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A Textbook of Advanced Oral and Maxillofacial Surgery

Volume 3

Edited by Mohammad Hosein Kalantar Motamedi

A TEXTBOOK OF ADVANCED ORAL AND MAXILLOFACIAL SURGERY VOLUME 3

Edited by **Mohammad Hosein Kalantar Motamedi**

A Textbook of Advanced Oral and Maxillofacial Surgery Volume 3
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Notice

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Meet the editor

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Contents

Preface

Just as Volume 2 was published, I came across an email from **InTech** regarding the astonishing number of chapter downloads of **"A Textbook of Advanced Oral and Maxillofacial Surgery" Volume 1.** It had practically "gone viral" with over 132,000 chapter downloads in the past year or so. I was also surprised to note the logarithmically increasing number of chapter downloads of the recently published **Volume 2**, which was well-over 13,000! This issue as well as the eagerness of distinguished world renown national and international colleagues to contribute to the next volume **(Volume 3)**provided me with the incentive and motivation to complete this trilogy. Below are some of the email testimonials of world renown oral and maxillofacial surgeons regarding the first volume:

"Many thanks. Great job!! "
Daniel M. Laskin, DDS, MS, Professor and Chairman Emeritus VCU Oral and Maxillofacial Surgery, USA

"Thank you for sharing your lovely textbook."
Edward Ellis III, DDS, MS, Professor and Chair, Oral and Maxillofacial Surgery, University of Texas Health Science Center at San Antonio, USA

"Thank you very much for the opportunity to have a closer look at this great book and congratulations for this successful, tremendous work."
Christoph Kunz, MD, DDS, PD, Associate Professor, Oral and Craniomaxillofacial Surgery, University Hospital Basel, Switzerland

"Excellent book; I would like to congratulate you for the fine work you did. You have chosen outstanding specialists to write each chapter. All topics that concern the oral and maxillofacial surgeon are nicely covered. We will use this book in our residency program."
Professor **Wilson Delgado**

"I just dowloaded your valuable book. Thank you very much for your contribution and efforts to our speciality of OMFS."
Dr. Zekai Yaman, American Hospital OMFS Specialists Istanbul, Turkey

Volume 3 is the work of **93** contributors from **nine** countries culminating in **18** sections and **32** chapters and essentially complements **Volumes 1** and **2**; interesting new topics discussed herein include:

- NANOANTIBIOTICS - VIRTUAL APPOINTMENTS - TRIGEMINAL NERVE REPAIR - TRIGEMINAL NEURALGIA - OFFICE ANESTHESIA MANAGEMENT OF COAGULOPATHIES - FACIAL SKIN LESIONS - GUIDED-BONE-REGENERATION - RIDGE AUGMENTATION FOR IMPLANTS - MANAGEMENT OF FISTULAS - TOTAL TMJ RECONSTRUCTION - THREE-DIMENSIONAL PRINTING - FACIAL OSTEOTOMIES - DEN-

TOALVEOLAR SURGERY TECHNIQUES - FACE LIFTING - FACIAL TRANSPLANTATION - RHINOPLASTY - ADVANCED IMPLANTOLOGY - OSMOTIC EXPANDERS - ADVANCED CRANIOFACIAL SURGERY

This undertaking would not be possible without the help of my national and international colleagues. Thus, I find it prudent hereby to take this opportunity and express my sincere thanks to the national and international contributors below:

From USA:

• Alexandra Radu • Curtis Holmes • Francesco R. Sebastiani • Golaleh Barzani • Ho-Hyun Sun • Jeffrey A. Elo • Maximillian Beushausen • Paul Bermudez • Peter R. Hunt • Robert Pellecchia • Michael P. Horan

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Keyhan • Kambiz Hasrak • Nader Zarinpour • M. Hosein Amirzade Iranaq • Saeed Khosravi • Reza Tabrizi • Hossein Behnia • Sarang Saadat

I would like to dedicate this work to my mother Zakie - my ardent supporter, my father Mohammad Reza, MD, FACS - my mentor, and my wife Maryam - my companion, who patiently put-up with me "day in and day out" while I was sending emails and editing book chapters 24/7; I also thank my son Mostafa and my daughter Marzieh, and also Ms. Danijela Duric - Head of InTech Book Department and the publishing process managers Ana Pantar and Iva Lipovic who made all this possible.

I hope that this humble and altruistic undertaking, which I did free of charge, was time well spent and to the benefit of all practitioners and academicians involved in the study and practice of the fascinating discipline of Oral and Maxillofacial Surgery.

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Section 1

Antibiotic Management of the Maxillofacial Patient, Complications and Nanoantibiotics

Chapter 1

Antimicrobial Therapy and Surgical Management of Odontogenic Infections

Robert Pellecchia, Curtis Holmes,
Golaleh Barzani and Francesco R. Sebastiani

Additional information is available at the end of the chapter

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Abstract

Dentoalveolar infections include a wide range of conditions from localized abscesses to deep-neck space infections or more severe cases of necrotizing fasciitis. Odontogenic infections and emergencies are a significant part of an oral and maxillofacial surgeon's daily practice. On a daily basis, an oral surgeon needs to be prepared to deal with any infection-related emergencies ranging from a toothache, localized vestibular abscess to deep head and neck abscesses. Management of these odontogenic infections could propose a challenge due to complex microbiology of the odontogenic infection and the potential for advancement to a life-threatening emergency. It is crucial that the oral and maxillofacial surgeon has knowledge of anatomic boundaries and fascial spaces to be able to make an accurate diagnosis and perform prompt surgical management. For the patient, odontogenic infections may carry high incidence of morbidity and mortality if not treated promptly. Management of patient with an odontogenic infection is a multifaceted approach involving (1) an examination and assessment of the patient, (2) identifying the source of the infection, (3) anatomic considerations, (4) surgical intervention, (5) administration of the appropriate antimicrobial therapy, and (6) referral to an appropriate provider if indicated. This chapter provides the clinician with a better understanding of diagnosis and pharmacological management as well as surgical treatment of patients with odontogenic infections.

Keywords: odontogenic infection, cellulitis, abscess, multifascial space abscess, management of odontogenic infections, ludwigs angina

1. Introduction

1.1. Patient examination and assessment: review

A comprehensive and thorough clinical examination is a critical component of treatment of odontogenic infections. A good clinician will need to accurately evaluate and examine the patient, to formulate a prompt diagnosis and plan for surgical management accordingly. Every examination should begin with an accurate history and physical examination with focus on the evaluation of airway. Airway evaluation perhaps is the most important step in evaluating odontogenic infections and will guide the clinician and dictate the next appropriate course of treatment. Information on the timing of initiation of symptoms will give the clinician an understanding on how quickly the infection is progressing. It is absolutely crucial that the clinician promptly recognize any signs of impending airway and take necessary steps to take control over the airway as soon as possible. Once the airway is deemed stable, the clinician can proceed to accessing patient's oral examination focusing on dentition, floor of the mouth, oral pharyngeal, pharyngeal space, and palatopharyngeal fold. This is then followed by a diagnosis and development of a treatment plan for patient care. Failure to complete a comprehensive history and examination of the patient can lead to improper treatment and/or delayed treatment of infections. This potentially leads to serious complications, including but not limited to airway compromise, mediastinitis, sepsis, and death [1].

A patient history includes attaining information regarding the symptoms, onset, and duration of the present illness. This information helps form an understanding of the severity of the patient's infection. Common signs and symptoms that should alert a provider of a developing or established infection include trismus, fever, difficulty swallowing, pain, difficulty breathing, dysphonia, and pain on swallowing [1–3]. The patient's medical history and current medications are key in assessing the patient's ability to fight infection as well as providing an insight to potential drug interactions.

The physical examination can start by the recording of vital signs; any fever chills or malaise should be the warning sign for a well-established infection. Oftentimes, clinicians can quickly assess the patient and severity of their situation over the initial few minutes they meet with the patient. Clinicians can quickly assess for airway compromise by observing patient's posture for sniffing position, any difficulty breathing, tolerating secretions, tongue position, and changes in voice, along with any obvious facial swelling. Clinicians should keep in mind that airway assessment is the most critical component of this examination and will help the clinician quickly determine should the patient require urgent surgical intervention. Clinicians should first establish whether the patient has a stable airway. Failure to recognize this crucial information will lead to more complications. Palpation, percussion, and thorough visual examination of the extra- and intraoral cavity provide necessary information for identifying the source and location of the infection. Providers should pay close attention to size swelling, tongue position, floor of the mouth swelling or elevation, visual disturbances, voice changes, vestibule, and uvula position. This should be followed by radiographic examination. If the clinician suspects that infection is diffused and involves multiple fascial spaces, then a maxillofacial or neck computed tomography (CT) with contrast should be obtained. The use

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of contrast should be avoided should the patient have any renal problems or any allergies to intravenous dye. A complete laboratory workup consisting of complete blood cell count and basic metabolic panel must be done. C-reactive protein levels must also be measured as markers to assess the severity of infection and response to treatment. It is important to note that the use of blood cultures is not indicated in dentoalveolar infections as they yield negative results. After gathering all clinical and radiographic findings, clinician should quickly establish a plan of care that can vary from establishing a secure and stable airway, emergent or urgent surgical management with intravenous or oral antibiotic therapy. These treatments could vary based on the clinical and radiographic findings. Clinicians should keep in mind that clinical-radiographic examination is the most crucial step in helping clinicians establish whether the patient will require to be managed in a hospital setting or in an outpatient setting. It is important to note that if the clinician suspects any possibility of airway embarrassment or quick progression to a toxic patient, prompt establishment of a secure airway should be the first and most important priority.

2. Stages of abscess development

Odontogenic infections are commonly caused by bacteria native to the oral cavity. They arise from either periapical or periodontal sources. Periapical infections are the most common cause of odontogenic infections. In periodontal infections, attachment loss of the gingival fibers and destruction of supportive structures expose the teeth and tissues to bacterial introduction. Periapical infections begin with a carious lesion causing pulpal necrosis that introduces the pulp to microorganisms. The infection can quickly spread to periapical tissues and may spread to other fascial spaces. Upon accessing the periapical tissues, the process can remain localized to the bony structures as a cystic lesion, granuloma, or focal osteomyelitis. Periapical infection can also spread through cortical bone causing cellulitis, localized and or deep-space abscess formation.

After inoculation of bacteria into deeper tissues, abscess development progresses from cellulitis to abscess formation without early intervention. Cellulitis is an acute disorder associated with warm, diffuse, painful, indurated swelling of soft tissues that also may present with erythema. Indurated swelling begins to soften as an abscess develops represented by localized area of fluctuation (**Table 1**). An abscess is a collection of purulent material containing necrotic tissue, bacteria, and dead white blood cells. Patients may present at varying stages of the process. Bacteria responsible for odontogenic infections have the ability to spread hematogenously due to the high vascularity of head and neck structures allowing infections to present in distant sites including the orbit, brain, and spine [2, 4].

2.1. Anatomic considerations

Odontogenic infections spread from the bony structures through the cortical bone along the path of least resistance with the affected fascial spaces determined by the structures in proximity to the tooth roots [5]. This necessitates an understanding of fascial spaces and

anatomy to effectively diagnose and develop a surgical plan for the management of infections. The spaces that are primarily affected by odontogenic infections are located adjacent to the origin. Those spaces are categorized as primary fascial spaces. They include buccal, canine, sublingual, submandibular, submental, and vestibular spaces.

Characteristics	Cellulitis	Abscess
Duration	1-5 days	4-10 days
Pain	Generalized	Localized
Size	Large	Small
Location	Diffuse	Well circumscribed
Palpation	Doughy-indurated	Fluctuant
Presence of pus	No	Yes
Degree of concern	High	Moderate
Bacteria	Mixed	Anaerobic
Color	Red	Shiny center

Adapted from Flynn TR: Principles of Management and Prevention of Odontogenic Infections. In Peterson LJ, Ellis E, Hupp J, editors: Contemporary Oral and Maxillofacial Surgery, ed 6, St Louis, 2014, Mosby, pp 296–318.

Table 1. Cellulitis versus abscess.

After infection spreads to primary spaces, they can progress to include secondary spaces. Secondary spaces include pterygomandibular, infratemporal, masseteric, lateral pharyngeal, superficial and deep temporal, masticator, and retropharyngeal.

A basic understanding of the spread of infections into the primary spaces is established by understanding the origin and insertions of the buccinator and mylohyoid muscles in relation to the maxilla and the mandible. The buccinator inserts superiorly into the alveolus of the maxilla and inferiorly in the alveolus of the mandible. An infection that spreads within the constraints of those insertions results in a vestibular abscess, and the spread of infection above or below these insertions forms a buccal space infection. The mylohyoid muscle's origin is from the mylohyoid line of the mandible. Teeth with root apices below this origin are the mandibular second and third molars. Infectious spread from these teeth through the lingual plate forms submandibular space infections. The roots of the mandibular premolars and first molars lie above the mylohyoid and therefore infectious spread lingually associated with these teeth creates sublingual space infections. The teeth most frequently identified as the source of an infection are the mandibular molars, followed by the mandibular premolars [1, 3, 5].

A special note should be made of an indurated cellulitis involving bilateral submandibular, sublingual, and submental spaces with drooling, tongue displacement, dysphagia, and patient head positioned in the "sniffing" position. This is the classic description of Ludwig's angina. This is a medical emergency in need of definitive airway management and timely surgical management and should be referred immediately to the nearest hospital for treatment. Patients

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with infections associated with maxillary molars may also present with maxillary sinusitis due to the close proximity of root apices with the floor of the maxillary sinus. Conversely, patients with maxillary sinusitis may also present with symptoms of an infection, so it is prudent to perform an examination to develop the appropriate diagnosis (**Figures 1–5**).

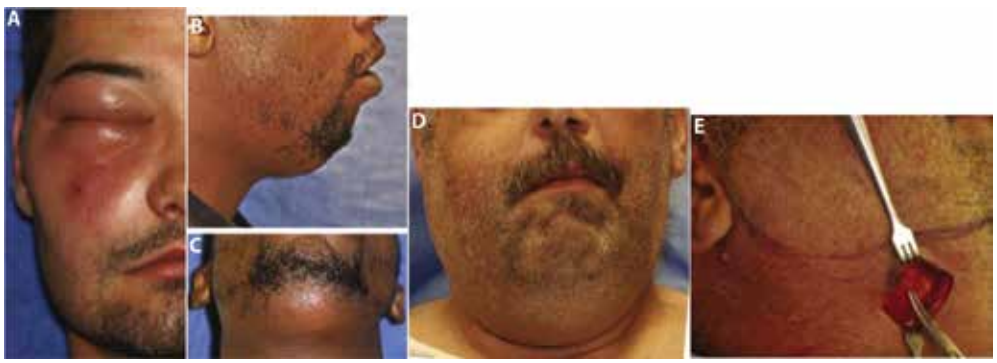

Figure 1. Fascial spaces of face and suprahyoid areas: (A) canine space infection; (B) masseteric space infection; (C) lateral pharyngeal and submandibular space infection; (D) submental space infection; (E) submental space infection surgical approach. Adapted from Cillo JE: Fascial Spaces of the Head and Neck. In Kademani D and Tiwana PS, editors: Atlas of Oral and Maxillofacial Surgery, St. Louis, 2016, Saunders.

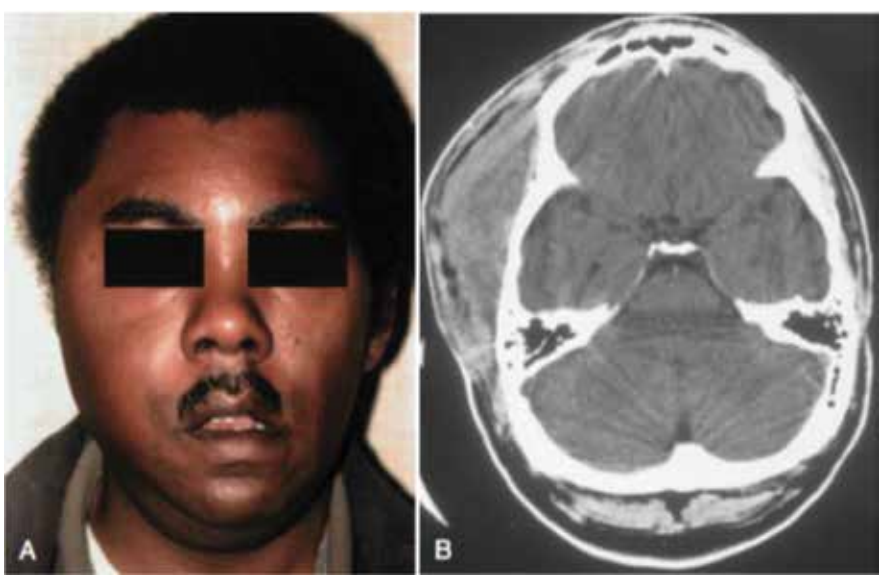

Figure 2. (A) Right masticator space infection (60-day duration); (B) right temporal space CT of abscess (same patient); 60 ml of pus aspirated. (A from Flynn TR: The swollen face. Emerg Med Clin North Am 15:481, 2000. B from Flynn TR: Anatomy of oral and maxillofacial infections. In Topazian RG, Goldberg MH, Hupp JR, editors: Oral and maxillofacial infections, ed 4. Philadelphia, 2002, Saunders.).

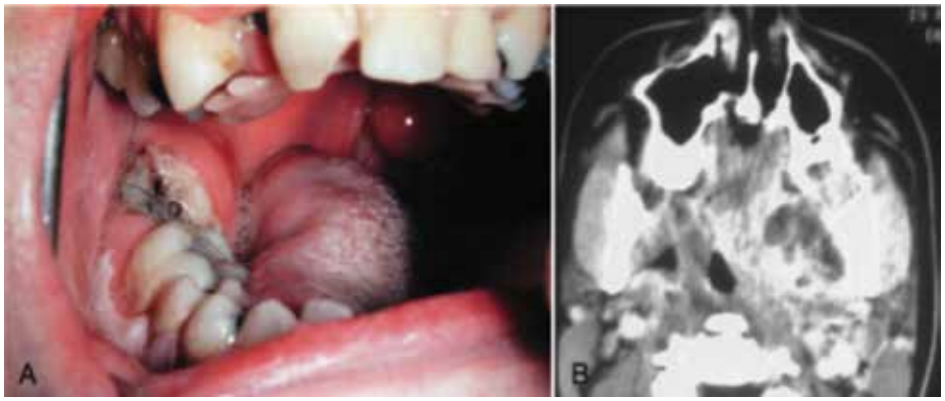

Figure 3. (A) Pterygomandibular space infection. Infected fracture of the mandible involving a partially erupted and carious right lower third molar, which was the source. Significant deviation of the uvula to the opposite side and the swelling of the right anterior tonsillar pillar. (B) CT of a pterygomandibular space abscess. Fluid collection seen between the ascending ramus of the mandible and the medially displaced medial pterygoid muscle. (A from Flynn TR, Topazian RG: Infections of the oral cavity. In Waite D, editor: Textbook of practical oral and maxillofacial surgery. Philadelphia, 1987, Lea & Febiger. B from Flynn TR: The swollen face. Severe odontogenic infections. Emerg Med Clin North Am 15:481, 2000.).

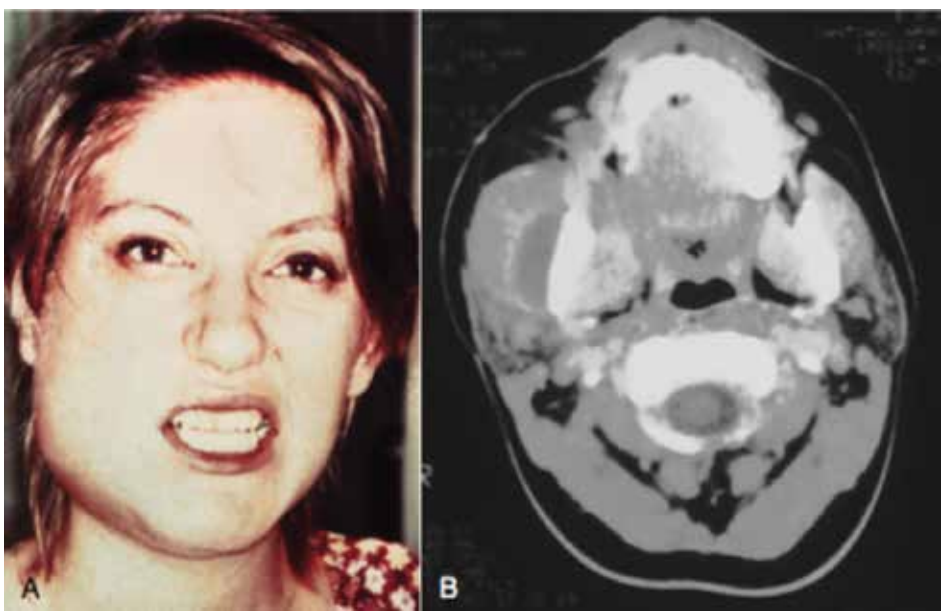

Figure 4. (A) Submasseteric space infection. Significant swelling over the right mandibular ascending ramus seen and severe trismus reported. (B) CT of a submasseteric space abscess. Collection of pus between the ascending ramus of the mandible and the overlying edematous masseter muscle. (A from Goldberg MH: Odontogenic infections. In Topazian RG, Goldberg MH, Hupp JR, editors: Oral and maxillofacial infections, ed 4. Philadelphia, 2002, Saunders. B from Flynn TR: Anatomy of oral and maxillofacial infections. In Topazian RG, Goldberg MH, Hupp JR, editors: Oral and maxillofacial infections, ed 4. Philadelphia, 2002, Saunders.).

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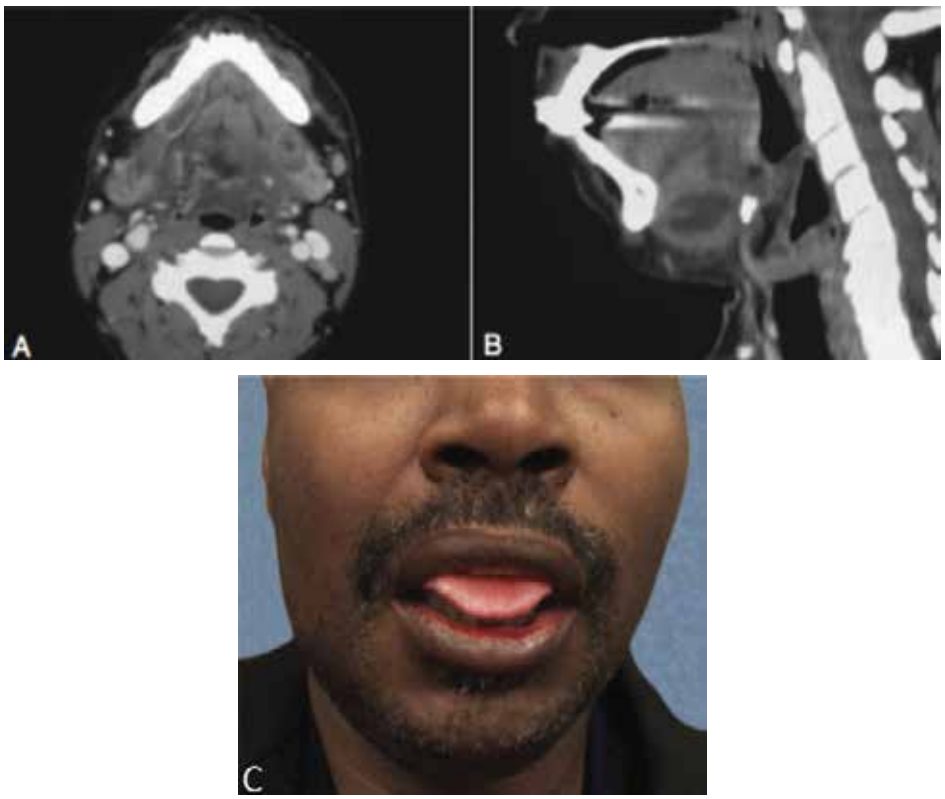

Figure 5. (A and B) Coronal and sagittal CTs with contrast of Ludwig's angina. (C) Inability to protrude the tongue is a sign of an infectious process involving the floor of the mouth. Adapted from Farnish SE: Ludwig's angina. In Bagheri SC, editor: Current Therapy in Oral and Maxillofacial Surgery, St. Louis, 2012, Saunders.

Computed tomography with intravenous contrast dye is the ideal modality for the identification of and delineation of the anatomic spread of severe deep fascial space infections. When the infection involves only the more superficial spaces, CT may not be necessary. Infections involving the deeper structures can be significantly more difficult to delineate using clinical methods alone. Contrast-enhanced CT (CECT) is useful in these cases. In head and neck infections, CECT may demonstrate ring enhancement, which is the hypervascular capsule surrounding a well-established abscess cavity. The combination of CECT and experienced clinical examination was able to identify clinically significant loculations of pus in the head and neck in 85% of cases [6].

2.2. Deep-space neck infection

If deep-space neck infection is suspected, it is imperative that the clinician makes an early diagnosis with a thorough clinical examination. These patients often present with nonspecific systemic signs, symptoms such as fever, chills, generalized malaise, and loss of appetite, but it is imperative that the clinician recognize more localized and specific symptoms such as

dysphagia, trismus, odynophagia, odontalgia, or dysphonia. According to a study by Mayor and colleagues, most commonly shared signs and symptoms shared by patients with deep-space neck infection were odynophagia, followed by dysphagia, fever, neck pain, and neck swelling [7]. In addition, these patients may show signs of neck swelling, floor of the mouth elevation, drooling, and inability to tolerate their secretions, diaphoresis, and bulging of pharyngeal wall. According to Osborn et al. [7], classic description of pharyngeal wall bulging is the presence of a midline bulge for prevertebral infections and a unilateral bulge for retropharyngeal space infections. It is important to note that submandibular space infections are the most common site of deep-neck space infections. Infection of lateral pharyngeal space can also be caused by nonodontogenic source such as tonsillar infections from peritonsillar space. Infection can spread from lateral pharyngeal or prevertebral space into the retropharyngeal space or danger zone (**Figure 6**) [7].

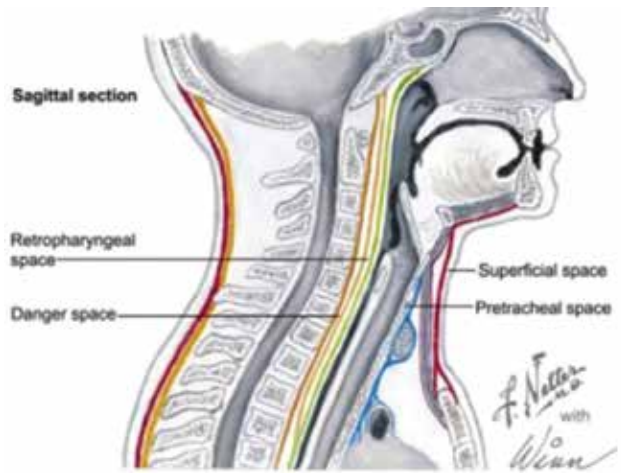

Figure 6. Deep spaces of neck infections. Adapted with permission from Osborn et al. [7]. PubMed PMID: 18603196.

2.3. Surgical intervention

Resolution of an odontogenic infection occurs after pharmacotherapy, but it is often studied in combination with surgical treatment [2, 3, 8]. Surgical intervention is believed by many to be the most important aspect of the management of odontogenic infection.

Odontogenic infection with abscess collection, detected clinically or radiographically, warrants incision and drainage by transcutaneous or transoral approach, in addition to dental extraction. The following eight steps are used to guide treatment of severe odontogenic infections (**Figure 7**).

Location and rate of progression determine the severity of the infection. In the various deep fascial spaces, infection can be classified as low, moderate, and high severity. Diligently taking the patient's medical history leads to proper evaluation of host defenses. Indications for hospitalization of a patient with odontogenic infections are as follows:

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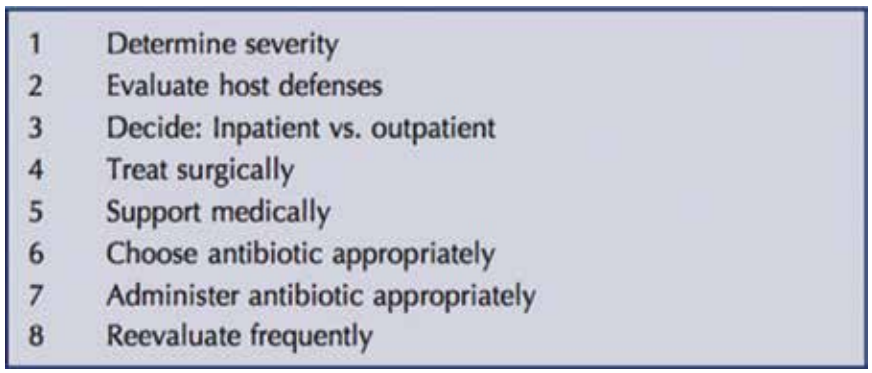

Figure 7. Steps in the management of severe head and neck infections. Adapted from Flynn TR: Principles and Surgical Management of Head and Neck Infections. In Bagheri SC, editor: Current Therapy in Oral and Maxillofacial Surgery, St. Louis, 2012, Saunders.

1. Impending airway compromise or threat to vital structures
2. Infection of deep-neck spaces or masticator space
3. Temperature of >101°F
4. Need for general anesthesia
5. Need for inpatient control of systemic disease.

The surgical goals in head and neck infections are (1) to secure the airway, (2) to establish dependent drainage, and (3) to remove the cause of infection. Incision and drainage decreases the bacterial load the immune system must face by physically removing pus. Intraoral incisions are generally made in the oral vestibule at the point of maximum swelling. After surgical treatment, the patient must receive adequate medical support including nutrition, rehydration, and control of systemic disease. Steps six and seven will be discussed in detail later in this chapter. For outpatients, appropriate follow-up is 1–4 days. With hospitalized patients, daily follow-up is standard.

3. Treatment techniques

The initial step in the treatment of odontogenic infections is to assure that a stable airway is established. A topical cleansing agent should then be applied and aspiration of abscess should be completed using a syringe connected to a needle in a sterile fashion. Aspirate should be sent for microbiologic culture examination. Prior to incision, local anesthetic infiltration can be administered. Depending on the involved fascial space, various skin incisions have been described (**Figure 8**).

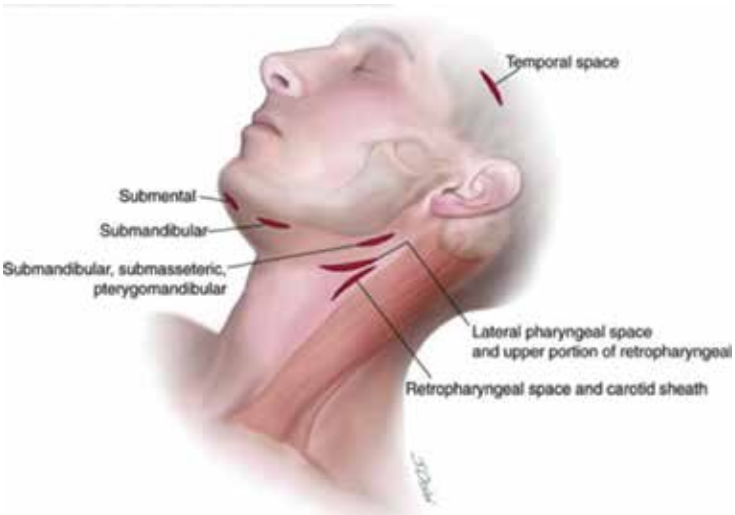

Figure 8. Typical incision sites for extraoral incision and drainage. From Lui DW and Abubaker AO: Odontogenic Infection. In Kademani D and Tiwana PS, editors: Atlas of Oral and Maxillofacial Surgery, St. Louis, 2016, Saunders.

On treating a submandibular abscess, the neck incision is approximately 2–4 cm below the angle of the mandible following a natural neck crease, inferior to the most inferior extent of inflammation. A mosquito hemostat is introduced through the skin, subcutaneous tissue, platysma muscle, and superficial layer of the deep cervical fascia until the inferior border of the mandible is encountered [9]. Subperiosteal instrumentation of the lateral and medial aspect of the mandibular ramus is then performed if masticator space is also involved. Normal saline solution should be used to irrigate all drainage sites. One-fourth inch penrose drains are then placed via incision sites and subsequently secured with 5/0 Prolene sutures. Dental extraction (removal of the source of infection) should be followed up next. The decision on extubation should be made with the anesthesiologist.

For lateral pharyngeal abscess treatment, the submandibular approach allows exploration of the lateral pharyngeal space by blunt finger dissection. This occurs in the superomedial direction between the posterior belly of digastric and the sternocleidomastoid (SCM) muscles (**Figure 9**).

Finger dissection of the lateral pharyngeal space is complete when the surgeon can palpate the endotracheal tube medially, the ipsilateral transverse processes of the vertebrae posteromedially, and the carotid sheath posterolaterally [9].

On treatment of the retropharyngeal abscess, the submandibular approach allows for exploration of the suprahyoid component. If the infrahyoid portion was also involved, the anterior SCM approach should be used. Finger dissection of the retropharyngeal space is a continuation of the complete dissection of the lateral pharyngeal space. Palpation of the contralateral transverse processes of the vertebrae, the endotracheal tube from its posterior aspect, and, if necessary, the contralateral carotid sheath ensure completion of dissection [9]. If necessary, the

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danger space is entered by finger dissection through the alar fascia. It can be safely explored inferiorly as far as the T4 level.

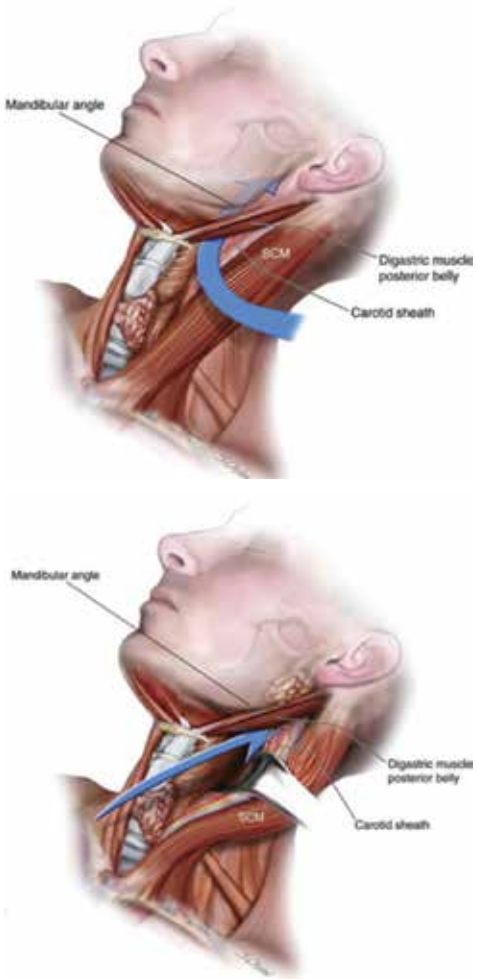

Figure 9. (A) Lateral pharyngeal space abscess incision and drainage. (B) Retropharyngeal abscess surgical access for incision and drainage. Adapted from Lui DW and Abubaker AO: Odontogenic Infection. In Kademani D and Tiwana P, editors: Atlas of Oral and Maxillofacial Surgery, St. Louis, 2016, Saunders.

Oral and maxillofacial surgeons should keep in mind that on treating descending mediastinal infection, thoracic surgical consultation is necessary. In a series of 10 patients, Freeman and colleagues reported no mortality when using the following treatment regimen: immediate thoracotomy incision and open-direct exploration, debridement, irrigation, and drainage of the mediastinum. Cervical incisions were used to explore and debride infection in the neck when necessary. Postoperative CT scans were obtained every 48–72 h, or more frequently if the clinical condition deteriorated [10]. These were used to guide additional surgeries to

aggressively drain any new loculations of pus. In 30% of cases, extension of the infection into the abdomen through the diaphragm was found. The subjects underwent a mean of six operations and six CT scans. The length of hospital stay was 14–113 days, with a mean of 46 days [10]. In these series cases, early, aggressive, and additional surgeries combined with frequent postoperative CTs reduced the mortality of mediastinitis from 20 to 0% (**Figure 10**).

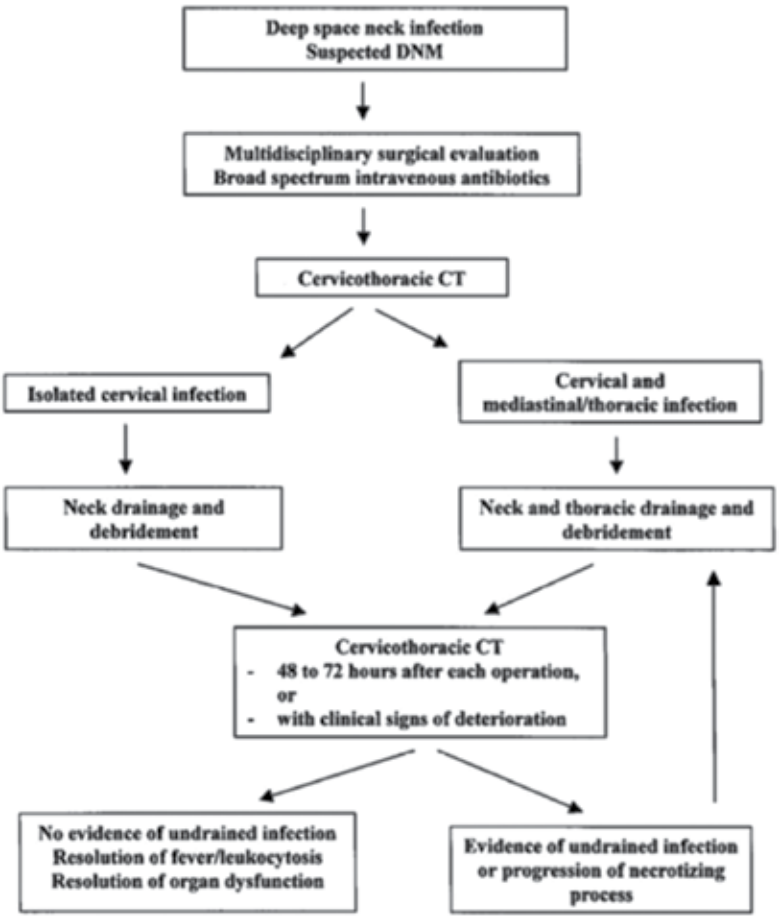

Figure 10. Treatment algorithm for patients with descending necrotizing mediastinitis (DNM). From Freeman RK, Vallieres E, Verrier ED, et al: Descending necrotizing mediastinitis: an analysis of the effects of serial surgical debridement on patient mortality, J Thorac Cardiovasc Surg 119:260, 2000.

3.1. Microbiology of an odontogenic infection

It has been stated that odontogenic infections arise from bacterial introduction in the deeper tissues of the head and neck. There is vast array of bacterial species all residing contemporaneously in the oral cavity and contribute to the normal oral flora. Odontogenic infections are characterized as a combination of aerobic and anaerobic bacteria. This is why they are

considered mixed infections. Streptococcal species are often responsible for orofacial cellulitis and abscess. Aerobic bacteria including *Streptococcus viridans*, *S. milleri* group species, beta-hemolytic streptococcus, and coagulase negative staphylococci have been cultured from odontogenic infections. Within the *S. milleri* group, the members *S. anginosus*, *S. intermedius*, and *S constellatus* are most often associated with cellulitis. Anaerobic bacteria are often isolated from sites with chronic abscess formation. These pathogens include *Peptostreptococcus*, *Prevotella*, *Prophyromonas*, *Fusobacterium*, *Bacteroides*, and *EIkenella* [2, 3, 9, 12, 13, 16]. The most common microorganisms isolated from odontogenic infections have been consistent over the years [3, 8]. However, what has changed is the prevalence, the ability to isolate, and the ability to classify them due to changes in nomenclature [2, 5, 14].

Over the years, studies have shown that there has been a change in the antibiotic susceptibility of isolated organisms. While many streptococci are still penicillin-sensitive, especially those that are prevalent during the first 3 days of clinical symptoms, the gram-negative obligate anaerobes, present abundantly after 3 days, are producing penicillin-resistant strains [12, 17]. Recently, an increase in aerobes and anaerobes that are resistant to clindamycin regimens has been documented [2, 18]. This complicates recommendations for therapeutics for orofacial infections; however, traditionally used empirical antibiotics are excellent options if culture and sensitivity testing are not performed at or prior to the time of surgery. Nonetheless, providers must not forget the potential resistant organisms to empirical antibiotics. As a result of new resistant strains, antibiotic management of odontogenic infections has become increasingly more complex to cover a broader spectrum of offending microorganisms.

3.2. Antibiotics of choice

Antibiotics are antimicrobials used for the treatment and prevention of infections. They are classified as either bactericidal or bacteriostatic. Bactericidal antibiotics kill bacteria by inhibiting cell wall synthesis and bacteriostatic antibiotics inhibit bacterial growth and reproductions. **Table 2** lists common antibiotics and their classification. The choice of antimicrobial therapy for patients with odontogenic infections can be complex due to numerous variables that must be considered. Factors involved in antibiotic selection include host-specific factors and pharmacologic factors.

Host factors include the microbiology of odontogenic infections, history of allergic responses or intolerance, previous antibiotic therapy, age, pregnancy status, and immune system status [12]. Traditional pathogens found to be in association with orofacial infections are mixed in origin and consist of facultative and obligate anaerobic bacteria. The duration of the infectious process aids in deciphering which organisms predominate. Allergy to antibiotics is noted during acquisition of the medical history as well as information regarding antibiotic intolerance. Previous antibiotic therapy, especially on a consistent basis, yields a propensity for resistant organisms to an antibiotic. Certain antibiotics should be avoided in children as well as pregnant patients. The immunocompetence of a patient may direct antibiotic therapy toward bactericidal, rather than bacteriostatic types.

Empiric antibiotics of choice for odontogenic infections in outpatient setting	
No penicillin allergy	Penicillin allergy
PO	PO
-Pen VK 500 mg Q6h 7 days or Amoxicillin 500 mg Q8h, 7 days	
-Clindamycin 300 mg Q6h, 7 days	-Clindamycin 300 mg Q6h, 7 days
-Cephalexin (or first generation cephalosporin) 500 mg Q 12h 7-10 days	-Cephalexin (or first generation cephalosporin) 500 mg Q 12h 7-10 days
-Azithromycin 500 mg Q24, 5 days	-Azithromycin 500 mg Q24, 5 days
	-Metronidazole 500 mg TID, 7 days
	-Moxifloxacin 400 mg Q24 5 days
Empiric antibiotics of choice for odontogenic infections in inpatient setting	
No penicillin allergy	Penicillin allergy
IV	IV
Clindamycin IV, 600 mg Q8h	Clindamycin IV, 600 mg Q8
Ampicillin + metronidazole, 0.5-2 g Q6h/500 mg Q8h	Moxifloxacin 400 mg Q24
Ampicillin + sulbactam, 1.5-3 g Q6h	Cefotaxime, 1-2g Q12
Adapted from Flynn.	

Table 2. Empiric antibiotics of choice for odontogenic infections in outpatient and inpatient setting.

Pharmacologic factors of interest include spectrum of antibiotics, pharmacokinetics, tissue distribution of antimicrobials, cost of antibiotics, adverse reactions, and potential drug interactions [12]. The antibiotic spectrum is of important consideration, because it is best for the patient to receive therapy with antibiotics that are effective against the involved microorganisms. Pharmacokinetically, the effectiveness of such antibiotics is dependent upon serum concentration needed to kill bacteria or the time necessary to maintain adequate serum levels. Beta-lactams and vancomycin are time dependent, whereas fluoroquinolones are concentration dependent. The ability of an antibiotic to reach the site of an infection should be considered, because abscess cavities are avascular. Thus, antibiotic effectiveness is based on the ability to penetrate an abscess. Adverse reactions and potential drug interactions will be discussed later in the chapter.

Pathogen-specific antibiotic therapy is driven by results of culture and sensitivity testing. Site cultures are not obtained until surgical intervention is done; patients with orofacial infections warrant timely therapeutic management. Empirical antibiotic therapy for odontogenic infections is based on an understanding of common pathogens cultured from the infection site. Empiric antibiotics may be difficult to ascertain due to the complex microbiology of such infections; the timing of antibiotic administration and antibiotic resistance are important. **Table 2** shows empiric antibiotics of choice for odontogenic infections in the outpatient setting.

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Penicillin still remains the antibiotic of choice in the outpatient setting for the management of odontogenic infections when there is no history of allergy [1–3], especially in infections of less than 3-day duration [3, 12]. Clindamycin is the antibiotic of choice for patients with an allergy to penicillin [1–3, 8]. This may also be considered for infections of longer than 3 days of duration due to the increase in penicillin-resistant organisms present at this stage [12, 17]. Of the macrolides, azithromycin has fewer drug interactions and is used to treat infections; however, resistance to macrolides has been reported [17]. Cephalosporins have been found to be effective in the treatment of orofacial infections, but there are pathogens that produce cephalosporinases. There also must be consideration for cross-allergy in penicillin-allergic patients. Metronidazole is excellent for obligate anaerobes and studies have shown its effectiveness in the outpatient setting; however, it is often used in the inpatient setting in combination with other antibiotics [2, 8, 12]. Moxifloxicin, a fourth-generation fluoroquinolone, has a spectrum of coverage including oral aerobes and anaerobes, including *E. corrodens*, which is clindamycin resistant. Moxifloxicin is an excellent antibiotic choice when initial antibiotics and surgery have remained ineffective (**Table 3**).

Bactericidal	**Bacteriostatic**
Beta-lactams	Macrolides
Penicillins	Erythromycin
Cephalosporins	Clarithromycin
Carbapenems	Azithromycin
Monobactams	
Aminoglycosides	Clindamycin
Vancomycin	Tetracyclines
Metronidazole	Sulfa antibiotics
Fluoroquinolones	
Adapted from Flynn.	

Table 3. Bactericidal and bacteriostatic antibiotics.

3.3. Duration of antibiotics

A common antibiotic course for orofacial infections is 7–10 days. Flynn et al. hypothesized that antibiotic therapy for 4 days or less combined with appropriate surgical treatment results in equal or better clinical outcomes, as measured by time to resolution, morbidity, selections for antibiotic-resistant strains, and expense. In this systematic review, it was found that no clinically significant difference was found at day 7 with antibiotic courses of 7 days or less with appropriately administered surgical treatment. Chardin and colleagues [19] found no significant difference in clinical cure rate of antibiotic therapy after surgical intervention with amoxicillin 1 g for 3 days versus the same therapy for 7 days. Lewis and colleagues [16] found similar results when comparing surgical intervention followed by 3-g amoxicillin for two doses

8 h apart from penicillin V of 250 mg by mouth four times per day for 5 days. These studies support the emphasis on prompt and efficient surgical intervention in combination with antibiotic therapy.

Antibiotic	Usual dose (mg)	Usual interval (h)	Wholesale cost 2010 ($)	1-week retail cost 2010($)	Amoxicillin cost ratio
Penicillins					
Amoxicillin	500	8	0.37	11.99	1.00
Penicillin V	500	6	074	12.29	1.03
Augmentin	875	12	5.05	51.99	4.34
Augmentin XR	20,000	12	7.38	108.99	9.09
Cephalosporins					
Cephalexin	500	6	1.23	15.19	1.27
Erythomycins					
Erythromycin	500	6	0.30	17.99	1.50
Clarithromycin	500	24	5.01	34.69	2.89
Azithromycin	250	12	7.78	120.99	10.09
Anaerobic					
Clindamycin (generic)	150	6	1.19	31.79	2.65
Clindamycin (2T)	300	6	2.38	59.99	5.00
Clindamycin (generic)	300	6	3.76	87.59	7.31
Metronidazole	500	6	0.73	34.49	2.88
Other					
Vancomycin	125	6	29.10	849.99	70.89
Ciprofloxacin	500	12	5.13	13.49	1.13
Moxifloxacin (Alyelox)	400	24	16.35	138.99	11.59

Table 4. Cost of oral antibiotics used in odontogenic infections.

3.4. Cost of antibiotics

The cost of antibiotics whether a factor that is often not considered during the treatment of odontogenic infections should be considered. The central focus is the resolution of infectious process with surgical treatment while providing effective and appropriate antibiotic therapy that will reduce the morbidity associated with the infection. Antibiotic cost can be compared based on the cost for a standard prescription for antibiotics of preference in oral formulations.

Amoxicillin is one of the least expensive oral formulations of antibiotics. Flynn considered the retail cost for a 1-week prescription that an uninsured patient would pay for antibiotic therapy. He obtained the cost of commonly prescribed antibiotics from a pharmacy chain in the Boston area. Then, he formulated a numeric cost comparison ratio by dividing the cost of the commonly prescribed medications by the cost of an amoxicillin prescription. This comparison found that the cost of a 150-mg Cleocin prescription is significantly less than the 300-mg prescription with a two 150-mg capsule regimen four times a day being 63% the cost of a 300-mg capsule four times a day therapy [8, 12] (**Table 4**).

3.5. Antibiotic resistance

A problem that has emerged regarding the effectiveness of selected antibiotic therapy for the management of odontogenic infections is antibiotic resistance. Antibiotic resistance occurs by four mechanisms namely alteration of a drug's target site, inability of a drug to reach its target, inactivation of an antimicrobial agent, or active elimination of an antibiotic from the cell [8, 17]. Alteration of the target site for an antibiotic occurs by genes allowing bacteria to synthesize peptides that prevent binding diminishing the affinity of the antibiotic. Some bacteria have bypass pathways that use alternate metabolic pathways when specific antibiotics are present. Antibiotics may be inactivated by bacterial enzymes; these enzymes can result in neutralization. Penicillinase and beta-lactamases are examples of this mechanism. Genes present in some bacteria produce proteins that prevent antibiotic uptake or signal for the removal of the antibiotic from the cell leading to antibiotic resistance as well. The genes necessary to drive antibiotic resistance are acquired through four mechanisms namely spontaneous mutation, gene transfer, bacteriophages, and mosaic genes [4, 8, 17]. Spontaneous mutation is considered the dominate source antibiotic resistance. Gene transfer occurs with transmissible DNA segments that transfer and insert genetic material after bacterial conjugation. Bacteriophages are viruses that infect bacteria and replicate to insert genetic material, subsequently highjacking the control of the bacteria's genetic and bacterial metabolism. Mosaic genomes are formed by bacteria incorporating fragmented DNA directly from dead members of related species. Collectively, these mechanisms allow the spread of genetic material from one bacterial species to another and can result in the resistant strain becoming the predominate strain of the species [8, 17].

Strides have been made to reduce the prevalence and manage antibiotic resistance. Non-antibiotic attempts relate to the hospital setting. This includes reduction of colonization sites, patient isolation, decreased length of hospital stay, and aseptic technique during intervention. Antibiotic-associated attempts include limiting antibiotic therapy to as narrow of a spectrum as possible to effectively manage the offending bacteria and utilizing broader spectrum antibiotics only when indicated. Culture and sensitivity testing of purulent exudate aid in identifying the susceptibility of bacteria to specific antibiotics. Kuriyama et al. examined a relationship between past administration of beta-lactam antibiotics and those patients producing increased amounts of resistant bacteria with odontogenic infections. It is beneficial to the clinician and patient to be diligent in obtaining history of previous odontogenic infections to guide treatment and consideration of possible antibiotic resistance.

4. Complications of antibiotic therapy and drug interactions

Antibiotic drugs have the potential to alter the effectiveness of other drugs and interfere with the metabolism of other drugs. The cytochrome p450 system is a complex set of drug-metabolizing enzymes in the liver and gastrointestinal (GI) system that breaks down many different drugs. When antibiotics that utilize this metabolic pathway inhibit cytochromes that are needed for metabolism of other drugs altering the bioavailability of one of the involved drugs, some of these interactions can lead to some severe adverse effects.

Providers should be mindful of some of the potential adverse reactions associated with antibiotic therapy and other medications. Erythromycin and other macrolides have been found to have drug interactions with numerous drugs including statins, theophylline, warfarin, carbamazepine, triazolam/midazolam, and antiarrhythmic. Side effects of these interactions range from bleeding issues, increased sedation, confusion, and seizures to cardiac dysrhythmias and death. Metronidazole has the potential for increased bleeding with the coadministration of warfarin due a decrease in the metabolism anticoagulants. Clindamycin may destroy gut flora and prevent absorption of vitamin K, which can cause an increase in anticoagulation. Metronidazole can also affect renal clearance of lithium and also has a disulfiram effect in combination with alcohol. Fluoroquinolones have been found to interfere with theophylline metabolism and cause seizures. These drugs have also been found to cause spontaneous tendon rupture. Fluoroquinolones should be avoided in children due to chondrotoxicity in growing cartilage.

Antibiotic allergy should be obtained while obtaining a patient's medical history. It is important to inquire about the nature of an allergy to access whether a true anaphylactoid allergy exists. Penicillin is a common antibiotic for which patients report an allergy. One to 10% of patients develop an allergic response to penicillin during an initial course and a less than 1% chance of development of an allergic reaction exists with additional courses [8, 21]. There is a possibility for cross-allergy to cephalosporins. This occurs in 10–15% of patients with an allergy to penicillin and often involves patients with a history of anaphylaxis.

Antibiotic-associated colitis (AAC) is another possible adverse effect of antimicrobial therapy. *Clostridium difficile* is an enteric anaerobe that produces an exotoxin found in a stool assay of affected patients. Diagnosis of *C. difficile* occurs after symptoms of fever, abdominal cramping, five or more episodes of diarrhea per day, or positive results in a stool sample. AAC has been found to occur with clindamycin, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins, and other antibiotic therapy, and is treated with the removal of the offending antibiotic and oral metronidazole or vancomycin. If no resolution occurs, these patients should be referred as soon as possible to rule out the potential need for surgical intervention.

A patient who is on oral contraceptive pills should be informed of the necessity to utilize other forms of birth control. Antibiotic therapy my kill enough gut flora that inhibits recirculation of estrogen which reduces the serum levels of estrogen and may allow for the patient to become pregnant. This has been found to only involve oral contraceptives, not implantable or injectable forms [8].

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5. Management of medication-related osteonecrosis of the jaw

The American Association of Oral and Maxillofacial Surgeons (AAOMS) in 2014 as described in their position paper changed the nomenclature from bisphosphonate-related osteonecrosis of the jaw (BRONJ) to medication-related osteonecrosis of the jaw (MRONJ). The change in designation signals the increasing number of osteonecrosis cases secondary to the use of alternative antiresorptive and antiangiogenic therapies [23]. The oral and maxillofacial surgeon often encounters patients treated with antiresorptive medications via either oral or parenteral route. Most of those patients who require treatment with antiresorptive medications are afflicted with metastatic bone tumors with primary sites from the breast, prostate, and lung. Lytic bone lesions are more often associated with multiple myeloma. Included in the antiresorptive medication regimen are receptor activator of nuclear factor (RANK) ligand inhibitors and in particular, Denosumab. The RANK ligand inhibitors work by the inhibition of osteoclast formation thus reducing the risk of fracture of vertebral, nonvertebral, and hip in the osteoporotic patient [23]. Controversy persists as to the mechanism and pathophysiology of MRONJ. Theories include altered bone remodeling or oversuppression of bone resorption, angiogenesis inhibition, constant microtrauma, suppression of innate or acquired immunity, vitamin D deficiency, soft-tissue BP toxicity, and inflammation or infection [23]. In the context of managing MRONJ, as a bacterial infection one must be cognizant of postsurgical risks following extraction of teeth especially those with existing periodontal disease and or periapical pathology [23]. Dentoalveolar surgery is still considered a major risk in developing MRONJ. Approximately 52–61% of those patients following dentoalveolar surgery are at risk to develop MRONJ [23]. *Actinomyces* species was one of the first bacteria identified in osteonecrosis of the jaw. Biopsied specimens of bone have recently identified a combination of bacteria and fungi associated with the biofilm on exposed bone [23]. As a result, a regimen of complex therapies is often required to treat the osteonecrosis-related biofilm of bone.

5.1. Staging of MRONJ

Stage 1:
Exposed and necrotic bone asymptomatic with no evidence of infection localized to the alveolus.

Stage 2:
Exposed and necrotic bone with evidence of infection and symptoms.

Stage 3:
Exposed and necrotic bone with evidence of infection and one of the following:

- Exposed and necrotic bone beyond the alveolus with extension to the inferior border of the mandible and or maxillary sinus and zygoma.
- Pathologic fracture.
- Extraoral fistula.

- OA or oronasal fistula.
- Osetolysis beyond the inferior border of the mandible or sinus floor.

Those patients afflicted in Stages 1–3 can be treated empirically with long-term use of Chlorhexidine rinses [23]. Presurgical management with Chlorhexidine and a regimen of broad-spectrum antibiotics have been used as a modality of care with the initial management of symptomatic MRONJ. It appears that a specific antibiotic regimen is not universally accepted and is often the preference of the surgeon as to what is found to be most effective. Clearly, the approach to the use of antibiotics for those afflicted with MRONJ identifies this condition with a bacterial component. Developing a strategy as to what antibiotics would be effective is found on the understanding and identification of the bacterial flora. Coverage for *Actinomyces* is essential, as it is one of the most predictable bacterial organisms isolated in patients with MRONJ. *Actinomyces* is a gram-positive organism that thrives best in an anaerobic environment. This is an opportunistic organism that is best treated with Amoxicillin for 6 months to a year.

6. Summary

Odontogenic infections are emergencies that may present in the outpatient setting. Management of such emergencies can occur in the dental office; however, there are circumstances that warrant referral for definitive treatment. Clinicians treating orofacial infections should be able to effectively examine and assess patients, have an understanding of common microorganisms associated with an abscess, head and neck anatomy, and vectors of development and spread of an abscess. Providers choosing to engage in management should promptly provide treatment of odontogenic infections with a combination approach, involving surgical intervention and antimicrobial therapy. It is important to confirm that the patient does not have any medical condition that necessitates antibiotic prophylaxis prior to surgical intervention. If so, the provider should refer to the current American Heart Association guidelines for antibiotic prophylaxis regimen (**Table 5**).

Antimicrobial therapy is complicated by the mixed flora of an abscess and varied responses of microorganisms to penicillin. Antibiotic therapy selection should be chosen according to safety, cost, consideration for a patient's medical history, effectiveness of antibiotic, and stage in abscess development. The use of clindamycin has increased in dentistry; however, multiple clinical studies comparing clindamycin to penicillin or ampicillin have found clinical success rates of 97% or higher with penicillin [3]. Penicillin continues to be the drug of choice in odontogenic infections, while clindamycin is an excellent alternative in patient with penicillin allergy. A 7-day antibiotic therapy has traditionally been effective; however, studies have shown that a 3- to 4-day regimen should suffice in healthy patients [6]. Regardless of the empirical antibiotic choice, surgical intervention that removes the source of the infection is considered the primary treatment modality.

Situation	Agent	Regimen: single dose 30-60 min before procedure	
		Adults	**Children**
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin OR	2 g IM or IV	50 mg/kg IM or IV
	Cefazolin or cefriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins or ampicillin oral	Cephalexin OR	2 g	50 mg/kg
	Clindamycin OR	600 mg	20 mg/kg
	Azhithromycin or clarithromycin	500 mg	15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxone OR	1 g IM or IV	50 mg/kg IM or IV
	Clindamycin	600 mg IM or IV	20 mg/kg IM or IV

IM, intramuscular; IV, intravenous.

Table 5. Antibiotic prophylaxis regimen.

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Chapter 2

Complications of Antibiotic Therapy and Introduction of Nanoantibiotics

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Additional information is available at the end of the chapter

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Abstract

Oral and maxillofacial surgeons play a major role in therapy, preventing morbidity, mortality from odontogenic and non-odontogenic maxillofacial infections; therefore, it is essential to have knowledge of current advancements in microbiological diagnosis and antibiotic therapy for odontogenic maxillofacial infections. Fortunately, we live in an era where antibiotics are readily available to prevent and treat against infections. The exact cause should be determined once the specific antibiotic is prescribed; additionally, the empirical, definitive treatments, side effects, pharmacokinetics and pharmacodynamics of antibacterial agents have to be considered.

Nowadays, antimicrobial resistance which is spreading rapidly is of great concern, because it is common in hospitals where acquired infections can be perilous. This situation compels scientists to synthesize new antibiotics and treatment modalities. The reason of microbial resistance can be due to increased misuse of antibiotics in foods (livestock, poultry and agriculture). A number of significant factors, such as organism identification, antibiotic sensitivity testing and host factor situations, should be taken into account in order to treat various infections effectively.

Currently, investigations are ongoing to impede antibacterial resistance by nanoscience technology seeking new chemotherapeutic agents. Scientists focusing on microbiological investigations aim to invent novel nanoantibiotic agents with high efficiency, low toxicity and low percentage of resistance. In recent years, nanoantibiotics have been applied against infections intelligently. The average size, polydispersity and composition of generated nanomaterials can be controlled by various methods in order to make them appropriate for biomedical applications.

The goal of this chapter is to provide an overview of the complications of various antibiotics used for therapeutic and prophylactic purposes in the oral and maxillofacial regions; furthermore, some essential nanoantbiotics are introduced and discussed.

Keywords: antibiotics, complications, nanoantibiotics, resistance, adverse effect

1. Introduction

Antibiotics can improve cell defense effectively; some key factors should be considered in antibiotic therapy, including the health of the host, identity of the organism and the antibiotic susceptibility; moreover, adverse reactions, interactions, resistance and other complications should be taken into account. The origin of most orofacial infections is odontogenic. The major relevant organisms of dental origin infections are aerobic and anaerobic Gram-positive cocci and anaerobic Gram-negative rods. The predominant aerobic bacteria in odontogenic infections are *Streptococcus milleri* genus [1]. Oral Gram-negative anaerobic rods are cultured in three quarters of the infections; however, several Gram-positives and Gram-negatives play more important pathogenic roles [1, 6]. Pure aerobic infections are less common (5%) [7]. Brook et al. detected that 50% of odontogenic deep facial infections yielded anaerobes, and only 44% of infections are a combination of aerobic and anaerobic flora [8]. Most sinus infections are viral, and only a small proportion develop a secondary bacterial infection in which the most common bacteria are Gram-positive and anaerobic bacteria [7, 9]. It is reasonable to use narrow-spectrum antibiotics for simple infections and broad-spectrum for complex infections to prevent resistance. Penicillin, clindamycin, metronidazole are narrow-spectrum, while amoxicillin+clavulanic acid, ampicillin+sulbactam, azithromycin, tetracycline, cephalosporin, moxifloxacin, ciprofloxacin and co-trimoxazol are broad-spectrum antibiotics [10]. Recently, there has been an alarming increase in the incidence of resistant bacterial isolates in odontogenic infections. Many anaerobic bacteria have developed resistance to beta-lactam antibiotics via beta-lactamase [7]. Inappropriate use of antibiotics causes the emergence of resistant bacteria. Today, many common and life-threatening infections are becoming difficult or impossible to treat and sometimes turning a common infection into a life-threatening one [11]. The antibiotic resistance is facilitated by repeated exposure of bacteria to antibiotics and access of bacteria to a large antimicrobial pool. Pathogenic and nonpathogenic bacteria are becoming increasingly resistant to conventional antibiotics. The focus has now shifted to multi-drug-resistant Gram-negative bacteria, while initial studies were investigated on antibiotic resistance such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant Enterococcus spp. [12]. Gram-negative pathogens are particularly troublesome as they are becoming resistant to nearly all drugs. Bear in mind that resistance occurs for the Gram-positive infections (Staphylococcus and Enterococcus) but not on the same scale [13].

Nanoantibiotic drug delivery with low toxicity and extended release would be an appropriate alternative to reduce antibiotic resistance. When an antibiotic is administered, strains of resistant organisms may proliferate; therefore, the antibiotic becomes ineffective. An antibiotic can act as an antigenic stimulus and produce an allergic reaction. They can kill or

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halt the proliferation of sensitive bacteria. This may include normal flora. Thus, an antibiotic may cause diarrhea, increased risk of bleeding especially in patients taking warfarin. Once the susceptible bacteria are killed, they may be replaced by more resilient organisms such as *Candida albicans* and *Clostridium difficile*; moreover, hepatobiliary dysfunctions and nephrotoxicity are the other complications that may occur [14].

2. Mechanisms of resistance

- Mutations of bacterial genes (chromosomal) leading to cross-resistance.
- Gene transfer from one microorganism to other by plasmids, transpositions (conjugation), integrons and bacteriophages (transduction). After these, they can use various biochemical types of resisting mechanisms (**Figures 1** and **2**).
- Antibiotic inactivation (with cell wall synthesis by beta-lactams and glycopeptide).
- Target alteration (inhibition of protein synthesis for tetracyclines and macrolides).
- Interfering with nucleic acid synthesis for rifampin and fluoroquinolones.
- Altered permeability (modifications of the cell surface for aminoglycosides).
- Bypass metabolic pathway (metabolic route inhibition for co-trimoxazole) [2–4].
- In recent studies, Lee et al. recommended that not all interactions of bacteria with antibiotics can be clarified within the standard theory; however, the new Kin selection hypothesis

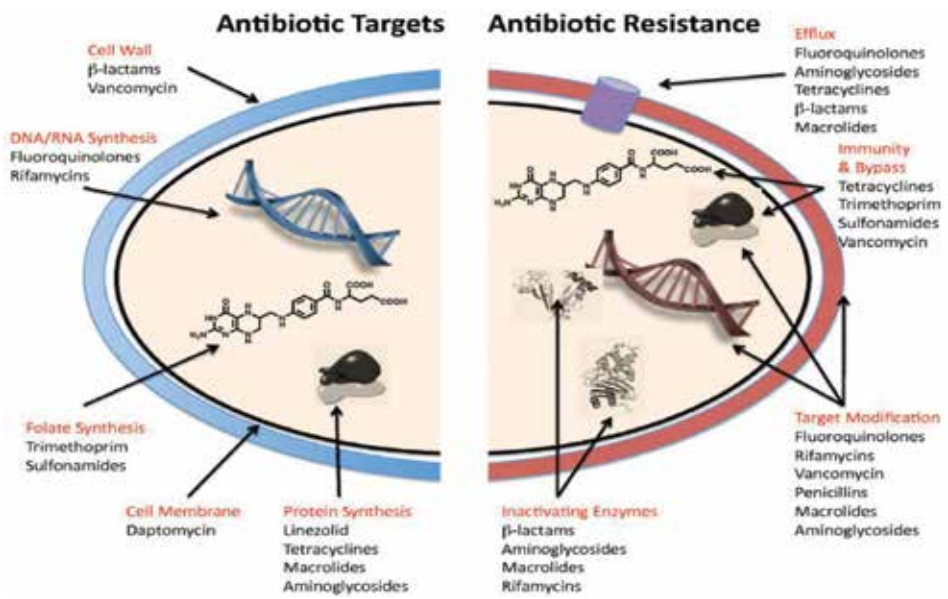

Figure 1. Gerard D Wright. Antibiotic targets and mechanisms of resistance. BMC Biology 2010 8:123.

proposed by W.D. Hamilton in 1964 suggested if one group of microorganisms is going to be resistant or destroyed, then others with similar genes have an opportunity to resist and mutate [15, 16].

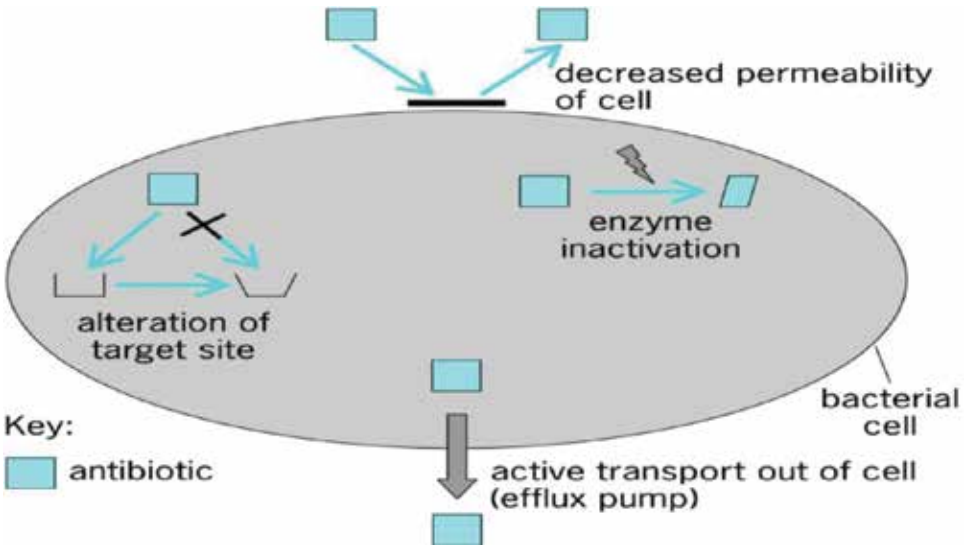

Figure 2. Four common mechanisms of antibiotics resistance. McGraw-Hill Concise Encyclopedia of Bioscience. 2002 by the McGraw-Hill Companies, Inc.

Resistance is formed by the lack of proper diagnosis, the widespread use of antibiotics in hospital, wrong use for patients with a viral infection or still undiagnosed illness and livestock farming and exploiting antibiotics in poultry and food industry (may cause some resistance in the long term) [11]. Clinical signs of resistance include prolonged and chronic infections, increasing disease manifestations and outbreaks, distributing diseases to other organs and increasing the probability of other diseases due to immune system weakening, malnutrition and organ failure. Adverse effects include hypersensitivity reactions to agents, that is, interaction between drugs, cells, organ functions and normal electrolyte concentration. In addition, the presence of background diseases, organ disorders, and physiologic factors such as old age and pregnancy may increase side effects [17].

3. The adverse effects and resistance of the several common antibiotics which are used in oral and maxillofacial surgery

3.1. Penicillins

The base structure of penicillins is a thiazolidine ring which is adherent to the beta-lactam and carries the subordinate amino group (RNH), and in fact, substituents can attach to the amino chain [3]. Natural penicillins are beta-lactam antibiotics and the most important ones are as follows [18]:

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- Penicillins (penicillin G) have little activity against Gram-negative rods, and they are susceptible to hydrolysis by beta-lactamases.
- Anti-staphylococcal penicillins (nafcillin) are resistant to staphylococcal beta-lactamases. They are active against staphylococci and streptococci but not against anaerobic bacteria, Gram-negative cocci or rods.
- Extended-spectrum penicillins (aminopenicillins and antipseudomonal penicillins). They are relatively susceptible to hydrolysis by beta-lactamases [3].

More than 10% of patients receiving penicillin may have some reactions from a mild rash to anaphylaxis. Anaphylaxis is a life-threatening reaction that most commonly occurs with parenteral administration. It appears as severe hypotension, bronchoconstriction and abdominal pain. Other manifestations of hypersensitivity reactions include fever, eosinophilia, angioedema and serum sickness. Before penicillin therapy begins, the patient's history should be assessed for reactions to penicillin, in case of positive background, alternative drugs should be used; however, hypersensitivity reactions may occur even in patients with a negative history [18].

3.1.1. Adverse effects

Penicillins are bactericidal and act by interfering with bacterial cell wall synthesis. They infiltrate well into body tissues and fluids. Penetration into the cerebrospinal fluid is poor except when the meninges are inflamed. Allergic situations happen in 1–10% of patients, but anaphylactic reactions occur in less than 0.05% of treated patients. Patients with a history of atopic allergy are at higher risk of anaphylactic reactions to penicillins. Patients who are allergic to one penicillin will be allergic to all. Patients with the background of immediate hypersensitivity to penicillin may also have a reaction to cephalosporin and other beta-lactam antibiotics. Individuals with a history of a minor rash (non-confluent, non-pruritic) or a rash that occurs more than 72 hours after penicillin administration are probably not allergic to penicillin, and penicillin should not be withheld unnecessarily for serious infections [19]. Other side effects are rare, but serious toxic effects of the penicillins are encephalopathy due to intrathecal injection. In renal failure, the accumulation of electrolytes may occur due to either sodium or potassium content in injection. Diarrhea frequently occurs during oral penicillin therapy, and it can also cause antibiotic-associated colitis in a prolonged case [19]. Penicillins are classified as category B. Penicillin is excreted into breast milk in low concentrations and is considered safe to use in breastfeeding women [20, 21]. Exfoliating dermatitis and Stevens-Johnson syndrome are the most severe dermatologic signs. Gastrointestinal adverse effects are most common in response to ampicillin [22]. Aqueous crystalline penicillin G and procaine penicillin G have been implicated in neurological reactions including seizures, neuromuscular instability, confusion and hallucinations [21]. Rarely, penicillin G causes hemolytic anemia [23, 24]. Candidiasis is more common in patients taking broad-spectrum aminopenicillins. Other side effects of natural penicillins include bone marrow suppression, and with high-dose therapy, seizures may occur [18].

3.1.2. Significant interactions

Probenecid increases blood levels of penicillins and may be given alongside for this purpose. Antibiotic antagonism occurs when erythromycin, tetracycline or chloramphenicol is given within an hour after taking penicillin. Prolonged reactions may arise in utilizing penicillin G procaine and benzathine. Penicillin G procaine should not be injected into or near an artery or nerve due to possible permanent neurological damage [3, 18].

Penicillinase-resistant penicillin is not hydrolyzed by beta-lactamases. These agents include methicillin, nafcillin, the isoxazolyl penicillin, dicloxacillin and oxacillin. The penicillinase-resistant group can cause hypersensitivity reactions. Methicillin may cause nephrotoxicity and interstitial nephritis. Oxacillin may be hepatotoxic. The most dangerous situation is methicillin-resistant *Staphylococcus aureus* (MRSA). This bacterium resists numerous antibiotics including methicillin, amoxicillin, penicillin and oxacillin [25]. Wide-ranging cross-resistance exists among the penicillinase-resistant penicillins. Methicillin sodium and nafcillin have been reported to be incompatible with aminoglycosides, acidic and alkaline drugs [26]. Aminopenicillins, because of their broader range, are identified as broad-spectrum penicillins. The incompatibility of ampicillin sodium and aminoglycosides appears to be more evident at higher concentrations and with glucose-containing solutions [26].

Extended-spectrum penicillins have the extensive antibacterial spectrum of all penicillins. Also called antipseudomonal penicillins, this group includes the carboxypenicillin and ureidopenicillin [18]. Hypersensitivity reactions are the other penicillins. Ticarcillin may cause hypokalemia. The high sodium content of ticarcillin can pose a danger to patients with heart failure (HF) and inhibits platelet aggregation [26].

3.1.3. Resistance

Modification of drug penicillin-binding proteins (PBPs) impairs penetration of drug to target PBPs and efflux. Beta-lactamase production is the most common mechanism of resistance. Altered target PBPs are the basis of methicillin resistance in staphylococci and penicillin resistance in pneumococci. These resistant organisms produce PBPs which have low affinity for binding beta-lactam antibiotics. PBP targeting is decreased only in Gram-negative species because of their water-resistant outer cell membrane. Reduced penetration is not sufficient to confer resistance because enough antibiotic ultimately enters the cells. However, this barrier can become important in the presence of the beta-lactamase as long as hydrolyzing the drug is faster than entering the cells. Gram-negative organisms may produce an efflux pump that efficiently transports some beta-lactam antibiotics from the periplasm back across the outer membrane [27].

3.2. Cephalosporins

The cephalosporins are a class of beta-lactam antibiotics originally derived from the fungus Acremonium, and they also constitute a subgroup of beta-lactam antibiotics called cephems, and both are based upon the cephem nucleus. Unlike most cephalosporins, cephamycins are a very effective antibiotic group against anaerobic microbes. Cephamycins include cefoxitin,

cefotetan and cefmetazole which are often grouped with the second-generation cephalosporins. The structure of most of the cephalosporins contains N-methylthiotetrazole side chain, and when it becomes metabolized in the body, it releases free N-methyl-thiotetrazole which can cause hypoprothrombinemia (due to the inhibition of vitamin K enzyme, epoxide reductase) and a reaction with ethanol similar to performing by disulfiram, due to inhibition of aldehyde dehydrogenase [3]. Cephalosporins are similar to penicillins but more stable to many bacterial beta-lactamases; therefore, they have a broader spectrum of activity.

3.2.1. First generation

They are very active against Gram-positive cocci; however, they are not active against methicillin-resistant strains of staphylococci. Oral therapy should not be relied on in serious systemic infections.

3.2.2. Second generation

They have extended Gram-negative efficacy. Cephamycins have activity against anaerobes. The oral second-generation cephalosporins are active against beta-lactamase-producing organisms [3].

3.2.3. Third generation

They have an expanded Gram-negative coverage, and some of them are able to cross the blood-brain barrier. Third generation acts against beta-lactamases; however, they should be avoided in enterobacter infections because of the emergence of resistance [3, 5].

3.2.4. Fourth generation

They are more resistant to hydrolysis by chromosomal beta-lactamases (those produced by Enterobacter) [3].

3.2.5. Fifth generation

Beta-lactam antibiotics with activity against methicillin-resistant staphylococci are currently under progress, for instance ceftaroline fosamil is the first drug to be approved for clinical use. Ceftaroline has better binding to penicillin-binding protein 2a which facilitates methicillin resistance in staphylococci. It is not active against AmpC or extended spectrum beta-lactamase-producing organisms [3].

3.2.6. Adverse effects

Reactions can be allergic or toxic or both [3]. Common adverse drug reactions (>1%) include rash, diarrhea, electrolyte instabilities, nausea, pain and inflammation at injection site. Rare side effects (0.1–1%) include vomiting, headache, dizziness, oral candidiasis, pseudomembranous colitis, eosinophilia, neutropenia, hemolytic anemia, nephrotoxicity, thrombocytopenia and fever. Some other adverse reactions are pruritus, Stevens-Johnson syndrome, vaginitis,

increased hepatic transaminases, thrombocytosis, phlebitis, increased BUN and creatinine, renal failure and anaphylaxis. Some cephalosporins have reactions when they are combined and utilized such as encephalopathy, asterixis neuromuscular excitability, seizure, aplastic anemia, interstitial nephritis, PT prolonged, agranulocytosis, cholestasis and erythema multiform [5]. A potentially life-threatening arrhythmia has been reported in patients who received a rapid bolus cefotaxime injection via central line, and granulocytopenia and more rarely agranulocytosis may develop through long treatment (>10 days) [3, 5]. Secondary to biliary obstruction possibly due to ceftriaxone-calcium precipitates, pancreatitis has been reported rarely by using ceftriaxone [3, 5]. Cross-allergenicity appears to be most common among penicillins, carbapenems, aminopenicillins and early-generation (group I and II) cephalosporins due to sharing the same R-1 side chains. Patients with documented penicillin anaphylaxis have an increased risk to cephalosporins. Previously, extensive warnings of 10% cross-reactivity had been given, but nowadays, in the absence of proper alternatives, oral cefixime or cefuroxime, injectable cefotaxime, ceftazidime and ceftriaxone are used with precaution [4]. Local irritation can produce pain after intramuscular injection and thrombophlebitis after intravenous injection [3, 5, 28]. Cephalosporins may cause increased international normalized ratio (INR) particularly in nutritional-deficient patients, extended treatment, hepatic and renal disease. Long usage may result in fungal or bacterial superinfection particularly with renal impairment [5]. The pregnancy risk factor is B. Small amounts of cephalosporins are excreted in breast milk but most are not harmful, however, have influence on bowel flora [5].

3.2.7. Drug interactions

Uricosuric agents may decrease the excretion of cephalosporins. Cephalosporins may increase the anticoagulant effect of vitamin K antagonists. Tablets containing sodium caseinate can cause allergic reactions in patients with milk protein hypersensitivity. Cephalexin may increase the serum concentration of metformin. Antacids, H2-antagonists and food may decrease the absorption of cephalosporin [5]. Calcium salts (intravenous) and every fluid containing calcium may enhance the adverse/toxic effect of ceftriaxone due to the formation of an insoluble precipitate. Some test interactions might be changed such as positive direct Coombs, false-positive urinary glucose, false-positive serum or urine creatinine [5, 16].

Resistance to cephalosporin antibiotics can involve either reduced affinity of existing PBP components or the acquisition of a supplementary beta-lactam-insensitive PBP. Currently, some *Citrobacter freundii, Enterobacter cloacae, Neisseria gonorrhea* and *Escherichia coli* strains are resistant [3, 28]. Other beta-lactam drugs such as monobactams and aztreonam are drugs with a monocyclic beta-lactam ring; their spectrum of activity is limited to aerobic Gram-negative rods. Their Gram-negative spectrum is similar to the third-generation cephalosporins.

3.3. Beta-lactamase inhibitors (clavulanic acid, sulbactam and tazobactam)

These substances look like beta-lactam molecules and have weak antiseptic action. They can protect hydrolysable penicillins from inactivation. Beta-lactamase inhibitors are available only in fixed combinations with specific penicillins [5].

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Carbapenems are structurally related to other beta-lactam antibiotics. It is resistant to most beta-lactamases but not carbapenemases or metallo-beta-lactamases. Methicillin-resistant strains of staphylococci are resistant. The dosage must be reduced in the case of renal insufficiency [3]. The most common adverse effects of carbapenems as imipenem are gastrointestinal signs, skin rashes and reactions at the infusion sites. Patients allergic to penicillins may be allergic to carbapenems, but the incidence is low [5].

3.4. Glycopeptide antibiotics

Vancomycin is an antibiotic produced by Streptococcus and *Amycolatopsis orientalis*. It is active only against Gram positives [3]. Resistance to vancomycin is due to reform of the D-Ala-D-Ala binding site of the peptidoglycan building block with conversion to D-lactate and thickened cell wall with increased numbers of D-Ala-D-Ala which serve as dead-end binding sites for vancomycin. Vancomycin is effective against staphylococci, including those producing beta-lactamase and those resistant to nafcillin and methicillin [5, 6, 29].

Adverse reactions take place in almost 10% of cases. Most reactions are rather slight and reversible. Vancomycin is an irritant to tissue because of phlebitis at the site of injection. Chills and fever may occur. Ototoxicity is rare, and nephrotoxicity is uncommon. However, prescribing another ototoxic or nephrotoxic drug increases the risk of these toxicities. Ototoxicity can be minimized by maintaining peak serum concentrations below 60 mcg/ml. The more common reaction is "red man" syndrome which is caused by the release of histamines. It can be prevented by prolonging the infusion period to 1–2 hours or pretreatment with an antihistamine [3]. Other side effects include tinnitus or vertigo which can be the symptoms of vestibular injury and future bilateral irreversible damage. Elongated therapy or total doses above 25 g may increase the risk of neutropenia. Oral vancomycin is only specified for pseudomembranous colitis due to *C. difficile* and enterocolitis due to *S. aureus* and is not effective for systemic infections. Pregnancy risk factor is B for the oral type and C for intravenous type. Vancomycin may develop the neuromuscular-blocking effect. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease the elimination of vancomycin [5].

3.5. Other glycopeptides

Teicoplanin is very similar to vancomycin in the mechanism of action and antibacterial spectrum; telavancin is active with Gram-positive bacteria and potentially teratogenic; hence, it must be avoided in pregnant women. Daptomycin is a new cyclic lipopeptide fermentation creation of *Streptomyces roseosporus*. It may be active against vancomycin-resistant strains of enterococci and *S. aureus*. It should be used with care in renal impairment [3, 29].

3.6. Tetracyclines (tetracycline, doxycycline, minocycline, tigecycline)

Tetracyclines chelate divalent metal ions which can restrict their absorption and activity. Tetracyclines are broad-spectrum bacteriostatic antibiotics that inhibit protein synthesis.

3.6.1. Resistance

Three mechanisms of resistance to tetracycline analogs have been described: 1) impaired influx or increased efflux, 2) ribosome shield due to the production of proteins that interfere with tetracycline binding to the ribosome regularly by Gram positives and 3) enzymatic inactivation. The most important of these is the formation of an efflux pump and ribosomal protection [3, 30].

3.6.2. Adverse reactions

Hypersensitivity reactions to tetracyclines are uncommon. Most adverse effects take place due to direct drug toxicity or modification of microbial flora; moreover, gastrointestinal adverse effects are the most common symptoms. Tetracyclines are readily bound to the calcium deposited in newly formed bone or teeth in young children under 8 years and in the fetus. It can accumulate in fetal teeth, leading to fluorescence, discoloration and enamel dysplasia; therefore, tetracyclines are avoided in pregnancy (category D). Tetracyclines in breast milk can chelate with calcium and interferes with growing teeth. Hepatic necrosis has been reported with daily doses of 4 g or more with intravenous injection. Renal tubular acidosis and Fanconi syndrome have been attributed to the administration of outdated tetracycline; if it is given along with diuretics it may cause nephrotoxicity. Intravenous injection can lead to venous thrombosis. Intramuscular injection produces painful local irritation and should be avoided. Demeclocycline can induce sensitivity to sunlight or ultraviolet light mainly in fair-skinned people [3]. An erythematous rash in sun-exposed parts of the body has been reported to appear in 7–21% of people taking doxycycline. Unlike some other members of the tetracycline group, it may be used in those with renal impairment. Doxycycline is contraindicated in the pediatric treatment of acute bacterial rhinosinusitis. Other reactions of doxycycline are similar to other tetracyclines [3, 5, 17]. Oral tetracyclines should be given in an empty stomach. Meals containing aluminum and magnesium may reduce tetracycline absorption. Other side effects include pericarditis, intracranial pressure increase, bulging fontanels in infants, pseudotumor cerebri, paresthesia, pigmentation of nails, exfoliative dermatitis, insipidus syndrome, discoloration of teeth enamel hypoplasia (young children) and anaphylaxis [5].

3.6.3. Drug interactions

Antacids, bile acid, bismuth, iron, magnesium and zinc salts may decrease the absorption of tetracyclines. Tetracycline derivatives can boost the neuromuscular-blocking effect and may diminish the therapeutic effect of penicillin and increase the toxic effect of retinoic acid and the anticoagulant effect of vitamin K antagonists [3, 5].

3.7. Macrolides (azithromycin, erythromycin)

The macrolides are categorized by a macrocyclic lactone ring to which deoxy sugars are attached. Erythromycin loses activity rapidly at 20°C and at acidic pH. Its activity is enhanced at alkaline pH [3, 17].

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Clarithromycin is derived from erythromycin by the addition of a methyl group and has an improved acid stability, but erythromycin-resistant streptococci and staphylococci are also resistant to clarithromycin. The advantages of clarithromycin are lower incidence of gastrointestinal intolerance and less regular dosing [3].

Macrolides resistance to erythromycin is usually plasmid encoded. Three mechanisms have been recognized: 1) Reduced permeability of the cell membrane, 2) production of esterases that hydrolyze macrolides and modification of the ribosomal binding site and 3) efflux and methylase production are the most important resistance mechanisms in Gram-positive organisms. Fundamental methylase construction confers resistance to structurally unrelated but systematically similar compounds such as clindamycin which share the same ribosomal binding site. However, constitutive mutants which are resistant can be selected and emerge during therapy with clindamycin [3, 17].

3.7.1. Adverse reactions

Anorexia and gastrointestinal signs are common, and they occur due to a direct stimulation of gut motility, and it is the most common reason for discontinuing erythromycin and substituting another antibiotic. Erythromycins, particularly the estolate type, can produce acute cholestatic hepatitis probably as hypersensitivity reaction but is reversible. Macrolides have been associated with rare (QTc) = QT Interval of the electrocardiogram prolongation and ventricular arrhythmias, including torsade de pointes; extensive use may result in fungal or bacterial superinfection [3, 5].

3.7.2. Disease-related concerns

Macrolides should be used with caution in coronary artery disease (CAD), in the elderly, myasthenia gravis, with narrowing of the gastrointestinal (GI) tract (may cause obstruction) and severe renal impairment. Pregnancy risk factor is B for erythromycin and C for clarithromycin. Macrolides can decline the metabolism of benzodiazepines, calcium channel blockers, carbamazepine, cisapride, antifungal agents, clozapine, colchicine, corticosteroids, cyclosporine, theophylline derivatives and vitamin K antagonists and may increase the serum concentration of alosetron, cardiac glycosides, fentanyl, salmeterol and tacrolimus. Macrolides may diminish the therapeutic effect of clopidogrel, the metabolism of HMG-CoA reductase inhibitors and some SSRIs [3, 5, 17].

Azithromycin is derived from erythromycin by the addition of methylated nitrogen into the lactone ring and different from clarithromycin mainly in pharmacokinetic properties. However, azithromycin penetrates into most tissues (except cerebrospinal fluid) and phagocytic cells extremely well. Antacids do not alter the bioavailability but delay absorption and reduce peak serum concentrations. Because they have a 15-element (not 14) lactone ring, they do not inactivate cytochrome P450 enzymes [3]. Other reactions are similar to macrolides [5, 17].

Ketolides are semisynthetic 14-membered-ring macrolides, differing from erythromycin by substitution of a 3-keto group for the neutral sugar L-cladinose which is permitted for limited clinical use. It is active in vitro against *Streptococcus pyogenes, S. pneumonia* and *S. aureus*. Many

macrolide-resistant strains are susceptible to ketolides because the basic modifications of these compounds change as poor substrates for efflux pump-mediated resistance, and they bind to ribosomes of some bacterial species with higher affinity than macrolides. It may slightly prolong the QTc interval. The use of ketolides can cause hepatitis and liver failure and are also contraindicated in patients with myasthenia gravis [3, 17].

3.8. Lincosamides

Clindamycin is a chlorine-substituted derivative of lincomycin, an antibiotic that is produced by *Streptomyces lincolnensis* [3]. Clindamycin, like erythromycin, inhibits protein synthesis by interfering with the formation of initiation complexes and with aminoacyl translocation reactions. The binding site for clindamycin is on the 50S subunit. It is often active against community-acquired strains of methicillin-resistant *S. aureus* [5, 17]. Ordinary adverse effects are diarrhea, nausea and skin rashes. Impaired liver function and neutropenia occur occasionally [3]. Physicians must use clindamycin carefully in patients with hepatic impairment. Some products may contain benzyl alcohol which has been related to "gasping syndrome" in neonates, and some others may have tartrazine which causes allergic reactions in certain persons. Elderly patients have a higher risk of developing severe colitis. Clindamycin is excreted in breast milk, and thus it is suggested to suspend drug intake. Lincosamide may diminish the therapeutic effect potential of erythromycin [3, 5, 17].

3.9. Streptogramins

They share the same ribosomal binding site as macrolides and clindamycin, and it is active against Gram-positive cocci, multidrug-resistant strains of streptococci, penicillin-resistant strains of *S. pneumoniae*, methicillin-susceptible and resistant strains of staphylococci. Resistance may occur due to alteration of the quinupristin binding site (MLS-B type resistance), enzymatic inactivation of dalfopristin or efflux. Quinupristin-dalfopristin is permitted for the treatment of infections caused by staphylococci or by vancomycin-resistant strains of *E. faecium*. The major toxicities are infusion-related events, such as pain at the infusion site and an arthralgia-myalgia syndrome [3, 31].

3.10. Oxazolidinones

Linezolid is an affiliate of the oxazolidinones, a novel class of synthetic antimicrobials. It is active against Gram-positive organisms. Its resistance is caused by the mutation of linezolid binding site on 23S ribosomal RNA. Linezolid is confirmed for use in vancomycin-resistant *E. faecium* infections, health care-associated pneumonia and community-acquired pneumonia. Tedizolid is a next-generation oxazolidinone with high potency against Gram-positive bacteria such as methicillin-resistant *S. aureus*. Possible benefits over linezolid include bigger impact against staphylococci and one daily dosing [3, 6]. The main toxicity of linezolid is hematologic which is reversible and commonly minor. Thrombocytopenia is the most common sign when the drug is ordered for use more than 2 weeks. Optic and peripheral neuropathy and lactic acidosis have been reported with long courses of linezolid. There are reports of serotonin syndrome arising when linezolid is co-participated with serotonergic drugs [3, 5].

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3.11. Aminoglycosides

They are used broadly in combination with a beta-lactam antibiotic in serious infections with Gram-negative bacteria and with vancomycin or a beta-lactam antibiotic for Gram-positive endocarditis. Acidic pH and anaerobic conditions inhibit the passage across the cell membrane into the cytoplasm by reducing the gradient. Transport may be improved by cell wall-active drugs such as penicillin or vancomycin [3, 32]. Aminoglycosides are absorbed very poorly from the intact gastrointestinal tract.

3.11.1. Adverse effects

The threshold is not precisely defined for the beginning of toxicity, but concentrations above 2 μg/mL are perilous [5]. All aminoglycosides are ototoxic and nephrotoxic, and they are more likely to emerge when therapy is persistent for more than 5 days, with higher doses, in the elderly and in renal failure. Parallel consumption with loop diuretics or other nephrotoxic antimicrobial agents (vancomycin or amphotericin) can create nephrotoxicity. Ototoxicity can appear as auditory damage (tinnitus and high frequency hearing loss) or as vestibular impairment (vertigo, ataxia, loss of balance). Neomycin, kanamycin and amikacin are the most ototoxic drugs. Streptomycin and gentamicin are the most vestibulotoxic. Neomycin, tobramycin and gentamicin are the most nephrotoxic. Aminoglycosides can produce a curare-like effect, in high doses, with neuromuscular blockade. This reaction is usually reversible by calcium gluconate or neostigmine. Hypersensitivity occurs intermittently [3, 5].

Gentamicin is effective against both Gram-positive and Gram-negative organisms and has no activity against anaerobes. Resistance emerges in staphylococci during monotherapy. Gram-negative bacteria resistance is most commonly due to plasmid-encoded aminoglycoside-modifying enzymes. Gram negatives which are gentamicin-resistant generally are vulnerable to amikacin. Low pH and low oxygen pressure create poor environment for drug activity [5, 32].

3.11.2. Gentamicin adverse reactions

Nephrotoxicity is usually reversible. It occurs in 5–25% of patients consuming gentamicin for longer than 3–5 days. Ototoxicity, which is permanent, shows itself as vestibular dysfunction. Gentamicin has a rare hypersensitivity reaction. Pregnancy risk factor is C (ophthalmic, topical) and D (injection).The nephrotoxic effect of aminoglycosides may be enriched with amphotericin B, cisplatin, cyclosporine, colistimethate, loop diuretics and vancomycin. Aminoglycosides may increase the hypocalcemic effect of bisphosphonate derivatives and the neuromuscular-blocking effect of Botulinum toxin type A and Botulinum toxin type B. Some penicillins may accelerate the degradation of aminoglycosides in vitro. This may be clinically significant for certain penicillin (ticarcillin, piperacillin, carbenicillin) and aminoglycoside combination therapy in patients with significant renal impairment. Close monitoring of aminoglycoside levels is warranted [5, 32].

Tobramycin, like other aminoglycosides, is ototoxic and nephrotoxic. Nephrotoxicity of tobramycin may be slightly less than that of gentamicin.

Amikacin is semisynthetically derived from kanamycin; it is less toxic than the near relative molecule. It is resistant to many enzymes that inactivate gentamicin and tobramycin; therefore, it can be used against some resistant microorganisms. Similar to all aminoglycosides, amikacin is nephrotoxic and ototoxic [3, 5, 17].

3.12. Sulfonamides

The basic structure of the sulfonamides has similarity to p-amino benzoic acid (PABA). Sulfonamides are more soluble in alkalosis than in acidosis. It can be prepared with sodium salts which are utilized for intravenous injection. Sulfonamides deter Gram-positive and Gram-negative bacteria. Its activity is reduced against anaerobes. *Pseudomonas aeruginosa* is certainly resistant to sulfonamide antibiotics. A mixture of a sulfonamide with an inhibitor of dihydrofolate reductase (trimethoprim) is synergistic due to sequential inhibition of folate synthesis [3, 5].

3.12.1. Resistance

Several bacteria, like mammal cells, do not have the crucial enzymes for folate synthesis from PABA and depend on exogenous sources; therefore, they are not vulnerable to sulfonamides. Sulfonamide resistance may take place by mutations that cause high production of PABA and production of a folic acid-synthesizing enzyme that has low affinity for sulfonamides or impermeability to the sulfonamide. In significant renal failure, the dosage must be reduced. The previous susceptible species such as meningococci, pneumococci, streptococci, staphylococci and gonococci are now resistant [3, 5, 32].

3.12.2. Adverse reactions

Traditionally, drugs with the basic structure of sulfonamide including antimicrobial sulfas, diuretics, diazoxide and the sulfonylurea hypoglycemic drugs are measured to be cross-allergenic. The most common adverse effects are fever, skin rashes, exfoliative dermatitis, photosensitivity, gastrointestinal signs and difficulties due to urinary tract problems. Stevens-Johnson syndrome is uncommon, and potentially fatal type of skin or mucous membrane eruption may be appeared. They may precipitate in acidic urine producing crystalluria or obstruction. This is rarely a problem with the more soluble sulfonamides such as sulfisoxazole. Sulfonamides have also been associated in various types of nephrosis. They can cause hemolytic or aplastic anemia and may incite hemolysis in patients with G6PD. Sulfonamides taken near the end of pregnancy increase the risk of kernicterus [3, 5].

3.13. Trimethoprim and trimethoprim-sulfamethoxazole

Trimethoprim selectively inhibits bacterial dihydrofolic acid reductase for repelling the synthesis of purines and DNA. Trimethoprim or pyrimethamine by merging with a sulfonamide can block folate synthesis (synergism). It is active against most *Staphylococcus aureus* strains, both methicillin-susceptible and methicillin-resistant and against respiratory tract pathogens.

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Resistance to trimethoprim results from reduced cell permeability, overproduction of dihydrofolate reductase or production of an altered reductase with reduced binding. Mutation due to plasmid-encoded causes rapid and widespread trimethoprim resistance.

3.13.1. Adverse effects

Anti-folate activity causes megaloblastic anemia, leukopenia and granulocytopenia, and with the trimethoprim-sulfamethoxazole mixture, all reactions connected to sulfonamides may occur. Patients with AIDS and pneumocystis pneumonia have a particularly high frequency of reactions to this mixture (fever, rashes, leukopenia, diarrhea, hepatic enzymes rising, hypoglycemia, hyperkalemia, hyponatremia) [3, 5, 29]. It should be used with cautiousness in patients with allergies or asthma, hepatic and renal impairment, thyroid dysfunction, in the elderly, G6PD deficiency and folate deficiency. Trimethoprim can increase the hyperkalemic effect of ACE Inhibitors and the adverse effect of amantadine. It may decrease the metabolism of thiazolidinedione, repaglinide, procainamide and the excretion of lamivudine. Sulfamethoxazole can boost the myelosuppressive effect of azathioprine and cyclosporine. Procaine may reduce the activity of trimethoprim. Sulfonamides and trimethoprim may decrease the metabolism of phenytoin [5, 29].

3.14. Fluoroquinolones—DNA gyrase inhibitors

Quinolones are synthetic fluorinated analogs of nalidixic acid. They are active against Gram-positive and Gram-negative bacteria. Methicillin-resistant strains of staphylococci are often resistant [3, 33]. Quinolones as whole are divided into three groups including nalidixic acid, the first generation with better effect on Gram negatives, ciprofloxacin as the second and moxifloxacin as the third generation. In some references they are divided into two groups based on antimicrobial spectrum and pharmacology [3, 34]. Gemifloxacin and moxifloxacin have better action against Gram-positive organisms while older fluroquinolones have moderate effects on Gram positive as well as Gram negative [3, 34].

Resistance appears in around one of every 107–109 bacteria, especially staphylococci, *P. aeruginosa* and *Serratia marcescens*. Resistance will be appeared in the quinolone-binding region of the target enzyme with mutations or by changing the permeability; recently, two forms of plasmid-mediated resistance have been defined. The first utilizes Qnr proteins which protect DNA gyrase from the fluoroquinolones; the second is an aminoglycoside acetyltransferase capable of modifying ciprofloxacin. Resistance to one fluoroquinolone normally confers cross-resistance to all of this class [3, 34].

3.14.1. Adverse effects

Fluoroquinolones are typically well tolerated. The most common side effects are nausea, vomiting and diarrhea. Intermittently, some interactions are headache, dizziness, insomnia, skin rash and high liver function tests. Prolongation of the QTc interval may occur with levofloxacin, gemifloxacin and moxifloxacin; therefore, it must be used with care to QTc interval prolongation and hypokalemia. Due to impaired cartilage growth and arthropathy by

fluoroquinolones, they are not prescribed for patients under 18 years. Nevertheless, if arthropathy is reversible, it may be feasible for the treatment of pseudomonal infections in some patients with cystic fibrosis. Fluoroquinolones should be suspended during pregnancy due to lack of data verifying their safety. Neuropathy can appear and may continue for several months or years during and after treatment; in some cases it may be perpetual [3]. Fluoroquinolones have been related to serious and occasionally fatal hypoglycemia especially in elderly patients with diabetes, but it has been reported in cases without a previous history of diabetes [5, 33].

3.15. Moxifloxacin

It is effective on Gram-positive bacteria. Side effects include tremor, restlessness, confusion and rarely hallucinations or seizures; must be used with caution in cases with known or suspected CNS disorders [5]. Reactions may present as typical allergic symptoms or can present as severe idiosyncratic dermatologic disorder (Stevens-Johnson, toxic epidermal necrolysis, vasculitis). Pneumonitis, nephritis, hepatic failure or necrosis and cytopenias are frequently seen after multiple doses. Patients must avoid excessive sunlight because of moderate-to-severe phototoxicity reactions [5, 6]. Prolonged use can produce fungal or bacterial superinfection. It should be used carefully in patients with significant bradycardia or acute myocardial ischemia, hepatic impairment, myasthenia gravis, rheumatoid arthritis, elderly and G6PD deficiency. Safety and efficacy of moxifloxacin have not been established in children, but in pregnancy, the risk factor is category C [5]. All these adverse effects are rare or about 1–2%, and it may also have some other reactions less than 1% such as hyperlipidemia, hyper or hypotension, hypoesthesia, laryngeal edema, nightmares, paresthesia, pelvic pain, peripheral neuropathy, decreased prothrombin time, speech disorder, taste loss, abnormal thinking, tinnitus, tongue discoloration, arrhythmia and vision abnormalities [3, 5]. It may increase the QTc-prolonging effect. Antacids, magnesium, iron and zinc salts may decrease the absorption of quinolone antibiotics (oral tables), but it is not affected by taking with a high-fat meal, yogurt or sodium bicarbonate. Quinolone antibiotics may expand the toxic effect of corticosteroids (systemic) and the effect of vitamin K antagonists. Insulin and sulfonylureas may increase the hyperglycemic or hypoglycemic effects. The neurotoxicity or seizure-potentiating effect might increase with NSAIDs [5, 33].

3.16. Ciprofloxacin

It has moderate effects on both Gram-negative and Gram-positive bacteria. In consequence of its extensive usage even for minor infections which are curable with older and narrower spectrum antibiotics, many bacteria have developed resistance in recent years. Numerous pathogens, including enterococci, *Streptococcus pyogenes* and *Klebsiella pneumonia*, have become resistant [33]. Most side effects are similar to other fluoroquinolone drugs above. Alkaline urine may escalate the risk of crystalluria. In patients over 60 years, rupture of the Achilles' tendon may take place. Due to secretion in breast milk and because of damage to joint cartilage, it should be avoided during breast feeding; the pregnancy risk factor is C [3, 5, 17]. Intravenous injection must be slow to avoid the risk of venous irritation. Oral tablets should be taken with

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food to minimize GI distress. Consuming large quantities of caffeinated drinks may pose a danger due to cardiac or CNS reactions. Ciprofloxacin can reduce the serum concentration of phenytoin and theophylline derivatives [3, 5].

3.17. Metronidazole

It is a nitroimidazole antibiotic and antiprotozoal drug. Metronidazole is absorbed selectively by anaerobic bacteria and sensitive protozoa and does not affect any human cells directly or aerobic bacteria [3, 17].

3.17.1. Adverse reactions

It has been found to be carcinogenic in rats [35]. Chronic treatment causes seizures and neuropathies; if this occurs, therapy must be withdrawn. It should be used with restriction in patients with a history of seizure disorder and CNS disease. Metronidazole should be utilized carefully in patients with blood dyscrasias, the elderly, heart failure or other sodium-retaining states, liver impairment and severe renal failure (creatinine clearance less than 10 mL/min). The pregnancy risk factor is B and should be avoided in the first trimester. Other reactions include flattening the T-wave, flushing, ataxia, dizziness, fever, headache, insomnia, irritability, seizure, vertigo, erythematous rash, Disulfiram-like reaction, dysmenorrhea, nausea (very common), abdominal cramping, constipation, diarrhea, furry tongue, stomatitis, metallic taste, xerostomia, cystitis, darkened urine (rare), incontinence, neutropenia (reversible), thrombocytopenia (reversible), peripheral neuropathy, nasal congestion, rhinitis, sinusitis, pharyngitis, flu-like syndrome and moniliasis [3, 5, 35].

Metronidazole can increase the toxic effect of alcohol (ethyl). It may augment the toxic effect of amprenavir, tipranavir, disulfiram and mebendazole (risk for Stevens-Johnson syndrome). It may increase the serum level of busulfan, fentanyl and salmeterol. This drug may reduce the metabolism of calcineurin inhibitors and vitamin K antagonists. It may affect the enzymes aspartate transaminase (AST), and alanine transaminase (ALT) for Liver function test, triglycerides, glucose and LDH tests. Metronidazole may possibly cause mood fluctuation [36].

4. Nanoantibiotics

4.1. Introduction

Nanoscience in association with medicine can bring new opportunities for scientists to introduce novel solutions against medical complications. In recent years, the development of innovative drugs to combat multi-drug resistant (MDR) bacteria is growing strongly [28–30, 32, 37–40]. The advantage of nanoantibiotic therapy is to proficiently decrease a variety of side effects which originate from conventional antibiotics; furthermore, a specific nanostructure can be synthesized for a distinctive goal since the production process is safe, inexpensive and innovative.

As biocompatibility, low toxicity and noticeable purity of antibacterial nanoparticles are vital for medical treatments, in the near future the conventional methods of nanoantibiotic assembly such as sonication [41–43] and chemical routes [44] will be replaced by laser-assisted generation of nanoparticles (NPs) in liquids since no chemical precursors are required [45–49]. Shape and size of the nanoparticles play an essential role in the antibacterial behavior of nanoparticles, as a case in point the average size of 1–10 nm demonstrated a dominant antibacterial activity [50]; therefore, laser ablation in particular liquids along with controlled laser parameters can design nanomaterials with desired shape, size and composition in a very strategic mechanism without using surface active agents which can trigger surface impurity and toxicity. The large surface area to volume ratio is a main property of nanomaterial which increases the antibacterial activity. Co-delivery process of two or more drugs can be efficiently achievable by using nanomaterials [51]; antibiotic resistance is significantly avoided since nanoparticles do not enter the bacterial cell, and its mechanism of killing bacteria is fundamentally done via direct contact with the bacterial cell wall [52]. There are critical procedures which occur during nanoantibiotic therapy; as nanomaterials electrostatically bind to the bacterial cell wall, they can induce membrane destruction and depolarization which initiate cell death [53–55]. Nanomaterials with extremely high surface area can catalyze the production of reactive oxygen species (ROS) which have a critical potential to damage bacterial cells [56].

4.2. Essential nanocarriers for drug delivery

Antibacterial drugs due to their fast degradation, low water-solubility, cytotoxicity to healthy tissues and weak membrane transportation are fairly hard to manage; nanoparticles including dendrimers, liposomes and polymer-based nanoparticles can simplify drug delivery against infectious diseases. Dendrimers as a tree-like structure with many branches with typical size of 10 nm were used in drug delivery and diagnostic systems. Liposome nanoparticles in the size range of 50–200 nm were broadly used for drug delivery system initially proposed in the 1970s [57]. Liposomes with a distinctive bilayer lipid structure are able to transfer hydrophobic and hydrophilic compounds without any chemical alteration; they can proficiently combine with bacterial membranes and release antibacterial agents to their cell membranes. In order to extend liposome longevity and stability in the blood stream, they can easily be functionalized with biocompatible polyethylene glycol (PEG) by forming a stealth layer on the liposome surface [58, 59]. Biocompatible chitosan nanoparticles with nontoxic nature, high antibacterial activity and high stability can encapsulate or embed drugs in the polymeric network. Hydrogels with biocompatible hydrophilic networks allow delivery of hydrophilic and small-molecule drugs. Highly porous silica nanoparticles are well known for local drug delivery to reduce cytotoxicity and side effects [60–62].

Metal-based nanoparticles including nickel, tungsten, gadolinium, gold, silver, zinc oxide, titanium dioxide and iron oxide nanoparticles were commonly used for diagnosis and delivery. A critical disadvantage is toxicity from the accumulation of metal nanoparticles in the human body after treatment; therefore, drug delivery process should be performed in a very strategic way.

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Zinc oxide nanoparticles (ZnO NPs) with potent antibacterial activity were designed as enzyme-nanoparticle conjugates in order to improve mono-dispersity and stability of nano-antibiotics during treatment; extremely greater antibacterial behavior was obtained by using positively charged lysozyme enzyme covalently bonded to ZnO nanoparticles [63].

Interestingly not only nanoparticles but also ions can demonstrate very strong antibacterial activity. Researchers at Rice University discovered that only silver ions behave destructively to the bacteria. Delivered silver ions can stimulate lysis in which the membrane of the bacterial cell breaks down and causes bacterial cell death [64].

The release of antibiotics can be prolonged by using nanocarriers for drug delivery systems to reduce extremely antibiotic resistance. Gold nanoparticles capped with glutathione can bring a higher rate of gentamicin loading; these capped gold nanoparticles which were covalently attached to gentamicin revealed strong antimicrobial activity with extended release of antibiotic over several days [65].

4.3. Antibacterial activity of core-shell nanoparticles

Recently, scientists were accentuated over designing of biocompatible core-shell nanoparticles for antibacterial activity, controlled drug release and targeted drug delivery [66]. Core-shell nanoparticles are advantageous in contrast to single nanoparticles because of their advanced properties such as high stability, great dispersity and efficient functionality.

Silver-titanium dioxide (Ag-TiO_2) core-shell nanoparticles presented strong antibacterial activity against infectious diseases as a result of releasing silver ions from silver cores through the porous matrix of titanium dioxide shells; one can assume in such a core/shell assembly is the extension of the release time of silver ions which can be beneficial for a persistent antibacterial effect [67].

Gold-copper sulfide (Au-CuS) core-shell nanoparticles demonstrated extreme capability to deactivate *B. anthracis* cells by disordering and damaging its cell membrane; furthermore, antibacterial activity depends on nanoparticle concentration and treatment time [68]. The antimicrobial activity of nanoparticles and microbial cell death can be related to the electrostatic interaction between negatively charged bacterial cells and positively charged nanoparticles which stimulates the loss of membrane integrity [69]. The negatively charged bacterial cell wall composition has a thick layer of peptidoglycan which is linked to teichoic acid. Osmotic imbalance and cytoplasmic content leakage of the damaged membrane probably initiate the cell disintegration.

Alumina-coated iron oxide magnetic nanoparticles (Fe_3O_4-alumina core-shell MNPs) as a photothermal factor under near-infrared (NIR) illumination were used to selectively destroy bacteria. Alumina coating triggers the targeting ability of Fe_3O_4 magnetic nanoparticles in the direction of bacteria. The magnetic behavior of Fe_3O_4/alumina nanoparticles allows them to accumulate in the desired region under a magnetic field and photothermally destroys them by NIR irradiation at the populated region. Remarkably, the cell growth of nosocomial bacteria (Gram positive, Gram negative) and antibiotic resistance can be efficiently avoided in over

95% by applying 10 minutes irradiation via NIR laser beam at the accumulated region of core/shell Fe3O4-alumina MNPs [70].

Core-shell silica-gold nanoparticles were represented loading a significant amount of gentamycin about 87 μg/mg for drug targeting process. Silica core particles were prepared by Stober's method and functionalized with amine groups. Amine group of gentamycin was attached to the gold nano shell surface, and the drug releasing from core-shell nanoparticles was simply prepared by breaking the gold-gentamycin coordinate linkers [71].

Core-shell silica-polyrhodanine nanoparticles were synthesized by chemical oxidation polymerization; they revealed brilliant antimicrobial activity against Gram-positive *Staphylococcus aureus*. In fact, biocidal activity of these nanoparticles was improved by increasing the surface area to volume ratio; core/shell NP size can be experimentally modified by changing the silica core diameter [72].

Novel mesoporous silica nanoparticles were efficiently loaded with chlorhexidine (CHX) which is generally used as antimicrobial agent in dentistry; they were synthesized with an average particle diameter of 140 nm and pore size of around 2.5 nm. Nano-CHX core-shell nanoparticles exhibited promising antimicrobial activity against critical oral pathogens including *S. mutans, S. sobrinus, F. nucleatum, A. actinomycetem comitans* and *E. faecalis* [73].

Hybrid core-shell zinc oxide-silver (ZnO-Ag) nanorods presented remarkable antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Silver nanoparticles with an average size of about 7 nm were designed on heterojunctions at the surface of the ZnO nanorods. The probable mechanism derives from the generation of reactive oxygen species due to electron transfer between zinc oxide nanorods and silver nanoclusters which triggers physical destruction of the bacterial cell wall [74].

5. Conclusion

The normal human body has an intrinsic order which is known as physiology; when a bacterial infection occurs, human cells occasionally need help to defend themselves; therefore, various antibiotics have roles to assist cells, and at the same time, some interactions may take place among antibiotics and human cells then side effects appear. Adverse reactions can be predicted by recognizing the normal situation, background diseases, spectrum of antibiotic effects and mechanism of action. Nowadays, due to extensive use of antibiotics in many fields such as veterinary, agriculture, farming, food industries, and exaggerative prophylaxis, bacteria have a greater chance to resist with mutation, selection and gene transferring; therefore, action against bacterial infection should be with caution, proper drug doses, good background hygiene, adequate therapy, synergism, novelty in treatment and enhanced diagnosis should be considered; one of these innovative treatments is nanoantibacterial therapy. Nanoantibiotics revealed innovative mechanisms against infectious diseases in comparison with conventional drug delivery procedures. Biocompatibility, low toxicity and pronounced purity of antibacterial nanomaterials have prepared them appropriately for therapeutic processes as an

auspicious alternative in medicine to decrease antibiotic resistance and cytotoxicity in a very efficient way.

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Section 2

Virtual Appointments in Oral and Maxillofacial Surgery

Chapter 3

Shared Medical and Virtual Surgical Appointments in Oral Surgery

Alexandra Radu and Michael P. Horan

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/63011

Abstract

Access to care and patient satisfaction are primary objectives in most, if not all, surgical practices. With current healthcare reform and implementation of The Affordable Care Act of 2010, surgeons are more frequently being challenged by their administrative counterparts to improve clinical efficiency and quality of care while maintaining current profit margins. This chapter describes two non-traditional, innovative concepts that can be incorporated into full scope, oral and maxillofacial surgery practices in order to allow more efficient delivery of care while maintaining quality. The two programs outlined herein are shared medical appointments (SMAs) and virtual surgical appointments (VSAs). These programs, when implemented in a busy academic or group private practice, have the potential to allow for efficient delivery of care while simultaneously improving patient satisfaction.

Keywords: shared medical appointments, virtual surgical appointments, telemedicine, third molar surgery, cost-effective medicine

1. Shared medical appointments

1.1. Introduction

An SMA can be defined as a medical appointment where multiple patients with similar medical conditions or needs are seen in a group setting. The appointment is moderated by the physician, surgeon, or medical team. Being in a group setting allows patients to share experiences, voice concerns, and receive feedback from others with similar conditions as well as with their provider. Whereas individual medical appointments are typically 15–20 minutes long, SMA

can last up to 90 minutes. Patients are allotted more time to their provider and medical team, and most often indicate increased satisfaction relative to individual appointments.

The concept of the SMA was first established by Dr. John Scott, a Kaiser Permanente staff internist and geriatrician, in 1991. Dr. Scott's cooperative healthcare clinic model for geriatric patients helped to shape early SMAs. At that time of its inceptions, Dr. Scott's model focused on 15–20 patients with a chronic medical condition. The appointment was staffed by a physician, nurse, and medical assistant [1]. Even though medical SMAs geared toward chronic illnesses have maintained this basic structure over the years, this model is currently being adopted by medical specialists in an attempt to provide knowledge to a larger group of patients in an environment that is more welcoming and nurturing for patients [2]. In addition, several surgical specialties have adopted this model as a pre-operative consultation or informational session, as in the case of breast [3] or dermatological surgery [4]. SMAs are also currently being utilized for post-operative monitoring of patients who have undergone bariatric [5] or cardiac surgery [6].

Participating in SMAs provides patients with the benefit of a longer visit with their physician and other members of the healthcare team, including nurses, physician's assistants, or health educators. Studies by Prescott et al. and Bartley et al. have both demonstrated that SMAs improved patient access to care, enhanced outcomes, and patient understanding by offering the same information at varied levels of literacy, and promoted patient satisfaction, while at the same time providing education for self-management in a more efficient manner for practitioners and patients [7, 8]. Giladi and co-workers showed that patients also benefit from developing a sense of camaraderie, peer support, and group education [3]. In the case of patients with morbid conditions undergoing cardiac surgery, Harris demonstrated that SMAs can reduce depression, anxiety, or the sense of isolation related to the severity of the patients' medical condition and the post-operative course [6].

Utilization of SMAs has not yet taken hold in the field of oral and maxillofacial surgery despite its potential to improve the accessibility and efficiency of care. Although SMAs were initially developed to manage patients with chronic diseases, the format is easily adaptable to meet the needs of patients who require minor oral surgical procedures, such as third molar surgery, or in patients with chronic conditions treated by oral and maxillofacial surgeons (e.g., temporomandibular joint disease, obstructive sleep apnea).

1.2. Economics of SMAs

The cost-effectiveness of SMAs has been shown in several studies since the beginning of the 1990s. Not only is the physician's productivity increased, but SMAs also provide many other economic and patient care benefits, while reducing the costs by leveraging staff [9]. In a case study performed by Caballero at Sutter Medical Foundation in California, the productivity among primary care physicians improved by 200% and specialty clinics by 300% [10]. When this model was introduced in the management of diabetic patients in Australia, it was calculated that the lifetime cost reduction of diabetes was estimated at over $126,000 per person. In addition, by reducing one individual appointment for the diabetic population in

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Australia (~2 million diabetic patients nationwide), the annual cost reduction would be an estimated $100 million, considering one individual appointment to cost $50 per patient [11].

When discussing about SMAs, it is also important to understand the billing aspect of the process. In general, medical insurance companies do not reimburse for group visits. However, an SMA is not a class or seminar but an actual office visit. Because the same documentation for individual appointments is required for SMA (e.g., history, physical examination, vital signs, laboratory testing, plan), it is possible to bill each patient according to the current procedural terminology (CPT) code based on the level of care provided. It is not advisable, however, to bill according to the time spent with patients [7].

1.3. Measuring patient satisfaction

Since the model of SMA is fairly new and not commonly used, there is a perceived skepticism on the patients' side that the medical team should consider and address at the time the appointment is made. In a controlled study done for patients undergoing post-operative bariatric surgery, 47 patients were asked to complete the same 13-question survey before and after the SMA. The patient's opinion of the SMA improved from baseline levels after taking part in one, and patients were generally happy with the level of confidentiality relative to individual appointments [5].

Figure 1. Structure and flow of the SMA.

We have implemented the concept of shared medical appointments over the past year in our Oral and Maxillofacial Surgery clinic for patients who needed third molar surgery. The patients are briefly explained the SMA model at the time that the appointments are made. **Figure 1** shows the flow of events and the approximate time allotted for each step in our SMA model.

Eighteen surveys were collected from the patients who participated in such appointments throughout this period. The surveys asked 7 questions that were graded by the participants on a scale of 1 to 5 (1-Strongly Disagree, 2-Disagree, 3-Neutral, 4-Agree, 5-Strongly Agree). Additionally, there were two questions asking the patient to provide qualitative short answers (questions 8 and 9). The questions in the survey are shown below:

1. Scheduling my shared medical appointment was easy

2. I gained valuable information from responses to other patient's questions

3. There was adequate time for my questions

4. I gained a sense of group support

5. I would participate in a shared medical appointment again

6. I would recommend shared medical appointments to other patients

7. I feel my medical information is secure in the group setting

8. How would you compare an SMA to a one-on-one appointment?

9. Do you have any further comments about the SMA?

After data collection was finalized, the survey results were analyzed by calculating averages, standard deviations, and standard errors for the first seven questions (**Table 1**).

Question	Average	Standard deviation	Standard error
1	4.33	1.08	0.25
2	4.11	0.83	0.19
3	4.50	0.98	0.23
4	3.94	1.05	0.24
5	4.55	0.75	0.17
6	4.44	0.51	0.12
7	4.61	0.50	0.11

1—Strongly disagree, 2—Disagree, 3—Neutral, 4—Agree, 5—Strongly agree.

Table 1. Summary of the data collected for the seven questions that had numerical quantification.

For Questions 8 and 9, there were no numerical data to analyze. The answers were generally favorable, with six neutral (i.e., the SMA was the same as a typical one-on-one appointment) and two negative responses (i.e., the one-on-one appointment was a better fit). One positive

recurrent answer found in the surveys was that SMAs benefited the patients in learning about the condition and treatment while benefiting from questions and concerns raised by others.

The data presented in **Table 1** indicate that SMAs were predominantly received well by patients, with respondents strongly agreeing that they would participate in a shared medical appointment again. With the exception of Question 4, all other question ranked in the 4–5 range. One of the main goals of SMAs in oral and maxillofacial surgery is to increase accessibility, and based on the answers received for Question 1, the patients had scheduled their appointments with ease in a timely manner.

2. Virtual surgical appointments

Telemedicine is the use of telecommunication technology to provide clinical care at a remote location. Telemedicine was first adopted in the 1990s. With the low cost and wide availability of mobile devices, the field continues to grow. Virtual appointments can aid practitioners by fostering the patient–doctor relationship and improve practice efficiency. Virtual appointments have the potential to reduce the wait times by offering more online services, such as virtual consultation (VCA) and post-operative appointments (VPAs). Telemedicine has been successfully employed in various medical and surgical fields, including primary care, psychiatry, dermatology, oncology, otolaryngology, and orthopedics, resulting in increased patient satisfaction while providing high-quality care [12]. Virtual patient–doctor relationships have been used for several purposes, such as scheduling of appointments, referrals to other doctors, the writing of prescriptions, discussion of test results, and certificates of health [13].

VSA can be effectively incorporated into oral and maxillofacial surgery practices in the form of VCAs and VPAs. VCAs allow surgeons to meet and screen potential surgical candidates whom otherwise may need to travel nationally or internationally, to be evaluated. The patient's medical history can be reviewed and bidirectional communication can be established to determine the patient's chief complaint and history of present illness. With the use of image exchange servers, previous clinical photographs, radiographs, and virtual surgical plans can be reviewed. A determination can then be made as to whether or not this patient would be an appropriate candidate for treatment in the surgeons practice. The use of virtual appointments for post-operative monitoring has not been greatly explored, most likely due to the potential oversight of surgical complications and the perceived importance of performing a "hands on" physical examination. However, VPAs are ideal for monitoring outcomes of minor surgical procedures performed on an outpatient basis (e.g., dentoalveolar surgery, third molar surgery, implant surgery, minor bone grafting procedures) that have a low risk for post-operative complications.

As defined by the American Dental Association (ADA), teledentistry is the electronic exchange of dental patient information from one geographic location to another for interpretation and/or consultation among authorized healthcare professionals [14]. Teledentistry employs both information and communication technologies to accomplish the electronic exchange of diagnostic image files, such as radiographs, photographs, video, or optical impressions. The

ADA released a policy on teledentistry in 2012. However, the policy was resolved in November 2015, explaining the scope of teledentistry and encouraging dentists to consider conformance with the Digital Imaging and Communications in Medicine (DICOM) standards when selecting and using imaging systems [14]. The 2015 resolution included more detailed guidelines addressing licensure of practitioners providing teledentistry, patient privacy, and billing issues. More specifically, the resolution states that dental benefit plans, and other paying public and private programs, should cover services provided through teledentistry at the same level as if the services were delivered in a traditional in-person encounter [15]. The ADA has encouraged both practitioners and patients alike to take advantage of teledentistry, as it greatly improves efficiency and access to care, respectively.

Teledentistry is a growing field that is currently utilized to virtually supervise the oral health care of patients in skilled nursing facilities, residents in rural areas, or others who do not have immediate access to a dentist [15]. According to the 2015 resolution, teledentistry can take multiple forms namely:

- Live video, which is a two-way interaction between patients and dental providers using audiovisual technology, such as smart phones, tablets, and computers equipped with webcams. This could include VPAs.
- Store and forward, which takes advantage of recorded health information that is transmitted through a secure electronic communications system to a practitioner at a distant site. The practitioner can then use the information to evaluate the patient's condition and render a consulting service outside of a real-time or live interaction. The health information communicated through this method includes radiographs, photographs, video, digital impressions, or photomicrographs.
- Remote patient monitoring is a method that could be used in the setting of a nursing home facility. It is the collection of personal health and medical information from an individual in one location and electronic transmission to another provider in a different location. This procedure differs from "store and forwards" in that it implies long-term monitoring.
- Mobile health, which involves the use of mobile communication devices to perform education projects in public health. This could include apps that monitor patient brushing (**Figure 2**).

In the field of oral and maxillofacial surgery, VPAs can be used to effectively and efficiently follow up patients who have undergone minor surgical procedures. These procedures include third molar surgical extraction, dental implant placement, allogenic bone grafting for ridge augmentation, adjunct implant procedures, and biopsies, and minimally invasive temporomandibular joint (TMJ) surgical procedures (e.g., arthroscopy, arthrocentesis, and intra-articular injections). Using a camera-equipped mobile device (e.g., cell phone, tablet, laptop, etc.) or desktop computer, patients can participate with their clinician in video conferences that are compliant with the Health Insurance Portability and Accountability Act (HIPAA). The clinician is able to do everything that would normally be done during a traditional post-operative appointment, except for a "hands-on" clinical examination. If the clinician has any concern about the patient's recovery, an in-office visit can be scheduled.

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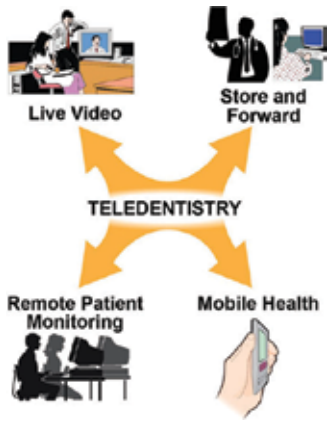

Figure 2. Four major practices employed through teledentistry [15].

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Section 3

Nerve Surgery and Repair of Trigeminal Nerve Injuries

Chapter 4

Cranial Nerves and Nerve Surgery in the Oral and Maxillofacial Region

Shahram Nazerani and Tina Nazerani

Additional information is available at the end of the chapter

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Abstract

The head and neck surgeon is confronted with cranial nerves in the course of operations and he or she must know the anatomy and the ways to treat complications should they happen. In this chapter we focus on the subject of cranial nerves and begin with the history and anatomy and then to individual nerves and maladies of these nerves and complications of surgical procedures involving these nerves.

Keywords: cranial nerves, cranial nerve disorders, cranial nerve surgery, nerve repair, nerve transfer

1. Introduction

Ancient Egyptian mummification artisans had no consideration for the brain; the internal organs such as the liver, intestines, lung, and heart were preserved in separate jars; they broke the skull bone through the nose with a tool like a hook and a tool to blend lift the brain and then allowed it to drain out the nose or flushed it out with water. The Egyptians thought the heart was the site of bravery and gave no importance to the brain for afterlife preservation (**Figure 1**).

The history regarding exploration of the cranial nerves and their anatomy is ancient. Galen's classification of the cranial nerves, excluding the olfactory nerve, was composed of seven pairs; the sixth pair included the glossopharyngeal, vagus, and accessory nerves all traveling through the jugular foramen [1].

The cranial nerves were essentially identified and numbered based on the opening through which they exited the skull base. Our knowledge of the cranial nerves grew more clearly by

medieval Middle Eastern and European scholars such as Rhazes, Avicenna, Jorjani, Mundinus, Benedetti, Achillini, Massa, and Berengario deCarpi [2].

Figure 1. Mummification process with internal organs set aside in jars.

Italian anatomists in the fourteenth and fifteenth centuries identified the olfactory nerve as a cranial nerve. The work of these anatomists laid the foundation for the doctoral thesis of the German anatomist Samuel Sömmerring (1755–1830 AD), who in 1778 classified the 12 cranial nerves as we recognize them today [3, 4]. In his thesis, Sömmerring made no meaningful anatomical discoveries, and his classification is essentially no less different from previous anatomists. Nonetheless, the Sömmerring system was rapidly adopted across continental Europe, although it was only slowly accepted in England [5].

2. Anatomy and naming of the cranial nerves

The cranial nerve nomenclature is an ordinal system introduced presumably by Galen, by which the nerves are named by their location on the undersurface of the brain, this system has stood the test of time and has not been changed during the ages, although the olfactory nerve has been mentioned even before Galen's ordinal classification. Modern anatomists argue that the olfactory and optic nerves are tracts and not true cranial nerves and should be removed from the "twelve-nerve" classification system [5]. To memorize these nerves, several mnemonics have been devised (**Figure 2**).

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Figure 2. A mnemonic of the cranial nerves.

Galen's classification of cranial nerves is depicted below; he identified seven pairs but he assigned no names to them. The modern classification is shown below, Galen identified seven pairs of nerves, and the interesting point is that the old scholars saw the brain as a whole and not two hemispheres of an organ.

Modern classification:

I. Olfactory nerve

II. Optic nerve

III. Oculomotor nerve

IV. Trochlear nerve

V. Trigeminal nerve

VI. Abducens nerve

VII. Facial nerve

VIII. Vestibulocochlear nerve

IX. Glossopharyngeal nerve

X. Vagus nerve

XI. Accessory nerve

XII. Hypoglossal nerve

3. Surgical importance of cranial nerves

There are 12 cranial nerves, but only some of the nerve problems were identified and reported in the early ages. Of the 12 cranial nerves, the trigeminal and facial nerves have been under more scrutiny: the trigeminal due to its excruciating pain and the facial nerve due to its characteristic facial disfigurement in nerve palsy (**Figure 3**).

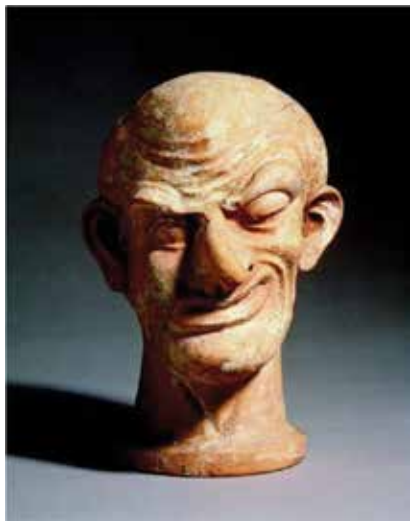

Figure 3. A sculpture of facial palsy.

Other cranial nerves are usually noticed when traumatized, involved in tumoral conditions or injured during an operation.

Multiple cranial nerves are usually involved in procedures such as carotid endarterectomy, anesthesia, and cancer surgery. In a review article, Thiruvenkatarajan et al. investigated cranial nerve injury (CNI) during anesthesia and they found that cranial nerve injuries are unusual complications of supraglottic airway use. Branches of the trigeminal (V), glossopharyngeal (IX), vagus (X), and hypoglossal (XII) nerves may be injured. Lingual nerve (LN) injury was the most commonly reported, followed by recurrent laryngeal, hypoglossal, glossopharyngeal, inferior alveolar, and infraorbital. The culprit is usually poor technique and inappropriate pressure on the nerves due to wrong size or misplacement or overinflation of the cuff. Injury to the recurrent laryngeal nerve (RLN) is usually more long lasting than other nerves involved [6]. In a multicenter prospective study, Fokkema et al. investigated the prevalence of CNI in carotid endarterectomy; 6878 patients were included for analyses. CNI rate at discharge was 5.6%. Sixty patients (0.7%) had more than one nerve affected. The hypoglossal nerve was most frequently involved (2.7%), followed by the facial (1.9%), the vagus (0.7%), and the glossopharyngeal (0.5%) nerve. The vast majority of these CNIs were transient; only 47 patients (0.7%) had a persistent CNI at their follow-up visit [7]. Isolated cranial nerve injuries are herein with special attention to the nerves more prone to injury during maxillofacial surgery.

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3.1. The olfactory nerve

The first cranial nerve is composed of receptor neurons which connect the nasal cavity to the brain (**Figure 4**). The nerve dendrites reside in the nasal cavity on the apical side and the axons pass through the cribriform plate of the skull into the olfactory area of the brain [8].

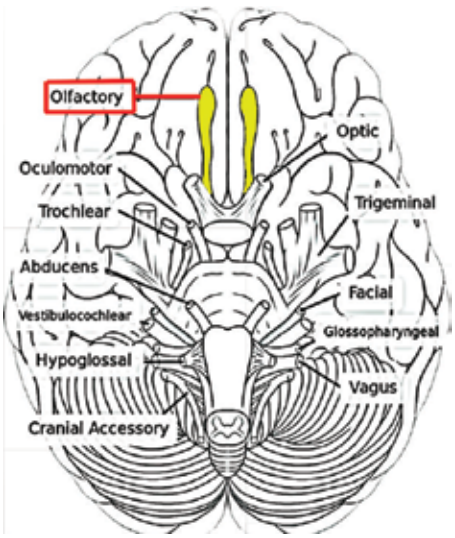

Figure 4. Skull base schematic diagram and the olfactory nerve marked in yellow.

Esthesioneuroblastoma (ENB) is a rare malignant neoplasm arising from the olfactory neuroepithelium. ENB constitutes only 3% of all malignant intranasal neoplasms. Because of the rarity, the number of patients of ENB treated in individual departments is small. Most of these patients present in locally advanced stages and require multimodality surgery, chemotherapy, and radiotherapy [9]. Impairment of smell may occur following injury to any portion of the olfactory tract, from the nasal cavity to brain. A thorough understanding of the anatomy and pathophysiology combined with comprehensively obtained history, physical exam, olfactory testing, and neuroimaging may help to identify the mechanism of dysfunction and suggest possible treatments. Although most olfactory deficits are neuronal mediated and therefore currently unable to be corrected, promising technology may provide novel treatment options for those most affected. Until that day, patient counseling with compensatory strategies and reassurance is essential in this unique and challenging patient population [10].

3.2. Optic nerve

Optic nerve injury may have several etiologies such as tumor, trauma, and inflammation, but in the context of maxillofacial surgery, trauma to the optic nerve is the most important (**Figure 5**); two types of trauma to the optic nerve are seen, primary and secondary; injury to the nerve fibers and/or vascular supply can be due to direct injury at the time of trauma or secondary as the result of compromised blood supply to the nerve.

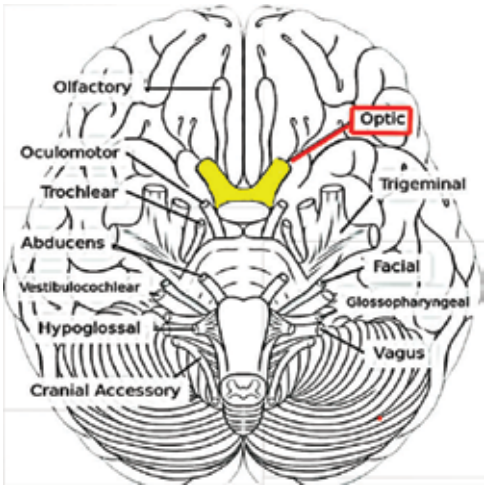

Figure 5. Optic nerve marked in yellow.

3.3. Oculomotor nerve

Injuries to the oculomotor nerve present with nerve palsy manifestations (**Figure 6**); the etiologies can be sellar chordoma, odontogenic abscess, non-aneurysmal subarachnoid hemorrhage, polycythemia, sphenoiditis, brucellosis, interpeduncular fossa lipoma, metastatic cancer, and blood and lymph cancers. Surgical options are correction of nerve palsy, i.e., strabismus surgery. New globe fixation procedures may include fixation to the medial orbital wall, apically based orbital bone periosteal flap fixation, and the suture/T-plate anchoring platform technique [11].

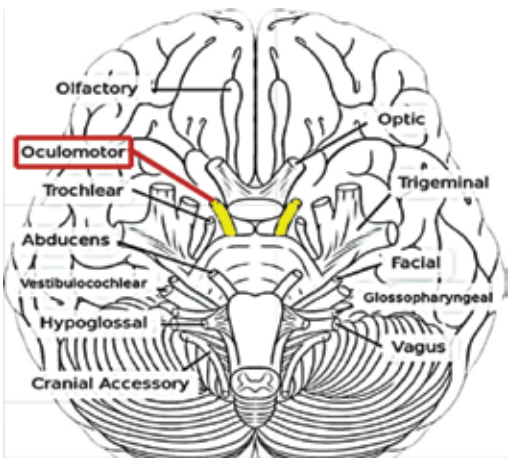

Figure 6. The third cranial nerve marked in yellow.

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3.4. Trochlear nerve

The trochlear nerve originates from the trochlear nuclei in the caudal midbrain (**Figure 7**) and carries primarily motor fibers destined for the superior oblique muscle; the nerve may be encountered in many areas such as the supracerebellar, middle cranial fossa, parasellar, and orbital regions. This nerve was the last cranial nerve found, due its small size and lack of fixation techniques in the earlier periods of anatomical studies. Trauma, tumors, viral infection, and surgery can all injure this nerve with impaired eyeball movement.

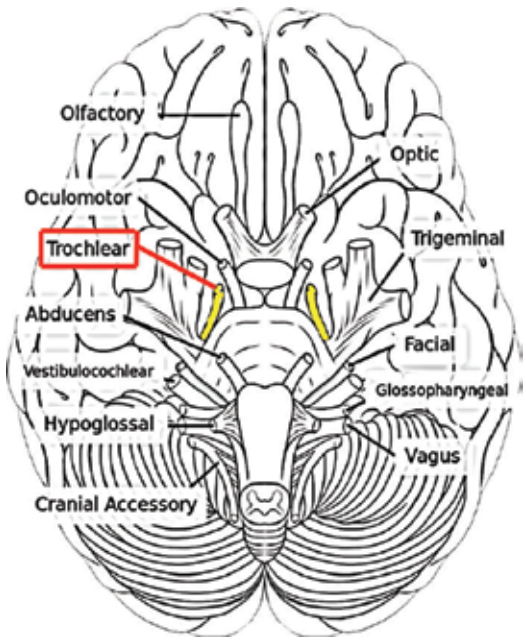

Figure 7. The fourth cranial nerve seen from undersurface of the brain.

3.5. Trigeminal nerve

The trigeminal nerve is the largest and most complex of the 12 cranial nerves (**Figure 8**). The three branches of the trigeminal nerve (the ophthalmic, maxillary, and mandibular branches exit the skull through three separate foramina, namely, the superior orbital fissure, the foramen rotundum, and the foramen ovale, respectively). The mandibular branch had mixed sensory and motor neurons and of all the branches lingual and inferior alveolar are more prone to injury during maxillofacial operations. Injury to the LN and/or inferior alveolar nerve (IAN) is a known complication associated with several oral and maxillofacial surgical procedures. Bagheri et al. in a retrospective study have shown that microsurgical repair of LN and IAN injury has the best chance of successful restoration of acceptable neurosensory function if done within 9 months of the injury. As in all other nerves, the likelihood of recovery decreases progressively when the repair is done more than 9 months after injury [12].

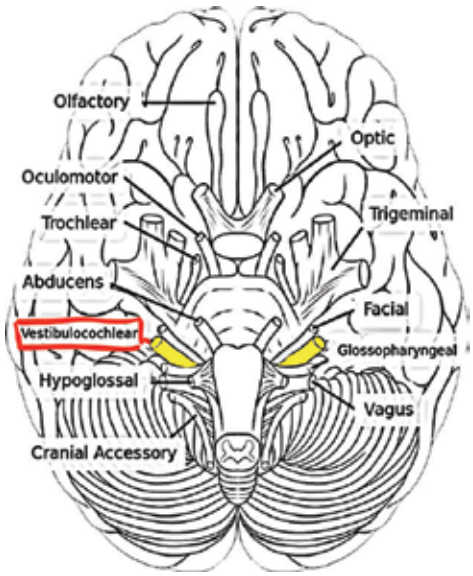

Figure 8. The fifth cranial nerve, the largest cranial nerve.

3.6. Abducens nerve

The sixth cranial nerve is a motor nerve with diplopia as its presenting symptom when injured (**Figure 9**). Binocular diplopia occurs from misalignment of the eyes. The fixation object is imaged onto the fovea of one eye and a non-foveal region of the misaligned eye, creating diplopia. The nerve can be injured in head trauma, autoimmune diseases, and several other conditions. Treatment options include ocular occlusion, mono-vision optical correction, prism glasses, strabismus surgery, and chemo-denervation.

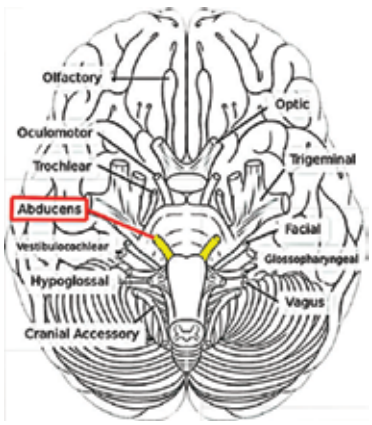

Figure 9. The sixth cranial nerve.

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3.7. Facial nerve

Facial nerve paralysis involves orifice control for the eye, nose, and mouth, as well as facial expression (**Figure 10**). The lack of orifice control for the eye can lead to corneal exposure, keratopathy, and potential visual loss. The orifice control relating to the nose can cause difficulties in breathing with lack of normal opening of the involved nostril.

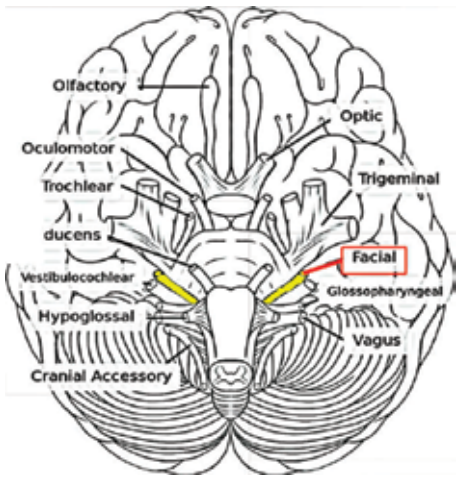

Figure 10. The seventh cranial nerve.

The lack of orifice control for the mouth can affect the symmetry of the face with drooping of the involved side, as well as problems related to speech, chewing, and oral competence leading to drooling. In some cases, the lack of dental protection can lead to dental decay. Some partial facial palsies are seen as attractive (**Figure 11**).

Figure 11. Sylvester Stallone with his "trademark smile."

The mimetic function, however, of the facial nerve is critical for social interactions. Nonverbal communication is conveyed by facial expression and is essential for normal interpersonal interactions. A smile invokes a smile in others and conveys feelings that cannot be transmitted in any other way. Consequently, a spontaneous dynamic smile is critical for personal interactions. Treatment modalities in facial paralysis and associated movement disorders are numerous and vary based on individual needs and preferences.

3.7.1. Congenital facial paralysis

The anatomical presentation of developmental facial paralysis can be summarized into four categories:

1. Aplasia or hypoplasia of cranial nerve nuclei
2. Nuclear agenesis
3. Peripheral nerve abnormalities
4. Primary myopathy [13]

3.7.2. Acquired facial paralysis

Three stages of facial nerve paralysis are acute, intermediate, and chronic; the treatment modalities are discussed below.

3.7.3. Acute facial paralysis

Identifiable causes of acute paralysis are treated with appropriate medical therapy, following proper identification of the cause. In rare instances, surgical intervention may be necessary to control infection and/or swelling around the facial nerve. In trauma or resection of cancer invading the facial nerve, several reconstructive options are available. These minimize the sequelae of paralysis, optimize immediate patient recovery, and promote the return of facial nerve function.

3.7.4. Intermediate facial paralysis

During this stage (3 weeks to 2 years), facial nerve recovery is monitored with serial electrophysiological studies, which provide useful prognostic data. In a setting of poorly recovering facial nerve, several procedures can be considered to restore facial appearance and rehabilitate function around the eye and mouth. In the early stages gold weight placement to aid upper eyelid closure (lagophthalmos) and static sling suspension of the midface and lip can be performed with minimal associated downtime. Lagophthalmus (**Figures 12** and **13**) can be treated by a range of techniques, including tarsorrhaphy, facial slings, and canthopexies. Gold plates provide a solution for temporary or permanent lagophthalmos resulting from facial paralysis. Amer et al. studied the use of gold plates in two different positions in the upper lids.

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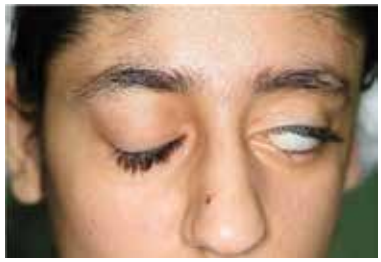

Figure 12. Bell's palsy and lagophthalmos.

Figure 13. Gold plate inserted, but is not esthetically appealing.

They concluded that gold plate insertion at a higher than usual place of insertion can reduce the drawbacks of lower placement such as "plate show," thinning of the skin over the plate [14].

These procedures do not interfere with the recovering facial nerve. In the later stages, if the facial nerve continues to display poor recovery on EMG, consideration is given to nerve transfer procedures designed to maintain neurological input of facial muscles. A graft from a nearby nerve, most commonly the hypoglossal, can provide such input. Terzis and Karypidis show that cross-facial nerve grafting and concomitant mini-hypoglossal transfer are the procedures that yield higher improvement in blink scores and ratios compared with the rest of the dynamic procedures. Direct orbicularis oculi muscle neurotization achieves a fair blink improvement [15].

3.7.5. Chronic facial paralysis

3.7.5.1. Paralysis

Management of chronic facial paralysis, more than two years, depends on numerous factors, including patient preferences, age, and desires. Medical considerations may also limit the available procedures. Reconstructive options range from static suspensions to reanimate via muscle transfer to the paralyzed side.

Static slings such as native fascia (5) or permanent sutures (6) are the easiest methods in facial reanimation. These slings hold the paralyzed side in midline and help hold the lips and prevent

drooling to a degree. Static slings relax and descend over time, thus potentially requiring additional tightening [16, 17] (**Figures 14–18**).

Figure 14. Chronic Bell's palsy, first-stage sural nerve transfer already done.

Figure 15. Gracilis muscle bisected and ready for insertion.

Figure 16. Two months after the operation and the static splint for maintaining the muscle suture.

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Figure 17. Four months after operation, minimal muscle function has returned; lagophthalmos will be addressed later.

Figure 18. Tendon transfer for the eye with the face contour nearly normal.

One- or two-stage free vascularized muscle transfers are the best options for facial reanimation but they are lengthy operations and more sophisticated than the static slings. Interest in the temporalis muscle transfer has been renewed but the results are inferior to the muscle transfers [18] (**Figures 19** and **20**).

Figure 19. Facial palsy in a patient after reconstruction of the mandible due to childhood radiation-induced lower face atrophy.

Figure 20. Temporalis transfer for right facial palsy.

The procedure of choice to regain involuntary smile is a two-stage transfer of the gracilis muscle. There are several candidate muscles in the literature, such as the pectoralis minor and latissimus dorsi (LD) as a one-stage muscle transfer (**Figure 21**).

Figure 21. The one-stage LD muscle transfer, which can be done in one stage due to its long nerve.

At the first operation, a branch of the facial nerve on the healthy side is grafted and carried across by a sural nerve graft to the paralyzed side. The recommended route for nerve graft is across the face, through the upper lip and actually lying in the midface area, where at the second stage, a skin elevation is needed to insert the flap. Due to hazardous route of the cable graft, we think that a submental or frontal route is better suited for this operation because the nerve graft is safe when elevating the flaps at the second stage and also in future revision surgeries (**Figure 22**).

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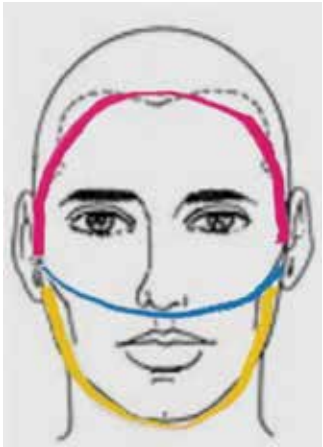

Figure 22. Blue is the recommended route; yellow and red routes are our preferred ways to transfer the nerve graft from one side of the face to the other side.

Six to nine months later, a segment of the gracilis muscle is transferred to the face and connected to the grafted nerve. The muscle becomes functional, providing movement on the paralyzed side. The gracilis transfer affords a better precision to the smile angle and greater movement of the commissure, when compared to temporalis transfer.

Terzis and Anesti used platysma muscle transfer to augment the function of or regulate the overactive previously transferred free vascularized muscle for oral sphincter control [19].

3.7.5.2. Synkinesis

Synkinesis is abnormal involuntary facial muscle movement during the voluntary movement of different muscle groups. For example, eye closure can result in simultaneous contraction of orbicularis oris or platysma contraction during smile. Other cranial nerves such as ocular and abducens have also synkinesis problems.

The problem seems to be the random growth or "miswiring" of facial nerve.

Management is a multimodality protocol which includes multiple session chemo-denervation with botulinium toxin and biofeedback facial muscle retraining and also surgical procedures such as small nerve graft or repair [20].

Choi et al. in a study of botulinum toxin injection in facial paralysis showed significant suppression of synkinesis and improvement of facial symmetry with resulting elevated quality of life, social interaction, personal appearance, and food intake [21].

Radiofrequency ablations are theoretically capable of reducing the injection sessions but are still in investigative stages. At present the best method of treatment for synkinesis is chemo-denervation with physical therapy [22–24].

3.8. Vestibulocochlear nerve

The vestibulocochlear nerve (eighth cranial nerve) is a pure sensory intracranial nerve (**Figure 23**). This nerve has two functions and hence two nerves: sound transmission and balance. The nerves originate from sensory receptors of internal ear to the brain stem and thence to the post-central gyrus and auditory cortex. The two most frequent etiologies of eighth nerve pathology are skull base trauma and vestibular schwannomas with the latter being the most common lesion.

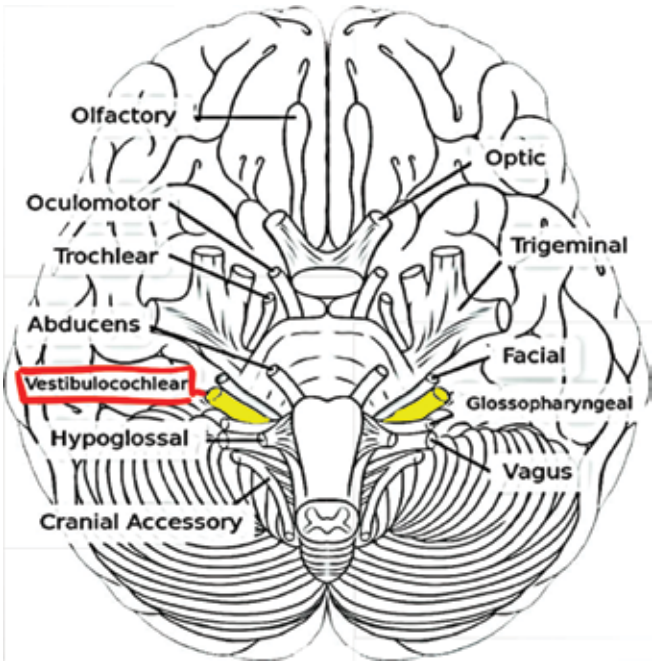

Figure 23. The eighth cranial nerve.

3.9. Glossopharyngeal

The ninth cranial nerve or glossopharyngeal nerve is a mixed nerve consisting of both sensory and motor nerve fibers (**Figure 24**). The origins of sensory fibers are pharynx, middle ear, posterior one-third of the tongue (including taste buds), and the carotid body and sinus. The motor fibers terminate at the parotid gland, the glands of the posterior tongue, and the stylopharyngeus muscle. Hwang et al. in a review article found that frequency of communication between the facial nerve and the vestibulocochlear nerve was the highest (82.3%) and the frequency of communication between the facial nerve and the glossopharyngeal nerve was the lowest (20%). Surgeons should be aware of the nerve communications, which are important during clinical examinations and surgical procedures of the facial nerves such as those communications involved in facial reconstructive surgery, neck dissection, and various nerve transfer procedures [25].

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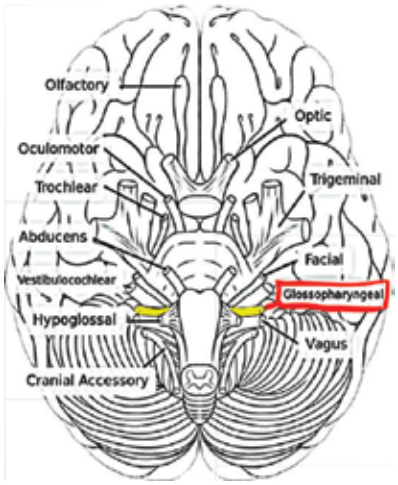

Figure 24. Ninth cranial nerve location at the undersurface of the brain.

The glossopharyngeal nerve is in danger of iatrogenic injury during tonsillectomy and the bilateral injury can be devastating [26].

3.10. Vagus nerve

The vagus nerve (**Figure 25**), from the Latin root meaning "wanderer," is the longest cranial nerve with far reaching functions, from vocal cords to the heart and finally the stomach and gallbladder. This nerve is at greatest risk in head and neck re-exploration.

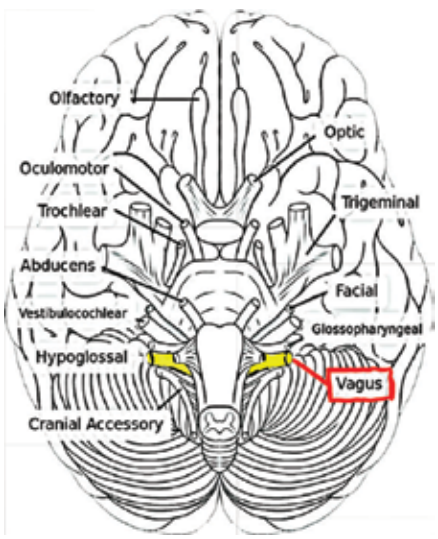

Figure 25. The 10th and the longest cranial nerve.

One of the important branches of the vagus nerve is RLN, the nightmare of head and neck surgery and especially thyroid surgery. Unrecognized RLN injury entails delayed phono-surgical intervention and laryngeal reinnervation.

Unilateral RLN damage is usually the complication of thyroid cancer surgery; in these instances when the nerve is involved in cancer, unilateral nerve resection or resection and nerve graft have been proposed [27].

Hong et al. [28] performed immediate direct anastomosis of RLNs injured during surgery for thyroid cancer; they found that patients undergoing immediate direct RLN anastomosis demonstrated better phonation and perceptually rated voice quality than those who did not undergo repair.

3.11. Spinal accessory nerve (SAN)

The accessory nerve is unique in that its name is based on a historical misunderstanding regarding its origin although it retains its original cranial nerve terminology; but contemporary nomenclature is more inclined toward spinal origin of this nerve, since the cranial part immediately joins the vagus nerve and the spinal part is considered the only and main part of the eleventh nerve [29] (**Figure 26**).

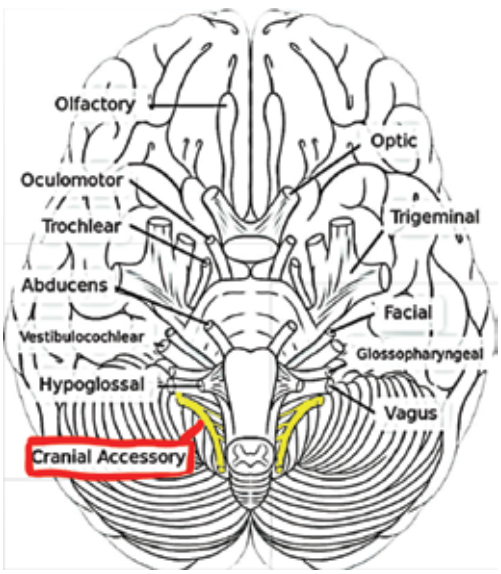

Figure 26. The 11th nerve; as the name implies, some authors think of this nerve as a spinal nerve.

During the past century, the anatomy and blood supply of SAN have been better understood (**Figure 27**). The importance of almost all of the SAN plexus to head, neck, and upper extremity motor and sensory functions has come to be realized. Because of this understanding, surgical neck dissection has become progressively more conservative toward preserving this nerve as much as possible.

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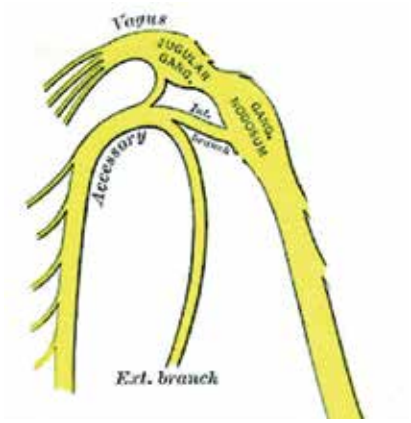

Figure 27. The relations of the SAN to vagus nerve (Gray's anatomy).

Iatrogenic injuries to the spinal accessory are not uncommon during lymph node biopsy of the posterior cervical triangle.

Park et al. review the operative techniques and surgical outcomes of 156 surgical repairs of the SAN following iatrogenic injury during lymph node biopsy procedures. SAN injuries present challenges for surgical exploration and repair because of the nerve's size and location in the Posterior cervical triangle. They concluded that patients with diminished or absent function achieved favorable functional outcomes by corrective surgery. Surgeons performing lymph node biopsy procedures in Zone I of posterior cervical triangle should be aware of the potential risk of injury to the SAN [30].

Nerve transfer between the SAN and the suprascapular nerve is a standard technique in brachial plexus surgery for shoulder reanimation. In cases of global brachial plexus injury, donor nerves are few and at times severely traumatized owing to extensive traction forces. Bhandari and Deb [31] offer the use of the contralateral SAN as an additional option in the reinnervation of an injured Suprascapular nerve in such circumstances.

3.12. Hypoglossal nerve

Use of the entire hypoglossal nerve for nerve transfer in obstetric palsy is not recommended because of major donor nerve morbidity in terms of feeding and speech problems (**Figure 28**).

The hypoglossal nerve to facial nerve transfer is one of the facial reanimation procedures, care must be taken to preserve the hypoglossal nerve for its primary function, and end-to-side nerve transfer is also mentioned in the literature. Beutner et al. have described the modified technique of the hypoglossal-facial-jump anastomosis without an interposition graft [32].

Al-thunyan et al. used a hemi-hypoglossal nerve transfer for biceps reinnervation in obstetric palsy in three infants with multiple root avulsions.

Elbow flexion was seen in two of the three operated patients with no reported feeding problem. Speech assessment was done at the 20–27 months of age and early speech development was unaffected [33].

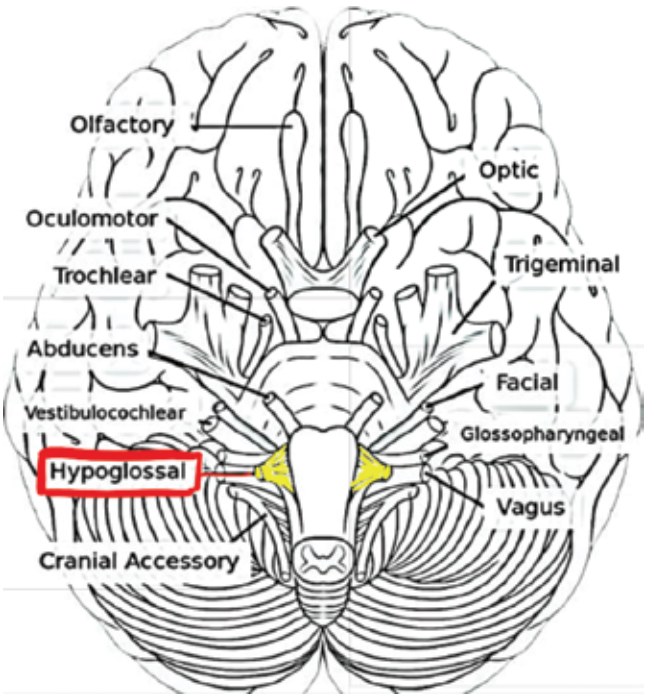

Figure 28. The 12th cranial nerve.

4. Summary

The knowledge of cranial nerves' anatomy is an important and integral part of head and neck surgery; we have discussed the cranial nerve anatomy and surgery, ablations, and reconstructions and several personal cranial nerve surgeries have been included in this chapter. The results indicate that patients are at greatest danger of cranial nerve damage during times of *stress* and that surgeons should take particular care to protect specific nerves in tough conditions.

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Chapter 5

Surgical Repair of Trigeminal Nerve Injuries

Ahmad Alshadwi and Mohammed Nadershah

Additional information is available at the end of the chapter

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Abstract

This chapter reviews the relevant surgical anatomy, clinical indications, and timing for surgical repair of the inferior alveolar and lingual nerve injuries. It will also present state-of- the-art reconstructive surgery and examine the factors influencing success as well as the scientific literature for outcome studies after surgical repair.

Keywords: trigeminal nerve, injury, surgical repair, microneurosurgery, nerve graft

1. Introduction

The trigeminal nerve and its peripheral branches are susceptible to injury from a wide variety of surgical procedures, trauma, and iatrogenic causes in the practice of dentistry and medicine. These types of injuries may result in significant morbidity due to their impact on speech, mastication, and social interactions. Although these sensory disturbances often recover spontaneously, some may be permanent with varying outcomes ranging from mild hypoesthesia to complete anesthesia. Some patients can also develop troublesome outcomes such as neuropathic responses, leading to chronic pain syndromes that may become quite debilitating.

The face and perioral region have one of the highest densities of peripheral nerve innervation in the body, which is why it is challenging for patients to tolerate neurologic disturbances in this region compared to other areas of the body. Pain, temperature, and proprioception are transmitted centrally through the lingual, mental, inferior alveolar, infraorbital, and supraorbital nerves. Different types of sensory nerve fibers transmit each sensation with different susceptibilities to injury and recovery. The goal of trigeminal nerve microsurgery is to create an environment in which these nerves that do not demonstrate spontaneous recovery are given the opportunity for regeneration to prevent the development of neuropathies.

1.1. Relevant surgical anatomy

The third division (mandibular branch) of the trigeminal nerve travels through the foramen ovale into the infratemporal fossa (**Figure 1**). The lingual nerve shortly branches off close to the skull base.

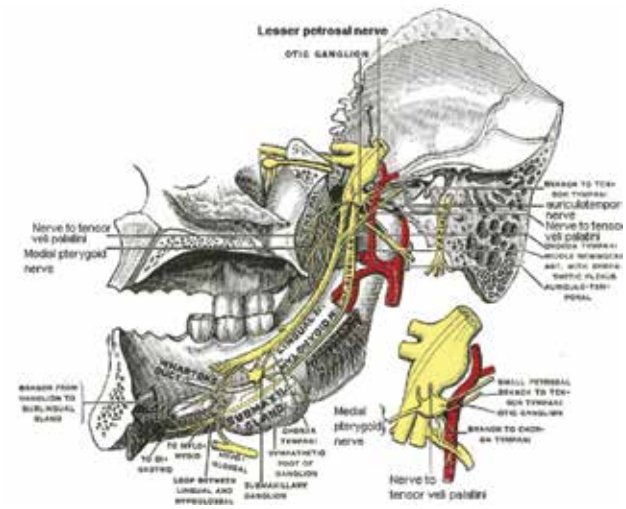

Figure 1. Anatomy of the mandibular division of the trigeminal nerve.

The lingual nerve lies anterior and medial to the inferior alveolar nerve and descends between the lateral and medial pterygoid muscles. At the lower end of the lateral pterygoid muscle, it receives fibers from the chorda tympani which carries special sensory fibers providing taste sensation (from the anterior two thirds of the tongue) and the presynaptic parasympathetic fibers to the submandibular ganglion, providing secretomotor innervation (to the sublingual and submandibular salivary glands). The nerve then follows the lateral surface of the medial pterygoid muscle and travels medial to the mandibular ramus for about 3 cm. In the third molar region, the lingual nerve may be intimately associated with the third molar and/or the alveolar bone, protected by periosteum or within the soft tissues of the retromolar region. While traversing the retromandibular region, the lingual nerve can potentially cross the internal oblique ridge with only a layer of oral mucosa covering and protecting the nerve. This is where the lingual nerve is most vulnerable to injury during removal of the third molar teeth.

The inferior alveolar nerve (IAN) winds around the lower border of the lateral pterygoid muscle and then turns sharply lateral to reach the inner aspect of the mandible and into the body of the mandible through the mandibular foramen; the foramen is identified by a bony elevation called the lingula on the medial aspect of the ramus. The IAN passes laterally within the mandibular canal and exits via the mental foramen. In the sagittal plane, the IAN begins approximately 10 mm below the sigmoid notch and reaches its lowest point at the second premolar/molar region. Just before existing the mental foramen, the nerve loops anteriorly and then superior and posteriorly in the premolar area. The IAN is most susceptible to iatrogenic

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injury at the third molar site and in the premolar area, given the nerve course in the mandibular canal.

Histologically, trigeminal nerve cell bodies are located within the trigeminal ganglion; trigeminal nerve ends synapse with sensory receptors in the anatomical area supplied by the trigeminal nerve to convey stimulation and pass it through the nucleus caudalis, medulla, and pons onto the cortex.

Generally, nerves are wrapped in a number of fascial structures beginning with the mesoneurium layer, which surrounds the whole nerve and contains blood vessels called vasa nervorum that provides the nutritional framework. Deeper than that is the epineurium that provides coverage for the perineurium layer, which separates fascicles into functional units; each fascicle is made up of joining axons and Schwann cells that are covered by endoneurium (**Figure 2**).

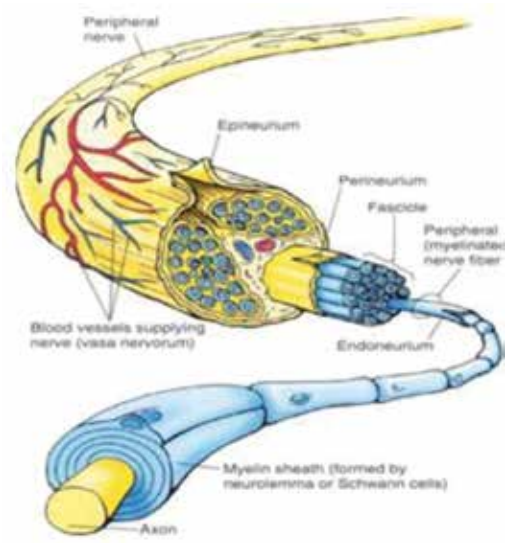

Figure 2. Microanatomy of a peripheral nerve.

The lingual nerve starts as oligofascicular proximally and then becomes polyfascicular after it is joined by the chorda tympani, whereas the IAN tends to be polyfascicular with decreasing number of fascicles as it travels distally [1].

1.2. Neurosensory testing and work-up

Documentation of sensory nerve injury is critical from legal perspectives and extremely important in determining the nature and type of injury. The first step is obtaining the patient's chief complaint, whether it is a loss of sensation, pain, or other abnormal sensation or functional impairment [2]. When noting the history, few key elements need to be documented namely, location and cause of injury, date of injury, development of the symptoms, etc. Return of sensation within the first 4 weeks indicates a neuropraxia that implies a great prognosis,

whereas a delay in return of function indicates a more serious injury, such as axonotmesis. Neurotmesis should be considered if loss of function/sensation continues for more than 3 months. Clinically, it is imperative to observe signs of traumatic injury, erythema, edema, or change in the state of local tissues (scar formation). Blanching, flushing, or changes in the overlying tissue temperature or sweating are indicative of hyperexcitability of the sympathetic nervous system. Tinel's sign (tingling over the distribution of the nerve) is another sign that clinicians should try to elicit as it may indicate neuroma development. If the pain follows an anatomical pattern, an in-continuity neuroma may be suspected and if there is pain without radiation, neurotmesis and neuroma formation may be suspected. Diagnostic nerve blocks are valuable tools in differentiating peripheral versus central pain. Radiographs and particularly

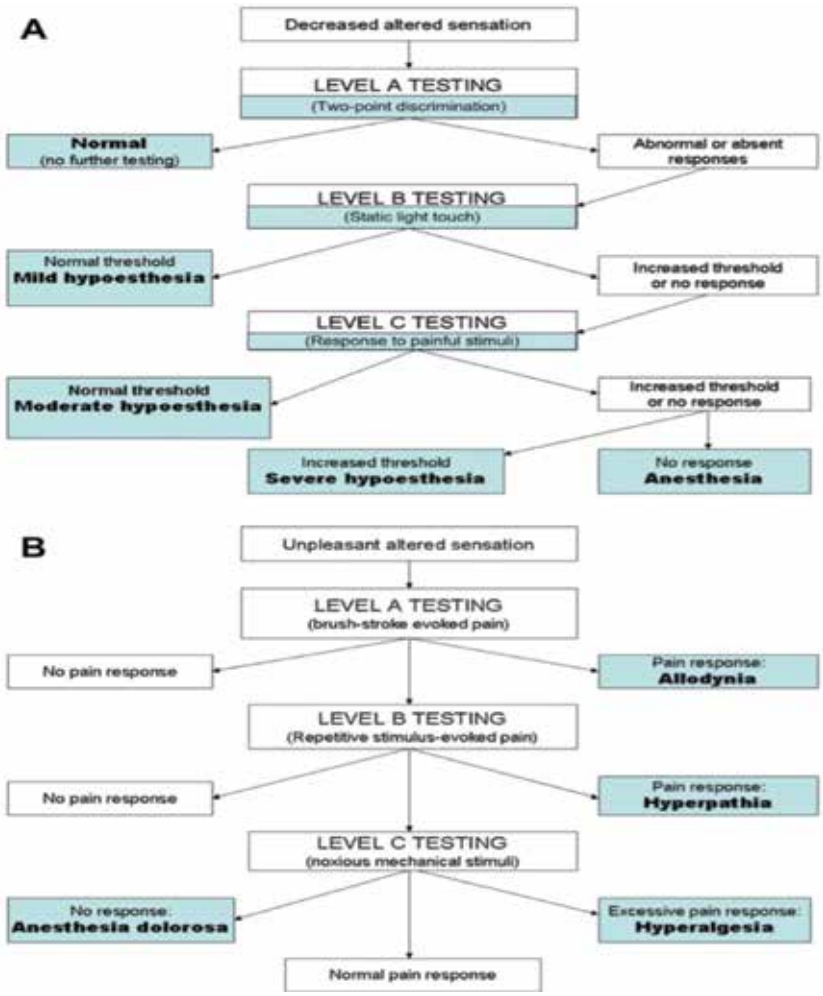

Figure 3. Algorithms for neurosensory testing to evaluate peripheral trigeminal nerve injuries and their recovery. (A) Evaluation of the patient with decreased altered sensation. (B) Evaluation of the patient with unpleasant/painful altered sensation.

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CT scans may indicate foreign bodies, such as screws, implants, or other alloplastic materials, which may be causing the problem.

The purpose of neurosensory testing is to determine and outline the sensory deficit, quantify the magnitude and character of the deficit, and record it for comparison in an objective manner over time. Usual tests include touch, directional touch, two-point discrimination, temperature change, and pinprick. Whether injured fibers are myelinated or non-myelinate is important; usually non-myelinated fibers recover quicker than myelinated nerves. Pain is the first sensation to return, whereas other sensations recover more slowly. Photographs or diagrams are helpful in documenting the extent of injury and its recovery [3]. More definitive and sophisticated tests (somatosensory-evoked potentials) can be used to record the return of function and monitor recovery after surgery (**Figure 3**) [4].

2. Indication and timing for surgical repair

Nerve injuries can be broadly classified into open and closed injuries. The patient who is undergoing repair of facial trauma or ablative oncologic surgery will often have the injured or intentionally resected nerve directly exposed and visible (open injury) during the procedure and this is the ideal time for repair of the nerve injury (immediate primary repair) if microsurgical expertise is available [5]. On the other hand, if conditions are unfavorable at that time, nerve reconstruction may be deferred. Delayed primary repair (within one week) or early secondary repair (after appearance of visible granulation tissue in the wound) has a favorable prognosis for sensory recovery approximating immediate primary repair [6, 7].

In recent years, however, the vascularized free flap has become the preferred method for reconstructing larger defects (>6 cm) of the mandible and all large soft-tissue defects unable to be restored by local rotational flaps [8]. Because free flaps often contain sensory nerves suitable as grafts to reconstruct important branches of the trigeminal nerve resected along with a tumor, they provide an excellent opportunity to restore important sensation to the tongue, lip, or face during the same operation. For instance, a microvascularized osseomyocutaneous scapulolatissimus dorsi free flap containing the long thoracic nerve has been used to successfully reconstruct mandibular defects and restore the sensation of the IAN after resection of oral carcinomas [9]. A radial free forearm flap containing either the medial antebrachial nerve or the lateral forearm cutaneous nerve provides a well-matched donor nerve to reconstruct the IAN or the lingual nerve after ablative cancer surgery [10–12]. Many cancer reconstructive teams now include a microsurgeon, who can enhance the opportunity for restoration of optimum osseous continuity, soft-tissue coverage, and nerve function.

A nerve injury may be unsuspected or unobserved (closed nerve injury), particularly during elective dentoalveolar surgery or when patients sustain facial trauma that do not require open reduction [13]. Excising a benign tumor or cyst near the inferior alveolar or lingual nerve can cause injury that is not visualized at that time. Surgery for benign submandibular or sublingual salivary gland disease may likewise pose a risk on the lingual nerve and may not be observed

by the surgeon [14, 15]. Sensory dysfunction in the distribution of the injured branch of the trigeminal nerve postoperatively should prompt the surgeon to investigate the situation.

Although guidelines have been proposed for indications and timing of surgical repair of trigeminal injuries [16], the exact optimal time for surgical intervention in the treatment of closed trigeminal nerve injuries remains uncertain, as shown by a recent literature review [17]. Seddon [18, 19], based on his extensive experience with treatment of missile injuries to the extremities during and after World War II, proposed a classification of closed peripheral nerve injuries. This classification, which emphasizes clinical factors, is helpful to the clinician in making timely decisions regarding treatment. Another classification devised by Sunderland emphasizes nerve pathophysiology. These two classifications are summarized in **Table 1** [20].

Seddon	**Neurapraxia**	**Axonotmesis**	**Neurotmesis**
Sunderland	I	II, III, IV	V
Nerve sheath	Intact	Intact	Interrupted
Axons	Intact	Some interruption	All interrupted
Wallerian degeneration	None	Some distal axons	All distal axons
Conduction failure	Transitory	Prolonged	Permanent
Potential for spontaneous recovery	Complete	Partial	Little or none
Time to spontaneous recovery	Within 4 weeks	Begins at 5–12 weeks, may take months	None, if not begun by 12 weeks

Table 1. Comparison of Seddon's and Sunderland's classifications of peripheral nerve injuries as applied to the trigeminal nerve (Adapted with permission from Bagheri and Meyer: Oral Maxillofac Surg Clin N Am; 2013. [58]).

Because of the progressive effects of Wallerian degeneration on nerve tissue distal to the site of nerve injury, time is of essence when attempting to achieve successful restoration of satisfactory sensory function [21–23]. Seddon [19], from his clinical experience, believed that the surgeon must be aggressive in the surgical treatment of closed peripheral nerve injuries, stating "If a purely expectant policy is pursued, the most favorable time for operative intervention will always be missed." Ideally, one should aim his repair while nerve regeneration is most active: According to Holmes and Young [24], Schwann cells' proliferative power peaks 2–3 weeks post injury and regress in about 3 months after injury.

As most of the injuries to the branches of the trigeminal nerve in relation to routine oral surgery procedures are of closed nature that would not be readily apparent to the clinician: that being said, patients may benefit from a period of observation prior to any surgical intervention. Generally, 3 months is the optimal time to wait between injury and attempted repair [25–28].

Indications for trigeminal nerve microsurgery include:

1. Observed nerve transection.
2. No improvement in sensation for more than 3 months.

3. Development of pain due to nerve entrapment or neuroma formation.
4. Presence of foreign body.
5. Progressively worsening hypoesthesia or dysesthesia (An unpleasant abnormal sensation, whether spontaneous or evoked).
6. Hypoesthesia that is intolerable to the patient.

Contraindications for trigeminal microsurgery may include

1. Development of central neuropathic pain.
2. Clinical evidence of improving sensory function.
3. Level of hypoesthesia that is acceptable to the patient.
4. Severely medically compromised patient unable to tolerate general anesthesia for microsurgery.
5. Excessive time elapsed since the initial injury.

3. Principles of surgical repair

Surgical treatment of peripheral nerve injuries has benefited from increased knowledge of neuropathophysiology and technical advances in equipment and surgical nuances over the past 30 years. The principles of treatment of peripheral nerve injuries elsewhere in the body apply equally to the trigeminal nerve and its peripheral branches [6, 7, 29, 30].

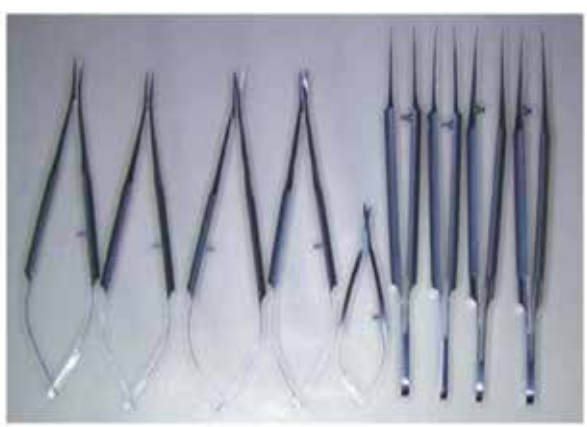

Figure 4. Basic set for microsurgery.

Microneurosurgical operations are performed with the patient under general with nasal endotracheal anesthesia in a sterile operating environment. The patient must remain perfectly

motionless while delicate maneuvers are performed on structures often less than 2 mm in diameter. This could be achieved with the use of muscle relaxant. Because most procedures are lengthy, the patient's bladder is catheterized and alternating compression pads are placed on the lower extremities when indicated. The surgical team usually consists of the surgeon, an assistant surgeon (preferably also trained in microsurgery), and a scrub nurse/surgical technician familiar with the instruments, objectives, and work habits of the surgeon. Specialized instruments including tissue forceps, scissors, small round burr mounted on high-torque high-speed handpiece and bone curettes, needle holders, and nerve hooks are sterilized and packaged in sets for each operation (**Figures 4** and **5**).

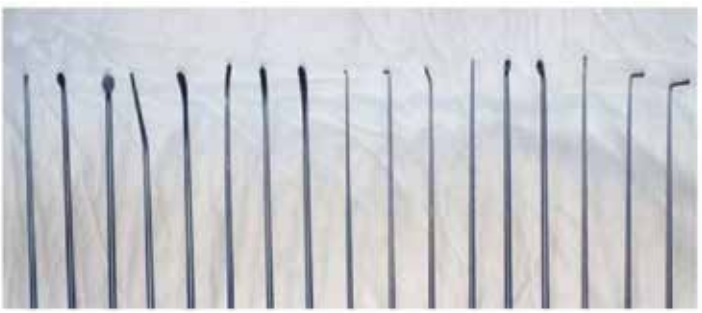

Figure 5. Rhotong curettes used to expose and dissect nerves from their bony canals.

Figure 6. Pentero microscope from Carl Zeiss Meditec AG, Goeschwitzer Strasse, 07745 Jena, Germany.

Small, nonreactive material (7-0 to 9-0 monofilament) is used for suturing nerves. In repair of the peripheral branches of the trigeminal nerve, sutures are generally placed only within the

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epineurium [31]. Wolford and Stevao [32] noted that the trigeminal nerve branches are polyfascicular in nature (non-grouped multiple fascicles of different sizes); hence, epineural repair offers better outcomes since perineural repair will likely yield more trauma due to the fact that dissecting each individual fascicle and suturing them together will lead to nerve atrophy and scarring. The operating microscope with hand controls and multiple ports for surgeon, assistant, and/or camera is essential for adequate magnification and visualization of delicate nerve structure (**Figure 6**).

O'Brien and Morrison [33] found no convincing evidence that a perineural repair is significantly better than an epineural repair if magnification is used, as magnification will allow more accurate alignment of the fascicles with the repair. The operating room table should be turned 90° relative to the anesthesiologist to allow for placement of the surgical microscope.

The surgeon and assistant are often seated and supportive rests for the wrists and forearms help to minimize hand tremors during surgical manipulations. Good hemostasis is required to aid in visualization and to minimize later formation of scar tissue in the operative site surrounding the repaired nerve. Hemostasis is achieved by control of the patient's blood pressure by the anesthesiology team, elevation of the operative site (patient head), placement of bone wax to staunch oozing from medullary bone, injection of epinephrine-containing local anesthetic solution, and the judicious use of bipolar cautery for electrocoagulation of small vessels within or adjacent to the nerve. Residual clotted blood in proximity to a nerve repair may increase the amount of connective tissue proliferation, leading to further scarring and compression-induced ischemia potentiating demyelination, hence the importance of maintaining a hemostatic surgical field. Miyamoto showed decreased axonal growth when repair tension exceeds 23 g [34]. Hausaman [35] emphasized that a tension-free co-adaptation is vital for functional return and recommended nerve grafting where nerve stumps cannot be repaired in a passive, tension-free fashion.

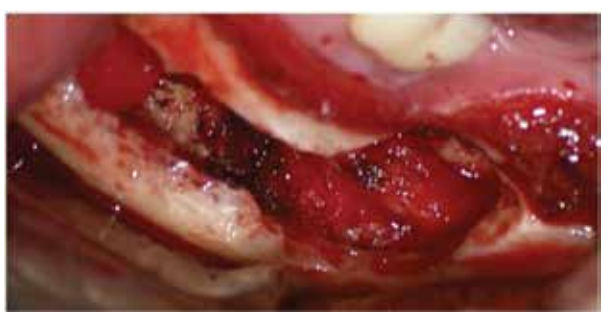

Figure 7. Lateral mandibular corticotomy to expose inferior alveolar nerve.

Generally, the mental and lingual nerves are exposed transorally, and the IAN may be approached either transorally or through a submandibular skin incision. The decision regarding which incision to use is largely determined by the degree of access and visualization afforded by a particular approach and, in some instances, by the surgeon's personal preference and experience. Exposure of the IAN can be accomplished after decorticating the lateral cortex

with skeletonization of the mental nerve branches. Regardless of which technique is used to access the mandibular bone, subsequent access to the nerve is achieved through lateral decortication (**Figure 7**).

The lingual nerve is approached transorally through either a paralingual or lingual gingival sulcus incision. The paralingual mucosal incision is made along the floor of the mouth parallel to the lingual plate, with dissection completed using blunt and sharp dissection to expose the nerve. Advantages of this approach include a smaller incision with direct visualization; however, transected nerve ends may retract from the field on exposure. The lingual gingival sulcus incision requires a lateral release along the external oblique ridge for complete flap mobilization and is extended along the lingual sulcus of the teeth to approximately the canine region. Once the flap is elevated in a subperiosteal plane and retracted, the nerve may be visualized from below through the overlying periosteum and bluntly dissected from the flap. This technique requires a larger incision than the paralingual incision; however, the proximal and distal nerve ends will not retract during surgical dissection (**Figure 8**).

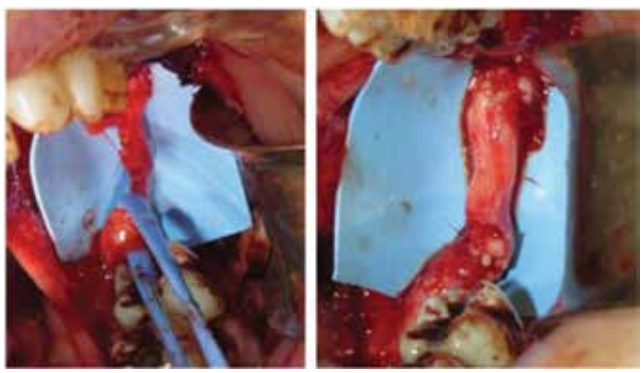

Figure 8. Lingual nerve repair with allograft Avance (AxoGen Inc, Alachua, FL, USA).

External neurolysis is the surgical procedure used to release the nerve from its tissue bed and remove any restrictions that can lead to conduction blockade or prevent recovery. Injury to soft tissues surrounding a nerve such as the lingual nerve can induce scar tissue and create a compressive neuropathic injury. The dissection of scar tissue from an intact nerve may potentiate the recovery of sensation. External neurolysis is usually performed under some magnification to grossly assess the nerve and to isolate any pathologic tissues. For patients with moderate sensory disturbances, external neurolysis may be the only surgical procedure indicated. Once the external neurolysis is completed, the nerve can be examined under magnification and clinical findings will dictate the need for any additional procedures such as removal of foreign bodies including endodontic filling material, tooth fragments, or dental implants.

Internal neurolysis may be indicated when there is evidence of nerve fibrosis or visible regions of nerve compression. The nerve may appear narrow or enlarged depending on the mechanism and type of injury. This procedure requires opening of the epineurium to examine the internal

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structure of the nerve. Because the trigeminal nerve has a scarce amount of epineurium, any manipulation could potentially lead to further scar formation, hence the need for a delicate surgical technique. A longitudinal incision is made through the epineurium using a beaver blade to expose the internal structures in a procedure referred to as an epifascicular epineurotomy. With release of the epineural fibrosis, the nerve may expand, indicating a successful internal neurolysis procedure. If this is ineffective, a circumferential portion of the epineurium may be removed in a procedure called epifascicular epineurectomy. If no expansion and fibrosis is observed, the affected nonviable segment can be excised and the nerve prepared for primary neurorrhaphy. The epineurectomy procedure is rarely indicated because of the potential for further nerve injury through the surgical manipulation itself.

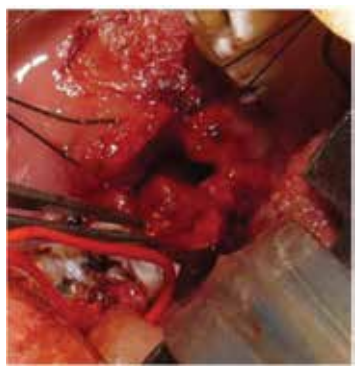

Figure 9. Exophytic neuroma of the lingual nerve.

Excision of neuromas is performed to prepare the nerve for co-adaptation by removing nonviable tissues in order to re-establish continuity. This procedure may be performed in cases of complete transection injuries or partial injuries in which there is an exophytic type of neuroma (**Figure 9**).

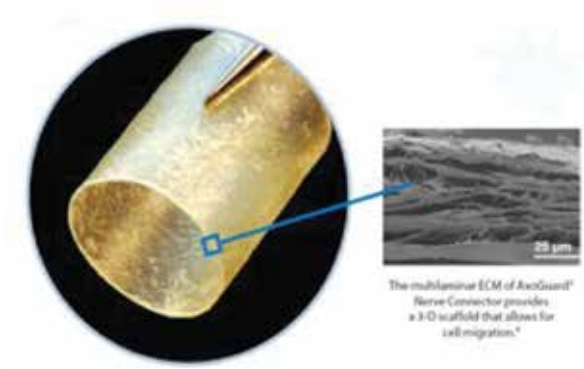

Figure 10. Axoguard Nerve Protector (AxoGen Inc, Alachua, FL, USA).

After excision of the neuroma-like tissue, the resulting stumps are examined under magnification to ascertain whether normal tissue is present as determined by the presence of herniated intrafascicular tissues. The goal is to allow the suturing of the two nerve ends together without tension in a process called primary neurorrhaphy. The two nerve stumps are approximated using 7-0 to 9-0 nonreactive epineural sutures. Three to four sutures are optimally placed to allow for nerve healing. It is the preference of the authors to wrap the nerve on completion with a resorbable membrane such as Axoguard Nerve Protector (AxoGen Inc, Alachua, FL, USA) to protect the surgical site and potentially minimize additional scarring in the region (**Figure 10**).

These materials may also provide a "seal" which ensures that growth factors released during nerve regeneration remain locally within the conduits themselves.

4. Factors affecting nerve repair success:

There are a lot of factors that determine the outcome of nerve repair. According to Wolford and Stevao [32], the factors affecting the success of the procedure are as follows:

1. Time between injury and repair.
2. Nature and extent of injury.
3. Vascularity.
4. Axons' orientation between the nerve and graft.
5. Distance between the injured nerve stumps.
6. Quality of the repair.
7. Tension of the repair.
8. Type and preparation of the graft.
9. Age and health of the patient.

Microneurosurgical repair outcome is greatly affected by number of elements, some of them pertain to the nerves themselves and others external to it. Type and degree of injury, blood supply to the surgical bed, and infections in addition to scarring are examples of external factors that affect the recovery of repaired nerves. Perhaps age and overall health of the patient are considered the most significant external factors, as better outcomes have been reported in younger healthier patients [36].

On the other hand, quality, technique, tension, and timing of the repair are the principle local factors that impact the repair outcome. Moreover, Wallerian degeneration is a unique phenomenon that will influence both the proximal and distal stumps of the injured nerve and may extend up to the first node of Ranvier [37]. Location of the injury along the nerve will affect the distance the axons have to travel, as the more proximally the injury is located, the more

regeneration is expected, however, the less access the surgeon will have. Finally, the type of nerve does have an impact on repair recovery as pure nerves (either motor or sensory), tend to recover more rapidly when compared to mix type (the trigeminal nerve is a mixed nerve).

5. Nerve grafting considerations

The gold standard for reconstructing a peripheral nerve gap when it is not possible to perform a tension-free primary neurorrhaphy has long been the autogenous nerve graft [38]. A nerve graft interposed between the proximal and distal nerve stumps eliminates tension across the repair and distal nerve regeneration approximates that occurring across a tension-free primary neurorrhaphy [39]. In the head and neck region, the great auricular nerve in the upper lateral neck has been the most frequently harvested donor for nerve gaps of less than 3 cm while the sural nerve in the lower extremity is more suitable for longer nerve gaps [40]. Each nerve harvest has its own morbidity, as patients will end up with a sensory deficit over the lateral aspect of the foot if the sural nerve is used, and to the ear plus lateral skull if the greater auricular nerve is harvested. The patient requires an informed discussion about the potential sensory loss as result of the harvest procedure, so they can determine which graft donor site they wish to choose. Miloro and Stoner [41] subjectively assessed outcomes following sural nerve harvest and found that most patients tolerated sural nerve harvest without significant donor site morbidity.

The donor nerve and the damaged nerve need to approximate one another in diameter, fascicular size, and numbers to ensure successful outcome. The average diameter of the inferior alveolar nerve is 2.4 mm and the lingual nerve is 3.2 mm [42, 43]. The greater auricular nerve is 1.5 mm in diameter and the sural nerve is 2.0 mm in diameter. There is also considerable difference between the size and number of fascicles of those nerves. Svane et al. [42] found that the inferior alveolar nerve has up to 18 fascicles at the third molar area, which decreases to about 12 fascicles at the mental foramen. The lingual nerve has been shown to have similar number of fascicles at the third molar site but wean down to about nine fascicles as it enters the tongue. As for the greater auricular and sural nerves, they have 9 and 12 fascicles, respectively [43], all of them are considered polyfascicluar in nature; when we look at the cross-section, it is noted that the sural nerve is more flattened whereas the rest of them are more round in shape and 2–4 cm of length can be harvested when considering the greater auricular nerve as the donor site; on the other hand, the sural nerve may give up to 20–30 cm of nerve graft [44, 45].

When the lost soft tissue or bone included in a tumor resection or an avulsive injury is planned to be reconstructed with a vascularized free flap, nerves contained in such flaps, including the long thoracic nerve (in scapulolatissimus dorsi flap) [9] or the medial antebrachial or lateral cutaneous nerve of the forearm (in a forearm flap) [12], provide easily accessible tissue for simultaneous trigeminal nerve reconstruction during the same operation. If the diameter of the donor nerve is less than that of the recipient, two or more cable grafts can be placed side by side to match the recipient nerve diameter and maximize neurotization of the distal nerve stump.

Reconstruction of the nerve gap with a processed allograft shows promise in laboratory research [46]. A product consisting of a human decellularized allograft, which has been made to be non-immunogenic and inert in the recipient's body but which provides a biological substrate for nerve regeneration (Avance; AxoGen Inc, Alachua, FL, USA) is available (**Figure 11**).

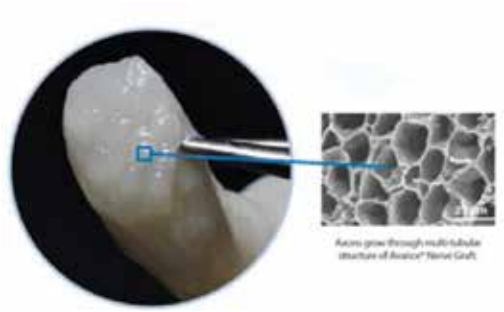

Figure 11. Allogenic nerve graft material Avance (AxoGen Inc, Alachua, FL, USA).

Successful inferior alveolar nerve reconstruction with a decellularized nerve allograft has been reported [47], and early results with repair of small gaps (<3 cm) are favorable in the authors' practice. This product is currently used to repair longer nerve gaps in the extremities. Although at present, this experience has not been reported for the reconstruction of large trigeminal nerve gaps, and the ultimate maximal length of a nerve gap that can be restored with the processed allograft has yet to be determined, it will undoubtedly play a greater role in nerve reconstruction in the maxillofacial region in the future.

Guided nerve regeneration with an autogenous vein graft conduit has been used to reconstruct short gaps in small digital nerves in the hand [48]. This technique is successful only in short nerve gaps (<3 cm) when used in peripheral trigeminal nerve repairs [49, 50]. An alloplastic nerve conduit (polyglycolic acid or polytetrafluoroethylene) has been used with limited success in trigeminal nerve injuries, but only in minimal nerve gaps [51, 52]. Such distances are commonly exceeded when reconstructing traumatic avulsive or oncologic surgical defects with nerve gaps of the trigeminal nerve; therefore, guided nerve regeneration has limited applicability.

6. Outcomes of surgical repair of trigeminal nerve injuries

Analyzing, interpreting, and comparing the results of microsurgical repair of trigeminal nerve injuries from multiple studies have frequently been a difficult task, because of lack of standardized methods for evaluating neurosensory function and a uniform grading system for surgical outcomes. In the past few years, studies conducted by experienced clinicians have established that microsurgical repair of trigeminal nerve injuries can result in improved sensory function for a large majority of selected patients. Pogrel reviewed his results, based on neurosensory testing, from microsurgical repair of 51 Trigeminal Nerve injuries (inferior

alveolar nerve = 17, lingual nerve = 34), and reported that 28 (54.9%) gained "some" or "good" improvement in sensory function. Nerve repair at more than 10 weeks after injury was less likely to be successful. No differences were observed in the results based on gender, with slightly better success in the inferior alveolar nerve group than in the lingual nerve group [53]. A long-term follow-up of repair of 20 lingual nerve injuries by Rutner et al. [54] using standardized neurosensory testing and patients' subjective evaluations of their degree of recovery of sensory function found that 15 patients (85%) gained improvement in all neurosensory testing parameters, whereas 18 patients (90%) judged the repair to have achieved "some improvement". Strauss et al. [55] reported microsurgical repair of 28 inferior alveolar nerve injuries evaluated by neurosensory testing produced "slight" (N = 12, 42.9%) or "significant" (N = 14, 50%) improvement, whereas only 2 repairs resulted in "no improvement" (7.1%).

Grade	Description
S0	No sensation
S1	Deep cutaneous pain in autonomous zone
S2	Some superficial pain and touch sensation
S2+	Pain and touch sensation with hyperesthesia
S3	Pain and touch sensation without hyperesthesia; static 2 point discrimination >15mm
S3+	Same as S3 with good stimulus, localization and static 2 point discrimination 7–15mm
S4	Normal sensation

Table 2. Medical Research Council Scale for grading sensory function of peripheral nerves as applied to the trigeminal nerve; Grades S3, S3+, and S4 are considered functional sensory recovery (Adapted with permission from Birch et al. Surgical disorders of the peripheral nerves. Philadelphia: Churchill Livingstone; 1998. p. 405–14.).

Subsequent studies have used neurosensory testing for preoperative and postoperative assessment of sensory function and have graded the outcome of surgical intervention for trigeminal nerve according to the Medical Research Council Scale (MRCS) for grading sensory nerve function (**Table 2**).

In a review of 60 surgically repaired trigeminal nerve injuries (inferior alveolar nerve = 4, lingual nerve = 56), 45 (75%) were found to have achieved functional sensory recovery (MRCS score of 3.0 or greater) in 1 year postoperatively [25]. The time from nerve injury to surgery did not statistically correlate with outcome, although all patients were operated on at less than one year after injury. Bagheri et al. [13, 56, 57] have reported their experience with microsurgical repair of a variety of trigeminal nerve injuries and causes. Among the total of 429 nerve repairs (inferior alveolar nerve = 186; lingual nerve = 222; mental nerve = 12; inferior orbital nerve = 7; labial branch nerve = 2), the success rate (achieving functional sensory recovery, MRSC grade of >3) varied from 81.7% for the inferior alveolar nerve to 90.5% for the lingual nerve [22, 23]. The success rate for inferior alveolar nerve repair increased to 87.3% when the nerve was reconstructed with an autogenous nerve graft in comparison with all other types of repair. In the most successful group of nerve repairs, the lingual nerve was repaired in the

overwhelming majority of cases by primary neurorrhaphy rather than an autogenous nerve graft [22]. This result probably reflects the much greater ease of creating sufficient mobilization of the lingual nerve to bring the proximal and distal nerve limbs together to close a nerve gap without tension than is the case with the IAN. Many of the patients were operated on more than one year following injury, allowing for an analysis of the effect of time on the outcome of nerve repair. At more than 9 months following lingual nerve repair or 12 months after IAN repair, there was a statistically significant decrease in successful outcome. Patient age was also a significant factor in outcome, with significant drop-off in success rate for inferior alveolar nerve repair after 51 years of age and a similar decline in favorable outcome for lingual nerve repair after age 45 years [58].

7. Summary

Patients who sustain large traumatic avulsive injuries or defects from ablative tumor surgery in the oral and maxillofacial region often have lost sensory function caused by injury or avulsion of one or more peripheral branches of the trigeminal nerve. Such injuries result in altered and/or painful sensation in the tissues previously supplied by these important sensory nerves. Normal orofacial functions, such as eating, drinking, oral hygiene, swallowing, and speaking, are dependent on adequate sensory input. Loss of this input creates significant orofacial dysfunction and jeopardizes the quality of life of afflicted patients. Nerve repair and reconstruction techniques have been revolutionized over time with the introduction of better instrumentation and improved knowledge of neurobiology. The successes of these techniques depend upon accurate assessment of the injury nature as well as early and meticulous repair so that the patient has the best chance for functional recovery. Whenever possible, repair or reconstruction of injured branches of the trigeminal nerve should be planned and performed in conjunction with reconstruction of other lost osseous or soft tissues in the oral and maxillofacial region. After surgery, an important aspect of global rehabilitation of such patients is a well-planned program of daily sensory re-education exercises to assist in achieving maximum potential sensory recovery and associated orofacial function and thus, an improved quality of life.

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Section 4

Management of Headaches, Migraines, TMJ Pain and Trigeminal Neuralgia

Chapter 6

Headaches, Migraine, and TMJ Pain Management: Medical and Surgical Intervention

Mazen Almasri

Additional information is available at the end of the chapter

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Abstract

The main objective of this chapter is to introduce to the readers the issue of head and neck pain, temporomandibular joint (TMJ) disorders, clicking, headaches, migraines, and neck discomfort that are likely to present in the clinic with similar signs and symptoms. This chapter deals with the introduction, clinical examination, investigation, and the use of splint therapy, muscle complex injection therapy with botox and prolotherapy, TMJ lavage, arthrocentesis, and TMJ surgery to treat such patients.

Keywords: TMD, migraines, headaches, botox, injection therapy, trigger points, TMJ surgery

1. Introduction

In the middle of a stressful lifestyle and busy working schedule, the scenario of patients complaining of headaches, migraines, neck sores, or painful temporomandibular joint (TMJ) is very common in medical practice. Some studies show that more than 5% of the population complain some kind of head and neck pain [1]. Another study reviewed the incidence in a German population focusing on signs or symptoms of temporomandibular disorder (TMD), the incidence was as high as 50%. Moreover, the percentage of patients whom had some form of pain was only 2.7% [2]. The cause of pain incidence in a variable number in the literature is the multifactorial disease process; clinical presentation and precipitating factors are sometimes difficult to identify. Anatomically, the entities that can contribute to pain are dental, muscular, gingival, skeletal, vascular, neurogenic, or psychogenic; not to mention personal susceptibility, medications, external, and life-style factors. Due to the frequency of the disease,

a lot of practitioners are bound to see such patients and may contribute to the treatment of pain in either a successful or an unsuccessful path. The unfortunate path is when attempts are performed improperly and make the situation worse. When a patient presents to a clinic complaining of pain, discomfort, or headache in the head and neck region, the presentation can be similar to a lot of conditions at first glance; however, the etiological factors differ in the magnitude and the degree of involvement. The dynamic relation of the muscles, skeleton, TMJ, gingival tissue, and occlusion does form a sophisticated relation that can modify the etiology of the disease and or extension as unilateral or bilateral. Therefore, the clinical assessment is as challenging as the management plan [3, 4]. In this chapter, the approach will be addressed in a unique way focusing on the problem in general and showing the span of management from the pain reduction to restoring function. In addition, examples of variable cases will be presented to illustrate different approaches to management, such as the use of night guard, botox therapy, trigger point injections, transcutaneous electro-neuro-stimulator (TENS) therapy, prolotherapy, medications, and surgical interventions.

2. Clinical examination

The clinical examination of a patient with head and neck pain complaints should start with the routine patient medical interview. Going through the chief complaint, history of present illness, medical history, medications, allergy, social history, eating habits, life-style, postural tendency, previous interventions, etc. As easy as it sounds, the patient may not be able to present all the pertinent information the physician is looking for very clearly. Hence, the expertise of the practitioner to "fish" for the information is needed. Such points can mainly be divided into pertinent positives, which will help in diagnosis of a disorder, and pertinent negatives, which usually rule out an entity. The same can be applied while performing the clinical examination, medical consultation via investigatory methods. Due to the complexity of head and neck pain, thorough knowledge and clinical training are needed to be able to work through the examination-diagnostic part in order to reach a proper diagnosis.

For example, some points may not be presented by the patient and which is of prime importance in diagnosis; this requires a trained physician to "probe" for this information such as life-style's habits, the amount of caffeinated drink intake, the number of cigarettes per day, the number of sleeping hours, the nature of work, and any postural tendency.

Another issue is the detailed medical status of the patient, vitamin D levels, exercise habits, and eating habits. The head and neck area should be examined thoroughly and routinely for every patient as part of the routine check; however, for head and neck pain patients, closer attention should be made to the major components of the maxillofacial skeleton. Lack of knowledge and expertise may lead practitioners to a false diagnosis, false management, and delay in proper treatment, thus complicating the definitive management.

A special care is required when examining the head and neck area as TMJ constitutes only part of the problem not all of it. Hence, in addition to examining the TMJ by palpation, inspection range of motion, excursions, and clicking, further correlation with other components are

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necessary. Dental occlusion, attrition of teeth or restorations, rotated teeth, edge-to-edge teeth, multiple fractured restorations on bicuspids and molars, sharp dental edges, and indentations on surrounding soft tissue such as cheeks or tongue should all be carefully inspected as signs dictating precipitating factors [3].

The muscles of the head and neck area should also be evaluated for size, symmetry, tenderness on occlusion or on palpation, presence of trigger points, radiating pain, pain extension to the scalp, back, neck, shoulder girdle, and the paravertebral musculature. The patients should be asked if pain is associated with any neurological deficits, such as tingling peripheries, or motor deficits. Such may dictates other associated problems especially at the cervical vertebral spine level, where consultation with a neurologist or orthopedic surgeon is necessary.

The maxillomandibular complex should be inspected thoroughly, and selectively to palpate the pertinent muscular origins and insertions. The most common muscles of attention are the zygomaticus, orbicularis oris, temporalis, ptyregoids, masseter, buccinator, occipitalis, suboccipitalis, and trapezius.

Assessment of the ear, nose, and throat region is definitely important. TMD pain can be present either at or about the ear. Palpating the TMJ or assessing the range of mouth opening is important (**Figure 1**).

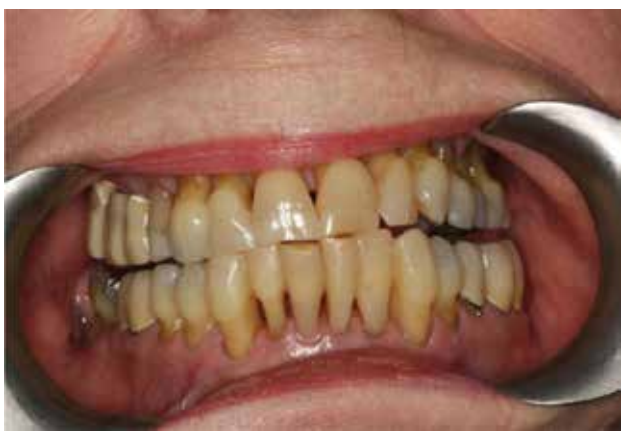

Figure 1. A patient presented with onset of abnormal occlusion just after completing a 2-h dental treatment. The picture shows open bite at the posterior teeth and barely touching anterior occlusion, which suggest acute TMJ derangement, likely in the form of disk displacement.

3. Investigation

Once the clinical interview and examination are accomplished, usually the clinical outcome can dictate the type of images that might be needed to correlate the findings. Of the most common ones is the orthopantomography or panoramic radiography. The advantage of this

image is that it is easy, available in most dental offices or medical centers, relatively has low cost, and shows a wide panoramic view of the maxillofacial complex. It includes the TMJ, the maxillomandibular skeleton, the associated erupted and impacted teeth, the mastoid—styloid complex, the maxillary sinuses, and other findings such as external objects and piercings (**Figure 2**). A lateral cephalometric or anteroposterior radiograph can be used as well to document the maxillomandibular relation or discrepancies in anteroposterior dimension [3–5].

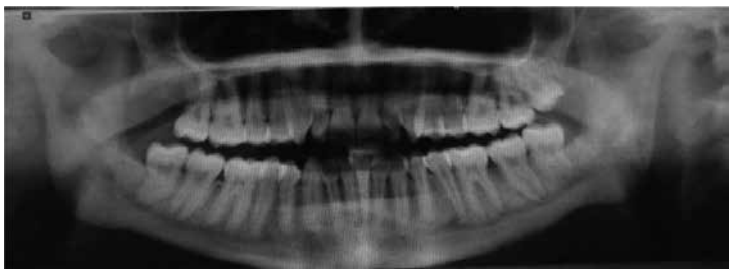

Figure 2. A panoramic radiograph of a 27-year-old patient with chronic pain of the head and neck muscles. The radiograph is showing signs of chronic condylar overload presented in the form of bilateral degenerative changes.

The CT scan of the head and neck is usually used as well to verify the relation of the maxillomandibular status with the base of skull. Conditions such as impacted teeth or associated lesions, or abnormal position of such an impaction are usually present. A hard bony lesion of the joint, condyle, coronoid, or base of skull is investigated and can be seen in difficult situations. An MRI of the head and neck region is of great value to investigate the internal status of the TMJ region, showing the disk, effusion, and abnormal enlargements [5]. In addition to evaluating soft tissue abnormalities more clearly when compared to CT scans, it is useful if neurogenic, vascular, or mesenchyme disease is anticipated (**Figure 3**).

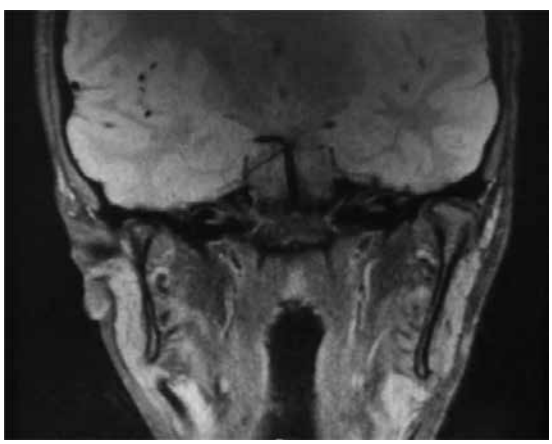

Figure 3. An MRI coronal view of a patient with left TMJ pain and hypomobility. The view shows left disk displacement toward the anterior-medial aspect.

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The use of 12.5 MHZ ultrasonography has been presented to be a useful aid for TMD evaluation with some limited application in detecting the presence or absence of derangements more than specifically identifying a precise type of the disease [6]. Some other investigatory tools have been used to help verify the status such as the stethoscope to listen closely to clicking or crepitus and the use of electromyography for objectively measuring the activity of some muscles of mastication especially temporalis and masseter but with limited application in the clinical field [4–7].

4. Management strategy

Managing such problems is thought to be easy by a lot of practitioners as considering the same regime for almost all their patients. The drawback of doing so, is worsening the situation over time, decreasing the pain threshold level, emotionally disturbs the patient and families, causing more depression, causing less tolerance to treatment, and further difficulty in treating those patients eventually when referred to a specialized center.

Management always begins with the correct diagnosis as discussed in the previous section. Furthermore, it is crucial to identify the contributing factors to address them while planning the treatment strategy. Hence, the primary visits are usually directed toward counseling the patients and identify the possible conservative strategy [2, 3]. Using soft diet, cutting food into smaller pieces, avoiding chewing gum, and minimizing extreme opening of the mouth are strategies that can be applied in order to alleviate the load on the joint and muscles. The addition of medications is commonly used; however, care should be taken to customize the medications to the appropriate case. Analgesics, nonsteroidal anti-inflammatory drugs, muscle relaxants, anxiolytics, opioids, antidepressants, anticonvulsants, antihistamines, and local anesthetics are all examples of extrinsic treatment that can be added carefully. The dose, frequency, duration, and possible combination are all aspects to consider [8]. The management protocol usually includes behavioral therapy as the case dictates, which include, self-determination, relaxation, meditation, yoga, self-hypnosis, cognitive therapy, and finally, a psychiatric evaluation if needed. It is imperative to understand that customizing a protocol is a difficult task, not to mention that the patient responded partially or completely to the treatment or did not respond at all. That's when the practitioner should revisit the case, starting from diagnosis, patient cooperation, and finally the treatment protocol as the response can vary according to the treatment given, the patient's cooperation, and the nature of the disease.

5. Occlusal evaluation

The physiologic harmony of occlusion in accordance with the TMJ and muscle complex is of prime importance. One of the reasons that lead to losing such harmony is the loss of occlusal equilibrium. Missing posterior teeth can be very devastating to the patient especially if more than one is missing. Such will lead to directing the occlusal force and chewing asymmetrically.

Abnormal high contacts in the form of fillings or prosthetics will disturb the occlusal balance and might lead to TMJ internal derangement, muscle abnormal reaction, or eventually fracture of the restoration or the tooth itself. The same might occur if abnormal maxillomandibular prosthetic occlusal compatibility was not evaluated and planned; as acrylic maxillary teeth might be incompatible when opposed by porcelains (**Figure 4**).

Figure 4. A lateral clinical view showing the posterior open bite acutely found after prolonged dental treatment took place for a 60-year-old female patient. She presented to the oral maxillofacial surgery center right after finishing the dental treatment complaining that she cannot bite normally as used to be with pain upon mouth opening and closure.

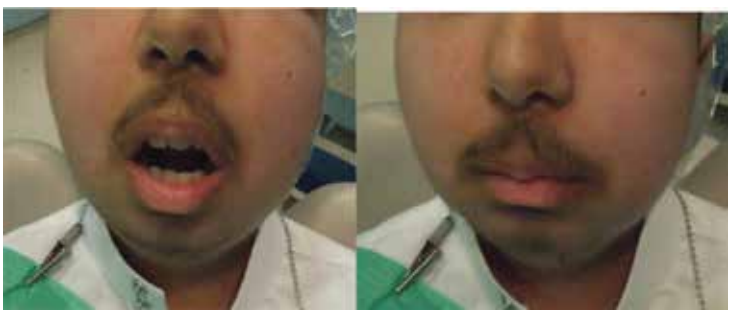

Figure 5. An 18-year-old patient presented with a tender TMJ and muscle complex in addition to hypomobility of the mandible. Thorough interview and examination revealed a medical background of juvenile rheumatoid arthritis that is affecting the TMJ bilaterally leading to hypomobility likely due to fibrous ankylosis (see **Figure 6**). Such deformity will require careful management to reconstruct the deranged TMJ, ramus height, mandible opening, occlusion, and the convex facial profile by mandible advancement surgery and possibly a chin augmentation procedure [11, 12].

Clenching, bruxism, or parafunctional habits can be devastating type of forces as they direct forces to unusual points of the tooth structure in a chronic continuous fashion. The phenomena might lead to unilateral or even bilateral disease at the muscle or TMJ aspects [9]. Such patients usually will show evidence of the habits on their teeth or surrounding soft tissue in the form of attrition, loss of restorations, frequently changing restoration, or fractured tooth. The soft tissue envelope might show evidence of continuous trauma as fibrosis, leukoplakia, or indentations on the tongue and cheek mucosa [9, 10]. Maxillomandibular skeletal discrepancies such as anterior open bite, long face syndrome, short ramus, and class 2 skeletal

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malocclusion are prone to have an abnormal load on the muscular or TMJ region. The patients usually complain from difficulty eating, cleaning, and mouth opening, in addition to the possibility of pain and discomfort. Such derangements can affect both the hard and soft tissue structures (**Figures 5** and **6**). Accordingly, practitioners must dictate the type of surgical intervention needed [11, 12].

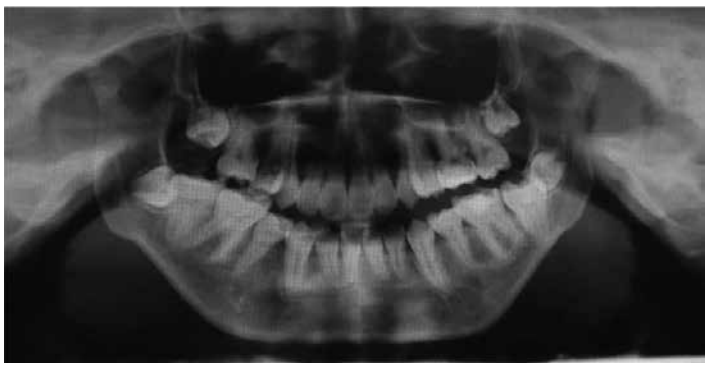

Figure 6. An orthopantomogrpahic (OPG) view of the patient in this figure, showing reduced ramus height bilaterally and abnormal condylar fossa shape in the form of flat condylar head, decortication, abnormal space, and osteophytic changes. Further images and CT scan are needed to investigate the joint and confirm the suspected ankylosis type and extension. An MRI scan can be used as well to confirm the soft tissue status such as the disk, joint effusion, and further fibrosis.

6. Splint therapy

A splint is defined as using an external device that can be worn on top of teeth as part of TMD management process. Splints can come in different forms or shapes or material. It can be hard, soft, or combined [9]. The extension of the device can be generalized to cover all the teeth or can be limited to specific teeth. Some splints are placed in the maxillary arch, mandibular, or even both, which are less commonly used nowadays. The occlusal surface of the splint can be flat, anatomical, or positional. As presented, variability in forms and shapes is available, and selections do depend mainly on the case, or according to the availability in the laboratory or the practitioner's expertise in handling one over the other. Hence, it is extremely discouraged to use similar device modality in all the patients without knowing the reasoning of prescribing so. It is unfortunate that this is considered to be one of the common pitfalls in dental practice that a specific theme is prescribed for all the patients for reasoning such as material available, lab technician skills, or dentist lack of knowledge or expertise.

The general idea of using splint therapy is to hold the occlusal units together against the extreme or abnormally directed force of occlusion. It can work as a habit-breaker, redistribute the amount of force all over instead of a single location, stretching the muscles of mastication, and finally to re-orient the condyle fossa relation targeting alleviating force, proprioception,

and retrodiscal tenderness. It can be beneficial to patients at the beginning of the disease and can be assuring if used during sleep where a lot of the bruxism usually takes place [10].

Splint therapy can be harmful if used on patients with occlusal disequilibrium, patients with hyperactive muscles of mastication, patients with multiple trigger points, or patients with advanced TMD and muscular disease, especially if not combined properly in the management protocol.

6.1. The muscle complex therapy

The muscles are the main structure stabilizing the skeleton and help in movement and functions. Muscles are integrated with their terminal tendons at the origin or insertion base, with capsules, and with the surrounding fascia of the head and neck. The anatomical and functional harmony between the muscular complex, the joint, and functional outcome can preserve a prolonged pain free well-being. However, minor disfigurement can lead to patient's dissatisfaction and discomfort. At some point during the disease process, the muscles of mastication can suffer by different pathophysiological lines. It can get hypertrophied, showing trigger points, and even worse—fibrosed or calcified. Trigger points (TPs) are defined as localized areas in the muscle, palpable, tender, and can cause extreme radiating pain if pressed for prolonged duration. TPs vary in size, shape, and number, where their presence is usually evidence of muscular advanced reaction to the disease process. Muscles can be approached by different techniques, where oral pills are usually the easiest and commonly approached by practitioners. The medications commonly used include analgesics, NSAIDS, or muscle relaxants. However, in situations of advanced muscular involvement presented by TPs and severe pain to the head and neck muscles, further interventions are needed, such as TP injection, botox, prolotherapy, TENS, or more types of systemic medications [13, 14].

TP injection is a well-known technique to manage muscle pain using variable materials such as local anesthetics, saline, or opioids. Studies of such material showed significant results with

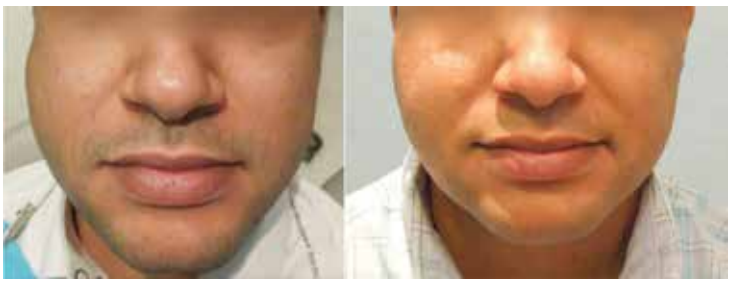

Figure 7. On the left side, a frontal clinical view of a client complaining of an increased size of the right facial contour that is more noticeable when eating or speaking. On clinical examination, the right masseter muscle showed significant trigger points on palpation with tenderness and general muscle hypertrophy. The temporalis muscle is involved as well. Upon reviewing the pertinent history, the client stated heavy clenching and bruxism likely due to the stressful busy work schedule. The picture on the right, taken approximately 2 months after starting the muscle therapy and trigger point injections resulting in a significant reduction of the contour with anticipation of further reduction concomitant with time.

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variable outcomes according to the confounding factors and study group criteria. When local anesthesia is used, non-epinephrine containing solution is used to get the advantage of the vasodilating effect on the muscle and trigger point. Such will facilitate better blood supply circulation and analgesic effect to allow more range of motion exercise [13, 14]. The disadvantage is that it might require multi-injection therapy over few weeks to show results that can be not convenient to the patients.

When botulinum toxin-A was introduced to treatment, it showed very good results for treating migraines, headaches, TPs, and neck pain with prolonged effect and much less visits to the hospital emergency department or hospitalization [14, 15]. Such made that choice of more convenience to the patients and practitioners with much fewer visits needed. The drawback is the possible high cost when compared to local anesthetic TP injection. Of the common pitfalls along this line is not explaining to the patients how botox works, not mixing the material in the right formula, or improperly injected by untrained practitioners. It is not uncommon that patients might think that a single visit of injection therapy might resolve a disease that has been there for few years which is unlikely. The treatment risks, benefits, and alternatives have to be discussed clearly with the patient in order to assure proper outcomes and continuity of care without unrealistic expectations. Patients will usually feel relieved and significantly improved when treated properly. However, it will still require to keep up with the instructions and other forms of the treatment strategy as well, such as, eating softer diet, changing the damaging postural habit, and possibly adding a stress reduction form into the stressful lifestyle (**Figure 7**).

6.2. Prolotherapy

Prolotherapy is defined as a mode of treating tender joint and surrounding tendons using hypertonic fluid injections to stimulate a proliferative regeneration process. It has been used for over 70 years in TMJ and other joints showing promising results. It was first described in

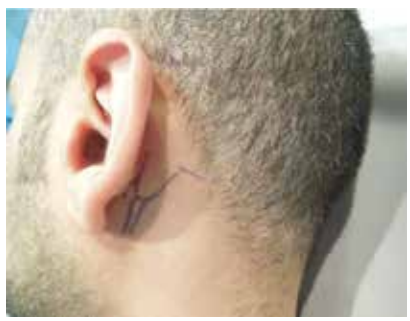

Figure 8. A 36-year-old male patient presented with tender muscles at the left side of the face, head, and ear region. Clinical examination revealed involvement of the mastoid-styloid-muscular complex as a major point eliciting the pain. A query Eagle's syndrome was suggested as the patient has the pain increased when turning his head to the sides, excessive articulation, or sometimes swallowing. An extensive muscle therapy and postural control took place with significant improvement of the condition. The clinical picture is showing the posterior side view of the mastoid-styloid region, landmarking the region for further muscle injection therapy.

the literature as a treatment modality for TMD and pain back in 1937. The technique of injecting hypertonic solution such as dextrose 10% mixed with sterile water and lidocaine can be effective if placed at the peri-discal tissue or at the muscle tender trigger points or terminal attachments [16]. The application is used on a case-by-case selection according to the origin of the pain and the response to treatment modalities. It requires three to four injection sessions done in 4–12 weeks intervals, which might be counted as a disadvantage (**Figures 8** and **9**). However, the availability of the injection material and the relatively lower cost is considered as advantages [16–18].

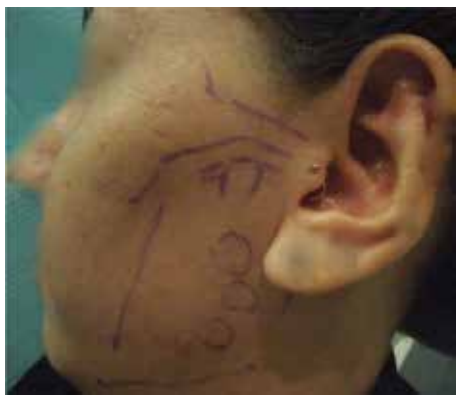

Figure 9. A 24-year-old female patient presented with chronic unilateral face, head, and neck pain that was diagnosed as TMD and myofascial disease with query Eagle's syndrome character. Part of the management protocol presented to her was prolotherapy injection at the TMJ complex. The marking is showing the anatomical topography of the area and illustrating the retrodiskal ligaments and anterior diskal attachment. The masseter muscle origin from the zygomatic arch is identified as well as the location of the major trigger points for evaluation and management. The patient responded very well to the TMJ/MFD protocol used and showed significant reduction of pain and improved functional ability.

6.3. TMJ lavage, arthrocentesis, and arthroscopy

Arthrocentesis is defined as using needles of particular size in order to reach inside the joint for the management of intracapsular disease. The procedure aims to flush the join from the inflammatory effusions, break the fibrous adhesions, mobilize the disc, and inject a lubricating viscoelastic agent, mainly comprising sodium hyaluronate [19]. Arthroscopy may add more to the benefit of this mode of treatment such as the ability to visualize any internal derangements using an endoscope, coagulate inflamed synovial lining with laser, and to manipulate or reposition of the disc as needed. Hence, the procedure is indicated toward cases of intracapsular disease primarily [20].

The success rate of this treatment modality is over 90% in some studies, and patients usually improve in a matter of 5–10 days postoperatively with increase in range of mouth opening. However, further follow-up visits, physiotherapy, occlusal therapy, and continuous care are necessary to avoid relapse. It is indicated in cases of internal TMD, painful clicks, decrease range of motion, or symptoms of disc displacement. MRI is usually performed preoperatively

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to confirm the type of derangements and stage of involvement. It might be contraindicated to use this treatment in cases of advanced TMD, ankylosis, or primary muscular disease that requires preemptive consideration [19–21]. The technique is directed toward inserting a circulatory flush to the superior joint space. The literature describes variable techniques to do so, starting from single-entry point, two, or even three while other literature reported that inferior joint space, although smaller in size, is reported to be effective in arthrocentesis [20, 21]. A line drawn from the mid-posterior tragus to lateral canthus can be used as an anatomical landmark to determine the entrance point. Points anterior to the mid-tragus of 10, 20, or 30 mm is another landmark to identify possible entry sites as following the area between the head of the condyle and inferior glenoid fossa margin. Asking the patient to slightly open the mouth or distracting the condyle antero-inferior can help locate the proper space. A lot of factors may change the entrance point such as age, remodeling, pathological disease, condyle shape, and different translational modes [20, 21].

Figure 10. a side view showing the needle entrance into the TMJ superior joint space as heading to arthrocentesis. The picture shows the landmarks as well as the tragus canthal line.

On occasions, practitioners might not succeed to establish the circulatory flow, which might be caused due to loss of the joint distention, false location, numerous fibrous compartments, or internal pathology such as ankylosis. The practitioner can indicate true entrance if the needles do touch inside or if the needles showed movement while moving the mandible. Flushing the joint usually takes place using either normal saline or Ringer's lactate. Volumes ranging from 100 to 500 cc reported in the literature. It is necessary that caution be taken while flushing the fluid as reckless forceful flush might destroy the joint anatomy and push the fluids elsewhere (**Figures 10–14**). Violation of the surrounding structures is rarely reported (such as the external auditory canal, lateral pharyngeal space, superficial masseteric space, or medial pterygoid space). Injuring the surrounding vascular bundle is possible (such as the superficial temporal vessels, branches of the facial nerve, or less likely the massteric vessels) [20, 21].

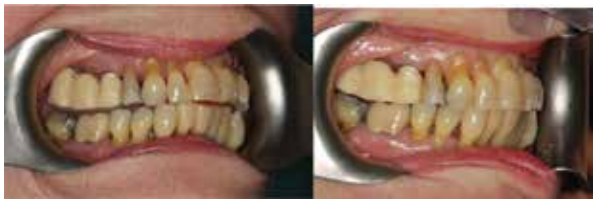

Figure 11. The left clinical picture showing a posterior open bite started immediately after prolonged dental care with a clinical diagnosis of acute disc displacement, and planned treatment with arthrocentesis under conscious sedation. The picture on the right showing the result illustrating the corrected occlusion position immediately after the procedure indicating replacing the acute disc displacement and allowing the condyle to move back in place.

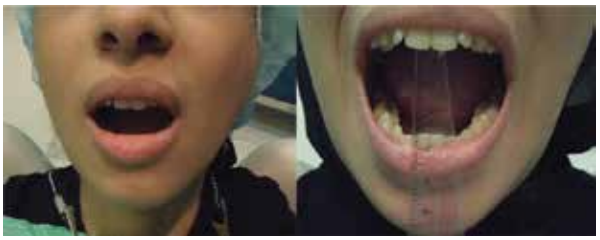

Figure 12. The left clinical frontal view showing another example of a patient that presented with disc displacement leading to hypomobility of the mandible and minimal mouth opening. On the right, improved mouth opening is indicated.

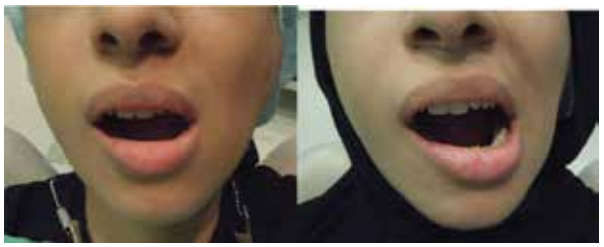

Figure 13. The same patient in Figure 11, showing limited excursion preoperatively (left picture) and improved mandible excursion post arthrocentesis on the right.

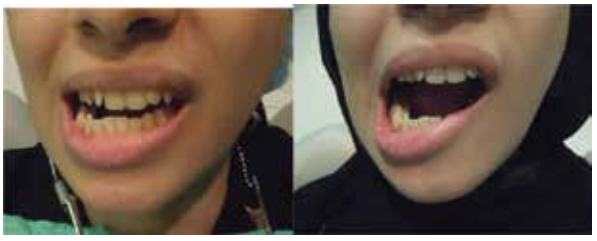

Figure 14. Pre- and post-arthrocentesis show the patient in Figures 11 and 12 with improved excursions toward the contralateral side.

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6.4. TMJ surgical intervention

Surgical intervention is defined as surgical maneuvers used to open the joint, violate the capsule, or/and surrounding structures to expose a diseased site and surgically correct it with or without reconstruction. Although description and classification of internal derangements took a lot of discussion in the literature in addition to descriptive classifications such as Wilk's being implemented, still the joint status classification is very descriptive and is not a clear indicator of the surgical intervention needed [22]. Hence, careful clinico-radiographic correlation is needed to design the best intervention. As pain, function, and patient satisfaction usually dictate further steps of the treatment modalities.

TMJ surgical maneuvers range from exposing the external joint structure and reorienting the capsule only, violating the capsule and manipulate the disc, or resecting and reconstructing the deformed structures. Once the joint is exposed, careful evaluation of the internal components takes place and search for signs of abnormalities such decortication, osteophytes, fibrous adhesions, erythematous linings, or deformed articular eminence. Once identified, correction can take place by reorientation, resection, and/or reconstruction.

Managing deformed joints can be in the form of gap arthroplasty where the internal surface of the joint is being investigated, prepared, and assure functioning capability. All osteophytes should be shaved to assure a healthy and smooth condylar surface. The use of temporalis muscle flap is advisable when discectomy is performed in addition to poor synovial lining to reduce the chances of ankylosis and for better joint structure compensation postoperatively [22, 23].

The disc and attachments can be more complicated to manage as commonly the disc is displaced or deformed to certain limit, where the operator has to decide either to repair, reorient, partially resect the disc, or completely remove the deformed disc. Afterward, a decision to reconstruct takes place according to the status. Disc conservative maneuvers found to be beneficial if the gross bow-tie shape and size are maintained, while it is not recommended to keep the disc if major deformation is identified. If the bony surfaces are presented to be deformation free, then disk procedures might be all that is needed, although rare. Since arthroplasty is commonly needed concomitantly with diskoplasty. Arthroplasty should be performed with caution and as conservative as possible to avoid further articular damage, unfavorable healing, and ankylosis. Arthroplasty is performed if osteophytes, bony spurs, and abnormal irregularities are identified, which can be smoothened using fine hand instruments, for example, bone file, to avoid heat generation. In case of poor access, partial eminectomy can be performed to allow better evaluation of cephalic and medial surfaces of the joint so better intervention can be delivered [22–24].

In case of disc perforation, it should be evaluated regarding the size of the perforation, the location, the degree of disc displacement, and the internal status of the joint and bone surface. Accordingly, a decision can be made to perform selective perforation margin excision and suturing, or, transferring the case into partial discectomy. Disc reposition and arthroplasty are commonly associated with such surgical interventions. Partial discectomy usually involves resecting the deformed portion of the disc, which is usually toward the latero-posterior aspect,

in addition to repositioning it more posteriorly, commonly called a "disc reshaping" procedure [22–24].

In situations where major deformity does exist at the disc joint complex, total discectomy is performed. It used to be a common procedure that took place in the 1980s with very promising results. As pain significantly subsides, condyle mobility and the joint maturation improve [24]. Usually, disk replacement takes place immediately rather than delayed. A lot of techniques introduced for replacement, such as temporalis pedicle flap, has an advantage of being harvested along the same surgical site, as a regional flap reconstruction [23]. Dermal grafts, conchal cartilage grafts, and synthetic materials have been used as well. The advantage of disk replacement is minimizing the chances of joint crepitation in comparison with the non-replacement option. The option of condylotomy is still advocated in cases of refractory pain to non-surgical management of TMDs. It is thought that it will change the condyle fossa relation and hence redistribute the force in the joint that might reduce the pain source.

Total joint reconstruction is used when a major deformity affects most of the joint structure that needs total reconstruction. The options vary between autogenous components and synthetics. Autogenous are mainly used in young growing patients especially if systemic rheumatic disease is not a factor destroying the joint. While synthetics are used in non-growing patients, a history of more than previous TMJ surgeries, previous alloplastic reconstruction, systemic rheumatoid disease, previously failed autogenous options, or the existence of major deformity secondary to tumor, trauma, or congenital anomaly that destroyed the anatomical boundaries. The success rate of reconstructing the joint is over 90% over 5 years and pain reduction of 89% [22, 25]. The addition of fat graft at and around the reconstruction area has increased the success rate, reduced pain, heterotrophic bone formation, and fibrosis incidents necessary to re-intervene at the surgical site post-reconstruction.

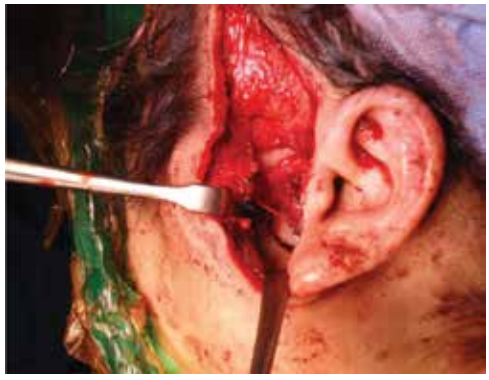

Figure 15. A 35-year-old female patient presented with history of rheumatoid arthritis affecting the TMJ leading to hypomobility and mouth opening of 10–15 mm for the last 2 years. The option of total joint reconstruction was not feasible at the time and hence, an attempt of gap arthroplasty, discectomy, and temporalis muscle flap transfer was planned. The picture showing the preauricular approach to the TMJ with the temporal extension for temporalis flap management. The wound shows the joint region after opening the capsule and identifying the internal structures.

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The major advantage of synthetic reconstruction is that it can be designed to custom fit the joint preoperatively, while the main disadvantages are the high cost of order and the possible prolonged delivery time (**Figures 15–19**).

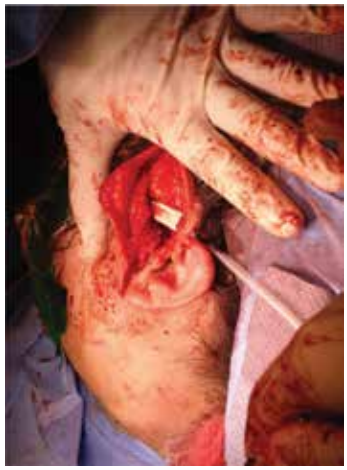

Figure 16. A drain is placed at the surgical site to avoid hematoma or seroma collection that might disturb the healing, the occlusion, and lead to infection.

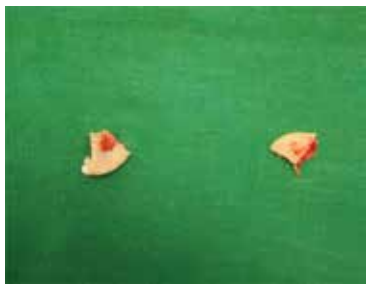

Figure 17. The coronoid process was removed bilaterally to facilitate better mandible mobility by removing the action of temporalis muscle.

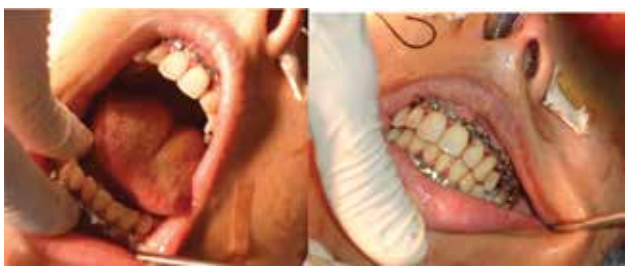

Figure 18. The left picture is showing the significant increase in mouth opening immediately intraoperatively as well as stable occlusion is maintained as seen on the right. The patient continued physical therapy postoperatively and proper medical follow ups including pain management protocol.

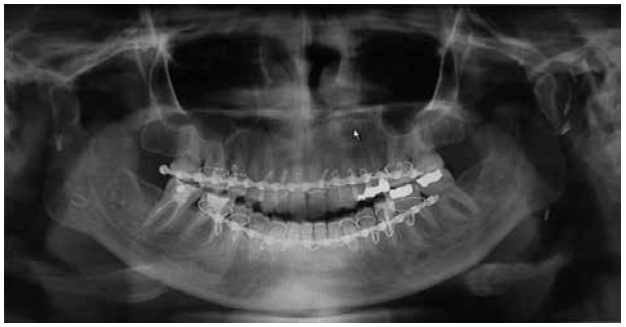

Figure 19. A postoperative panoramic radiograph showing the bilateral TMJ status, occlusion, and arch bars in place to aid in maintaining the occlusion using intermaxillary light elastics to guide the muscles and joint into the newly set status.

7. Conclusion

It is of prime importance toward the healthcare system and public health to carefully examine those patients in order to guide them in the right path of management. It has been discussed that delaying treatment can harm the patients and change their pain threshold level. It is necessary as well to understand that treatment modalities do vary, and the management strategy is customized to each case in particular. Hence, an expertise consultation is usually necessary early enough to come up with the best management plan.

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Chapter 7

Drug-Refractory Trigeminal Neuralgia: Treatment via Botulinum Toxin Type A

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Mohammad Hosein Kalantar Motamedi,
Misaq Heydari and Milad Heydari

Additional information is available at the end of the chapter

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Abstract

Trigeminal neuralgia (TN) is a disorder characterized by severe abrupt lancinating pains, limited to areas of distribution of the fifth cranial nerve—the trigeminal nerve. Numerous modals have been used to reduce or alleviate the intensity and frequency of pain. Drug therapy with anticonvulsive drugs is still the first choice. Migraine and occipital neuralgia have been treated via botulinum toxin type A (BTX-A). Symptoms of TN (pain duration, initiating factors, affected nerve branch, frequency of attacks, and severity of pain) are assessed before injections, and evaluated 1 week, 1 month, and 6 months after injection of 50 U reconstituted BTX-A solution in the trigger zones. Patients generally improve with regard to frequency and severity of pain attacks and in many, the pain is completely eradicated and there is no need for further medication. In some patients, nonsteroidal anti-inflammatory drugs (NSAIDs) may be needed to alleviate pain attacks. All patients develop higher pain thresholds after injections. Complications of BTX therapy include transient paresis of the facial nerve. BTX-A therapy is a minimally invasive method that can play a role in treating TN before other more invasive therapies, i.e., radiofrequency and surgery, are sought. In this chapter, we discuss the indication and method to treat TN via BTX-A in patients refractory to medical treatment.

Keywords: trigeminal neuralgia, botulinum toxin type A, treatment, drug-refractory, method

1. Introduction

The prevalence of trigeminal neuralgia (TN) in the population is about 1 in 25,000 people, and is slightly more in women. Patients are usually in midlife or older [1]. Numerous modals have been used to reduce or alleviate pain intensity and frequency. Drug therapy using anticonvulsive drugs is usually the first choice. Surgery (i.e., microvascular decompression [MVD], stereotactic rhizotomy, percutaneous balloon compression, and other methods) may be indicated [2]. Some of these treatment modalities may have severe complications. Confrontation of patients presenting with refractory cases also known as drug-refractory trigeminal neuralgia (DR-TN) show that further research is still warranted [3]. Botulinum toxin type A (BTX-A) is used to treat pains such as occipital neuralgia and migraine [4]. We have used BTX-A to treat DR-TN with good results.

1.1. Diagnosis

Patients were treated for DR-TN clinically documented according to the criteria defined for TN by the International Headache Society [5] and Winn's criteria (presence of paroxysmal unilateral sharp stabbing pain limited to a branch or branches of the trigeminal nerve, painful trigger zones (TZs), frequent pain-free intervals between paroxysms, unresponsive to anticonvulsants, and no neurologic deficit). Patients with a musculoskeletal disorder (considered to be a relative contraindication for BTX-A injection) or with a history of a surgical procedure on the cranial base for TN or pathologies (e.g., tumors) were not treated.

1.2. Trigger zones

TZs were identified by the patients and by clinical examination. Injection of lidocaine into TZs can both confirm the diagnosis (when the pain stops) and guide us to where we can inject the BTX (ensuring that we do not inject in the area of the branches of the facial nerve).

2. Treatment

Patients who have undergone medical treatment protocols (carbamazepine, antiepileptic drugs like gabapentin, cannabinoids, etc., for months to a year) can be treated with BTX-A. If they are or become ineffective then the patient is first injected with 1.8 ml lidocaine at the TZ. Injection of lidocaine into TZs alleviates the pain until the anesthetic wears off [6]. Pain recurs after the duration of the local anesthetic. This also ensures that the injection site (the TZ) is not on the facial nerve. The possibility of transient paresis is explained to the patients. Patient demographics, age, gender, presence of TZ, involvement site, involved nerve branch, total/partial success (after injection), and complications are documented. Pain symptoms, duration, provoking factors, nerve branch involved, frequency of attacks (per day), and pain severity (via visual analog scale) are documented just before injections and after 1 week, 1 month, and 6 months. The overall response to treatment is assessed and compared with that at baseline (before injection) [6].

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2.1. Technique

2.1.1. Preparation of the injection

Hundred patients between 22 and 70 years of age suffering from TN were treated at our center. The patients were first injected with 1.8 ml lidocaine at the TZ. This alleviates the pain until the anesthetic wears off [6]. This also ensures that the trigger point is not on the facial nerve. Three milliliters of normal saline solution is mixed in a vial of BTX-A; a fresh solution is prepared; 50 U of reconstituted BTX-A is injected at the TZs.

3. Outcomes

Data and pain characteristics of 100 patients between 22 and 70 years (mean 47 years) of age who were suffering from TN for 3 months to 24 years are presented in **Table 1**. In 35 patients, the mandibular nerve alone was the origin of pain and in 38 patients, it was the maxilla nerve. More than 1 branch of the trigeminal nerve was involved in 28 patients (both maxilla and mandible nerves in 4 patients, both maxilla and ophthalmic nerves in 1 patient). The ophthalmic nerve alone was involved in 5 patients. All of the patients improved regarding frequency and severity of pain attacks up to 6 months after injection (**Table 2**). In 35 patients, pain was completely eradicated; there was no need for further medication. In 34 patients, nonsteroidal anti-inflammatory drugs (NSAIDs) were enough to alleviate pain attacks, and 25 patients became responsive to anticonvulsive drugs after injection. Six months after the injection, a significant improvement in all the patients in the patient global assessment scale was seen. Complications included transient paresis of the buccal branch of the facial nerve in 3 patients; in 7 of them, it was not significant and resolved in 2 weeks; in the third patient, the paresis was severe, requiring physiotherapy for 3 months.

Patient	Gender	Age (y)	Provoking factors	Duration (mo)	Affected branch			Complications
					Mandible	Maxilla	Ophtalmic	
1	M	67	Spontaneous	36			x	Transient partial paralysis
2	M	28	Spontaneous	6	X	x		----
3	F	55	Spontaneous	24	×			Transient partial paralysis
4	M	62	Spontaneous	60		x		----
5	M	32	Spontaneous	12	×			----
6	M	48	Cold-Spontaneous	288		x	×	----
7	F	45	Touch-cold-stress	24	×	×		----
8	M	53	Speaking	48	×			----
9	M	65	Spontaneous	8		x		----
10	F	60	Spontaneous	60		x		----

Patient	Gender	Age (y)	Provoking factors	Duration (mo)	Affected branch			Complications
					Mandible	Maxilla	Ophtalmic	
11	F	29	Spontaneous-stress	18	x	x		----
12	M	34	Spontaneous	24	x			----
13	F	46	Spontaneous	6	x			----
14	F	51	Spontaneous	96		x		----
15	F	58	Spontaneous	24	x	x		Transient partial paralysis
16	F	**45**	Spontaneous-stress	**36**		X	X	----
17	M	**65**	Spontaneous	**12**	x			----
18	F	**22**	Spontaneous	**6**		x		----
19	M	**70**	Stress-touch	48	x			----
20	M	**34**	Spontaneous-touch	12	x			----
21	F	48	Spontaneous	6	x			----
22	M	61	Speaking-touch	48	x			----
23	M	66	Spontaneous	240		x		----
24	F	71	Spontaneous	8			X	----
25	F	65	Spontaneous	48		x		----
26	F	35	Speaking	48	x			----
27	M	46	Spontaneous	36	x	x		----
28	M	73	Spontaneous	240		x		----
29	F	51	Spontaneous	12		x		----
30	F	65	Spontaneous-touch-Speaking	120		x		----
31	M	74	Spontaneous	60	x			----
32	F	35	Spontaneous	6		X		----
33	F	55	Spontaneous	18	X			----
34	M	31	Spontaneous	12	X			----
35	M	59	Spontaneous	60	x			----
36	M	42	Spontaneous-touch	9		x		----
37	F	46	Spontaneous	12				----
38	F	32	Spontaneous	18	x	X		----
39	F	64	Spontaneous-touch	12		x		----
40	M	66	Spontaneous	180	x	X		----
41	M	44	Spontaneous	24		X		----

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Patient	Gender	Age (y)	Provoking factors	Duration (mo)	Affected branch			Complications
					Mandible	Maxilla	Ophtalmic	
42	M	71	Spontaneous-stress	240			X	Transient partial paralysis
43	F	65	Spontaneous	9		x		----
44	F	42	Spontaneous	120	x	x		----
45	M	44	Spontaneous	24	X	X		----
46	F	53	Spontaneous	48		X		----
47	F	32	Spontaneous	12			X	----
48	M	32	Spontaneous	12	x			----
49	M	65	Spontaneous	12		x	X	----
50	F	46	Cold-Touch	6	×			----

Table 1. Demographic data and pain characteristic of TN patients.

Patient	Severity of pain (VAS)			Frequency of attacks (per d)			Global assessment (after 6 mo)
	S_0	S_1	S_2	F_0	F_1	F_2	
1	10	3	2	60	5	3	3
2	8	0	0	10	0	0	4
3	7	2	2	25	2	3	4
4	10	4	2	40	5	5	3
5	9	0	0	20	0	0	4
6	6	0	0	30	0	0	3
7	7	0	0	15	0	0	4
8	5	0	0	45	0	0	4
9	10	5	5	50	10	10	1
10	9	2	2	60	5	8	3
11	5	0	0	5	0	0	4
12	8	2	1	10	2	2	4
13	10	3	2	50	20	20	2
14	6	0	0	25	0	0	4
15	10	2	2	50	5	10	3
16	7	1	1	22	3	3	RECENT CASE< 6 MO
17	5	2	1	12	1	2	RECENT CASE< 6 MO
18	8	0	0	16	0	0	RECENT CASE< 6 MO
19	10	3	3	34	2	2	RECENT CASE< 6 MO

Patient	Severity of pain (VAS)			Frequency of attacks (per d)			Global assessment (after 6 mo)
	S_0	S_1	S_2	F_0	F_1	F_2	
20	4	0	0	10	0	0	RECENT CASE< 6 MO
21	8	1	1	35	4	4	RECENT CASE< 6 MO
22	9	0	0	50	0	0	RECENT CASE< 6 MO
23	10	3	3	30	1	3	RECENT CASE< 6 MO
24	6	0	0	50	0	0	RECENT CASE< 6 MO
25	4	1	1	25	1	3	RECENT CASE< 6 MO
26	8	2	2	20	5	5	RECENT CASE< 6 MO
27	10	3	1	35	5	5	RECENT CASE< 6 MO
28	7	0	0	10	0	0	RECENT CASE< 6 MO
29	6	3	4	15	10	10	RECENT CASE< 6 MO
30	8	2	2	10	3	2	RECENT CASE< 6 MO
31	5	1	1	40	15	20	RECENT CASE< 6 MO
32	10	3	4	15	3	3	RECENT CASE< 6 MO
33	7	0	0	35	10	10	RECENT CASE< 6 MO
34	3	0	0	20	5	8	RECENT CASE< 6 MO
35	6	0	0	25	0	0	RECENT CASE< 6 MO
36	10	3	3	60	10	10	RECENT CASE< 6 MO
37	8	0	0	20	0	0	RECENT CASE< 6 MO
38	6	3	3	40	5	5	RECENT CASE< 6 MO
39	10	0	0	50	0	0	RECENT CASE< 6 MO
40	7	0	0	30	0	0	RECENT CASE< 6 MO
41	**6**	**4**	**4**	**30**	**10**	**15**	RECENT CASE< 6 MO
42	9	1	1	20	5	5	RECENT CASE< 6 MO
43	10	5	5	30	10	10	RECENT CASE< 6 MO
44	5	0	0	50	0	0	RECENT CASE< 6 MO
45	8	3	3	60	30	30	RECENT CASE< 6 MO
46	10	0	0	30	0	0	RECENT CASE< 6 MO
47	4	0	0	15	0	o	RECENT CASE< 6 MO
48	7	5	6	25	20	20	RECENT CASE< 6 MO
49	9	1	1	30	2	3	RECENT CASE< 6 MO
50	8	0	0	60	0	0	RECENT CASE< 6 MO

Table 2. Pain severity and frequency during the course of treatment.

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Because TN is a painful neuropathic disorder, it typically presents as paroxysmal or abrupt facial pain lasting from seconds to several minutes and rarely up to hours. The pain is described as stabbing electric shocks occurring spontaneously or after stimulation of a TZ. Idiopathic TN is seen in 1 in 100,000 people and more frequently in those aged more than 50 years. It may be typical (paroxysmal pain only) or atypical (association of a permanent background of pain). The facial skin is painful upon attacks in the area innervated by V1, V2, or V3 of the trigeminal nerve. An etiology often cannot be found. Pain is severe and may begin while talking or swallowing. Analgesics are usually ineffective. There may be a trigger point in the oral cavity that sparks the attack [7]. Treatment of TN is possible via medication or surgery.

4. Differentiation of dental pain and trigeminal neuralgia

4.1. Dental pain

Pulpitis or periapical infection can result in severe dental pain. In pulpitis, the patient often has nocturnal pain exacerbated by heat; radiographic findings may present caries or deep restorations. In a patient with the mentioned radiographic findings or endodontic treatment, there may be pain from a periapical infection not yet apparent on radiographs. In this case, the tooth may be felt to be extruded and painful upon percussion and to palpation over the apex of the tooth root in the vestibule; however, pain does not involve the facial skin. In dental pain, the cause is often apparent and the pain usually responds to analgesics. Radiographic findings are usually diagnostic and the origin of pain to the oral cavity, tooth or gum can be traced.

4.2. Trigeminal neuralgia pain

The pain from TN is said to feel like stabbing, electric shocks occurring spontaneously or following a TZ stimulation. TN pain is excruciating; this neuropathic disorder presents typically as paroxysmal or abrupt attacks lasting from seconds to one or more minutes and rarely up to several hours [7]. Idiopathic TN occurs in 1 in 100,000 people and is more frequently found in patients aged more than 50 years. It may be typical (i.e., with only paroxysmal pain) or atypical (i.e., association with a permanent background of pain). The skin of the face is painful upon TN attacks in the area innervated by V1, V2, or V3 of the trigeminal nerve; radiographic findings are often lacking and pain is not necessarily nocturnal. Often an etiology is not found. Pain is severe and may ensue when talking or swallowing. Analgesics are usually ineffective. Radiographs are not diagnostic and the origin of pain cannot be traced to the oral cavity upon examination. However, a trigger point in the oral cavity may be found that sparks the attack.

5. Other treatment approaches

5.1. Medical treatment approach

A medical approach is often used primarily in an attempt to treat TN noninvasively. This is usually accomplished using anticonvulsants. Carbamazepine is the classic medication chosen for this purpose. However, long-term studies have shown a gradual decrease in efficacy. Initial response is 80%. After 10 years, its effectiveness decreases by 50% [7]. Other antiepileptic drugs, such as gabapentin and cannabinoids, have also been used.

5.2. Neurectomy

Another method to treat TN is neurectomy. It has been reported to be successful in 88.2% patients. Balloon compression is another method used to treat TN, for which initial pain relief has been reported in 93% patients. Unilateral facial sensory loss has been reported in 61% of these patients [7].

5.3. Microvascular decompression

Use of MVD for TN which is caused by venous pressure is another effective method of treatment; pain recurrence ranges from 31.0% to 75%, within 1 to 3 years after operation, owing to development of new veins around the nerve root in 87.5% patients. Lee [8] did an electronic search of patient records from 1988 to 1998 and found that in 393 patients treated with MVD for TN caused by veins, the pain recurred in 122 patients (31.0%). MVD is a major neurosurgical operation that may have serious complications as well as prolonged convalescence [7].

5.4. Radiofrequency

Percutaneous radiofrequency thermocoagulation of the trigeminal ganglion (PRTTG) is an interventional treatment that is relatively safe and patients are treated as outpatients. It is less invasive in comparison to other invasive modes of treatment, is not very time consuming (30–60 minutes), and has a low complication rate. Motamedi and colleagues [7] did a study from 2000 to 2006, in which data from 65 patients treated for clinically documented TN (according to Winn's criteria) were assessed. Out of 65 patients, 36 (55.4%) females and 29 (44.6%) males with a mean age of 52.4 years (ranging from 21–75 years), a total of 51 (78.5%) patients were successfully treated; 14 (21.5%) were unsuccessful. The success rate was significantly higher for patients with defined TZs (74.5%) in comparison with those without defined TZs (25.5%). There was no need to repeat RF for the majority (72.3%) of the patients.

5.5. Botulinum toxin injection

Several studies have documented the beneficial effects of BTX-A on reducing the frequency and severity of TN. The actual mechanism is not well understood. Some believe that botulinum toxin injection inhibits secretion of acetylcholine in nerve endings, leading to relaxation of

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muscles and relief of pain; others think that the injection stops secretion of nociceptive neuropeptides in addition to acetylcholine, which helps prevent pain [9–11].

6. Conclusion

All our patients with DR-TN received 50–100 U BTX-A at each TZ. All experienced considerable pain relief and some were completely cured up to the time of writing. These findings were in accordance with the studies by Türk et al. [12] and Zúñiga et al. [13]. In both studies, the pain attacks were considerably alleviated. Türk et al. conducted a relatively similar study, in patients who were suffering from TN and injected with 100 U of botulinum solution below the zygomatic arch at the involved site [12]. Zúñiga et al. injected BTX into the subcutaneous tissue in patients suffering from TN and got good results [13]. In our study, partial paresis occurred in 3 patients, which resolved spontaneously in 2 cases and disappeared in the third patient after physiotherapy for 3 months. Injection of local anesthetic at the site before BTX injection may have prevented this. In series by Türk et al., no paresis was reported and complications were dysesthesia in one patient and difficulty in chewing in another [12]. In study by Zúñiga et al., paresis was reported in 1 patient who recovered spontaneously. In our study, complete cure was seen in 7 patients (1 had a 24-year history of severe pain).

In the other 8 patients, the severity and frequency of pain were reduced considerably. In all of these patients, pain threshold improved and a stronger stimulus was necessary to provoke TN pain, and pain attacks got weakened and duration got decreased. In conclusion, this study supports other similar studies and shows that BTX-A is a safe minimally invasive method that can play a role in treating TN before other more invasive therapies, i.e., radiofrequency and surgery are sought. However, long-term assessment is still under study.

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Section 5

Anesthesia and Sedation in Oral and Maxillofacial Surgery

Chapter 8

Anesthesia and Sedation

Jeffrey A. Elo and Ho-Hyun Sun

Additional information is available at the end of the chapter

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Abstract

Anxiety control and patient comfort are integral components of everyday oral and maxillofacial surgery (OMFS) practice. Moderate sedation, deep sedation (DS), and general anesthesia (GA) have been successfully administered by and in the offices of oral and maxillofacial surgeons (OMSs) and their anesthesia teams for more than 50 years. The goal of moderate sedation, DS, or GA in the OMFS office is to establish an environment in which patients are comfortable and cooperative while allowing the surgeon to safely perform the operation. This requires meticulous care in which the practitioner balances the depth of sedation and level of responsiveness while maintaining a patent airway, proper and adequate ventilation, and optimal cardiovascular hemodynamics. The record of safety among OMSs with this form of outpatient anesthesia is exemplary. The impressive morbidity and mortality statistics support the concept that the OMFS anesthesia team model is a safe, efficient, and cost-effective model for office-based ambulatory surgical-anesthesia care. Safe anesthesia practice depends on various items, including goals of anesthesia, selecting the proper patient, anesthetic technique utilized, drug regimen selection, monitoring, anesthetic team (staff and anesthesia provider) training, and the team's preparedness to handle unanticipated complications and medical/anesthetic emergencies.

Keywords: general anesthesia, pediatric anesthesia, levels of sedation, anesthetic agents, local anesthetics

1. Introduction

Moderate sedation, deep sedation, and general anesthesia have been successfully and safely administered by and in the offices of oral and maxillofacial surgeons (OMSs) and their

anesthesia teams for more than 50 years. [1–5]The goal of moderate sedation, deep sedation (DS), or general anesthesia (GA) in the oral and maxillofacial surgery (OMFS) office is to establish a safe environment in which the patient is comfortable and cooperative while allowing the surgeon to safely perform the indicated operation. This requires meticulous care in which the practitioner balances the patient's depth of sedation andlevel of responsiveness while maintaining a patent airway, proper and adequate ventilation,andoptimalcardiovascular hemodynamics. Several recent nationwide morbidity studies in the United States have demonstrated that these techniques are safe when used by OMSs who have completed an accredited OMFS residency program with formaltraininginanesthesiology. The impressivemorbidityandmortality statistics support the concept that the OMFS anesthesia team model is a safe, efficient, and cost-effective model for office-based ambulatory surgical-anesthesia care.

A preanesthetic patient assessment is a critical component of an OMS' practice. The standardization of the method of evaluating and documenting a patient's medical history and physical examination findings, as well as any pertinent diagnostic tests (laboratory and radiographic), is essential to formulating an accurate diagnosis and developing an effective anesthetic treatment plan. A comprehensive evaluation provides the basis for determining the surgical and anesthetic risk of each patient, and minimizes perioperative morbidity and complications associated with comorbid systemic health conditions. It is important to note that many comorbid medical conditions require consideration by the OMS. However, as each OMS has been trained during his/her surgical residency to complete a thorough pre-operative patient assessment, this chapter is not intended to describe the steps in how to perform an assessment; rather it will attempt to organize its process.

The processes described here establish a foundation for patient assessment and management as described in the American Association of Oral and Maxillofacial Surgeons' (AAOMS) Parameters of Care—2012 (AAOMS ParCare 2012) [9]. Specific diagnostic techniques and physical assessment protocols are purposely not defined, as it is not the authors' intent to dictate the methods for performing a patient assessment. The OMS has the freedom and ability to complete a patient assessment based on his/her training, the clinical circumstances of the patient, and the institutional standards under which the OMS practices.

The OMS is responsible for an initial history and physical examination necessary to determine the risk factors associated with the management of each patient. In some circumstances, the patient's primary care medical doctor may perform the history and physical examination, but it is ultimately the responsibility of the OMS to review such information and to ascertain whether it is complete to his/her level of satisfaction or whether further assessment and/or laboratory studies are indicated based on the specific patient and planned procedure. In cases when another health care provider (such as a primary care physician, cardiologist, or pediatrician) assesses the patient preoperatively, the OMS must ensure that the documented assessment also meets the parameters set forth in the AAOMS ParCare 2012 [9] The OMS is solely responsible for the final risk assessment of the patient and, ultimately, the decision to perform or not perform the surgical procedure. No other provider may assume this responsibility.

1.1. American Society of Anesthesiologists (ASA) Physical Status Patient Classification System

ASA class I	A normal healthy patient
ASA class II	A patient with mild systemic disease
ASA class III	A patient with severe systemic disease
ASA class IV	A patient with severe systemic disease that is a constant threat to life
ASA class V	A moribund patient who is not expected to survive without an operation
ASA class VI	A declared brain-dead patient whose organs are being removed for donor purposes

*Note: If a surgical procedure is performed emergently, an "E" is added to the previously defined ASA classification.

Table 1. American Society of Anesthesiologists Physical Status Patient Classification System

On the basis of a thorough patient assessment, an ASA physical status should be assigned to all surgical patients according to the guidelines set forth by the ASA (**Table 1**).

1.2. Preoperative fasting guidelines

Every healthy patient without a risk of gastroparesis who will undergo a sedation or general anesthetic procedure should maintain a "nothing per mouth" (NPO) status (**Table 2**). The ASA [10] recommends a 2-h fasting period of clear liquids for all patients. The ASA recommends a fasting period for breast milk of 4 h and for infant formula or nonhuman milk of 6 h for neonates and infants. For solid foods in most adult patients, the ASA recommends fasting periods of at least 6 h (light meal such as toast and clear liquid) or 8 h (fatty or fried foods or meat). For infants and children, the fasting period for solids should be at least 6 h.

Ingested material	Minimum fasting period
Clear liquids	2 h
Breast milk	4 h
Infant formula	6 h
Nonhuman milk	6 h
Light meal	6 h
Fatty meal	8 h

Table 2. American Society of Anesthesiologists Fasting Guidelines [10]

The preoperative use of gastric stimulants, gastric acid secretion blockers (histamine H_2 receptor antagonist agents), antacids, antiemetic agents, and/or anticholinergic medications (to decrease the risk of pulmonary aspiration) is not routinely recommended [10] Their use should be based on the individual patient assessment.

1.3. Discharge criteria

All patients who have undergone outpatient surgery using moderate sedation, DS, or GA must meet minimal criteria to permit safe discharge from the OMFS office or outpatient surgical facility. Such criteria may include either the use of an Aldrete Score (**Table 3**), Post-Anesthesia Discharge Scoring System (PADSS or modified PADSS), or another equivalent. The patient must arrive at the office or surgical facility with a responsible adult escort for discharge after surgery and anesthesia.

Criteria	Points
Oxygenation	
SpO_2 > 92% on room air	2
SpO_2 > 90% on oxygen	1
SpO_2 < 90% on oxygen	0
Respiration	
Breathes deeply and coughs freely	2
Dyspneic, shallow, or limited breathing	1
Apnea	0
Circulation	
BP ± 20% of normal	2
BP ± 20–50% of normal	1
BP ± > 50% of normal	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responsive	0
Activity	
Moves all extremities	2
Moves two extremities	1
No movement	0

A total score of 9 or 10 shows readiness for discharge.

Table 3. Post-anesthetic Aldrete recovery score.

1.4. Special considerations for pediatric patients

When performing physical examinations on pediatric patients, it is critical to remember the differences between children at various ages and adults with regard to anatomy (e.g., airway), vital signs (e.g., heart and respiratory rates), and physiology (greater body surface area or mass

and cardiac output). Cardiac output is more heart rate dependent in the child than in the adult. When assessing the child for anesthesia, the OMS must also pay particular attention to the patient's allergy history for the common childhood precipitants of asthmatic attacks: pollen, other indoor or outdoor airborne irritants, animal hair, physical exercise, and/or anxiety. Upper respiratory tract infections that produce airway irritability are exceedingly common in young children. Specific reactions to suspected drug allergens should be ascertained through allergy testing with, for example, an allergy panel. Noted differences between the pediatric and adult airways include: higher, more anterior position of the glottis opening in the child; relatively larger tongue in the infant; larger and more floppy epiglottis in the child; the subglottic region as the functionally narrowest portion of the pediatric airway versus the vocal cords in the adult; and larger relative size of the occiput in the infant.

1.5. Preoperative cardiac and pulmonary assessment

It comes as no surprise to the seasoned OMS/anesthesia provider that the two most important systems to consider on patient evaluation are the cardiac and pulmonary systems. Perioperative adverse cardiac events may occur in the OMFS patient. High-risk patients can usually be identified during a comprehensive history, review of systems, and physical examination. The history should elicit conditions such as stable (ASA 3) or unstable (ASA 4) angina, recent or past myocardial infarction with or without cardiac stent and appropriate anticoagulation, heart failure—compensated or decompensated, significant arrhythmias, valvular disease, and the presence of a pacemaker or a defibrillator. Patients should be questioned on their smoking status (current or former use, how many cigarettes per day, how many years), management and control of their blood sugars in diabetes mellitus, and renal insufficiency. Functional status should be quantified based on the metabolic equivalent (MET) (**Table 4**), which is used in the American College of Cardiology/American Heart Association Guidelines (ACC/AHA) [11]. For example, a person functioning at 1 MET is limited to simple activities such as eating, dressing, and using the toilet. A person with 4 METs can climb a flight of stairs, walk up a hill, or walk on level ground at 4 mph, and would generally not require an extensive cardiac workup. Physical examination should be used to look for jugular venous distention, arrhythmias, and abnormal heart sounds such as an S_3 gallop or murmur. The information obtained from the history and examination can be used to assess risk and to direct further testing.

MET	Functional levels of exercise
1	Eating, working at a computer, dressing
2	Walking down stairs or in your house, cooking
3	Walking 1–2 blocks
4	Raking leaves, gardening
5	Climbing 1 flight of stairs, dancing, bicycling
6	Playing golf, carrying clubs
7	Playing singles tennis

MET	Functional levels of exercise
8	Rapidly climbing stairs, jogging slowly
9	Jumping rope slowly, moderate cycling
10	Swimming quickly, running or jogging briskly
11	Skiing cross-country, playing full-court basketball
12	Running rapidly for moderate to long distances

MET, metabolic equivalent of the task. 1 MET is defined as the amount of oxygen consumed while sitting at rest and is equal to 3.5 mL O_2 per kilogram of body weight × min. The MET concept represents a simple, practical, and easily understood procedure for expressing the energy cost of physical activities as a multiple of the resting metabolic rate. The energy cost of an activity can be determined by dividing the relative oxygen cost of the activity (mL O_2/kg/min) by 3.5 [12].

Table 4. Estimated energy requirements for various activities (METs)

Indices for assessment of cardiac morbidity and mortality in noncardiac surgery have been established. The Revised Cardiac Risk Index (RCRI) is one such important assessment tool (**Table 5**). If it is determined that the patient is at significant risk for a postoperative cardiac event, further workup should be conducted and the condition should be optimized prior to the surgical procedure, if possible. Consultation with the patient's cardiologist should be sought when coronary or valvular disease is suspected or if assistance is needed with management of pacemakers or defibrillators.

Risk factors	
Ischemic heart disease	
Congestive heart failure	
Cerebrovascular disease	
Diabetes mellitus requiring preoperative insulin	
Serum creatinine > 2.0 mg/dL	
High-risk surgery (intraperitoneal, intrathoracic, or suprainguinal vascular)	
RCRI classification	**Event rate (%)**
Low risk (0 factors)	0.5
Low risk (1 factor)	1.3
Intermediate risk (2 factors)	3.6
High risk (3 or more factors)	9.1

Table 5. Revised Cardiac Risk Index (RCRI) [13].

1.6. Twelve-lead electrocardiogram (ECG)

A preoperative ECG is indicated within 30 days prior to the surgical procedure in patients with known coronary disease, peripheral vascular disease, or cerebrovascular disease. It may be

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reasonable to obtain an ECG in patients with a single clinical risk factor (e.g., diabetes mellitus, renal insufficiency, or congestive heart failure) who are to have an intermediate risk operation (more than "minor" oral surgical procedures). There is no evidence to support the routine use of ECG in patients without risk factors.

1.7. Noninvasive testing of left ventricular function

Evaluation of left ventricular function by radionuclide angiography or echocardiography is reasonable in patients with dyspnea of unknown origin or worsening dyspnea in the setting of known congestive heart failure (decompensated). The routine evaluation of left ventricular function is not otherwise indicated.

1.8. Noninvasive stress testing

Noninvasive stress testing involves radionuclide or echocardiographic imaging combined with pharmacologic stress to evaluate for ischemia and arrhythmias in patients who are unable to exercise. Patients with one or two clinical risk factors and poor functional capacity (<4 METs) should be considered for noninvasive stress testing. Routine noninvasive stress testing is not indicated in patients without clinical risk factors. Patients with active cardiac conditions should usually be evaluated by other methods.

1.9. Pulmonary and airway assessment

Patient-related risk factors for perioperative pulmonary complications include chronic obstructive pulmonary disease (COPD), pneumonia, sleep apnea, dyspnea, advanced age, obesity, and smoking [14, 15]. The most important part of a pulmonary risk assessment is a thorough history and physical examination. Specifically, the patient should be asked about shortness of breath, dyspnea on exertion, productive coughs, and symptoms of sleep apnea. A smoking history should also be obtained. Smoking cessation may reduce postoperative pulmonary complications. Patients experience increased mucociliary response and airway hypersensitivity shortly upon termination of smoking which will increase the risk of pulmonary complications. Ideally, patients should stop smoking for at least 8 weeks prior to the surgical procedure in order to reduce pulmonary morbidity.

Sleep apnea is a common and underdiagnosed problem [16]. Risk factors include obesity, male gender, a short/stout neck, macroglossia, and enlarged tonsils (**Table 6**). Symptoms and signs related to apnea are snoring, nighttime choking, or gasping, observed cessation of breathing by a partner, morning headaches, and daytime somnolence. Premedication with clonidine [17] given the night before and 2 h prior to surgery has been shown to reduce the need for operative anesthesia and to improve perioperative hemodynamics, anesthetic recovery, and pain control.

The Mallampati classification is a scoring system that relates the amount of mouth opening to the size of the tongue, and provides an estimate of space available for oral intubation by direct laryngoscopy. According to the Mallampati scale (**Figure 1**), class one is present when the soft palate, uvula, and pillars are visible, class two when the soft palate and base of the uvula are

visible, class three when only the soft palate is visible, and class four when only the hard palate is visible.

Degree of tonsils blockage	Ratio of the tonsil in the oropharynx
Degree 0	Tonsils in the fossa
Degree 1	Tonsil occupies < 25% of the oropharynx
Degree 2	Tonsil occupies 25–50% of the oropharynx
Degree 3	Tonsil occupies 50–75% of the oropharynx
Degree 4	Tonsil occupies > 75% of the oropharynx

Table 6. Brodsky tonsil classification system

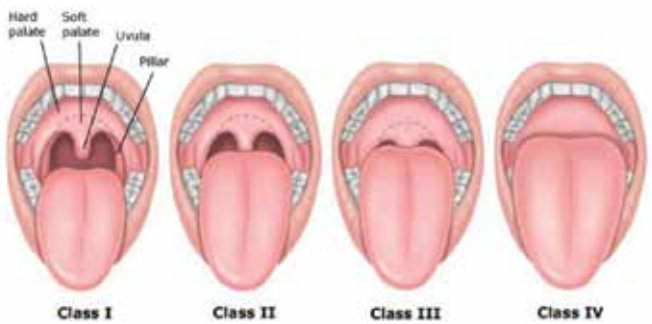

Figure 1. Mallampati classification.

1.10. Renal/endocrine systems assessment

Renal failure has been associated with increased risks of surgical infection and issues with wound healing [18]. It can also lead to disturbances in electrolytes and fluid balance, which may exacerbate the physiologic changes occurring during the perioperative period. In the patient with known or suspected renal failure, it may be prudent to evaluate the serum concentrations of the patient's potassium, magnesium, calcium, and phosphate. Blood urea nitrogen and creatinine assays should be obtained. Patients with newly diagnosed renal failure should be evaluated by a nephrologist prior to general anesthesia and surgery. Dialysis may be indicated if the uremia is found to be significant [19].

1.11. Diabetes and hyperglycemia

The prevalence of diabetes in the United States has been increasing and is currently estimated to be about 10%. Many more individuals likely remain undiagnosed. Hyperglycemia has been associated with immune dysfunction, elevation of inflammatory markers, vascular endothe-

lium dysfunction, and thrombosis. Clinically, hyperglycemia can lead to increased surgical site infection and postoperative mortality [20–23].

At-risk patients should be assessed for hyperglycemia prior to surgery. Known diabetics should have their hemoglobin A1c levels evaluated along with a fasting serum glucose test. Optimization of blood glucose control prior to surgical intervention should be undertaken, if possible. For nondiabetic patients at risk of hyperglycemia (e.g., the obese and the elderly), consideration should be given to measuring the preoperative and intraoperative fasting glucose level. If these levels are found to be elevated, measures to tightly control serum glucose (e.g., insulin infusion) should be initiated [21, 22, 24].

1.12. Summary of preoperative assessment

Risk evaluation should be done for every OMFS patient. A diligent evaluation using the presented guidelines will allow optimization of care throughout the perioperative period. The ultimate goal of achieving improved outcomes should encourage the consistent assessment of all potential risk factors for each patient.

2. Sedation

2.1. Levels of sedation

The American Dental Association (ADA) has incorporated the American Society of Anesthesiology (ASA) definitions for use in its own published guidelines. The categorization as detailed by both the ASA and ADA focuses on the concept that the spectrum of sedation and anesthesia is a continuum extending from mild sedation (anxiolysis) to moderate sedation and analgesia ("conscious sedation") to deep sedation and analgesia to general anesthesia. The ASA and ADA differentiate these levels based on four parameters, which measure responsiveness, airway integrity, spontaneous ventilation, and cardiovascular hemodynamics (**Table 7**).

Minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes, ventilatory, and cardiovascular functions are unaffected.

Moderate sedation/analgesia ("conscious sedation") is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

Deep sedation/analgesia is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

General anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

Characteristic	Minimal sedation	Moderate sedation and analgesia	Deep sedation and analgesia	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

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[†]Reflex withdrawal from a painful stimulus is not considered a purposeful response

Table 7. Continuum of depth of sedation: definition of general anesthesia and levels of sedation and analgesia

In most situations, the primary goal of outpatient sedation in the OMFS office is to achieve comfort and cooperation which is accomplished by a drug-induced alteration in consciousness. Responsiveness can be used as the primary parameter to assess the state of consciousness, which defines the desired anesthetic level. The terms mild, moderate, deep, and general descriptively imply both the desired response and depth of sedation. Given sufficient anesthetic medications, a patient will proceed from a state of relaxation with a normal response to verbal stimulation to a state in which they are unarousable.

Most anesthetic agents cause airway musculature relaxation and depress the hypoxic and hypercapnic respiratory drive, which have the potential to impair airway integrity and patency as well as spontaneous ventilation. As the level of sedation becomes deeper, both airway patency and spontaneous ventilation may and will ultimately require intervention and assistance.

Sedation is a continuous spectrum, and there is always a danger for the patient's airway to become compromised, which can go unnoticed in the absence of diligent monitoring. In addition, patient responsiveness and depth of anesthesia fluctuate depending on the level of stimulation. When the patient is more responsive, there may be a temptation to administer additional sedative medication. However, sustained procedural stimulation is rare and if

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additional anesthetic medication is administered to diminish patient responsiveness, respiratory depression may result upon cessation of the procedural stimulation. This presents one of the limitations with the lighter levels of sedation as patient comfort and cooperation may be unachievable without infringing on the potential of adverse events.

It is important for the OMS to be cognizant that levels of sedation are independent of the route of administration or the selection of anesthetic agent. The OMS must also be cognizant that there is a wide variability in patient response to the various anesthetic medications, which could produce a more profoundly sedated patient than desired or anticipated.

2.2. Monitoring in OMFS sedation

The OMS/anesthesia provider is responsible for continuously monitoring the sedated patient. This consists of direct observation as well as utilization and interpretation of cardiovascular and respiratory monitors. Adverse respiratory events have been the primary etiology resulting in adverse outcomes. Standard of care in OMFS offices dictates that the following monitors be applied: pulse oximeter, noninvasive blood pressure monitoring, electrocardiography, capnography, and pretracheal stethoscope auscultation.

Pulse oximetry has been the standard of care for monitoring oxygen saturation for almost three decades. Pulse oximetry measures the amount of oxygen carried by hemoglobin molecules in arterial blood (oxygen saturation), which is displayed as a percentage. Arterial oxygen content is inferred (but not directly measured) from the percent hemoglobin saturation on the oxygen-hemoglobin dissociation curve.

Partial or complete airway obstruction and ventilatory depression from anesthetic medication, if not remediated, will result in an eventual decrease in arterial oxygen content which can be detected by pulse oximetry. However, it is important to realize that there will be at least a 20–30-s delay in the detection of these events as pulse oximetry measures hemoglobin saturation at the fingertip where blood may take up to 20–30 s to travel from the core circulation. Administration of supplemental oxygen will further postpone the onset of desaturation with airway obstruction or ventilatory compromise. For these reasons, pulse oximetry is not an efficient ventilatory monitor.

Ventilation is the movement of gas in and out of the lungs. Ventilatory monitoring for deep sedation and general anesthesia can be best accomplished with both capnography and a pretracheal stethoscope. Capnography typically utilizes infrared gas analysis technology to assess the concentration of carbon dioxide in inspired and expired air. The capnographic unit provides both an absolute end-tidal carbon dioxide ($ETCO_2$) value as well as a graphic demonstration of the patient's ventilation pattern (**Table 8**). In an open system (e.g., nonintubated patient), the exhaled air may be diluted with ambient air, minimizing the benefit of capnography; however, the graphic display can provide visual cues for the respiratory rate as well as an impairment of gas exchange (e.g., obstruction, bronchospasm). In addition, changes in ventilation, such as a change in the graphic display suggestive of airway obstruction, are detected and displayed immediately. The practitioner must be cognizant that capnography can fail in an open system as there is no direct sealed conduit between alveoli and the monitor.

The combination of both capnography and pretracheal auscultation improves the accuracy of ventilatory monitoring, as $ETCO_2$ sampled from the nose in a mouth breather can be inaccurate, and pretracheal auscultation during slow ventilation in an open airway can be silent or difficult to hear.

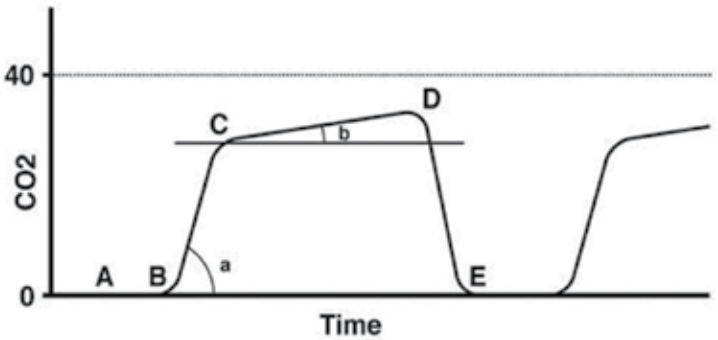

Table 8. End tidal CO_2 monitor graphical recording

3. Anesthetic agents

3.1. Clinical summary

An administered drug's activity is determined by its ability to cross the blood-brain barrier (degree of lipid solubility) to reach and bind respective central nervous system (CNS) receptors [the "vessel rich" group receives 75% of cardiac output (CO)] in sufficient concentration to exert its intended actions such as analgesia, sedation, hypnosis, and/or amnesia. A drug's side effects are usually due to its action at locations other than its targeted receptors. A drug's action is also dependent on the dose given, the rate of administration, and receptor number and

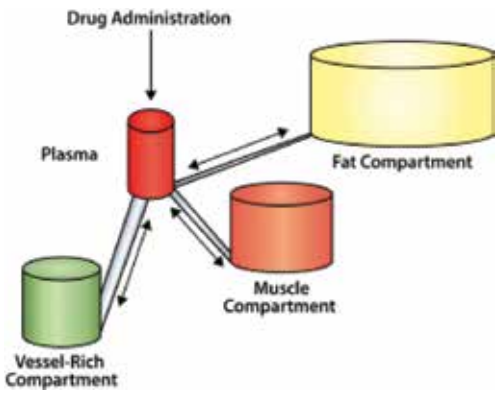

Figure 2. Drug distribution to various body compartments.

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sensitivity, with a wide range of variability among patients. The actions of most short-acting drugs are terminated by redistribution ($T_{1/2}\alpha$) to other compartments (**Figure 2**). Longer-acting drugs are terminated by metabolism ($T_{1/2}\beta$) in the liver into smaller, water soluble moieties which can then be filtered and excreted by the kidney (or in sweat, mucus from the lungs, and gastrointestinal excretions to a small extent). Drugs may also "hide" in muscular (20% of CO), adipose (5% of CO) tissues or remain bound to plasma proteins (**Figure 3**), in which cases the intended receptors are not activated and clinical effects are absent (**Figure 4**). "Hidden drugs" can subsequently redistribute from "hidden reservoirs" prior to metabolism, causing a return or additive clinical effect also known as hangover. Hypoproteinemia (e.g., cachexia, anorexia, liver disease) will similarly enhance drug availability and action.

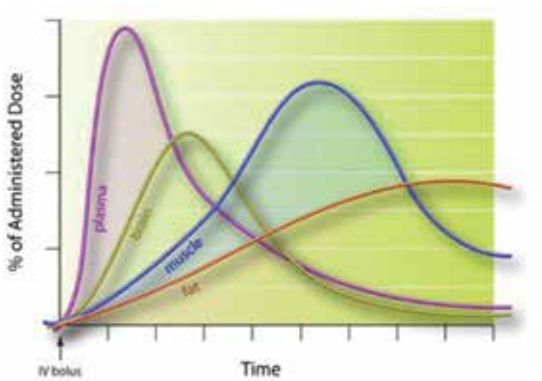

Figure 3. Drug distribution to various compartments over time.

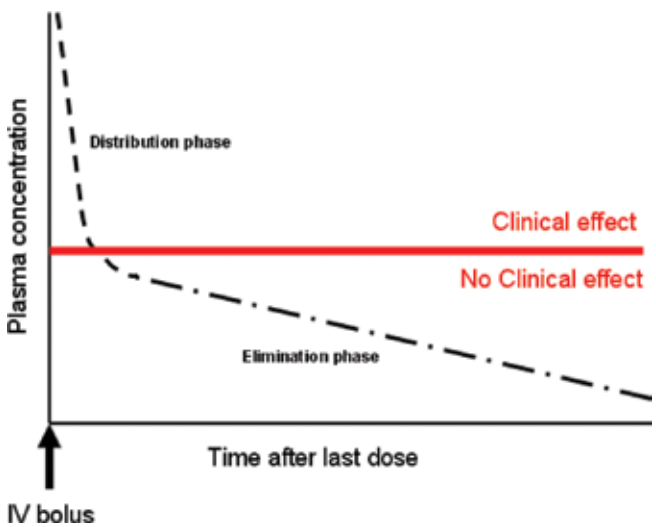

Figure 4. Plasma drug concentration versus time after an intravenous (IV) dose.

4. Review of anesthetic medications

This section focuses on describing many of the characteristics and properties of some of the most commonly used in-OMFS-office sedatives. The list of medications described here is not intended to be exclusive. The authors realize that with variations in OMFS training programs, variations in preferred drug regimens exist.

4.1. Benzodiazepines

Mechanism of action: bind to and enhance $GABA_A$ receptors to the actions of GABA ("GABAergic"), increase chloride conductance, and hyperpolarize neurons, thereby interrupting nerve transmissions. Benzodiazepines can be described as agonists of inhibitory GABA receptors.

Intended effects include sedation, anxiolysis, anterograde amnesia, muscle relaxation, and anticonvulsant activity. Benzodiazepines exert minimal cardiovascular effects and respiratory depression (decreased tidal volume and increased respiratory rate). They suppress psychotomimetic ketamine effects.

Adverse side effects include minimal cardiovascular or respiratory changes when used alone in therapeutic dose; however, benzodiazepines are synergistic with other agents. A paradoxical excitement (disinhibition) reaction is possible in patients at age extremes and in anxious teenage patients.

Benzodiazepines are metabolized via the liver and are excreted renally.

Midazolam: Water soluble until aromatic ring closes at pH > 4 (after injection), which enhances lipid solubility. Can be given by mouth (PO), intravenously (IV), or intramuscularly (IM). Midazolam has minimally active metabolites. Adult sedation/anxiolysis: 5 mg or 0.07 mg/kg IM; or 1 mg IV slowly q2–3 min up to 5 mg. Pediatric premedication dose ~0.25–1.0 mg/kg up to 20 mg maximum PO, or 0.1–0.15 mg/kg IM. Midazolam has an IV onset time of 1.5–5 min, peak effects at 4–8 min, and duration of 15–20 min.

Diazepam: Diazepam is a lipid soluble agent that requires propylene glycol to dissolve in water, which in turn creates a risk for thrombophlebitis. It features erratic IM absorption but can be given PO, IV, or IM. Physiologically, diazepam is metabolized to oxydiazepam, which is an active metabolite and contributes to a longer duration of action and hangover compared to midazolam. Diazepam has an IV onset time of 1.5–5 min, peak effects at 3–5 min, and duration of 15–60 min.

4.2. Flumazenil

Flumazenil is an inhibitory agonist of the GABA-benzodiazepine receptor complex (specifically) with no intrinsic activity. It will occupy a "free" receptor but will not displace other agonists and is therefore not very effective for quick reversal after an overdose. It is characterized by its high affinity, short duration, and possible contraindication in patients with seizure disorders as it may trigger seizures in patients who rely on benzodiazepines for seizure

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control. Other side effects may include agitation, arrhythmias, and dizziness, pain on injection, nausea/vomiting (N/V), sweating, headaches, and blurred vision. The dose for benzodiazepine sedation reversal is 0.2 mg IV over 15 s, then 0.2 mg q1 min as needed up to 1 mg total dose. The dose for benzodiazepine overdose reversal is 0.2 mg IV over 30 s, then 0.3–0.5 mg q30 s as needed up to 3 mg total dose.

4.3. Opioids

Mechanism of action: opioid medications bind to multiple opioid receptors, most notably at the central nervous system (brain and spinal cord) mu receptors.

Intended effects of opioids include analgesia, attenuation of the neuroendocrine stress response, blunted laryngeal reflex, sedation, euphoria, and mental clouding. Opioids also provide cardiovascular stability.

Adverse side effects include vagal nerve mediated bradycardia, decreased sympathetic tone (decrease in systemic vascular resistance leading to hypotension), pupillary constriction, respiratory depression (blunted response to hypercarbia), N/V, muscular rigidity with rapid or high dosing (which initiates at the small muscles of the larynx then progresses to the chest wall and skeletal muscles), pruritus, histamine release (seen with morphine and meperidine).

The majority of opioids are metabolized via the liver, though remifentanil is metabolized in the plasma.

4.4. Opioid receptors include the following: mu, delta, kappa, sigma

Mu (μ) receptors are located primarily in the brainstem and medial thalamus. Binding to these lead to supraspinal analgesia, respiratory depression, euphoria, sedation, decreased gastrointestinal motility, and physical dependence.

Delta (δ) receptors are localized largely in the basal ganglia and the neocortical regions of the brain, though their effects are not well studied. It is believed they may be responsible for psychomimetic and dysphoric effects.

Kappa (k) receptors are located in the limbic and other diencephalic areas, the brain stem, and the spinal cord. They primarily induce spinal analgesia, sedation, dyspnea, dependence, dysphoria, and respiratory depression.

Sigma (Σ) receptors have been described as being responsible for dysphoria and hypertonia.

Fentanyl is a commonly used in-office synthetic opioid medication (phenylpiperidine class) that is 100 times more potent than morphine (phenanthrene class). It acts at a variety of receptors within the central nervous system (mu, kappa, delta, and sigma). It produces venodilation, a decrease in heart rate via vagal response, and respiratory depression (dose dependent). It affects respiratory rate more than tidal volume, decreases stress response to surgery, and is metabolized by the liver to be excreted in the urine and bile. Potential side effects include: cough-suppression, constipation, urinary retention, biliary tract spasm, and muscle rigidity. It has an IV onset time of 5+ min, peak effects at 6 min, and duration of approximately 1 h.

Remifentanil is an atypical phenylpiperidine opioid that is metabolized by plasma esterases. It must be delivered as an IV bolus or via continuous infusion. Apnea and hypotension are more common with remifentanil than with other opioids. It has a very rapid onset (due to a small volume of distribution that is 1/10 that of fentanyl) and offset (esterase metabolism) and has a clearance that is more than 2.5 times as rapid as the other opioids'. It has an IV onset time of 1 min, offset time of 5+ min, peak effects at <1 min, and duration of 3–5 min regardless of the duration of infusion, age, or renal and hepatic status. It is supplied as a powder that must be reconstituted.

Meperidine is a pure synthetic opioid that has an active metabolite, normeperidine, which has half the potency but possesses proconvulsant potential. Meperidine has a slight anticholinergic effect, releases histamine, slightly elevates heart rate, and can be effective for controlling postoperative/post-anesthetic shivering, xerostomia, and mydriasis. It is contraindicated for us with monoamine oxidase inhibitors (MAOIs) as both drugs will increase serotonin and can trigger serotonin syndrome (too much serotonin), which consists of cognitive (confusion, agitation, and lethargy), autonomic (hyperadrenergic state), and somatic (myoclonic, twitching, and tremor) symptoms. It has an IV onset time of 5 min and duration of 2–3 h.

4.5. Opioid antagonist

Naloxone is a competitive antagonist of all opioid receptors—it can displace an agonist if the affinity and/or concentration of this antagonist are greater than the affinity and/or concentration of the agonist. The resultant effect is the reversal of the analgesic and ventilatory depressant effects of the opioid. There is a concern about a possible premature termination of the antagonistic effects. If naloxone is used to rescue overdose-induced ventilatory insufficiency, the practitioner must monitor the patient for an additional 1–2 h to ensure against re-sedation. Possible side effects can include flash pulmonary edema (usually in patients with cardiovascular diseases), dysphoria and withdrawal symptoms (in patients who are dependent on opioids for chronic pain relief and where rapid reversal will trigger intense pain), and sympathetic hypertension with possible pulmonary consequences. The usual dosing for adult post-op reversal is 0.1–0.2 mg q2–3 min as needed. Its duration is 30–45 min.

4.6. NMDA receptor antagonist

Ketamine is a phencyclidine derivative. Its pharmacodynamics involves analgesia, anesthesia, and sympathomimetic effects that are mediated by different receptor sites. Non-competitive NMDA (N-methyl-D-aspartate) receptor antagonism is associated with the analgesic effects, opiate receptors may contribute to analgesia and dysphoric reactions, and sympathomimetic properties may result from enhanced central and peripheral monoaminergic transmission. Ketamine blocks dopamine reuptake and therefore elevates synaptic dopamine levels [25]. Inhibition of central and peripheral cholinergic transmission could contribute to induction of the anesthetic state and hallucinations [26]. Ketamine is structurally similar to PCP (phencyclidine), but 10–50 times less potent in blocking NMDA effects. The exact mechanism of action is unclear. Ketamine produces dissociative anesthesia between the thalamocortical and limbic systems; that is, patients do not perceive painful, visual, or auditory stimuli and appear to be

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in a cataleptic state. Ketamine is also a direct myocardial depressant. Central sympathomimetics cause a non-dose dependent increase in the heart rate, cardiac output, and blood pressure. It relaxes bronchial smooth muscles but has a minimal effect on the respiratory drive. Ketamine's expected effects are excellent analgesia [27], strong anterograde amnesia, preserved laryngeal reflexes, suppression of convulsive neuronal activities, increased intraocular and intracranial pressures, and increased salivation and lacrimation. Its adverse effects include possible emergence delirium (especially seen with large doses in elderly and pediatric patients, females, and those with underlying personality disorders [28]), dose-related increases in muscle tone, random non-triggered movements, nausea, and vomiting. For common in-office OMFS sedation use, usual dosage (the "low dose IV regimen") is 0.1–0.5 mg/kg which is most often combined with additional benzodiazepines, an opioid, and propofol. Dosages of 1–2 mg/kg IV over 1–2 min or 4 mg/kg IM induce 10–20 min of a dissociative state. Its onset time is very rapid (<1 min), and its duration is 10–15 min. Ketamine is metabolized in the liver and is renally excreted.

4.7. Imidazole derivatives

Etomidate is a GABA agonist that is used for rapid induction of dose-dependent sedation/anesthesia when hypotension cannot be tolerated and cardiovascular stability must be maintained after bolus induction. It has a wide therapeutic index and is the induction agent of choice in patients with severe cardiovascular disease. Induction IV dose is 0.3 mg/kg with maintenance dosing of 5–20 μg/kg/min. It is metabolized by the liver and in plasma and is renally excreted. Possible adrenocortical suppression can be observed, especially when combined with benzodiazepines and opioids. Other potential side effects and precautions include injection pain and phlebitis, hiccups, myoclonic activity on induction, nausea, and vomiting.

4.8. Barbiturates

Barbiturates are both GABAergic and GABAmimetic—they do not require GABA for their intended effects. They are very lipophilic, producing rapid on and offsets but will accumulate in adipose tissue and can lead to a prolonged hangover with high doses.

Intended effects of barbiturates include hypnosis and anticonvulsant properties with no histamine release.

Possible adverse side effects include hyperalgesia in subanesthetic doses (paradoxical excitement), pain on injection (alkaline pH of 11), hypotension (especially with hypovolemia) with compensatory tachycardia, dose-dependent respiratory depression, and excitatory phenomenon such as tremors, twitching, heightened airway reflexes, and laryngospasm.

Methohexital is an ultra-short acting barbiturate that acts by GABA receptor activation and increasing chloride ion channels. It has a rapid onset (1 min) and offset (5–8 min) but does not accumulate in adipose tissue. Expected effects include venodilation, increases in heart rate with stable cardiac output, and central depression of respiratory rate and tidal volume. Methohexital is safe for asthmatics (no histamine release) but does not produce bronchodila-

tion. It is contraindicated in patients with acute intermittent porphyria. Adverse side effects may include nausea/vomiting, laryngospasm, bronchospasm, hiccups, and apnea. It is metabolized by the liver.

4.9. Sedative

Propofol (2, 6 diisopropylphenol) is a short acting ($T_{1/2}\alpha$ 2–8 min, $T_{1/2}\beta$ 4–7 h) hypnotic general anesthetic agent that increases the function of GABA receptors. It is GABAergic and GABA-mimetic and may inhibit the NMDA receptor. It does not provide analgesia or antalgesia but does produce sedation, amnesia, hypnosis, and is a profound antiemetic. There is notable dose-dependent respiratory depression, and it may produce apnea on induction. Propofol also helps relax bronchial smooth muscle and is safe to use with asthmatics (no histamine release). Systolic blood pressure may be reduced 20–40% by blocked sympathetic tone (hypotension without compensatory tachycardia); this effect may be more exaggerated in the medically compromised and elderly patients. Propofol may also reduce the heart rate by 20%. There is a more rapid awakening with propofol and less residual central nervous system side effects with only mild euphoria. There is a low incidence of N/V but patients may experience pain on injection if given in large bolus doses. Propofol is manufactured with no anti-microbial preservatives; therefore, it must be discarded after 6 h once drawn up. As some formulations contain soy or egg products, it may be prudent to use great caution in exposing allergic patients to such solutions. IV sedation infusion dose: 5–50 mcg/kg/min; deep sedation bolus dose: 1 mg/kg IV over 20–30 s, repeat 0.5 mg/kg IV as needed.

4.10. Succinylcholine

Succinylcholine is comprised of two acetylcholine molecules joined together and acts as a depolarizing neuromuscular blocker by binding acetylcholine receptors at the post-synaptic neuromuscular junction end plate. The resultant end plate depolarization initially stimulates muscle contraction; however, because succinylcholine is not degraded by acetylcholinesterase, it remains in the neuromuscular junction to maintain continuous end plate depolarization and subsequent muscle relaxation referred to as a "Phase I Block." Succinylcholine is metabolized by pseudocholinesterase. Its effects may be prolonged in approximately 20% of patients because of atypical or deficient expression of the pseudocholinesterase enzyme. This defect may be diagnosed via the use of the local anesthetic dibucaine, which drastically reduces the action of normal plasma cholinesterase. An atypical patient will not experience the full effects of dibucaine.

Succinylcholine use is a potential etiology behind hyperkalemia and cardiac arrest with expected 0.5–1 mEq/L increases in serum potassium levels following administration. This effect may be exaggerated in patients with neuropathies, denervation injuries, dystrophies, myopathies, strabismus, end-stage renal disease, and burns over a week old as a result of increased acetylcholine receptor expression.

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4.11. Volatile anesthetic (VA) agents

With the exception of nitrous oxide (N_2O), inhaled anesthetics do not provide any significant analgesia, though they produce immobility and amnesia. Other than N_2O (which increases skeletal muscle tone), inhaled anesthetics do not affect or, in some cases, decrease skeletal muscle tone. Volatile anesthetic (VA) agents produce immobility via actions on the spinal cord and anesthesia by enhancing inhibitory channels and attenuating excitatory channels. Whether or not this occurs through direct binding or membrane alterations is not known. VAs also depress the cardiovascular system, thereby reducing the mean arterial pressure. Desflurane, isoflurane, and sevoflurane decrease the systemic vascular resistance, which is reflected by a decrease in blood pressure. VAs cause dose-dependent decreases in ventilation. They lead to decreases in tidal volume and compensatory increases in respiratory rate, but a net decrease in min ventilation. A decrease in minute ventilation causes an increase in CO_2.

Ventilation is the most important factor affecting the elimination and dilution of sevoflurane, desflurane, and isoflurane. The time needed for a 50% decrease in sevoflurane, desflurane, or isoflurane is <5 min and essentially independent of case duration. The rate of onset of VAs is indirectly proportional to the blood/gas partition coefficient as a lower coefficient corresponds to rapid equilibration between alveolar gas and capillary blood. The rate is directly proportional to the oil/water partition coefficient as a higher oil/water partition signifies a more rapid uptake through the BBB. All three agents are bronchodilators in general anesthetic doses. However, desflurane and isoflurane are pungent and, upon induction, may precipitate bronchospasm and/or laryngospasm. VAs carry the very serious risk of developing malignant hyperthermia (MH). This risk is decreased with desflurane and sevoflurane (and possibly isoflurane) as compared to halothane, though all potent volatile agents should be avoided in the MH-susceptible patient.

Agent	MAC (potency)	Blood-gas partition coefficient (solubility)
Nitrogen	–	**0.014 (least soluble)**
Desflurane	6.0	0.42
Nitrous oxide	105 (least potent)	0.47
Sevoflurane	2.0	0.65
Isoflurane	1.2	1.4 (most soluble)

MAC: minimum alveolar concentration.

Table 9. Comparison of various common anesthetic agents, potency, and solubility

In general, volatile agents can exist in two phases: gaseous and in solution. The proportion of the agent in its gas phase compared to those dissolved in blood is determined by the blood/gas partition coefficient, which is described using solubility and ambient pressure. If an agent is largely soluble, it resides in solution and exerts no measurable pressure. Pressure—gas tension in an enclosed space—is necessary to drive movement of agents across membranes.

Highly soluble agents are slower in onset and offset, but conversely, they may be held more extensively within the circulating blood. **Table 9** compares various anesthetic gases, their potency, and their solubility.

4.12. MAC

The potency of anesthetic gases are often described using the minimum alveolar concentration (MAC), defined as the concentration of an anesthetic gas administered at 1 atmosphere of ambient pressure required to prevent skeletal muscle movement in response to pain (e.g., surgical skin incision) in 50% of patients. Factors that can increase the MAC include fever, young age, hyperadrenergic states, and chronic alcohol abuse while anemia, old age, hypotension, and other anesthetic agents (such as narcotics, propofol) can lead to its decrease.

4.13. Second gas effect into nitrogen-filled spaces

Nitrogen (N_2) is the least soluble gas and therefore diffuses most rapidly. Nitrous oxide (N_2O) also diffuses rapidly relative to halogenated vapors as the next least soluble gas. When N_2O leaves the alveoli more rapidly than other gases can enter, it creates a gaseous void that shrinks the alveolar volume and increases the concentration (partial pressure) of other gases present, subsequently facilitating their diffusion down the newly amplified concentration gradients. This contributes to the movement of slower moving, more soluble agents, which also creates/enhances a void that theoretically can cause a follow-up "Venturi effect" on other gases. Although N_2 moves more quickly than N_2O because it is less soluble, N_2O is carried in greater concentration in blood; hence, the rate determining step of N_2O moving in more quickly than N_2 moving out is in the blood flow and has little to do with relative solubility differences. N_2O moving in more quickly than N_2 moving out expands compliant nitrogen-filled spaces and pressurizes non-complaint nitrogen-filled spaces.

Nitrous oxide (N_2O) is a GABAergic anesthetic agent that is an NMDA antagonist. It provides analgesia and anxiolysis but can be emetogenic in higher doses. It works in synergy with other volatile anesthetic agents via the second gas effect to lower the MAC. No increased cardiovascular risk has been shown to result from its use; however, increased pressure is noted in non-compliant spaces such as the eyes, middle ears (especially with obstructed Eustachian tubes), and non-draining sinuses. Also noted is increased volume in compliant spaces such as air emboli, pulmonary blebs, bowel distension, and tamponading gas bubbles following retinal surgery. When used in higher elevations/altitudes, the concentration of N_2O must be higher because of less atmospheric pressure needed to drive gas diffusion.

4.14. Anticholinergics

Glycopyrrolate is a quaternary ammonium compound that does not cross the blood-brain barrier (BBB) and causes no sedation. Glycopyrrolate has a delayed onset and possesses more anti-sialagogue effect (its main indication for OMFS in-office use) and less tachycardia than atropine does. Expected effects with glycopyrrolate include tachycardia, bronchodilation, and a reduction in salivary flow. It is metabolized in the liver and renally excreted. Potential side

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effects include blurred vision, urinary retention, xerostomia, xerophthalmia, and tachycardia. Dosing for routine use as an anti-sialagogue is 0.1–0.2 mg (0.5–1.0 mL) IV.

Atropine is a tertiary ammonium compound that crosses the BBB. It has a rapid onset but possesses less anti-sialagogue effect and more tachycardia than glycopyrrolate. Expected effects with atropine include tachycardia, bronchodilation, and a smaller reduction in salivary flow. It is metabolized in the liver and renally excreted. Potential side effects include sedation/dysphoria, blurred vision, urinary retention, xerostomia, xerophthalmia, and hyper-vagal responses (tachycardia) with very small doses. Dosing for routine use as an anti-sialagogue is 0.4 mg via IV (1 mL).

4.15. Gastric prokinetics

Metoclopramide is a moderate central dopamine receptor (D_2) antagonist. It increases lower esophageal sphincter tone and upper gastrointestinal forward peristalsis. It is metabolized by the liver and is renally excreted. It must be avoided in patients with Parkinson's disease, and it may cause extrapyramidal reactions. Usual adult dose is 10 mg IV/IM.

4.16. Antiemetics

Patients at increased risk of perioperative/perianesthetic N/V include children, women, the obese, expectant mothers, gastroesophageal reflux disease (GERD) patients, those with a history of motion sickness, gastroparesis, the anxious, and those in acute pain.

Causes of perioperative/perianesthetic N/V include early ambulation, acute pain, unpleasant visual sights, odors, tastes, and physical stimulation of the pharynx. Anesthesia-related causes of N/V include high concentrations of N_2O, opioids, ketamine, gastric insufflation, hypoxia, and hypovolemia. Various surgical stimuli can also account for perioperative N/V. These might include blood in stomach (could be common following oral surgical procedures), throat drape that applies too much pressure on the skin over the larynx, and a Weider tongue retractor placed too deeply or too aggressively.

Treatment of perioperative N/V focuses on the following goals: prevent aspiration, avoid protracted recovery, prevent hypoxia, prevent hypovolemia, achieve meticulous hemostasis, prevent distress to patient, and correction of any possible electrolyte imbalances.

Ondansetron is a serotonin 5-HT3 receptor antagonist used to prevent N/V. It is produced in various forms, both for IV (4 mg) use as well as in oral dissolving tablets (8 mg). It is metabolized in the liver and renally excreted. It has no significant drug interactions and only demonstrates mild side effects such as constipation, dizziness, and headache.

Promethazine is a neuroleptic medication and a first generation histamine H_1 receptor antagonist. It has antiemetic and anticholinergic properties via actions on the Dopamine D_2 receptor. Promethazine can have an additive central nervous system action when combined with antidepressant medications. It is metabolized in the liver and is renally excreted. Possible side effects include excessive sedation, xerostomia, constipation, and rare neuroleptic malignant syndrome. It is recommended to avoid IV push when administering this medication as

extravasation can lead to tissue necrosis. For parenteral use, the IM route in encouraged. Usual dosage is 6.25–25 mg IV, and 12.5–50 mg PO/IM/PR.

Diphenhydramine is a first generation antihistamine and an H_1 receptor antagonist. Antagonism is achieved through inhibiting the effects of histamine more so than its production or release. Diphenhydramine inhibits most smooth muscle vasoconstrictor effects of histamine. This antagonism may also produce anticholinergic effects, antiemetic effects, and significant sedative side effects [29, 30]. Diphenhydramine is metabolized in the liver and renally excreted. Usual adult dosage is 6.25–25 mg IV, and 12.5–50 mg PO/IM/PR.

Dexamethasone is a glucocorticoid and a well-established antiemetic in patients receiving highly emetogenic cancer chemotherapy. Its antiemetic mechanism of action is not well understood. Dexamethasone may antagonize prostaglandin, stimulate the release endorphins that improve mood and a sense of well-being, and stimulate appetite. It is metabolized in the liver and is renally excreted. It may incur interactions with non-steroidal anti-inflammatory medications, and potential side effects include hyperglycemia and euphoria/mania. Usual adult dose is 2–10 mg IM/IV, and 4–10 mg PO.

4.17. Local anesthetics

Local anesthetics (LA) are classified as either esters or amides. Esters include Novocain, procaine, benzocaine, and tetracaine. They are metabolized by plasma pseudocholinesterase. Amides include lidocaine, mepivacaine, and bupivacaine. They are metabolized in the liver by its microsomal enzymes. A commonly used LA, articaine, contains both an amide and an ester link but is classified as an amide.

The mechanism of action of LAs is that once they are injected into tissue, they exist in both ionized and nonionized forms. The nonionized base is able to penetrate many layers of tissue —the lipid nerve sheath and membrane. Re-equilibration between the ionized and nonionized forms occurs once passage is completed. While in the nerve axon, the ionized form is able to block sodium channels, prevent the inflow of sodium, slow the rate of depolarization, and thus preventing an action potential from occurring.

Agent	Lipid solubility	Protein binding	Duration	pKa	Onset time
Mepivacaine	1	75	Medium	7.6	Fast
Lidocaine	4	65	Medium	7.7	Fast
Bupivacaine	28	95	Long	8.1	Moderate

Table 10. Properties of local anesthetics

An ideal LA is one that is very potent, has a quick onset time, and has an appropriate duration of action sufficient to accomplish the procedural goals and then wear off with no permanent adverse effects. Properties often used to compare one LA to another include potency, duration, and onset time (**Table 10**). Potency is determined by lipid solubility. Greater lipid solubility produces a more potent LA (bupivacaine > lidocaine > mepivacaine). Duration is determined

by the protein binding. Greater protein binding creates a longer duration (bupivacaine > mepivacaine > lidocaine). Onset time is determined by pKa. The closer the pKa of a LA is to the pH of tissue (7.4), the more rapid the onset (mepivacaine > lidocaine > bupivacaine). The pKa is the pH at which equal concentrations of ionized and nonionized forms exist.

Anesthetic	pKa	% Conc	Vasoconst	Pulpal (P)/Soft Tissue (ST) duration (min)	Max dose (mg/kg)	Max dose (absolute, mg)
Articaine	7.8	4	Epi 1:100k	P: 60–75 ST: 180–360	7 (adult)	500 (adult)
Bupivacaine	8.1	0.5	Epi 1:200k	P: 90–180 ST: 240–540	1.3 (adult)	90 (adult)
Lidocaine	7.7	2	None	P: 5–10, ST:60–120	4.5 (adult)	300 (adult)
		2	Epi 1:100k	P: 60, ST: 180–300	7.0 (adult)	500 (adult)
Mepivacaine	7.6	2	Levo 1:20k	P: 60, ST: 180–300	6.6	400
		3	None	P: 20–40, ST: 120–180	6.6	400
Prilocaine	7.9	4	None	P: 10–15 (infil), 40–60 (block); ST: 90–120 (infil), 120–240 (block)	6.0	400

Table 11. Comparison of various commonly used local anesthetics

Time	Blood levels of LA	Signs/symptoms
Initial	Minimal to moderate overdose	↑ HR, ↑ BP, ↑ RR Drowsiness, confusion, slurred speech, stuttering, talkative, excited, nystagmus, tinnitus, metallic taste
Progressive	Moderate overdose	Tremors, hallucinations, ↓ BP, ↓ HR, ↓ CO
Late	Moderate to high overdose	Unconsciousness, seizures, ventricular dysrhythmias, respiratory and circulatory arrest

Table 12. Clinical manifestations of local anesthetic toxicity

The most common drugs utilized by OMSs are LAs, so a detailed and intimate knowledge of these agents is essential to ensure a successful practice (**Table 11**). Occasionally, providers do not take into account special patient factors such as age, weight, or medical comorbidities; LA toxicity may result if maximum dosages are exceeded. Clinical manifestations of systemic LA toxicity are varied and may include only the (early) classic sign of circumoral numbness.

However, if left unnoticed, toxicity symptoms may progress and can involve the cardiovascular and central nervous systems (**Table 12**).

Should a toxic reaction or overdose from LA occur, several treatment options exist for the practitioner. One option for treating minimal to moderate LA overdose is to give a reversal agent. OraVerse (phentolamine) is a short-acting alpha blocker. It reverses the vasoconstrictor effect and shortens the LA duration. It is only for use with vasoconstrictor-containing LAs. It is packaged as 1.7 mg in a 1.8 mL cartridge, and the maximum dose is two cartridges. For moderate or high overdose as the symptoms worsen, Intralipid™ 20% IV emulsion can be administered. This drug increases the concentration of serum proteins available for binding the LA. Usual dosing is to administer 1 mL/kg over 1 min and to repeat twice more at 3- to 5-min intervals. Then (or sooner if stability is restored), the practitioner can convert to an infusion at a rate of 0.25 mL/kg/min, continuing until hemodynamic stability is restored. As a last resort, emergency dialysis can be considered.

4.18. Epinephrine

Lidocaine remains the most common local anesthetic medication administered in OMFS and dental offices; therefore, a deeper review of this medication, its properties, and its toxicity is warranted. **Table 13** lists adult dosages for the most common preparations of lidocaine in dental carpules (2% solutions, 1.7 mL total volume/carpule). Most OMSs prefer to use the lidocaine preparation with epinephrine due to its favorable vasoconstrictive properties. A 1:100,000 concentration of epinephrine translates to 0.01 mg/mL or 0.017 mg/carpule. The American Heart Association regards no more than 0.04 mg epinephrine generally as safe for patients with uncontrolled/poorly controlled hypertension or a significant cardiac history. This, however, is based more on anecdotal rather than empiric evidence as injection variables such as the time frame over which the medication is administered or whether the injection was given intravascular become important factors.

Agent	Cartridge size (mg)	Max dose (mg/kg)	Max dose (mg/lb)	Max dose (mg)
2% lidocaine	34	4.5	2	300
2% lidocaine w/1:100k epi	34	7	3.3	500

Maximum dosages are based on an adult weight of 150 lb or 70 kg and taken from the manufacturer (Astra).

Table 13. Adult dosages for lidocaine as commonly used in OMFS practice

Contrary to popular belief, epinephrine will not alter mean arterial pressure as α vasoconstriction is balanced by β dilation. Epinephrine will, however, accelerate heart rate, which will *increase* myocardial oxygen demand secondary to the tachycardia and *decrease* oxygen supply secondary to decreased diastolic fill time and decreased diastolic coronary perfusion time. Since most patients with known coronary artery diseases are stented, the epinephrine-induced tachycardia is only an issue with heart failure and other structural heart diseases. Epinephrine is direct acting and therefore has no interaction with monoamine oxidase inhibitors. It may

increase blood pressure when given to patients taking tricyclic antidepressants, and will increase blood pressure and decrease heart rate when used in patients taking non-selective β blockers.

4.19. Causes and clinical manifestations of local anesthetic (LA) toxicity

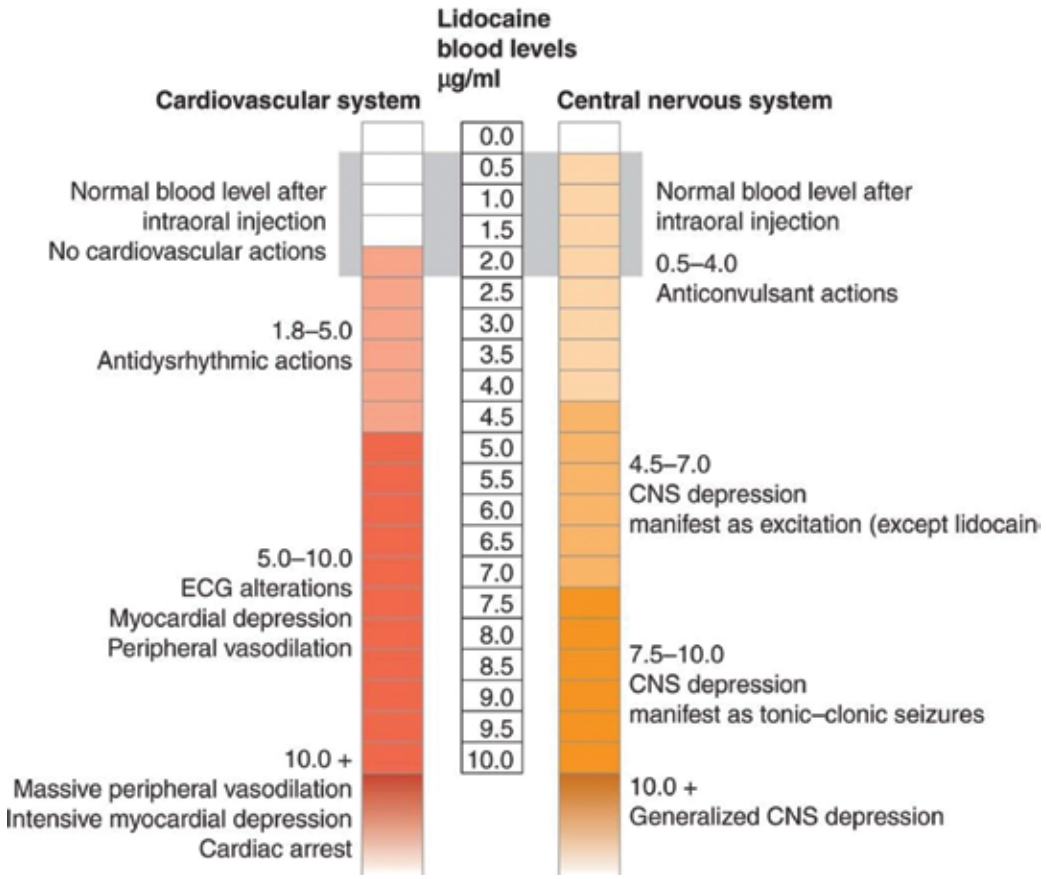

Table 14. Local anesthetic (Lidocaine) blood levels and their actions on cardiovascular and central nervous systems [31].

Elevated plasma levels of the anesthetic could lead to local anesthetic toxicity. This may be caused by an inadvertent intravascular injection or by iatrogenically violating the maximum (mg/kg) dose. Geriatric and pediatric patients are at greatest risks for LA toxicity. Older patients generally metabolize drugs at a slower rate. A geriatric patient who takes multiple medications may experience adverse drug reactions when lidocaine is administered. Cimetidine, a histamine H_2-receptor antagonist, inhibits the hepatic oxidative enzymes (P-450) needed for metabolism, thereby allowing lidocaine to accumulate in the circulating blood. This

adverse reaction is seen only with cimetidine and not with other H_2-receptor antagonists. Propranolol, a beta-adrenergic blocker, can reduce both hepatic blood flow and lidocaine clearance. Toxic reaction could result if high doses of lidocaine are given to patients taking either or both of these medications. A possible additive adverse drug reaction exists with the administration of LAs and opioids in the geriatric and pediatric populations as well. Opioids (fentanyl, meperidine, and morphine) may cause an amide LA additive effect because of their similar chemical structures (both are basic lipophilic amines) and a first-pass pulmonary effect. The lungs may serve as a reservoir for these drugs with a subsequent release back into the system.

4.20. Lidocaine toxicity and cardiovascular effects

Lidocaine has a depressive effect on the myocardium (**Table 14**). Toxic doses of lidocaine cause sinus bradycardia because lidocaine increases the effective refractory period relative to the action potential duration and decreases cardiac automaticity. If a very high dose has been administered, impaired cardiac contractibility, arteriolar dilation, profound hypotension, and circulatory collapse can result [32].

4.21. Lidocaine toxicity and central nervous system (CNS) effects

Lidocaine usually has a sedative effect on the brain (**Table 14**). Initially, lidocaine toxicity depresses brain function in the form of drowsiness and slurred speech. Its effects may progress to unconsciousness and even coma [33].

4.22. Cardiovascular *actions* of lidocaine

Lidocaine is frequently used in the management of various ventricular dysrhythmias, especially ventricular extrasystole (premature ventricular contractions) and ventricular tachycardia. Alterations occur in the myocardium as blood levels of lidocaine increase. In general, the minimal effective blood level of lidocaine for antidysrhythmic activity is 1.8 (μg/mL). In the range from approximately 2–5 (μg/mL), the actions of lidocaine on the myocardium consist only of electrophysiological changes. These include a prolongation or abolition of the slow phase of depolarization during diastole in Purkinje fibers and a shortening of the action potential duration of the effective refractory period. At this therapeutic level, no alterations in myocardial contractility, diastolic volume, intraventricular pressure, or cardiac output are evident. Both the healthy and diseased myocardia tolerate mildly elevated blood levels of lidocaine without deleterious effects. When used to treat dysrhythmias, lidocaine is administered intravenously in a 50–100-mg bolus (1.0–1.5 mg/kg). Overdose is a potential concern, but the generous benefit-to-risk ratio allows for the judicious use of IV lidocaine. Further elevation of the lidocaine blood level (5–10 μg/mL) produces a prolongation of conduction time through various portions of the heart and an increase in the diastolic threshold. This may be noted on the ECG as an increased P-R interval and QRS duration as well as sinus bradycardia. In addition, decreased myocardial contractility, increased diastolic volume, decreased intraventricular pressure, and decreased cardiac output become evident. Peripheral vascular effects observed at this level include vasodilation, which produces a decrease in blood pressure and

occurs as a result of the direct relaxant effect of lidocaine on peripheral vascular smooth muscle. Further increases in blood levels of lidocaine (>10 μg/mL) lead to an accentuation of the electrophysiological and hemodynamic effects such as massive peripheral vasodilation, marked decrease in myocardial contractility, and slowed heart rate, which may ultimately result in cardiac arrest.

4.23. Risk factors for lidocaine toxicity

Older age (>60) and pediatric patients are susceptible to lidocaine overdose and toxicity reactions. Those with decreased body weight, along with patients with medical comorbidities such as congestive heart failure, acute MI, and decreased hepatic function are also at risk. Continued risk includes patients with concomitant use of drugs decreasing P-450 activity (such as cimetidine) that triggers lidocaine accumulation in the blood. Like with other LAs, a possible additive adverse drug reaction exists with administration of lidocaine and opioids in the geriatric and pediatric populations [33].

4.24. Management of mild lidocaine overdose with rapid onset

An overdose in which signs and symptoms develop within 5–10 min following drug administration is considered rapid in onset (**Table 15**). Possible causes include intravascular injection, unusually rapid absorption, or administration of a large total dose. If clinical manifestations do not progress beyond mild central nervous system excitation and consciousness is retained, significant and definitive care is not necessary. The local anesthetic undergoes redistribution and biotransformation, with the blood level falling below the overdose level in a relatively short time.

Method of overdose	Likelihood of occurrence	Onset of signs and symptoms	Intensity of signs and symptoms	Duration	Primary prevention	Drug
Too large of a dose given	Most common	5–30 min	Gradual onset w/ increased intensity; may prove severe	5–30 min	Administer minimal doses	Amides; esters rarely

Table 15. Most common form of local anesthetic overdose

4.25. Toxicity reversal

Increasing evidence suggests that the intravenous (IV) infusion of lipid emulsions can reverse the cardiac and neurologic effects of local-anesthetic toxicity [32]. Although no blinded studies have so far been conducted in humans, studies in animal models and multiple case reports in human patients have shown favorable results. Indeed, case reports support the early use of lipid emulsion at the first sign of arrhythmia, prolonged seizure activity, or rapid progression of toxic manifestations in patients with suspected local anesthetic toxicity. Intralipid™ 20% emulsion IV may be administered at 1 mL/kg over 1 min. This is to be repeated twice more at

3- to 5-min intervals. Then (or sooner if stability is restored), convert to an infusion at a rate of 0.25 mL/kg/min, continuing until hemodynamic stability is restored. This increases the concentration of serum protein available for binding to lidocaine. As a last resort, the practitioner can consider emergency hemodialysis.

4.26. Stable versus unstable/symptomatic bradycardia

Bradycardia is defined as any rhythm disorder with a HR < 60 beats per minute (bpm). Stable bradycardia can be a normal non-emergent rhythm. For instance, well-trained athletes may have a normal HR < 60 bpm. Symptomatic bradycardia is defined as a rate that is <60 bpm that elicits signs (hypotension, congestive heart failure, myocardial infarction, and hypoxia) and symptoms (chest pain, shortness of breath, decreased level of consciousness). Symptomatic bradycardia will usually manifest with HR < 50 bpm.

4.27. Management of unstable/symptomatic bradycardia with pulse (HR < 50 and inadequate for clinical condition) [34]:

Includes following a treatment protocol resembling this algorithm:

- Establish a secure airway
- Obtain intravenous (IV) access
- Administer oxygen
- Monitor blood pressure and rhythm
- Administer atropine 0.5 mg via IV q3–5 min, maximum 3 mg
- Consider transcutaneous pacing, or
- Consider dopamine 2–10 μg/kg/min, or
- Consider epinephrine 2–10 μg/min, or
- Consider isoproterenol 2–10 μg/min

4.28. Anesthetic preparation

Though significant anesthetic complications in the OMFS office are rare, an American Society of Anesthesiology closed claims analysis reported that up to 80% of anesthetic mishaps were attributable to human error [35] Practitioners and their staff may not be fluent in management of these situations unless they routinely practice emergency scenarios and have made regular preparations for such events. Emergency management preparation must consist of the following components: thinking about the emergency (pathophysiology of the event and decision making), doing (taking responsibility), and interacting (communicating to staff and auxiliary personnel and maintaining leadership). This preparation can be enhanced by staging repeated and simulated rehearsals within the OMFS office.

For most OMSs, anesthetic management is routine, but uncertainties and emergencies are bound to arise. The OMFS office must develop, implement, and practice protocols to optimize

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patient care and emergency management that balances practicality with the premises of "do no harm" and "always be prepared."

5. Conclusion

Deep sedation and general anesthesia can be safely administered in the OMFS office. Optimization of patient care requires appropriate patient selection, thorough understanding of medical comorbidities and body systems, selection of appropriate anesthetic agents for the individual being treated, utilization of appropriate anesthetic monitoring, and a well-trained office anesthesia team. Achieving a highly trained team requires emergency management preparation that helps foster decision making in intense circumstances, develops leadership, formulates communication strategies, and perfects task management. Furthermore, the privilege and ability to provide patient care under anesthesia is a continuum that extends beyond this initial training. Safe anesthetic care can be provided, but doing so requires effort that entails constant maintenance of current knowledge, preparation, and teamwork.

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Section 6

Management of Inherited, Acquired and Iatrogenically-Induced Coagulopathies

Chapter 9

Management of Inherited, Acquired, and Iatrogenically Induced Coagulopathies in Oral Surgery

Paul Bermudez, Maximillian Beushausen and Michael P. Horan

Additional information is available at the end of the chapter

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Abstract

Hemostasis is the process of cessation of blood loss. Alterations of the hemostatic pathways can result in a hypercoagulable or hypocoagulable state resulting in thrombosis or hemorrhage. Common defects in hemostasis and their management, specifically the hypocoagulable state, are discussed as these defects often result in increased perioperative blood loss, which can result in compromised patient outcomes.

Keywords: hemostasis, platelets, coagulation, bleeding, hemophilia, von Willebrand disease, warfarin, Coumadin, heparin, fondaparinux, Arixtra, Aspirin, PGY12 blockers, clopidogrel, ticagrelor, direct oral anticoagulants, dabigatran, Pradaxa, rivaroxaban, Xarelto, apixaban, Eliquis, thrombocytopenia, ITP, liver disease, kidney disease, Surgicel, Gelfoam, topical thrombin, HemCon, CollaPlug, tranexamic acid, aminocaproic acid

1. Introduction

The process of hemostasis can be divided into four phases namely formation of the platelet plug, clot development via the coagulation cascade, termination of the coagulation cascade, and clot fibrinolysis [1]. The formation of the platelet plug can be described as primary hemostasis. Clot development via the coagulation cascade is subsequently termed secondary hemostasis. Primary hemostasis occurs immediately following endothelial cell damage and includes a vascular phase and a platelet phase. The vascular phase occurs following vascular injury and results in the vasoconstriction of the blood vessel. The platelet phase follows the vascular phase and consists of the formation of the initial platelet plug.

The formation of the platelet plug includes activation, adhesion, and aggregation. Platelet activation occurs via exposure of platelets to subendothelial collagen [2]. This results in a conformational change of the platelets as well as a release of granules within the platelets. This is followed by platelet adhesion to the subendothelial collagen in damaged blood vessels via von Willebrand's factor (VWF) and GP1b [3]. Platelet activation and the production of platelet products including thromboxane A2, ADP, and serotonin result in a conformational change in GPIIb/IIIa on platelets that allows platelets to bind to fibrinogen resulting in platelet aggregation (**Figure 1**) [4].

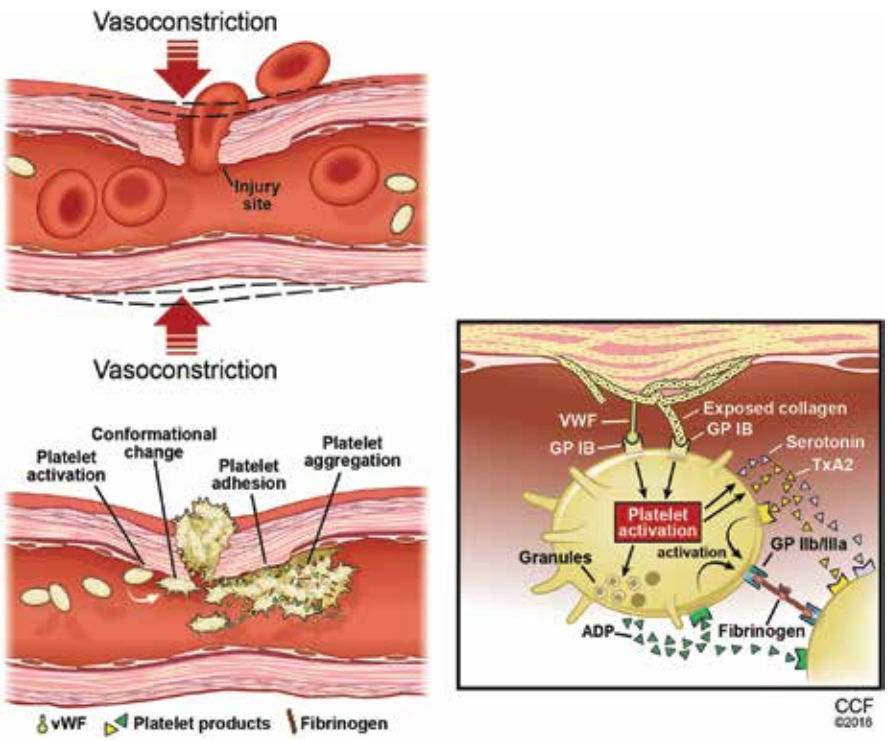

Figure 1. Primary hemostasis.

Secondary hemostasis results in clot development via the coagulation cascade, in which activation of serine protease zymogens results in the conversion of fibrinogen to fibrin and the cross-linking of fibrin that stabilizes the initial platelet plug. Traditionally, the coagulation cascade is broken down into the extrinsic and intrinsic pathways. The extrinsic pathway is initiated when tissue factor from damaged endothelial cells within the disrupted vasculature binds to factor VII, leading to the activation of factor X and the common pathway of the coagulation cascade. In the intrinsic pathway, activation of high molecular weight kininogen, conversion of prekallikrein to kallikrein, and activation of factors XII, XI, IX, and VIII leads to the activation of factor X and the common pathway of the coagulation cascade. The common pathway includes the activation of factors X, V, thrombin, and the conversion of fibrinogen to

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fibrin by thrombin, resulting in the formation of the fibrin clot. Thrombin also upregulates other upstream clotting factors including V, VIII, and XI, further promoting the formation of thrombin and the fibrin clot via the extrinsic pathway [5]. Termination of the coagulation cascade occurs via activation of antithrombin, tissue factor inhibitor, thrombomodulin, protein C, and protein S [6, 7]. In the fibrinolytic phase, plasminogen is converted to plasmin via tissue plasminogen activator. The effect of plasmin is to cleave fibrin and fibrinogen leading to the dissolution of the clot (**Figures 2** and **3**) [8].

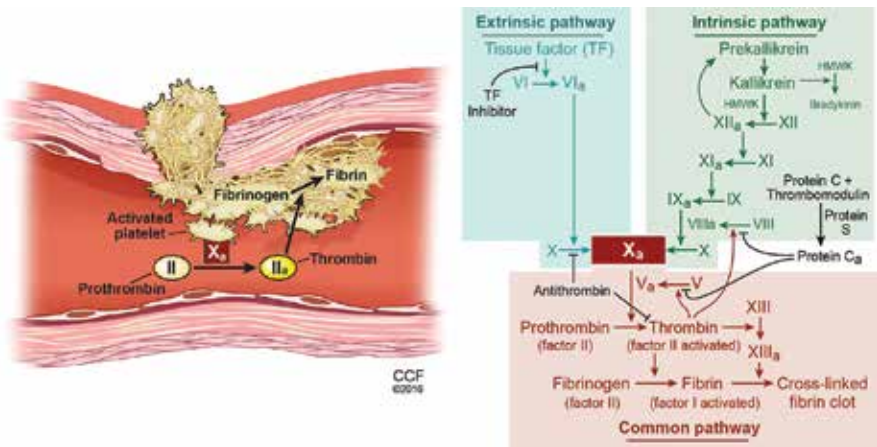

Figure 2. Extrinsic/intrinsic pathways. Termination of coagulation cascade.

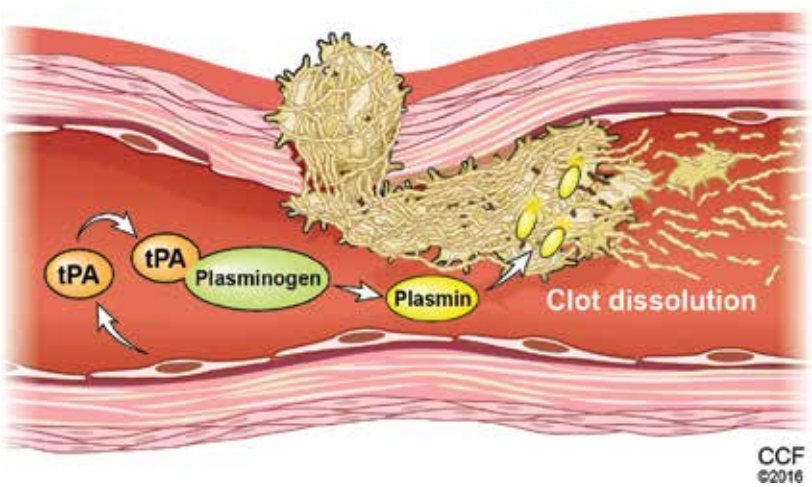

Figure 3. Fibrinolysis.

This chapter deals with the management of inherited, acquired, and iatrogenically induced coagulopathies in oral surgery.

2. Inherited and Acquired Coagulopathies

2.1. Overview

As hemostasis occurs via primary and secondary mechanisms, coagulopathies can be divided into similar categories. Defects in primary and secondary hemostasis typically have different presentations. Characteristically, primary hemostatic disorders, or defects in platelet function, result in mucocutaneous bleeding such as epistaxis, petechiae, menorrhagia, and ecchymosis [9]. Secondary hemostatic disorders, or defects in the coagulation cascade, result in deep bleeding such as hematomas and hemarthroses. Disorders of hemostasis can also be divided into congenital and acquired disorders of hemostasis. Acquired disorders are the most common cause of prolonged bleeding. In contrast to the congenital disorders in which only one factor is typically affected, the acquired coagulation disorders often have multiple factors affected. Congenital disorders of primary hemostasis include platelet function disorders **(PFDs)** and von Willebrand disease (VWD). Congenital disorders of secondary hemostasis include hemophilias A and B. Acquired disorders of hemostasis include immune thrombocytopenia (ITP), uremia-induced platelet dysfunction, defects due to chronic liver failure, and iatrogenic or medication-induced coagulopathies (**Tables 1** and **2**).

	Minor surgery		**Major surgery**		**Mild renal impairment**	**Moderate renal impairment**
	Pre-op	**Post-op**	**Pre-op**	**Post-op**		
Warfarin	INR <3.0	Adequate hemostasis/ next morning	Hold 5 days	Adequate hemostasis/ next morning		
Heparins						
Heparin	4–6 h	Once hemostasis achieved	4–6 h	48–72 h		
LMWH	24 h	24 h	24 h	48–72 h		
Fondaparinux	48 h	24 h	96 h	24 h	72–120 h	72–144 h
Platelet inhibitors						
Aspirin	None	None	None	None		
Clopidogrel	None	None	None	None		
Dual -antiplatelet therapy	None	None	None	None		

	Minor surgery		Major surgery		Mild renal impairment	Moderate renal impairment
	Pre-op	Post-op	Pre-op	Post-op		
Direct anticoagulants						
Dabigatran	48 h, PT or PTT compared to normal <1.2X	24 h	72 h, PT or PTT compared to normal <1.2X	48–72 h	48–72 h	72–120 h
Rivaroxaban	48 h, PT:PTT <1.2×	24 h	72 h, PT:PTT <1.2×	48–72 h	48–72 h	72–96 h
Apixaban	48 h	24 h	72 h	48–72 h	48–72 h	72–96 h

*Determination to bridge based on risk for thromboembolism in consultation with cardiologist.
**In patients with low risk for cardiovascular event aspirin may be discontinued 7–10 days prior to surgery.
***There are no RCTs evaluating bleeding risk with dental extractions.

Table 1. Perioperative management of antithrombotic therapy.

Hemostatic agent	Description	Features
Gelfoam	Gelatin sponge	Highly absorptive Matrix for coagulation cascade Neutral pH can be used in combination with topical thrombin
Surgicel	Oxidized regenerated cellulose	Bactericidal Acidic pH should not be used with topical thrombin Reported negative effect on nerve function
CollaCote, CollaTape, CollaPlug	Collagen product	Highly absorptive Matrix for coagulation cascade
Topical thrombin	Converts fibrinogen to fibrin	Converts fibrinogen to fibrin in final step of coagulation cascade Gelfoam can be soaked in liquid thrombin for increased hemostasis
Tranexamic acid	Inhibits conversion of plasminogen to plasmin	Gauze soaked in 5% tranexamic acid liquid for hemostasis Liquid 4.8% tranexamic acid q6h 2–5 days as postoperative mouth rinse for hemostasis
HemCon	Chitosan agent	Antimicrobial properties Sutures not required for placement

See Refs. [100, 164].

Table 2. Local hemostatic agents.

2.2. Inherited disorders of hemostasis

2.2.1. Platelet function disorders (PFDs)

Platelets are anucleate cellular fragments derived from megakaryocytes. Platelets are produced via the activation of the hormone thrombopoietin (TPO), have an average life span of 7–10 days, and are critical to primary hemostasis. The normal blood cell count of platelets is 150,000–450,000/μl [10]. When endothelial injury occurs, von Willebrand's factor is able to via bind to subendothelial collagen. Platelets then bind to von Willebrand's factor, the platelet GP1b glycoprotein. Platelet activation via exposed collagen and other platelet agonists is followed by aggregation via GPIIb/IIIa. Platelet activation leads to the secretion of thromboxane and the secretion of ADP and serotonin from the dense granules. This further promotes platelet activation and aggregation that propagates primary hemostasis [2–4, 9].

Historically, von Willebrand disease has been identified as the most common inherited defect of primary hemostasis, but recent studies suggest that platelet function disorders (PFDs) may actually be more common [11]. Individuals with PFDs commonly have symptoms of abnormalities in primary hemostasis including mucocutaneous bleeding, ecchymosis, menorrhagia, and epistaxis [9]. Severe forms of PFDs are rare and include Bernard-Soulier syndrome, a deficiency in GP1b, and Glanzmann thrombasthenia, a deficiency in GPIIb/IIIa. Less severe forms of platelet function disorder are more common and may include defects in receptors, platelet agonists, platelet storage granule defects, and signal transduction defects [9].

Traditionally, bleeding time was used to evaluate platelet function, but this has fallen out of favor. The platelet function screen (PFS) is used more often today and is readily available at most hospitals. The downside of the PFS is its low sensitivity, especially in cases of mild platelet function defect [12]. The best test for diagnosis of platelet function disorders is light transmission aggregometry (LTA), in which platelet aggregation is promoted via agonists leading to an increase in light transmission that can be quantified [12]. However, LTA is not readily available and is thus rarely utilized in clinical testing. Due to the limitations of clinical diagnostic testing as noted above, patients with symptoms of mucocutaneous bleeding without laboratory abnormalities may not be diagnosed. These patients can be identified as having mucocutaneous bleeding of unknown cause [9]. In patients with platelet function disorders, the use of local measures and antifibrinolytics, such as a 5% tranexamic acid mouthwash every 4–6 h perioperatively, should be a mainstay of therapy for patients undergoing oral surgery procedures. If moderate bleeding is expected, desmopressin at a dose of 0.3 μg/kg (max dose 20 μg) can be administered intravenously 1 h prior to procedure [13]. In patients with severe risk of bleeding or severe forms of PFDs, such as Bernard-Soulier syndrome or Glanzmann thrombasthenia, perioperative platelet transfusion may be indicated. Platelet transfusions are rarely used for patients with mild forms of PFDs [13]. Some risks associated with platelet transfusions include the development of HLA antibodies or antibodies to platelet glycoproteins. Additional risks of blood components include the transmission of infectious diseases, which is discussed.

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2.1.2. Von Willebrand disease

Von Willebrand disease (VWD) has been historically identified as the most common inherited bleeding disorder. VWD is caused by an inherited defect in the concentration, structure, or function of von Willebrand's factor [14]. VWD can be the result of a qualitative or quantitative defect in VWF. The prevalence of all types of VWD is estimated to be around 1 in 100 [15]. VWF is synthesized in vascular endothelial cells and megakaryocytes. Within the endothelial cells, VWF can be stored in Weibel-Palade bodies or released directly from the endothelial cells. In platelets, VWF is stored in the alpha-granules [16]. VWF plays a role in both primary and secondary hemostasis, and therefore, VWD may include symptoms of defects in both primary and secondary hemostasis. In primary hemostasis, VWF promotes subendothelium binding to platelets via GP1b. VWF further promotes binding between platelets via GPIIb. During secondary hemostasis, VWF stabilizes Factor VIII, promoting the coagulation cascade [17].

Type I VWD is the most common form of VWD, accounting for 60–80% of all cases. It is defined by 10–45% of circulating levels of VWF. Type I VWD is also inherited in an autosomal-dominant fashion, but is usually found incidentally during a surgical procedure.

Type II VWD is usually an inherited autosomal-dominant disorder and is considered a qualitative disorder. Subtypes of Type II VWD include IIA, IIB, IIM, and IIN. Type IIA VWD is due to a defect in the synthesis of high and medium molecular weight VWF multimers or an increase cleavage of VWF by ADAMS13 [17]. Type IIB VWD is caused by a gain-of-function mutation in the GPIb binding site of VWF. This results in activation of VWF and platelet aggregation, followed by clearance of VWF and platelets. Patients with Type IIB VWD may present with thrombocytopenia [17]. Type IIM is due to a decrease in interaction between VWF and platelets [17]. Type IIN is inherited in an autosomal recessive manner and is due to a mutation in the factor VIII binding site of VWF [17].

Type III VWD is inherited in an autosomal recessive manner and is considered the most severe form of VWD, as no VWF is produced [15]. There is great inter-individual variability between the different types and subtypes of VWD, resulting in variable risks of hemorrhage from minor to severe. Therefore, hemorrhage risk should be evaluated on a case-by-case basis.

VWD is diagnosed via the qualitative ristocetin cofactor assay (VWF:RCo) and the quantitative measurement of the amount of circulating von Willebrand's factor antigen (VWF:Ag) [18]. Type I and Type II VWD can be differentiated based on differences in ratios between the two assays, where a decrease in the VWF:RCo/VWF:Ag <0.6 is indicative of Type II VWD and a ratio VWF:RCo/VWF:Ag >0.6 is indicative of Type I VWD [17]. The PTT and bleeding time are often elevated in patients with VWD [19]. Management of Type I VWD includes the use of desmopressin, which results in a release of stored VWF. Due to inter-individual variability in response to desmopressin treatment, in patients with Type I VWD, a preliminary test dose to verify biological response to desmopressin is recommended [17]. Desmopressin is effective in most cases of Type I VWD, but is not used in Type II VWD or Type III VWD [20]. Type II VWD may actually be aggravated by the use of desmopressin. Specifically, in Type IIB VWD, there is a risk for the aggravation of thrombocytopenia [21]. The peak response to desmopressin

infusion occurs between 90 min and 2 h post-infusion, and therefore, surgery is recommended within 2 h post-infusion. Bornert et al. used a protocol of IV infusion (50 ml/30 min) of 0.2 μg/kg 1 h preoperatively, 10 h postoperatively, and 24 h postoperatively to obtain hemostasis in a pediatric patient with Type I VWD undergoing dental extractions [22]. This protocol can be used as a basic guideline for treatment of patients with Type I VWD undergoing dental extractions; alternatively, the use of 300 μg intranasal preoperatively in patients >50 kg, 150 μg intranasal in patients <50 kg, or subcutaneous 0.3 μg/kg max dose of 15 μg may also be considered [23–25]. The use of local hemostatic measures and antifibrinolytics is also recommended in the treatment of VWD. In cases of severe VWD, VWF/FVIII infusions have been used [17].

2.1.3. Hemophilias A and B

Hemophilias A and B are X-linked recessive bleeding disorders. Patients with hemophilia are unable to activate Factor X and therefore are unable to generate thrombin and fibrin necessary to stabilize the initial platelet plug. Hemophilia A is caused by a defect in Factor VIII and Hemophilia B, also known as Christmas disease, is caused by a defect in Factor IX. The incidence of Hemophilia A is approximately 1 in 5000, and the incidence of Hemophilia B is 1 in 30,000 [26]. Males are generally affected, whereas female carriers are generally asymptomatic, with some female carriers having symptoms similar-to-mild hemophilia [27]. While most cases of hemophilia have a family history of the bleeding disorder, approximately one-third of the cases arise spontaneously, with hemophilia occurring due to a de novo maternal mutation [28]. Hemophilias A and B can be further categorized based on the concentration of functional Factor VIII or IX. Severe hemophilia is identified as less than 1% of normal factor activity, moderate hemophilia 1–5% of normal factor activity, and mild hemophilia as 5–40% of normal factor activity [29, 30]. Two-thirds of patients with Hemophilia A have severe hemophilia, and one-half of patients with Hemophilia B have severe hemophilia. The average age of diagnosis of hemophilia for severe hemophilia is at 1 month of age, 8 months for moderate hemophilia, and 3 years for mild hemophilia. A family history of hemophilia or of mother carrier status increases the likelihood of diagnosis [31]. In mild hemophilia, the diagnosis may be challenging as diagnosis may only be made after a bleeding episode during surgery or trauma [32]. Symptoms in newborns include bleeding after circumcision and intracranial hemorrhage [33, 34]. Symptoms that present during early childhood include bruising, joint bleeds, and "goose-egg" hematomas of the forehead [35]. Symptoms that present later in childhood or during adult life include hemarthrosis and hematomas. Joints with frequent hemarthrosis are likely to develop arthropathy during adolescence [36]. In trauma patients with a history of hemophilia, there is an increased risk for life-threatening intracranial hemorrhage, which can present clinically as headache, vomiting, seizures, and lethargy [37]. In those patients with a family history of Hemophilia A, diagnosis can be made at birth by measuring Factor VIII levels on the umbilical cord blood [17]. In patients with a family history of Hemophilia B, diagnosis can be made between 6 and 12 months, as at birth Factor IX levels are low in all individuals [26]. Laboratory results in hemophilia indicate a prolonged PTT with normal PT and INR. A normal PTT does not exclude hemophilia due to a low sensitivity of the screening test. A prolonged PTT is then confirmed by identifying

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decreased functional Factor VIII or IX at less than 40% of normal [17]. In patients with suspected Hemophilia A, a normal VWF:Ag should be present to rule out decreased Factor VIII as a result of von Willebrand Disease.

Once a diagnosis of hemophilia is made, patients should be vaccinated against Hepatitis B. At one year of age, vaccination against Hepatitis A can be administered to prevent viral transmission during the transfusion of blood products [38]. Management of hemophilia with acute bleeding can be achieved with factor replacement, fresh-frozen plasma (FFP), local measures, antifibrinolytic agents, and desmopressin in patients with Hemophilia A. Today, factor replacement is preferred to FFP due to relative concentrations of the products and decreased risk of transmission of blood borne pathogens. Long-term management of patients with hemophilia includes prophylactic treatment with factor replacement. Prophylaxis is achieved by maintaining the missing clotting factor at a level of 1% or higher. These protocols have resulted in a decrease in the chronic morbidities associated with hemophilia, such as arthropathy [39]. For factor replacement, one unit of Factor VIII per kg of body weight increases the plasma FVIII level by 2%. For Factor IX replacement, one unit of Factor IX per kg of body weight increases the plasma IX level by 1%. The half-life of Factor VIII is 8–12 h so twice-daily dosing is required. The half-life of Factor IX is 24 h so dosing is limited to once daily [40–42]. The control of serious bleeding is usually achieved by maintaining factors levels at 50–100% for a period of 7–10 days [43, 44]. Prophylaxis to prevent serious bleeding complications in patients with hemophilia includes achieving 100% factor function for a period of 1 week prior to surgery. Factor replacement is typically maintained postoperatively for 1–3 days [39]. Desmopressin can also be used in the management of Hemophilia A. Desmopressin at 0.3 μg/kg body weight is expected to raise FVIII levels by twofold within an hour post-infusion. This can be repeated after 12 h and once daily thereafter [45, 46]. Intranasal administration of 300 μg of desmopressin preoperatively in patients >50 kg, 150 μg intranasal in patients <50 kg, or subcutaneous 0.3 μg/kg max dose of 15 μg may also be considered [23–25]. Desmopressin is dependent on existing Factor VIII as it promotes the release of VWF, allowing for stabilization of Factor VIII. Therefore, desmopressin is ineffective in severe hemophilia (<1% activity) and in treating Hemophilia B [17].

Factor replacement therapy has its potential complications, such as the development of antibodies against the replaced factors. The development of inhibitors is reported to develop in 20% of severe cases of Hemophilia A and 3–5% of patients with Hemophilia B [47]. The development of inhibitor antibodies is diagnosed via mixing studies where the addition of the missing protein to the plasma of a subject with an inhibitor does not correct an abnormal PTT. The Bethesda assay is used to qualify patients with inhibitors into low responders or high responders. Low responders are patients with BU <5 and respond well to high doses of factor replacement. High responders, or patients with BU >10, do not respond well to factor replacement and are treated with concentrates of other factors including Factor VII to promote the intrinsic pathway of the coagulation cascade [48]. The future of hemophilia treatment likely includes the development of long-acting factor replacements and gene therapy [49]. In patients born before 1985, the leading cause of death in patients with hemophilia is complications from HIV or Hepatitis C due to contamination of the plasma supply [50, 51]. Today, the preferred

use of recombinant factors and improved methods in removing viruses from the donor blood supply has decreased the viral rate of transmission. Complications related to liver failure as a result of Hepatitis C further increases difficulties in managing the coagulopathy in these patients.

2.1.4. Hemophilia C

Factor XI deficiency or Hemophilia C is the fourth most common inherited bleeding disorder after VWD, Hemophilia A, and Hemophilia B. Hemophilia C is most common in the Ashkenazi Jewish population with 8% of this population being heterozygous [52, 53]. Unlike Hemophilias A and B, Factor XI deficiency is not defined by spontaneous bleeding into muscles and joints [52]. Hemophilia C can also be seen in both sexes, whereas Hemophilias A and B are inherited in an X-linked recessive manner and therefore are more common in males. Hemophilia C was first identified in two sisters, one of which had a tonsillectomy and the other a dental extraction [54]. Factor XI deficiency is most commonly identified after trauma or surgery to tissues with high fibrinolytic properties including the oral mucosa. Bleeding occurs more commonly in tissues with high fibrinolytic properties because the normal function of Factor XI is to stabilize thrombin-activated fibrinolysis inhibitor (TAFI), an inhibitor of fibrinolysis [55]. An elevated PTT is seen in patients with Hemophilia C with confirmation of Hemophilia C via measurement of Factor XI levels. Patients with <20 μ/dl are identified as having a severe deficiency of Factor XI and patients with a Factor XI level of 20–80 μ/dl as having a partial deficiency [56]. The degree of Factor XI deficiency is poorly correlated with bleeding tendency for patients with partial deficiency. Overall, a history of bleeding episodes is more significant than the specific level of Factor XI [53]. In patients undergoing dental extractions, the use of tranexamic acid is an effective treatment. Berliner et al. reported no episodes of prolonged bleeding in patients with severe Factor XI deficiency <15 μ/dl when tranexamic acid was used 12 h prior to procedure and continued for 7 days post-extraction [57]. In surgeries where more severe bleeding is expected the use of fresh-frozen plasma (FFP), 15 ml/kg within two days prior to surgery is an effective treatment modality [53]. Prior to transfusion with FFP, patients should be tested for Factor XI inhibitors [58]. If inhibitors are present, alternative treatment modalities should be explored including Factor VIIa. A single dose of Factor VIIa (15–30 μl/kg) in combination with tranexamic acid perioperatively has been effective in obtaining hemostasis in patients with Factor XI inhibitors [58]. Patients with severe Factor XI deficiency should be transfused with FFP to Factor XI levels of 30–40 μ/dl, which can be identified via Factor XI testing or a normalized PTT [53]. Factor XI should not be normalized due to increased risk of thrombosis. Risks of FFP include fluid overload and those risks associated with blood products. Factor XI concentrate is another effective treatment modality, but due to the risk of thrombosis formation, Factor XI concentrate is not currently available in the United States [53].

2.1.5. Other inherited coagulopathies

Other rare forms of inherited coagulation disorders make up 3–5% of all coagulation disorders. These include deficiencies in fibrinogen, prothrombin, factor V, Factor V and VIII, VII, X, and XIII deficiency [17, 59–61]. These disorders can be screened for using PT, PTT, and INR assays.

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If positive results are present, then a secondary diagnostic assay of factor activity can be performed [17]. Unique to the rare forms of inherited coagulopathies a normal PT, PTT, and INR with symptoms of CNS bleeding or hemarthrosis may indicate a Factor XIII deficiency [17, 62]. Treatment for these coagulopathies usually includes factor replacement [60].

2.3. Acquired disorders of hemostasis

2.3.1. Thrombocytopenia

There are various causes of thrombocytopenia including decreased platelet production, increased destruction, sequestration, dilution and consumption within clots. Some causes of thrombocytopenia are associated with hemorrhage, while others are associated with increased risk of thrombosis. Thrombocytopenia associated with increased risk of thrombosis includes heparin-induced thrombocytopenia (HIT), disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), and drug-induced thrombotic microangiopathy. Thrombocytopenia occurs in these disorders as platelets are consumed during the formation of clots. Thrombocytopenia in the presence of pancytopenia is indicative of a defect in the bone marrow including nutritional deficiencies, myelodysplastic syndromes, and acute leukemia. Additionally, drugs used to treat malignancies may cause pancytopenia. Isolated thrombocytopenia may be indicative of congenital thrombocytopenia, thrombocytopenia during pregnancy, autoimmune diseases, immune thrombocytopenia (ITP), drug-induced thrombocytopenia, or liver disease [63]. Patients who present with thrombocytopenia with a recent change in medications should be evaluated for drug-induced thrombocytopenia. The mechanism of thrombocytopenia in patients with liver disease is via spleen sequestration of platelets secondary to splenomegaly due to portal hypertension. Thrombocytopenia can be associated with infections viral, bacterial, or parasitic. Thrombocytopenia has been reported to be an initial presentation of HIV [64]. Patients with unexplained thrombocytopenia have a complex differential diagnosis and should be referred to a hematologist for consultation and complete workup. The average platelet count is 150,000–450,000/μl representing great variability between individuals. While there is greater variability in platelet count between individuals, individuals typically have a consistent platelet level [65]. Therefore, a change in platelet count may be more indicative of an increased risk of hemorrhage compared to the platelet value itself. A platelet value below 150,000/μl is defined as thrombocytopenia with severe thrombocytopenia being defined as a platelet count below 50,000/μl. Severe thrombocytopenia may pose a risk for hemorrhage during surgical procedures, while spontaneous bleeding does not typically occur unless the platelet count is less than 10,000/μl. Bleeding time should be evaluated in patients with thrombocytopenia. The bleeding time can be estimated by bleeding time = 30.5 (platelet count/3850) [66]. Patients with thrombocytopenia should be transfused to a platelet count of 50,000/μl prior to minor procedures and 100,000/μl for more invasive procedures [66]. Patients should be transfused with platelets the morning of surgery due to the high rate of platelet consumption or sequestration. A platelet count should be taken post-transfusion. A history of prior transfusions is important to identify due to increased alloimmunization of the recipient against platelet products. Additional transfusions intraoperatively or postoperatively may be necessary. In addition to platelet transfusions,

local hemostatic measures including gelatin sponge, oxidized regenerated cellulose, topical thrombin, aminocaproic acid, and tranexamic acid should be used to obtain and maintain hemostasis. In patients undergoing dental extractions with a platelet count of <100,000/μl and when <50,000/μl were transfused with platelets, Fillmore et al. reported a 7.4% risk of postoperative bleeding, all of which were controlled via local measures [67].

2.3.2. Immune Thrombocytopenia

Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is an immune-mediated thrombocytopenia in children, adults, or during pregnancy. ITP is a disease of exclusion with a differential diagnosis including thrombotic thrombocytopenic purpura (TTP), chronic liver disease, aplastic anemia, leukemia, Type IIB von Willebrand disease, drug-induced thrombocytopenia, myeloproliferative disorders, and HIV [68]. The presentation of ITP in children and adults differs, as in children ITP typically occurs after a viral infection and typically resolves spontaneously. ITP in adults is typically a chronic disease. ITP in adults is identified as either primary ITP or secondary ITP.

Primary ITP occurs suddenly with no apparent precipitating event. Secondary ITP occurs in patients with other morbidities including HIV, Hepatitis C, malignancies, or other autoimmune diseases. The cause of ITP is the production of IgG autoantibodies to platelet proteins, notably GPIIb/IIIa [69]. Once opsonized, platelets are destroyed by the reticuloendothelial system [68]. Clinical manifestations of ITP include bleeding consistent with a platelet defect. Symptoms include petechiae, purpura, epistaxis, and most severely intracranial hemorrhage. Intraoral blisters or bleeding known as "wet purpura" has historically been identified as a more concerning presentation than petechiae or purpura of the skin [70]. Typically, spontaneous bleeding does not occur in patients with platelet counts greater than 30,000/ml, and patients with a platelet count greater than 30,000/ml have mortality risks equal to the general population [71, 72]. Patients with ITP typically have less bleeding risk than would be anticipated by the reduced platelet count. This is likely related to the majority of platelets being younger with greater hemostatic activity, as the autoimmune nature of ITP results in a shortened platelet life span [73, 74]. Patients do not need to be treated for ITP unless platelet counts are <10,000/ml, there is the presence of spontaneous bleeding, patients are scheduled for surgery, or patients have lifestyles or occupational demands that increase the risk for trauma [73]. The presence of comorbidities including chronic liver disease, hypertension, infection, and uremia-induced platelet dysfunction is another factor that should be considered when deciding to treat patients with ITP [73]. Recommendations for safe practice in patients undergoing surgical procedures are platelet count >30,000/ml for a single simple extraction, >50,000/ml for minor surgery, and >80,000/ml for major surgery [68]. Typical first-line therapy in consultation with a hematologist includes prednisolone at 1 mg/kg for 2–4 weeks, followed by tapering over several weeks. If corticosteroids are unsuccessful or not indicated, IVIG 1 g/kg for 2 days or anti-D 50 μg/kg once can be used. For patients who fail first-line therapy, second-line therapy includes splenectomy, followed by additional pharmacotherapy [73]. In the patient with ITP necessitating emergency surgery, a protocol including IVIG and platelet transfusions is used [73–76].

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2.3.3. Liver disease

Common causes of chronic liver disease include viral hepatitis and alcoholic liver disease. Candidates for liver transplantation due to liver cirrhosis are required to have dental clearance as part of a preoperative evaluation prior to being placed on the transplant list. This often includes extraction of carious dentition that is deemed to be an infection risk. The liver plays a crucial role in hemostasis as the liver is the site of synthesis of thrombopoietin, most of the coagulation factors, the inhibitors of the coagulation cascade and fibrinolytic proteins. In addition to the site of synthesis, the liver is the site of metabolism of these factors. Due to diminished procoagulant and anticoagulant factors, there is a rebalancing of hemostasis, and most patients with liver disease undergoing surgical procedures do not exhibit excessive bleeding [77]. Additionally, von Willebrand's factor (VWF) is not produced in the liver and is elevated in patients with chronic liver disease. Increased VWF may contribute to maintenance of primary hemostasis [78]. Patients with liver disease should be treated with caution, as the balance between procoagulant and anticoagulant factors can easily be disrupted resulting in either a hypercoagulable or hypocoagulable state. PT, INR, and PTT are commonly prolonged in patients with liver failure, but this does not necessarily indicate an increased bleeding risk as PT and PTT are unable to account for the decreased production of the anticoagulant factors protein C, S, and antithrombin [77]. Prophylactic correction of prolonged PT with fresh-frozen plasma is not recommended prior to procedures due to limited reduction in bleeding risk and the risks of blood products [79]. Additionally, volume overloading can increase the possibility of varices rupturing as a consequence of portal hypertension [80]. Patients with liver disease commonly present with moderate thrombocytopenia (50,000–100,000/μl) due to a decreased production of thrombopoietin in the liver, as well as platelet sequestration in the spleen due to portal hypertension [81]. For platelet count >50,000/μl, there is limited risk for significant bleeding. For patients with a platelet count <50,000/μl, platelets should be transfused to >50,000/μl. The use of antifibrinolytic agents such as tranexamic acid oral rinse preoperatively is indicated to prevent bleeding complications. Stanca et al. successfully used intranasal desmopressin (300 μg) in patients with INR of 2–3 and platelet count <50,000/μl prior to dental extractions to promote hemostasis [82]. Additionally, platelet and coagulation factor deficiencies may occur in alcoholics due to nutritional deficiencies in folic acid and vitamin K associated with poor diets. Correction of folic acid and vitamin K (10 mg orally for 3 days) prior to surgical intervention may be indicated. For pain management, NSAIDs should be avoided in patients with liver disease due increased bleeding risk. Comorbidities that may increase bleeding risk including current infection, uremia that impairs degranulation of platelets, and medications that may affect coagulation. Infections should be treated and renal status optimized prior to surgical intervention [77]. As liver disease does not prevent against thrombosis, prior to surgery, anticoagulant therapy should not be suspended solely based on liver disease status [83].

2.3.4. Renal Dysfunction

In patients with renal dysfunction, there is an increased susceptibility to bleeding. This increased bleeding risk is multifactorial and includes platelet dysfunction due to uremia,

platelet dysfunction due to anemia, and the anticoagulant effects of heparin used during dialysis. Platelet dysfunction due to uremia can affect all stages of platelet function including adhesion, secretion, and aggregation [84]. This includes an increase in prostacyclin and nitric oxide levels, decreased production of thromboxane A2, abnormal intracellular calcium mobilization, and decreased production of ADP, epinephrine, and serotonin [85–88]. Well-characterized effects of uremia on platelet function include intrinsic platelet dysfunction in GPIIb/IIIa resulting in decreased platelet aggregation and adhesion [89]. Uremia can also induce platelet dysfunction extrinsic to platelets via the production of inhibitors including guanidinosuccinic acid that increase nitric oxide levels [90]. Nitric oxide is a potent inhibitor of platelet aggregation.

Anemia occurs in patients with renal dysfunction due to a decrease in erythropoietin. In a patient with a normal hematocrit, red blood cells occupy the center of the blood vessel, while the platelets are located at the periphery of the blood vessel. The peripheral location of platelets in the blood vessel allows platelets to easily contact the subendothelial collagen when the endothelium is damaged. In patients with anemia, the platelets are mixed with the red blood cells and are less able to contact damaged endothelium [84].

Nishide et al. published a case report of increased hemorrhage in a patient with renal dysfunction undergoing full mouth dental extractions and removal of hyperplastic gingiva two months prior to kidney transplantation [91]. The authors noted no abnormalities in PT, PTT, or bleeding time on preoperative laboratory tests. Abnormal laboratory results included decreased hemoglobin of 7.2 g/dl and an elevated creatinine of 8.9 mg/dl consistent with renal failure. In patients undergoing dialysis treatment, it is recommended that patients undergo surgical procedures the day after dialysis when the anticoagulant effects of heparin have subsided. To limit the negative effects of anemia on hemostasis, it is recommended to transfuse patients to a hemoglobin of 10 g/dl preoperatively [92]. Additional strategies to promote hemostasis preoperatively include the use of desmopressin single dose IV 0.3 μg/kg or 300 μg intranasally 2 h prior to procedure [93]. The use of desmopressin increases the release of vWF, therefore increasing the binding of platelets to subendothelial collagen in the damaged endothelium. Estrogen 0.6 mg/kg IV or 2.5–25 mg orally beginning 5 days preoperatively can also be used [94]. Estrogen promotes platelet function by limiting the production of nitric oxide [95]. Additionally, the use of local hemostatic measures is recommended. Patients with chronic renal failure may be at an increased risk of bleeding due to the presence of comorbidities such as cardiovascular disease that are managed with antiplatelet therapy or vitamin K antagonists [96, 97]. Patients with uremia should avoid NSAIDs as analgesics, as there is an increased risk of bleeding.

3. Iatrogenically induced coagulopathies

3.1. Vitamin K antagonists (Warfarin)

Warfarin is a commonly used anticoagulant in patients with atrial fibrillation, history of pulmonary embolism, possibility of deep vein thrombosis, and in patients with prosthetic

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heart valves. Warfarin management can be challenging based on the narrow therapeutic range and other variables, such as drug interactions, diet, and systemic illnesses. Warfarin functions by inhibiting the enzyme epoxide reductase, which reduces vitamin K from its oxidized form so that it may participate in the carboxylation and activation of glutamate residues on coagulation factors II, VII, IX, X, protein C, and protein S.

Protein C and protein S are endogenous anticoagulant proteins and have shorter half-lives than factors II, VII, IX, and X [98]. Therefore, the initial effect of warfarin is a hypercoagulable state, with the anticoagulant effects of warfarin occurring after 2–3 days [99]. Due to the initial hypercoagulable state, patients at a high risk for a thromboembolic event may undergo bridging therapy with heparin for a period of 5–7 days. The effects of warfarin can be evaluated via PT or INR testing. Warfarin has an oral bioavailability of 100%, and over 99% of warfarin is bound to albumin. Due to the high protein binding of warfarin, the presence of other highly protein bound drugs may lead to the displacement of protein bound warfarin resulting in an increase in anticoagulation. Medications that promote the effects of warfarin include broad-spectrum antibiotics, fluconazole, metronidazole, erythromycin, cimetidine, phenytoin, and propranolol [98]. Additionally, broad-spectrum antibiotics may disrupt the normal gut flora, resulting in a decrease in vitamin K absorption and an increase in the effect of warfarin [100]. Medications that antagonize the effects of warfarin include steroids, cholestyramine, griseofulvin, rifampin, barbiturates, and carbamazepine [98]. There is also great inter-individual variation in dose to achieve therapeutic anticoagulation due to genetic variation in the cytochrome p450 enzymes, further necessitating the need for regular INR monitoring. Despite genetic variation in p450 enzymes, genetic testing prior to initiation of warfarin therapy is not recommended, as there is limited evidence to support reduced risk of bleeding or thromboembolism with altered initial dosage; 5.0 mg once per day is the standard initial dosage for patients initiating warfarin, as higher dosages have been associated with increased bleeding events [101, 102]. In elderly patients or patients at increased sensitivity to warfarin, a lower initial dose of 2.5 mg per day may be indicated [103]. In patients with thrombotic disease, the INR is usually titrated to 2.0–3.0 and in patients with valvular disease it is titrated from 2.5 to 3.5.

Due to balancing the risk of hemorrhage while on warfarin and the increased risk for thromboembolism in patients whose anticoagulation is discontinued, Ward and Smith determined there remains a disparity in perioperative management of patients on warfarin undergoing dentoalveolar procedures [104]. In most clinical situation, the trend is to limit modifications to warfarin therapy and promote hemostasis with use of local hemostatic agents. In a randomized controlled trial comparing maintenance of warfarin therapy to bridging with low molecular weight heparin (LMWH), Bajkin et al. determined there was no statistical difference in post-extraction bleeding between the two groups when local hemostatic measures were used. The authors concluded that in patients on warfarin with an INR of less than or equal to 4, simple dental extractions could safely be performed without modification to the patient's oral anticoagulant therapy [105]. Morimoto et al. determined that patients on antiplatelet therapy and anticoagulant therapy with INR <3.0 can safely undergo dental extractions without risk of excessive bleeding [106]. Cocero et al. determined in patients with comorbid-

ities such as diabetes, liver disease, and kidney failure that the INR safety window should be adjusted to <2.3 [107].

In patients undergoing surgical procedures with a higher risk of bleeding including head and neck surgery and reconstructive plastic surgery, warfarin should be stopped 5 days preoperatively [108]. The use of bridging anticoagulation with unfractionated heparin or low molecular weight heparin should be based on the thromboembolic risk of the patient. The American College of Chest Physicians (ACCP) as part of the Perioperative Management of Antithrombotic Therapy of the Antithrombotic Therapy and Prevention of Thrombosis 9th ed. has developed a three-tiered thromboembolic risk stratification of patients with mechanical heart valves, atrial fibrillation, and history of venous thromboembolism [108]. The risk stratification includes high risk (>10%/years of ATE or >10%/months of venous thromboembolic events (VTE)), intermediate risk (4–10%/years risk of ATE or 4–10%/months risk of VTE), and low risk (<4%/years risk of ATE or <2%/months risk of VTE). In patients at a high risk for thromboembolism bridging anticoagulation is recommended [102]. In patients at low risk for thromboembolism, bridging anticoagulation is not recommended [102]. In patients at moderate risk for thromboembolism, use of bridging anticoagulation should be determined on a case-by-case basis [108]. In cases of excessive anticoagulation, the effects of warfarin can be stopped by the administration of parenteral vitamin K, prothrombin complex concentrate (PCC), or fresh-frozen plasma; 4 factor PCC including factors II, VII, IX, and X are preferred over FFP based on an increased rate of INR correction with fewer side effects [109].

3.2. Heparin and derivatives

3.2.1. Heparin (HMWH, unfractioned heparin

Heparin is an endogenously produced linear polysaccharide with anticoagulant effects [110]. Heparin binds to antithrombin, formerly known as antithrombin III, increasing the anticoagulant effect of antithrombin by a factor of 1000. The binding of heparin to antithrombin results in a conformational change allowing for increased binding to clotting factors. Antithrombin activation leads to the inactivation of thrombin, Factor IX, and Factor X [104]. HMWH is unique compared to low molecular weight heparin and fondaparinux due to its ability to inhibit thrombin. HMWH is able to inhibit thrombin by the formation of a complex between HMWH, antithrombin, and thrombin that requires the long chains found in HMWH [111]. The molecular weight HMWH is 5000–30,000. In patients on HMWH, close monitoring via PTT is necessary. The therapeutic levels of heparin are typically 1.5–2.5 normal PTT [112]. Typically, the therapeutic range is 0.3–0.07 units/ml (anti-Xa units), which is achieved via a bolus of 80–100 units/kg, followed by 15–20 units/kg/h [113]. The onset of parenteral HMWH is nearly immediate with a half-life of 45 min to 1 h [114]. Low-dose prophylaxis can be achieved with 5000 units subcutaneously every 8–12 h. Peak plasma concentration of subcutaneous heparin occurs at 2–4 h post-administration. In patients on bridging anticoagulation with heparin, it is recommended that patients have HMWH discontinued 4–6 h prior to surgery with postoperative resumption of HMWH after hemostasis has been achieved [108]. In surgeries with a high risk of bleeding, resumption of HMWH is done after 48–72 h [108]. The most common serious

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side effect of heparin treatment is heparin-induced thrombocytopenia (HIT). HIT is a hypercoagulable state that occurs in 1–4% of patients receiving unfractionated heparin due to antibodies to platelet factor 4 and heparin [115]. The formation of a thrombus or sudden decrease in platelet levels should raise suspicion for HIT. HMWH is metabolized by the liver and is unaffected by renal function. Reversal of the anticoagulant effect of heparin is achieved with the antagonist protamine. Protamine binds avidly to heparin reducing its anticoagulant effect. For every 100 units of heparin remaining in the patient, 1 mg of protamine is administered. Protamine should be administered slowly at a maximum rate of 20 mg/min (not to exceed 50 mg in a 10-min period).

3.2.2. Low molecular weight heparin (enoxaparin, dalteparin, and tinzaparin)

Low molecular weight heparin (LMWH) is derived from HMWH to produce a polysaccharide with a molecular weight of 2000–9000 Da [116]. LMWH, like heparin, leads to anticoagulation by promoting antithrombin to inactive Factor X and II. LMWH has a greater effect on Factor X compared to its effect on thrombin [98]. Advantages of LMWH over heparin include less frequent dosing and more predictable anticoagulant response compared to HMWH, limiting the need for laboratory monitoring. LMWH is unable to cross the placenta and is therefore the ideal anticoagulant during pregnancy. Disadvantages of LMWH include delayed onset, decreased effectiveness of protamine as a reversal agent, limitations in patients with renal failure and inability to monitor by PTT [117]. For enoxaparin, full-dose therapeutic levels should be titrated to 0.5–1.0 units/ml antifactor Xa for twice-daily dosing or 1.5 units/ml for once-daily dosing. Antifactor Xa should be used to measure activity of LMWH when indicated. For enoxaparin, prophylaxis 30 mg twice daily or 40 mg once daily should be given subcutaneously. Prophylactic dalteparin is typically administered as 5000 units every 8–12 h. Plasma concentrations peak at 2 h for IV administered LMWH and after 3–5 h for subcutaneously administered LMWH. The half-life is approximately 2 h. In patients receiving therapeutic subcutaneous LMWH as part of bridging anticoagulation, it is recommended that LMWH be discontinued 24 h prior to surgery and continued 24 h post-surgery pending hemostasis. In higher bleeding risk surgeries, LMWH should be continued 48–72 h post-surgery [108]. Protamine may be used to reverse the effects of LMWH. For LMWH administered in the last 8 h, 1 mg of protamine should be administered for every 1 mg of LMWH. For administration of LMWH longer than 8 h, prior 0.5 mg of protamine should be administered for every 1 mg of LMWH [118].

3.2.3. Fondaparinux (Arixtra)

Fondaparinux (Arixtra; GlaxoSmithKline, Mississauga, Ontario) is a small synthetic pentasaccharide fragment of heparin with a molecular weight of 1700 Da. Fondaparinux is an inhibitor of Factor Xa with high affinity for antithrombin compared to HMWH [98]. Fondaparinux is approved for prophylaxis of venous thromboembolic events (VTE) for up to one-month post-orthopedic surgery of the lower limbs, prophylaxis of VTE for patients undergoing abdominal surgery with high risk of thromboembolic events and in the acute treatment of DVT and pulmonary embolism [119]. Fondaparinux is not currently used for

long-term anticoagulation therapy. For prophylaxis, 2.5 mg of fondaparinux is administered subcutaneously once daily beginning 6–12 h post-surgery [120]. For VTE therapy, 5–10 mg is administered subcutaneously once daily in a weight-dependent manner. The half-life of fondaparinux is 17–21 h in patients with good renal function. The excretion of fondaparinux is highly dependent on renal function as 77% of fondaparinux is excreted unchanged in the urine within 72 h post-administration in patients with good renal function under the age of 75 years [119]. In patients with moderate renal insufficiency, creatinine clearance 30–50 ml/min, the half-life of fondaparinux is 29 h, and in patients with severe renal insufficiency, creatinine clearance <30 ml/min, the half-life of fondaparinux is 72 h [119]. Due to its renal excretion and concerns of prolonged bleeding, fondaparinux is contraindicated in patients with severe renal insufficiency. Fondaparinux has advantages over traditional heparin in terms of a reduced risk for heparin-induced thrombocytopenia. Fondaparinux is not currently approved for the use of "bridging," and there are currently no randomized controlled trials with fondaparinux used as a bridging therapy. There are limited case studies with fondaparinux used as bridging therapy, with Wei et al. publishing a case report in a patient with a history of HIT requiring perioperative bridging due to mitral valve replacement prior to resection of esophageal squamous cell carcinoma. The patient was successfully bridged used 2.5 mg of fondaparinux subcutaneously, with the last dose of fondaparinux given 30 h preoperatively and resumed 24 h postoperatively [121]. In patients with HIT or antithrombin deficiency, where heparins are contraindicated, the use of fondaparinux for perioperative bridging may be indicated but further investigation is required. Initial recommendations for discontinuation of fondaparinux preoperatively would be 3–5 half-lives, similar to other anticoagulants. This recommendation is based solely on expert opinion, with no differentiation between the 2.5 mg prophylaxis dose and 5–10 mg therapeutic dose [122]. In patients with good renal function, this would be at least 2 days prior to a surgical procedure with minimal bleeding risk and 4 days prior to a surgical procedure with a high risk of bleeding. In patients with mild-to-moderate renal dysfunction, these time points should be adjusted accordingly [122].

3.3. Antiplatelet Therapy

3.3.1. Aspirin

Aspirin is used in the prophylactic treatment of myocardial infarction, stroke, and acutely in acute coronary syndrome. For prophylaxis, patients regularly take 75–100 mg/day indefinitely [123] with 81 mg being the most common dose in the United States. Aspirins mechanism of action is the irreversible inhibition of cycloxygenase-1 (COX-1). By inhibition of COX-1, there is a decrease in formation in thromboxane A2 in platelets and therefore a decrease in platelet aggregation [56]. As aspirin is an irreversible inhibitor of COX-1, its effect is for the life span of the platelet. For dentoalveolar surgery, rarely is discontinuation of aspirin recommended. This is supported in the literature by Medeiros et al. who determined no difference in the amount of bleeding that occurred during tooth extraction between patients who continued prophylactic doses of aspirin therapy compared to those who suspended aspirin therapy [124]. In patients who are undergoing procedures with a high risk of bleeding including head and

neck surgery and reconstructive plastic surgery, cessation of aspirin should be based on the cardiovascular risk of the patient. In patients with a high risk for a cardiovascular event, aspirin therapy should be continued perioperatively, and in patients with a low risk of a cardiovascular event, aspirin therapy should be discontinued 7–10 days prior to surgery [108]. Patients at high risk for a cardiovascular event include those patients with congestive heart failure, diabetes mellitus, renal insufficiency, ischemic heart disease, and cerebrovascular disease [108].

3.3.2. P2Y12 receptor blockers

The P2Y12 blockers receptor blockers include clopidogrel, ticlopidine, prasugrel, ticagrelor, and cangrelor. The P2Y12 blockers function by blocking the binding of ADP to the P2Y12 receptor on platelets, resulting in an inhibition of platelet aggregation [125]. Clopidogrel, ticlopidine, and prasugrel are irreversible inhibitors of P2Y12 via prodrug conversion to active metabolites, while ticagrelor and cangrelor are direct reversible inhibitors of P2Y12. As a result of being irreversible inhibitors, there is a slower offset of action of clopidogrel, ticlopidine, and prasugrel compared to the reversible inhibitors [126]. Clopidogrel is the prototypical P2Y12 receptor blocker, but it is not an ideal anticoagulant due to its slow onset of action due to being a prodrug, unpredictable pharmacodynamics due to its p450 interactions, and slow offset as an irreversible inhibitor. Ticlopidine use is limited due its side effect of severe neutropenia. Prasugrel and ticagrelor have come into favor due to increased prevention of cardiovascular events [127, 128]. Prasugrel and ticagrelor also carry a high risk of bleeding compared to clopidogrel due to their faster onset and more consistent platelet inhibition [126]. P2Y12 blockers are commonly used along with aspirin for dual-antiplatelet therapy in patients with NSTEMI or coronary stent placement [129]. The current recommendation for patients with drug eluding stents is at least 12 months of dual-antiplatelet therapy, followed by an additional 18 months of dual-antiplatelet therapy considering the increased risk for bleeding [130]. The recommendations for bare metal stents are the same as for drug eluding stents with improved outcomes at greater than 12-month dual-antiplatelet therapy [131]. In patients undergoing dental extractions, Bajkin et al. determined that there was no increased risk in postoperative bleeding in patients on dual-antiplatelet therapy with clopidogrel and aspirin compared to patients on no antiplatelet therapy [132].

3.4. Direct oral anticoagulants (DOACs)

Direct oral anticoagulants (DOACs) including thrombin and Factor X inhibitors are being used in treatment of stroke prevention in patients with atrial fibrillation, prophylaxis for venous thromboembolism post-surgery, in management of venous thromboembolism, in secondary prevention of thromboembolism, and in heparin-induced thrombocytopenia. DOACs are contraindicated in patients with prosthetic heart valves, severe renal impairment, and during pregnancy. Compared to warfarin, the DOACs have several advantages. This includes a rapid onset of action, a relatively wide therapeutic range, and a decrease in need for regular coagulation monitoring. Compared to heparin, DOACs have the advantage of oral bioavailability. Direct factor inhibitors are also reported have an overall lower bleeding risk compared

to warfarin [133]. With a decreased necessity for close monitoring, there is an increased concern for patient compliance. While compliance between patients taking vitamin K antagonists and DOACs may be equal, missing a single dose of a DOAC has an increased risk of anticoagulation outside the therapeutic window compared to missing a single dose of warfarin [134]. Other concerns include a current lack of specific antidotes. Direct thrombin inhibitors include parenteral bivalirudin (Angiomax; The Medicines Company Parsippany, NJ, USA), argatroban, and desirudin. Bivalirudin is a synthetic analog to hirudin, a natural anticoagulant in the saliva of leeches. Bivalirudin is renally excreted and in patients with adequate renal function has a half-life of 25 min. Similar to other DOACs, there is no antidote for bivalirudin. Bivalirudin has been used as an alternative to heparin in patients with HIT [135, 136]. The only oral direct thrombin inhibitor is dabigatran (Pradaxa; Boehringer Ingelheim Ridgefield, CT, USA). There are no parenteral Factor X inhibitors. Oral Factor X inhibitors include rivaroxaban (Xarelto; Janssen Pharmaceutica, Belgium), apixaban (Eliquis; Bristol-Myers Squibb, New York, NY, USA), and edoxaban (Lixiana; Daiichi-Sankyo, Japan).

3.4.1. Dabigatran (Pradaxa)

Dabigatran is a competitive direct thrombin inhibitor. Thrombin is the final enzyme of the coagulation cascade that cleaves fibrinogen into fibrin. In addition, thrombin also activates factors V, VIII, XI, and XIII [137]. Dabigatran is able to block the action of both circulating and clot bound thrombin therefore preventing the propagation of clots. This is unique from heparin, which only blocks circulating thrombin [138]. Dabigatran is approved to reduce the risk of stroke in atrial fibrillation, treatment of venous thromboembolism, and secondary prevention of venous thromboembolism with a dosing of 150 mg twice a day in patients with good renal function. In post-surgical patients for prevention of venous thromboembolism, 110 mg is administered post-surgery followed by 220 mg once daily for one to four weeks. The prodrug dabigatran etexilate has a 6–7% oral bioavailability [139, 140]. Peak plasma concentration is achieved in 1–2 h and the half-life ranges from 12 to 17 h [141]. The anticoagulant effects of dabigatran last for 2–3 days. The drug is cleared renally and should be avoided in patients with severe renal impairment [142]. Dabigatran has fewer drug interactions than warfarin as it is not metabolized by the p450 system, but should be avoided in patients taking amiodarone, verapamil, quinidine, and rifampin as these drugs increase the effects of dabigatran [139, 140]. The antidote for dabigatran is idarucizumab (Praxbind Boehringer Ingelheim, Germany), a monoclonal antibody that can be used in emergency situations for reversal of dabigatran [143]. In the RE-LY trial, Eikelboom et al. determined that there was no increased risk of bleeding with warfarin titrated to an INR of 2–3 compared to dabigatran 150 mg twice a day [144]. There are currently no randomized controlled trials evaluating the risk of bleeding in patients on dabigatran undergoing dental extractions. The limited evidence in managing patients undergoing dental extractions indicates continuing anticoagulant treatment, delaying extractions as long as possible since the last dosage of dabigatran, and the use of local hemostatic agents [145]. If dabigatran is to be interrupted preoperatively, renal function should be considered. In patients with normal or mild impairment of renal function undergoing surgery with low bleeding risk, the last dose should be administered 2 days before surgery, and in patients with moderate renal impairment, the last dose should be administered 3 days before

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surgery. In patients with normal or mild impairment of renal function undergoing surgery with a high bleeding risk, the last dose should be administered 3 days before surgery, and in patients with moderate renal impairment, the last dose should be administered 4–5 days before surgery [146]. In emergency situations, the safe concentration for dabigatran at which surgery can be performed without the risk of major bleeding is less than 30 ng/ml. A PTT and PT ratio of <1.2 compared to normal is indicative of a dabigatran concentration of <30 ng/ml. If PTT and PT concentration is greater than 1.2 compared to normal, treatment should be delayed for 24 h and new laboratory tests taken prior to treatment [147].

3.4.2. Rivaroxaban (Xarelto)

Rivaroxaban is a competitive direct Factor X inhibitor. Activated Factor X cleaves prothrombin to thrombin. Rivaroxaban is able to bind to both circulating and clot bound Factor X, preventing the propagation of clot formation. This is unique from heparin, which only binds to circulating Factor X. Rivaroxaban is approved for prevention of stroke in patients with atrial fibrillation, prevention of venous thromboembolism following surgery, and in the treatment and prevention of venous thromboembolism [108]. There is no prodrug for rivaroxaban. For post-surgical prophylaxis of VTE, 10 mg is used daily for 2–5 weeks; for treatment and prevention of VTE, 15 mg is given twice daily for 3 weeks followed by 20 mg once daily; for stroke prevention in atrial fibrillation, 20 mg is used once daily in patients with good renal function. The oral bioavailability is ~80%. Peak plasma concentration is achieved in 2.5–4 h [108, 109]. Rivaroxaban has a half-life of 5–9 h, and the anticoagulant effect lasts for 1–2 days [110]. One-third is excreted renally, and two-thirds are converted by CYP 3A4 to inactive metabolites. Therefore, strong p450 inhibitors and inducers may have significant drug interactions [148]. Rivaroxaban is not recommended in patients with poor renal function or poor liver function [149]. There is no known antidote for rivaroxaban. There are currently no randomized controlled trials evaluating the risk of bleeding in patients on rivaroxaban undergoing dental extractions. As part of the ROCKET AF Trial, Sherwood et al. determined that there was a higher risk of major and minor GI bleeding compared to warfarin, but no difference in severe bleeding [150]. The limited evidence in managing patients undergoing dental extractions indicates continuing anticoagulant treatment, delaying extractions as long as possible since the last dosage of rivaroxaban, and the use of local hemostatic agents. If rivaroxaban is to be interrupted preoperatively, renal function should be considered. For patients with normal, mild, or moderate impairment of renal function undergoing surgery with a low bleeding risk, the last dose should be given 2 days prior to surgery, for a surgery with a high bleeding risk the last dose should be given 3 days before surgery. For patients with severe impairment of renal function, creatinine clearance less than 30 ml/min, undergoing surgery with a low bleeding risk the last dose should be given 3 days before surgery and for a surgery with a high bleeding risk the last dose should be given 4 days before surgery [106]. The concentration for rivaroxaban at which emergency surgery can be performed without major risk of bleeding is less than 30 ng/ml. Regular laboratory testing of rivaroxaban concentration is not always available, but analysis of PT and PTT can act as a good indicator. A PTT and PT ratio of <1.2 compared to normal is indicative of a rivaroxaban concentration of <30 ng/ml. If PTT and PT concentration

is greater than 1.2 compared to normal, treatment should be delayed for 24 h and new laboratory tests taken prior to treatment [107].

3.4.3. Apixaban (Eliquis)

Apixaban is a direct oral Factor X inhibitor. The half-life of apixaban is 5–9 h [101]. Apixaban can be used in post-surgical VTE prophylaxis, treatment and prevention of VTE, and stroke prevention patients with atrial fibrillation. Compared to other DOACs, apixaban has the least risk for bleeding complications [151]. There are currently no randomized controlled trials evaluating the risk of bleeding in patients on apixaban undergoing dental extractions. The limited evidence in managing patients undergoing dental extractions indicates continuing anticoagulant treatment, delaying extractions as long as possible (since the last dosage of apixaban) and the use of local hemostatic agents. If apixaban is to be interrupted preoperatively, renal function should be considered. In patients with normal or mild impairment of renal function undergoing surgery with low bleeding risk, the last dose should be administered 2 days before surgery, and in patients with moderate renal impairment, the last dose should be administered 3 days before surgery. In patients with normal or mild impairment of renal function undergoing surgery with a high bleeding risk, the last dose should be administered 3 days before surgery, and in patients with moderate renal impairment, the last dose should be administered 4 before surgery [106].

4. Local hemostatic agents

In many patients, local hemostatic agents are an efficient and cost-effective way to limit blood loss. By limiting blood loss in the perioperative period, there is a decreased need for additional interventions and their associated morbidities, including blood transfusions and their associated risks. The use of local hemostatic agents aids in preventing the need for the discontinuation of anticoagulant therapy that would place patients at risk of thromboembolic events. Additionally, the use of local hemostatic agents is cost-effective by decreasing the need for follow-up due to incidence of "rebleeding." Local hemostatic agents can be divided into two main categories: physical agents that provide scaffolding for clot formation and biologically active agents that include clotting factors or antifibrinolytics that promote clot formation or inhibit clot dissolution. Physical agents include bone wax, oxidized regenerated cellulose (Surgicel; Ethicon, Neuchatel, Switzerland), and gelatin matrix (Gelfoam; Pfizer, New York, NY, USA). Biologically active agents include topical thrombin (RECOTHROM; Zymogenetics, Seattle, WA, USA), aminocaproic acid (AMICAR; Clover Pharmaceuticals, Marietta, GA, USA), and tranexamic acid (IV Cyklokapron; Pfizer, New York, NY, USA) (oral tablet LYSTEDA; Ferring Pharmaceuticals Saint-Prex-Switzerland).

Oxidized regenerated cellulose (Surgicel) is a resorbable sterile mesh that can be layered at a bleeding surgical site. Surgicel has bactericidal properties due to its acidic pH [152]. This is an advantage of Surgicel over other hemostatic agents, as the highly absorptive properties of other physical hemostatic agents at a neutral pH have been shown to be a nidus for infection. The

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acidic pH of Surgicel may have a negative effect on other hemostatic agents, such as thrombin. Surgicel is known to inhibit topical thrombin; thus, Surgicel and topical thrombin should not be used together to promote hemostasis. Additionally, Alkan et al. and Loescher and Robinson in two separate animal models have determined that Surgicel when placed in close proximity to nerves may have a negative effect on peripheral nerve function [153, 154].

Gelfoam is a highly absorbable gelatin matrix prepared from purified porcine. Gelfoam is highly pliable, can easily be placed in bleeding extraction sockets, and completely reabsorbs in 4–6 weeks [155]. The main effect of Gelfoam is to act as a scaffold for coagulation. Gelfoam has a neutral pH. The use of Gelfoam as a physical matrix combined with topical thrombin as a biological agent is an effective way to obtain hemostasis. The highly absorptive property of Gelfoam has been reported to act as a nidus for infection and granuloma formation.

HemCon Dental Dressing (Zimmer Holdings, HemCon Medical Technologies Inc., Beaverton, OR, USA) is an absorbable chitosan derived dressing used for hemostasis in dental extraction sites [156]. Advantages of HemCon include its antimicrobial properties and its ability to be placed over extraction sockets compared to being placed in extraction sockets and sutured in place [157]. CollaPlug (Zimmer Dental, Carlsbad, CA, USA) is an absorbable collagen based agent that acts a physical matrix to promote the coagulation cascade in extraction sockets. The absorbable collagen membrane is also marketed as CollaTape for closure of graft sites and repair of Schneiderian membrane tears, as well as CollaCote to be placed over soft-tissue donor sites [158]. In a recent study, Pippi et al. compared HemCon to CollaPlug and found favorable outcomes in patients on anticoagulant therapy undergoing dental extractions with INR less than 3.5 with both hemostatic agents. The authors reported advantages of HemCon, such as reduced operative time and improved soft-tissue healing, which they attributed to obviating the need for suturing [156].

Bone wax, a mixture of beeswax and isopropyl palmitate, is an inexpensive and effective way of occluding small bleeding vessels in bone. Bone wax does not act as a scaffold for coagulation or contain coagulation factors, but rather a compressive and occlusive dressing. Increased risk of infection is reported with the use of bone wax [159].

Topical thrombin is able to convert fibrinogen to fibrin in the final step of the coagulation cascade. Topical thrombin is available in a liquid form and can be an effective way to obtain hemostasis when combined with Gelfoam or collagen matrices. As mentioned previously, Surgicel and thrombin should not be used together.

Tranexamic acid and aminocaproic acid are antifibrinolytic agents composed of synthetic lysine residues capable of blocking plasminogen and plasmin binding to fibrin. Tranexamic acid can be administered intravenously or topically. In patients undergoing orthognathic surgery, Choi et al. determined that a bolus of tranexamic acid (20 mg/kg) preoperatively significantly reduced intraoperative bleeding compared to controls [160]. In a recently published randomized control trial, Eftekharian et al. used tranexamic acid (1 mg/mL) in combination with normal saline as an irrigant during orthognathic surgery and concluded that there was a statistical significance in blood loss between the tranexamic acid irrigant and the saline control irrigant, with the tranexamic acid irrigant reducing mean blood loss by >25%

[161]. Gauze soaked in topical tranexamic acid is an effective way of gaining the hemostatic effects of tranexamic acid post-dental extraction patients. The use of a tranexamic acid mouthwash as a hemostatic agent in post-dental extraction patients is supported by Carter et al. who found favorable outcomes of a 4.8% tranexamic mouthwash four times a day for 7 days post-dental extraction compared to a fibrin glue preparation in patients on anticoagulant therapy [162, 163] (**Table 2**).

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Section 7

Diagnosis and Management of Facial Skin Lesions

Chapter 10

Common Skin Lesions of the Face

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Additional information is available at the end of the chapter

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Abstract

Skin lesions are common and range from acute inflammatory dermatoses, such as urticaria, to malignant melanoma, which may be life-threatening. When confronting skin diseases, it is important that the maxillofacial surgeon collaborate with both the dermatologist and pathologist. The clinical history, gross appearance, and course of any disease are as important as the microscopic findings. In this chapter, we discuss the more common skin lesions of the face.

Keywords: acute and chronic dermatoses, infectious, auto immune, blistering, skin lesion

1. Introduction

In this chapter, the more common skin lesions of the face are discussed. These include the following:

- **Acute inflammatory dermatoses:** urticaria, acute eczema dermatitis, and erythema multiforme
- **Chronic inflammatory dermatoses:** psoriasis and lichen planus
- **Infectious dermatoses:** bacterial infections (impetigo, cat-scratch disease), fungal infections, and viral infections (herpes simplex, chickenpox, herpes zoster)
- **Autoimmune diseases:** systemic lupus erythematosus, chronic cutaneous (discoid) lupus erythematosus, scleroderma, and angioedema
- **Blistering (bullous) disorders:** pemphigus, bullous pemphigoid, and dermatitis herpetiformis

- **Benign and premalignant epithelial lesions and nevi:** melanocytic nevus, dysplastic nevus, actinic keratosis, seborrheic keratosis, and keratoacanthoma
- **Malignant epidermal tumors:** basal cell carcinoma, squamous cell carcinoma, and malignant melanoma
- **Miscellaneous:** Sturge-Weber syndrome, *Paederus* dermatitis, and melasma

2. Acute inflammatory dermatoses

2.1. Urticaria

Urticaria ("hives") is a common disorder mediated by localized mast cell degranulation, which leads to dermal microvascular hyperpermeability. The resulting erythematous, edematous, and pruritic plaques are termed "wheals". In most cases, urticaria stems from an immediate (type 1) hypersensitivity reaction in which antigens trigger mast cell degranulation by binding to immunoglobulin E (IgE) antibodies displayed on the mast cell surface. The responsible antigens include pollens, foods, drugs, and insect venom (**Figure 1**) [1].

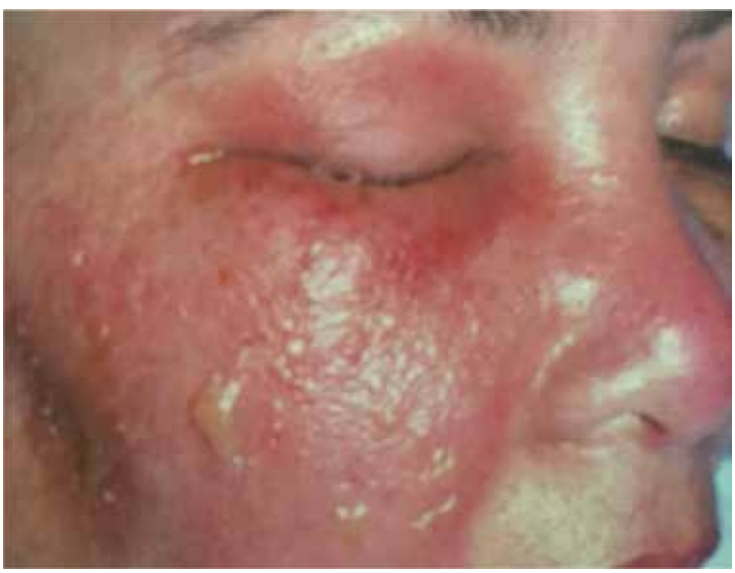

Figure 1. Urticaria.

2.2. Acute eczematous dermatitis

"Eczema" is a clinical term that embraces a number of conditions with varied underlying etiologies. New lesions take the form of red papules, often with overlying vesicles, that ooze and become crusted. With persistence, these lesions develop into raised, scaling plaques. The

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nature and degree of these changes vary among the clinical subtypes, which include the following:

- **allergic contact dermatitis**, which stems from topical exposure to an allergen;
- **atopic dermatitis**, which has traditionally been attributed to allergen exposure but is now thought to stem from defects in keratinocyte barrier function, many with a genetic basis;
- **drug-related eczematous dermatitis**, a hypersensitivity reaction to a drug;
- **photoeczematous dermatitis**, in which eczema appears as an abnormal reaction to UV or visible light;
- **primary irritant dermatitis**, which results from exposure to substances that chemically, physically, or mechanically damage the skin.

In most cases, these skin lesions resolve completely when the offending stimulus is removed or exposure is limited, stressing the importance of investigating the underlying cause. Only contact dermatitis, the most common form, is considered here.

Contact dermatitis is triggered by exposure to an environmental contact sensitizing agent, such as poison ivy, that chemically reacts with self-proteins (**Figure 2**) [2].

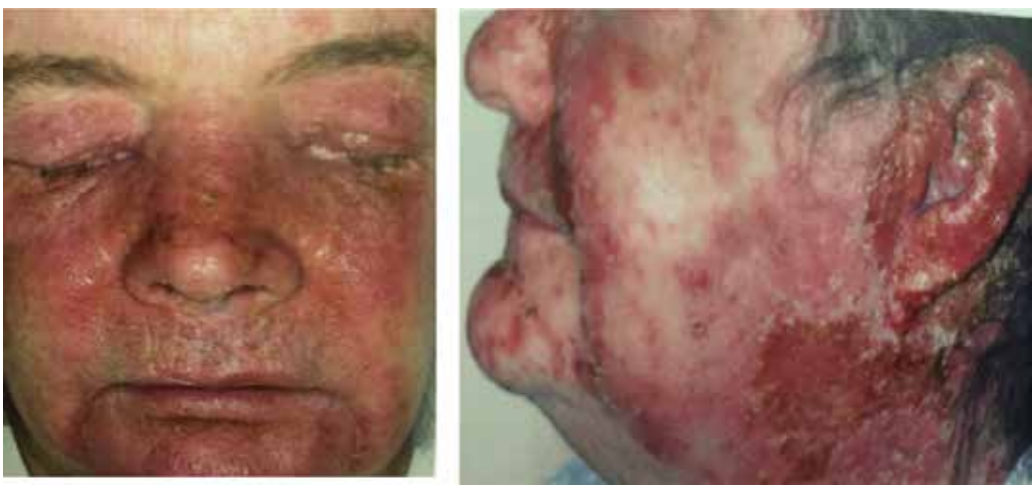

Figure 2. Acute eczematous dermatitis.

2.3. Erythema multiforme

Erythema multiforme is a self-limited, sometimes episodic, disease of the skin that may also involve the mucous membranes. It is characterized by a pleomorphic eruption consisting of erythematous macules, papules, urticarial plaques, vesicles, and bullae. Individual lesions may evolve through a papular, vesicular, and target (iris) stage in which bullae surmount an

erythematous maculopapule. Lesions tend to be distributed symmetrically with a predilection for the extremities, particularly the hands.

In the past, erythema multiforme was classified into erythema multiforme minor and erythema multiforme major, the latter being characterized by a severe and sometimes fatal illness in which fever, systemic symptoms, and severe oral lesions were usually present. Stevens-Johnson syndrome was also diagnosed in these severe cases with oral involvement. Recently, an attempt has been made to distinguish Stevens-Johnson syndrome from erythema multiforme major with mucosal lesions on the basis of their different cutaneous lesions and their etiology; their mucosal lesions are similar. Stevens-Johnson syndrome is said to be characterized by flat atypical target lesions or purpuric macules that are widespread or limited to the trunk. Erythema multiforme major with mucosal lesions has typical or raised atypical target lesions, located on the extremities and/or the face. With these definitions, Stevens-Johnson syndrome is usually related to drugs and erythema multiforme to herpes or other infections.

Erythema multiforme major occurs in younger males, has frequent recurrences, and is marked by mild fever, milder mucosal lesions, and a lack of association with collagen vascular diseases, human immunodeficiency virus (HIV) infection, or cancer. Recent or recurrent herpes simplex infection is the principal risk factor. The criteria used to distinguish the component diseases that form this spectrum have been criticized on fundamental clinical differences between the two related conditions. Stevens-Johnson syndrome is associated with systemic symptoms and the involvement of internal organs, whereas erythema multiforme is not.

Toxic epidermal necrolysis has been widely regarded as a separate entity or as representing the severe end of the spectrum of erythema multiforme major or Stevens-Johnson syndrome. Some clinicians have arbitrarily diagnosed toxic epidermal necrolysis when blisters and

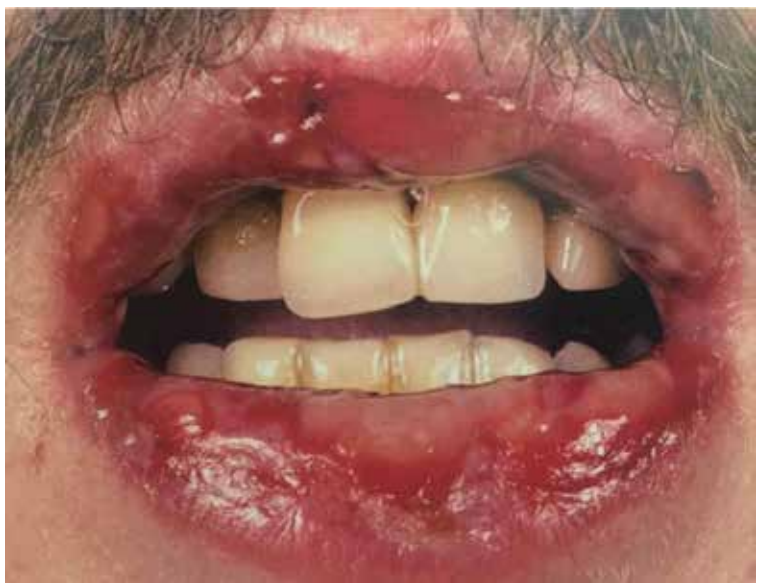

Figure 3. Erythema multiforme.

peeling involved more than 30% of the total body surface area and Stevens-Johnson syndrome when mucosal lesions were present and blistering involved less than 30% of the body surface (**Figure 3**) [3–5].

3. Chronic inflammatory dermatoses

3.1. Psoriasis

Psoriasis is a chronic inflammatory dermatosis that appears to have an autoimmune basis. It is a common disorder, affecting as many as 1% to 2% of people in the United States. Persons of all ages may develop the disease. Approximately 15% of patients with psoriasis have associated arthritis. Psoriatic arthritis may be mild or may produce severe deformities resembling the joint changes seen in rheumatoid arthritis. It can affect any joint in the body and may be symmetrical or unilateral only. In addition, psoriasis may also be associated with myopathy, enteropathy, and AIDS. Psoriasis results from interactions of genetic and environmental factors. As in the case of many autoimmune diseases, it is linked to genes within the HLA locus, most frequently affecting the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal cleft, and glans penis.

The typical lesion is a well-demarcated, pink to salmon-colored plaque covered by loosely adherent silver-white scales (**Figure 4**) [6–8].

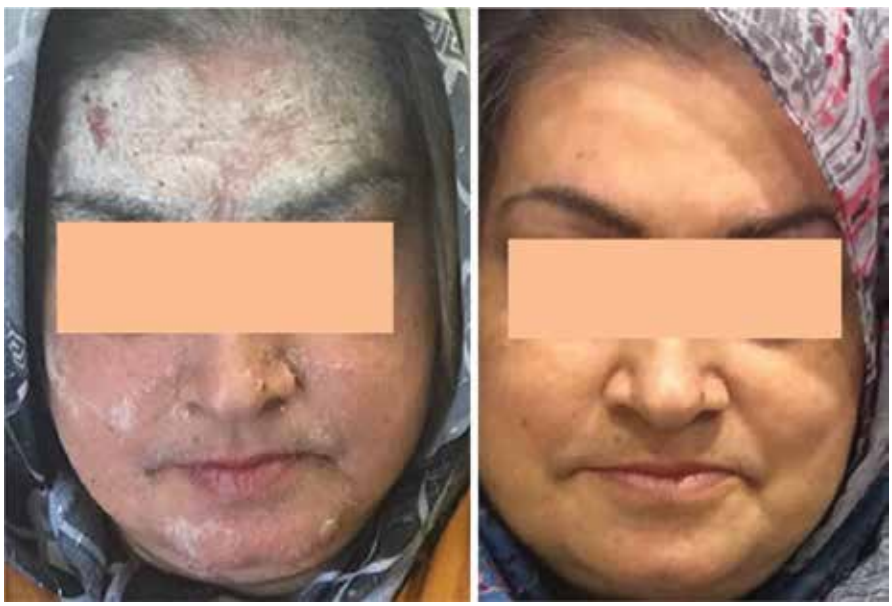

Figure 4. Psoriasis (before and after treatment).

3.2. Lichen planus

Lichen planus, a relatively common eruption of unknown etiology, displays violaceous, flat-topped papules that are usually pruritic. A network of fine white lines (Wickham striae) may be seen on the surface of the papules. There is a predilection for the flexor surface of the wrists, the trunk, the thighs, and the genitalia. Oral lesions are common; rarely, the esophagus is also involved. Lesions localized to the vulva and eyelids have been reported. Lichen planus localized to a radiation field may represent an isomorphic response. It has also developed in a healed herpes zoster scar. Nail changes occur, and, as with oral lesions, these may be the only manifestations of the disease. Clinical variants include atrophic, annular, hypertrophic, linear, zosteriform erosive, oral, actinic, follicular, erythematous, and bullous forms. An eruptive variant also occurs. Spontaneous resolution of lichen planus may occur and is usual within 12 months, although postinflammatory pigmentation may persist for some time afterwards. Familial cases are uncommon, and rarely these are associated with HLA-D7. An association with HLA-DR1 has been found in nonfamilial cases (**Figure 5**) [9–14].

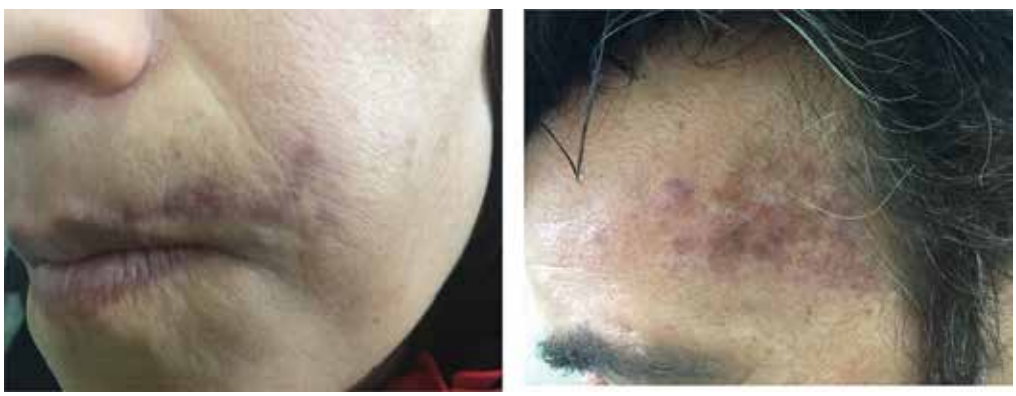

Figure 5. Lichen planus.

4. Infectious dermatoses

4.1. Bacterial infection

4.1.1. Impetigo

Impetigo is a superficial infection of the skin that is caused by *Staphylococcus aureus*, alone or in combination with *Streptococcus pyogenes* (group A, β-hemolytic). Two main patterns are seen: Seventy percent of the cases are **nonbullous impetigo**, which typically demonstrates a mixture of *S. aureus* and *S. pyogenes*, whereas **bullous impetigo** is less common and predominantly caused by *S. aureus*. The term "impetigo" is derived from a Latin word meaning "attack" because of its common presentation as a scabbing eruption. Intact epithelium normally is

protective against infection; thus, most cases arise in damaged skin, such as preexisting dermatitis, cuts, abrasions, or insect bites. Secondary involvement of an area of dermatitis has been termed **impetiginized dermatitis**. An increased prevalence is associated with debilitating systemic conditions, such as HIV infection, type 2 diabetes mellitus, and dialysis. **Nonbullous impetigo** (**impetigo contagiosa**) is the more prevalent pattern and occurs most frequently on the legs, with less common involvement noted on the trunk, scalp, and face. Facial lesions usually develop around the nose and mouth. In an infrequent pattern of impetigo termed **ecthyma**, the central area of the crust becomes necrotic and forms a deep indurated ulceration. Weakness, fever, and diarrhea may be seen. Lymphadenopathy and cellulitis are unusual complications. Meningitis and pneumonia are very rare but may lead to serious complications, even death (**Figure 6**) [15, 16].

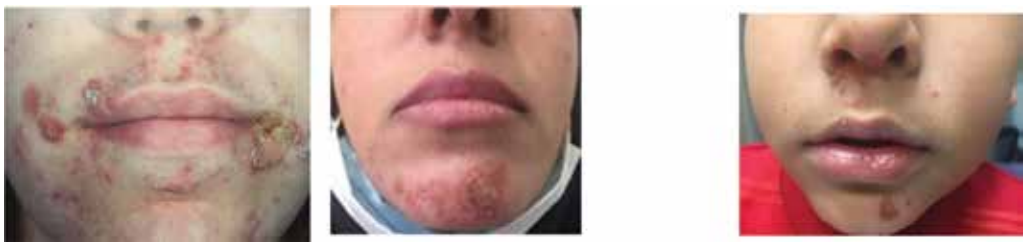

Figure 6. Impetigo.

4.1.2. Cat-scratch disease

Cat-scratch disease is an infectious disorder that begins in the skin but classically spreads to the adjacent lymph nodes. This infection is the most common cause of chronic regional lymphadenopathy in children, with an estimated 22,000 cases occurring annually in the United States. The causative organism was initially named *Rochalimaea henselae* but was reclassified as *Bartonella henselae* when the genera *Bartonella* and *Rochalimaea* were combined. Almost all cases arise after contact with a cat. The spread of the infection between cats appears to occur through cat fleas. The organism becomes an intraerythrocytic parasite and may be transmitted to humans via saliva or from a scratch. Infection from other sources is highly unlikely, but the disease rarely has been described in dogs, monkeys, porcupine quills, and thorns. Person-to-person transmission has not been documented. Eighty percent of the cases occur in patients younger than 21 years. Cat-scratch disease begins as a papule that develops in 3 to 14 days along the initial scratch line. The lesion typically progresses through erythematous, vesicular, and papular-crusted stages, with resolution usually occurring within 1 to 3 weeks. About the time the skin lesion heals, lymph node changes arise and may be accompanied by fever or malaise. In about half of the cases, a single node is involved. Multiple regional nodes are affected in about 20%, and nodal enlargement is discovered in multiple sites in about 33%. Suppuration is noted in approximately 10% of affected patients. The most frequently affected nodes are those in the head and neck, axillary, epitrochlear, and groin regions. Although the

vast majority of affected patients present with typical cat-scratch disease as described above, a variety of systemic manifestations may be seen. Of these, prolonged fever of unknown origin and hepatosplenic disease are the most common. Less common problems include cardiac, hematologic, neurological, ocular, orthopedic, and pulmonary manifestations (**Figure 7**) [17].

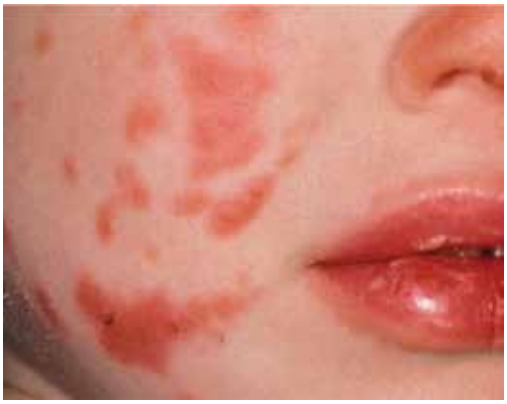

Figure 7. Cat-scratch disease.

4.1.3. Cutaneous leishmaniasis

Cutaneous leishmaniasis is a chronic self-limited granulomatous disease of the skin usually caused by *Leishmania tropica*. It is common in children. It is endemic in the Middle East, around the Eastern Mediterranean, in North Africa, and in areas of Asia. The term "Old World" leishmaniasis has been used for such cases (**Figure 8**) [18, 19].

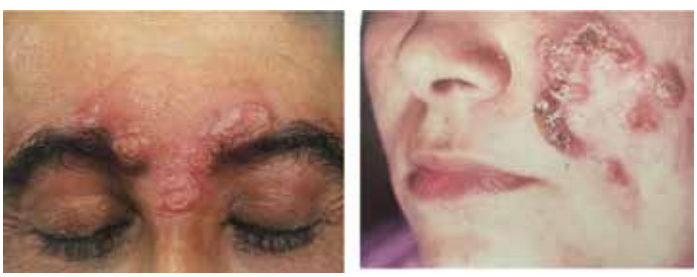

Figure 8. Cutaneous leishmaniasis.

4.2. Fungal infections

4.2.1. Mucormycosis

Mucormycosis is an opportunistic, frequently fulminant fungal infection that is caused by normally saprobic organisms of the subphylum Mucoromycotina, including such genera as

Absidia, *Mucor*, *Rhizomucor*, and *Rhizopus*. The presenting symptoms of rhinocerebral mucormycosis may be exhibited in several ways. Patients may experience nasal obstruction, bloody nasal discharge, facial pain or headache, facial swelling or cellulitis, and visual disturbances with concurrent proptosis. Symptoms related to cranial nerve involvement (e.g., facial paralysis) are often present. With progression of the disease into the cranial vault, blindness, lethargy, and seizures may develop, followed by death (**Figure 9**) [20].

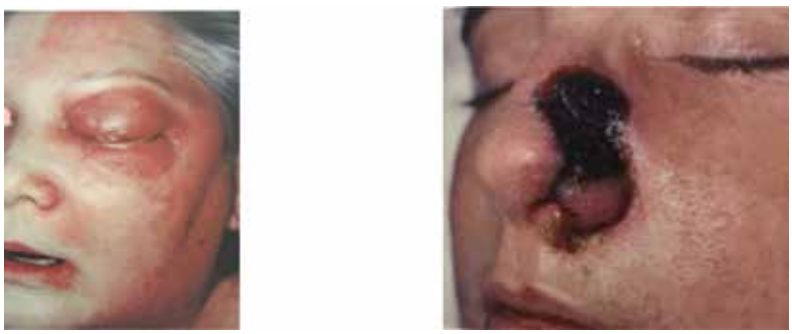

Figure 9. Mucormycosis.

4.3. Viral infections

4.3.1. Herpes simplex virus

The two herpes simplex viruses (type 1 and type 2) are similar in structure and disease mechanisms but differ in antigenicity, anatomical site predilection, and epidemiology. Differences in envelope glycoproteins account for their distinct antigenicity. Nevertheless, there is potential for antibody cross-reactivity and antibodies directed against one type may decrease the likelihood or severity of infection with the other type. HSV-1 is spread predominantly through infected saliva or active perioral lesions of the oral, facial, and ocular areas. The pharynx, intraoral mucosa, lips, eyes, and skin above the waist are involved most frequently. Genital HSV-1 infection is uncommon, although recent studies have shown an increase in the proportion of genital herpes caused by HSV-1 in developed nations. This trend has been attributed to an increase in oral-genital sexual behavior and lower rates of nonsexual HSV-1 acquisition in childhood. **Primary infection** refers to initial exposure of an individual without antibodies to the virus. Primary infection with HSV-1 typically occurs at a young age, often is asymptomatic, and usually does not cause significant morbidity. For symptomatic cases, the usual incubation period is 3 to 9 days. After primary infection is established, the virus is taken up by sensory nerves and transported to the associated sensory or, less frequently, autonomic ganglia where the virus remains in a latent state. The most common site of latency for HSV-1 is the trigeminal ganglion. The virus uses the axons of the sensory neurons to travel back to the skin or mucosa. **Recurrent** (**secondary** or **recrudescent**) **infection** occurs with reactivation of the virus. Old age, ultraviolet light, physical or emotional stress, fatigue, heat, cold, pregnancy, allergy, trauma, dental treatment, respiratory illnesses, fever, menstru-

ation, systemic diseases, and malignancy have been associated with reactivation. Symptomatic recurrences are fairly common and affect the epithelium supplied by the sensory ganglion; however, reactivation with asymptomatic viral shedding greatly exceeds clinically evident recurrences. Spread to an uninfected host can occur from symptomatic active lesions or asymptomatic viral shedding. In addition, the virus may spread to other sites in the same host to establish residency at the sensory ganglion of the new location (**Figure 10**) [21, 22].

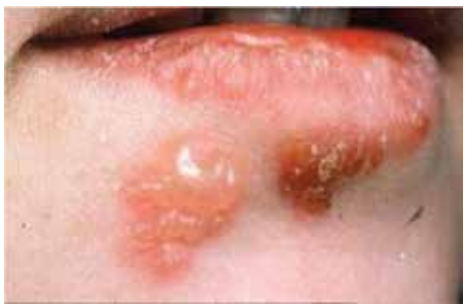

Figure 10. Herpes simplex virus.

4.3.2. Herpes zoster (shingles)

After primary infection with varicella virus (chickenpox), the virus is transported up the sensory nerves and establishes latency in the dorsal root ganglia. Clinically evident herpes zoster develops after reactivation of the virus, with involvement of the distribution of the affected sensory nerve.

Immunosuppression, HIV infection, treatment with cytotoxic or immunosuppressive drugs, radiation, malignancy, old age, alcohol abuse, stress (emotional or physical), and dental manipulation are additional predisposing factors for reactivation. The long-term impact of varicella virus vaccination on herpes zoster prevalence is controversial and presently under evaluation. Interestingly, it is possible to develop herpes zoster by reactivation of either the wild type or the vaccine strain virus, although the risk for vaccine strain zoster seems to be much lower than that for wild-type zoster. The clinical features of herpes zoster can be grouped into three phases: prodromal, acute, and chronic. During initial viral replication, ganglionitis develops with resultant neuronal necrosis and severe neuralgia. This inflammatory reaction is responsible for the prodromal pain present in more than 90% of cases. The virus travels down the nerve (dermatome) and may be accompanied by fever, malaise, and headache. Typically, one dermatome is affected, but involvement of two or more can occur. The thoracic dermatomes are affected in about two thirds of the cases. This prodromal pain normally precedes the acute phase rash by 1 to 4 days and, depending on which dermatome is affected, may masquerade as sensitive teeth, otitis media, migraine headache, myocardial infarction, or appendicitis.

The acute phase begins as the involved skin develops clusters of vesicles set on an erythematous base. The lesions tend to follow the path of the affected nerve and terminate at the midline.

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Within 3 to 4 days, the vesicles become pustular and ulcerate, with crusts developing after 7 to 10 days. The lesions are contagious until they crust, although the rate of varicella zoster virus (VZV) transmission from herpes zoster lesions is lower than that from varicella lesions. The exanthema typically resolves within 2 to 3 weeks in otherwise healthy individuals. On healing, scarring with hypopigmentation or hyperpigmentation is not unusual. Infrequently, there is dermatomal pain without development of a rash; this pattern is called **zoster sine herpete** (zoster without rash). Ocular involvement is present in approximately 10% to 25% of cases and can cause significant morbidity, including permanent blindness. The ocular manifestations are highly variable and may arise from direct virus-mediated epithelial damage, neuropathy, immune-mediated damage, or secondary vasculopathy. Lesions on the tip of the nose (Hutchinson sign) indicate involvement of the nasociliary branch of the trigeminal nerve and an increased risk for severe ocular infection. In these cases, referral to an ophthalmologist is mandatory. Reactivation of VZV in the geniculate ganglion may cause **Ramsay Hunt syndrome**, which is characterized by cutaneous lesions of the external auditory canal and involvement of the ipsilateral facial and auditory nerves. Affected individuals may exhibit facial paralysis as well as hearing deficits, vertigo, and other auditory and vestibular symptoms. In addition, some patients may develop loss of taste in the anterior two thirds of the tongue. By using PCR or serology, investigators have detected active VZV infections in approximately 30% of patients thought to have Bell's palsy. Similar associations also have been demonstrated with HSV and EBV. These findings suggest an underlying viral cause for many cases of "idiopathic" facial paralysis. Approximately 15% of patients progress to the chronic phase of herpes zoster (termed **postherpetic neuralgia**), which is characterized by persistent pain after resolution of the rash. In defining postherpetic neuralgia, there is a lack of consensus regarding the duration of pain persistence following the rash, although many investigators consider a minimum period of 1 to 3 months. Risk factors include female sex, older age, history of prodromal pain, moderate to severe rash and/or pain during the acute phase, and ophthalmic involvement (**Figures 11** and **12**) [23–27].

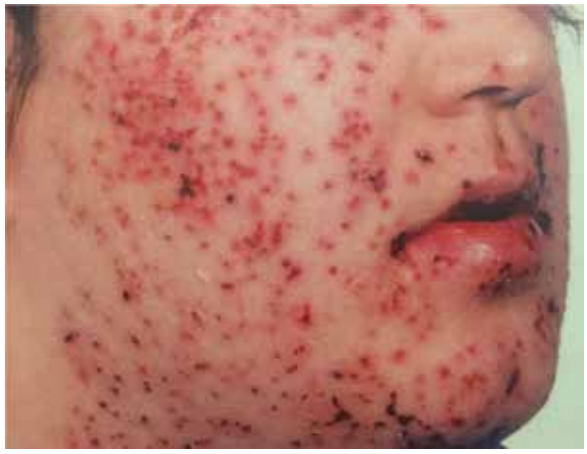

Figure 11. Chickenpox.

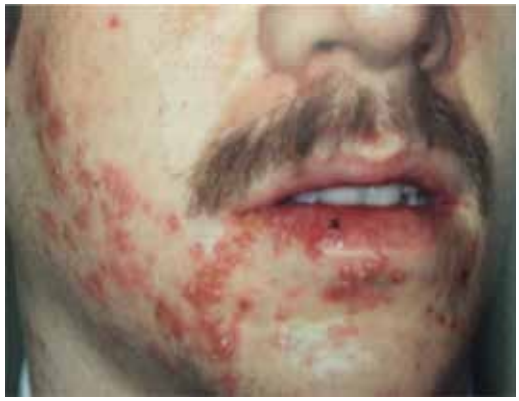

Figure 12. Herpes zoster.

5. Autoimmune disease

5.1. Systemic lupus erythematosus (SLE)

SLE is an autoimmune disease involving multiple organs that is characterized by a vast array of autoantibodies, particularly antinuclear antibodies (ANAs), in which injury is caused mainly by deposition of immune complexes and binding of antibodies to various cells and tissues. The disease may be acute or insidious in its onset and is typically a chronic, remitting, relapsing, and often febrile illness. Injury to the skin, joints, kidney, and serosal membranes is prominent. SLE predominantly affects women, with the female-to-male ratio being 9:1 (**Figure 13**) [28–30].

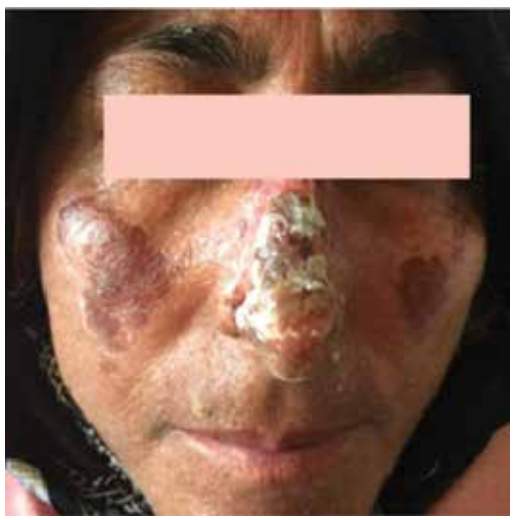

Figure 13. Systemic lupus erythematosus.

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5.2. Chronic cutaneous lupus erythematosus (CCLE)

Patients with CCLE usually have few or no systemic signs or symptoms, with lesions being limited to skin or mucosal surfaces. The skin lesions of CCLE most commonly present as **discoid lupus erythematosus**. They begin as scaly, erythematous patches that are frequently distributed on sun-exposed skin, especially in the head and neck areas. Patients may indicate that the lesions are exacerbated by sun exposure. With time, the lesions may heal spontaneously in one area but only to appear in another area. The healing process usually results in cutaneous atrophy with scarring and hypopigmentation or hyperpigmentation of the resolving lesion (**Figure 14**) [31, 32].

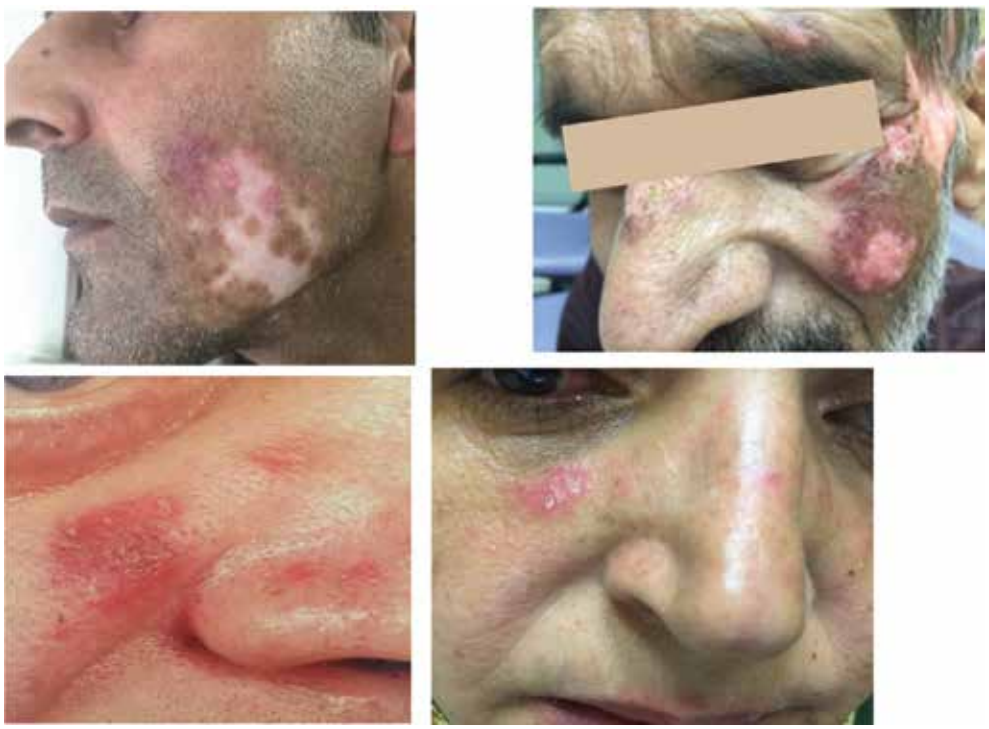

Figure 14. Chronic cutaneous lupus erythematosus.

5.3. Systemic sclerosis (scleroderma)

Systemic sclerosis is autoimmunity of chronic inflammation with damage to small blood vessels and perivascular fibrosis in the skin and multiple organs. The skin is most commonly affected, but the gastrointestinal tract, kidneys, heart, muscles, and lungs also are frequently involved. In some patients, the disease seems to remain confined to the skin for many years, but in the majority, it progresses to visceral involvement with death from renal failure, cardiac failure, pulmonary insufficiency, or intestinal malabsorption, in which the skin involvement is often confined to the fingers, forearms, and face. Visceral involvement occurs late; hence,

the clinical course is relatively benign. Some patients with the limited disease also develop a combination of calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia, collectively called the CREST syndrome (**Figure 15**) [33].

Figure 15. Systemic sclerosis (scleroderma).

5.4. Angioedema (angioneurotic edema)

Angioedema is a diffuse edematous swelling of the soft tissues that most commonly involves the subcutaneous and submucosal connective tissues but may affect the gastrointestinal or respiratory tract, occasionally with fatal results. The disorder has been referred to as **Quincke's disease**, after the clinician who initially related the changes to an alteration in vascular permeability. The outdated term **angioneurotic edema** also has been used because affected patients often complained of a choking sensation and were labeled neurotic. The most common cause is mast cell degranulation, which leads to histamine release and the typical clinical alterations. IgE-mediated hypersensitivity reactions caused by drugs, foods, plants, dust, and inhalants produce mast cell degranulation and are fairly common. Contact allergic reactions to foods, cosmetics, topical medications, and even dental rubber dams have been found responsible. Mast cell degranulation can even result from physical stimuli, such as heat, cold, exercise, emotional stress, solar exposure, and significant vibration. Angioedema also can result from activation of the complement pathway. This may be hereditary or acquired. Two rare autosomal dominant hereditary forms are seen: type I and type II. Type I, comprising 85% of the hereditary cases, is caused by a quantitative reduction in the inhibitor that prevents the transformation of C1 to C1 esterase. Without adequate levels of C1 esterase inhibitor (C1-INH), C1 esterase cleaves C4 and C2 and results in angioedema. Type II exhibits normal levels of C1-INH, but the inhibitor is dysfunctional. The acquired type of C1-INH deficiency is seen in association with certain types of lymphoproliferative diseases (Caldwell syndrome) or in patients who develop specific autoantibodies. In lymphoproliferative diseases, monoclonal antibodies directed against the tumor cells activate C1 and lead to consumption of C1-INH.

An unusual pattern of drug reaction that can produce severe forms of angioedema that are not mediated by IgE is the type associated with use of drugs called angiotensin-converting enzyme (ACE) inhibitors (**Figure 16**) [34–36].

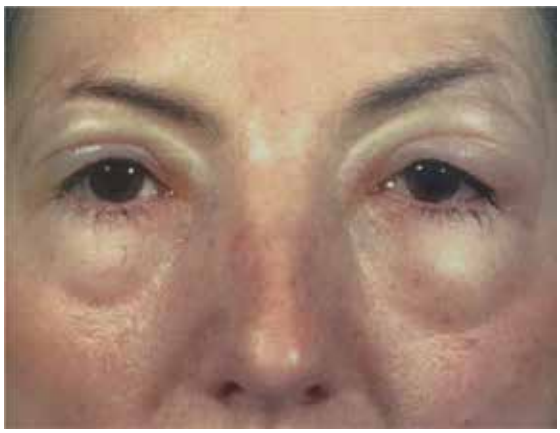

Figure 16. Angioedema.

6. Blistering (bullous) disorders

6.1. Pemphigus

Pemphigus is a rare autoimmune blistering disorder resulting from loss of normal intercellular attachments within the epidermis and the squamous mucosal epithelium. There are three major variants: pemphigus vulgaris (the most common type), pemphigus foliaceus, and paraneoplastic pemphigus.

Pemphigus vulgaris is a rare disorder that occurs most commonly in the elderly and more often in women than men. Lesions are painful, particularly when ruptured, and secondary infections are common. Most cases are associated with oropharyngeal involvement at some point in their course. Most patients require immunosuppressive therapy, sometimes for the remainder of their lives. Medications can cause pemphigus, and when they do, patients most often present with pemphigus foliaceus rather than pemphigus vulgaris. There is also an unusual endemic form of pemphigus foliaceus in South America (fogo selvagem) that is putatively associated with the bite of a black fly.

Pemphigus vulgaris, by far the most common type, involves both mucosa and skin, especially on the scalp, face, axillae, groin, trunk, and points of pressure. The lesions are superficial flaccid vesicles and bullae that rupture easily, leaving deep and often extensive erosions covered with a serum crust.

Pemphigus foliaceus, a rare, more benign form of pemphigus, results in bullae confined to skin, with only infrequent involvement of mucous membranes. The blisters in this disorder

are superficial, such that more limited zones of erythema and crusting of ruptured blisters are seen (**Figure 17**) [37–39].

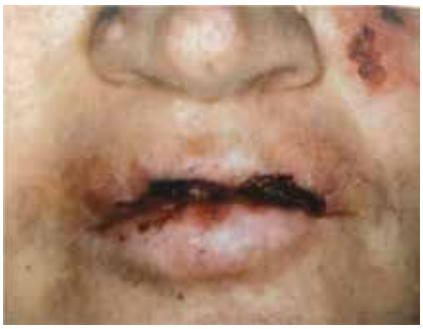

Figure 17. Pemphigus vulgaris.

6.2. Bullous pemphigoid

Bullous pemphigoid is another distinctive acquired blistering disorder with an autoimmune basis. Blistering in bullous pemphigoid is triggered by the linear deposition of IgG antibodies and complement in the epidermal basement membrane. The bullae do not rupture as readily as in pemphigus and, if uncomplicated by infection, heal without scarring. The disease tends to follow a remitting and relapsing course and responds to topical or systemic immunosuppressive agents. Gestational pemphigoid (also known as herpes gestationis, a misnomer) is a clinically distinct subtype that appears suddenly during the second or third trimester of pregnancy. It is also caused by autoantibodies against BPAG. It typically resolves after childbirth but may recur with future pregnancies (**Figure 18**) [40].

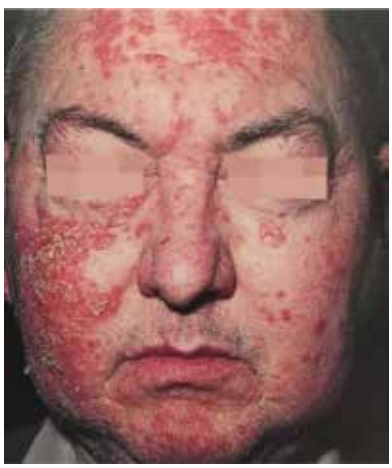

Figure 18. Bullous pemphigoid.

6.3. Dermatitis herpetiformis

Dermatitis herpetiformis is another type of autoimmune blistering disorder characterized by extremely pruritic urticaria and grouped vesicles. The disease affects predominantly males, often in the third and fourth decades of life. In up to 80% of cases, it occurs in association with celiac disease; conversely, only a small minority of patients with celiac disease develop dermatitis herpetiformis. Similar to celiac disease, dermatitis herpetiformis responds to a gluten-free diet. The lesions of dermatitis herpetiformis are bilateral, symmetrical, and grouped and preferentially involve the extensor surfaces, elbows, knees, upper back, and buttocks. Initially, neutrophils accumulate selectively at the tips of dermal papillae, forming small microabscesses. The basal cells overlying these microabscesses show vacuolization and focal dermoepidermal separation that ultimately coalesce to form a true subepidermal blister (**Figure 19**) [41].

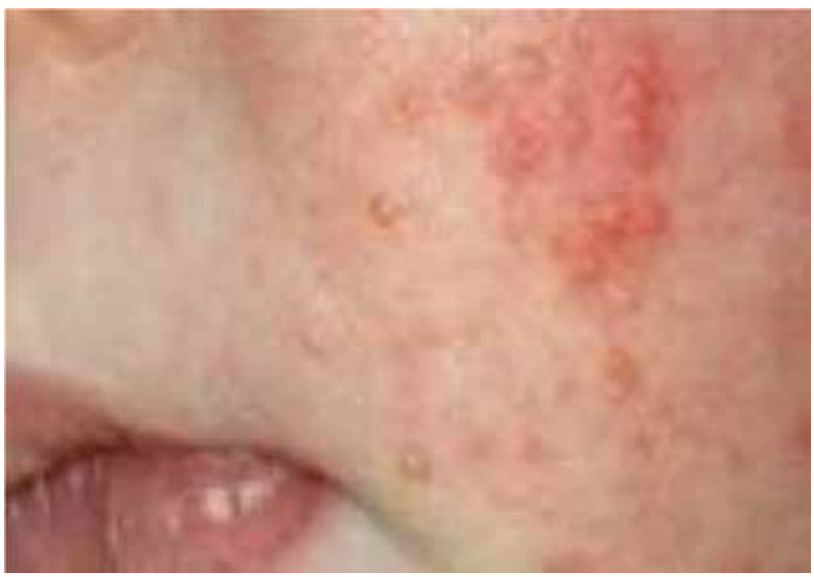

Figure 19. Dermatitis herpetiformis.

7. Benign and premalignant epithelial lesions and nevi

7.1. Melanocytic nevinevus

Strictly speaking, the term "nevus" denotes any congenital lesion of the skin. Melanocytic nevus, however, refers to any benign congenital or acquired neoplasm of melanocytes. There are numerous types of melanocytic nevi, with varied appearances. Although these lesions usually are of only cosmetic concern, they can become irritating or mimic melanoma, requiring their surgical removal (**Figure 20**).

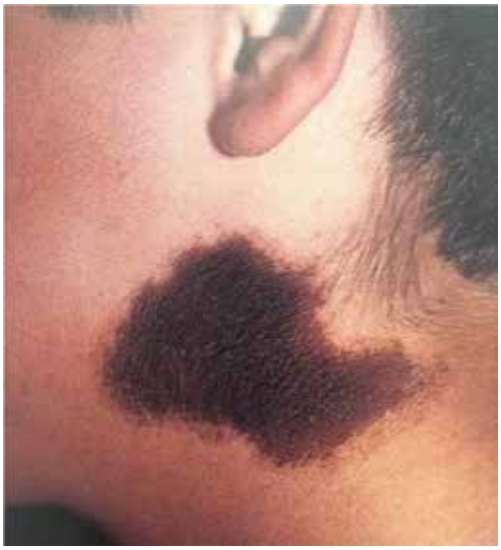

Figure 20. Melanocytic nevus.

7.2. Dysplastic nevus

Dysplastic nevi may be sporadic or familial. The latter ones are important clinically because they are considered potential precursors of melanoma. As with conventional melanocytic nevi, activating NRAS or BRAF mutations are commonly found in dysplastic nevi and are believed to have a pathogenic role. Unlike ordinary nevi, dysplastic nevi have a tendency to occur on body surfaces not exposed to the sun as well as on sun-exposed sites. Familial dysplastic nevus syndrome is strongly associated with melanoma, as the lifetime risk for the development of melanoma in affected persons is close to 100%. In sporadic cases, only individuals with 10 or more dysplastic nevi appear to be at an increased risk for melanoma (**Figure 21**) [42].

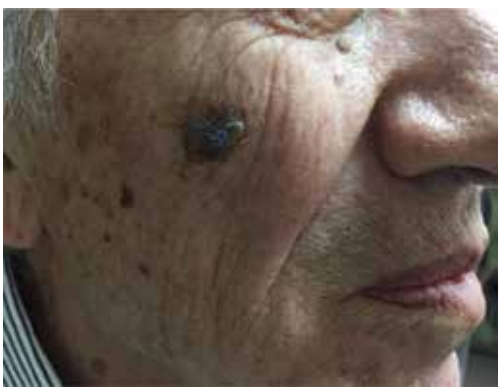

Figure 21. Dysplastic nevus.

7.3. Actinic keratosis

Actinic keratosis is sun-damaged skin with hyperkeratosis that exposure to ionizing radiation, industrial hydrocarbons, and arsenicals may induce similar lesions. Actinic keratoses are usually less than 1 cm in diameter (**Figure 22**). The lips may also develop similar lesions (termed "actinic cheilitis") [43–47].

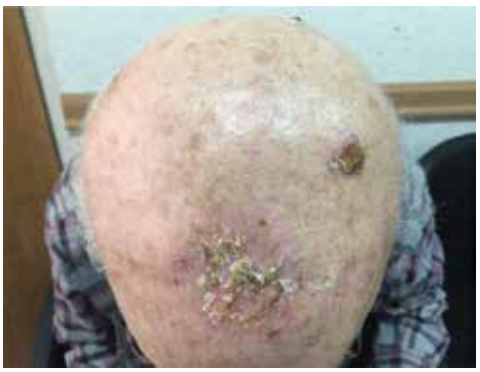

Figure 22. Actinic keratosis.

7.4. Seborrheic keratoseskeratosis

Seborrheic keratoses are characterized by round, flat, coin-like, and waxy plaques that vary in diameter from millimeters to several centimeters and occur most frequently in middle-aged individuals. They arise spontaneously and are particularly numerous on the trunk, although the extremities, head, and neck may also be involved (**Figure 23**) [47, 48].

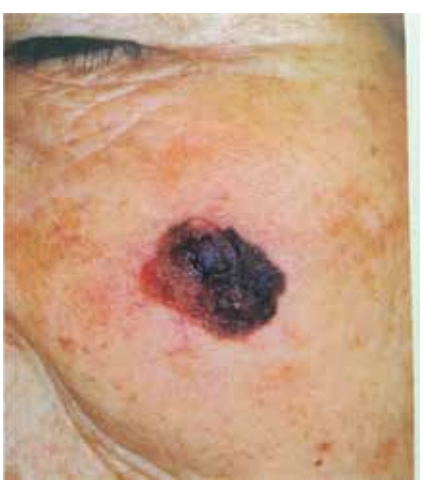

Figure 23. Seborrheic keratosis.

7.5. Keratoacanthoma

Keratoacanthoma is a self-limited epithelial proliferation with a strong clinical and histopathological similarity to well-differentiated squamous cell carcinoma. Indeed, many dermatopathologists consider it to represent an extremely well-differentiated squamous cell carcinoma. Cutaneous lesions presumably arise from the infundibulum of hair follicles. An association with sun damage is suggested by the fact that most solitary lesions are found on sun-exposed skin in older adults. Additional potential contributing factors include tar exposure, HPV, immunosuppression, certain drugs (e.g., BRAF inhibitors and tyrosine kinase inhibitors), tattooing, and burns or other trauma. Keratoacanthoma-like lesions have been produced in animals by the cutaneous application of carcinogens. Keratoacanthoma shows a male predilection and rarely occurs before 45 years of age. Almost 95% of solitary lesions involve sun-exposed skin, and 8% of all cases involve the outer edge of the vermilion border of the lips, with equal frequency on the upper and lower lips (**Figure 24**) [49, 50].

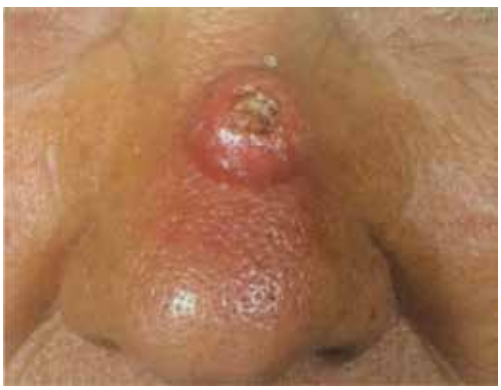

Figure 24. Keratoacanthoma.

8. Malignant epidermal tumors

8.1. Basal cell carcinoma

Basal cell carcinoma is the most common invasive cancer in humans, reaching nearly 1 million cases per year in the United States. It is a slow-growing tumor that rarely metastasizes. The vast majority of cases are recognized at an early stage and cured by local excision. However, a small number of tumors (<0.5%) are locally aggressive and potentially disfiguring or exceedingly rarely that they may metastasize to distant sites. They occur at sun-exposed sites in lightly pigmented elderly adults. As with squamous cell carcinoma, the incidence of basal cell carcinoma is increased in the setting of immunosuppression and in disorders of DNA repair, such as xeroderma pigmentosum. Basal cell carcinomas usually present as pearly papules containing prominent dilated subepidermal blood vessels (telangiectasias) (**Figure 25**) [51, 52].

Figure 25. Basal cell carcinoma.

8.2. Squamous cell carcinoma

Squamous cell carcinoma is the second most common tumor arising on sun-exposed sites in older people. The most important cause of cutaneous squamous cell carcinoma is DNA damage induced by exposure to UV light. Other risk factors for squamous cell carcinoma include industrial carcinogens (tars and oils), chronic ulcers and draining osteomyelitis, old burn scars, ingestion of arsenicals, ionizing radiation, and (in the oral cavity) tobacco and betel nut chewing (**Figure 26**) [53].

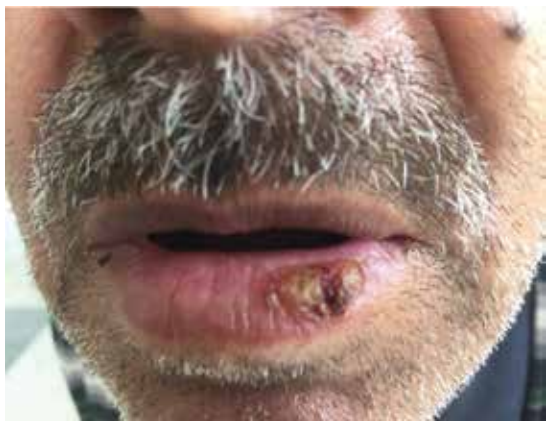

Figure 26. Squamous cell carcinoma.

8.3. Malignant melanoma

Melanoma is the most deadly of all skin cancers and is strongly linked to acquired mutations caused by exposure to UV radiation in sunlight. It is a relatively common neoplasm that can be cured if it is detected and treated when it is in its earliest stages. The great preponderance of melanoma arises in the skin; other sites of origin include the oral and anogenital mucosal surfaces (i.e., oropharynx as well as gastrointestinal and genitourinary tracts), esophagus,

meninges, and the uvea of the eye. Today, as a result of increased public awareness of the signs of cutaneous melanoma, most are cured surgically. Melanoma has two growth phases: radial and vertical. Radial growth describes the horizontal spread of melanoma within the epidermis and superficial dermis. During this initial stage, the tumor cells seem to lack the capacity to metastasize. Tumors in radial growth phase fall into several clinicopathological classes, including lentigo maligna, usually presenting as an indolent lesion on the face of older men that may remain in the radial growth phase for several decades; superficial spreading, the most common type of melanoma, usually involving sun-exposed skin; and acral/mucosal lentiginous melanoma, which is unrelated to sun exposure. In vertical growth phase, the tumor cells invade downward into the deeper dermal layers as an expansile mass (**Figures 27** and **28**) [54–57].

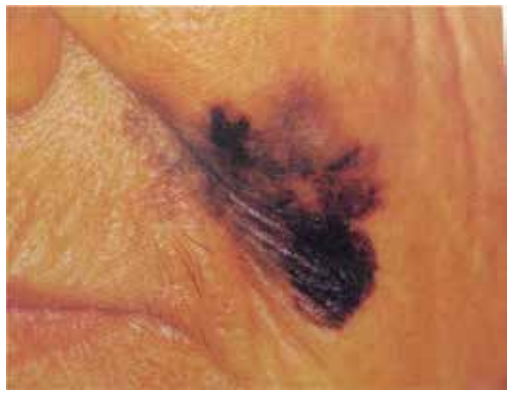

Figure 27. Melanoma.

Figure 28. Lentigo maligna melanoma.

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9. Miscellaneous

9.1. Sturge-Weber syndrome

Sturge-Weber syndrome is a rare, nonhereditary developmental condition that is characterized by a hamartomatous vascular proliferation involving the tissues of the brain and face. Patients with this disease are born with a dermal capillary vascular malformation of the face known as a port-wine stain or nevus flammeus because of its deep purple color. This port-wine stain usually has a unilateral distribution along one or more segments of the trigeminal nerve. Occasionally, patients have bilateral involvement or additional port-wine lesions elsewhere on the body. Only 8% to 10% of patients with facial port-wine nevi will have Sturge-Weber syndrome. Risk for the condition occurs primarily in patients with involvement along the distribution of the ophthalmic branch of the trigeminal nerve (V1). If the port-wine stain involves the entire distribution of V1, the risk for neurological and ocular involvement is 78% (**Figure 29**) [58–62].

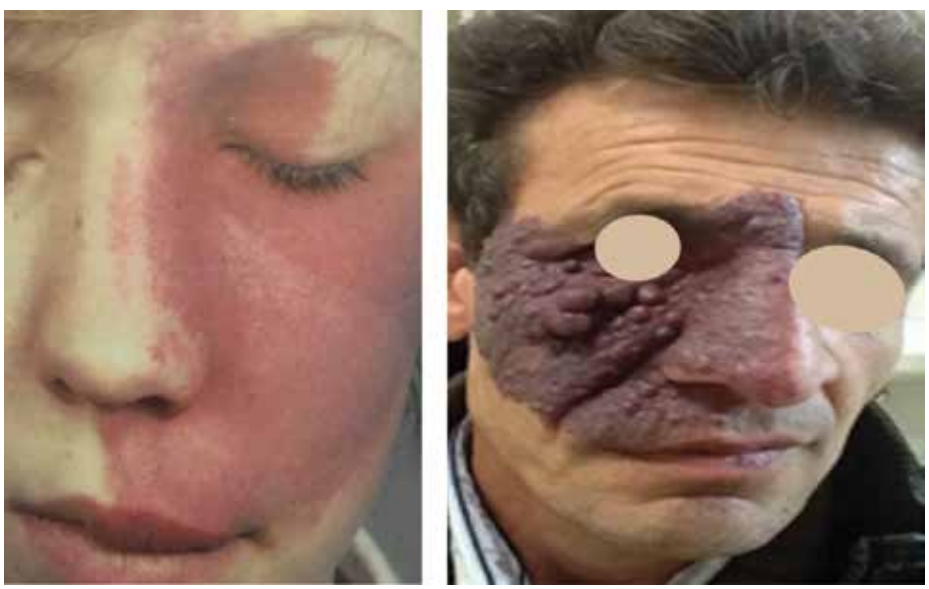

Figure 29. Sturge-Weber syndrome.

9.2. Paederusderus dermatitis

Paederus dermatitis (also known as night burn) is a peculiar irritant dermatitis following contact with an insect belonging to the genus *Paederus* and its fluid, which contains a blistering toxic amide, the chemical pederin. The dermatitis is characterized by erythemato-bullous lesions of sudden onset on exposed areas of the body: the neck is the most common site involved, followed by the face (**Figures 30** and **31**) [63].

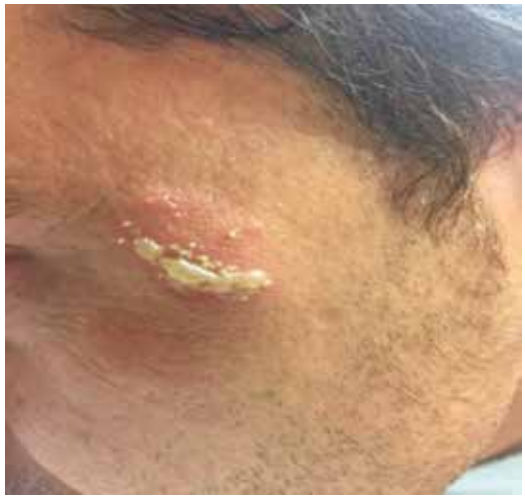

Figure 30. *Paederus* dermatitis.

Figure 31. *Paederus* insect.

9.3. Melasma

Melasma is an acquired symmetrical hyperpigmentation of the sun-exposed skin of the face and neck. Its exact cause is unknown, but UV light exposure and hormonal influences appear to be important etiological factors. Studies suggest that UV light stimulates production of dermal stem cell factor and α-melanocyte-stimulating hormone, resulting in proliferation of melanocytes and increased melanin production. Melasma classically is associated with pregnancy. In addition, an association with oral contraceptives, hormone replacement therapy, thyroid disorders, phototoxic medications, antiepileptic agents, and cosmetics has been described. Several studies suggest a genetic predisposition. The condition most commonly

affects medium- to dark-complexioned persons—particularly Asian and Hispanic women. In the United States, melasma affects more than 5 million individuals. It typically appears in adult women as bilateral brown or grayish cutaneous macules that range from a few millimeters to more than 2 cm in diameter. Lesions develop slowly with sun exposure and primarily involve the skin of the midface, forehead, upper lip, chin, mandibular ramus region, and (rarely) the arms. The pigmentation may remain faint or darken over time. Melasma only rarely affects men (**Figure 32**) [64–68].

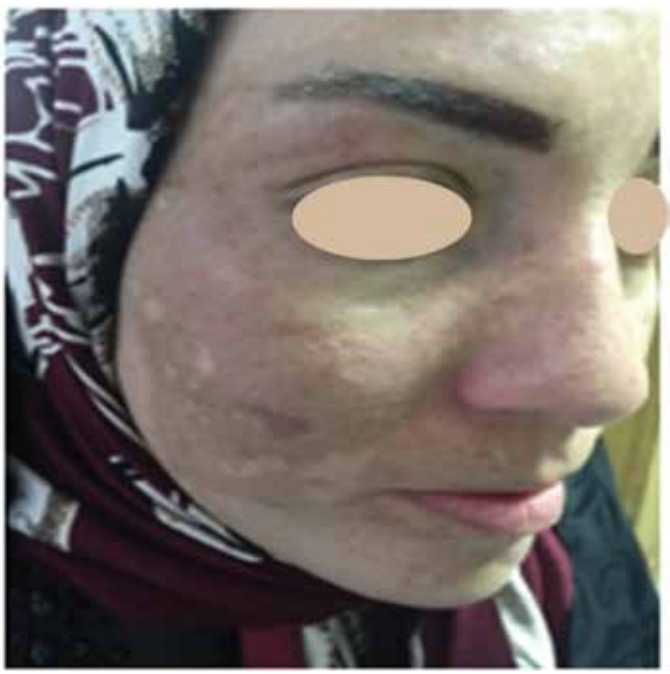

Figure 32. Melasma.

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Section 8

Advanced Dentoalveolar and Implant Surgery

Chapter 11

Ridge Augmentation Techniques in Preprosthetic Implant Surgery

Bahattin Alper Gultekin, Erol Cansiz and Serdar Yalcin

Additional information is available at the end of the chapter

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Abstract

Rehabilitation of missing teeth with dental implant-supported restorations has become a predictable treatment option in dentistry. The stability of hard and soft tissues around the implant is fundamental for long-term success. However, due to factors such as trauma, oncologic diseases, and missing teeth, vertical and horizontal bone loss is expected, and the available bone may not be suitable for optimum implant placement. Ridge augmentation procedures are applied to increase in the volume of the deficient sites for implant treatment. Autogenous block bone augmentation and guided bone regeneration (GBR) are two surgical approaches for implant placement. Autogenous bone is widely used for augmentations because of its osteogenic potential. A myriad of biomaterials, including xenografts, allografts, alloplasts, and composite grafts, are available for GBR. The aim of this chapter is to provide a brief summary of these methods and to discuss the advantages and pitfalls of ridge augmentation techniques.

Keywords: Alveolar ridge deficiency, guided bone regeneration, iliac block bone augmentation, biomaterials, autogenous bone

1. Introduction

Rehabilitation of edentulous sites with implant-supported restorations is a reliable technique with a predictable outcome. Alveolar ridge resorption after tooth loss is very common and may compromise the placement of implants. Trauma, oncologic diseases, oral infections, and congenitally missing teeth may also cause severe bone deficiency. A wide range of surgical procedures, such as guided bone regeneration (GBR) through the use of resorbable and non-

resorbable membranes, intra- and extra-oral block grafting, and distraction osteogenesis, can be applied for reconstruction of alveolar ridge deficiencies [1–3].

Defect morphology plays an important role in the success of alveolar ridge augmentation techniques. Defects can basically be classified as intrabony or extrabony defects [4]. It is easier to maintain space, stabilize the augmented site, achieve primary soft tissue closure, and protect the grafting site in intrabony defects than in extrabony defects. Therefore, intrabony defects are much easier to augment through techniques such as socket augmentation and sinus floor elevation. Extrabony defects can be more challenging in cases such as lateral and vertical augmentations (**Figure 1**) [5].

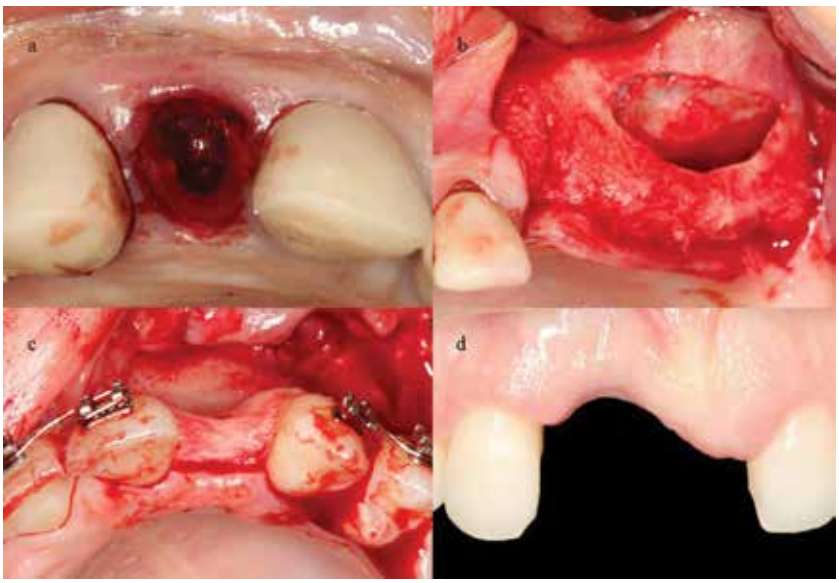

Figure 1. Intrabony (a, b) and extrabony (c, d) alveolar ridge defects.

The amount of augmentation may also influence the risk assessment of the operation. Particularly for vertical augmentation, complications are more likely if a large amount of height is needed outside the natural bone after bone regeneration.

This chapter is focused on GBR and extra-oral bone block techniques that are widely used for ridge augmentation.

2. Alveolar ridge augmentation techniques

2.1. Guided bone regeneration (GBR)

GBR is a surgical technique that increases the amount of alveolar ridge for implant placement using barrier membranes with or without bone substitutes [4]. Regeneration at the deficient

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site depends on the exclusion of soft tissue (epithelial cells and fibroblasts) from osteogenic tissue (osteoblasts) during organization of the bone [6]. Osteoblasts are mainly responsible for increasing the amount of regenerated alveolar ridge. However, osteoblasts do not regenerate the alveolar ridge as quickly as epithelial and connective tissue cells grow. The success of the GBR approach mainly depends on the exclusion of soft tissue cells during bone remodeling by slowly working osteoblasts [6]. Aghaloo et al. evaluated the success of ridge augmentation techniques (GBR, onlay block grafting, distraction osteogenesis, ridge splitting, and mandibular interpositional grafting) based on implant survival in a systematic review [7]. They found that GBR may be the best way to augment the ridge according to implant survival.

The GBR technique can be applied in two stages (delayed approach) or in one stage (simultaneous approach with implant placement). If the bone deficiency is low and implant stability can be achieved, the one-stage approach can be applied (**Figure 2**).

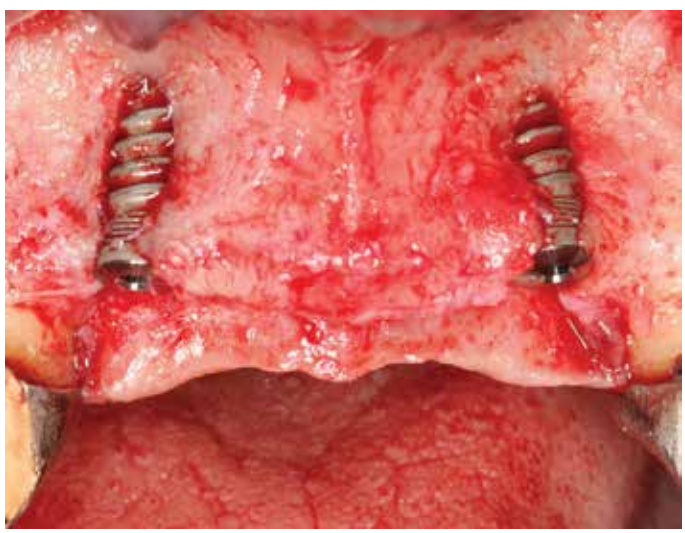

Figure 2. Labial bone deficiency.

However, if a greater amount of bone must be regenerated, then the two-stage approach is preferable and the complication risk will be reduced.

The predictability of GBR is based on several principles, such as space maintenance, stability, nutrition, and primary closure [5]. In this section, these principles are introduced in detail according the morphology of the bone defects, the grafting material, and the chosen technique.

2.2. Space maintenance

Maintenance of space at the augmented site is one of the fundamental principles of the GBR technique. A protected space is needed for hard-tissue cells to regenerate bone that excludes soft-tissue cells during healing and maturation.

Bone substitutes, membranes, tenting screws, titanium, and bone plates are suggested for the maintenance of space. Jovanovic et al. evaluated the treatment groups in a pre-clinical study on GBR. They found that significant bone gain could be achieved when membrane and graft material were used than when no membrane was used [8]. Space maintenance can be challenging depending on the properties of the defect site. When significant bone augmentation is required in a severely resorbed alveolar ridge, creating space is more critical for the success of GBR.

2.3. Grafting biomaterials

Currently, the use of a bone substitute material in GBR applications is the standard of care. The primary types of bone substitutes are autogenous bone, xenografts, allografts, and alloplasts [4]. An ideal biomaterial for bone regeneration should have the ability to form new bone, and bone formation must be balanced with the speed of resorption [4, 6]. Autogenous bone is the gold standard for augmentation because of its osteogenic potential. It has the ability to regenerate bone through the mechanisms of osteogenesis, osteoinduction, and osteoconduction [4, 6]. Osteogenesis is the production and evolution of bone at every site, even in the absence of local undifferentiated mesenchymal stem cells. Osteoinduction is the transformation of undifferentiated mesenchymal cells into pre-osteoblasts and osteoblasts. Therefore, the graft material should be in contact with living bone. Osteoconduction provides a non-living scaffold for the regeneration of bone [9]. By using local bone harvesting techniques, morbidity can be lowered during autogenous bone collection. Scraping autogenous bone from a location near the recipient site may simplify bone harvesting, decrease morbidity, and reduce the treatment time (**Figure 3**).

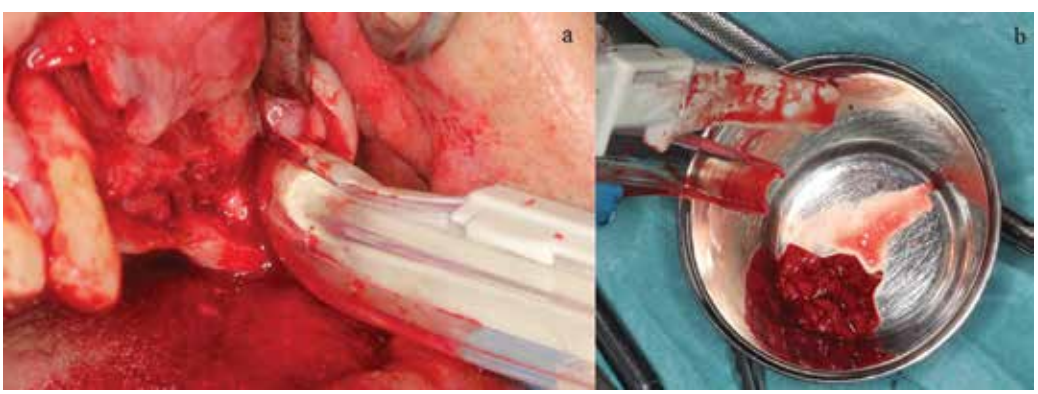

Figure 3. Bone harvesting from tuber site.

Peleg et al. found that the use of a bone scraper to harvest autogenous bone at the ramus resulted in no neurosensory injuries to the anatomical tissues and minimal morbidity in the patients [10]. There are also novel rotary tools to harvest bone easily from local sites (**Figure 4**).

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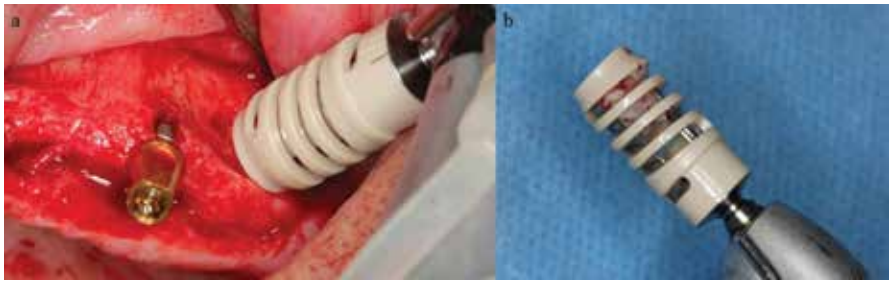

Figure 4. Bone harvesting rotary instrument.

These autogenous particulate grafts can be used alone or with biomaterials as a composite. Composite grafts greatly reduce the amount of autogenous bone required and therefore reduce morbidity.

Bone graft substitutes have osteoconductive properties. However, the use of bone grafting material is very popular among clinicians because of benefits such as the unlimited availability, lack of a need to harvest bone (hence, reduced donor-site morbidity), reduced operation time, and reduced risk of postoperative complications [4, 6].

Xenografts are bone grafts obtained from animals such as cows, horses, or species other than human [4, 6]. Deproteinized bovine bone (DBB) is a xenograft material that is frequently used in GBR applications. DBB is osteoconductive and has an interconnecting pore system that serves as a scaffold for the migration of osteogenic cells; the inorganic bone substance has a microscopic structure similar to that of natural cancellous bone [11, 12]. DBB particles are incorporated over time within the living bone, and DBB resorbs very slowly and has low-substitution rates. Therefore, it can provide space maintenance over a very long term [4, 6]. It was shown that DBB graft particles remain present even after 10 years postoperatively [13]. Chackartchi et al. reported that the mean percentage of new bone was 28 ± 6% using DBB alone 6–9 months after sinus augmentation [14]. Materials with low-substitution rates are good scaffolds for host bone growth during healing, and they inhibit resorption of the augmented site [4, 6]. However, increased amounts of residual graft particles may negatively impact the healing of the augmented site and decrease the rate at which the implant surface area is integrated with the newly formed bone [15]. In challenging cases that require a greater amount of bone augmentation, such as vertical, horizontal, or both, DBB can be mixed with autogenous particulate bone and applied as a composite [2]. The authors recommend allowing 6–9 months for healing of lateral/vertical augmentations before implant placement. During long-term healing, DBB particles prevent the shrinkage of the augmented site, and autogenous particles facilitate the incorporation of this scaffold with the living natural bone. The authors do not recommend implant placement during the early stages of bone healing (less than 4–5 months) for two-stage augmentations because implant stability may be compromised or severe marginal bone loss may occur before loading [4, 6].

Allografts are bone grafts obtained from the same species but are genetically dissimilar from the recipient [4, 6]. Allograft donors are meticulously screened, and specimens are carefully

processed to reduce the possibility of disease transmission. Freeze drying is a commonly used process. Mineralized allografts (MAs) provide stability and space by maintaining their physical properties during the bone remodeling phase [4, 6]. Osteoconductive scaffolds provide volume enhancement and effective site management for successful dental implant placement after augmentation [16]. MAs can be composed of cortical and cancellous particles. Mineralized cortical particles with slow resorption rates offer a scaffold, whereas cancellous particles that have faster resorption rates and are prone to resorption may provide a space for the ingrowth of bone cells and angiogenesis. Therefore, if the amount of cortical graft particles is increased in the composite, less resorption can be expected [17]. Demineralized allograft (DA) contains bone morphogenic proteins and stimulates osteoinduction. However, DA is highly biodegradable and has less compressive strength than DBB and MA. Therefore, it is often mixed with other slowly resorbed graft materials to maintain space [18]. The authors recommend using MAs in challenging cases, and demineralized grafts are recommended in well-protected defects such as socket augmentation. Implants can be placed safely after 4 months of healing in well-protected defects [17, 18]. The authors do not recommend using DA in challenging cases, such as vertical and lateral augmentation, because a great amount of bone loss can be expected after long-term healing [17, 18].

The possibility of disease transmission from xenografts and allografts to humans has drawn attention to synthetic bone graft substitutes [19]. Alloplasts are synthetic and also have osteoconductive properties that provide a scaffold for bone regeneration [20]. Various synthetic graft materials have been developed for crestal ridge augmentations, such as synthetic hydroxyapatite (HA), beta-tricalcium phosphate (β-TCP), and calcium sulfate (CS) [4]. HA has a low or very limited resorption rate [4]. β-TCP and CS are highly biodegradable and have less compressive strength than synthetic HA and DBB [21, 22]. CS can be completely resorbed within 1 month [23]. Therefore, according to the defect properties, these materials can be mixed with slow resorbable materials in different ratios to maintain space during healing [21, 22]. By increasing the amount of resorbable material in the composite, the rate of new bone formation can also be increased. However, the space maintenance capacity will be reduced, even in sinus augmentation applications [24].

The particle size in the graft may also affect the resorption time and the success of the procedure. There are conflicting articles in the literature regarding graft particle usage [14, 25]. Particles that are too small may be resorbed too rapidly, and advanced shrinkage of the augmented site can be observed. Particles that are too large may prevent angiogenesis and delay and/or reduce new bone formation [25]. Chackartchi et al. compared the use of small and large particles in grafts during two-stage sinus floor augmentation with regard to new bone formation and vertical bone height stability. The authors could not detect any statistically significant differences between the small and large graft particles [14].

Several factors, such as the graft properties, membrane choice, surgical technique, use of compression during packing of the graft material, availability of natural bone, composition of the graft, and activity of the host bone, may influence the resorption rate at the augmented site and may therefore affect space maintenance [26].

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2.4. Barrier membranes

Barrier membranes are routinely used to maintain space. There are two kinds of barrier membranes: resorbable and non-resorbable [4, 6].

2.5. Resorbable membranes

The most important advantages of resorbable membranes are the elimination of membrane removal after healing, resulting in decreased morbidity, easy manipulation, and lower rate of complications. However, resorbable membranes are not very successful in comparison with non-resorbable membranes with regard to space maintenance. These membranes must be used with bone graft substitutes and additional tools, such as tenting screws or plates for space maintenance.

Resorbable membranes that are made of native collagen (non-cross-linking) show high biocompatibility resulting in good tissue integration and rapid vascularization (**Figure 5**) [27].

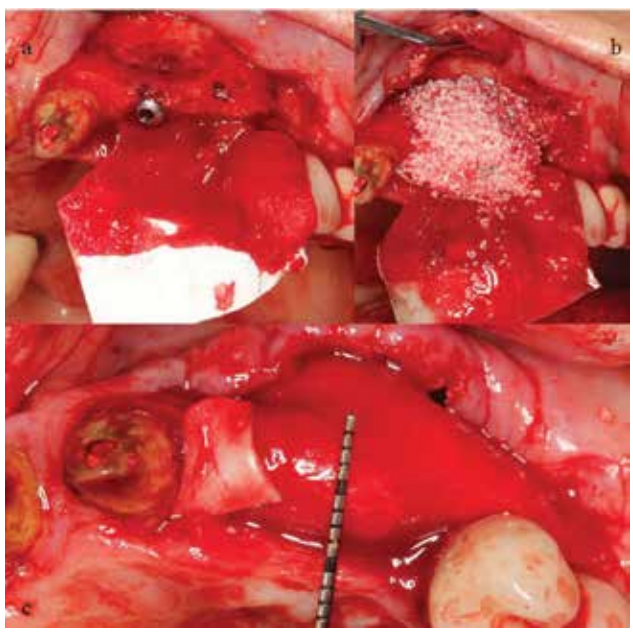

Figure 5. Native collagen resorbable membrane.

However, these membranes may lose their barrier function early due to rapid biodegradation [28]. The resorption time depends on the membrane's properties, the cellular activity of the native bone, and exposure [29]. One of the most important benefits of non-cross-linked collagen membranes is the spontaneous closure of membrane exposure during the healing period [30]. Epithelization of the exposed membrane occurs within weeks after mucosal dehiscence. Although spontaneous healing of the exposure occurs, the grafting volume may be negatively affected during healing, and some bone loss may be expected

[4, 6]. Simion et al. compared the effects of exposed and non-exposed membranes on bone regeneration at the site of implant insertion [31]. Bone regeneration was 99.6% with non-exposed membranes and 48.6% with exposed membranes [31]. There are also studies showing predictable results with late membrane exposures up to 6 months [5]. Therefore, every effort should be made to ensure primary closure of the grafted site during healing. Some clinicians recommend using double non-cross-linked membrane over the grafted site to extend the resorption time for better barrier function [6].

Cross-linking resorbable collagen membranes were produced to extend the degradation time in GBR applications. In a preclinical study, different collagen membranes were compared to evaluate the resorption time [32]. It was found that if the amount of cross-linking collagen fibrils was increased, the resorption time was also extended. However, tissue biocompatibility was decreased. There are also studies showing good results regarding tissue integration and bone regeneration using these membranes [33, 34]. Various types of cross-linked membranes may affect biocompatibility and tissue integration differently [6].

Membranes made of polylactic acid/polyglycolic acid copolymer (PGLA) are also available. These synthetic membranes simplify the clinical manipulation and reduce the application time [6]. Although studies have shown that this material is highly biocompatible and degrades without acidic products, concerns about the healing mechanism remain (**Figure 6**) [35, 36].

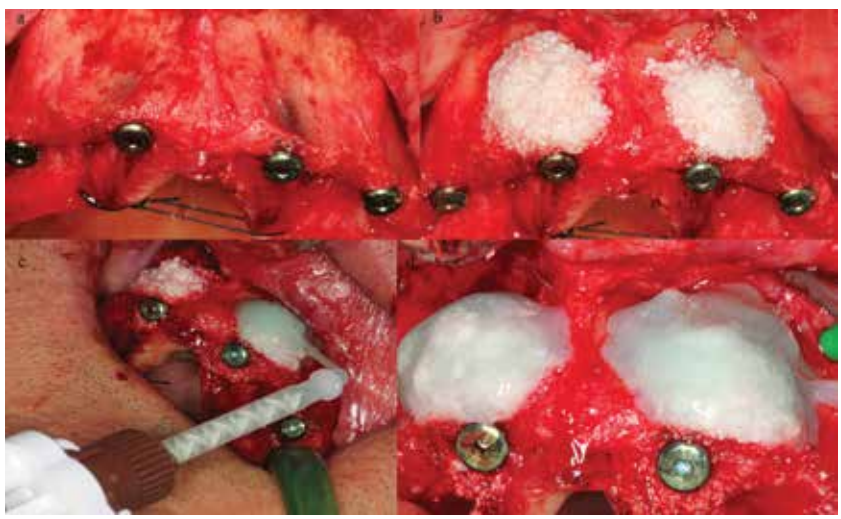

Figure 6. PGLA resorbable membrane.

2.5.1. Non-resorbable membranes

When a higher amount of bone augmentation is required, reinforced non-resorbable membranes are used. Reinforced membranes withstand the pressure from the surrounding tissues, resulting in the prevention of membrane collapse and allowing the bone to be regenerated during healing. Titanium mesh, titanium-reinforced expanded polytetrafluoro-

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ethylene (e-PTFE), and dense polytetrafluoroethylene (d-PTFE) membranes are most commonly used, and their benefits have been demonstrated in published studies [2, 4, 6]. Urban et al. augmented alveolar ridges vertically using e-PTFE membranes [37]. The mean vertical augmentation was 5.5 mm after 6–9 months of healing. They concluded that vertical augmentation with e-PTFE membranes and particulate autografts are a reliable method for the reconstruction of deficient alveolar ridges.

Currently, e-PTFE membranes are not used in oral surgery due to high rates of complications related to membrane exposure. d-PTFE membranes are novel titanium-reinforced non-resorbable membranes that have replaced e-PTFE membranes and are used for the reconstruction of critical-sized defects, such as sites requiring vertical augmentation. The highly porous structure of e-PTFE membranes allows ingrowth of the oral microflora when the membrane is exposed. Exposure results in high rates of infection, regardless of whether it occurs early or late during healing. Due to the high porosity of the membrane, it is almost impossible to mechanically or chemically clean the exposed site of the membrane; therefore, early removal of the membrane is required. After removal, it is generally discovered that GBR has failed due to infection, and re-augmentation is needed. e-PTFE membranes must be completely healed in primary closure, and they have no tolerance for exposure [4, 6].

Novel d-PTFE membranes are manufactured in a dense micro-porous form that prevents oral bacteria from entering the grafted site when exposed. These membranes are also easy to mechanically and chemically clean. The removal of a d-PTFE membrane after healing is also easy to perform and takes less time than the removal of titanium-mesh membranes (**Figure 7**).

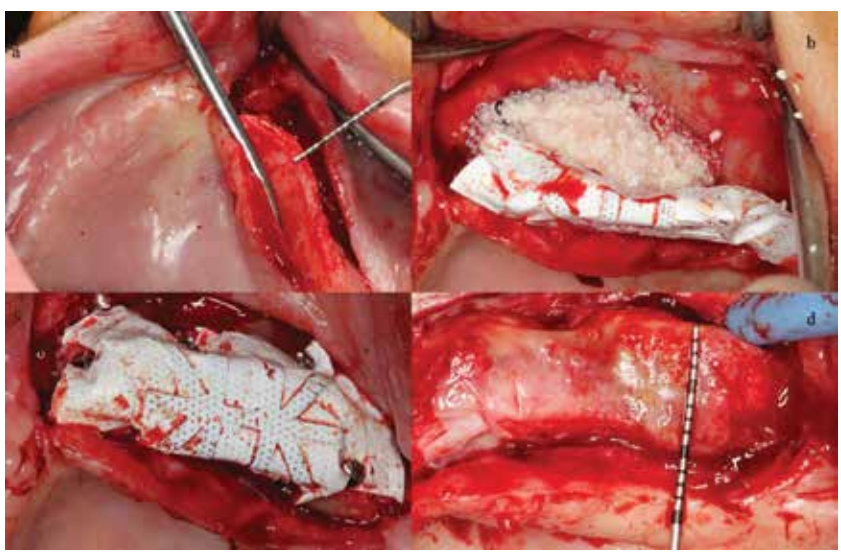

Figure 7. Titanium reinforced non-resorbable membrane.

Ronda et al. reported a mean defect fill of 5.49 mm after 6 months of healing at vertically augmented sites using d-PTFE membranes [38]. Urban et al. observed an average bone gain

of 5.45 mm using d-PTFE membrane with a mixture of bovine bone and autogenous particulate bone [2]. They also found a high rate of new bone formation (36.6%) on core biopsies that were taken at the time of implant placement. They concluded that treatment of vertically deficient alveolar ridges with GBR using a mixture of particulate autogenous bone and bovine grafts with d-PTFE membrane is a reliable method.

Although a high level of success with non-resorbable titanium-reinforced d-PTFE membranes has been reported in the literature, these membranes must be applied cautiously in selected patients. Non-resorbable membranes have higher complication rates than resorbable membranes [39]. If a d-PTFE membrane begins to be exposed, the amount of exposure can increase incrementally during healing [5]. Therefore, if early exposure of this membrane occurs, the prognosis may not be predictable. However, late exposures may be better tolerated with meticulous mechanical cleaning. If an infection does not occur 3–4 months after grafting, removal of the membrane may preserve the regenerated bone [5]. Complications regarding membrane exposure are less likely with resorbable membranes. The cost of GBR with titanium-reinforced membranes may also be higher than with resorbable membranes. Jensen et al. reported comparable amounts of bone gain between resorbable and non-resorbable membranes used for horizontal augmentation [40]. If minor augmentation is planned at a deficient site, resorbable collagen membranes should be considered first due to their low risk of complications. If the natural bone is not too thin, lateral augmentation can be successfully performed using collagen membranes with mixed autogenous particulate grafts and low-substitute graft materials such as DBB.

Titanium mesh is another alternative to non-resorbable membranes, and this type of mesh has a good space maintenance advantage [41]. It can be easily trimmed and bent according to the defect site. Another advantage, and also a disadvantage, of mesh over a PTFE membrane is that the holes within the membrane allow vascularization and nutrition from the periosteum to the grafting site [4–6]. However, bone can also grow from inside these holes over the mesh. After healing, the mesh can integrate with newly formed bone and complicate removal during surgery at the second stage [42, 43].

2.6. Stability

The stability of the augmented site in GBR applications during healing is an important factor for achieving success. The initial blood clot formation and stabilization of graft particles will result in predictable bone formation [5]. Although barrier membranes will cover the augmented site and exclude epithelial and connective tissue cells from the regenerating bone, additional tools are needed to provide stability and also to increase the resistance of the augmented site from the flap, lip, and mastication force pressure [5].

Membrane fixation systems can be used to secure resorbable membranes effectively. By using manual or automatic handles, tacks stabilize the membrane to the natural bone and prevent migration of the graft and soft tissue invasion (**Figure 8**).

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Figure 8. Bone tacks.

Another advantage is that tacking membranes simplify suturing because the membrane does not move during suturing. If lingual or palatal tacking is needed, the angled neck of the handle can be used to simplify the application. Generally, the tacks are made of titanium, and they do not need to be removed at the second-stage surgery. The authors recommend removing tacks that are placed coronally and leaving apically positioned ones to reduce morbidity from excessive flap elevation at the time of implant placement. If tacks are left, they may disturb the patient in the future, and they can be easily removed using a small circular incision around the tack.

Tacks may not be strong enough to secure non-resorbable membranes. Generally, membrane fixation screws are used for stabilization. The aggressive tip and thread design engage the membrane and bone and allow for precise placement in soft and dense bone (**Figure 9**).

Figure 9. Bone screws.

The authors recommend using short screws in the mandible and longer screws in the maxilla due to its low density; it is easier to engage longer screws in soft bone. If lingual or palatal

screwing is needed, surgical hand pieces can be used to simplify the application. At the second surgery, the non-resorbable membrane and all screws must be removed. If any screw is left, the membrane may not be removed easily.

Tenting screws can also be used under resorbable or non-resorbable membrane to prevent pressure from the environment and also to stabilize the augmented site. The treaded part of these screws engages the natural bone, and the smooth part remains at the augmented site (**Figure 10**).

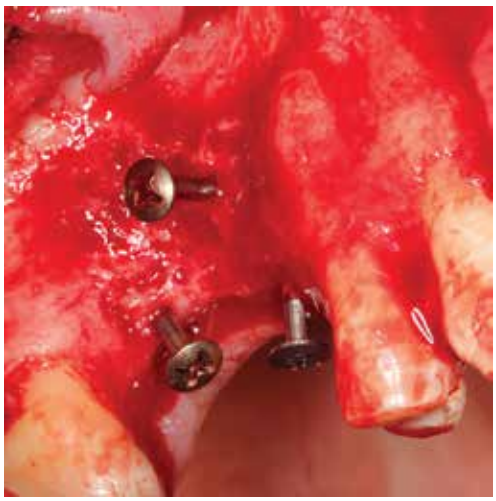

Figure 10. Tenting screws.

Another advantage of using tenting screw is that the clinician may estimate the amount of future bone gain at the time of the operation based on the length of the smooth part. For example, if 5 mm of bone gain is needed, an 8-mm tenting screw can be used and 3 mm of bone will stabilize the screw.

Metal plates that are generally used for orthognathic or trauma surgery can be used for space maintenance [4, 6]. The plate is fixed to the natural bone with screws, and the space between the bone and plate is filled with graft material. A resorbable membrane covers the augmented site. The authors recommend avoiding the use of overly thick plates to prevent soft tissue exposure during healing. Thin cortical strut allografts can also be used for space maintenance in a method known as the Shell technique. Space is created between the cortical strut and the host bone as with metal plates, but there is no need to remove the cortical struts during the second-stage surgery. However, these bone struts are very vulnerable during screwing, and they can be easily broken into pieces [4, 6].

2.6.1. Nutrition

The osteogenic potential of the defect site is also very important for the success of GBR. At the augmented site, the formation of a blood clot begins and granulation tissue invades over the

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following days and weeks [44]. Blood vessels that are in the granulation tissue serve in osteoid formation and subsequently bone formation. Therefore, the remaining bone walls are an important source of vessels and native cell transformation. When there are fewer walls around the defect, the regenerative capacity is reduced and the total treatment time is increased [5]. Hammerle et al. observed that grafted sites were regenerated with new bone at least 6–9 months after surgery [45].

Buser at al. recommend perforating the cortical bone before bone grafting for better migration of vessels to the augmented site [46]. There are also conflicting studies suggesting that decortication is not needed for better augmentation [47, 48]. Decortication of both the buccal and lingual aspects of the recipient site has been shown to increase the bone healing capacity by 2–10 times when compared to non-decorticated sites [49]. Several benefits of decortication of recipient site have been demonstrated [50]. First, revascularization is increased after decortication, particularly in the mandible. Second, the release of growth factors can improve healing. Finally, the roughed surface of the recipient site may integrate with the graft materials and increase the stability [50]. If the osseous defect is in the mandible, the authors recommend decortication of the recipient site with a drill under copious cold sterile irrigation (**Figure 11**).

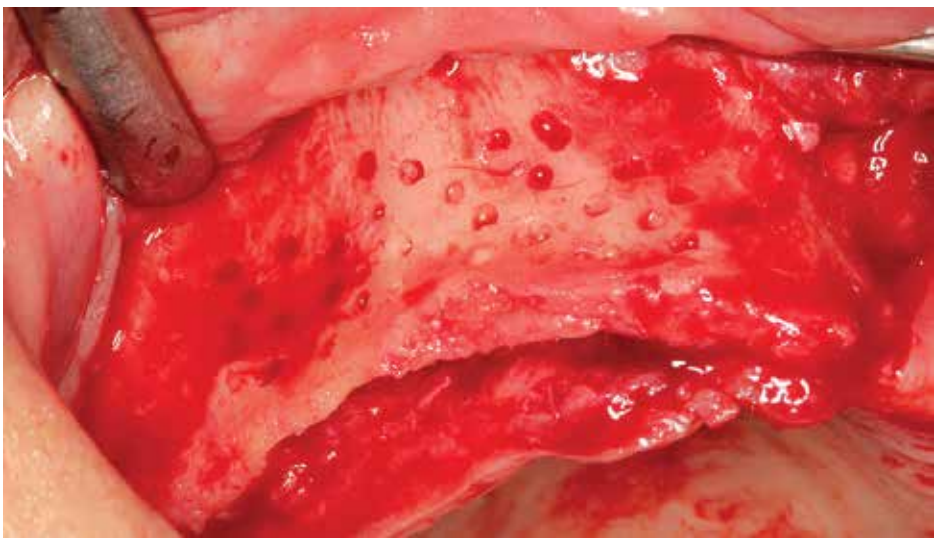

Figure 11. Decorticated bone.

Generally, decortication does not take a considerable amount of time or prolong the operation.

2.6.2. Primary closure

Protection of the grafted site during is an important factor. Wound healing in soft tissue can be achieved by primary or secondary intention. In primary intention, the edges of the flap are brought close and are in the same position as before the incision (**Figure 12**).

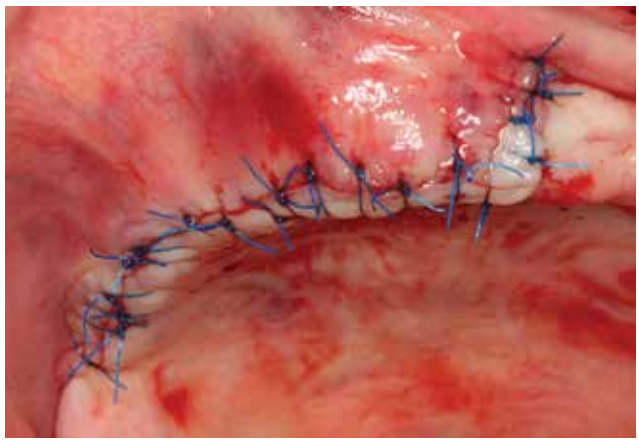

Figure 12. Primary closure.

In secondary intention, the edges of the flap are not closely approximated, and the membrane or grafting material can be seen visually [5]. Secondary intention prolongs the healing and increases the risk of infection at the grafted site [4–6]. Protection of the augmented site begins from a primary tension-free flap closure. If secondary intention healing occurs inadvertently, a series of complications may be encountered, and re-augmentation may be required [5].

Many factors may affect the predictability of GBR outcomes upon primary closure, including the grafting volume of the deficient site. The rate of soft tissue complications may increase in direct proportion with the grafting volume [4, 6]. Therefore, in challenging cases such as vertical augmentation, failures due to soft tissue dehiscence are more frequently seen [6]. Another factor that may affect the clinical outcome is the usage of the appropriate materials and technique. Multifilament sutures, such as silk sutures, are not recommended to use in augmented sites due to the high incidence of infection. Monofilament sutures may help to reduce the infection rate [4–6]. Most importantly, the clinician should be familiar with different suturing techniques to reduce the pressure on the edges of the flap. The authors recommend removing sutures 2–3 weeks after the operation. For vertical augmentations, sutures are generally removed after 3 weeks.

Incision design is also a key factor for tension-free flap closure. In particular, if large deficient sites are planned to be grafted, a greater number of releasing incisions will be needed for tension-free flap closure. Therefore, soft tissue surgical interventions may be needed before or after the operation to increase the vestibular depth and keratinized mucosa [6]. Clinicians should not only focus on hard tissue grafting. For the achievement and maintenance of success, soft tissue conditions such as the gingival biotype, the amount of keratinized mucosa, the vestibular depth, and previous surgical interventions due to failures should be evaluated meticulously during treatment planning [6].

Postoperative care during the initial weeks of healing may affect the outcome of GBR [51]. Chlorhexidine and hyaluronic acid mouthwash after the operation are recommended to reduce infection and improve soft tissue healing [5].

Postsurgical medications should also be prescribed, including antibiotics starting on the day of surgery and lasting for 7 days (1000 mg amoxicillin and clavulanic acid, twice daily), analgesics (to be taken as needed every 6 h), and corticosteroid (e.g., dexamethasone 4 mg daily) for 2–3 days to minimize edema [4, 6, 52]. Patients should be informed in detail with written postoperative instructions after the operation. Solely verbal instructions are not recommended because patients are generally tired after the operation and may forget these instructions.

2.6.3. Iliac crest block bone grafting

Iliac crest block bone grafting is widely used in oral and maxillofacial surgery for the reconstruction of major deficient alveolar ridges. Although both the anterior and posterior ilium can be a source of extra-oral bone grafts, clinicians generally choose the anterior ilium as a donor site because it allows convenient access to the recipient site. Patients remain in a supine position during the operation, and this approach reduces the operation time. Generally, the patient remains in a prone jackknife position during harvesting of the posterior iliac bone, and the patient must be switched to a supine position during the procedure. This may increase the operation time by at least 1–2 h. The anterior ilium can provide both cortical and cancellous bone blocks. Uni-, bi-, or tri-corticocancellous blocks can be harvested under general anesthesia. A bone volume of 50 cc or less can be harvested from a single anterior ilium [53]. If large corticocancellous blocks are needed, harvesting from the posterior iliac bone is appropriate.

The block is harvested according to the dimensions of the bone graft required for the reconstruction of the alveolar ridge. Under general or neuroaxial blockade anesthesia, a skin incision is made approximately 2 cm above the anterosuperior iliac spine, along the anterosuperior margin of the anterior iliac crest. The medial and lateral cortical surfaces of the iliac crest are exposed directly after the subperiosteal dissection. A micro-saw and chisel are used to harvest an autogenous bone block from the anterior iliac crest (**Figure 13**).

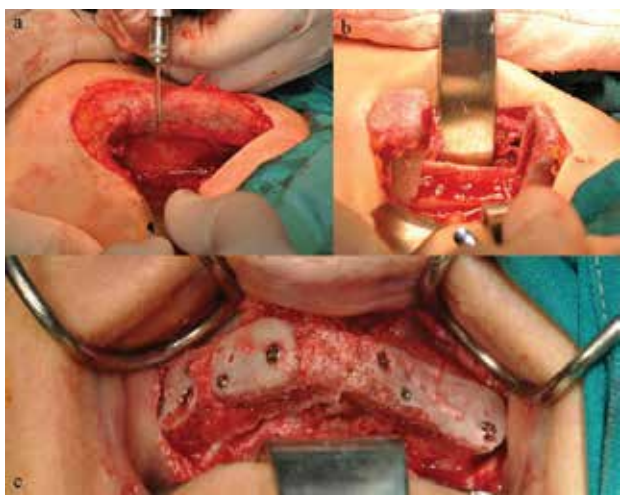

Figure 13. Iliac bone block application.

The block bone grafts are recontoured with diamond burs for optimum adaptation to the recipient site as an onlay technique, and they are fixed to the residual ridge with multiple screws to inhibit micro-movement during the healing process. The corners of the graft are smoothed out to avoid any undesirable exposure during the healing process. Suction drains can be used after harvesting before closure. The periosteum, fascia, and subcutaneous tissues are closed with sutures.

Numerous studies report low-to-moderate morbidity at the time of grafting. Major and minor complications, such as seroma, hematoma, fracture, paresthesia, pain, and gait disturbances, may occur after the operation [54]. Patients should remain in the hospital for at least 1 day; therefore, the total treatment cost is higher than the cost for intra-oral harvesting applications. Iliac bone block grafting morbidity is higher than that of local bone harvesting techniques, such as ramus or chin intra-oral autogenous block harvesting [54]. The experience of the surgeon and technique used plays important roles in reducing morbidity.

Sbordone et al. evaluated the resorption rate in alveolar ridge augmentation after iliac bone block grafting using computerized tomographic scans [53]. The authors reported an average resorption rate of 87% for maxillary grafts after 6 years follow-up [53]. Vermeeren et al. observed a resorption rate ranging from 44% to 50% after 5 years using two-dimensional images [55]. Other studies found a resorption rate ranging from 42% to 87% for onlay grafted bone [56, 57]. The use of a bone block for the reconstruction of a deficient alveolar ridge may be easier than GBR with regard to space maintenance. However, the use of a collagen membrane is still recommended, even in block grafting, to reduce bone resorption [4, 6]. The use of a collagen membrane with block grafting may reduce resorption by almost 25% [4, 6].

Jensen at al. compared GBR and block grafting techniques and found that in 11.1% of cases using GBR and in 2.8% of cases using block grafting, re-augmentation was needed [40]. Contour augmentation can be applied during the second-stage surgery, particularly during implant placement at an esthetically appropriate site. This second augmentation may not only limit bone resorption around implants in the future, but it may also support soft tissue and improve the esthetic appearance [4, 6]. The authors recommend using only slowly resorbable grafting materials such as DBB at the buccal site for re-augmentation with a collagen membrane. Tacked collagen membrane with grafting material will increase the bone thickness horizontally and facilitate anterior esthetic success.

More bone can be regenerated using iliac blocks than GBR [40]. However, iliac bone blocks may be more prone to resorption during healing [53]. Therefore, clinicians should estimate the rate of resorption and increase the amount of harvested bone block. Caution should be taken during treatment planning, and it is preferable to increase the number of implants used in iliac block-augmented patients to decrease the detrimental effects of loading forces [58]. Implant designs that include platform switching may also help to reduce marginal bone loss [52]. One important advantage of block grafting over GBR is the healing time. Four to five months are sufficient for a bone block integrates with the host bone and allow for implant placement [53, 54, 56]. However, particularly for vertical augmentations, 7–9 months are needed for the GBR technique to achieve implant stability [2, 37]. Therefore, it is easier for patients to accept a two-stage GBR treatment if temporary prostheses are provided during long-term healing. A

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temporary prosthesis can be manufactured using a provisional implant with a fixed or removable prosthesis. If the available bone is appropriate for the stabilization of four provisional implants, fixed temporary restorations can be provided during long-term healing. Soft tissue-supported removable prostheses are not recommended because they may adversely influence the stability of the augmented site.

According to the literature, the survival rates of dental implants inserted at augmented sites are similar to the survival rates of implants placed in natural bone [59, 60]. Marginal bone loss was also similar between implants placed in augmented and pristine bone [61, 62].

2.6.4. The future of tissue engineering

The field of biomaterials and tissue engineering is rapidly growing, and growth factors have great potential for promoting bone regeneration at the resorbed alveolar ridge. Among the various growth factors, recombinant human bone morphogenic protein-2 (rhBMP-2) and recombinant human platelet-derived growth factor (rhPDGF) have received a great deal of attention [63]. Although there are numerous graft materials available, such as xenograft, allograft, and alloplast, most have only osteoconductive properties and provide only a scaffold for bone regeneration during healing. Researchers are attempting to completely eliminate the use of autogenous bone at severe augmentation sites to decrease patient morbidity. Therefore, studies regarding growth factor use with graft materials are increasing [63, 64].

The bone morphogenetic proteins (BMPs) are members of the transforming growth factor-β superfamily. BMPs regulate differentiation, chemotaxis, growth, and apoptosis of osteogenic cells and induce significant bone regeneration [65, 66].

Platelet-derived growth factor (PDGF) is released from aggregated platelets during the early healing phase at the wound site and exerts chemotactic and mitogenic effects on inflammatory cells and undifferentiated mesenchymal cells [67]. PDGF-BB shows potential effects on cells that influence bone regeneration, and it stimulates type I collagen synthesis in osteoblasts, directs cell migration or chemotaxis of progenitor cells, and participates in the initiation angiogenesis [68, 69]. Of the five PDGF isoforms, PDGF-BB is the most biologically potent and has the greatest binding affinity for osteoblasts [69].

In a preclinical study, Simion et al. found that a significant amount of new bone formation was achieved using DBB blocks and rhPDGF-BB in the rehabilitation of severe mandibular ridge defects [70]. Wallace et al. applied rhBMP-2-wetted absorbable collagen sponges in extraction sockets [71], and they found 49.6% vital bone in core biopsies taken after 4 months of healing. These authors suggested that rhBMP-2 and collagen sponges may replace the use of barrier membranes and graft materials to rehabilitate extraction sockets for future implant placement. In another study, Misch et al. used rhBMP-2/collagen sponges and a titanium mesh for augmentation of the atrophic mandible prior to implant placement [72]. All dental implants were placed after 6 months of healing, and healing of the augmented sites was uneventful.

The Food and Drug Administration has approved the usage of rhBMP-2/collagen sponges (INFUSE Bone Graft kits; Medtronic, Minneapolis, MN, USA) in extraction socket and sinus floor augmentation (well-protected defects). The number of published pre-clinical and clinical

articles regarding the use of growth factors in reconstruction of hard tissue defects is growing. The use of growth factor instead of autogenous bone offers several advantages, such as decreased patient morbidity, reduced operation time, increased amounts of vital bone at the augmented site in comparison with scaffold biomaterials, and simplification of the surgical technique [70–72]. Clinicians need to be familiar with properties, limitations, and techniques associated with these materials before application. In the future, there can be no doubt that growth factors will play an important role in hard and soft tissue engineering.

3. Conclusion

Many novel techniques, biomaterials, and tools have been described in the literature that clinicians may use to reconstruct bone deficiencies. However, most importantly, the success of alveolar ridge augmentation procedures mainly depends on clinician experience and skill. The surgical risks may be increased for challenging reconstructions. Therefore, the clinician and patient should carefully evaluate the benefits and risks of the operation and decide on the most ideal treatment option. Prosthetic-driven augmentation is recommended for a better outcome. If the clinician focuses only on ridge augmentation techniques to solve bone deficiency problems, he or she may overlook other treatment options that may have lower risks and less morbidity, such as using short, narrow, or tilted implants. After all, ridge augmentation is being performed for the ideal placement of dental implants.

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Chapter 12

Bone Regeneration in Implant Dentistry: Role of Mesenchymal Stem Cells

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Additional information is available at the end of the chapter

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Abstract

This chapter focuses on a review of the activity of non-embryonic mesenchymal stem cells used to regenerate jaw bones in dentistry. Recent research of non-embryonic stem cells provides new possibilities for noninvasively obtaining new autologous bone from stem cells provided by various tissues from the same patient. Disaggregation of biologic tissue harvested from the patients during surgery permits extraction of stem cells from a small sample of connective tissue obtained from the patient's lingual mucosa or from the postextraction surgical site where the endosseous implant will be inserted.

Keywords: Bone regeneration, mesenchymal stem cells, scaffold, micrografts, socket preservation

1. Bone regeneration in implant dentistry

1.1. Bone components

Bone is formed by organic and inorganic components. Two-thirds of the volume comprises inorganic salts, including calcium, phosphate, carbonate, citrate, and hydroxyl ions (magnesium, sodium, and fluoride) in the form of crystals of hydroxyapatite [1]. The organic portion comprises 99% collagen type I and growth factors, such as osteocalcin, osteonectin, phosphoproteins, proteoglycans, and bone morphogenetic proteins [2].

Bone also includes cellular components, such as pre-osteoblasts, osteoblasts, osteocytes, and osteoclasts. Osteoblasts arise from mesenchymal pluripotent cells, which are cuboidal

mononuclear cells located along the bony margins, and are able to form new bone tissue. About 10–20% of osteoblasts are trapped within the matrix they produce by developing into osteocytes, which are considered mature osteoblasts. Osteocytes are smaller than osteoblasts, and have a higher nucleus-to-cytoplasm ratio and a larger number of extensions that allow for intercellular communication. Osteocytes are likely the cells responsible for bone regeneration [3]. Osteoclasts are large multinucleated cells that are polarized, have an average lifespan of 15–20 days, and are derived from bone marrow monocytes [4]. Osteoclasts facilitate bone resorption by reducing the surrounding pH.

1.1.1. Stem cells—mesenchymal stem cells

Stem cells are characterized by their ability to renew by cell division and to differentiate into a diverse range of specialized cell types. The two broad types of mammalian stem cells are embryonic stem cells, which are found in blastocysts, and adult stem cells, which are found in adult tissues such as the bone marrow. In adult organisms, stem cells give rise to progenitor cells that act as a repair system for the body by replenishing specialized cells and tissues. Because adult stem cells are obtained from a developed organism, their use in research and therapy is not as controversial as that of embryonic stem cells, which entail the destruction of an embryo [5].

Mesenchymal stem cells (MSCs) are multipotent adult stem cells with unique biologic properties that are typically associated with their mesodermal lineage (adipogenic, chondrogenic, osteogenic, or myogenic) [6–8]. MSCs were first discovered in 1968 by Friedenstein et al. [9], and are defined as adherent fibroblast-like cells that reside in the bone marrow and are capable of differentiating into bone. MSCs and an adequate blood supply are essential for the bone deposition process and healing. MSCs also contribute to the homeostasis of various tissues, including bone, in adults [10].

MSCs can be expanded in vitro for several passages, are easily accessible, and possess minimal immunogenic or tumorigenic risks, and are thus an excellent cell source of stem cells used in dental, craniofacial, and orthopedic regenerative surgery [11].

In 2006, the International Society for Cellular Therapy established the following definition of MSCs [12]:

1. Cells that are adherent to plastic under standard tissue-culture conditions;

2. Cells that are positive for surface markers CD105, CD73, and CD90, but negative for CD34, CD45, CD14, or CD11b, CD79a, or CD19, and human leukocyte antigen-D-related (HLA)-DR surface molecules;

3. Cells with the capacity to differentiate into osteoblasts, chondrocytes, and adipocytes;

MSCs, which represent ~10% of human stem cells, are rare and heterogeneous; they are part of the connective tissue and support hemopoiesis [13]. MSCs can be expanded in vitro and rapidly reach the desired cell counts for use in vivo [14].

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Despite having some common features, MSCs have different characteristics depending on the tissue of origin. MSCs can be isolated from several different tissues, including bone marrow [15], placenta, cord blood [16], adipose tissue [17], muscle [18], periosteum [19], synovium [20], deciduous teeth [21], and brain, kidney, heart, epidermis, and periodontal ligaments [22–24]. Among these, bone marrow and adipose tissue are the most commonly used sources of MSCs because of their relative ease of harvesting. MSCs can differentiate into osteoblasts, adipocytes, chondrocytes, myoblasts, cardiomyocytes, hepatocytes, neurons, astrocytes, endothelial cells, fibroblasts, and stromal cells [25].

2. Bone regeneration

Since Horwitz et al. [26] first demonstrated that MSCs can improve osteogenesis in children with osteogenesis imperfecta, the role of MSCs in bone formation and regeneration has been intensively studied. Studies performed in several animal models revealed that the transplantation of MSCs improves bone regeneration and healing of bony defects [27, 28]. The therapeutic options clinically available for bone reconstruction and regeneration, however, are often unsatisfactory due to morbidity at the donor site or the complexity of allograft procedures.

Bone regeneration in maxillofacial reconstruction is one of the most important applications of MSCs [29]. The repair of craniofacial bone defects remains a challenge, however, and the results depend on the size of the defect, the quality of the soft tissues that cover the defect, and the reconstructive techniques used. In Europe, ~1.5 million patients undergo craniofacial reconstructions annually; ~20% of them continue to experience functional deficiency despite the intervention, and 30,000 patients per year develop donor-site morbidity following oral and maxillofacial reconstruction [30].

Traditional bone regeneration techniques involve autologous, homologous, heterologous, or allogeneic grafts. Autologous bone grafts are considered the best option for damaged tissue repair because of the low risk of immunogenicity or disease transmission compared with allografts (genetically different donors from the same species) or xenografts (donors from another species). Autologous bone grafts are limited due to the scarcity of available autologous tissue for repairing larger bone defects, donor-site morbidity, and potential wound-based infections, as well as the prolonged operative times. In addition, autologous bone grafts require additional surgical procedures, which increase the risk of both donor-site morbidity and significant resorption [31]. Alternative therapies continue to be explored [32], and researchers are attempting to identify the best material for bone regeneration.

Bone regeneration following the use of stem cells occurs through two mechanisms: a direct mechanism, which comprises the integration and differentiation into tissue-specific cells, and begins when transplanted cells take root in the target tissue [33]; and an indirect mechanism, which involves paracrine effects [34].

Differentiation of MSCs into osteoblasts was demonstrated in vitro by cultivating the cells in the presence of ascorbic acid, inorganic phosphate (beta-glycerophosphate), and dexa-

methasone. In vivo studies suggest that transplanted adult stem cells can integrate into tissues that are different from those of the donor and, in some cases, contribute to their regeneration [35]. Demonstrating the in vivo differentiation of implanted cells is challenging, and researchers often assume that differentiation is the result of interactions between grafted cells and host-site cells, but the capacity of MSCs to release a number of trophic factors could also explain their therapeutic benefit.

Some recent reports suggest that the therapeutic properties of paracrine factors are a common feature of stem cells [36]. The paracrine effect could contribute to bone regeneration via the secretion of trophic and angiogenic molecules such as angiopoietin (Ang)-1, Ang-2, Ang-like-1, Ang-like-2, Ang-like-3, Ang-like-4, vascular endothelial growth factor (VEGF), and fibroblast growth factor-2. These molecules can activate local MSCs, promote tissue regeneration and angiogenesis [37], and inhibit fibrosis, apoptosis, and inflammation [38, 39]. They also have neurogenic, neuroprotective, and synaptogenic effects [40, 41]. Because the survival and differentiation of MSCs at the site of the lesion is limited, paracrine signaling is considered to be the primary mechanism of their therapeutic effects [42]. This hypothesis is supported by in vitro and in vivo studies showing that many cell types respond to paracrine signaling from MSCs, which leads to the modulation of a large number of cellular responses, such as survival, proliferation, migration, and gene expression [39].

The secretion of bioactive factors is thought to play a critical role in the paracrine activity of MSCs. These factors and cytokines can be collected in a conditioned medium (CM), which, when transplanted into animal models of different diseases, has effects that are similar to those exerted by MSCs and can increase the tissue-repair process in acute myocardial infarction [43], wound healing [44, 45], and neuroprotection [46]. Encouraging results have also been obtained following the graft of MSCs obtained from the bone marrow cleft at the level of the maxillary sinus and alveolar schisis [47, 48].

Preliminary studies of bone regeneration used MSC populations that were not expanded from bone marrow due to the reduced number of MSCs in the bone marrow (0.01% of the bone marrow cell population). The use of unexpanded MSCs, however, produced unpredictable results [49], and later advances made it possible to cultivate and characterize MSCs. The osteogenic potential of expanded and purified MSCs has been studied extensively, but with mixed results [50, 51]. Factors that may affect the results relate to the donor site, blood supply, and inadequate osteoblastic differentiation of the implanted cells.

In summary, stem cells are effective for tissue regeneration and future research is warranted despite the low number of clinical studies compared to those in preclinical animal models. The use of MSCs is still limited because of their low accessibility, difficult collection, and poor long-term stability. Stem cells are used mainly in combination with scaffolds or biomaterials to improve their efficacy and stability. Scaffold material is often used to provide mechanical support and as a substrate for cell attachment, proliferation, and differentiation. Regardless of the scaffold used for bone reconstruction, however, bone healing depends mainly on two pivotal factors: the capacity to recruit progenitor cells to the injury site and the presence of healthy vasculature near the injury site. Researchers have identified several different tissue types that can be considered valid MSC donors.

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2.1. Dental pulp stem cells

Dental pulp is a source of neural crest-derived stem cells that is easily accessible and characterized by low morbidity after collection [52, 53]. Dental pulp comprises both ectodermic and mesenchymal components, and is divided into four layers (outer to inner). The external layer is made up of odontoblast-producing dentin. The second layer, called the "cell-free zone," is poor in cells and rich in extracellular matrix. The third layer, called the "cell-rich zone," contains progenitor cells that exhibit plasticity and pluripotent capabilities [52]. Finally, the inner layer comprises the vascular area and nerve plexus.

In the context of the oral and maxillofacial area, dental pulp stem cells (DPSCs) and periosteal stem cells may be optimal alternatives to MSCs and display high potential for differentiating into a variety of cell types, including osteocytes, suggesting their effective use in bone regeneration, although clinical studies are limited. In addition to DPSCs and periosteal stem cells, adipose tissue also serves as a source of MSCs [17]. In fact, adipose-derived stromal cells can differentiate into chondrocytes, osteocytes, or myocytes, as indicated by several studies in animal models [54–57], although clear and conclusive data about their osteogenic potential are limited.

In 2005, Laino et al. [58] successfully isolated and selected a distinctive and highly enriched population of stem cells derived from dental pulp in adult humans. This stem cell population was self-expanding and differentiated into pre-osteoblasts able to self-maintain and renew. These stem cells differentiated into osteoblasts and produced living autologous fibrous bone tissue in vitro after 50 days of culture. Transplantation of this tissue in vivo led to the formation of lamellar bone with osteocytes without the need for scaffolding. The differentiated cells and living autologous fibrous bone could be frozen at −80°C and stored for extended periods of time with no clear effect on their bone-forming ability. The same research group subsequently demonstrated that DPSCs differentiate into osteoblasts that secrete abundant extracellular matrix [59].

In 2007, d'Aquino et al. [60] provided direct evidence that osteogenesis and angiogenesis mediated by human DPSCs are regulated by distinct mechanisms that lead to the organization of adult bone tissue after stem cell transplantation. In this study, stromal stem cells from human dental pulp were extracted, cultivated, and characterized in vitro. After 30 days of culture, the cells began to differentiate, lost their stem cell markers, and expressed differentiation markers. After 40 days, the cells differentiated into two cytotypes from a common progenitor: osteogenic progenitor cells (70% of total cells) and endothelial progenitor cells (EPCs, 30%), demonstrating synergic differentiation into osteoblasts and endotheliocytes. After 50 days, woven bone was obtained in vitro and its transplantation into immunocompromised rats resulted in a tissue structure with an integral blood supply similar to that of human adult bone. These findings suggest that osteogenesis and vasculogenesis are interdependent, and that this process is essential to obtain adult bone tissue suitable for transplantation and surgical or clinical applications in tissue repair.

DPSCs grafted into immunosuppressed rats generated complete and well-vascularized lamellar bone [61]. DPSCs are easily managed because they have a long lifespan, can be safely

cryopreserved, and are able to interact with biomaterials [62]. Finally, in vitro and in vivo experiments revealed that both the quality and quantity of bone regenerated by DPSCs blended from stem cells and biomaterials [58, 60, 61, 63].

DPSCs can be applied for oral and maxillofacial bone repair in the maxillofacial area and, on appropriate resorbable scaffolds, promote the formation of an efficient biocomplex in patients with a mandibular defect, as reported by d'Aquino et al. [60]. In that study, a biocomplex constructed from dental pulp stem/progenitor cells and a collagen-sponge scaffold was used for oral and maxillofacial bone tissue repair. Stem/progenitor cells obtained from the upper third of molars previously extracted were gently placed with a syringe onto a collagen-sponge scaffold and used to fill the space left by the lower third of the molar extraction procedure. Thirty days after surgery, X-ray controls exhibited a high rate of mineralization; 3 months after the surgery, samples collected from the regeneration site showed well-organized and well-vascularized bone with a lamellar architecture surrounding the Haversian canals. Bone from control sites was immature and showed fibrous bone entrapped among new lamellae, incomplete and large Haversian canals, and evidence of bone resorption. Moreover, immunofluorescence analyses showed high levels of bone morphogenetic protein-2 and VEGF in regeneration samples. This clinical study demonstrated that dental pulp stem/progenitor cells can be used for oral and maxillofacial bone repair and that collagen sponges can be considered an optimal support for stem/progenitor cells in cell-guided regeneration.

The same group published a 3-year follow-up [64]. Histology and in-line holotomography revealed that regenerated bone was uniformly vascularized and qualitatively compact rather than the physiologic type of bone found in that region—cancellous (i.e., spongy). The authors speculated that the regeneration of compact bone probably occurs because grafted DPSCs do not follow the local signals of the surrounding spongy bone. Although the bone that regenerated at the graft site was not the proper type found in the mandible, it seemed to have a positive clinical outcome because it created steadier mandibles, increased implant stability, and may have improved resistance to mechanical, physical, chemical, and pharmacologic agents.

Although the use of DPSCs is valid for tissue regeneration in the maxillofacial area, the identification of an accessible site from which to collect these cells can be challenging, and the amount of cells that can be obtained is very limited. DPSCs can be cultured by two methods. In the enzyme-digestion method, pulp tissue is collected under sterile conditions and digested with the appropriate enzymes, and the resulting cell suspensions are seeded in culture dishes [65]. In the explant outgrowth method, the extracted pulp tissues are cut, anchored via microcarriers onto a suitable substrate, and directly incubated in culture dishes [66]. From a clinical point of view, these methods are not appropriate for therapeutic applications because of the manipulation of dental pulp. A new, efficient, and safe method for isolating dental pulp was reported by Brunelli in 2013 [67], in which a new instrument called a Rigenera® (Torino, Italy) machine was used to create micrografts of disaggregated dental pulp that was subsequently poured onto a collagen sponge. This micrograft was injected into the sinus cavity, and 4 months after the intervention newly formed bone was observed with twice the mineral density of native bone [67].

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2.2. Periosteal stem cells

In addition to dental pulp, the periosteum is a surprising source of stem cells. After bone fracture in animal models, periosteal progenitor cells undergo an impressive expansion, followed by differentiation into osteoblasts and chondrocytes [68]. This remarkable property of the periosteum has prompted extensive research into the use of periosteum-derived cells for regenerative approaches, and preclinical studies have demonstrated the potential of these cells. The success of periosteal cells in preclinical animal models has also given rise to several exploratory clinical studies using ex vivo expanded periosteal cells for bone regeneration.

In 1992, chick tibial periosteal cells were cultured, combined with porous calcium phosphate ceramics, and subcutaneously implanted into athymic mice [69]. These cells eventually gave rise to bone tissue via two different mechanisms. Intramembranous bone formation occurred early in the peripheral pores of the ceramics, and endochondral bone formation occurred later in the central pores. These results raised the possibility that composite grafts of cultured periosteal-derived cells and porous ceramics could be clinically used as bone-graft substitutes for bone augmentation or regeneration.

In 2001, Vacanti et al. [70] first used culture-expanded periosteal cells derived from the radius in combination with a porous hydroxyapatite scaffold to replace the distal phalanx of the thumb. In this study, coral alone seeded with cells derived from the periosteum and placed in the subcutaneous tissue that was not adjacent to native bone formed new bone.

The use of periosteum-derived bony matrix for augmentation in the posterior maxilla before implantation results in bone formation 4 months after transplantation with trabecular bone containing viable osteocytes [71, 72]. The graft provides a reliable basis for the simultaneous or secondary insertion of dental implants.

Springer et al. [73] compared mandibular periosteum cells that were cultured and seeded onto a collagen matrix and maxillary bone cells that were cultured and seeded onto natural bone minerals. They concluded that the first method produced a significantly higher amount of new living bone.

Taken together, these reports demonstrate the clinical potential of periosteal-derived cells for bone regeneration therapies. The last three studies described, however, did not use stem cells but rather only cultures of differentiated periosteal cells.

2.3. Bone marrow-derived MSCs

Bone marrow-derived mesenchymal stem cells (BMSCs) are a readily available and abundant source of cells for tissue-engineering applications. BMSCs may be useful tools for regenerating bone, but the method of bone marrow aspiration from patients is associated with significant morbidity at the donor site [74].

BMSCs can differentiate into osteoblasts in vitro [75] and have osteogenic ability in vivo [76]. The addition of BMSCs to a biomaterial improves the quality of regenerated lamellar bone [77]. In 2008, BMSCs were successfully used in association with biphasic hydroxyapatite/β-tricalcium phosphate in a sinus-augmentation procedure [78].

In a recent study [79], tissue repair cells isolated from bone marrow were successfully used to repair bone defects in a human model. In this study, bone marrow cells were collected, cultivated, and characterized. Flow cytometry demonstrated the presence of mesenchymal and vascular phenotypes. The cellular suspension, carried by a gelatin sponge, was implanted in a postextraction site and covered by a resorbable collagen membrane. Six weeks after the implantation, biopsy revealed the presence of highly vascularized and mineralized bone tissue. McAllister et al. [5] used an MSC-heterologous bone graft harvested from cadavers for sinus-augmentation procedures. The authors demonstrated the presence of MSCs in the commercial bone preparation derived from cadavers and harvested within 24 h of death and stored at −80 °C. Moreover, they rapidly formed bone from a commercially available cellular bone matrix that contained heterologous MSCs.

In one study [80], researchers seeded Geistlich Bio-Oss (GeistlichPharma North America, Princeton, NJ, USA) with stem cells and found that this construct was superior to Bio-Oss mixed with autogenous bone in terms of bone formation 3–4 months after surgery. This study, however, presented some issues regarding data reporting and statistical analysis.

In a well-documented preliminary report, Behnia et al. [81] used BMSCs in association with platelet-rich plasma. They used biphasic hydroxyapatite/tricalcium phosphate as a scaffold and implanted the graft in an alveolar cleft, achieving cleft closure and a mean postoperative defect filling of 51.3% at 3 months after surgery. The same research group used demineralized bone mineral and calcium sulfate in association with BMSCs to treat alveolar clefts, but did not achieve similar positive results [47]. They concluded that the latter material was not a suitable scaffold for MSC-induced bone regeneration.

Bone marrow aspiration, however, is severely painful for donors, often requires general anesthesia, and may be associated with adverse events [74, 82].

2.4. Blood-derived stem cells

Peripheral blood is a source of MSCs that can be isolated with minimal invasiveness compared to extraction from bone marrow [83, 84]. According to some authors [85], blood-derived stem cells have characteristics and bone-regeneration abilities that are similar to those of BMSCs both in vitro and in vivo and are a promising source for bone regeneration for clinical use; by contrast, other authors [83] report that blood-derived stem cells have less multipotency than bone BMSCs.

2.5. Adipose-derived stem cells

Adipose tissue is an alternative source of MSCs that can differentiate into chondrocytes, osteocytes, or myocytes [17, 54, 86, 87]. An in vivo study demonstrated that adipose-derived stem cells are capable of bone regeneration and are useful for reconstructing critical-size defects in rats [55].

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2.6. Secretomes

MSCs enhance wound healing, but the mechanisms are unclear. The use of MSCs for tissue repair was initially based on the hypothesis that these cells migrate to and differentiate within injured tissues, becoming specialized cells. It now appears that only a small proportion of transplanted MSCs actually integrate into and survive in the host tissue. Thus, the predominant mechanism by which MSCs participate in tissue repair seems to be related to their paracrine activity. Indeed, MSCs provide a suitable microenvironment that includes a multitude of trophic and survival signals, including growth factors and cytokines. Factors secreted from stem cells into a medium are called *secretomes* and have attracted much attention [45] because of their ability to support regenerative processes in the damaged tissue, induce angiogenesis, protect cells from apoptosis, modulate the immune system, and recruit endogenous stem cells to the grafted site. Compared to stem cells from other sources, BMSCs secrete distinctively different cytokines and chemokines, including greater amounts of VEGF-alpha, insulin-like growth factor 1, epidermal growth factor, keratinocyte growth factor, Ang-1, stromal-derived factor 1, macrophage inflammatory protein-1 alpha and -1 beta, and erythropoietin [45], which are important for normal wound healing.

In vitro, the CM from the culture of BMSCs (MSC-CM) enhances the migration, proliferation, and expression of osteogenic marker genes such as alkaline phosphatase, osteocalcin, and Runt-related transcription factor 2 of MSCs, and contains cytokines such as insulin-like growth factor 1, VEGF, transforming growth factor-β1, and hepatocyte growth factor. The concentrations of cytokines contained in MSC-CM are relatively low, and the use of MSC-CM does not induce the severe histologic inflammatory responses observed with the clinical use of recombinant human bone morphogenetic protein 2 [88]. Implantation of MSC-CM in association with a collagen sponge or agarose produced early bone regeneration in rat calvaria, suggesting that MSC-CM has potential for cell-free bone regeneration [88, 89].

MSC-CM recruits endogenous stem cells to the graft site and promotes early bone and periodontal regeneration in rat calvarial bone defects and periodontal tissue [88, 90]. Some authors [88] noted a stronger effect on bone regeneration and autogenous MSC migration when MSC-CM, rather than MSCs alone, was used in the graft, demonstrating that MSC-CM induces bone regeneration via mobilization of endogenous stem cells. The recent use of MSC-CM in various oral and maxillofacial bone regeneration procedures demonstrated osteogenic potential [91].

The use of MSC-CM for bone regeneration is a unique concept in which the paracrine factors of stem cells are used without cell transplantation.

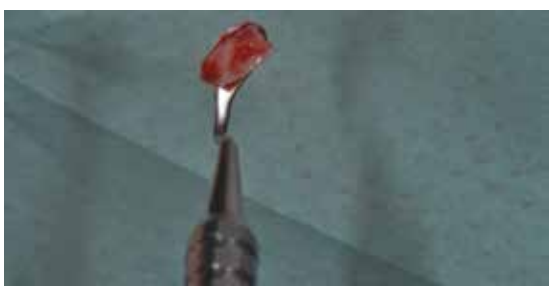
3. Cell isolation

The isolation of cells is often difficult, and the methods of extraction, such as enzymatic digestion or mechanical disaggregation, require several minutes to a few hours, which can reduce cell viability. A recent study [92] demonstrated the efficacy of a new medical device

called Rigeneracons® (CE certified Class I; Human Brain Wave, Turin, Italy) (**Figures 1** and **2**) to provide autologous periosteal micrografts (**Figure 3**) for clinical practice that are enriched with progenitor cells and are able to regenerate and differentiate.

Figures 1. Rigeneracons® medical device.

Figures 2. Detail of the blades system which disaggregate the periosteal tissue.



Figures 3. 1-2 mm^2 of periosteal tissue harvested after flap elevation can be disaggregate to get progenitor cells that will be seeded on a scaffold to be grafted in the bone defect.

The protocol is very simple. A 1–2-mm periosteal tissue harvested from the flap elevated at extraction or other surgical site is disaggregated mechanically (2 min at 15 Ncm and 75 round/min) after adding 1 ml sterile saline. The Rigeneracons® has 100 holes each provided with six microblades. A filter allows only the cells smaller than 50 μ (eight progenitor cells) to drop into a tank. The solution is then seeded on a polymeric scaffold (polylactic-co-glycolic acid-hydroxyapatite (PLGA-HA)) and grafted in the bone site (socket preservation, sinus lifting,

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periodontal defects, etc.) Although in vitro data about the Rigenera protocol are limited, a recent study demonstrated the efficacy of the Rigenera machine for obtaining stem cells from dental pulp [67]. These cells were positive for mesenchymal cell-line markers and negative for hematopoietic and macrophage markers. The percentage of viable cells derived from periosteum samples was high, however, suggesting that the device provides effective extraction.

4. Scaffold

MSCs grafted from a cell suspension require scaffolds to provide support, cohesion, and stability. Several types of materials are used as scaffolds. Advances in cell therapy have been accompanied by advances in novel scaffold fabrication techniques, yielding greater control over the surface topography, internal microstructure, and pore interconnectivity. Porous scaffolds have been widely explored for cell attachment because of the importance of allowing adequate room for tissue ingrowth and vascularization (i.e., pore size of 150–500 nm) [93]. Although natural materials retain their bioactivity, synthetic scaffolds present several advantages, including added flexibility in manufacturing, reproducibility, sterilization, storage times, and nonimmunogenicity. Solid free-form fabrication, a rapid three-dimensional printing technology for prototyping, was recently adapted for use in bone regeneration. Other researchers have developed hydrogels to encapsulate stem cells for tissue engineering, some with tunable degradation rates, but hydrogels may not provide the strength necessary for bone repair in load-bearing locations [94–96].

Not all researchers agree about the efficacy of combinations of stem cells and scaffolds, and a recent study reported that tissue-engineered complexes did not significantly improve bone-induced regeneration processes. Further studies are needed to elucidate the role of stem cells and scaffolds in tissue regeneration [97].

5. Epigenetic regulation

Epigenetic factors play a fundamental role in regulating the regenerative processes of MSCs [98, 99]. In stem cell differentiation processes, some genes may be upregulated and others repressed. Epigenetic modifications result in significant functional genomic alterations without changes in the nucleotide sequence [100].

Well-known epigenetic mechanisms include DNA methylation and histone modifications. Cytosine methylation downregulates gene expression, and the absence of methylation is essential for gene expression. In bone regeneration, however, methylation is essential. During MSC differentiation into osteoblasts in vitro, methylation of the osteocalcin promoter is significantly decreased, leading to the upregulation of osteocalcin [98]. Also, during osteoblast differentiation, increased methylation of the promoter of LIN28, a gene responsible for the maintenance of stem cell characteristics, reduces the expression of this gene, which facilitates osteogenesis [101].

Gene transcription is also regulated by histone modifications [100]. Histones are positively charged proteins that strongly bind the light-chain bearing structure of the double strand of phosphate-deoxyribose DNA. The binding of histone DNA determines the accessibility of transcription factors [102]. The most studied modifications are acetylation and methylation. Acetylation reduces DNA binding, allowing for greater gene expression. Conversely, deacetylation leads to a more compact chromatin structure, thus decreasing gene expression [103]. During differentiation, osteoblastic regions of the osteocalcin and osteocalcin promoters exhibit high levels of acetylation, which allows for greater accessibility of transcription factors. In addition, the downregulation of histone deacetylase-1 is an important process during osteogenesis [104]. These examples highlight the complexity of the effects of epigenetic regulation during bone regeneration.

6. Issues

Despite the initial success regarding the use of MSCs, some challenges remain as follows:

1. MSC removal requires invasive procedures that are associated with morbidity.
2. MSC proliferation and osteogenic differentiation potential decrease with age.
3. Inadequate vascular grafts of MSC carriers lead to cell death.
4. Difficulty accessing the repair site may limit the application of MSCs.

Recent studies revealed that implanted cells do not survive long [105]. One study showed a significant loss of cells within 24 h, and low numbers of transplanted cells survived at 12 weeks. Cells that did survive, however, underwent differentiation [106].

A crucial issue for autografts is cell viability; after collection, viability decreases to less than 50%, thereby reducing the regenerative capacities of the autografts. Cell death results from vessel interruption and subsequently reduced nutrition. Inadequate graft dimensions and tissue-size reductions to facilitate feeding can also lead to cell death. A promising approach to address this problem is the use of an instrument that preserves graft viability, such as by selecting small cells that are less susceptible to cell lysis.

Graft vascularization is a determining factor in cell survival, engraftment, and bone regeneration. In 1997, circulating EPCs were identified [107, 108]. EPCs participate in neovascularization processes [109], angiogenesis, vascular repair, restoration of blood flow after ischemia, distraction osteogenesis [110, 111], healing of fractures [111], and bone regeneration [112], and have an osteogenic potential. They are located mainly in the bone marrow and are mobilized as a result of biologic signals. The in vitro cultivation of mononuclear cell fractions under favorable conditions produces two EPC subtypes: early- and late-outgrowth endothelial cells [113]. Early-outgrowth endothelial cells survive less than 7 days in vitro, are characterized by a low rate of duplication, and induce transient angiogenesis principally for paracrine effects; late-outgrowth cells can expand to 100 cell population doublings, take root at the site of

engraftment, and can differentiate into osteoblasts [114]. A 2009 study demonstrated the successful application of blood-derived EPCs for healing bone defects [115].

7. Safety of transplanted MSCs

Clinical trials to evaluate the safety of MSCs for the treatment of graft-versus-host disease, ischemic heart disease, spinal cord injury, and systemic lupus erythematosus have not revealed any significant adverse effects [116–119]. While pluripotent cells have been obtained from adult somatic tissues by reprogramming methods [120], these cells can differentiate into different tissues and have wrongly been considered a source of MSCs for tissue regeneration. Indeed, they are known to cause teratoma formation and significant efforts to address the safety concerns are required before their application in patients [120]. By contrast, MSCs obtained without genetic reprogramming have a high capability to differentiate into many tissues without developing into tumor cells.

Studies of the role of MSCs in tumorigenesis have identified the ability of MSCs to interact with tumor cells and to support angiogenesis by providing a matrix to support cancer cells [121, 122]. MSCs may thus facilitate the growth of existing tumors [123, 124]. Transdifferentiation of MSCs has been observed in vitro, but this phenomenon could be due to contamination by tumor cells [125, 126].

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Chapter 13

Novel Techniques in Dentoalveolar and Implant Surgery

Mohammad Hosein Kalantar Motamedi and
Ali Hassani

Additional information is available at the end of the chapter

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Abstract

The topics of this chapter can help manage or prevent several common intraoperative problems facing clinicians during dentoalveolar and implant surgery. Three novel techniques are presented: (1) a technique for the stabilization of mucoperiosteal flaps following exposure of an impacted tooth requiring the apical repositioning of the gingival flap to allow for bonding of an orthodontic bracket, (2) a technique for the management of bone loss after tooth extraction and immediate dental implant placement, and (3) a technique to repair maxillary sinus membrane perforations during sinus lifting for implant placement.

Keywords: apical reposition flap, sinus membrane repair, bone grafting, implants, dentoalveolar surgery

1. Introduction

Dentoalveolar surgery may be associated with intraoperative complications; these complications may impede treatment, hinder healing, preclude immediate implant placement, or complicate delayed implantation [1–3]. Several new concepts and techniques presented in this chapter can help manage or prevent some of the common intraoperative sequels facing clinicians during dentoalveolar surgery. Three novel techniques in dentoalveolar surgery are presented herein, including "bone anchorage" (the stabilization of mucoperiosteal flaps following exposure of an impacted tooth requiring the apical repositioning of the gingival flap to allow for bonding of an orthodontic bracket), "crescent graft" (a technique to manage bone loss after tooth extraction and immediate dental implant placement), and "sinus membrane repair" [a simple technique to repair maxillary sinus membrane perforations (SMPs) during sinus lifting].

2. Bone anchorage: a fail-proof technique for the apical repositioning of the gingival flap following exposure of impacted teeth

Exposure of impacted teeth is a prerequisite for bracket bonding and orthodontic therapy. Sometimes, exposure of an impacted tooth requires the apical repositioning of the gingival flap to allow for bonding of an orthodontic bracket. In some cases, this procedure can be very difficult; this is particularly true in the posterior regions of the mandible where anatomical hindrances such as the external oblique ridge and muscle insertions are obstacles preventing the apical fixation of the flap [1]. In the anterior regions, we may also face difficulties if the impacted tooth requiring exposure is in the depth of the oral vestibule. In these cases, the mobility of the oral mucosa and muscle pull in the vestibule precludes the fixation and stabilization of the gingival flap impeding orthodontic bracket bonding. We present an effective approach by which these obstacles can be overcome. Our technique can effectively reposition the attached gingival flap apically after exposing the crown of the impaction and secure it until orthodontic bracket bonding.

2.1. Technique

To apically reposition the gingival flaps of attached gingiva after exposure of an impacted tooth and allow for orthodontic bracket bonding, surgery is indicated. After injection of local anesthesia, a full-thickness trapezoid-shaped mucoperiosteal flap is reflected using periosteal elevators to expose the bone. Buccal bone removal is then started laterally over the impacted tooth using an electric-driven hand piece and a rose bur. After tooth exposure, the buccal cortical bone is removed towards the cervix to sufficiently expose the crown. Care is taken not to remove the bone over or below the cervix of the tooth, as this may endanger the bifurcation or trifurcation in molar teeth. Using a 704 fissure or rose bur, a hole is drilled through the buccal cortex; this is often possible when there is a gap created via the dental follicle separating the tooth from the buccal bone or when a tooth adjacent to it has been removed (i.e. third molar). This gap provides room for passing the suture. Next, a 3-0 silk or polyglactin suture is passed through the superior part of the flap and then through the buccal cortex and tied securely to

Figure 1. Bur hole drilled through the buccal cortex after the removal of an impacted third molar. A polyglactin or silk suture is passed through the mucosa and then through the hole drilled in the buccal cortex.

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the bone to anchor down the flap apically below the crown of the tooth. The crown should be exposed sufficiently for bracket bonding (**Figures 1** and **2**).

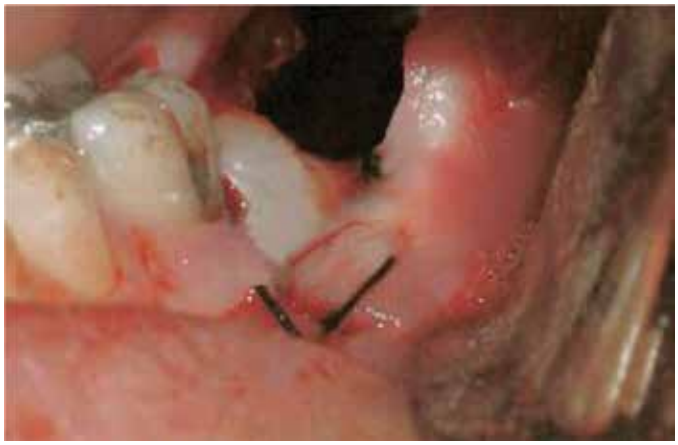

Figure 2. The suture is tied down to anchor the flap securing the exposure of the horizontally impacted second molar tooth for orthodontic bracketing.

2.2. Discussion

The apical repositioning of the gingiva for orthodontic bracketing is problematic in the posterior part of the mandible because of the external oblique ridge and shallow vestibule. The disruption of the gingival attachments and flap reflection of the attached gingiva will cause an immediate loss in vestibular depth due to the upward pull of facial muscles, such as the buccinator. In the anterior regions, we may also face difficulties if the impacted tooth requiring exposure is in the depth of the oral vestibule, because, in these cases, the mobility of the oral mucosa and muscle pull in the vestibule precludes the fixation and stabilization of the gingival flap impeding orthodontic bracket bonding. Securing the flap to the overlying bone is an optimal way to manage such cases [1].

3. Managing alveolar bone loss after tooth extraction for immediate implant placement: the "crescent graft"

3.1. Introduction

Although immediate implantation after tooth extraction has its merits, it may not always be feasible. The most common dilemma in such cases is the confrontation of postextraction bone loss due to difficult extraction of the tooth or preexisting periodontal disease. Many techniques exist with which to manage such complications, namely, autogenous bone grafts (the gold standard), which possess osteoinductive properties and other graft materials with osteoconductive properties. There are numerous sites from which to harvest autogenous bone, each

having inherent advantages and disadvantages. Chronic periodontitis is one of the major causes of excessive bone loss. After initial evaluations, the pocket depth must be assessed upon tooth extraction; periodontal bone defects may be encountered (vertical defects, crater defects, bone dehiscence, etc.) in the tooth socket of the extracted tooth. Defects may also be caused by traumatic extraction of a tooth without a defect preoperatively. Such defects may preclude immediate insertion of dental implants and require reconstruction either before or simultaneously upon insertion of the implant. It is generally believed that autogenous bone grafts are better than alloplasts; this is because of their osteoconductive and, more importantly, osteoinductive properties [4, 5]. Many sites exist from which to harvest bone and many techniques exist from which to do so. Herein, we present a new site and a novel technique for graft harvesting and restoring bone loss in implantology.

3.2. "Crescent graft" technique to manage bone loss after tooth extraction and immediate implant placement

When the clinical and radiographic examination of a tooth shows evidence of cortical bone loss, the patient may be a candidate for corrective bone grafting of the defect site after tooth extraction and immediate implant placement (**Figure 3**).

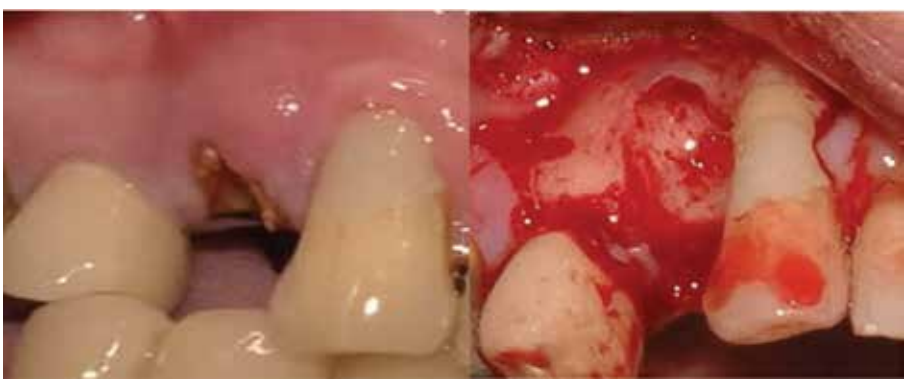

Figure 3. Patient requiring extraction of a hopeless "first" maxillary premolar. After the reflection of a mucoperiosteal trapezoid flap, a large cortical bone defect was seen.

After tooth extraction, the recipient site must be assessed and the amount of autogenous bone needed should be determined. Cross-sectional tomography or cone beam computerized tomography can be used to estimate the amount and thickness of available bone and the safest graft harvesting site.

3.3. Surgical technique

After local anesthesia and tooth extraction, a buccal mucoperiosteal flap is reflected. The defect is exposed and measured with a periodontal probe. The implant is inserted into the extraction socket. Then, the exposed implant surface area needing coverage is assessed; the volume of bone needed is reestimated (**Figure 4**).

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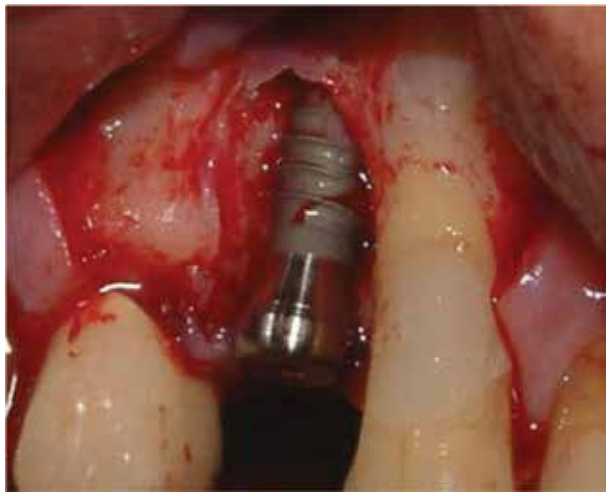

Figure 4. Implant inserted into fresh tooth socket.

The donor site and the size of the trephine bur are determined and a mucoperiosteal envelope flap in the palate is reflected. In our case, we used a trephine bur (5 mm in diameter); two overlapping insertions of the trephine are made parallel to the roots of the incisors and 2 to 4 mm away from them (**Figure 5**).

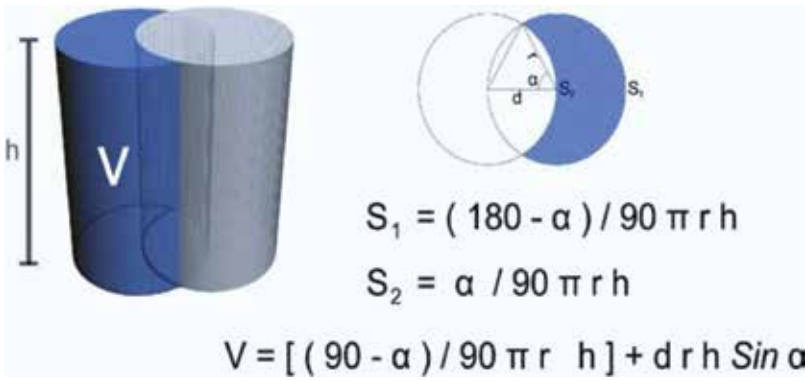

Figure 5. Two circles overlapping each other shape two crescents. S_1, area of outer surface of graft; S_2, area of implant facing surface of graft; V, volume of graft; h, depth of bur penetration; r, radius of trephine bur; d, intercentral distance; a, arcos (d/2r).

The trephine penetration depth is predetermined according to the sagittal tomogram. Extreme care should be taken not to penetrate the nasal floor by perforating the anterior palate. However, should this occur, it is not a problem because the palatal mucosa is intact and this precludes the formation of an oronasal fistula. It is essential to have a proper three-dimensional concept of the incisor roots to prevent iatrogenic damage [4]. A periodontal probe is used to determine the bur penetration depth during bone removal. Bone harvesting from the palate

produces two crescents, one of which is used in the procedure as a free graft with the concave inner side of the graft placed to cover the convex outer surface of the implant (**Figure 6**).

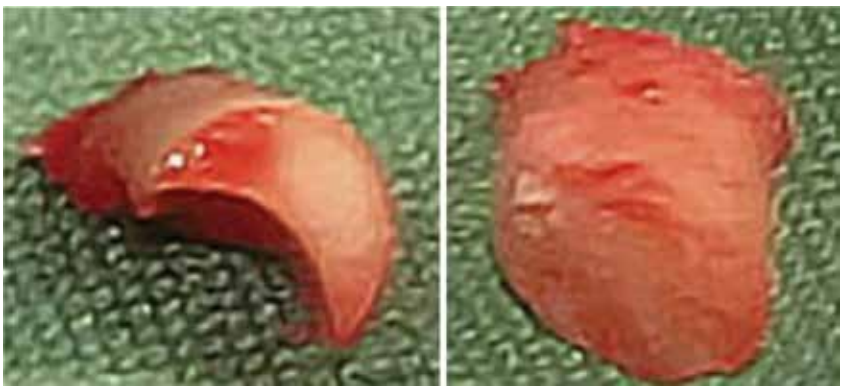

Figure 6. Two insertions of the trephine bur are done to harvest bone; two crescents are produced, one of which is used in the procedure as a free graft. The remaining harvested bone is blended and placed over the recipient site.

The crescent graft is placed into the recipient site (**Figure 7**). The remaining harvested bone is blended and placed over the recipient site.

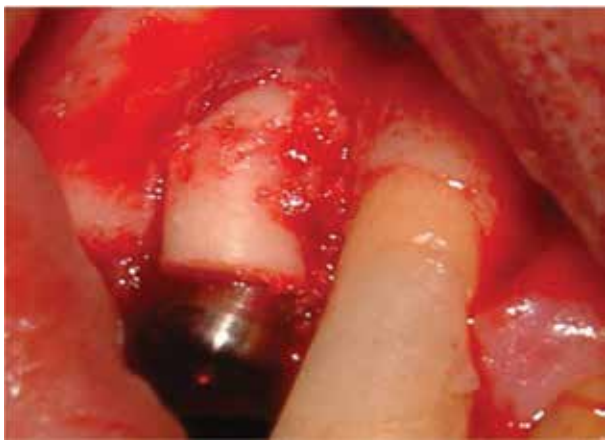

Figure 7. Crescent graft placed into the recipient site.

The small size of the graft precludes fixation with mini-screws. Therefore, a slot is made in the defect via a fissure bur, and the crescent graft is wedged into it. Then, the flap is repositioned and sutured. Postoperatively, the patient is prescribed antibiotics and instructed to use normal saline rinses the next day. The sutures are removed after 7 to 10 days. After 3 months, the cover screw is removed, and the abutment is placed and restored by the use of a cement-retained metal-ceramic crown. The patient is examined at 6 and 12 months after surgery. Vitality tests of the maxillary canines and incisors are performed to ensure vitality.

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3.4. Discussion

Dental implants can improve the quality of life, especially in edentulous patients [6]; however, implants are not without complications [4, 7, 8]. A common problem is bone loss or defects. Many studies have assessed the use of different grafts in such defects [9]. Several have shown advantages in using guided bone regeneration on autogenous grafts to avoid soft-tissue ingress [10–12]. Behneke et al. [13] advocated the use of autogenous bone grafts. Common sites in the jaws used as donor sites in autogenous harvesting procedures include the anterior border of the external oblique ridge, lingual exostosis, maxillary tuberosity, and the chin (**Figure 8**) [5, 14–16].

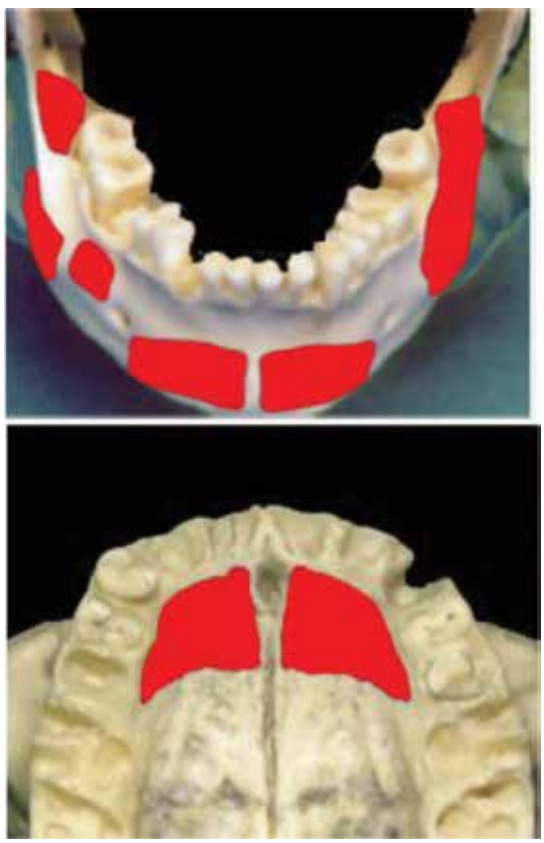

Figure 8. Intraoral donor sites.

The anatomic form of the donor site is as important as the bone quantity and quality [16]. Hassani et al. [17] first introduced the anterior palate of the maxilla as a quantitative donor site in cadavers. The bone is corticocancellous in nature despite its small volume. However, the curvature of the hard palate conforms conveniently to the implant. When two circles with equal radii cross each other in such a way that the perimeter of one circle crosses the center of the other, two crescents result. The use of a trephine bur to achieve this produces a favorably

shaped bone graft for implants. This design (the "crescent" graft) has a concave surface (cortex) that conforms nicely to the dental implant surface for coverage. Harvesting chin grafts should be done primarily in those presenting with an edentulous anterior mandible or a large chin protuberance with short roots of the anterior mandibular teeth [18]. Using a local donor site has the advantage of convenient surgical access, which means shorter duration of surgery and anesthesia [19, 20]. Bone harvesting can be performed in the office setting or at the hospital. The procedure is more cost-effective and is estimated to have less donor site morbidity than procedures involving extraoral approaches. Cross-sectional tomograms and lateral skull images can help prevent injury to the anterior maxillary teeth. The intramembranous origin of the harvested bone causes rapid vascularization and improves bone formation [17]. The bone harvested from the anterior palate has a corticocancellous nature. Revascularization occurs more rapidly with cancellous autografts than with cortical grafts. Cancellous autografts tend to be completely integrated with time, whereas cortical grafts tend to remain as admixtures of necrotic and viable bone [21, 22].

4. Sinus membrane repair: a novel technique to repair maxillary sinus membrane perforations during sinus lifting

4.1. Introduction

Boyne and James [23] first reported maxillary sinus lifting in an atrophic maxilla. Sinus lifting for implant placement has now become an established procedure in implantology. It is a predictable method used to augment bone in the posterior maxilla. Increased sinus lifting procedures and bone grafting for the implant placement in the posterior maxilla has in turn increased the complication rate. The most common complication in sinus lifting is the inadvertent perforation of the sinus membrane; if left untreated, it may result in the loss of graft material into the sinus cavity, infection, oroantral fistula, or impairment of the physiologic function of the antrum [24–27]. Fugazzotto and Vlassis [28] classified sinus membrane perforations or SMPs into three groups (class I, class II, and class III) based on their location [29, 30]. The most common location of perforation is the apical wall of the cavity (class I) followed by the mesial surface of the lateral wall (class II) and within the window extension (class III). SMPs are usually classified based on two factors, namely, perforation size and site. SMP has been reported to be as high as 58%, and it is more common in cases where the membrane is too thin or when septae are present [31, 32]. Thus, a method to manage this complication is warranted. We introduce a new, simple, feasible, and effective method to manage SMPs during sinus lifting.

4.2. Technique

Should inadvertent SMP occur after access to the maxillary antrum, the initial step is to evaluate the perforation size and determine whether biomaterials are necessary or not. After severe perforation (class I or II) of the sinus membrane (class II, mesial wall) during sinus lifting, if the quality of the sinus membrane is acceptable, first the membrane margins are gently

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released. For class II perforations or class I perforations in the apical wall, two holes are made 3 to 4 mm from one another using a fissure bur in the lateral wall near the access window. Next, a 4-0 absorbable suture with a round needle is passed through one of the cortical holes from the outer surface then into the antrum and then passed through 2 sites in the membrane (to reduce tension and prevent membrane tearing). The suture is then passed through the other hole, exiting from inside of the sinus outward; the knot is tied outside the antrum via a horizontal mattress technique; the sinus membrane abuts the bone as a result of the tension applied (**Figures 9** and **10**).

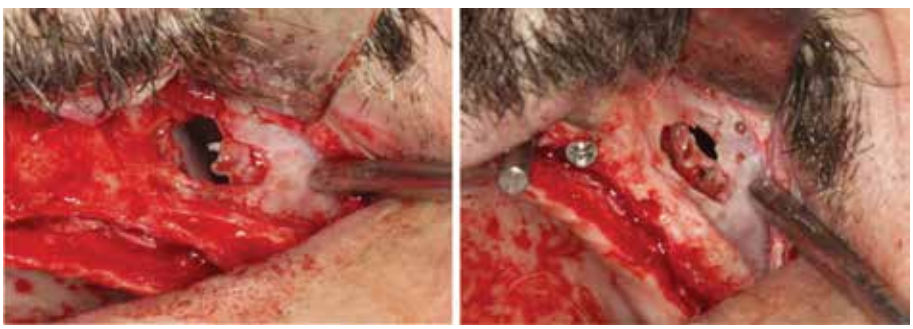

Figure 9. The sinus membrane is carefully released. Two holes are gently made 3–4 mm from one another using a fissure bur.

The perforation is closed in this manner; the integrity of the maxillary sinus floor is preserved, and the sinus lift procedure is resumed; bone grafting and the insertion of biomaterial under the sinus membrane can be done and implants may also be placed. For large perforations, it is prudent to place a membrane to ensure the closure and prevention of graft material from migrating into the sinus cavity. Alternatively, buccal fat can be used for perforation closure or as a barrier between the sinus membrane and the graft material. This fixation method can be used along with a variety of biomaterials.

4.3. Discussion

The growing popularity of implant treatment runs hand in hand with procedural complications. One example is SMP during sinus lifting in the atrophic posterior maxilla, complicating implant placement. In 1980, Boyne and James [23] performed the first sinus lift procedure. Since then, sinus lifting has been the treatment of choice for implant placement in an atrophic maxillary ridge. Like every other conventional treatment, sinus lifting has its inherent risks and complications. The most common potential complication of open sinus lift surgery is SMP intraoperatively, which if left untreated, may result in the leakage of graft material into the sinus, infection, oroantral fistula, and impairment of physiologic sinus function [24–27]. The risk of SMP has been reported to be as high as 58%, especially when the membrane is thin or when bone septae are present [31, 32]. The most common factor that can cause SMP is the use of excessive force upon elevation of the sinus membrane [33] or the inadequate reflection or release of the periphery [29]. Anatomic variations can also increase the risk of SMP [30]. These

anatomic variations associated with the risk of SMP are as follows: thin sinus membrane (28%), presence of septae (22%), membrane adhesion (17%), previous surgery (17%), presence of scar tissue(11%), and presence of cysts (5%) [11].

4.4. Repair

In SMPs smaller than 5 mm, the perforation can usually be closed by applying a direct suture, covering it with a collagen membrane or fibrin tissue sealant [34–36]. Larger perforations require application of other techniques. Various methods have been used [35–40]. Some recommend to abort the procedure and postpone it for 6 to 9 months to let the membrane heal [41]. In contrast, others believe that the perforation can be managed efficiently using biomaterials and grafts placed at the same time of repair [42]. Shin and Sohn [43] repaired SMPs using fibrin adhesive and implant placement. These were only for small perforations and not medium or large perforations. Pikos [27] offered a method for the repair of sinus perforations. He created four notches in four corners of the membrane, adapted it to the cavity, and used a tack to stabilize it. Testori et al. [32] introduced a method for repair of large SMPs. They used a few stitches on the sinus wall and created a strut for placement. However, a membrane was not attached to these sutures, and the stitches only worked as a strut. In general, suturing the two edges of the perforated membrane inside the sinus or keeping them close to each other for use of fibrin adhesive is not an easy task. In contrast, fixing the perforated membrane to the bone is simple.

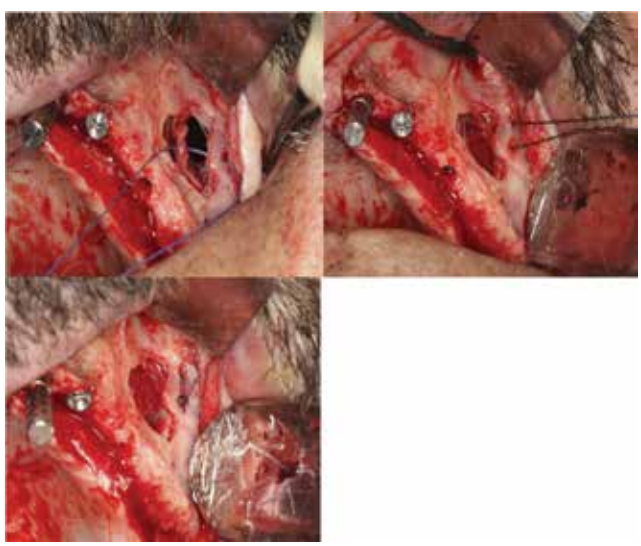

Figure 10. The suture enters through the first hole from the outside, towards the inside of the cavity and traverses the sinus membrane. The suture exits through the second hole. After tension is applied, the membrane is pulled adjacent to the bone.

The suture is tied and the knot is tightened on the external sinus wall. The perforation is completely closed. The perforated membrane will be fixed to the bony sinus wall. In our study,

14 patients in whom perforations of maxillary sinus membrane developed and who were treated using our technique were assessed; perforations developed after sinus lifting in 10 patients, after the removal of impactions in 3 patients, and after cyst removal in 1 patient. There were six perforation sites on the apical part of the window (class I), six on the lateral part (class II), and two within the window extension (class III). Patients were followed for an average of 13.7 months (range, 12–18 months). All were treated and complications were minor.

5. Conclusion

Our technique is an easy, feasible, and predictable technique that helps the surgeon easily manage SMP during sinus lifting. Other operations not related to implant placement might also be associated with this complication. In such situations, it is necessary to use a simple applicable method for management. Using the double-hole bone fixation technique allows for safe repair.

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Chapter 14

State-of-the-Art Immediate Implant Therapy

Peter R. Hunt and Laura M. Ceccacci

Additional information is available at the end of the chapter

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Abstract

Implantology is the newest major branch of dentistry and one that is rapidly becoming more and more important. A subject that was ridiculed 40 years ago is now transforming dentistry. Implantology gives hope for the end-stage edentulous patient unable to wear dentures. It enables those facing loss of a tooth to avoid bridgework or removable partial dentures. It is often simpler, faster, and far more effective over the long term to replace a failing tooth with an implant with a restoration than to do a root canal, post-core, and crown. This chapter discusses immediate implant therapy, which greatly reduces surgical interventions and shortens total treatment time, while preserving the alveolar structures which are rapidly lost when a tooth is extracted.

Keywords: immediate implant therapy, socket regeneration with implants, single-stage implant surgery, immediate placement, immediate loading

1. Introduction

Traditionally, implants have been placed into healed ridges where the teeth had been removed from a previous procedure. For an edentulous patient there was no other option, but to remove the teeth quickly before placing implants, which became a standard. The traditional protocol was then to reflect a soft tissue flap, to prepare a channel in the bone, to place the implant with a cover screw, and then to cover the soft tissue flap back over the region for a period of three to six months. At that time, another soft tissue flap was raised and a connection made to bring the implant transgingivally so that it could be brought into function. This meant the patient was subject to three surgical interventions: the extraction, the implant placement, and the second-stage exposure. With healing cycles in place, therapy from extraction to second-stage exposure and final restoration could take a year or more to complete.

Although this protocol can ensure a stable and functioning implant, it has some unfortunate sequelae. Most obvious are the time, expense, and discomfort for the patient associated with the three surgical procedures. Only recently have we started to appreciate that there is another, more significant issue with this three-stage protocol. This is the significant loss of alveolar bone and the periodontal soft-tissue complex in the region of the extraction. This can be extremely difficult to correct with augmentation procedures. Aesthetic and functional deformities remain. Immediate implant therapy can reduce the number of surgical procedures and expedite therapy, while at the same time minimizing the loss of alveolar and gingival structures, thus reducing aesthetic and functional deformities.

2. Post-extraction course

2.1. Ridge collapse

When a tooth is removed, the hard and soft tissue complex surrounding the tooth undergoes a series of changes. The soft tissues immediately collapse down, having lost the support from the tooth (**Figure 1**).

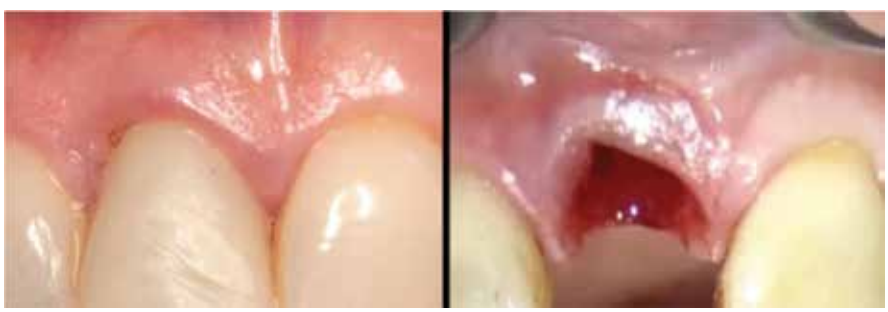

Figure 1. As soon as the right central incisor is removed, the soft-tissue complex starts to collapse.

Bleeding into the socket rapidly turns to a blood clot. Very quickly epithelium starts to migrate over the top of the blood clot. By this time blood vessels have invaded the blood clot and stem cells are proliferating, differentiating, and maturing. The region becomes progressively organized so that connective tissue and then bone start forming (**Figure 2**).

In time, there are major changes in the soft tissue covering the ridge. After the ridge epithelializes over, the new "Ridge" gingiva blends with the remnants of the original marginal attached gingiva. This lasts for a relatively short time because the region of attached gingiva starts to shrink, sometimes so much that only a very narrow band of attached gingiva remains on the alveolar crest (**Figure 3**).

As time passes, the bone in the crestal region shrinks, more so on the labial than on the lingual. The ridge height diminishes and the overall bone volume decreases. The tough cortical bone thins and the medullary bone starts to atrophy as there is less function with the teeth missing.

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The more time that passes, then the more bone loss that is likely to occur [1–3]. All these factors suggest that it would be better to do everything possible to stop the shrinkage process starting when the tooth is removed. Immediate interceptive therapy is required.

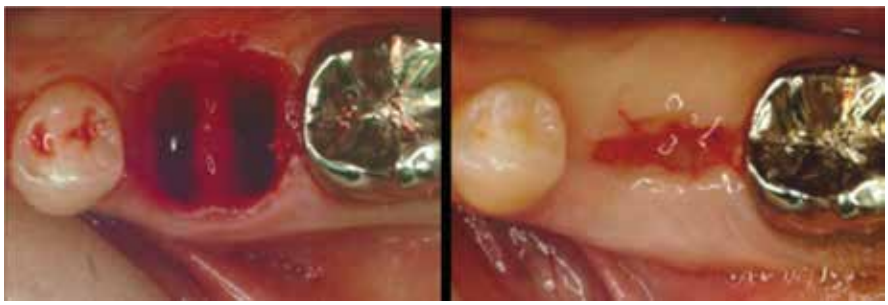

Figure 2. Left: The first molar has just been removed. Right: One month later.

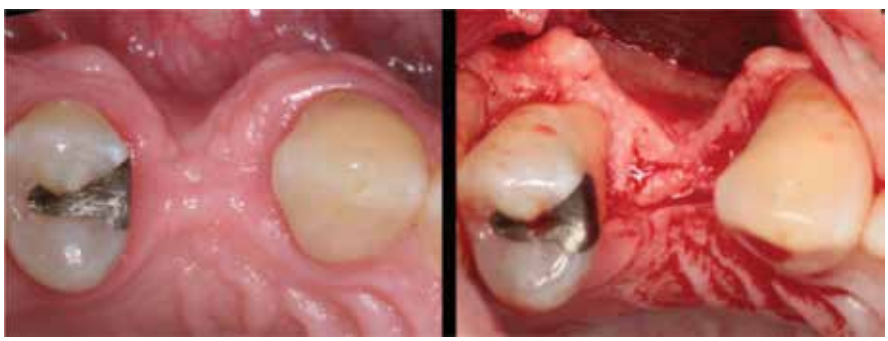

Figure 3. In this case, following the loss of the premolar, both the attached gingiva and the alveolar bone shrunk down extensively.

3. Requirements for immediate implant placement

3.1. Successful removal of the tooth

Immediate placement is precluded upon careful removal of teeth. The prime aim is to leave a socket with intact bone walls with sufficient residual bone to stabilize an implant. Unfortunately, this is one of the major uncertainties in the whole protocol, because some teeth can be extremely resistant to removal, others can fracture readily. If not careful, the bone housing for the tooth can easily be lost in the tooth removal process. For these reasons, it is quite standard to split multi-rooted teeth into their individual roots. Each root can then be removed individually. Removing labial bone to get at decayed or fractured off at the gum level teeth is generally quite harmful as this reduces the height of the residual socket. Instead, periotomes are better

used for loosening and elevating the roots. Ultrasonic periotome tips are particularly useful to expedite root removal (**Figure 4**).

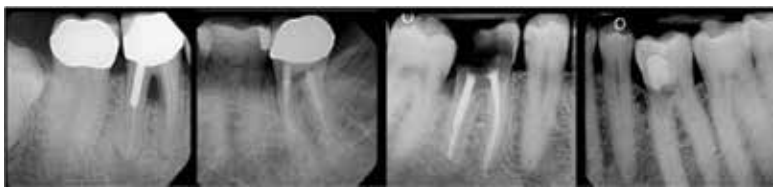

Figure 4. Teeth difficult to remove. Left: Large post in distal root with bulbous root end. Left Center: Long, thin deep roots. Right Center: Deep decay, poor tooth structure, large root canal fillings. Right: External resorption, very deep roots, proximity to neighboring tooth.

3.2. Removal of infection and granulation tissues in the region

Once the tooth has been removed from the socket, it is critical to remove three tissues from the socket: Remnants of the gingival complex, deeper granulomas, and periapical lesions.

3.2.1. Remnants of the gingival complex

Where the teeth have been periodontally involved it may take some time to work around the socket to remove any soft tissue remnants with curettes and excavators. In some sockets, there may be infected epithelial remnants which pass down quite deep. These need to be removed so that they are not taken down deeper into the region when an implant is placed. Both infections and epithelial down-growths are both associated with loss of osseointegration; removing them allows for successful implant therapy (**Figure 5**) [4].

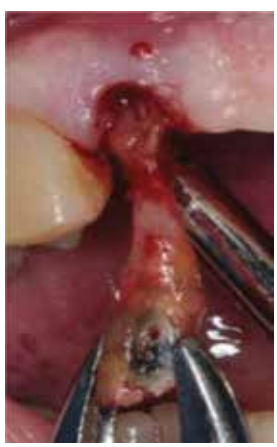

Figure 5. When this tooth was being removed, a considerable amount of epithelial remnants and connective tissue granulations came out with it. Granulations can often be more extensive than expected. They take time and considerable effort to remove.

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3.2.2. Deeper granulomas

More difficult to remove are deeper granulomas residing between roots. These can be of periodontal or endodontic origin. It is necessary to work around and under the granuloma with spoon excavators. Once they have been separated then they can be lifted up and out of the socket. Ultrasonic debridement and/or de-granulation with rough-cut burs can speed the process (**Figure 6**).

Figure 6. This molar has obvious trifurcation involvements and periapical infection. With the tooth removed, the granulations are apparent, considerably more than expected. When cleaned out, a large sinus perforation to the distal was apparent. There was no ability to stabilize an implant, so the procedure was changed to a "Socket Regeneration" procedure.

3.2.3. Periapical endodontic lesions

The most difficult region to remove residual infection from is the apical region. Sometimes an apical granuloma will come out with the root and this is always good to see. There are other times where it may be necessary to open up the apical region beneath the root space or to access the lesion from a lateral approach. No matter what, it is critical to do this de-granulation for an implant placed in the region to be successful (**Figure 7**).

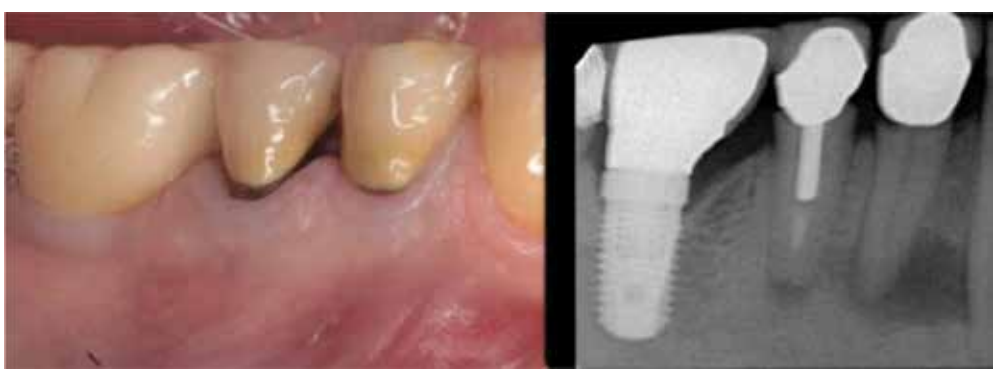

Figure 7. Both these premolars have apical infections and may break off at the gum level because of marginal decay. A procedure is needed to remove the teeth, debride the region and place implants. See **Figures 35** and **36** for treatment.

4. Ability to position and stabilize an implant in the remaining bone volume

Once the tooth has been removed and the region de-granulated, attention must turn to positioning and stabilizing an implant correctly. There are two different and sometimes incompatible considerations.

4.1. Implant positioning

These days it is the abutment which produces the desired emergence form as it exits the soft tissue collar. An implant platform is round but the form of a tooth as it emerges from the gingiva is highly variable. So the abutment that starts out round at the implant platform needs some vertical height, thickness of gingiva or "running room" to change to the desired form as it exits the gingiva. This implies two things: first, positioning the implant platform is critical, as it needs to serve as the base for the abutment; second, the angle of the implant, the diameter of the implant, and the length of the implant are less critical (**Figure 8**).

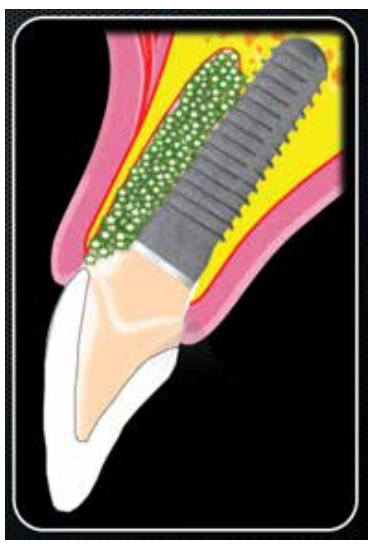

Figure 8. Modern implant environment principles.

Implant: oriented into palatal bone wall to gain stability.

Platform Placement: deeper to allow room for Emergence Profile Development

Augmentation: to fill out the residual socket, preserve labial bone wall, and prevent resorption

Abutment: to develop the desired "Tooth Form" and to support hard and soft tissue contours

Positioning an implant into a healed bony ridge is in many respects simpler than placing one into an extraction socket for several reasons.

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4.1.1. The original socket may divert drills and take them off course

This is most common in multi-rooted sockets where the central core of bone can be very hard and it can be very difficult to establish a starting point for a pilot drill. The drill tends to be diverted down and into one of the root spaces (**Figure 9**).

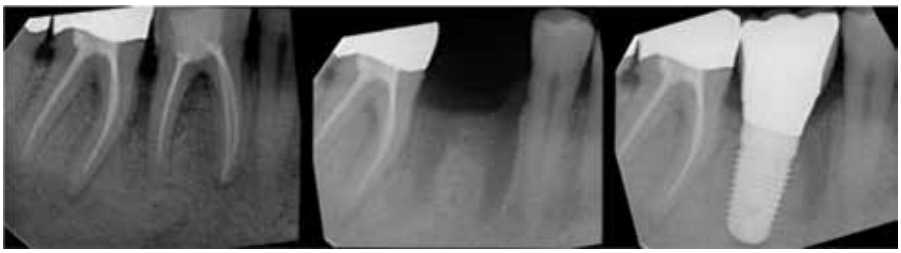

Figure 9. This vertically fractured molar was removed. Instead of the channel being established centrally in the furca region, it was diverted down the distal root space. A custom abutment was needed to manage the situation.

4.1.2. The original socket is not where implant support is available

A common example of this is in the maxillary anterior region where it is not a good idea to place an implant down the socket as this will mean that the implant gets placed too labial. This jeopardizes the thin labial bone wall of the socket. It is better to intentionally angle the implant into the palatal wall of the socket to gain the desired stability and position (**Figure 10**).

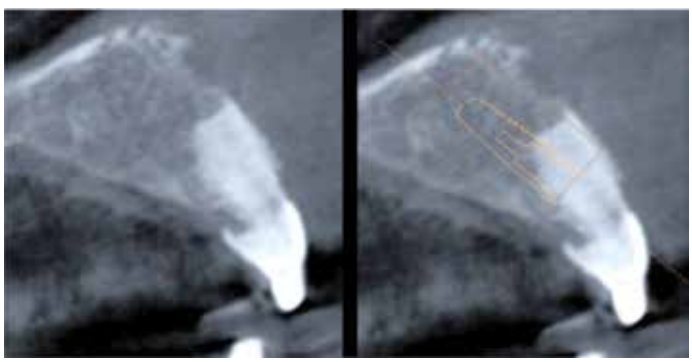

Figure 10. This central incisor needs replacing. The labial bone wall is very thin. The implant needs to be set into the palatal bone wall. The proposed position is outlined.

4.1.3. The original position of the tooth may not be the best position for an implant

The tooth may have an original malocclusion or have drifted, rotated, or changed position as part of a mesial drifting or bite collapse process. This can mean that it would be better to have the implant in a slightly different position (**Figure 11**).

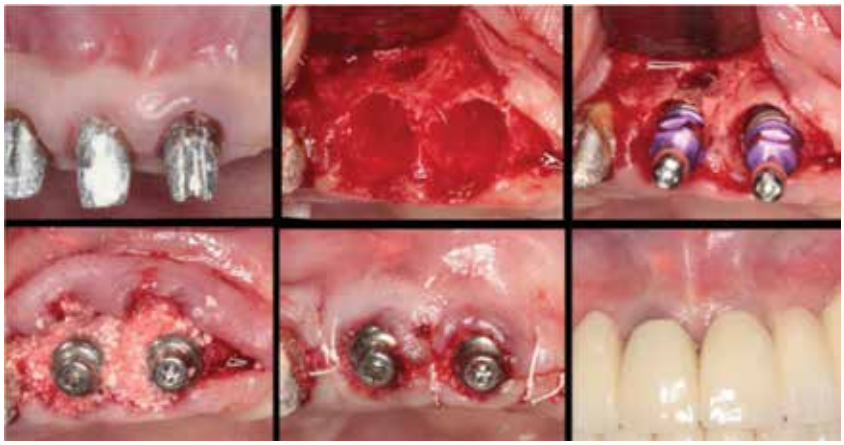

Figure 11. This case shows failing incisor teeth. These were extracted and immediately replaced with Camlog® implants and gingivaformers. Notice how the implants were moved laterally in the sockets to improve the midline of the final case.

4.2. Stabilizing regions

The ability to gain stability for a dental implant in extraction sockets very much depends on the form of the socket. The bone walls in a socket are generally quite firm and stable, so a small amount of bone can provide adequate stability for an implant. Of course, if immediate loading is required at the same time then a much higher level of stability is required [5, 6].

The region providing stabilization for an implant within a recent extraction socket can be quite limited and requires careful planning. Most times the socket will be larger than the implant. Often the only place where the implant engages the bone is in the apical region where the bone walls converge. However, one must be careful because all too often the socket is compromised in one way or another. For example, many sockets have little or no labial bone and this means that the implant needs to be positioned more centrally within the available bone complex. In socket management, it is always necessary to appreciate how the socket is liable to heal, both with or without an implant.

Sometimes, particularly in the molar regions, there is no obvious place for stabilizing an implant in the former socket. If bone is available beyond the residual socket, it may be possible to use as little as 2–3 mm to stabilize the implant. In the mandible, it is necessary to carefully check the location of the mandibular nerve as this may prevent this "Going beyond the socket" procedure. All that is needed is to make sure that the implant is stable. Obviously, it will not be possible to immediately load the implant with this limited amount of stabilization (**Figure 12**).

In the maxilla, it may be necessary to perform an intentional sinus lift to gain stability for the implant. The bone of the sinus floor, though it may be thin, is generally very stable. All that is necessary is to penetrate the floor in a safe way, such as with an ultrasonic device. The hole is

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then expanded with a hand-held osteotome. The final diameter of the channel should be matched to the apical diameter of the tapered implant that will be placed.

The sinus floor membrane is lifted with the osteotome. Bone graft is then placed and taken up into the sinus with the osteotome. A tapered, screw-threaded implant is placed into the channel. As it is screwed to place, the implant will gain increasing stability as the wider part of the implant gains traction. The sinus-lifted portion will also provide enhanced long-term stability (**Figure 13**).

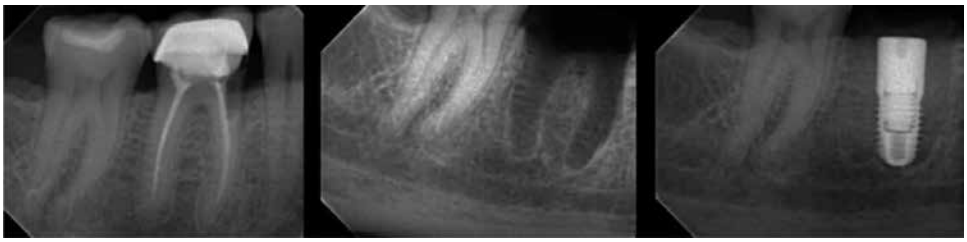

Figure 12. It would not have been sensible to take the channel deeper to gain stability because of the proximity of the nerve. Instead, the Pilot Drill was angled down the mesial root space, and then the channel was uprighted and expanded with progressively larger drills. The final implant placement was nicely centered and the implant was stable.

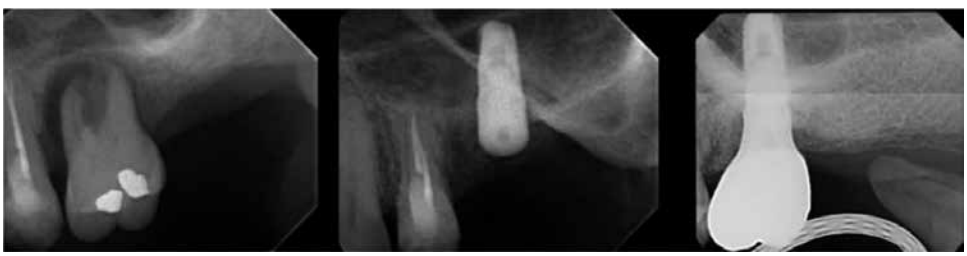

Figure 13. There was nothing much holding this molar in place. It was removed, the region debrided, and an intentional sinus lift performed to gain additional bone volume to stabilize an implant, so gaining additional support. Both the sinus region and the residual socket were grafted. Both regions healed to provide adequate support for the implant and restoration.

5. Provision of an osseous coagulum surrounding the implant

If an implant is adequately stabilized in a fresh socket, then much of the implant surface is liable to be exposed to the oral environment, allowing it to become contaminated; the result is that the implant will fail to osseointegrate. Instead of just leaving a blood clot around the implant, most operators feel more comfortable with filling the voids between the implant and the bony walls of the socket with a bone graft; this not only helps with implant osseointegration but also helps in preventing ridge collapse [7]. The term "Osseous Coagulum" implies supplying all the components which surround and protect the implant following placement.

These help stabilize the blood clot and allow a secure environment for it to develop stem cells, to re-organize, develop osteoblasts, and develop native bone ready to osseointegrate to the implant.

Certain types of bone graft, the slow-resorption materials, have been shown to resist or slow down the ridge resorption process which starts as soon as a tooth is removed [7–9]. At the same time, they encourage new bone to develop. The two aspects are synergistic. They help each other, so the term "osseous coagulum" implies a region which will in time become bone.

New bone formation occurs most predictably within the four walls of a socket. This is why everything possible is done to preserve the four walls of a socket during tooth removal and why the implant platform is placed down below the bone crest. If one bone wall is missing, then a membrane is always placed to provide the environment for its regeneration (**Figure 14**).

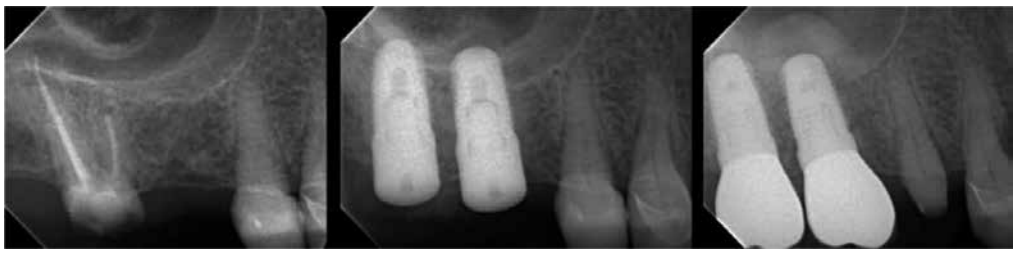

Figure 14. In this case an Osseous Coagulum Zone was needed in the region of the extracted roots of the second molar and also in the sinus lift region for the first molar implant. This was all managed in one surgical procedure when the second molar was extracted.

6. Wound closure

Closing the wound is the last part of the procedure. The aim is to protect the implant within the osseous coagulum, contain the graft materials, prevent early contamination and infection, stabilize the blood clot, and prevent bleeding. It is not just a matter of flap closure. One also has to consider the devices used to cover the implant including cover screws, extended height healing caps, and abutments of one form or another. Each of these components has a specific indication.

6.1. Component options

6.1.1. Cover screw

Cover screws are flat, low-profile devices often supplied with the implant. These are mostly used in traditional therapy where primary closure of the flaps over the region containing the new implant is desired (**Figure 15**).

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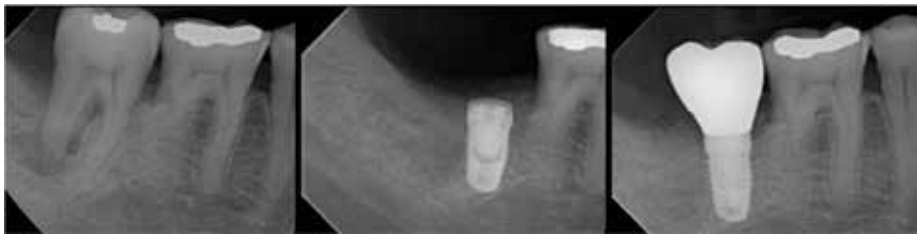

Figure 15. This case had a large periodontal defect with complete involvement of the distal root. The tooth was extracted, the region debrided and an implant with a cover screw placed at the same time. The deficient region in the distal root region was augmented with Bio-Oss Collagen® (Geistlich). There was primary closure over the implant. The region recovered and was restored with a custom abutment and final crown.

6.1.2. Gingivaformer

Gingivaformers come in various heights and configurations. Traditionally they have been placed at second-stage implant exposure surgery to form a trans-gingival passage into the mouth. These days they are often placed at the time of implant placement, with flaps being brought up around the outside of the gingivaformer (**Figure 16**).

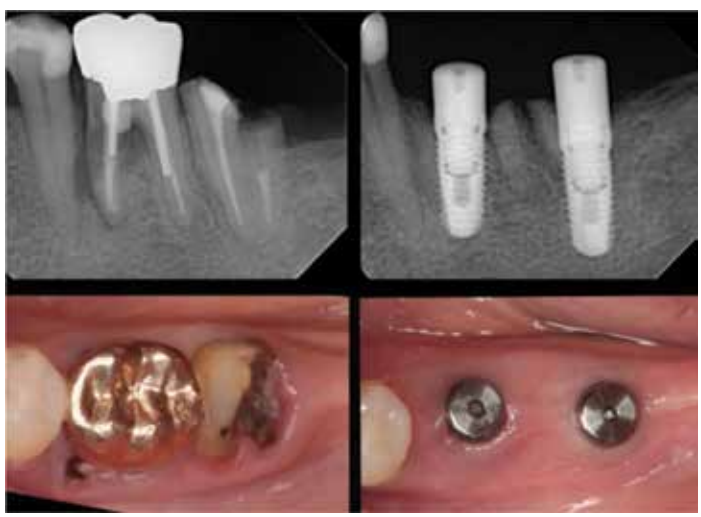

Figure 16. Left: Two failing molars. They were removed and immediately replaced with implants and hard- and soft-tissue augmentation. Right: Three months later, healing is evident. The case is now ready for restoration.

6.1.3. Abutment

Abutments provide an emergence and form which is more tooth-shaped. They also carry a restorative post, so these devices are used for immediate implant placement where immediate loading and a provisional restoration are required. Custom zirconia sleeves secured to a Ti-CAD base devices are generally more useful than off-the-shelf components because they allow

for custom form, good gingival reaction, and tooth-like color. Zirconia has better gingival adhesion than Titanium or PEEK plastic components. We use them for both temporary and final restorations (**Figure 17**).

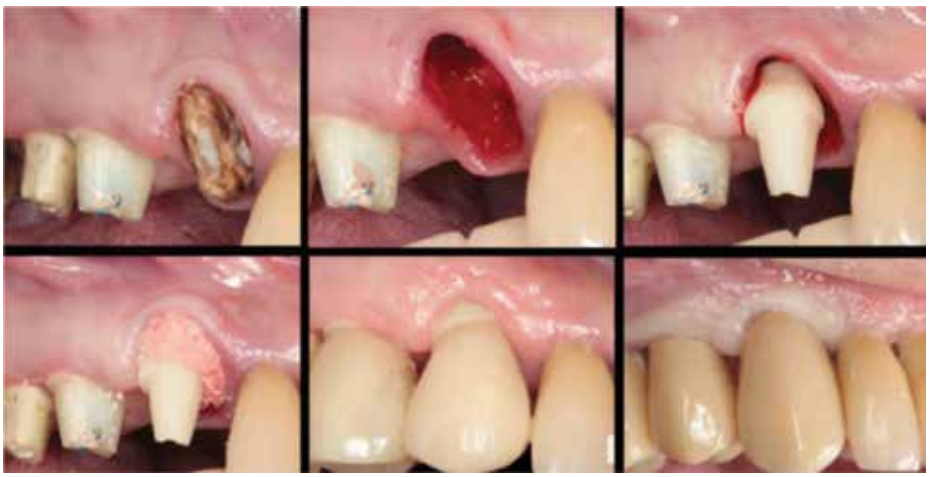

Figure 17. In this case, when the tooth was extracted, an implant was placed which supported a provisional abutment. Graft material was placed around the abutment to fill the channel defects. Despite the exposed graft material which was stabilized by cyanoacrylate (not shown), the wound healed-over fast and at one month appears very normal. Notice how the gingival margin healed well up on the abutment. The final implant-supported restoration improved the form and appearance of the original tooth.

6.2. Soft tissue closure

6.2.1. Primary closure

Traditionally, implant placement has been done by raising soft tissue flaps in the region adjacent to the implant site to allow access to prepare the bone channel and to place the implant(s). At the end of the procedure, the soft tissue flaps were closed back over the wound with what is called Primary Closure. With immediate placement of implants into extraction sockets, getting primary closure is more complex. To accomplish this, it is necessary to raise flaps and advance them to cover over the socket. The bigger the socket the more difficult it is to close over. If bone and soft tissue augmentation has been done, then more bulk has been added to the region, and this can increase the problems of getting closure. Finally, swelling and hematoma formation can make obtaining and maintaining primary closure still more difficult. The traditional solution to this problem is to make the flaps more mobile by raising them further and by severing the periosteum under the free mucosal part of the flap. However, this has the effect of moving attached gingiva from the sides of the socket to the top of the socket. There's no real problem with that in the short term, but in the long term it's essential to have attached gingiva attached to the alveolar bone outside and around an implant. It means

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an additional surgical procedure is needed not only to place a trans-gingival component, but also to raise the attached gingiva in the region and to displace it out and around the gingivaformer.

However, unless large-scale augmentation is being used, or the patient has a predisposition to implant failure, then primary closure is not required. Partial closure is quite adequate in most situations.

6.2.2. Partial closure

"Partial closure" is where the flaps are brought up around a gingivaformer or abutment placed in the implant, instead of a cover screw. This has several advantages. The surgical procedure is less invasive and it makes for a "single-stage" procedure. This is where there is no need for a secondary implant exposure procedure. It means that the overall treatment time is reduced by several months. The soft tissue complex is also more mature and stable than would be normal in a traditional two-stage procedure. It is easy to provide augmentation under the flaps, with bone graft and thickness increasing membranes, thus increasing the gingival thickness and providing a "safety zone" to protect the rough surface of the implant from becoming contaminated at an early stage. Finally, it means that attached gingiva surrounds the gingivaformer or abutment and this provides better protection for the implant and a more "Natural" appearance as the implant restorative component emerges through the gingiva. We tend to add a collagen-based bone graft at the base of the gingivaformer to fill any channel defects that may be present between the implant and the inner walls of an extraction socket. This is heaped up to increase gingival thickness. This provides a "safety zone" to protect the rough surface of the implant from becoming contaminated and infected at the outset (**Figure 18**).

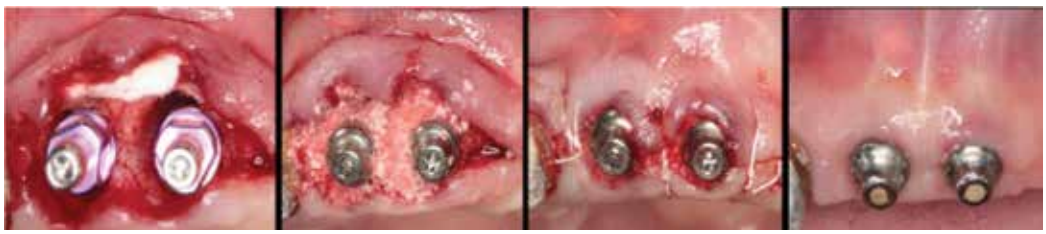

Figure 18. These front teeth were failing, so they were removed. Camlog® implants and gingivaformers were placed. The region was augmented with Mucograft® and Bio-Oss Collagen® (Geistlich) and the flaps were approximated. Healing proceeded nicely and a good final outcome was obtained.

6.2.3. Membrane closure

It is useful to think of ways which avoid extensive soft tissue mobilization and primary closure, one which leaves the attached gingiva where it is, or increases and thickens it. The trend is to use membranes of one form or another to cover the socket, the implant, the gingivaformer, and the bone graft within the osseous coagulum and the whole area.

Essentially, this is taking up the well-established principles of "socket regeneration" [7–9]. This is where extraction sockets are filled with bone graft of one form or another, and then covered over with various membranes. These range from Teflon-based plastic membrane, to collagen membranes to artificial membranes derived from polylactic acid or biodegradable co-polymers. Most of these seem to work quite satisfactorily, although as healing occurs, some shrinkage of the complex can be anticipated. The key is to get "wall-to-wall" regeneration within the socket. The membrane has several functions. First, it stabilizes the blood clot and bone graft mixture which enables it to consolidate, start healing, and become organized. With some membranes such as collagen membranes, the membrane material becomes partly or completely incorporated into the blood clot. The region soon becomes epithelialized. In others, such as the Teflon membranes, epithelialization starts to occur underneath the membrane. The individual processes do not matter too much as all the membranes serve to protect the healing wound and to reduce the potential for trauma, contamination, and infection. By about three weeks, the region is able to manage on its own because it is covered by epithelium with connective tissue immediately underneath. In short, it is not essential for complete primary closure of soft tissue flaps over a socket regeneration site. Instead, it is possible to achieve wound closure, implant osseointegration, bone regeneration, and good soft tissue healing by using artificial membrane; all the more reason to use these proven socket regeneration techniques to provide protection in a healing socket which contains a newly placed implant. Another benefit is with the implant there will be less shrinkage of the complex. A 4.0 mm height gingivaformer is generally placed into the implant instead of a cover screw and this helps "tent up" and stabilize the region. Bone graft generally fills up to and slightly over the top of the gingivaformer, and then the membrane covers the whole region.

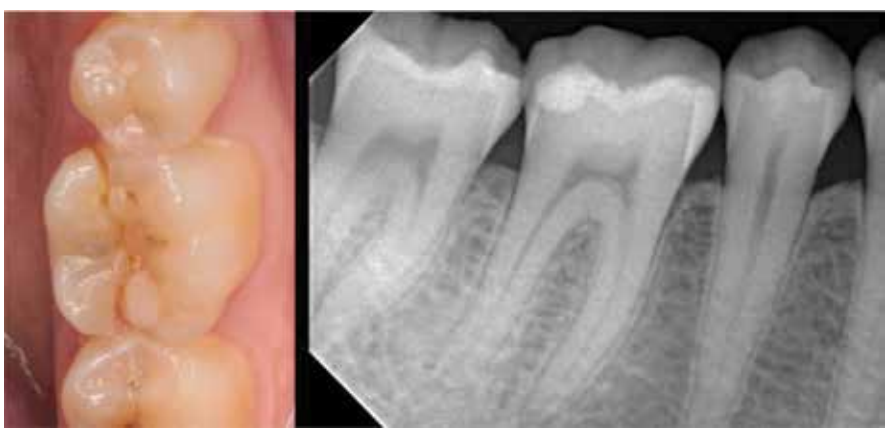

Figure 19. This mandibular first molar is vertically fractured and the crack extended sub-osseously.

As healing progresses there is some shrinkage. The top of the gingivaformer generally becomes exposed and at the appropriate time, it can easily be removed for impression taking. Emergence profile development and placement of a final abutment and restoration are then routine (**Figures 19–21**).

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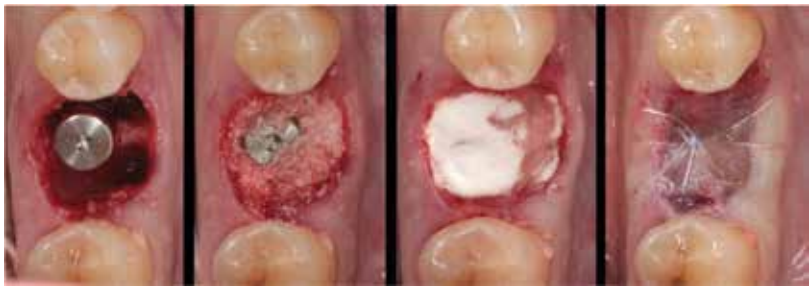

Figure 20. The tooth was removed and a Camlog® implant and gingivaformer placed. Bio-Oss Collagen® was placed down and around the implant. A Mucograft® membrane was placed over and the region sutured and sealed with Tissue Glue.

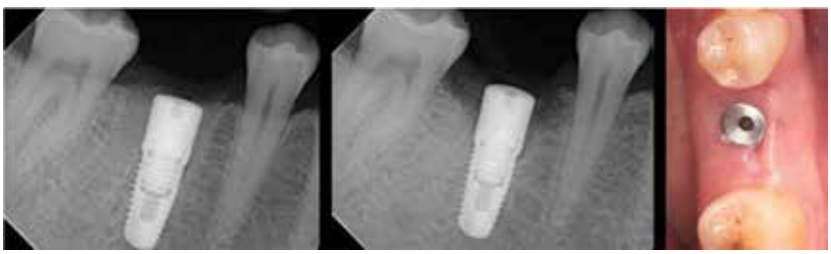

Figure 21. The radiograph on the left was taken immediately following the procedure. The one alongside was taken 3 months later as was the photograph. The case is now ready for a final restoration.

7. Regional considerations

7.1. Maxillary anteriors

Maxillary anterior teeth immediate replacement is very demanding. It can be very difficult to provide a final result where it is hard to know if a crown is implant-supported or tooth-supported. All too often, the give-away is that the implant-supported unit has recession of the interproximal papillae and labial gingival margin. This can be very difficult to reverse surgically. The obvious way to approach these situations is to be prepared for an immediate implant replacement and to make sure that the original hard and soft tissues in the region are maintained.

It's critical not to place the implant directly down the extraction socket as this will lead to the implant being set far too labial, leading to greater recession of the labial bone and soft tissue complex [9–14]. What is needed instead is to reinforce and regenerate the labial plate of bone. This is done by generating an osseous coagulum by placing a slow-resorbing bone graft between the labial bone and the implant. This allows adequate time for native bone to grow into the region. Instead of stabilizing the implant into the bone at the apex of the socket, the

implant needs to be stabilized into the palatal bone wall. This requires an abutment which can be angled towards the palatal which means the screw access channel will come out labially. To manage, this requires a separate abutment with an angle change and a separate crown. To facilitate the desired abutment form and angle change, it is necessary to set the implant platform quite deep within the bone complex. The case shown below illustrates all of these considerations (**Figures 22–28**).

Figure 22. The patient had the misfortune to have a crown on a maxillary central incisor fracture off while she was under anesthesia for a minor surgical procedure.

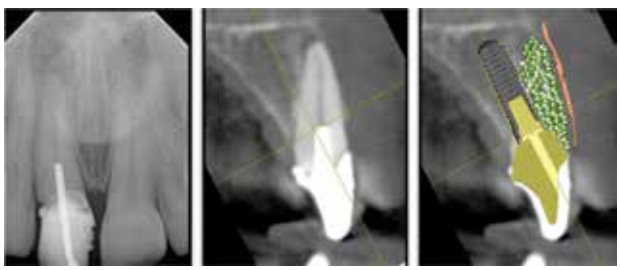

Figure 23. The cross-sectional CBCT cut showed that the tooth had little or no labial bone plate, but that there was a good volume of stable bone in the palatal wall of the socket. The principle of the procedure then is to anchor an implant into this palatal wall. The empty bone socket then needed to be filled with a bone graft and the outer wall of the socket needed to be protected with a membrane.

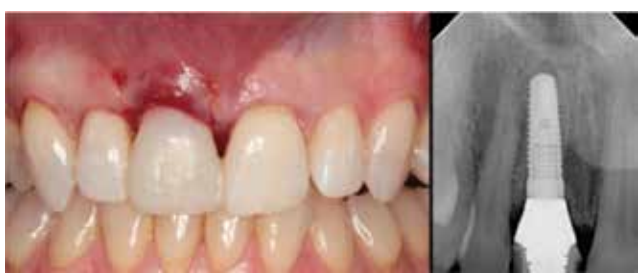

Figure 24. Here was the situation immediately following the procedure. An implant has been placed, all the augmentation materials are present and a temporary abutment with a provisional crown has been secured. It is screw-retained.

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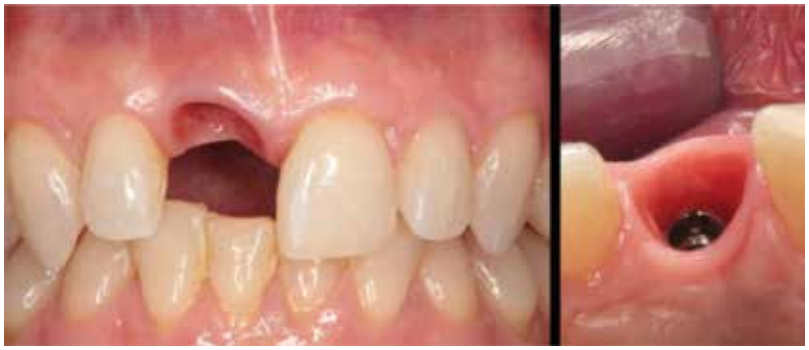

Figure 25. Four months later when the temporary abutment and crown are removed, the region looks very healthy. Notice the well-keratinized sulcus and freedom from inflammation.

Figure 26. Now the final abutment is placed. This is a custom Zirconia sleeve secured onto a Titanium Base CAD-CAM component.

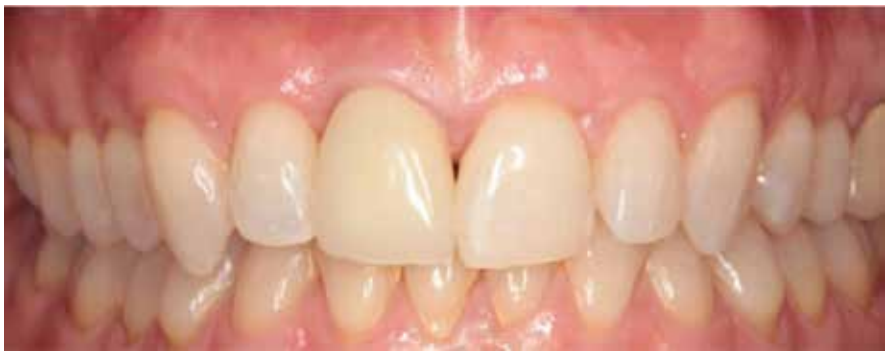

Figure 27. The final result.

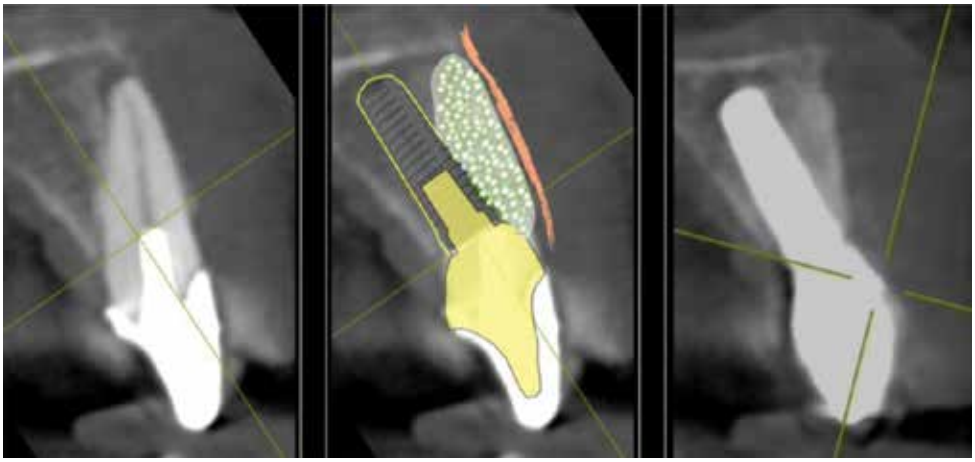

Figure 28. On the right is a cross-sectional CBCT slice taken 6 months following treatment showing that the labial region is stable and has filled in nicely.

7.2. Mandibular anteriors

The guidelines for mandibular anterior replacements are completely different from those of the maxillary anteriors. The situation can be much more variable and requires very careful analysis. The essential thing to appreciate is that one has to be very careful to make sure there is adequate bone volume within which to place an implant. The case which follows is a good illustration of some of the problems that can occur (**Figures 29–32**).

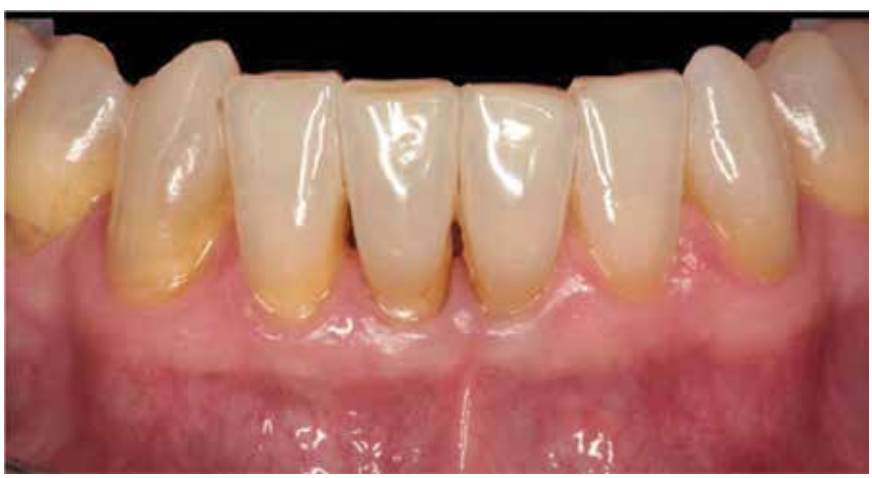

Figure 29. These lower anterior teeth seem almost perfect. On a routine examination the general dentist noticed there was a radiographic defect in the root canal chamber of the right central incisor. He referred the case to an endodontist for evaluation who diagnosed an external resorption of the tooth. He declined to treat the case and recommended an implant consult.

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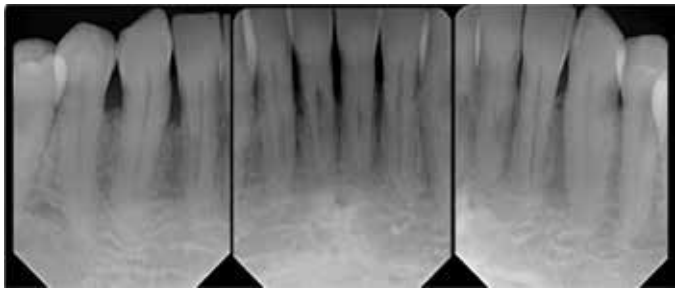

Figure 30. The patient came to see us. We took a CBCT and in the cross-sections it was obvious that the two central incisors had minimal supporting bone on the lingual and very little on the labial aspect.

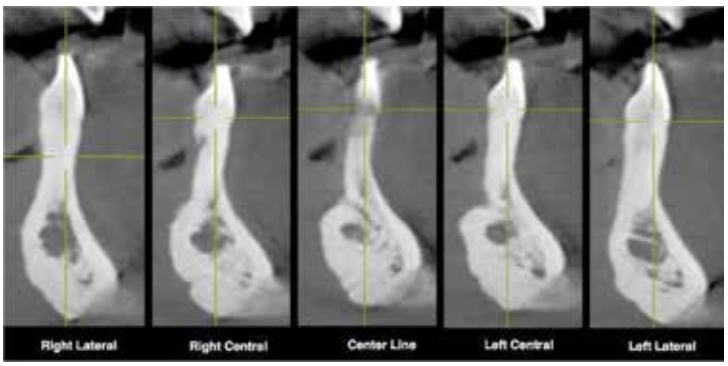

Figure 31. In addition in the midline, there was a very strange invagination of the bone structure. In short, this was not a suitable place for an implant.

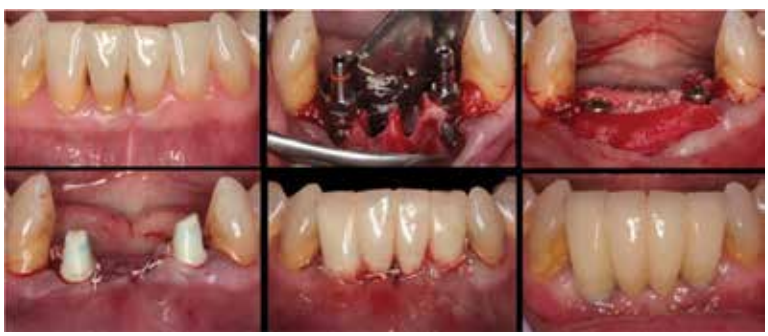

Figure 32. Two implants were placed in the lateral incisor regions, with extensive regional augmentation. An immediate provisional restoration was placed at the same time. After healing, for 6 months a final restoration was able to be constructed by the referring dentist, Dr. Peter Flaherty, Devon, PA.

One last point, the mandibular anterior region is the only region of the mouth where the bone width can decrease from the crest to the apical region. Although there may appear to be ample

bone at the crest it can be relatively easy to perforate out of the bone during the channel preparation and implant insertion. Usually the perforation is out to the labial.

7.3. Maxillary premolars

Maxillary premolars can be quite difficult to replace with implants. There can be two, sometimes even three roots of a premolar, particularly the first premolar, so the tooth can be difficult to remove in the first place. The labial roots are generally set very close to the outer plate of bone, so in this respect they are similar to the maxillary anterior teeth. It can be tempting to want to choose a palatal root space to place the implant into, but this may be set too palatally. It is better to prepare the initial channel down between the labial and the palatal roots. An ultrasonic tip can establish the ideal starting point for a pilot drill which allows the channel to be finalized using drills. Premolar roots are much wider palatal-to-buccal than they are mesial-to-distal, so it may not be possible to get great initial stability. What stability can be achieved is obtained in the apical one third of the channel. It can be tempting to use a larger diameter implant to get greater stability but this should be resisted because it can leave minimal interproximal space.

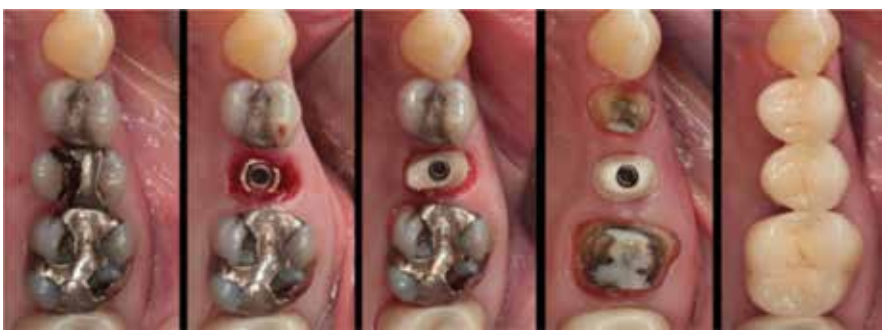

Figure 33. This case started with the sub-osseous fracture of the palatal cusp of a maxillary second premolar. The tooth was not restorable. It was extracted and immediately replaced with an implant to which a temporary Zirconia Sleeve abutment was then attached.

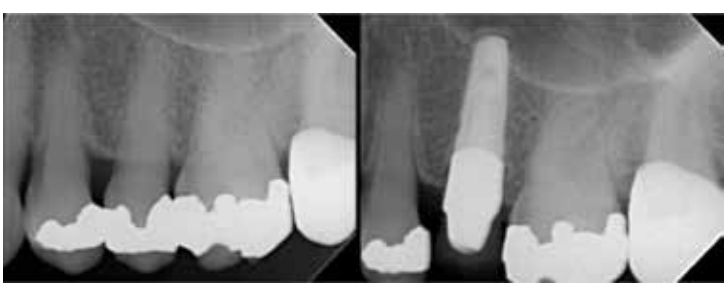

Figure 34. As is often the case with premolars, there was not enough initial stability of the implant to load it immediately. By taking the implant a little higher, into the sinus region, additional stability was gained.

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One relatively common problem is for the implant to penetrate out of the bone apically. The reason for this is that the operator fails to appreciate that the bone housing tapers in medially as the alveolus progresses apically. This can be avoided if the drill path parallels that of the outer plate of bone. It is also necessary to sink the implant platform deeper than usual so that the abutment placed on the platform can flare out buccally and lingually to develop an elliptical, pre-molar form (**Figures 33–35**).

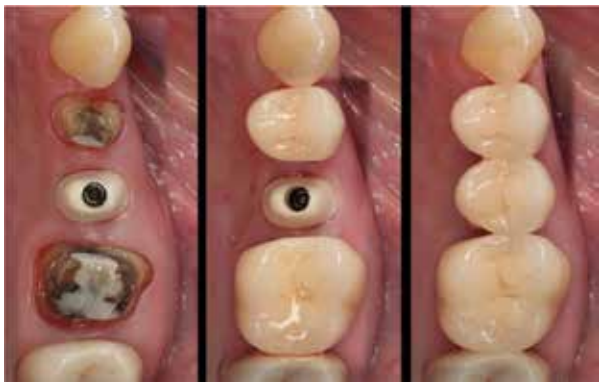

Figure 35. The deep position of the implant platform made it easy to develop the optimal emergence form for the abutment and for the final crown.

7.4. Mandibular premolars

The anatomy of the mandibular premolar region can be challenging. The labio-lingual bone dimension can be narrow even when it contains teeth. When the teeth are removed, the ridge shrinks more. The labial bone can be particularly thin and rapidly disappears after an extraction. The mandibular nerve can be very close which makes it impossible to gain extra stability for an implant by preparing the implant channel deeper (**Figures 36** and **37**).

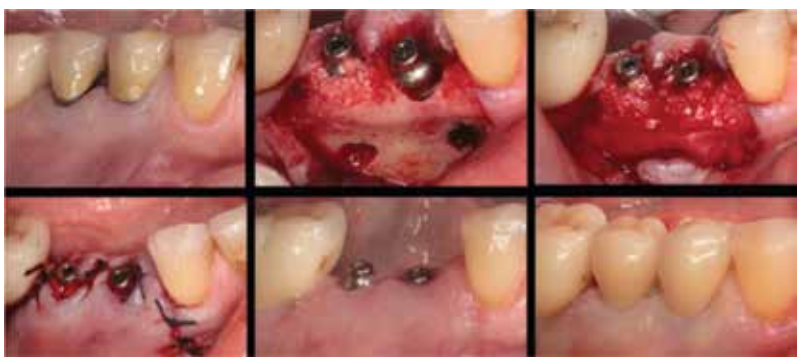

Figure 36. These two premolars were painful and had apical lesions. A labial flap allowed access to remove the teeth, to debride the region and to place implants and gingivaformers.

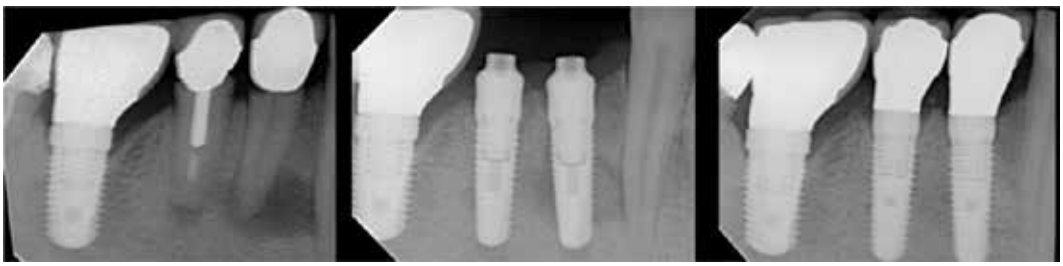

Figure 37. The radiographic series shows good healing. The molar implant was one with a 1.4 mm machined collar placed five years earlier.

7.5. Maxillary molars

The critical factor to appreciate with maxillary molars is that they have relatively little bone supporting them in the first place. What bone there is usually closely follows the form of the roots with the covering of bone around each root being quite thin. This bone covering can easily be taken away by recession, occlusal trauma, and furcation involvements. What is left can be inadequate to support an implant. It is critical to retain what bone there is in the region. An adequate volume of bone to support an implant is found in less than 5% of cases in our experience. This is why when replacing a maxillary molar with an implant it is necessary to consider providing a sinus lift. Once these principles are appreciated, then immediate molar replacement is both predictable and successful (**Figures 38–40**) [15].

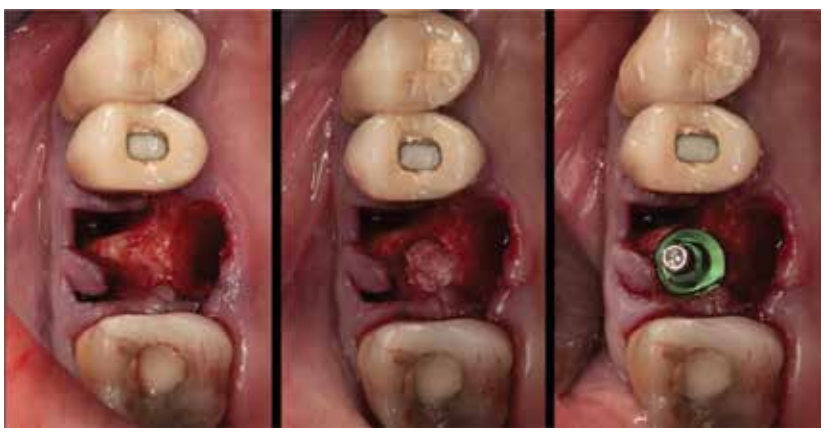

Figure 38. The first molar was failing and was removed. The labial and lingual walls were almost non-existent and the socket was expected to collapse. The central core bone in the trifurcation region was adequate to prepare a trephine channel, to raise the sinus floor, to augment the sinus region with bone graft and to place an implant.

Where the trifurcation region of bone is unable to stabilize an implant, such as when there is a large furcation involvement, it will be necessary to obtain apical stabilization by an intentional sinus lift procedure.

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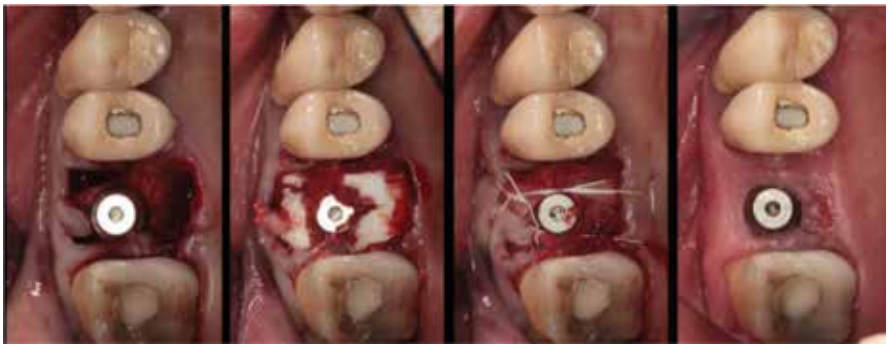

Figure 39. The former root spaces are then filled with bone graft, covered with a membrane and sutured. There was no advancement of the marginal gingival flaps.

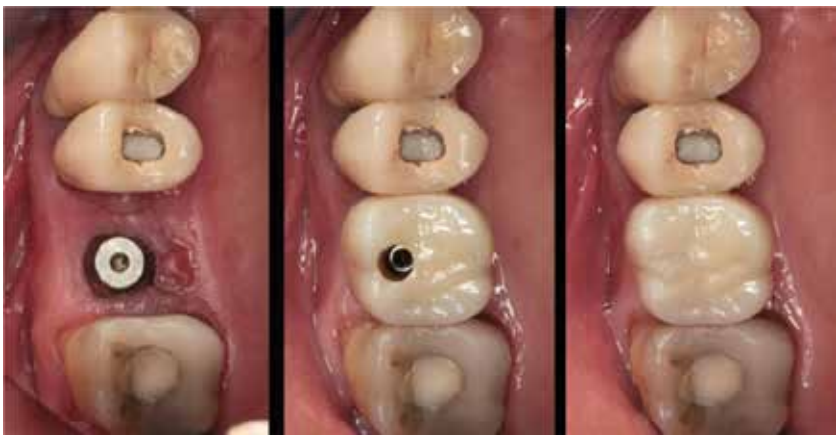

Figure 40. The region healed well and a restoration was placed.

Here is an example of such a case (**Figures 41–44**).

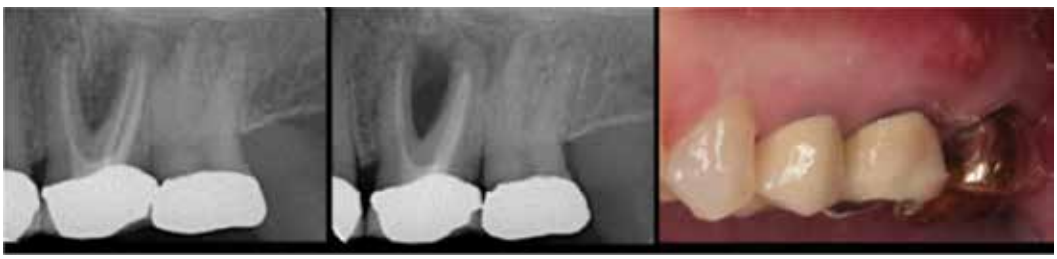

Figure 41. Left: On initial presentation the patient was advised to have the molar replaced by an implant. Center: Five months later, with no therapy, the furcation defect had increased greatly. Right: An abscess is now pointing out labially.

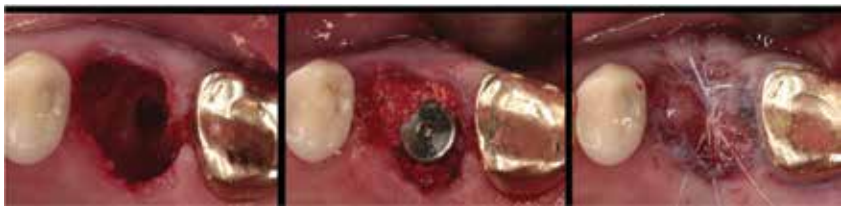

Figure 42. The tooth was sectioned and removed. A sinus floor perforation was obvious, so this was used as the starting point for the stabilization of the implant, even though it was a little distal. After a small sinus lift with bone graft, the implant was placed, surrounded by more bone graft, sutured and covered by a membrane.

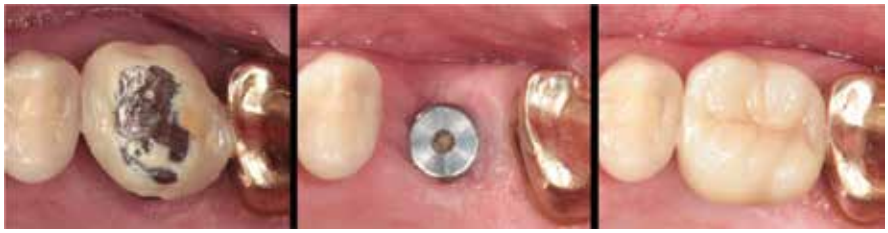

Figure 43. Here is the original, after healing and with the final restoration.

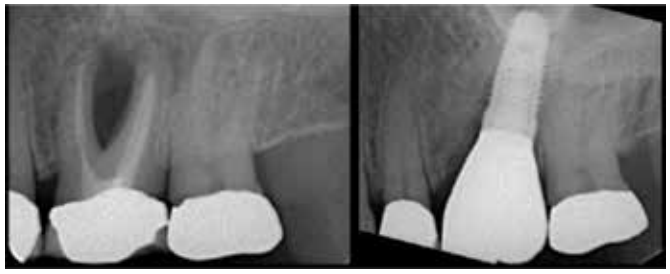

Figure 44. Before and after radiographs.

7.6. Mandibular molars

When mandibular molars are extracted, there tends to be a fairly rapid collapse of the labial plate with loss of ridge height and recession of the ridge to the lingual. Part of the reason for this is that the buccal roots of mandibular incisors often have very little bone coverage. In addition, traditional extractions with forceps can be fairly destructive on the labial bone plate. In short, it can be very difficult to rebuild a collapsed mandibular ridge. Prevention of ridge loss is better, simpler, easier, and faster. In the extraction procedure, everything possible should be done to preserve the labial and lingual plates.

Removing the roots can be difficult and time-consuming. Once this is done and granulation tissues have been removed, there should be a four-wall defect. Establishing the right position

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for and stability of the implant can be difficult. Sometimes this is possible in a former root socket. It may be possible to use the inter-radicular septum. Often it is necessary to make the channel for the implant a little deeper than the socket of the tooth. However, it is critical to ensure that there is clearance above the mandibular nerve. If this is not available, then it will be necessary to perform a socket regeneration procedure. The case which follows is typical of a situation which could be managed immediately (**Figures 45–47**).

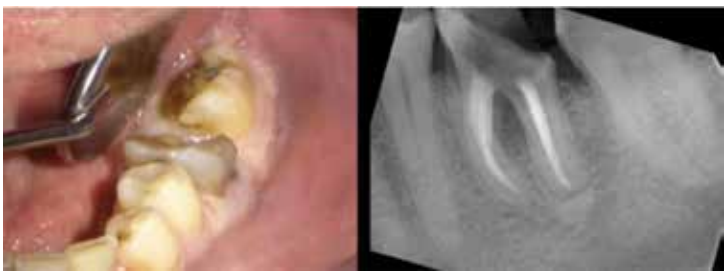

Figure 45. This mandibular molar had never been restored after the root canal therapy. Now the tooth is hopeless and there is considerable bone destruction in the region.

Figure 46. The tooth was removed, the region debrided, stabilization for the implant was generated apically, an osseous coagulum was developed with a bone graft and a membrane covered over the region while it healed. The final restoration was placed five months following the procedure.

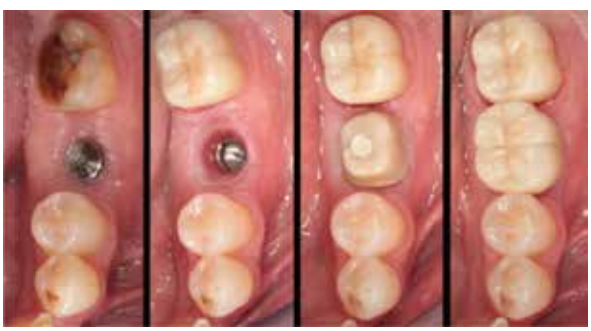

Figure 47. As is typical the gingivaformer is exposed by the time the case is ready to be restored. A custom zirconia emergence attached to a Camlog® Titanium Base CAD-CAM component is placed. This allows the final crown to appear very natural.

8. Larger scale immediate replacements

The success of immediate single tooth replacement has led us to take on larger scale cases with multiple missing teeth. These are always difficult situations because the hard and soft tissue defects that can arise from the loss of multiple adjacent teeth are more extensive and much more difficult to repair. The principles applied are much the same as for the individual tooth situation. The teeth are removed carefully with care being taken to preserve whatever bone is in the region. The region is thoroughly debrided, implant channels prepared, implants placed with adequate stability, an osseous coagulum with membrane coverage provided, and closure. The one real difference in these cases is that flap access to the region is required. The case shown below would generally not be treated using an immediate protocol. Traditional therapy would have been very complex because the teeth would have been removed, the ridge would shrink away almost completely, and re-building the region would have been exceedingly difficult, multi-staged, and lengthy. The patient, a graduate student in his late twenties, was about to leave the region and requested an accelerated protocol (**Figures 48–52**).

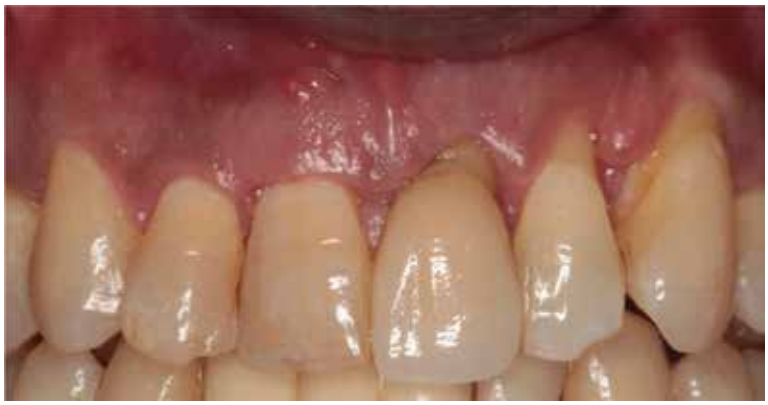

Figure 48. Clinical view of the dentition.

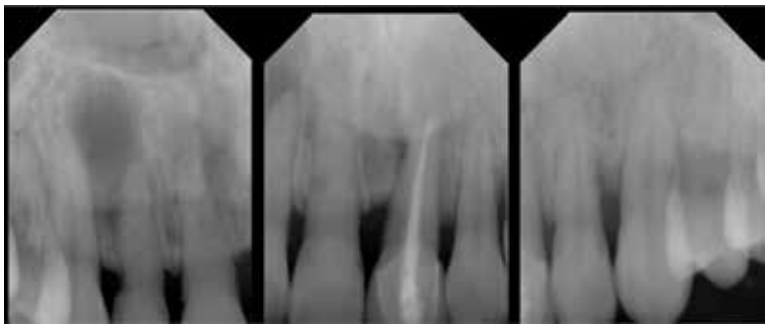

Figure 49. Periapical radiographs of the region.

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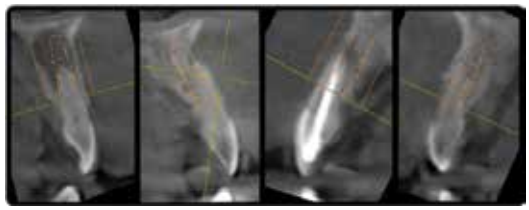

Figure 50. CBCT slices through the teeth show a variety of advanced lesions including almost complete loss of facial bone on three teeth.

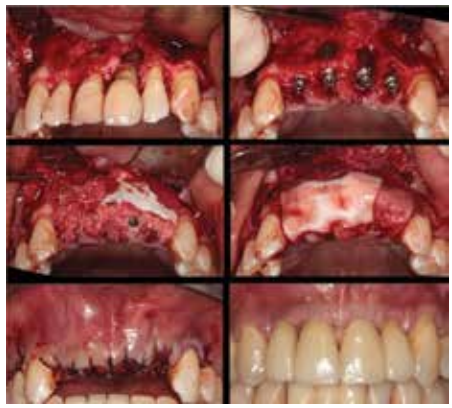

Figure 51. The region was open flapped for debridement. Camlog® implants were placed in all four sockets. An osseous coagulum was developed using BioOss Collagen particulate bone graft and covered with Bio-Gide® and Mucograft® collagen membranes (Geistlich). The region was closed without primary closure. Five months later the case was restored with individual abutments and restorations.

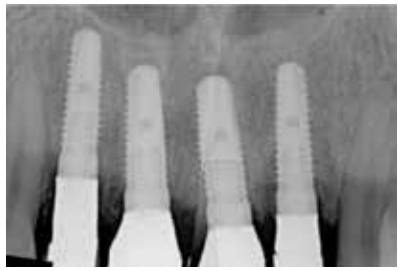

Figure 52. Post-therapy radiographs show that the region is continuing to recover.

Traditional therapy for this case would have been extremely complex, time consuming, and difficult. While this result cannot be considered ideal, it was relatively simple, fast, and effective. The basic principles of debridement, positioning, and stabilization of implants, developing an osseous coagulum and wound closure described above were used throughout therapy. All things being considered, the result in this case is very encouraging.

8.1. Failing individual teeth with aesthetic concerns

The case shown below also has many problems. They can all be handled individually, but what is really needed is to blend them all into a treatment plan that works towards a harmonious end result. It is a real challenge to make implant-supported restorations look natural alongside restorations supported on natural teeth but that was what was needed in this case (**Figures 53–56**).

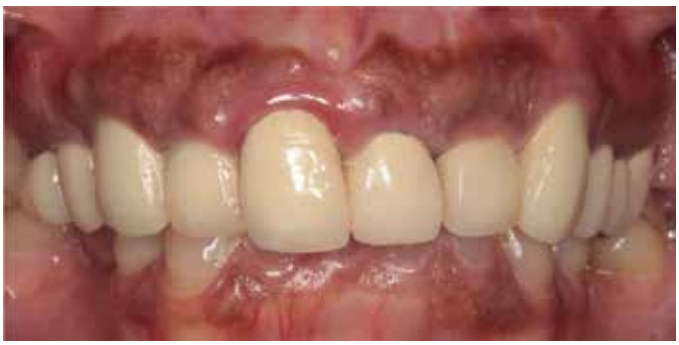

Figure 53. The patient was concerned about the puffy gums and the poor appearance of the teeth.

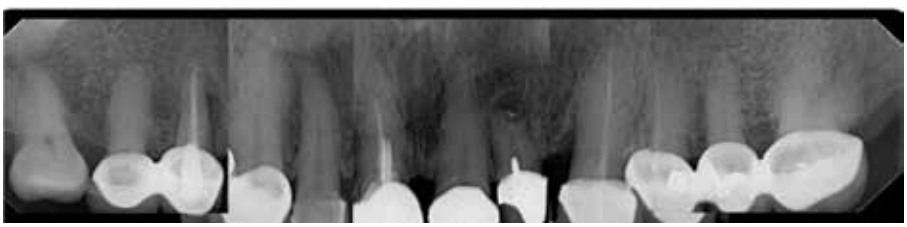

Figure 54. The radiographs show some failing teeth but the bone support is basically good.

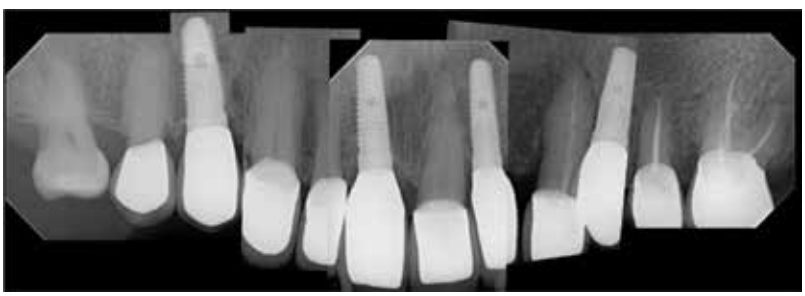

Figure 55. Four implants have replaced the failing teeth using an immediate replacement protocol. In the process the gingival lines have been re-aligned and the gingival health of the implants and natural teeth is now good. The aesthetics have been greatly improved.

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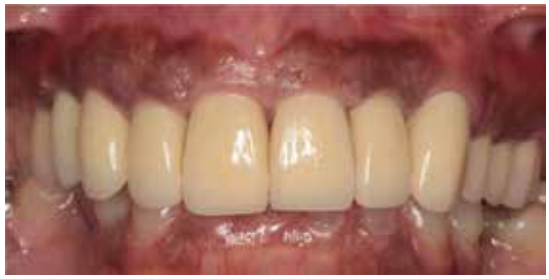

Figure 56. Therapy is completed, the appearance is now very natural.

9. Complications

Complications can occur with any procedure, but in immediate replacement these tend to be infrequent and relatively insignificant. The critical requirement is for careful monitoring of healing during the post-surgical process. If problems arise they should be managed as rapidly as possible.

9.1. Early loss of implant stability

This is an infrequent but very serious complication, usually occurring on immediately loaded implants with restorations. Loss of implant stability requires immediate action.

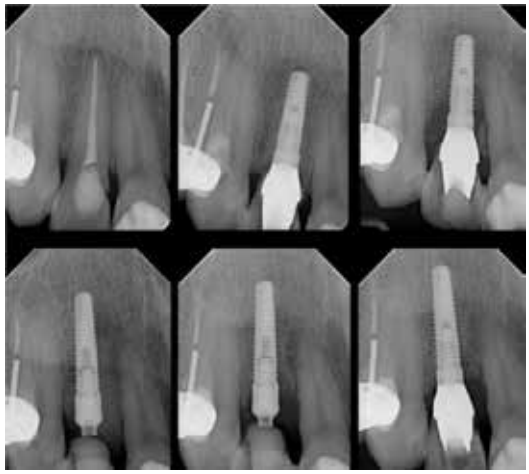

Figure 57. This lateral incisor was fractured at the gum level. It was removed and immediately replaced with an immediate load implant and provisional. Four weeks later he reported it was mobile. The referring dentist bonded it to the adjacent teeth. He was referred back to us 10 days later when it was more obvious that the region was quite compromised.

There are three options. First is to remove the abutment and to replace it with a gingivaformer. For this to work there must be no signs of inflammation or infection in the region, just slight mobility. The second alternative is to remove the implant, clean the region, and to replace it with another fresh, un-contaminated implant. Preferably this will gain additional stability with a larger size or length. However, it should be converted to a gingivaformer procedure to be sure of getting rid of the potential for breakdown. The third alternative is to remove the implant, to clean out the region, and do socket regeneration in the region. The case shown below was managed with the second option protocol (**Figure 57**).

The implant was removed and the region thoroughly cleaned out. A longer implant was then placed, with a gingivaformer positioned; the region was then augmented extensively with more bone graft before the region was closed. Three months later the healing was satisfactory, though there was some medial papillary recession.

9.2. Connection abscess (abutment screw loosening)

These occur because of loosening of the abutment retaining screw. Usually an abscess is a rather late occurrence. At an earlier stage there is inflammation of the marginal gingiva. If this is allowed to continue for too long, then the abscess may penetrate through the gingiva as seen in the case below. The way to check this is to rock the crown and to see if there is any mobility. The axis of the rotation will be at the connection. It is important to differentiate this from mobility of the implant which is where the axis of rotation would be more apical.

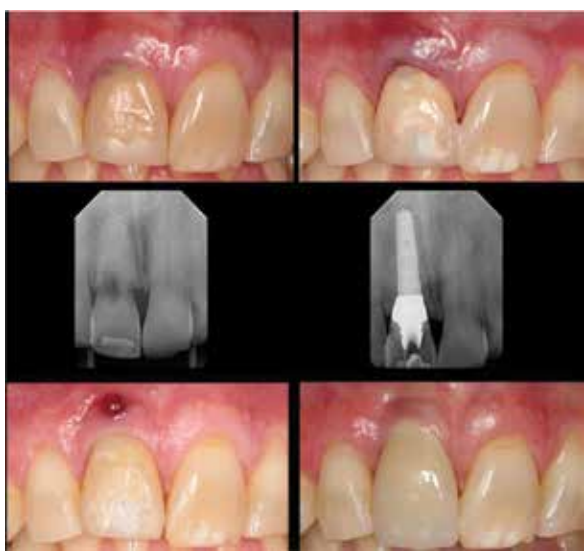

Figure 58. Top left: Situation with internal tooth resorption. Top Right: Following immediate replacement. Center left: Original radiograph. Center right: With implant and provisional. Bottom left: Four months later with connection abscess due to mobility of connection. Bottom right: Final case with healed situation but with increased marginal recession.

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This sometimes occurs because at the time of implant placement, there is a hesitance about over-tightening the abutment retaining screw, as this may cause the implant to rotate. If this rotation does occur, it can be interpreted as the wrong choice of post-surgical restoration in that the implant was really not stable enough to immediately load.

There can be one other cause for this problem. It occurs when bone graft used for the augmentation gets trapped between the abutment and the implant platform when the abutment is placed. A radiograph should always be taken at the end of the procedure to check that this has not occurred. Although the connection may be tight at the outset, as the graft softens, the joint will loosen (**Figure 58**).

9.3. Marginal gingival recession

This is a rather complex subject. Stability of the marginal gingival complex depends on many factors which can be grouped into three main considerations: structure, replacement structure, and pathology.

Structure: We start working with the pre-existing condition. A normal gingival complex is supported over marginal bone; if that bone is lost for one reason or another then the gingival margin can more easily recede. Gingiva is usually differentiated into attached gingiva and free marginal gingiva. Everybody appreciates that attached gingiva should be attached to the tooth, but there is not so much appreciation for it also being attached to the marginal bone complex. Many of our surgical procedures raise up and move this marginal attached gingiva, sometimes to places where there is no bone for it to re-attach to, for example when a flap is mobilized to cover over a socket. When replacing a tooth with an implant, it is critical that it be surrounded by attached gingiva, which is attached to the bone and then comes up over the gingivaformer or abutment.

Replacement Structure: Some teeth when replaced by an implant will have considerable amounts of native bone remaining in the region. Although this will be affected by the change-over, in most cases the hope is that it remains, regenerates, and starts to support the implant. However, in some of our most critical situations, such as in the maxillary anterior region, the implant is set back palatally and at an angle to get stability in the palatal bone. The void between the implant and the labial wall of the socket has to be augmented with a bone graft. We usually over-augment to make sure that this consolidates without receding. Similarly, the gingival complex is usually augmented with a gingival allograft or more traditionally a connective tissue graft. Another factor to take into account is the material and form of the temporary abutment as this is often used to bulk out and support the augmented regions. These should be of materials which are bio-compatible with the soft and hard tissues in the region. We use custom formed Zirconia sleeves secured on a titanium base to accomplish this in our cases.

Pathology: Inflammation and infection can affect marginal soft and hard tissues. They can induce a wide-range of responses ranging from swelling to hyperplasia, from fibrosis to tissue breakdown, and for attached tissues to become detached (**Figure 59**).

Figure 59. This patient had marginal recession and recurrent decay around the maxillary anterior teeth. Neither the patient nor the referring dentist was comfortable with another round of conventional restorative therapy. The teeth were all replaced with implants. Notice the change in gingival form and structure. Restorative dentistry by Dr. Chris Furlan, Havertown, PA, USA.

9.4. Peri-implantitis

Peri-implantitis is an inflammatory reaction in the tissues surrounding an implant, both gingiva and bone. One has to be careful to differentiate it from marginal gingivitis or inflammation of the gingival tissues about an implant. If there are changes in the marginal bone below the rough surface of the implant, then one should assume that osseointegration in that region has broken down and that the rough surface on the implant has become contaminated. If this is the case then it is doubtful if it can be "re-treated" or made so that re-osseointegration can develop. It may be possible to get short-term benefits, but it is often better to replace the implant (**Figure 60**).

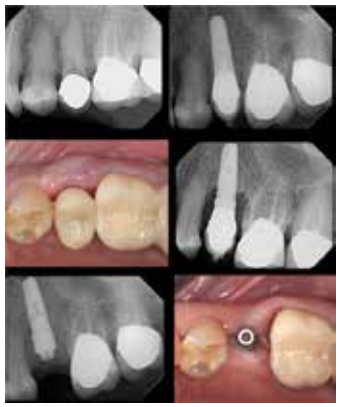

Figure 60. Top: Deep decay was under the margin of the crown on the second premolar, so the tooth was replaced with an immediately loaded provisional restoration. Center: Six weeks later, she returned with pain and gross inflammation of the marginal gingiva. A radiograph showed rapid breakdown around the collar of the implant. It was removed, and the region debrided. A fresh implant was placed with a bottleneck gingivaformer and closed after further augmentation. Bottom: Four weeks later, the inflammation in the soft tissue complex is resolving well and further healing can be expected.

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9.5. Apico-implantitis

This is a problem where infection breaks down the apical bone surrounding an implant. Generally there can be two sources of the infection. The first is a residual apical infection left from a tooth in the region that was extracted previously. The second source can be from an apical infection on an adjacent tooth. Diagnosis may be difficult and access to the region for debridement can be more complex (**Figure 61**).

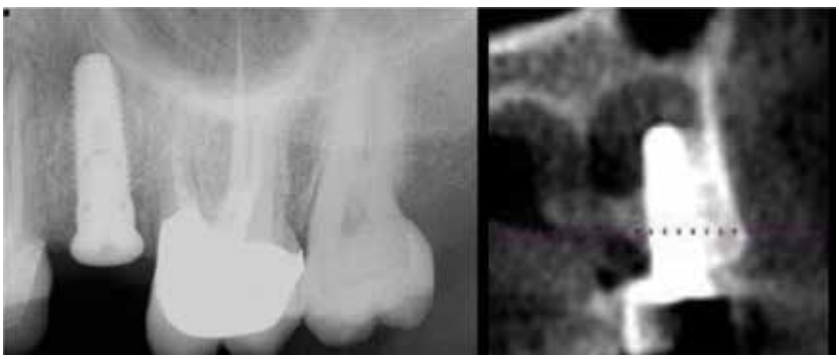

Figure 61. This implant was placed and appeared to integrate well, but a check radiograph at a later time showed apical pathology. The implant was removed, the region debrided and allowed to heal.

9.6. Sequestrum formation

Sequestra are portions of bone which lose vitality and then become a nidus of infection. Most of these occur in the mandible. Bone fragments may lose much of their surrounding support and blood supply during the extraction process or during implant placement. Most common are inter-radicular septa, followed by bone walls of adjacent teeth. Part of the issue can be that these regions may have been traumatized or even fractured during the extraction process. These can delay healing in the region, become a source of infection about an implant, and be painful. Once identified, it is best to remove the sequestrum and allow the region to heal. They can happen in any extraction socket, not just when implants are placed.

10. Summary and conclusions

Bone regeneration within four-wall sockets seems to be relatively easy to achieve. Socket regeneration is based upon using this principle. Immediate implantation is simply taking the concept one step further by stabilizing an implant in the middle of the regenerating socket. It is becoming increasingly obvious that immediate implantation procedures can be successful, that they can minimize the extent and number of surgical interventions, and return the patient to function within the shortest possible time. In addition, they help retain the supporting complex of a tooth being extracted and replaced by an implant. In comparison, traditional techniques seem increasingly outdated.

We have come to believe that it is easier to retain than regain an alveolar supporting complex. For immediate implantation procedures to be successful, it is necessary is to pay attention to some basic principles:

1. The tooth needs to be removed with minimal damage to the socket walls.
2. The socket needs to be debrided of soft tissue granulations and infected tissues.
3. Correct positioning and adequate stabilization of the implant must be established.
4. An osseous coagulum needs to surround the implant and fill the socket. Using a slow-resorbing bone graft material can help prevent ridge resorption.
5. A gingivaformer or abutment placed in the implant can provide a "tenting" effect, which assists augmentation and helps prevent early contamination of the rough surface of the implant.
6. The socket does not need to be covered with gingiva, it can be covered and protected by membranes as in socket regeneration procedures.
7. If high initial stability of the implant is achieved, then immediate provisionalization can be considered.

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Chapter 15

Guided Bone Regeneration Technique Using Hyaluronic Acid in Oral Implantology

Fatih Özan, Metin Şençimen, Aydın Gülses and Mustafa Ayna

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/63101

Abstract

Guided bone regeneration is a term used to describe the use of the barrier membranes to enhance complete osteogenesis by preventing the rapid ingrowth of fibroblasts into a bony defect and promoting the migration of osteogenic cells from adjacent bony edges or bone marrow into the defect in an unimpeded fashion. Hyaluronic acid (HA) is a glycosaminoglycan of the general formula $(C14H22NO11)_n$ and is an essential component of the extracellular matrix in connective tissue, which is found in abundance in the alveolar environment. The most important function of HA is its involvement in tissue healing and repair. It has been shown that HA stimulates cell proliferation, migration and angiogenesis, re-epithelialization and proliferation of basal keratinocytes and reduces collagen and scar tissue formation. This text presents our clinical experiences and outcomes following HA applications in various implant surgery procedures. According to our clinical outcomes, HA is a highly promising material for improving therapeutic outcomes for oral implantology.

Keywords: guided bone regeneration, hyaluronic acid, oral implantology, bone reconstruction, advanced oral surgery

1. Introduction

Loss of alveolar bone can result in secondary to periodontal diseases, periapical pathologies, maxillary sinus pneumatization or trauma to teeth and adjacent structures. Damage of the osseous structures during tooth extraction procedures may also result in bone loss of various types and severity. Sufficient alveolar bone volume and favorable architecture of the alveolar

ridge are essential to obtain ideal functional and esthetic prosthetic reconstruction following implant therapy [1]. In order to overcome the problems related to osseous defects adjacent to implants and/or implant recipient sites, Dahlin and colleagues spearheaded early research on guided bone regeneration (GBR) techniques [2–4]. Herein, we present the technique.

2. Guided bone regeneration

GBR is a term used to describe the use of barrier membranes to enhance complete osteogenesis by preventing the rapid ingrowth of fibroblasts into a bony defect and promoting the migration of osteogenic cells from the adjacent bony edges or bone marrow into the defect in an unimpeded fashion [5]. Nowadays, various types of dental GBR materials have been developed, which can be grouped together as either non-resorbable or resorbable membranes.

3. Non-resorbable membranes

The first and recently mostly used commercial membrane was produced from Teflon® (e-PTFE). According to the results of various studies focusing on the efficacy of e-PTFE, predictable outcomes were observed, especially in ridge augmentation using it either alone or in combination with osseous grafting. However, membrane exposure, which permits a communication between the oral environment and newly forming tissues, increasing the potential for infection and decreasing the likelihood of regeneration, has been a frequent post-surgical complication associated with the use of non-resorbable membranes [6]. Moreover, non-resorbable membranes must be retrieved by employing a second surgical procedure [7].

4. Resorbable membranes

There are mainly three types of biologically resorbable membranes: (1) polyglycoside synthetic copolymers, (2) collagen and (3) calcium sulfate.

Collagen is the principal component of connective tissue and provides structural support for them. Collagen membranes are the most widely used resorbable membranes in implant surgery. They have various advantages such as hemostasis, chemotaxis, biotolerability, bioresorbtion, slow absorbtion and ease of manipulation compared to e-PTFE.

Hyaluronic acid (HA) is a glycosaminoglycan with a chemical formula $(C14H22NO11)_n$ **and also found in abundance in the connective tissues of maxillary and mandibular tooth bearing areas** [8]. HA is particularly dense in the superficial layers of the buccal mucosa where it contributes to the epithelial barrier effect, at the same time enhancing both the stability and the elasticity of the peripheral connective tissue.

The most important function of HA is its involvement in tissue healing and repair [9, 10]. In the literature, it has been shown that HA stimulates cell proliferation, migration and angio-

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genesis, re-epithelialization and proliferation of basal keratinocytes and reduces collagen and scar tissue formation [11, 12].

In covalently cross-linked condition, HA forms a hydrophilic polymer network which may absorb its dry weight in water a multiple of times [13]. This lubricious property combined with its biocompatibility has led to different medical applications of HA in dermatology, ophthalmology, orthopedics, plastic surgery, and more recently, implantology, in order to benefit from its properties against inflammation and infection together with its capacity to promote wound healing.

Owing to that, HA is used as an effective medication for treatment of recurrent aphthous ulcers [14], as an adjuvant treatment for gingivitis [15], to enhance healing of tooth extraction socket [16] and interdental papillae reconstruction [17]. More recently, cross-linked HA products were used as gel barriers to cover the osseous defects around the implants and implant recipient sites and thereby promoting GBR. Claar performed a lateral coverage of the augmentation followed by use of cross-linked HA in gel form, which was developed especially for GBR [18].

The principles of GBR applications are as follows [19, 20]:

Cell exclusion: Crating a barrier to prevent forming fibrous connective tissue by epithelial cells.

Tenting: New wound space beneath the membrane must be regenerated solely from around soft tissues so that high quality of new tissue can be gained.

Scaffolding: At first, a fibrin clot is seen in this space which is a scaffold for progenitor cells. Adjacent hard tissues serve as a storage for stem cells.

Stabilization: To gain successful healing, the defective area must be protected from environmental effects such as flap movement, bacterial invasion, exposure of region, etc. by fixing the membrane into position.

It is well known that HA is a biodegradable, biocompatible, non-toxic, non-immunogenic and non-inflammatory linear polysaccharide. These properties demonstrate the superiority of HA by providing high biocompatibility and tissue integrity as a barrier membrane.

As mentioned above, the placement and stabilization of the membrane play a key role in the success of GBR. Therefore, the surgeon's skill and experience are of great importance. In addition, the need for removal of the mini bone screws placed for the stabilization of the membrane during implant insertion surgery necessitates a larger flap design and excessive exposure of the surgical field, especially in lateral sinus elevation procedures. Claar [18] has also proclaimed that, because of its high viscosity, HA is readily applicable and has high positional stability.

Marinucci *et al*. [21] evaluated the effects of bioabsorbable and non-resorbable membranes on human osteoblast activity *in vitro*. Human osteoblasts were cultured on bioabsorbable membranes made of collagen, HA, and poly DL-lactide, and e-PTFE. The results showed that collagen and HA increased secretion of TGF-β1, a growth factor involved in bone remodeling. It may be concluded that bioabsorbable membranes, particularly collagen and HA, can

promote bone regeneration through their effects on osteoblasts. Besides that, HA and bioabsorbable membranes significantly increased collagen synthesis and alkaline phosphatase activity.

Membranes must remain in place until cells capable of regeneration are established at the wound site. Blumenthal [22] showed that collagen membranes cross-linked with formaldehyde can last 6 to 8 weeks before being absorbed, whereas non-cross-linked membranes lose their structural integrity in 7 days. HA gel in cross-linked form can last up to 3–4 weeks in the surgical field, which could be accepted as an appropriate term for enhancement of osteopromotion. HA is a highly promising material for improving therapeutic outcomes in dental implantology.

The aim of this section is to present clinical outcomes following HA applications in different implant surgery procedures.

5. Technique

5.1. Bone defects around dental implants

A 43-year-old healthy male patient admitted to our department due to the loss of his upper left lateral incisor was assessed. According to his history, the tooth was extracted 4 months ago following an unsuccessful endodontic treatment. A computerized tomography revealed the presence of a bone defect located adjacent to the missing tooth (**Figure 1**).

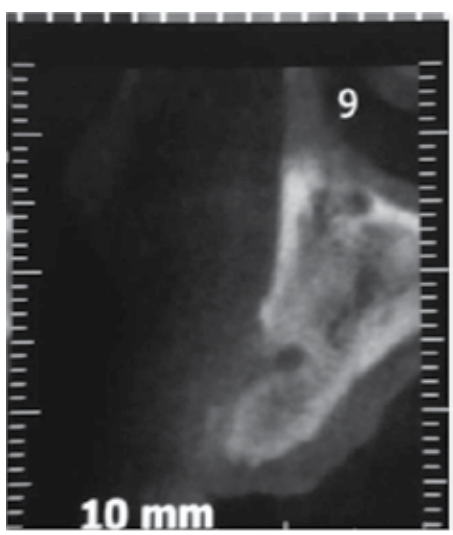

Figure 1. A computerized tomography scan revealed the presence of a bone defect located adjacent to the missing tooth.

After consultations with the prosthodontist, it was decided to insert an implant into the corresponding area. Under local anesthesia, a full thickness flap was raised and the bone defect

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and the implant recipient site were exposed. The granulation tissue were thoroughly curetted and the defect became more apparent (**Figure 2**).

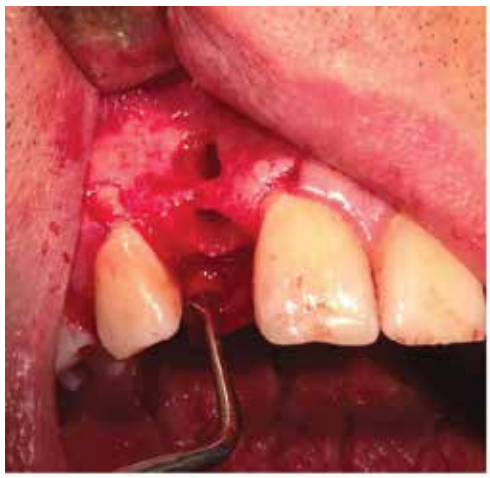

Figure 2. The remaining granulation tissues were thoroughly curetted and the defect became more apparent.

The implant site was prepared. A 3.4 × 11 mm implant (Bone Trust, Medical Instinct Zahn Implantate, Bovenden, Germany) was placed (**Figure 3**).

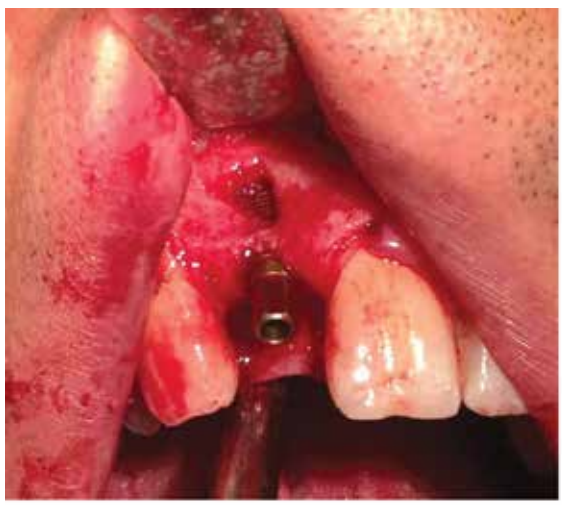

Figure 3. Placement of the implant.

The defect was grafted by using bioactive glass material (Leonardo, Naturelize, Hirschberg, Germany) mixed with non-cross-linked HA (Tissue Support Hyaluronic Acid Liquid Gel, Hyadent Bioscience GmbH, Ransbach-Baumbach, Germany) (**Figure 4**).

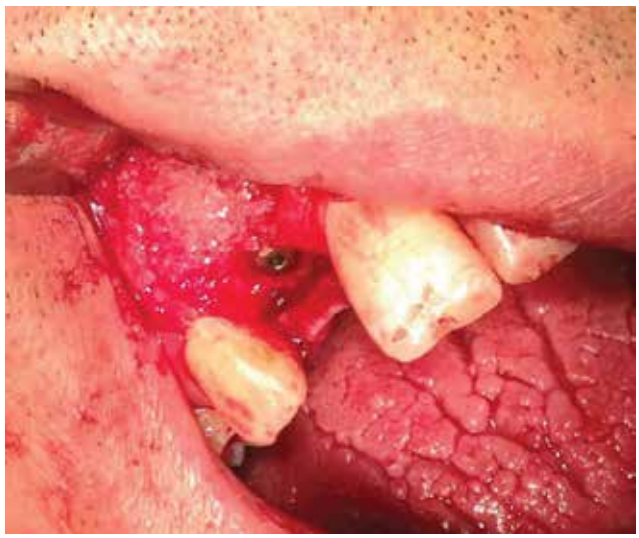

Figure 4. The defect was grafted by using bioactive glass material mixed with non-cross-linked HA.

The surgical field was covered by using cross-linked HA gel to avoid epithelial ingrowth to the grafted area. After closure of the surgical field with 4/0 silk sutures, the remaining cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) was injected into the surgical field in order to obtain a more predictable soft tissue profile and benefit from antibacterial properties of the material (**Figure 5**).

Figure 5. The injection of the remaining cross-linked HA into the surgical field.

Four months after implant placement (**Figure 6**), an ideal implant-bone contact was observed and the implant was functionally loaded. The patient was functionally and esthetically satisfied.

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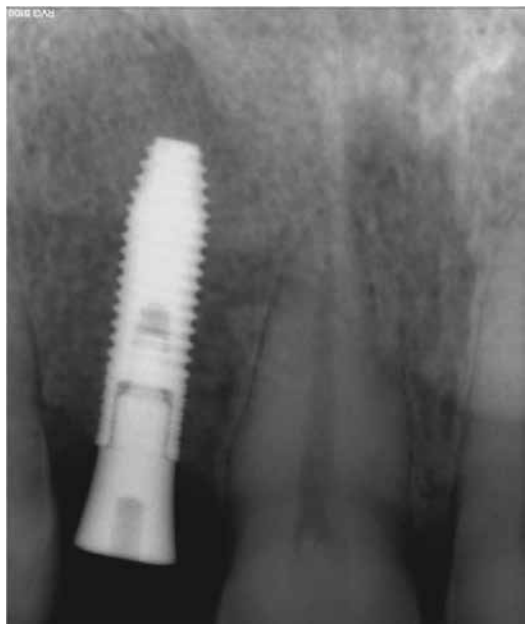

Figure 6. Four months after implant placement, an ideal implant-bone contact was observed.

5.2. Immediate post-extraction implant placement

A 34-year-old healthy female patient was admitted following the fracture of her upper left second premolar. On the clinical and radiographical examination, it was observed that upper left first and second premolars were unrestorable (**Figure 7**).

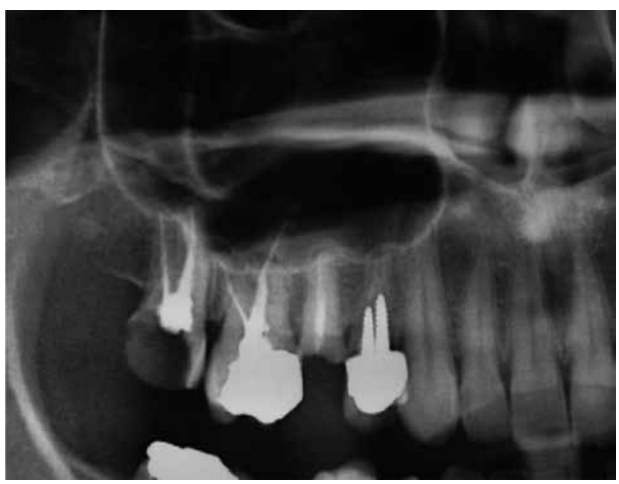

Figure 7. Radiological view of the upper right quadrant.

After consultation with the department of prosthodontics, it was decided to extract both teeth and to place implants simultaneously. Under local anesthesia, a full thickness flap was raised, both teeth were extracted (**Figure 8**) and two 5 × 11 mm Bone Trust implants (Bone Trust, Medical Instinct Zahn Implantate, Bovenden, Germany) were placed (**Figure 9**).

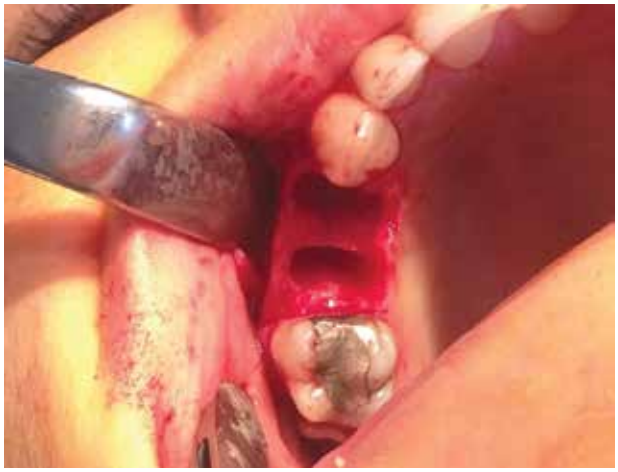

Figure 8. Intra-oral view after extraction of the upper first and second premolars.

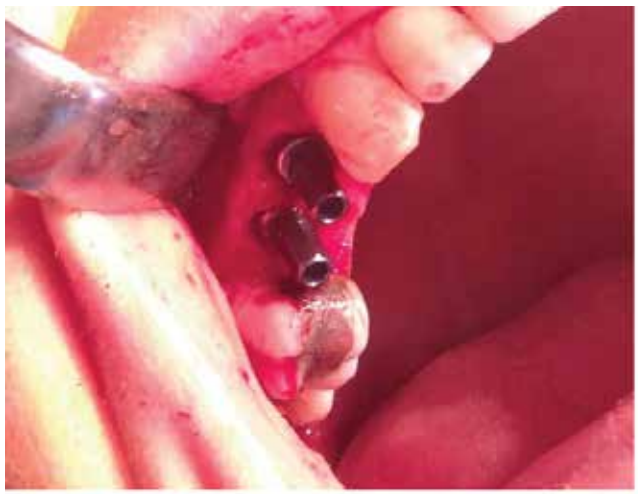

Figure 9. Placement of the implants. Please note the gap between the implants and the alveolus.

A gap was observed between the implant and the extraction socket, and these defects were grafted by using bioactive glass material (Leonardo, Naturelize, Hirschberg, Germany) mixed with non-cross-linked HA gel (Tissue Support Hyaluronic Acid Liqui Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) (**Figure 10**).

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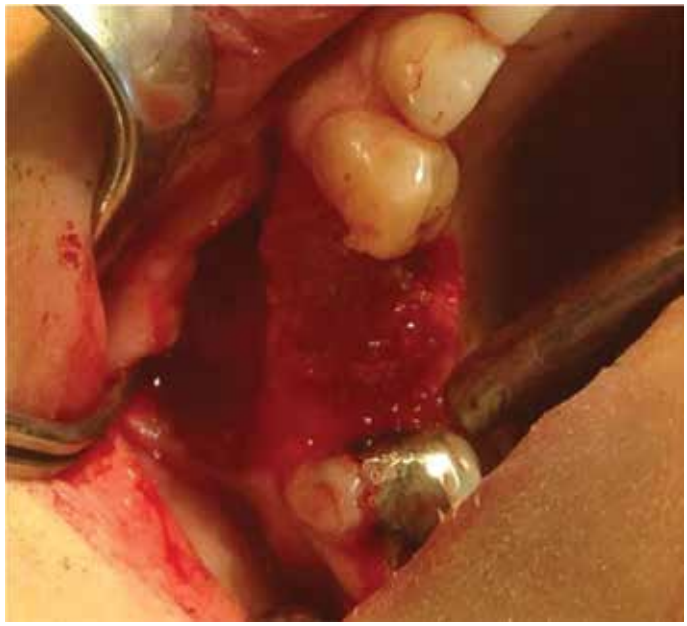

Figure 10. Grafting of the area with bioactive glass material mixed with non-cross-linked HA.

A cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) was injected over the implants and the graft material. Three months after implant placement (**Figure 11**), the implant was functionally loaded. The patient was satisfied both esthetically and functionally (**Figure 12**).

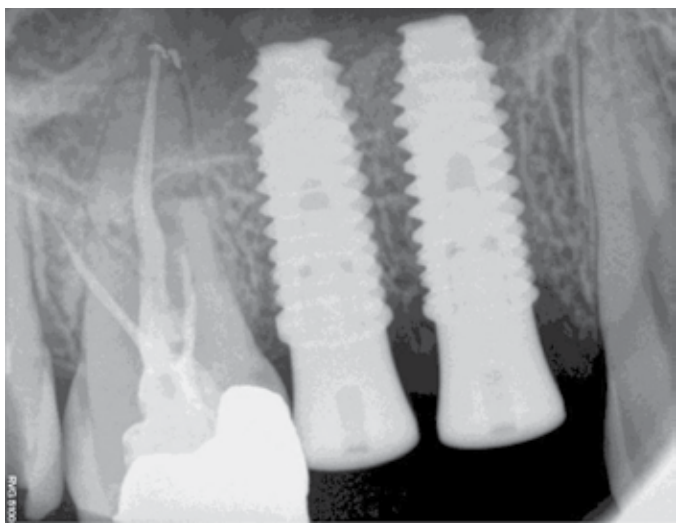

Figure 11. Three months after implant placement, an ideal implant-bone contact was observed.

Figure 12. Clinical view after prosthetic procedure.

5.3. Sinus bone grafting

A 44-year-old healthy female patient presented to our department and requested a fixed prosthesis of the right maxillary posterior region. The teeth had to be removed at another clinic as a result of failed endodontic procedures. Clinical and radiological examinations showed the lack of an adequate vertical bone, but sufficient width of the alveolar ridge. Given that the residual vertical bone height was ≤3 mm (**Figure 13**), we planned to insert the implants following the sinus floor augmentation procedure.

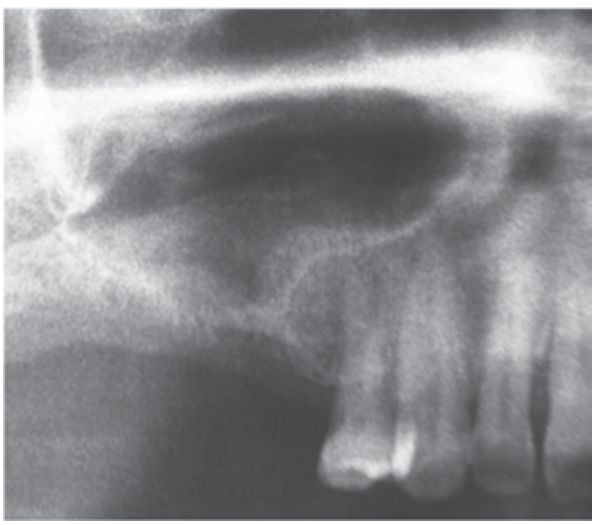

Figure 13. Preoperative radiological view.

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A trapezoid incision was made under local anesthesia to reflect a mucoperiosteal flap. The vestibular portion of the maxillary sinus was exposed, a maxillary sinus window was prepared and the sinus membrane was elevated. The sinus cavity was augmented with a bioactive glass bone graft material (Leonardo, Naturelize, Hirschberg, Germany), which we had mixed with non-cross-linked HA (Tissue Support Hyaluronic Acid Liqui Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) extra-orally (**Figure 14**), and the lateral coverage of the augmentation site was made by using cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) (**Figure 15**).

Figure 14. Mixing procedure of the bioactive glass bone graft material with non-cross-linked HA.

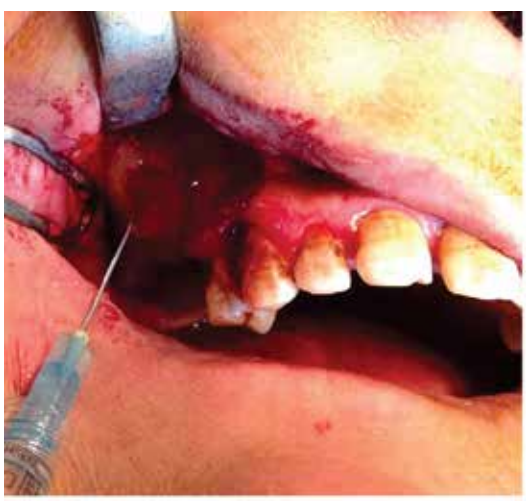

Figure 15. Augmentation of the sinus cavity with bioactive glass material mixed with non-cross-linked HA. Lateral coverage of the augmentation site was made by using cross-linked HA gel.

On radiographic examination 5 months postoperatively, particulated structure of the graft material was not seen and radio-opaque structure resembling the newly formed bone was observed (**Figure 16**).

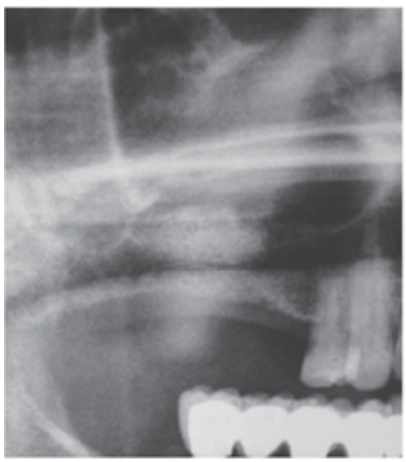

Figure 16. On the radiographic examination 5 months postoperatively, radio-opaque structure resembling the newly formed bone was observed.

Two implants (Oxy Biomec SRL, Colico, Italy) of 4, 5 × 10 mm were placed (**Figure 17**).

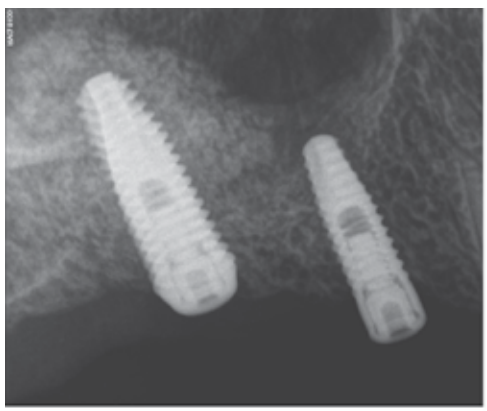

Figure 17. Placement of the implants.

The implants were surgically exposed and the prosthetic procedures were performed.

5.4. Covering of the autologous bone graft recipient sites (as a barrier membrane)

A 54-year-old female patient was admitted due to the difficulties in eating secondary to edentulousim of her lower left posterior mandible. According to her medical history, she

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was under steroid therapy due to lupus erythematosus. Clinically and radiographically, the corresponding area was extremely thin and it was decided to perform a ramas grafting procedure prior to implant placement. Under local anesthesia, a full thickness flap was raised, the recipient site and the ramus area were exposed, a bone block of 10 × 15 mm was harvested by using piezotome (Variosurg, NSK, Japan). Decortication of the recipient site was made by using round burr and the bone block was adapted and secured via three titanium screws. In order to avoid soft tissue ingrowth into the existing minimal gap between the bone block and the alveolar bone, the entire surface of the bone block was covered with cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) (**Figure 18**).

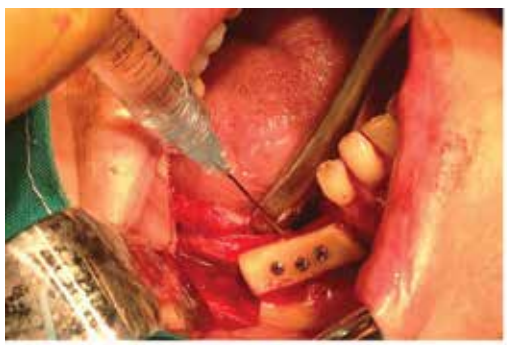

Figure 18. In order to avoid soft tissue ingrowth into the existing minimal gap between the bone block and the alveolar bone, the entire surface of the bone block was covered with cross-linked HA gel.

The postoperative period was uneventful. Three months postoperatively, radiological examination showed successful healing at the grafted site (**Figure 19**) and two implants were inserted into the grafted site (**Figure 20**).

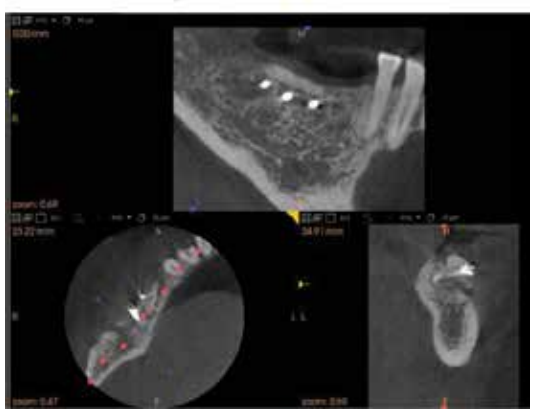

Figure 19. Three months postoperatively, radiological examination showed successful healing at the grafted site.

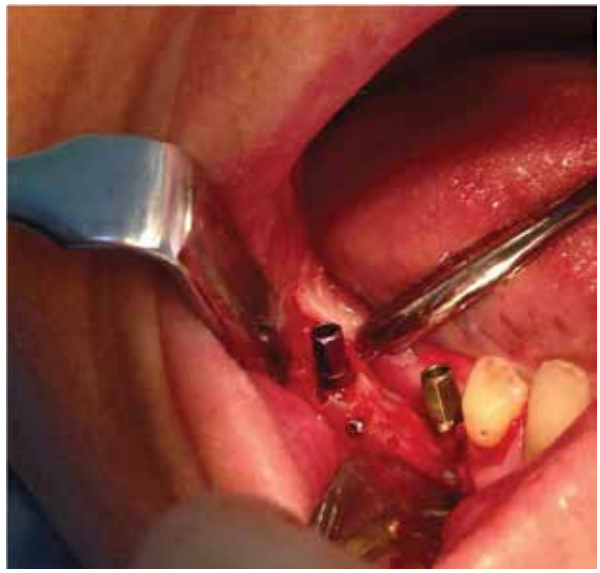

Figure 20. Two implants were placed into the grafted site.

5.5. Ridge splitting

A 44-year-old female patient was admitted due to the difficulties in eating. Clinically and radiographically, her left posterior mandible area was extremely thin and it was decided to perform a ridge splitting procedure prior to implant placement (**Figure 21**).

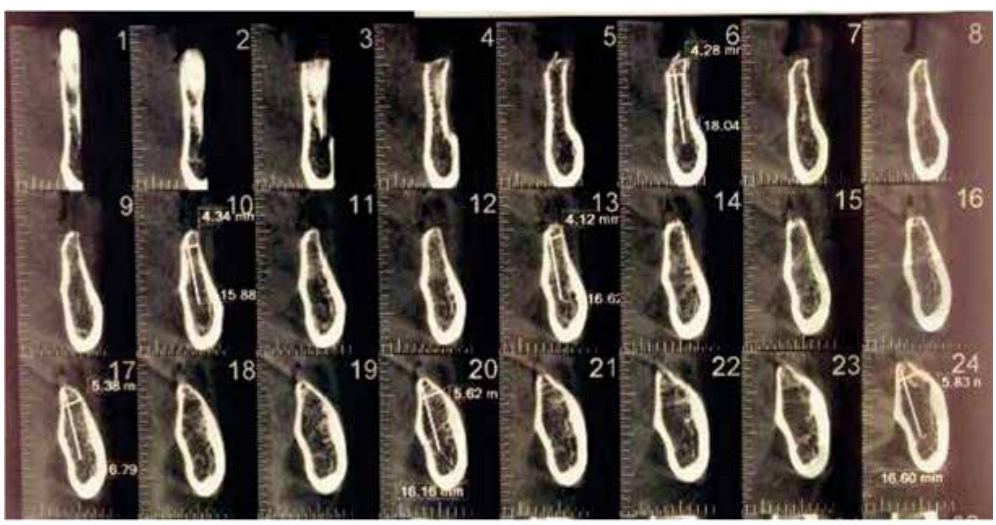

Figure 21. Radiographically, the corresponding area was extremely thin.

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Under local anesthesia, a full thickness flap was raised, the recipient site and the ramus area were exposed, the alveolar ridge was decorticated and then splitted via osteotomes (**Figure 22**).

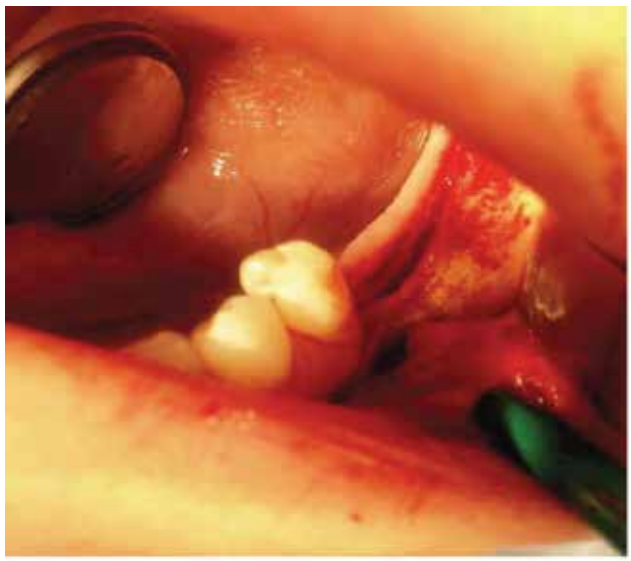

Figure 22. The alveolar ridge was split via osteotomes.

A bone spreader was used to prepare the implant sockets (**Figure 23**).

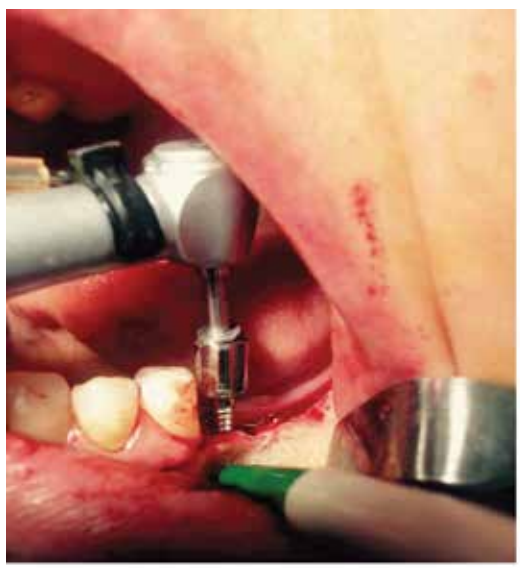

Figure 23. Bone spreader was used to prepare the implant sockets.

Two implants (Bone Trust, Medical Instinct Zahn Implantate, Bovenden, Germany) were inserted into the grafted area (**Figure 24**).

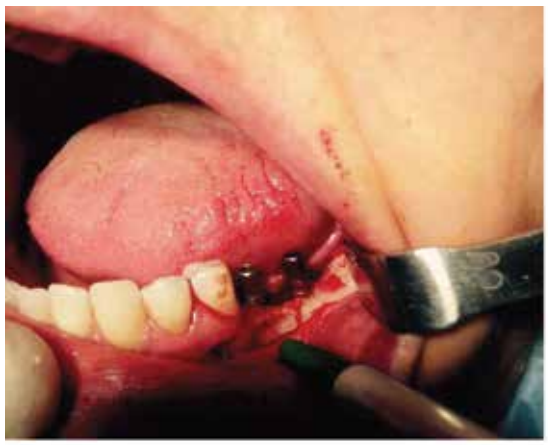

Figure 24. Two implants (Bone Trust, Medical Instinct Zahn Implantate, Bovenden, Germany) were inserted into the grafted area.

The gap between the splitted fragments were grafted with bioactive glass bone graft material (Leonardo, Naturelize, Hirschberg, Germany), which we had mixed with non-cross-linked HA (Tissue Support Hyaluronic Acid Liqui Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) (**Figure 25**).

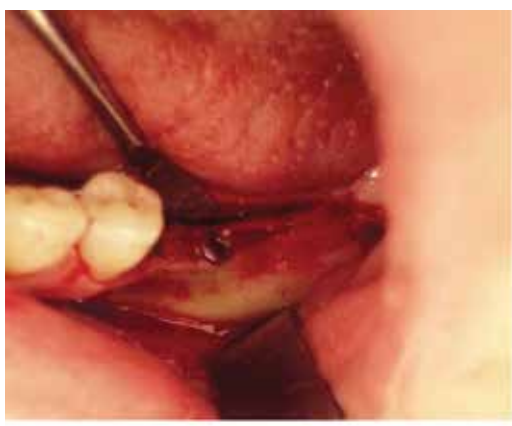

Figure 25. The gap between the splitted fragments were grafted with bioactive glass bone graft material (Leonardo, Naturelize, Hirschberg, Germany), which we had mixed with non-cross-linked hyaluronic acid (Tissue Support Hyaluronic Acid Liqui Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany).

In order to avoid soft tissue ingrowth into the existing minimal gap between the bone block and the alveolar bone, the entire surface of the splitted area was covered with cross-linked HA

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gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) (**Figure 26**). The postoperative period was uneventful.

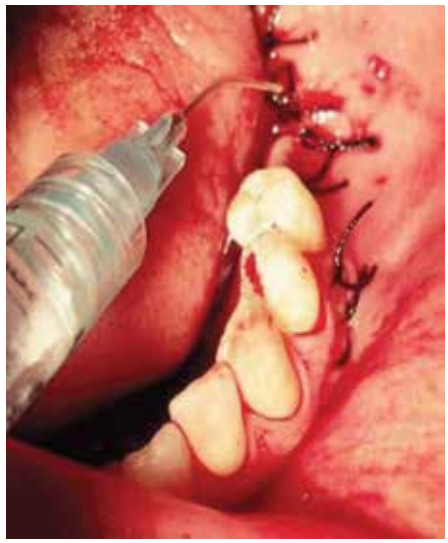

Figure 26. In order to avoid soft tissue ingrowth into the existing minimal gap between the bone block and the alveolar bone, the entire surface of the splitted area was covered with cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) before and after primary closure.

5.6. Filling of the bone defects following removal of oral lesions

A 64-year-old male patient was admitted due to swelling of his upper edentulous right maxilla. Radiographically, a radio-opacity resembling a residual root tip surrounded by a radiolucency was observed (**Figure 27**).

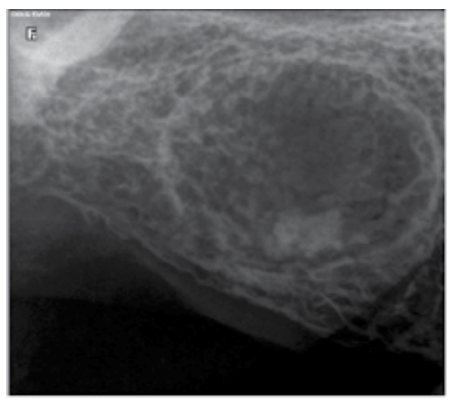

Figure 27. A radio-opacity resembling a residual root tip surrounded by a radiolucency.

Under local anesthesia, a full thickness flap was raised, the corresponding area was exposed (**Figure 28**) and the cyst was curetted.

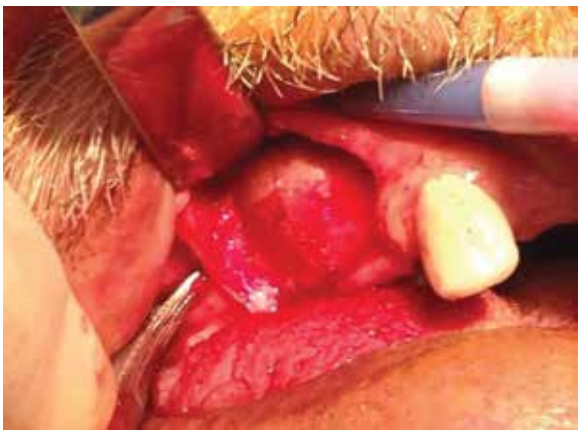

Figure 28. Surgical exposure of the cyst.

The cavity was filled with a bioactive glass bone graft material (Leonardo, Naturelize, Hirschberg, Germany), which we had mixed with non-cross-linked HA (Tissue Support Hyaluronic Acid Liqui Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany) extra-orally and the lateral coverage of the augmentation site was made by using cross-linked HA gel (Flex Barrier Hyaluronic Acid Gel, Hyadent Bioscience Gmbh, Ransbach-Baumbach, Germany). On the radiographic examination 2 months postoperatively, particulated structure of the graft material and radio-opaque structure resembling the newly formed bone were observed (**Figure 29**).

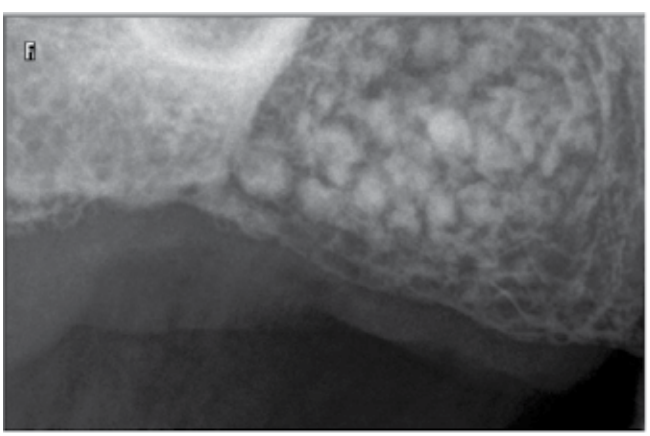

Figure 29. Two months postoperatively, radiological examination showed successful healing and particulated structure of the bone graft material.

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The patient underwent implant surgery 3 months after cyst removal (**Figure 30**).

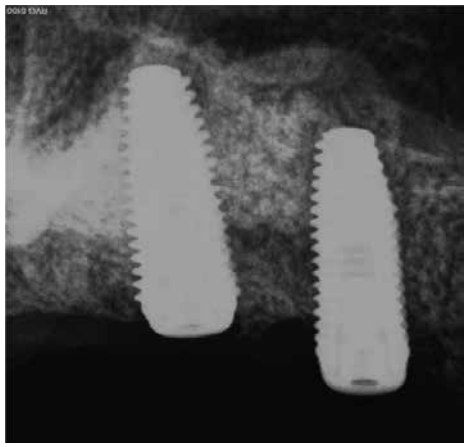

Figure 30. The patient underwent an implant surgery 3 months after cyst removal.

Two implants (Oxy Biomec SRL, Colico, Italy) were placed into the grafted site. As can be seen from our clinical outcomes, HA is a highly promising material for improving therapeutic outcomes for oral implantology.

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Section 9

Management of Oral Fistulas

Chapter 16

Management of the Oroantral Fistula

Guhan Dergin, Yusuf Emes, Cagrı Delilbası and Gokhan Gurler

Additional information is available at the end of the chapter

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Abstract

Communication between the maxillary sinus and oral cavity is a common complication in oral surgery. It results mainly from maxillary premolar and molar extractions when the sinus floor is close to the tooth apex. It can also occur after an infection involving the maxillary teeth, invasion of the sinus cavity by a cyst or carcinoma, trauma, the Caldwell-Luc operation, or other dentoalveolar or implant procedures. Openings smaller than 2 mm may heal spontaneously, whereas larger openings require surgical treatment. An oroantral fistula (OAF) may develop as a complication of dental extractions, as a result of infection, or as sequelae of radiation therapy, trauma, and removal of maxillary cysts or tumors. Various techniques have been examined for the closure of oroantral communications. However, the most common question is how to provide better healing of the defect area and the donor site. In this chapter, etiology, clinical features, medical and surgical managements of OAFs, and advantages and disadvantages of different closure methods of closure techniques are discussed in this chapter.

Keywords: oroantral fistulas, maxillary sinus, flaps, oral surgery, oral cavity

1. Introduction

An abnormal connection between the oral and antral cavities is defined as an oroantral communication (OAC). OAC between the maxillary sinus and oral cavity is a common complication in oral surgery, resulting mainly from premolar and molar extractions when the sinus floor is close to the tooth apex and separated by a thin bony lamella [1–3]. In physiologic circumstances, maxillary sinus mucosa thickness ranges from 1 to 7 mm [4, 5] but in some cases, when the bony floor of the antrum is resorbed by periapical infections or cysts the risk of an

OAC increases. It can also occur after an invasion of the sinus cavity by cysts and tumors, maxillofacial surgical procedures such as indirect or direct sinus lifts, dentoalveolar-grafting operations or corrective surgery such as orthognathic surgeries. OACs can also occur due to trauma [1, 3]. Epithelialization of a communication between the oral cavity and the maxillary sinus forms a pathologic tract, which is called an oroantral fistula (OAF). Various techniques have been described for the closure of OAFs. However, the question is how to provide better healing of the defect area and the donor site. In this chapter, etiology, clinical features, and medical and surgical management methods of OAFs are discussed.

2. Etiology

The most common cause of the OACs is the extraction of the posterior teeth, which have their roots in close relationship to the maxillary sinus. Even though earlier studies have pointed to the second premolars as the highest risk of OAC during extraction [6], later studies have reported that the molar teeth have their roots in the closest proximity to the sinus floor [7–10]; Güven [11] has stated that in his study, second molar extraction followed by first molar had the highest risk. OACs as a result of tooth extraction are the most common in the third decade of life and encountered mostly in adults with few posterior teeth, in which the maxillary sinuses are enlarged. Due to their underdeveloped small maxillary sinuses, the risk of OAC during extraction is very low in children. General consensus is that the OACs must be closed within 24–48 h to prevent fistula and sinusitis [12, 13].

Infections, cyst-, and tumor-removal operations performed in the posterior maxilla and trauma can also lead to the formation of an OAC. OACs can be encountered following a sinus augmentation procedure due to infection of graft material or an improper incision during the operation. Nedir et al. [14] reported the formation of an OAC after the failure of a dental implant in the second molar region. The implant, which was placed 10 years after a sinus-lift procedure and the loss of osseointegration, led to the removal of the implant, causing an OAC. Maxillary osteonecrosis due to the use of bisphosphonates can cause sinusitis and OAF, and when indicated in these patients, the removal of the necrotic bone may cause an OAC [15].

3. Clinical findings and diagnosis

Air and fluids passing into the nose and mouth are the main clinical findings following the formation of an OAC. The clinician may see blood bubbles in the defect or the patient may sense the leakage of air when blowing while nostrils are closed. Usually, patients complain of an unpleasant salty discharge into the mouth from the opening, odor, and reflux of fluids and foods into the nose from the mouth or leakage of air, which sometimes makes it difficult to smoke. Patients may also experience resonance of their sound and speech problems if the defect is large. Suctioning of the socket may create a hollow sound that shows communication. Sinus membrane can be sometimes intact. Therefore, great attention should be paid during the exploration of the perforation with probing or suctioning methods that may lacerate the sinus membrane, which may sometimes be intact [16, 17].

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The presence of one or more of these mentioned symptoms could be the indicator of an OAC or a fistula, while some patients may not show any of these findings if the passage is too small or closed by a large polyp. To validate clinical findings, the clinician needs to radiologically examine the site via a panoramic radiograph or a computed tomography (CT). Dental tomography gives clear data about the perforation and its size if the defect is closed by a polyposis or a granulation tissue [18].

4. Management of OACs/fistula

As almost all of posterior teeth have the risk of OAC, the clinician must evaluate the patient thoroughly prior to extraction. The relationship between the maxillary teeth apices and the maxillary sinus, cortical thickness of the sinus floor, apical granulomas, and cysts, which may have caused the sinus floor resorption, should be evaluated radiographically. After the extraction, it is safer if wound edges are well approximated and stabilized with sutures if the surgeon suspects a small perforation. Larger perforations may be closed with local flaps [1, 19, 20].

An accidental small perforation during a dentoalveolar surgical intervention, such as drilling in implant surgery, apicoectomy of maxillary teeth, and excision of cysts and tumors, can be repaired intraoperatively if the sinus is not infected. The surgeon should be careful not to close the defect with the excessive tension of the tissues, which may enhance the risk of postoperative wound dehiscence [21].

The main goal of the clinician in the management of OAC/fistula is the closure of the defect and prevention of oral bacteria and food debris penetrating the sinus. These oral contaminants may infect the sinus or induce inflammation, which may cause impaired ciliary function, problems of sinus areolation, congestion, and sinusitis. But before the closure of OAF, symptoms associated with inflammation in the sinus such as persisting pus discharge from OAF, malodor, nasal congestion and discharge, and postnasal drip should be eliminated medically with antibiotics, frequent antral irrigations, and decongestants. Patients should be carefully monitored and should be assessed often if the OAC or fistula has any acute sinusitis symptoms. Regardless of the chosen technique, two main points should be taken into account. First, sinus infection must be treated with adequate nasal drainage. This can be obtained by Caldwell-Luc procedure with nasal gastrostomy or endoscopic sinus surgery. Second is decreasing congestion by nasal decongestant and sterile saline water to obtain natural drainage and areolation from ostium. Avoid using long-term topical nasal decongestants that may cause rebound nasal congestion [16, 22].

5. Surgical management of OAFs

The preference of the technique to close an OAC depends on the size of the defect (which is sometimes difficult to estimate clinically), the health of the surrounding tissues, the health of

the maxillary sinus, and the time of diagnosis. Also, postoperative prosthetic planning (e.g., dental-implant planning) should be taken into consideration [19, 23].

Success of the closure of an OAC, or an OAF, is closely related to the health of the involved maxillary sinus. If the drainage of the antrum via mucociliary transportation is impaired and osteomeatal complex is obstructed, a combined approach to the OAC may be necessary [23]. Even though an open approach to the maxillary sinus was used for a long time (Caldwell-Luc operation), functional endoscopic sinus surgery in combination with an intraoral closure technique is currently the treatment of choice in these patients [10, 21, 24].

The closure of the OAFs rarely requires a bony reconstruction except in patients with cleft repair or implant rehabilitation. When intraoral donor sites are insufficient, extraoral sites such as calvarial or anterior iliac crest may be used. Various authors previously described a variety of techniques for the closure of OACs. Agarwal [24] et al. have proposed the suturing of platelet-rich fibrin rolls to the communication site even though they did not mention their indication criteria for this technique. Noel et al. [17] used a pedicle nasoseptal flap in a patient who had previously undergone radiotherapy. The patient they described had an opening of 10 mm, which was closed successfully. The use of allogeneic materials or xenograft or alloplastic materials and the placement of a third molar tooth or a dental implant into the defect have all been proposed for the treatment of OACs. But all these methods are rarely used in the literature and are replaced with soft-tissue management techniques [16].

Several surgical techniques for OAF closure have been introduced in the literature. Buccal and palatal flaps are commonly used methods, while the other local flaps are mostly variations of the two techniques. Distant flaps such as the buccal pedicle fat pad, tongue, and temporal muscle flaps are also used techniques to close OAF. The size and localization of the defect, the presence of acute or chronic infection in the sinus, and the absence of sufficient vestibular depth or keratinized tissue surrounding the defect are all determinately important factors for the preference of surgical technique to close the defect. Additionally, during planning of the flap design, the surgeon should take into account whether it is immediate or delayed, whether there is thick and healthy tissue surrounding the defect, and whether the patient is healthy or medically compromised [16].

5.1. Buccal approach

5.1.1. Buccal advancement flaps

Buccal advancement flaps are among the most commonly used techniques for the OAC closure. This is due to the simplicity of the technique. Even though the literature states that OACs can heal spontaneously when the defect size is smaller than 1–2 mm, this may not be true in every small defect. [8, 11, 25, 26]. Some studies have even reported the spontaneous healing of OACs up to 5 mm size [8]. When there is infection in the communication site and the communication remains open for an extended period of time, this may lead to the formation of an OAF. Due to these facts, most surgeons may prefer buccal advancement flaps as the first treatment of choice even in small communications where closure may be possible by simple suturing [27].

Rehrman's flap and Môczár flap are the two most commonly used buccal advancement flaps. These two flaps may also have disadvantages when compared to simple suturing, because the reflection of a mucoperiosteal flap may result in swelling, and also requires the dentist to have proper training to perform this operation. Another disadvantage of the buccal advancement flap is the risk of losing the depth of the vestibular sulcus, even though the Môczár flap results in less vestibular sulcus flattening according to Vowern [8].

There are flapless closure methods which are simply the placement of resorbable materials into the socket such as oxidized cellulose [28]. These materials maintain a closure by stabilizing the blood clot in the socket. It must be kept in mind that there are currently no generally accepted guidelines to choose the method of closure. This is the reason why these flapless techniques are very commonly used by general practitioners due to their simplicity, which do not require extensive surgical skill. Even though some studies show these simple methods are as effective in obtaining closure as the buccal advancement flap, these studies are not always considered reproducible in terms of the method of analysis of the complications [27, 28]. It is generally not possible to know the exact size of the opening in the sinus floor without reflecting the flap. Therefore, dentists must be careful when deciding to use the flapless techniques and must keep in mind that the defect may be larger than they think it is. A plain radiograph (periapical film or orthopantomograph) can give an idea about the defect size. When an OAC occurs, success rate is very high when immediate closure is obtained. This rate drops significantly when the closure is performed secondarily [1, 29]. Infected tissues, apical cysts, and foreign bodies must be removed from the socket in case they may prevent healing [1, 11, 26].

To perform the buccal flap, two vertical diverging incisions are made at the mesial and distal ends of the socket. The incisions must extend beyond the defect and must lie on healthy bone. After elevation of the mucoperiosteal flap, the gingival edges of the socket are de-epithelialized by a sharp instrument. Then, the flap is positioned palatally and primary closure is obtained by multiple sutures. An apical periosteal release of the flap can sometimes be necessary. Following surgery, an antibiotic should be prescribed. Surgeons may sometimes prescribe postoperative nasal decongestants. When a fistula with sinus infection is present, the infection must be treated first. Some authors recommend daily irrigation of the perforated antrum by antibiotic solutions prior to surgery [30].

Falci et al. [30] have described a modification of this technique in a patient with OAF. They have sutured together the mucosal margins of the fistula prior to the reflection of the buccal flap. Then, the buccal flap was pulled over this sutured site and tucked under the palatal flap, which was elevated simultaneously with the buccal flap.

The main disadvantage of this simple and safe technique is the weak perfusion of the flap, which may lead to failure in the closure of large defects. Yalçın et al. [12] recommend this technique be used for smaller defects. As mentioned earlier, this technique may lead to a flattening of the vestibular sulcus, and in edentulous patients, a secondary vestibuloplasty may be required. In edentulous patients, a palatal flap technique can be preferred especially if the alveolar ridge is severely atrophied. In their study of 23 cases, Yaçın et al. have performed the buccal flap in 10 patients, and a loss of vestibular depth was observed only in 2 patients at the end of 6 months.

Buccal advancement flaps can be safely preferred in dentate patients with no alveolar resorption and a bony defect of less than 5 mm size in the sinus floor for the immediate closure of the OAC. Buccal flaps can be used in edentulous patient also if the fistula is on the buccal side of the alveolar crest [12]. Despite an initial successful closure, both the patient and the surgeon must be aware that there is always a risk of a recurring OAF formation [21]. Neuschl et al. [31] have reported a very rare complication, in which the duct of the parotid gland was iatrogenically sutured into the maxillary sinus during the closure of an OAC using a buccal flap.

5.1.1.1. Technique

After the fistula tract is excised, the trapezoidal buccal mucoperiosteal flap is reflected and the lateral wall of the maxilla exposed. Horizontal releasing incisions are made at the most apical part of the flap, which helps to move and extend the flap to the defect without tension. After flap release, it can be advanced upon the defect and sutured to palatal tissue (**Figure 1a–c**).

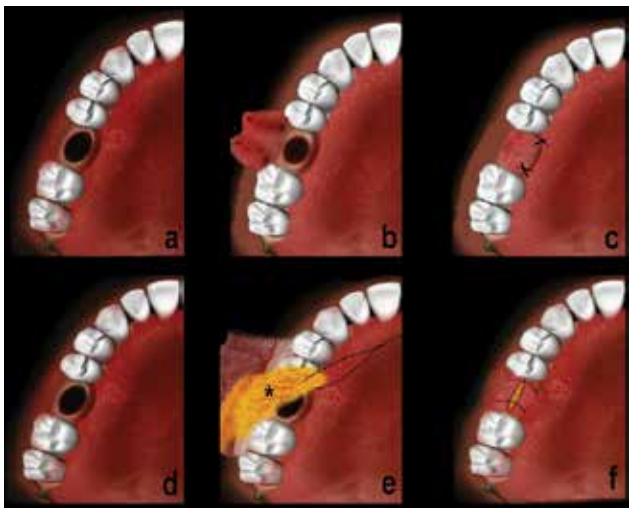

Figure 1. Illustration of buccal flaps: (a—c) Buccal advancement flap technique, (d—e) buccal fat-pad flap.

5.1.2. Buccal fat-pad flap

Another common buccal approach to OACs is the use of the buccal fat pad (BFP). The use of the BFP for the treatment of OAFs was first simply an alternative to the closure of small- and medium-sized defects; however, nowadays it is also used for large bony defects. The technique was first described by Egyedi in the late 1970s [32], and its use became more common following a study by Tideman et al. [33], which showed that the BFP epithelialized within 3–4 weeks. The technique is used not only in the treatment of OAFs but also in the reconstruction of medium-sized maxillary defects (as in tumor excisions) [34–36]. The buccal fat-pad flap has 10 ml of fat tissue. The fat pad is approachable through the oral cavity, and the buccal and temporal branches of the maxillary artery, facial artery, and superficial temporal artery perfuse

it sufficiently, which make it a good choice as a material to close medium-sized defects of the maxilla [37].

The incision is similar to the buccal flap technique. In order to expose the BFP, the periosteum is incised behind the zygomatic buttress. The fat pad is manipulated by pressing extraorally below the zygomatic arc. Then, the fat pad is sutured to the palatal tissues, covering the fistula.

The success of the technique has been reported by many authors. Mohan et al. used the technique in 11 patients for various pathologies including pleomorphic adenoma excision, and observed partial loss of the graft only in one patient and hematoma in another patient [38]. Martin-Granizo et al. [39] have reported the successful application of the technique in their patients, even in those who have had partial necrosis of the flap. Nezafati et al. [40] performed a study comparing the buccal flap and buccal fat-pad flap techniques, and concluded that both were similarly successful. Infection of fat tissue is the main problem of this technique.

5.1.2.1. Technique

A circular incision with a 3-mm margin is made around the defect (**Figure 2**), the epithelial tract with any inflammatory tissue was completely excised, and two vertical incisions extended into the vestibule are made.

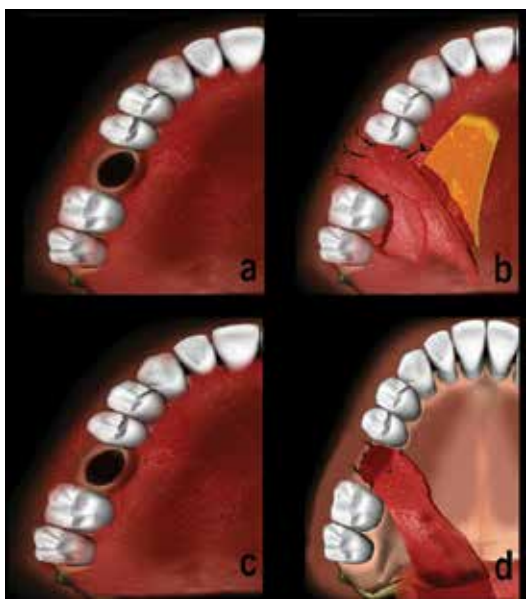

Figure 2. (a—c) Illustration of full-thickness rotational flap, (b—d) tongue flap technique for closure of large oroantral defects.

The trapezoidal buccal mucoperiosteal flap is reflected and the lateral wall of the maxilla is exposed. Buccal fat is exposed with a vertical incision through the periosteum posterior to the zygomatic buttress. Applying external pressure below the zygomatic arch helps herniation of

the BFP. Following gentle extraction, the BFP is released with meticulous dissection via scissors. After gaining sufficient length, the flap is advanced to the oral defect from behind the molar teeth and was fixed on the fistula by absorbable polydioxanone sutures over the fat pad, which was gently advanced over the bong defect (**Figure 3**), and secured with sutures (**Figure 4**). Finally, the mucoperiosteal flap is replaced in its original position with sutures inserted between the BFP and the buccal flap. The fat is left exposed in the mouth without any coverage (**Figure 1d–f**).

Figure 3. Excised fistula wall at the right maxillary molar region.

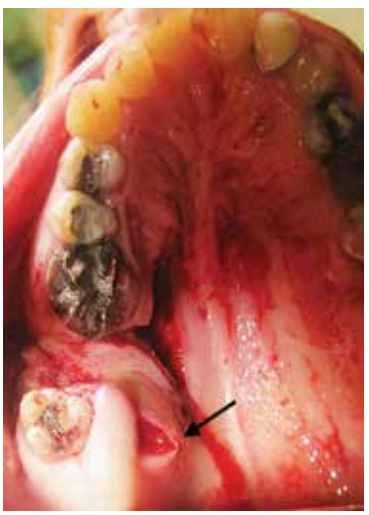

Figure 4. Dog-ear formation at full-thickness rotational flap at rotating point (marked with arrow).

5.1.3. Palatal flaps

The palatal flap has different forms that can be classified as straight-advancement, rotation-advancement, hinged, pedicle island, anteriorly based, submucosal connective tissue pedicle, and submucosal island flaps [1, 10].

5.1.4. Full-thickness palatal flap

Full-thickness rotational palatal flaps have the advantages of keratinized tissue, preservation of vestibular depth, and sufficient blood supply for better healing. However, the thick keratinized tissue limits rotation if the OAF is located at the maxillary tuberosity [1, 41]. With full-thickness palatal rotational flaps, at the pivot point, kinking or "dog-ear" formation can occur during flap rotation, which may compromise the vascular supply, predispose the patient to venous congestion, and impair the adaptation of the distal part of the flap. Kruger suggested that a V-shaped section be excised in the area of the greatest bend in the flap to prevent folding and wrinkling [3]. With full-thickness palatal rotational flaps, the technique exposes the bony structure of the hard palate and sometimes is required for re-epithelialization, causing severe complaints such as pain, burning, and edema of the hard palate.[13] There is also a risk of necrosis of the exposed bone at the donor site, especially in systemically compromised patients. Erdogan et al. [42] reported unexpected palatal bone necrosis in diabetics after the use of full-thickness palatal rotational flaps. Using a palatal stent is recommended after palatal rotational flap operations to reduce the edema and to stabilize the flap in its new position [43].

5.1.4.1. Technique

In the full-thickness mucoperiosteal palatal rotational flap technique, the flap design is arranged according to the greater palatine artery. About 1-cm length of additional flap is created to achieve tension-free closure of the fistula on the buccal bony base. Bone defect and

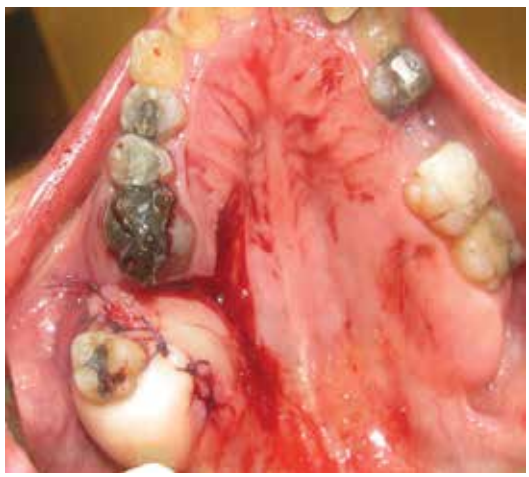

Figure 5. Dog ear was removed and adapted to defect and closed with full-thickness rotational flap.

angle of rotation are the key points in determining the width of the flap. Kinking formation at the rotation point of the flap should be evaluated; if dog-ear formation exists, it should be excised to obtain a better adaptation (**Figures 2 a–c** and **3–6**).

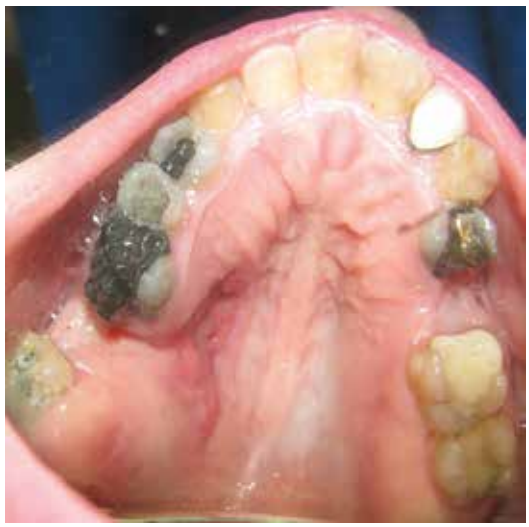

Figure 6. Healing of the fistula. After closing with FTPF (full-thickness palatal flap).

5.1.5. Modified submucosal connective tissue flap

Dergin et al. [44] reported a modified submucosal connective tissue flap for OAF repair. With a modified connective tissue flap, there is no folding or dog-ear formation because of its elasticity and it allows for better manipulation and adaptation in the closure of an OAF in the second and third molar region. In modified connective tissue flap techniques, all of the donor sites were closed with mucosal flaps that covered the underlying bone. In the modified connective tissue flap, no palatal acrylic plate is required postoperatively.

Ito and Hara [45] modified the pedicle palatal flap by developing a submucosal connective tissue pedicle flap, and reported that dividing the flap into an upper mucosal layer and underlying connective tissue layer overcomes the problem of bone exposure at the donor site. Healing at the donor site occurs within 1 month. The technique owes its success to the good blood supply and mobility without tension [46]. The only disadvantages of this technique are the difficulty of the dissection, possibility of injuring the blood supply, and the need for an experienced surgeon [45, 46].

The connective tissue-based pedicle palatal flap technique described by Dergin et al. [44] differs from the technique of Ito and Hara [45] in the design of the mucosal flaps and the preparation of the submucosal tunnel. Preparing a long, narrow mucosal flap carries a risk of necrosis and infection of the overlying mucosal flap at the donor site.

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5.1.5.1. Technique

In the modified palatal connective tissue flap technique (**Figure 7a**), an H-type window-like incision was made in the palatal mucosa 4 mm from the gingival margins of the molar and premolar teeth, with the medial incision 2–3 mm from the midline. The fistula wall is excised circumferentially and the granulation tissue is curetted (**Figure 8**).

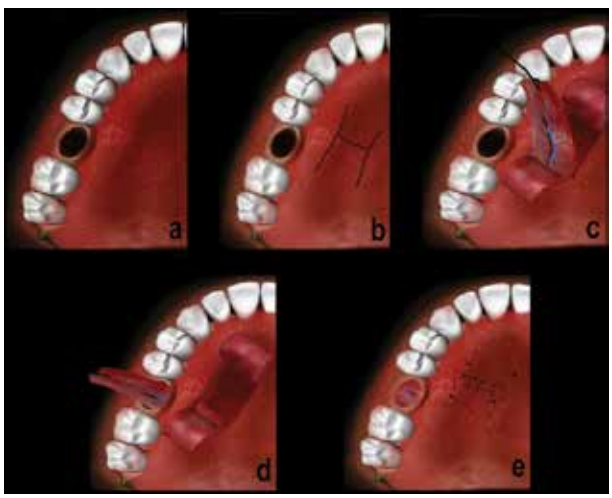

Figure 7. Illustration of the modified connective tissue technique a: excised fistulas wall, b: H incision, c: arterial palatal connective tissue window-like flaps and dissection of arterial connective flap, d: palatal tunnel maneuver, e: suturing.

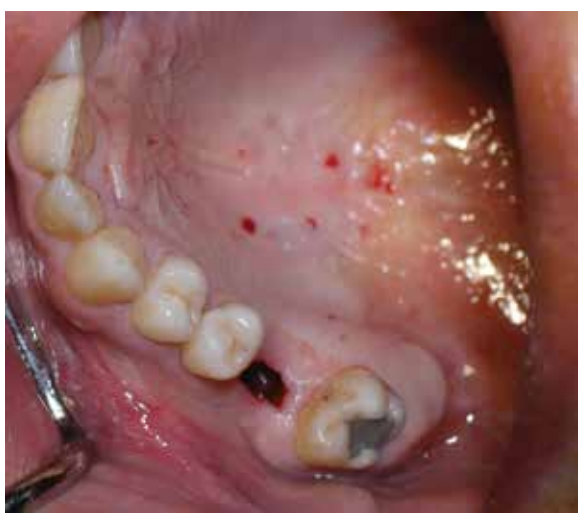

Figure 8. Oroantral fistula with excised fistula wall.

After excising the fistula, the mucosa of the two minor flaps of the H-type window-like incision (**Figures 7b** and **10**) was elevated and separated from the underlying connective tissue without jeopardizing the continuity of the mucosal flap (**Figure 9**).

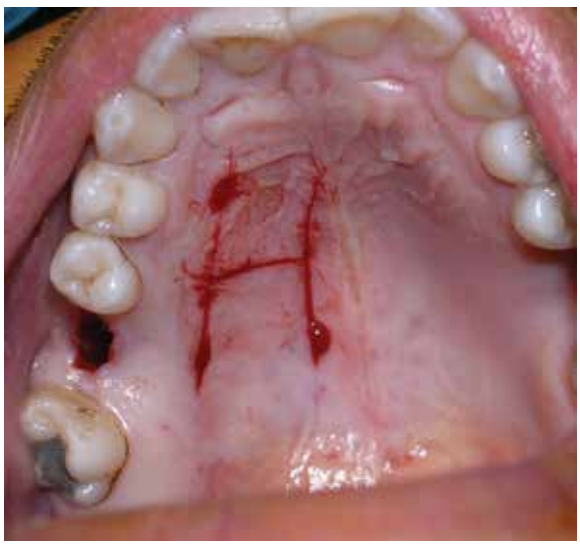

Figure 9. Intraoperative view of H-type incision.

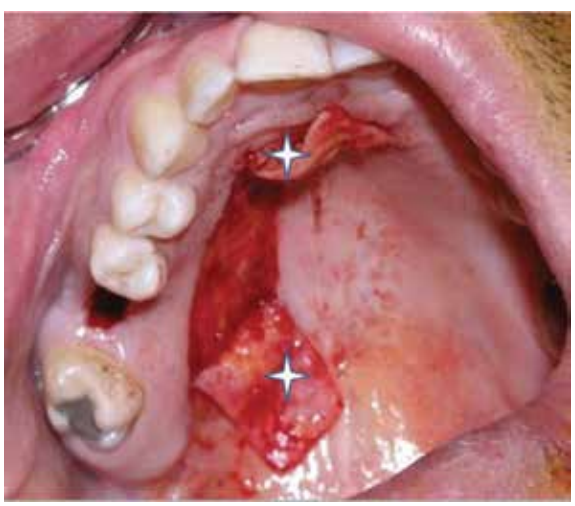

Figure 10. Elevated window-like mucosal H flap (marked with stars).

The underlying arterialized connective tissue was first dissected in the premolar-canine region, where the incisive and greater palatine arteries anastomose (**Figures 7c** and **11**).

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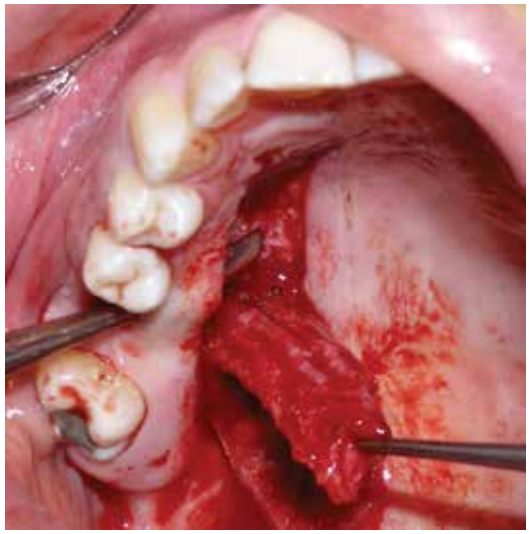

Figure 11. Intraoperative view of the elevated palatal connective tissue flap.

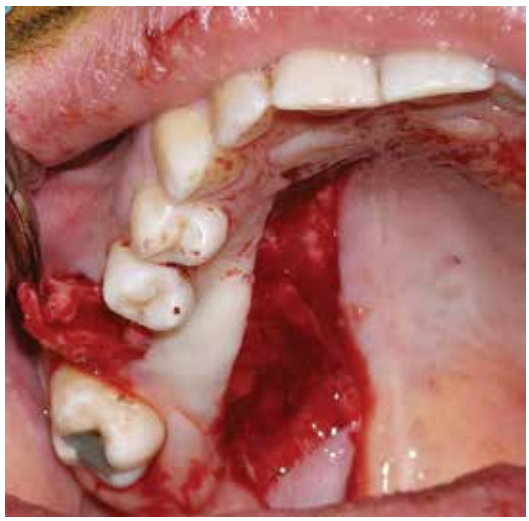

Figure 12. Orientation of the flap passing through the palatal tunnel to the underlying fistula during the operation.

The connective tissue was elevated with periosteum, as in palatal rotational flaps. The rotated flap was passed through a full-thickness tissue tunnel that was previously prepared on the palatal side of the OAF (**Figures 7d** and **12**).

The flap was inserted under the buccal mucosa and sutured with 4/0 polyglycan without any tension. The H-type minor flaps were sutured with 4/0 polyglycan and left for primary healing (**Figures 7e**, **13**, and **14**).

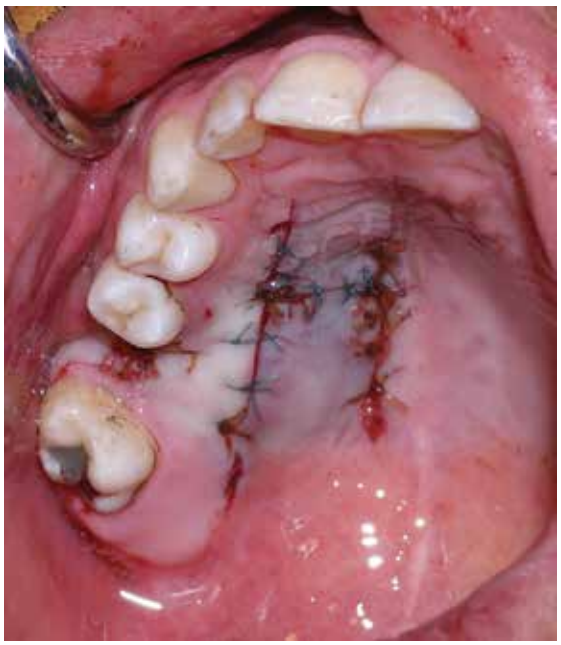

Figure 13. After the minor mucosal flaps were sutured, no area was left for secondary healing.

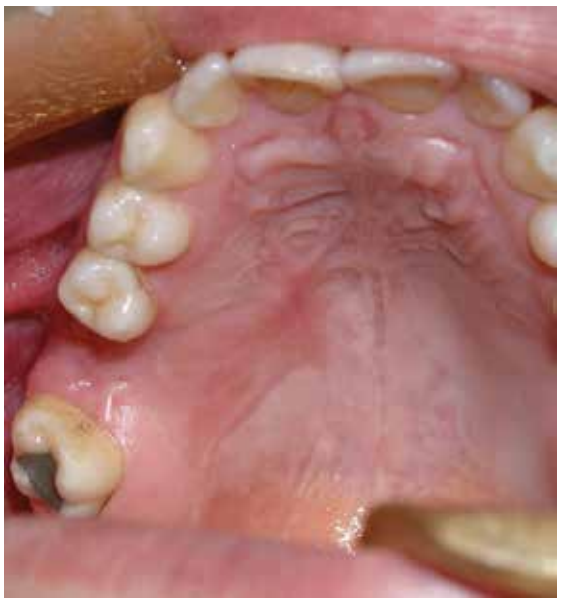

Figure 14. Healing of the fistula. After closing with MPCF (modified palatal connective tissue flap).

5.1.6. Distant flaps

Local flaps are the treatment of choice in most cases of OACs. However, sometimes these flaps may fail, and pedicle flaps from distant sites may be utilized in order to treat especially large defects. These flaps are usually selected from the anatomical sites in close proximity to the defect. Lateral tongue flap has been described as a method for the closure of OAF [47]. Lateral tongue flaps are used for the treatment of defects in the lateral palate and lateral alveolar process, and on the postoperative 14th day, the pedicle is severed [48] (**Figure 2c** and **d**).

The use of the temporalis flap has been described previously for intraoral reconstruction [49–51] and can be used for the reconstruction of large defects of the maxilla, especially following ablative tumor surgery. It is a well-vascularized flap with enough volume for the closure of large defects. The large bulk of this flap can also provide a soft-tissue bed if further bony reconstruction is planned for the defect site in the future. Distant flaps are preferred rarely, compared to local flaps [52].

6. Conclusion

OACs can be successfully treated if diagnosed at the time of occurrence or at an early stage. The size of the defect is an important factor in deciding which technique to use. Small openings can heal spontaneously, but the health of the sinus is an important factor which may lead to an incomplete healing and the formation of an OAF.

The clinician must make the correct diagnosis and decide the correct indication for treatment.

Local buccal and palatal flaps are the most proper for the closure of OACs resulting from dental procedures. However, large defects following tumor resection or trauma may require the use of more refined techniques for successful healing.

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Chapter 17

Treatment of Oral Fistulas

Erol Cansiz, Alper Gultekin, Melek Koltuk and Sirmahan Cakarer

Additional information is available at the end of the chapter

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Abstract

The term "fistula" can be defined as an improper connection between different body compartments. It can occur in different parts of the body. Although, fistulae mostly develop due to untreated chronic infections, traumatic injuries and congenital deformities, specific infections or diseases, and post-surgical healing abnormalities can also cause fistula formation. Although, there is a general classification system made by the World Health Organization to identify fistulae, specifically, in this chapter oral fistulae are divided into four different categories, namely dentoalveolar, oroantral, oronasal and orocutaneous fistulae. The diagnosis and the treatment protocols for oral fistulas are described using this specific classification and with additional new techniques introduced for the correction of the lesions. Conventional surgical methods also are summarized. The importance of the radiological examination is emphasized and the practitioners are informed of possible complications.

Keywords: fistula, dentoalveolar, oroantral, oronasal, orocutaneous

1. Introduction

The term "fistula" can be defined as an improper connection between different body compartments. They may be acquired or congenital and can occur in different parts of the body. Although, fistulae mostly develop due to untreated chronic infections, traumatic injuries, congenital deformities, specific infections or diseases, post-surgical healing abnormalities may also cause fistula formation.

The diagnosis and treatment of oral fistulas are well-described subjects in the literature. However, they are often misdiagnosed by dentists and physicians as cutaneous lesions or

non-odontogenic infections. The diagnosis of an oral fistula may be challenging because of the complex oral anatomy, and it requires the aid of radiological, microbiological, and/or pathological methods. In addition, detailed history taking and clinical examination are key factors for the diagnosis of oral fistulas.

Although, dentoalveolar, oroantral, oronasal, and orocutaneous fistulae are the most frequent types related to the oral cavity, an oral fistula may vary depending on the origin. Consequently, determining the source of the fistula is the first step in treatment, which must be directed primarily to the underlying cause.

The present chapter reviews classification, etiological factors, diagnosis, and the treatment of the four major fistula types related to the oral cavity. The chapter also focuses on the different surgical techniques of treatment of fistulae according to the clinical causes of the lesions.

2. Types of oral fistulas

2.1. Dentoalveolar fistula

Dentoalveolar fistula is a pathological pathway between the oral cavity and alveolar bone. They mostly occur as a result of infected cysts, mandibular or maxillary fractures, periodontal inflammation, necrotic teeth, and trauma. But the most common causes are pulpal necrosis and apical periodontitis [1–4]. On the other hand, differential diagnosis should include osteomyelitis, syphilis, tuberculosis, noma, actinomycosis, trauma, pyogenic granuloma, and neoplasia [2, 3].

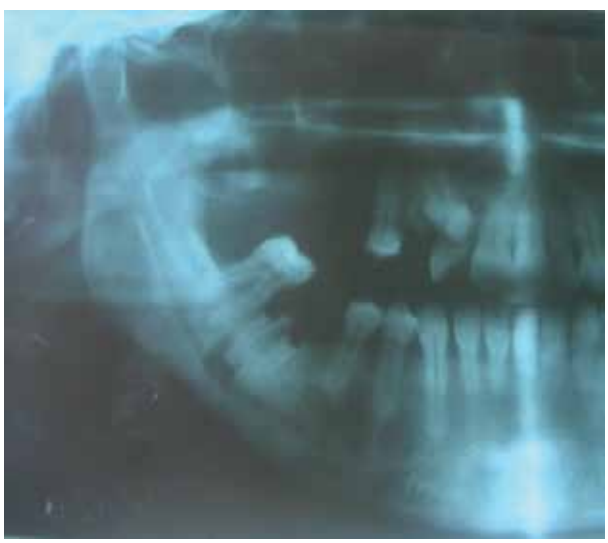

Figure 1. Periradicular infection due to necrotic teeth.

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Necrotic teeth usually have a history of trauma, tooth decay, periodontal disease, or orthodontic tooth movement. When the dental pulp becomes necrotic, the root canal becomes a potential site of bacterial colonization. At this stage if the treatment is not performed, infection spreads into the periradicular area, resulting in apical periodontitis and follows the path of least resistance in the bone and soft tissue (**Figure 1**).

The location of muscle attachments and the position of root tips determine the direction and the location of the fistula to the surface. Once the periradicular infection spreads and the cortical wall of the alveolar bone is perforated, the fistula follows the interstitial spaces. Although most of the periradicular infections end within the loose connective tissue compartments and cause abscess formation, they can reach to the skin or the oral mucosa and induce fistula formation (**Figure 2**).

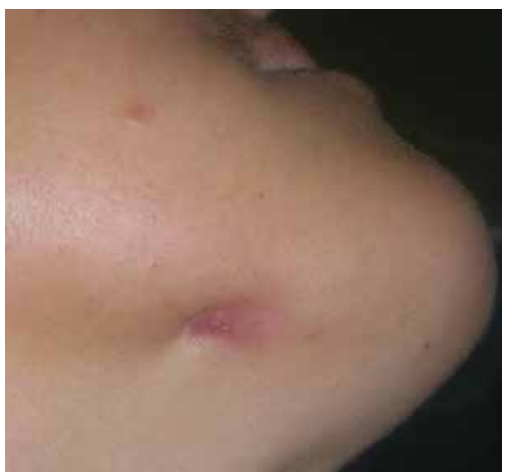

Figure 2. Extaoral view of the patient in **Figure 1**. Extraoral fistula formation.

The direction of a fistula differs for the maxilla and mandible due to the location of muscle attachments, root inclinations, and the localization of the root tips.

In the maxilla, generally, fistula tract formation from incisors exit on the labial vestibular mucosa, but lateral incisors may exit the palate due to distal inclination of the root. On the other hand, canines may lead to canine fossa abscess without fistula formation, if the root apex position is above the levator anguli oris attachments. For the molars and premolars, the fistula may occur in the buccal sulcus or spread to the buccal space. However, infected roots located palatally can lead to palatal abscess or fistula formation. In addition, they can easily spread to the maxillary sinuses that can lead to odontogenic maxillary sinusitis especially if there is a close relationship between the sinus floor and root apices [5–7].

In the mandible, periradicular infection of the incisors mostly leads to labial vestibular fistula formation. On the other hand, if the root tip of the canine is located under the mentalis muscle attachments, the fistula may spread to the subcutaneous area and can lead to an orocutaneous fistula formation on the chin (**Figures 3** and **4**) [8].

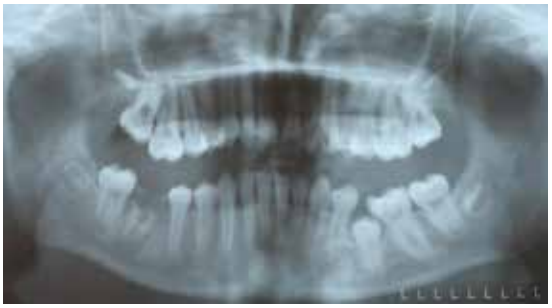

Figure 3. Necrotic mandibular incisors.

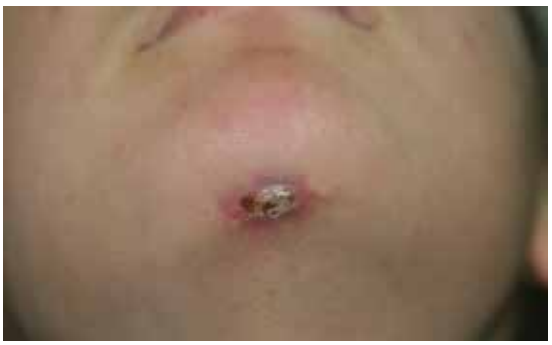

Figure 4. Fistula formation on the chin due to necrotic mandibular incisors.

The location of the mylohyoid muscle is an important factor in submental and submandibular abscess formation. The root tips of mandibular premolar and molar teeth are mostly located

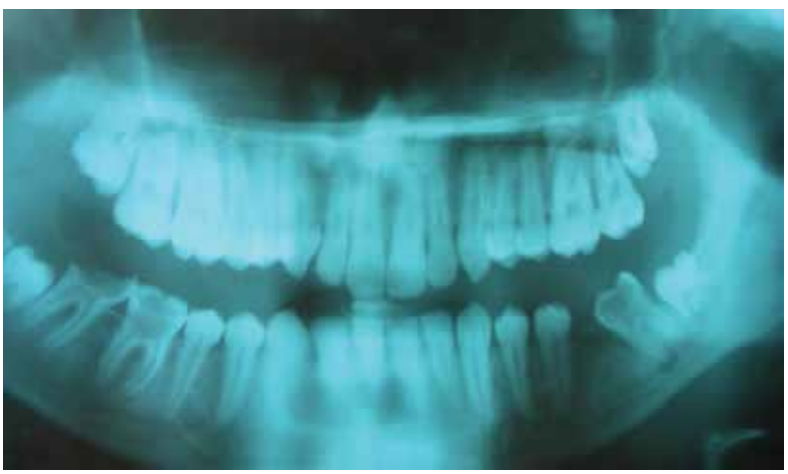

Figure 5. Submandibular abscess due to periradicular infection of the molar tooth.

below the mylohyoid muscle attachments, and the periradicular infection of these teeth spreads mostly under that muscle directly to the submental or submandibular spaces (**Figures 5** and **6**).

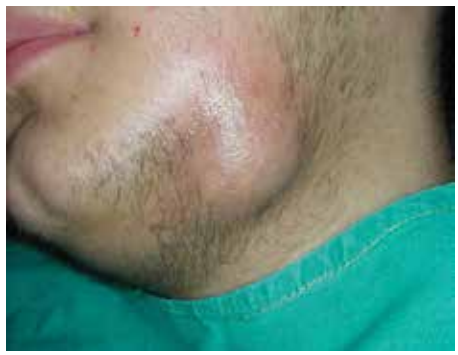

Figure 6. Radiograph of periradicular infection of the left mandible.

On the other hand, if the root tips are located at the buccal side of the mandibular alveolar bone, they may lead to fistula formation in the vestibular sulcus. However, if the buccally positioned root apices are located below the buccinator muscle, they may lead a buccal space abscess or orocutaneous fistula formation at the base or the mandibular [9].

Although the diagnosis of a dentoalveolar fistula is not challenging generally, they can be misdiagnosed by dentists and physicians. Furthermore, they may be mistaken for a neoplastic lesion because of their clinical appearance. For the determination of the origin, periapical and panoramic radiographs are helpful. On the other hand, Cone Beam Computed Tomography (CBCT) or MRI can be used when conventional radiography is insufficient. Placement of radiopaque material, such as gutta percha, during radiologic examinations is a useful method for the determination of the length, the localization of the fistula tract, and identifying the tooth causing it.

The principle of managing such lesions is to remove the source of the infection. Prescribing an antibiotic drug for the treatment of a dentoalveolar fistula is a common mistake. The removal of the infected pulp tissue by appropriate endodontic treatment is a simple and effective treatment modality for eradicating periradicular infection in a very short time. On the other hand, if there is a periradicular granuloma formation, apical resection in addition to endodontic treatment may be required. However, if there is no indication for endodontic treatment or apical resection, extraction of the infected tooth and curettage of the periradicular region may be required.

2.2. Oronasal fistulas

A tract unnaturally leading from oral cavity to the nasal cavity is defined as oronasal fistula (ONF). Although tumor resections are the major reason of ONF formation, these openings are also seen frequently as a complication of cleft lip and palate reconstructive surgery. After the

velopharyngeal insufficiency, fistulae are the second most common complication of cleft palate operations.

Fistulae that occur after primary repair of cleft palate appear in specific locations, such as intersection between the hard and soft palate or junction of the primary and secondary palate. They can also take place anywhere along the line where the cleft was situated (**Figures 7** and **8**).

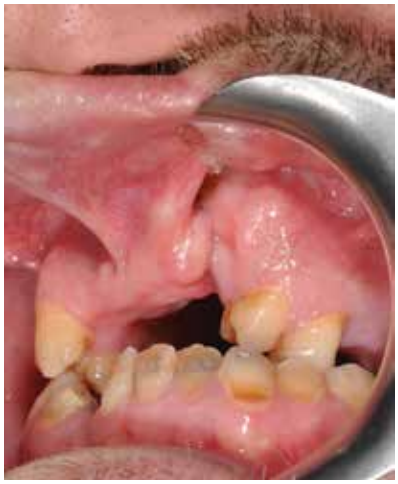

Figure 7. Nasoalveolar and palatial fistula formation after cleft surgery.

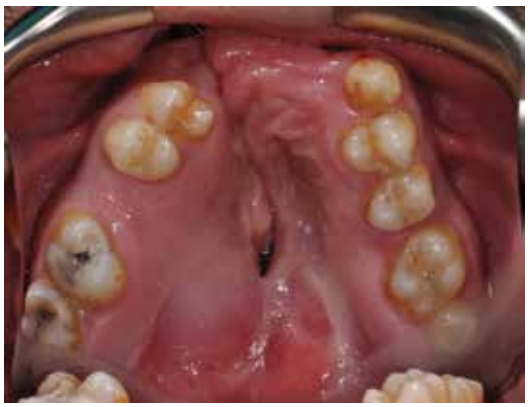

Figure 8. Nasoalveolar and oronasal fistula formation after cleft surgery.

Predisposing factors that may cause fistulae include cleft type, surgical technique, surgeon's inexperience, patient healing capability, and the age at the time of palatoplasty [10].

The more severe the cleft, the more likely a fistula may occur [11]. The incidence of formation of a fistula is higher in complete primary and secondary palate cleft reconstruction site rather

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than isolated clefts. Similarly, a fistula is more likely in a patient who has bilateral cleft lip and palate (40.9%), in comparison to unilateral clefts (16.9%) [12]. The Veau classification is a classification that divides the cleft lip and palate into four groups according to cleft severity [13]. Patients with a Veau IV cleft (complete bilateral soft, hard, and/or lip and alveolar ridge cleft) are more prone to develop an ONF [14].

Numerous causes lead to fistulation in cleft patients after surgery, such as infection, hematoma formation, flap necrosis, inadequate occlusion, or excessive tension on the cleft repair site. Infection can be caused by the absence of oral hygiene or upper respiratory system infection. Hematoma formation between the nasal and oral layers that may generate excessive tension at the wound site also causes infection. Needless trauma during repositioning the flap, lacerations, or any movement that disrupts perfusion of the flap can lead to flap necrosis. Especially, later wide cleft closure operations, using inadequate material, absence of multilayer seal, or faulty suturing can cause openings in the surgery area. Trying to seal the gap with inadequate tissue produces excessive tension and leads to failure [15].

ONFs cause problems due to their size. Food remnants pileup into the fistula track can cause bacterial accumulation, which leads to mucosal inflammation and bad breath. Fistulae also cause an excessive formation of thick phlegm or mucus, which can be seen in an airway or cavity and regurgitation of fluid into the nasal cavity during eating and drinking. Nasal secretions can seep into the oral cavity and create a bad taste, malodor, and cause poor oral hygiene. Even a fistula as small as 4.5 mm can cause speech problems such as hypernasal resonance, deficiency of pressure consonants, audible nasal air escape, and retracted tongue positioning while articulating speech sounds [16]. Air escapes create socially undesirable sounds that corrupt speech quality and intelligibility. Additionally, these functional problems add to social problems because of bad breath and the nasal fluid leakage. These issues can emerge after unsuccessful closure of the clefts, just like that in unoperated cleft patients.

ONFs are classified according to size such as small (1–2 mm), medium (3–5 mm), and large (>5mm) [14]. Smith et al. [17] created a classification system based on anatomic location of fistulae and named it the Pittsburg classification. In this classification system, ONFs are divided in to seven different subgroups such as; (1) bifid uvula, (2) soft palate, (3) soft and hard palate junction, (4) hard palate, (5) primary and secondary palates junction, (6) lingual alveolar, and (7) labial alveolar [17]. ONF is also described by shape as pinpoint, oval, slit, and total dehiscence [18]. The most common fistula type is the small size and slit-shaped ones. Small fistulas can remain asymptomatic, but it should be considered that after orthodontic treatment to expand the alveolar arch, fistulae can enlarge and become symptomatic.

2.2.1. Closure of ONFs

2.2.2.1. Non-invasive procedures

Symptomatic fistulae that can cause speech problems or nasal regurgitation should be reconstructed as early as possible. The small ones with minimal problems can be delayed for a couple of years or even be left untreated.

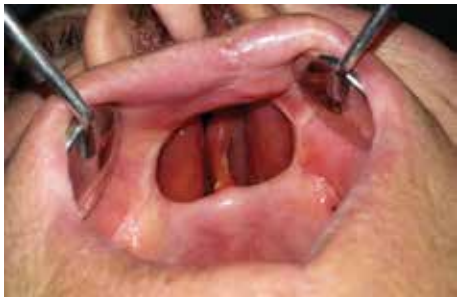

Figure 9. ONF after tumor resection surgery.

Figure 10. Obturator prosthesis.

There are plenty of surgical and prosthetic options for ONF closure. Openings can be managed using obturators/palatal prosthesis. Although use of this prosthesis significantly improves the aerodynamic characteristic of speech with temporary occlusion, obturators should not be considered as final treatment [19]. Some disadvantages of using these prosthesis are dramatic increase in oral bacteria count, rise in the incidence of carries, and chronic gingivitis at the areas where the denture fit is close to the neck of the teeth [20]. Obturator prosthesis should be

Figure 11. Application of an obturator prosthesis after tumor resection surgery.

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considered as a practical alternative for patients who had resective tumor surgery and when surgical procedures are contraindicated (**Figures 9–11**) [21].

2.2.2.2. Surgical procedures

Timing of reconstruction should be at least 6 months after the previous surgery. During the assessment, the amount of scar tissue caused by earlier operation is more important than size and location of the ONF [22]. Sometimes a successful closure cannot be managed because of the presence of this scar tissue. Most of the fistulas can be closed with palatal local tissue transfer. When extra tissue is needed, variable options are available (i.e., free flaps, cartilage grafts, distraction osteogenesis, osmotic tissue expansion, allografts, and bone grafts) [23–27]. Small ONFs can be repaired easily with local tissue. For closure, an adjacent palatal mucoperiosteal flap is raised and slided to the fistula area. This procedure can be performed under local anesthesia.

For large fistulas a tongue flap is a useful option. Tongue flap is a type of myomucosal flap that has many advantages. Abundant tissue for closing defected site, low donor site morbidity, flap is possible in different directions (anterior, posterior, lateral, medial based, and central island flaps), ease of rotation, excellent blood supply, and high success rate are some of these benefits. Besides these advantages, it has some drawbacks such as need to stabilization of the flap, two stage procedure, and 3-week waiting period between flap surgery and division [28].

Tongue flaps are indicated for large ONF repair where there is tissue deficit and when there is a persistent palatal fistula where earlier attempts have been unsuccessful. Thickness of the flap should be at least 6 mm, optimal references are 7–10 mm, and it should include a layer of underlying muscle tissue to ensure its vascularity. The width of the flap should fill the defect and allow movements of the tongue after turnover. The base must be two-thirds or at least the half of the ONF's width to ensure abundant blood supply [19–22].

To lower flap mobility, fixing the tip of tongue to the upper lip or anterior maxillary incisors may be done. Also prefabricated flap retainers or intermaxillary fixation can be used for this aim [29]. After 3 weeks, with a second operation, the pedicle should be divided and the contouring should be done.

Repairing ONF with bone grafts has some significant advantages. Bone tissue helps form continuity and stability on the palate surface and attain its natural contour [30]. Hard tissue supports the oral mucosa above and the alar base beneath [31]. For this purpose, several autogenous donor sites are available, such as anterior iliac crest, scapula, radial forearm, tibia, calvarial bones, and ribs. Iliac crest graft is accepted as the gold standard because of its benefits, such as containing all the three of osteoinductive, osteoconductive, and osteogenic capacity with its corticocancellous structure. While the cortical part provides support, cancellous component contains viable precursor cells that help to form new bone tissue [32]. Based on its advantages, patient's ONF repaired with anterior iliac crest bone grafting. After palatal and buccal flaps are raised, harvested bone is fixed to the related site with mini screws. In control sessions, the patient's vestibular ONF is usually seen to be completely closed (**Figures 12–16**).

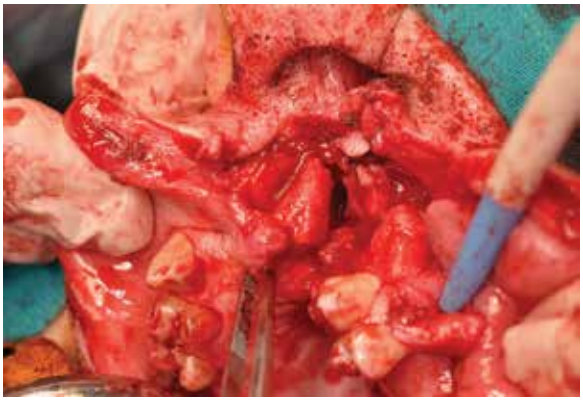

Figure 12. Recreating the defect for the closure of ONF.

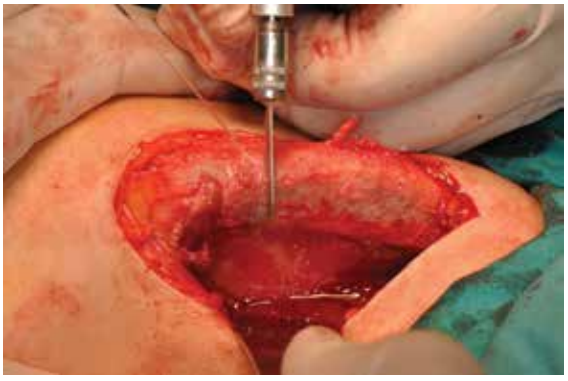

Figure 13. Anterior iliac bone harvesting.

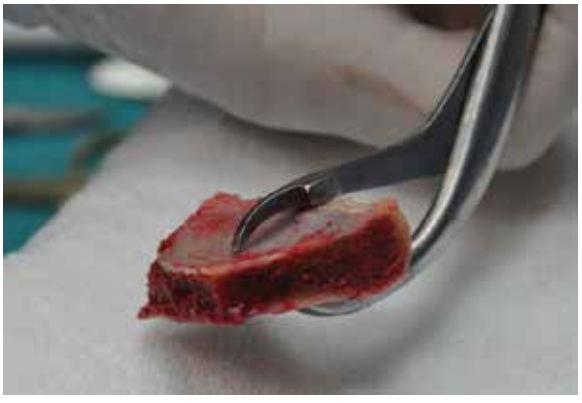

Figure 14. Anterior iliac bone.

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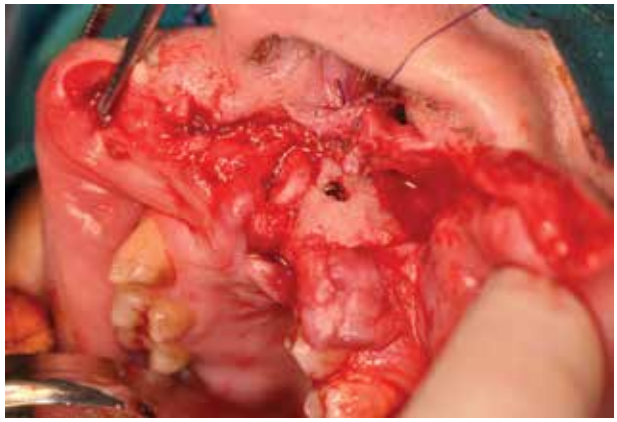

Figure 15. Anterior iliac bone graft placed.

Figure 16. Anterior iliac bone graft for the closure of ONF.

2.3. Oroantral fistulas

Oroantral communications are not rare in dentoalveolar surgery due to close relationship between maxillary posterior region and sinuses. Surgical procedures involving maxillary posterior region, such as cyst or tumor surgeries, impacted third molar operations, removal of ectopic teeth located in the maxillary sinuses, or traumatic extraction of premolar and molar teeth are the main predisposing factors of surgery-related oroantral communications [33, 34]. Generally, there is a thin bone between maxillary sinus floor and posterior teeth, and also, root apices of the maxillary posterior teeth may be located in the maxillary sinuses. Consequently, oroantral communications are very frequent during the extraction of maxillary posterior teeth because of this anatomical proximity [35, 36]. In addition, maxillary sinus floor perforations due to apicoectomy of maxillary premolar and molar teeth are not rare [37, 38].

Although rehabilitation of edentulous patients with dental implants has become popular, the incidence of complications has increased simultaneously with this popularity. Perforation of sinus floor during dental implant surgery or sinus floor augmentation procedures is quite often encountered, and this may induce complications [39, 40]. In addition, maxillofacial trauma is another predisposing factor causing maxillary sinus-related complications. Malunion of dentoalveolar or zygomatic fractures may lead to oroantral fistula formation [41]. Besides the mechanical and iatrogenic factors, chronic or specific infections may cause sinus perforation and oroantral fistula formation. Chronic infection of necrotic teeth or maxillary sinusitis may lead to bone resorption and communication between maxillary sinuses and the oral cavity. On the other hand, some specific infections such as syphilis may cause severe bone resorptions and oroantral communications [42].

If oroantral perforation occurs following surgical procedures or iatrogenic effects, perforation diameter, depth, and the presence of infection around the oral mucosa, alveolar bone and sinus membrane must be evaluated. Although small diameter, non-infected perforations are generally managed using simple surgical interventions such as buccal advancement flaps, more severe cases may require complicated surgical methods such as palatal rotational flaps or bone grafting procedures combined with soft tissue augmentations [43]. If the initial treatment of an oroantral perforation fails and fistula formation occurs, the treatment of the oroantral fistula may require the combination of medical and surgical interventions.

Various surgical methods and approaches have been described in the literature for the treatment of oroantral fistulas and each of them has its specific pros and cons. Although most of the local rotational-advancement flaps are useful to treat small-sized oroantral fistulas, the palatal rotation flap is the most preferred technique in our practice especially if the patient has had a previous unsuccessful fistula closure operation (**Figures 17–20**).

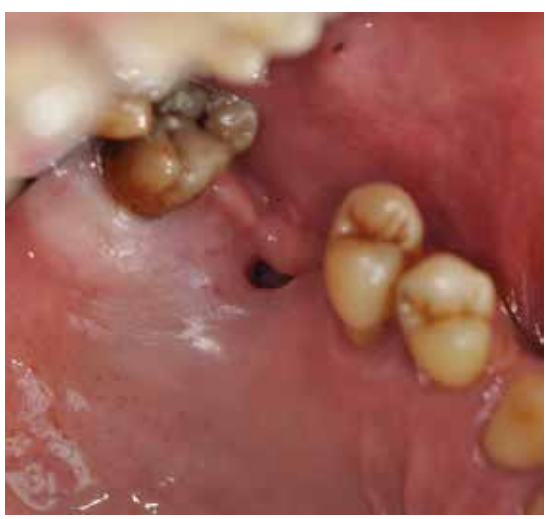

Figure 17. Oroantral fistula.

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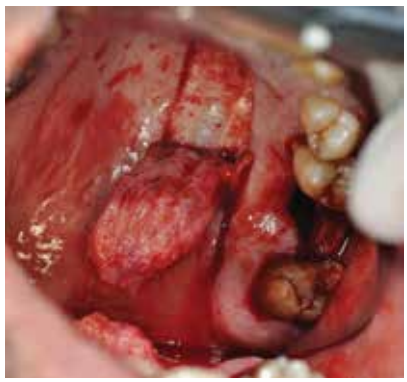

Figure 18. Palatal rotational flap for the closure of oroantral fistula.

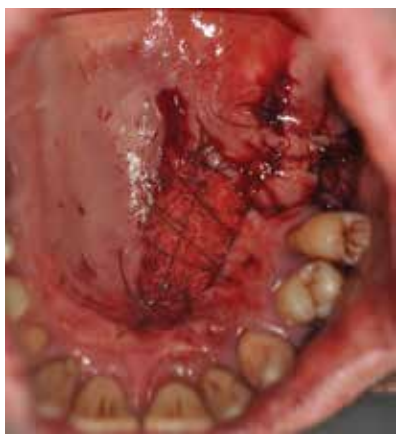

Figure 19. Post-operative appearance.

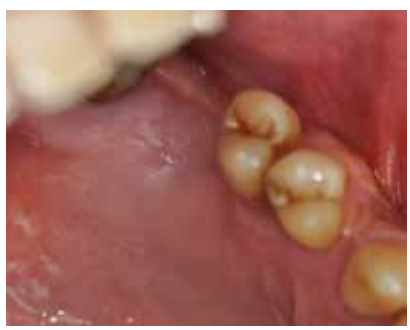

Figure 20. Post-operative appearance after 9 months.

In addition to conventional methods, there are some newly developed alternative approaches for the closure of oroantral fistulas and one of these newly described method is the closure of oroantral fistulae using auricular cartilage [44]. Cartilage is biocompatible, non-absorbable, easily manipulated, structurally durable, non-carcinogenic, readily accessible, resistant to infection, and cost-effective. Failure incidence is low due to the fact that it does not require vascularization to integrate to the recipient site. Additionally, cartilage graft acts as a separating barrier between the sinus membrane and the oral mucosa, which helps maintaining a successful healing.

The standard care for the closure of oroantral fistulae with an autogenous cartilage graft would be the utilization of nasal septal cartilage [45]. On the other hand, auricular cartilage is also a valuable alternative not only because of the lack of significant amount of defect formation at the donor site, but also because of the advantage of being able to harvest a larger graft in size using the auricle of the ear instead.

The operation technique for the closure of oroantral fistulae using auricular cartilage is recently described [44]. In this method, an anterior auricular approach is used and the incision line passes parallel to the semi-circular bulge in between the antitragus and the antihelix. Although scar formation is usually minimal, rarely some post-operative aesthetic complaints of the incision line were also observed due to scar formation. Taking this into account, the method was modified, using a posterior auricular approach. This operation is planned due to the failure of an autogenous bone graft for the closure of an oroantral fistula (**Figure 21**).

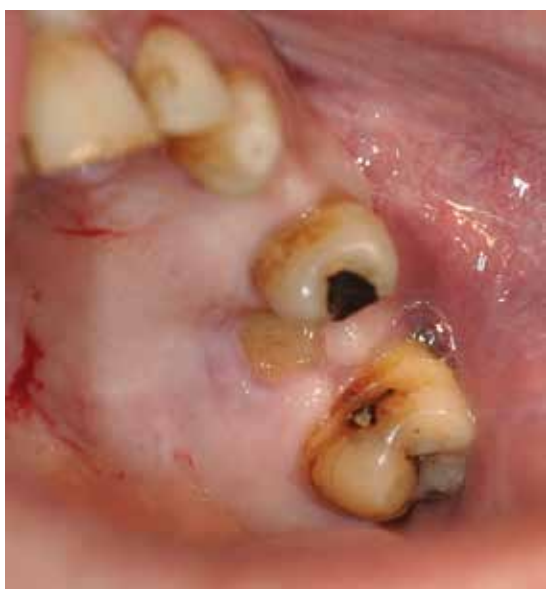

Figure 21. Failed autogenous bone graft for the closure of OAF.

Under local anesthesia, exposed necrotic block graft was removed and the site was cleaned from granulation tissue (**Figures 22** and **23**).

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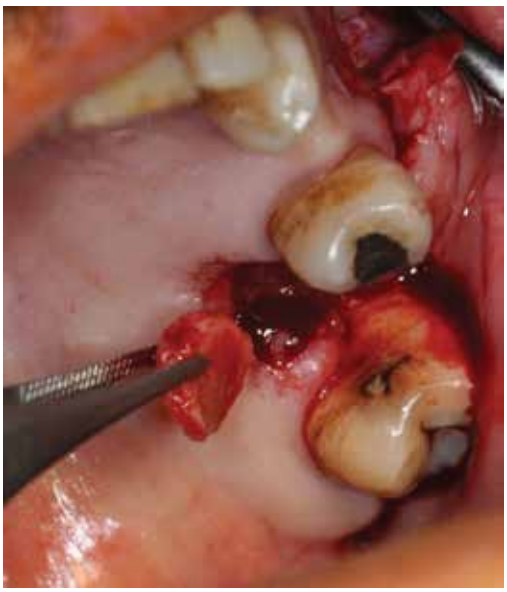

Figure 22. Removal of exposed bone graft.

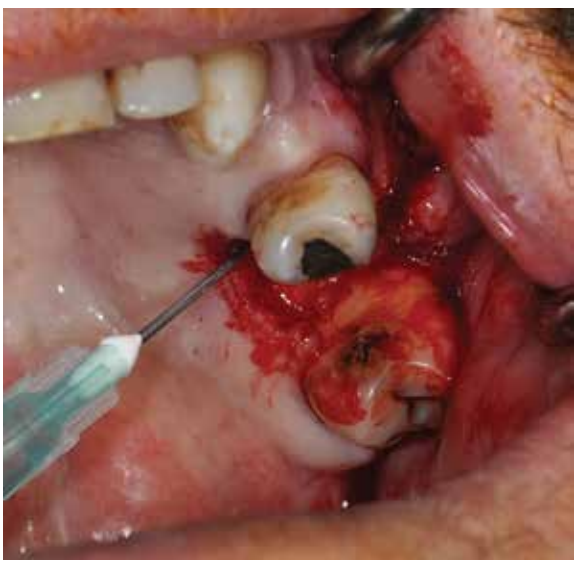

Figure 23. Identifying the OAF following removal of granulation tissue.

A buccal flap was elevated for the preparation of a recipient bed for the palatal rotational flap. Then, the palatal rotational flap was prepared and descending palatal artery was protected during the elevation of the flap. After, tension-free connection of the flaps was controlled by rotating palatinal flap to the buccal site (**Figure 24**).

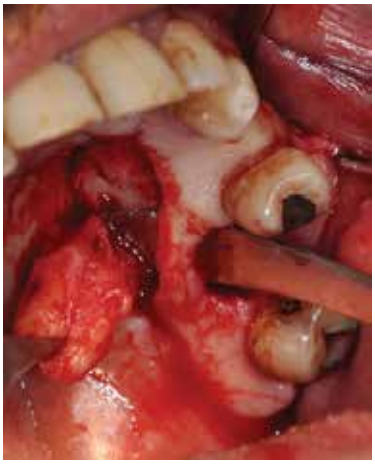

Figure 24. Preparation of a palatal rotational flap.

Following the recipient site preparation, a curved, split-thickness incision following the curvature of the helix on the posterior side of the auricle was made, and the skin overlying the auricular cartilage was gently elevated. Circular incision was made on the auricular cartilage and the graft was extracted by preserving the perichondrium (**Figure 25**).

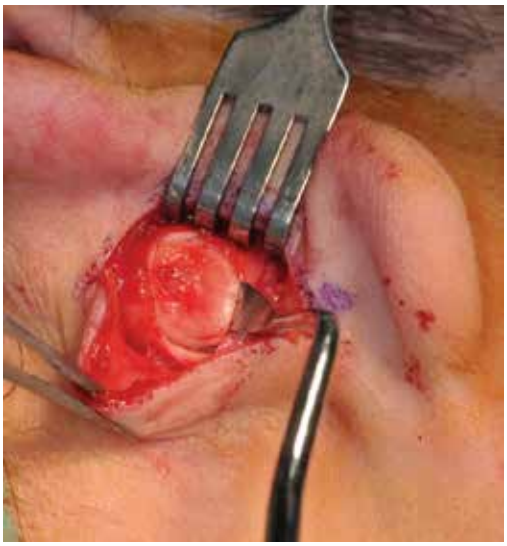

Figure 25. Auricular cartilage graft harvesting by posterior auricular approach.

Finally, posterior auricular skin flap was sutured using 5/0 polyglactin 910.

Auricular graft containing perichondrium was then adapted to the recipient bed (**Figure 26**) and sutured to the bone with 3/0 polyglactin 910 for stabilization.

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Figure 26. Adaptation of cartilage graft to the recipient site.

De-epithelization was achieved on the keratinized layer of the palatal flap by a round diamond bur, and it was rotated under the previously prepared full-thickness palatinal soft tissue tunnel. Finally, the buccal flap and the rotated palatinal flap were joined using 3/0 polyglactin 910 sutures (**Figure 27**).

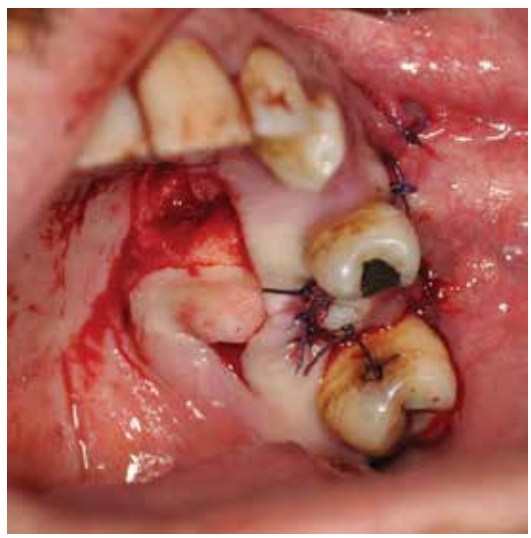

Figure 27. Connection of the palatal and the buccal flaps.

Any complication was not observed during the post-operative period and ideal healing was achieved after 4 months (**Figure 28**).

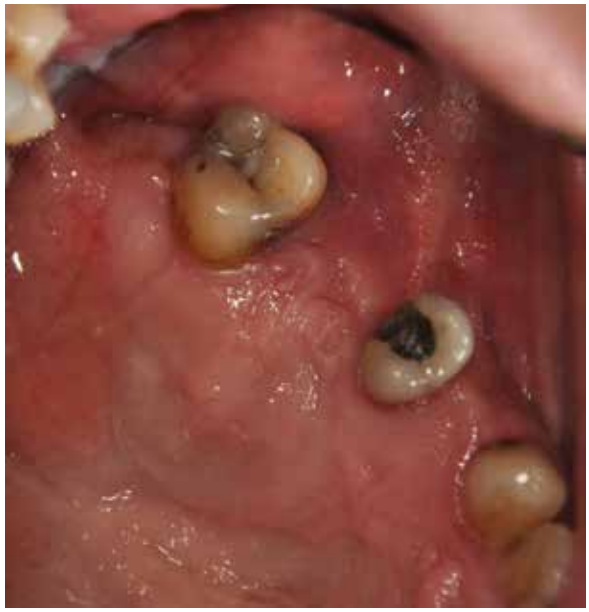

Figure 28. Post-operative appearance after 4 months.

We believe, using this modification in the surgical technique not only improves the aesthetic results but also decreases the resorption rate of the cartilage graft since the perichondrium is well-protected during the harvest of the graft.

2.4. Orocutaneous fistulae

An orofacial or orocutaneous fistula is a pathological communication between the cutaneous surface of the face and the oral cavity. An oral cutaneous fistula leads to esthetic problems due to the continual leakage of saliva from the oral cavity to the face. Malignancy, inflammation, and trauma are the most common causes [46].

The literature does not clearly demonstrate the incidence or treatment of the orocutaneous fistulas. This situation may be explained that the fistulas were not considered as a major complication in OMF practice. On the other hand, the fistulas that do not heal spontaneously may cause discomfort for the patients [46, 47].

This part of the present chapter evaluated the common causes of the orocutaneous fistulas by demonstrating some of the cases which were managed in Istanbul University, Faculty of Dentistry at the Department of Oral and Maxillofacial Surgery. The surgical management is emphasized for practitioners.

Some of the orocutaneous fistulae may be presented due to the use of miniplates or reconstruction plates and screws. The removal of these materials is not a routine procedure, and there are conflicting ideas about removal. **Figure 29** demonstrates an orocutaneous fistula that occurred 5 years after the placement of miniplate and screws in the mandible.

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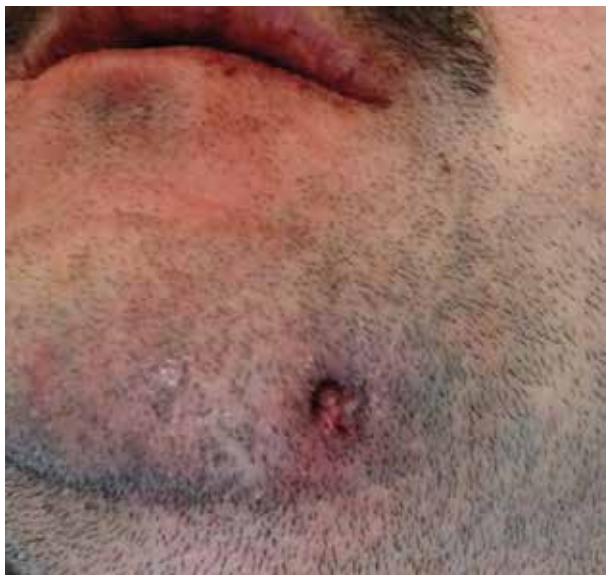

Figure 29. Orocutaneous fistula.

The orthopantomograph demonstrated the plates which were placed 5 years ago for the management of the fractures of the mandible (**Figure 30**).

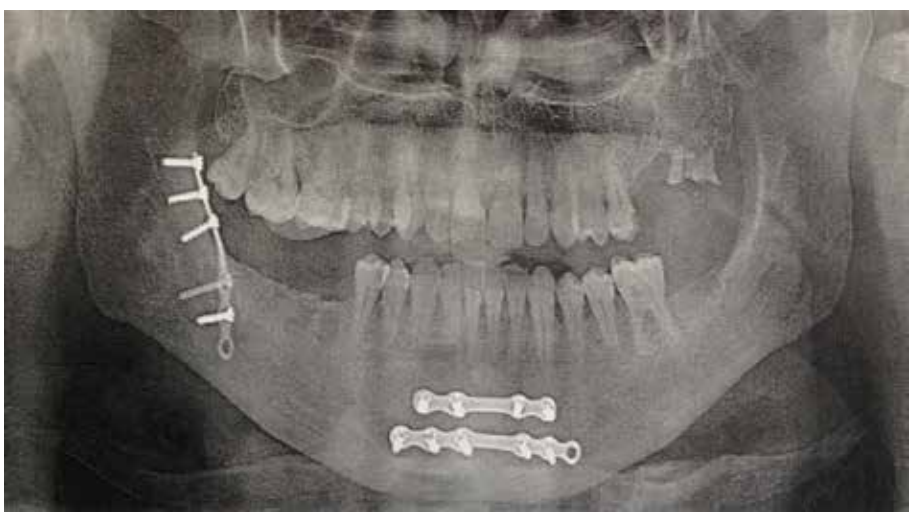

Figure 30. Preoperative orthopantomograph.

All the plates and screws placed at the symphysis were removed, and the infection site was curetted (**Figures 31** and **32**). The patient did not demonstrate any complaint after the operation and the fistula healed.

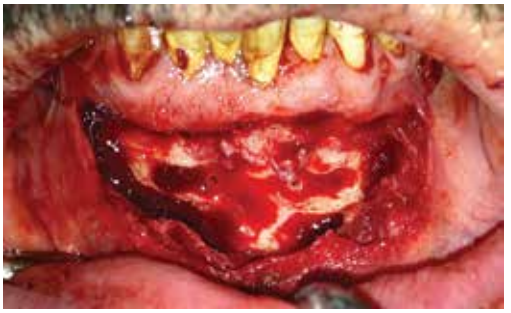

Figure 31. Intraoperative view of the operation site.

Figure 32. Removed plates and screws and excised remnants of the infected site.

Residual lesions of the cysts and the tumors of the jaws may cause formation of orocutaneous fistulae also. The second case is a residual keratocystic odontogenic tumor at the condyle, which causes an orocutaneous fistula formation. A panoramic radiograph showed a multilocular radiolucency with sclerotic margins located in the ramus up to the processes coronoideus and condylaris (**Figure 33**).

Figure 33. Pre-operative orthopantomograph which shows the affected right side of the ramus and condyle.

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Four months later after marsupialization, the lesion was excised under general anesthesia. The definitive diagnosis was reported as keratocystic odontogenic tumor. Ten years after the operation he presented with an extraoral fistula at the right mandibular angle region (**Figure 34**).

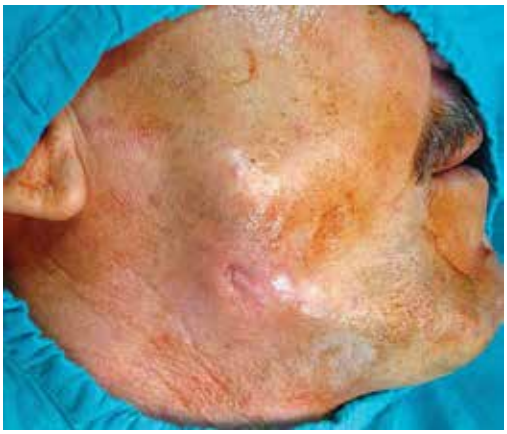

Figure 34. Orocutaneous fistula.

Three-dimensional views demonstrated cortical perforation and the borders of the lesion (**Figure 35**).

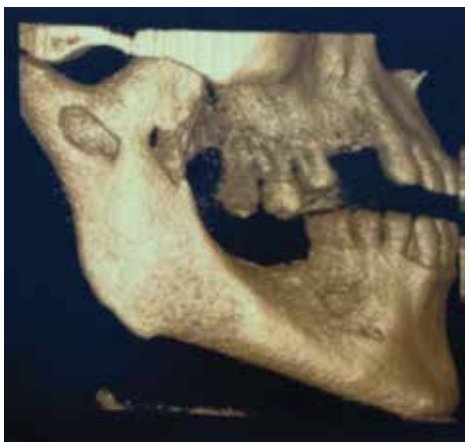

Figure 35. 3D view shows the tumor in the right condyle.

The patient was operated under general anesthesia. Extraoral approach was performed to access to the coronoidal part of the ramus. The lesion was excised (**Figures 36–38**). The definitive diagnosis reported by the pathology department was keratocystic odontogenic tumor. The fistula healed subsequently.

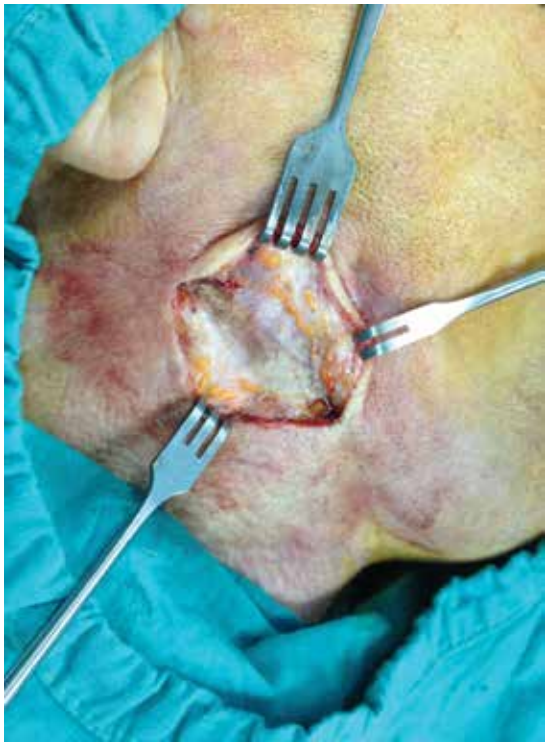

Figure 36. The view of the extraoral approach.

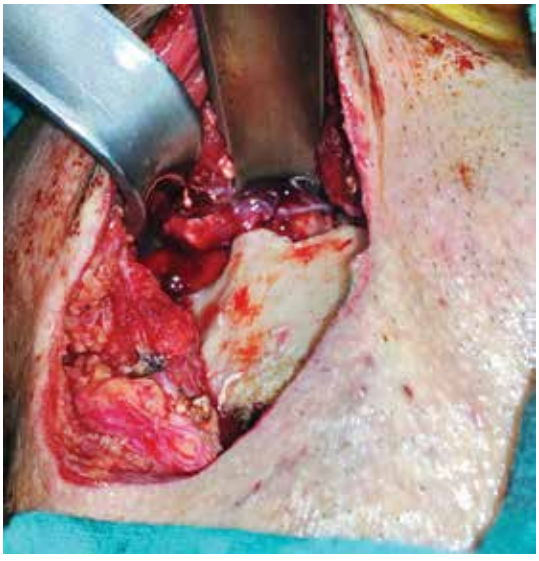

Figure 37. Intraoral view of the lesion.

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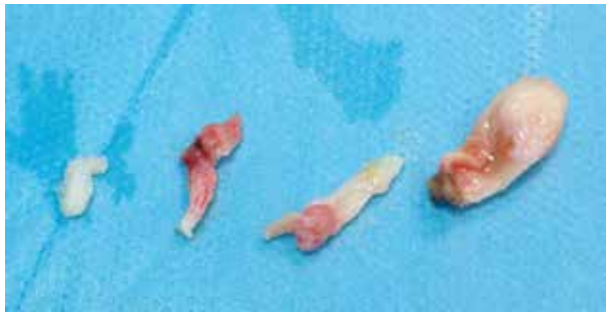

Figure 38. Excised tumor remnants.

Osteoradionecrosis (ORN) of the jaws is one of the most severe and debilitating complications following radiation therapy for head and neck cancer patients. It is a radiation-induced ischemic necrosis of bone with associated soft tissue necrosis, occurring in the absence of primary tumor, recurrence, or metastatic disease. The incidence of ORN ranges from 5 to 15% and is the most frequently noted (>70%) in the first 3 years after completion of treatment. Mandibular ORN is more prevalent when compared to the maxilla due to the relatively poor vascularization and the dense structure of mandibular bone.

Several risk factors have been implicated including tumor stage, tumor infiltration of adjacent bone, preradiation mandibular surgery, radiation modality, tooth extractions, and poor oral health. ORN can also develop spontaneously. Controversy exists over the management of ORN. Conservative measures include antiseptic mouthwashes, antibiotics, sequestrectomy, ultrasound therapy, and hyperbaric oxygen therapy. Surgical management includes more radical procedures with or without the use of conservative measures [48].

The third case demonstrates the formation of orocutaneous fistulas, which occurred after radiotherapy of head and neck cancer. The patient informed us that he had undergone head and neck radiotherapy due to nasopharyngeal carcinoma diagnosed 2 years ago. An extraction was performed also at the left side of the mandible. The OPG demonstrated a pathological fracture due to the osteoradionecrosis. It was noted that a sequestrum of bone from the fracture side was under the mandibular basal bone (**Figure 39**).

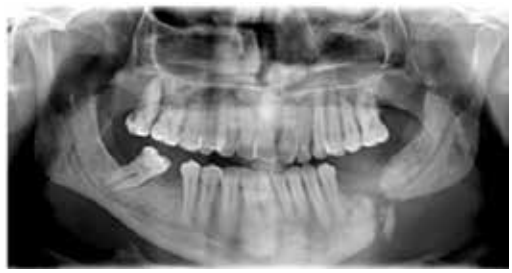

Figure 39. The view of the pathological fracture.

The replaced bone was removed and the fracture site was debrided. The fracture segments were stabilized with a long plate and four screws temporarily. A slight bone regeneration was observed on the control radiograph (**Figure 40**).

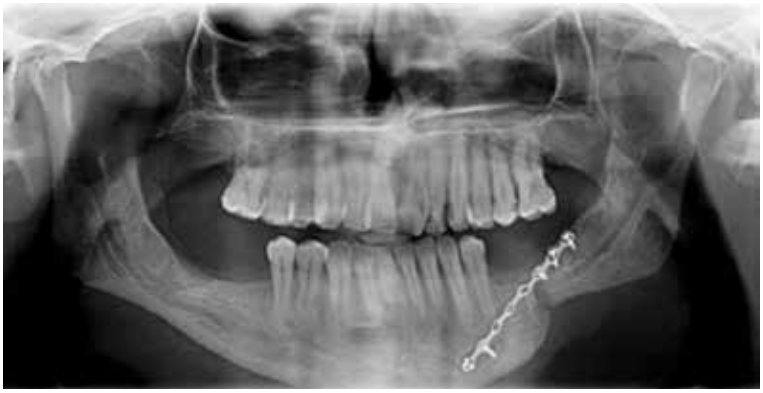

Figure 40. Intraoral temporary stabilization of the fractured segments.

The patient was informed regarding the permanent operation which included an iliac crest augmentation for the treatment of the bone loss at the fracture site, but the patient refused another operation. The extraoral fistula healed and the patient did not have any complaints (**Figure 41**).

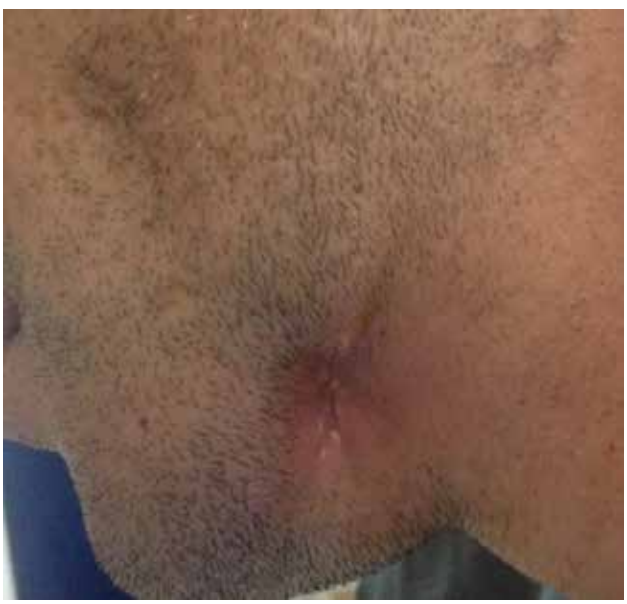

Figure 41. Healed fistula.

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2.5. Odontogenic orocutaneous fistula

Chronic dental infections may cause odontogenic cutaneous fistulae which may occur intraorally or extraorally. When the treatment is delayed, the pulp becomes necrotic and apical periodontitis may occur. This situation results bone resorption which may lead to the formation of an odontogenic cutaneous fistula [49].

Cutaneous sinus tracts on the face from odontogenic infection are commonly misdiagnosed and subsequently incorrectly treated. The differential diagnosis includes local skin infection, pyogenic granuloma, osteomyelitis, and basal or squamous cell carcinoma. Therefore, many patients refer to numerous physicians to evaluate their sickness. They sustain several inappropriate surgeries and courses of antibiotics before conclusive therapy is established. Early correct diagnosis and treatment of these lesions can help preventing unnecessary and ineffective antibiotic therapy or surgical treatment [50].

Diagnosis is established by tracing the sinus tract with gutta-percha or similar radiopaque material, dental examination, and radiologic evaluation. Dental panoramic or periapical radiographic views reveal evidence of a radiolucent periapical disease process [51].

Patients should be evaluated with orthopantomograph and, if possible, with cone-beam computed tomography. The pulp vitality test should be used to determine whether the diseased tooth is restorable. Histologically, the cutaneous sinus usually consists of granulomatous tissue or epithelium. Diagnostic errors can result in multiple surgical excisions and biopsies, antibiotic therapy, and even radiation therapy [51].

When assessing these patients, intraoral examination may reveal a carious tooth or signs of previous dental trauma. Bimanual examination may identify a cord-like track between the oral cavity and the skin, probing the external opening or performing a fistulogram may help establish the diagnosis.

Patients often seek treatment from a physician and present with chronic suppurative lesions that resemble a cyst, furuncle, or ulcer. The most common sites for a cutaneous sinus of dental origin are the chin and the jaw. The sinus tract's exit is determined by the location of muscle attachments and fascial planes. Of the reported cases, 80% arise from mandibular teeth. Mandibular incisors and cuspids typically drain to the chin or submental region [51–53].

Mandibular premolar and molar infections drain to the posterior mandible or below the inferior border in the submandibular region. Dental fistulae may arise from infection of the maxillary teeth, resulting in sinus tracts erupting intranasally or the inner canthal areas. Tracts in the mandibular, submandibular, and neck regions are most often associated with disease of the mandibular molars [52, 53].

Extraoral fistulae typically present as erythematous, symmetrical, crusting, smooth, and nontender nodules with periodic drainage. However, the dermal lesions are non-specific and can also present as abscesses, cysts, scars, and ulcers [54].

An understanding of the draining of cutaneous sinus tracts leads to more appropriate treatment. Most cases respond to conservative, non-surgical root canal therapy. Endodontic

treatment is recommended. Extraction may be required in non-restorable fractured or carious teeth, or in cases associated with extensive alveolar bone loss. The retention of natural teeth preserves function, arch integrity, and esthetics eliminates the need for a costly restorative procedure. After appropriate dental therapy, the sinus tract resolves spontaneously within a few weeks, but a retracted dimple or scar may develop. Because odontogenic sinus tract is a localized entity, systemic antibiotic administration is not indicated in healthy patients. The sinus tract will recur unless the source of infection has been eliminated. Early correct diagnosis, based on radiologic evidence of a periapical root infection, and treatment of these lesions can help prevent unnecessary and ineffective antibiotic therapy or surgical treatment, reducing the possibility of further complications such as sepsis and osteomyelitis [51].

Elimination of dental infection through endodontic treatments or tooth extraction is vital for the management of cutaneous sinus tracts. CBCT imaging facilitates successful endodontic treatment by aiding the diagnosis of odontogenic cutaneous sinus tract and enabling better understanding of unusual canal morphology [54].

Various types of intraoral infections may develop extraoral cutaneous fistulae, including odontogenic infections, osteomyelitis, osteonecrosis, midfacial fractures, cysts, and tumors of the jaws. The first attempt should be to reveal the cause of the fistula using clinical and radiological examinations. The treatment is to eliminate the causative factor. Early correct diagnosis and treatment of these lesions can help in preventing unnecessary and ineffective antibiotic therapy or surgical treatment.

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Chapter 18

Applications of the Buccal Fat Pad in Oral and Maxillofacial Surgery

Ali Hassani, Solaleh Shahmirzadi and Sarang Saadat

Additional information is available at the end of the chapter

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Abstract

The buccal fat pad (BFP) has become more and more popular in oral and maxillofacial surgery. Originally, it was described as an anatomic structure without any obvious function; it was even considered to be a surgical nuisance. Nowadays, the most reported application of the BFP is the closure of oroantral communications. In this chapter, different aspects of the BFP such as its applications, anatomy, physiology, and complications are explained.

Keywords: buccal fat pad, oral reconstruction, oroantral communication, oroantral fistula, cleft palate, surgical defects

1. Introduction

Although descriptions of the buccal fat pad (BFP) are typically very brief and lacking in detail in anatomical textbooks, they have recently received increased attention in the clinical literature [1]. After the first clinical use of the BFP by Egyedi in 1977, its use has increased rapidly during these years. The BFP has become more and more popular for closing oronasal and oroantral communications (OACs) and as a versatile pedicle graft for closing postsurgical maxillary defects [2].

The BFP initially believed to be an anatomic structure without any noticeable function was even considered to be a surgical nuisance [3–5]. However, with time, the use of the BFP as a pedicle graft has become more common; the relatively easy use and [6–8] the location of the BFP are anatomically favorable and minimal dissection allows it to be harvested and mobilized; good rate of epithelialization and low rate of failure have made it the preferred option for oral and maxillofacial applications [7]. The repair of oroantral and oronasal defects, the repair of pathological or traumatic defects (especially in the posterior maxilla and palate), the repair of congenital cleft palate defects, use as a biologic membrane for covering bone grafts, and its application in temporomandibular joint surgery are some of its common applications that are addressed here in this chapter.

2. History

Heister et al. introduced the BFP for the first time in 1732. They believed that the newly introduced structure was glandular and named it "glandula molaris" [9, 10]. Bichat in 1802 described this anatomic mass and realized its true nature. Therefore, it is commonly referred to as the boule de Bichat or bolle graisseusse in French; it is called "wangenfettpfropf" or "Wangenfettpolster" (Wangen means cheek, fett means fat, and polster means pad) in German, and the sucking pad, sucking cushion, masticatory fat pad, or BFP in English [10]. Samman was the first to explain the anatomy of the BFP and Goughram completed his description [11]. BFP's clinical importance was not discovered for years and due to its sudden egression during the surgical operations, it was known more as a nuisance factor [3, 4]. Egyedi for the first time in 1977 reported the use of the BFP in the regeneration of oral defects [2]. Neder introduced the use of the BFP as a pedicle and free graft in two patients with trauma of facial structures, but there were no reports available on the vascularization and functional anatomy of the BFP [12]. Tiedman et al. presented a complete report on anatomy, vascular supply, and operation method of the BFP for the first time [13]. Rapidis et al., Dean et al., and Hao used pedicle BFP for the reconstruction of medium-sized postsurgical oral defects of malignant lesions [11, 14, 15].

3. Anatomy, physiology, and embryology

3.1. General structures

The BFP is a simple lobulated mass described as consisting of a central body and four extensions: buccal, pterygoid, pterygopalatine, and temporal. The body consists of three independent lobes: anterior, intermediate, and posterior. Each lobe is encapsulated by an independent membrane and separated by a natural space [16] (**Figures 1–3**).

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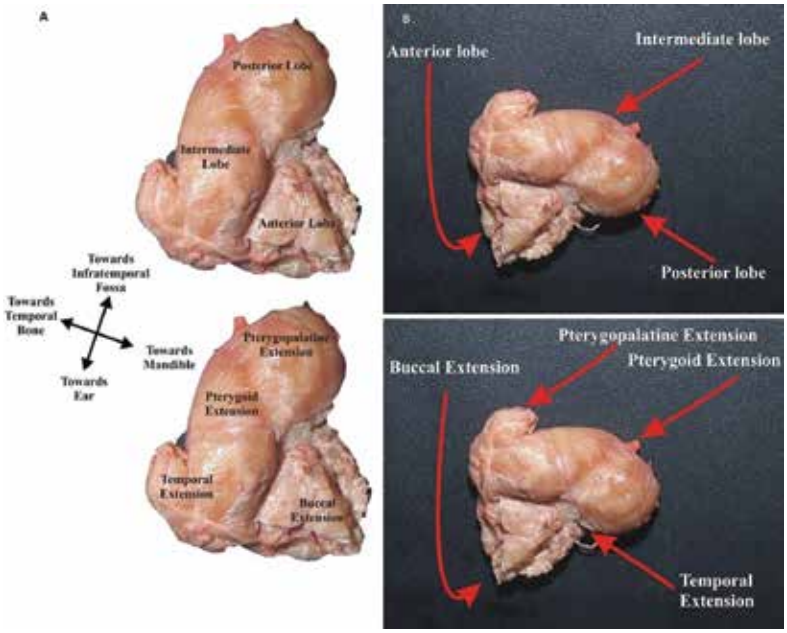

Figure 1. The BFP lobes and extensions (A, B) (Loukas M, et al. [1]).

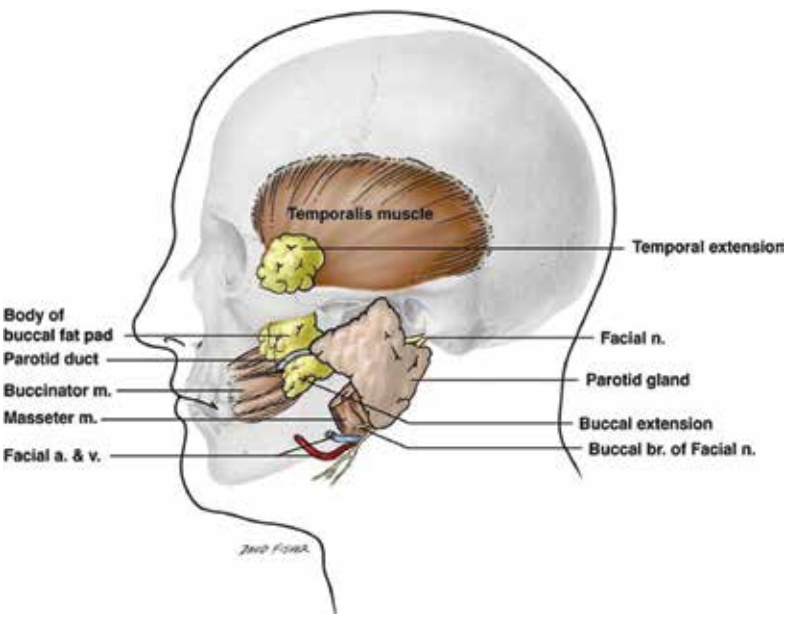

Figure 2. Anatomical relation of important adjacent structures (parotid duct, facial artery, parotid gland, and buccinator muscle) with the BFP, the temporal and buccal extensions of the BFP are present (Yousuf et al. [28]).

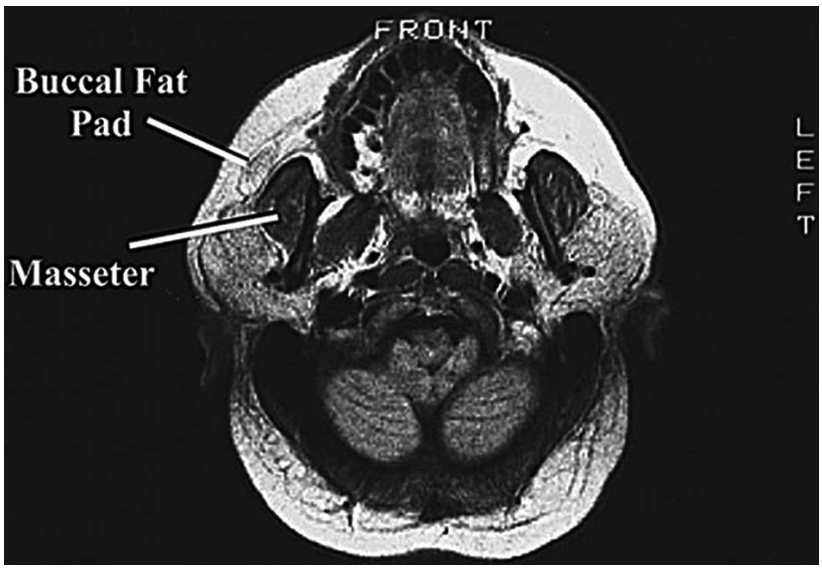

Figure 3. Cross-section of T1 MRI at the level of the oral cavity and the hard palate. The BFP is evident anteriorly to the masseter. Notice the volume of the BFP in relationship to the masseter (Yousuf et al. [28]).

The main body is situated deeply along the posterior maxilla and upper fibers of the buccinators, covered with a thin capsule.

The cheek contour is made generally by the buccal extension of the BFP, which is located superficially in the cheek. More than half of the total weight of the BFP mass is the body and the buccal extension together. Another extension of the BFP is pterygopalatine. It extends to the inferior orbital fissure and pterygopalatine fossa. The third extension is the pterygoid extension. It extends into the pterygomandibular space. The pterygoid extension packs the lingual nerve and mandibular neurovascular. The last extension of the BFP is the temporal extension. It has two parts, superficial and deep temporal extension. Actually, the superficial part is a distinct fat pad, its appearance is different, and has a different blood supply. Therefore, it is believed to be a distinct anatomical feature for the BFP.

A specific capsule covers each part of the BFP. Also, each part of the BFP is connected to the adjacent anatomical structures by ligaments. When the size of extensions is compared, the temporal, pterygopalatine, and pterygoid extensions are smaller and located deeper [1, 14, 16, 17].

3.2. Relation to the parotid duct and branches of the facial nerve

The parotid duct and zygomatic and buccal branches of the facial nerve cross the anterior and lateral surfaces of the BFP.

The parotid duct and zygomatic and buccal branches of the facial nerve cross the anterior and lateral surfaces of the BFP. The duct pierces the buccinators and presents in the oral cavity adjacent to the maxillary second molars [18]. It is established that the parotid duct either runs

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along the lateral surface of BFP or perforates the body of the posterior lobe before it comes up to the surface of the buccinators [19]. With respect to the BFP, the parotid duct is seen in three different situations. In 42% of cases, it travels over the buccal process (type A), in 26% of the cases, through the buccal process (type B), and 32% of the cases superior to the buccal process of the BFP (type C) (**Figure 4**).

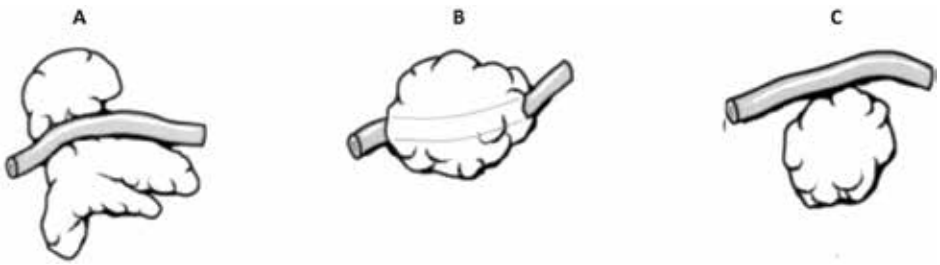

Figure 4. Relationship of the BFP with the parotid duct. (A) Type A: the parotid duct travels over the buccal extension. (B) Type B: the parotid duct travels through the buccal extension. (C) Type C: the parotid duct travels superior to the buccal extension of the BFP (Hwang et al. [18]).

The anterior surface of the BFP is covered by buccal branches of the facial nerve in 75% of cases, while the lateral border of the BFP is covered by the zygomatic branches in 90% of cases [1] (**Figure 5**).

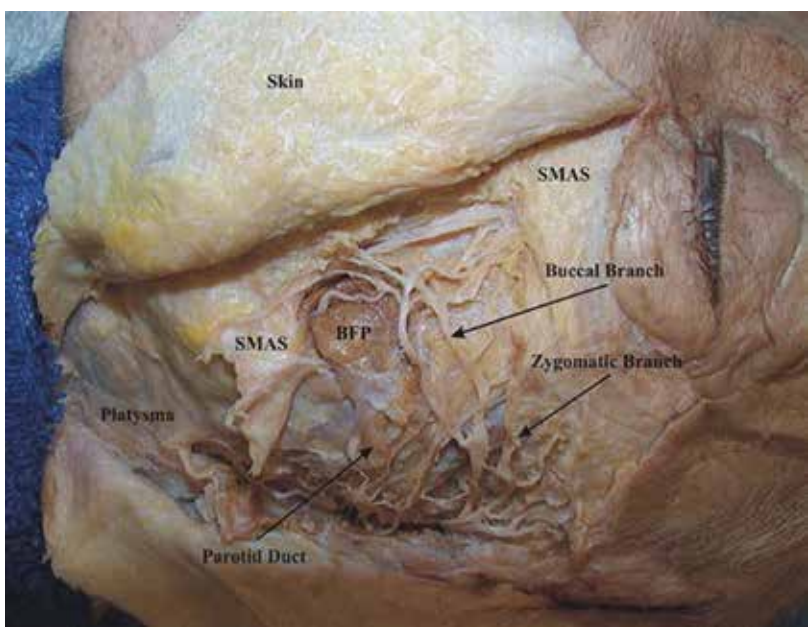

Figure 5. The relationship of the BFP with the branches of the facial nerve. Superficial musculoaponeurotic system (SMAS) (Loukas et al. [1]).

There are different types of the relations between the facial nerve and the BFP. Two different kinds of interrelations are present. First, in 73% of cases buccal branches of the facial nerve travel on the surface of the BFP (type one). Second, in 27% of cases the branches travel through into the buccal extension [18, 19].

3.3. Blood supply

There are three main sources of the BFP's blood supply. The maxillary artery (buccal and temporal branches), the superficial temporal artery (transverse facial branches), and the facial artery provide the blood supply for the BFP. These branches make a subcapsular plexus. Due to this rich blood supply, the BFP can be used as a pedicle graft. Also, it explains the great success rate of the BFP flap [17, 20–23]. The BFP has a very rich subcapsular capillary plexus. Arterioles go into the capsule, travel along the septa of the BFP, and finally make a capillary network among adipocytes. This circulation system is similar to the other white adipose tissues. However, the capillary plexus of the BFP is smaller and its capillaries are wider [19, 24]. The BFP venous system drains via the facial vein [23].

3.4. Volume and size

The mean volume of BFP is 10 cm^3 (average 9.6 ml, range 8.33–11.9 ml); weight is 9.3 g; if flattened, it can cover the surface of 10 cm^2, preserving a thickness of 6 mm [1, 2, 19, 25]. The size of the BFP is fairly constant among different individuals regardless of overall body weight and fat distribution; even cachectic patients have BFPs that are of normal weight and volume [10]. Investigation of age-related changes in BFP volume reveals that the most important alterations are found between two age groups namely 0–10 years and 21–50 years. Moderate decrease in volume after the age of 50 years is noted [25].

3.5. Embryology and physiology

Poissonnet et al. [26] reported that fat tissue differentiation begins in the second trimester of gestation. The size of fat lobules increases until the 29th week of gestation. However, the number of them is approximately constant. Cheek fat is the first fat that develops [26]. Like adults, the BFP has an important role in the cheek prominence of newborns. Among fetal adipose tissue, the BFP is one of the initial adipose tissues that develop.

Some functions were introduced for the BFP in newborns. First, the BFP prevents the negative pressure while a newborn is sucking. Second, it separates the masticator muscles from one another and nearby bony structures. Third, it protects the neurovascular bundles. Finally, it enhances the intermuscular movement; this function is performed by a specialized type of fat which is called syssarcosis [16, 17, 20, 22].

Bagdade and Hirsch are the first who measured and tabulated the fatty acid composition of the BFP. They used gas-liquid and thin-layer chromatography for this purpose [27]. Ranke claims that the amount of lipolysis of the BFP is different from subcutaneous fat. Like the periorbital fat, the BFP is constant during emaciation while subcutaneous fat is lost [8, 15, 20, 29, 30].

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One of the desirable features of the BFP as a flap is its quick epithelialization property [10, 31, 32].

4. Surgical approach

The most direct access to the BFP is found at the distobuccal depth of the maxillary tuberosity, and it may be dissected through a vestibular incision if it has not been encountered during the resection [33]. Under either local or general anesthesia, an upper mucosal incision posterior to the area of the zygomatic buttress is made, followed by a simple incision through the periosteum and fascial envelope of the BFP [8]. After a single sharp scissor stab through the periosteum and scant buccinator muscle, the BFP extrudes into the operative site [33] (**Figure 6**).

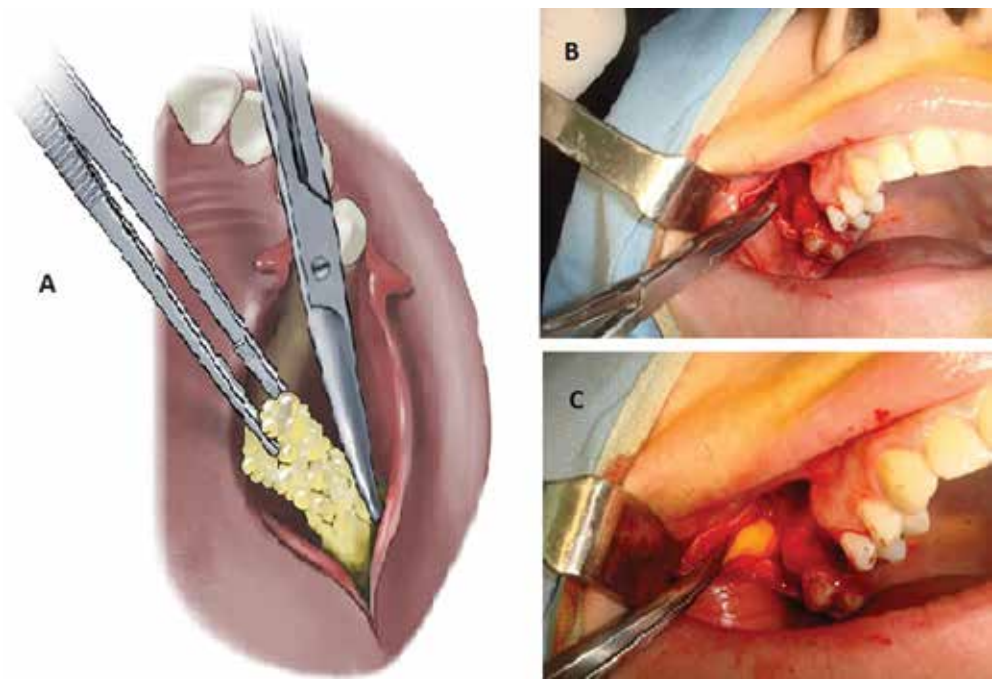

Figure 6. (A) Schematic view of the BFP intraoral approach (Arce [33]). Clinical view of intraoral approach. (B) The use of a hemostat to explore the site. (C) Pulling out the BFP very gently.

Mechanical suction must be avoided once the BFP is exposed. It easily herniates into the defect with a little teasing and is gently pulled out from its bed with a vascular clamp [8]. Since the main cause of sensory disturbances is the impairment of the metabolic supply due to the disturbed microvascular circulation of the nerve fibers by the mechanical trauma [34–36], surgeons should avoid the excessively and unnecessarily manipulating of the surgery site for finding the BFP. At this time, the external pressure helps the removal of the temporal extension

of the BFP. Surgeons should evaluate the amount of fat required, then based on their need manipulate the site and extract various processes of the BFP [8].

Clinically, the color of the oral aspect of the exposed BFP changes to yellowish-white within three days; then, it changes to red within the first week. It is a consequence of the formation of granulation tissue. In the second week, the granulation tissue becomes firmer and completely epithelialized [9, 37].

5. Applications of the BFP

The BPF has different applications in oral and maxillofacial reconstruction. It has some physiological functions, such as filling deep tissue space, has a role of gliding pad for facial and masticatory muscles during contraction, and has a role of cushion for some structures from outer force impulsion [21]. Besides its physiological functions, it serves as a versatile flap in reconstructive procedures [38].

Applications of the BFP in oral and maxillofacial surgeries have increased rapidly [7], and nowadays, the BFP is used in different kinds of surgeries. Particularly in recent years, scientists have been working on regenerative properties of the BFP, which rely on adipose-derived stem cells.

5.1. OAC and oroantral fistula

The BFP flap, preferably pedicle type, has been used most commonly for the closure of OACs and oroantral fistula (OAF) [2, 8, 39–43].

There is no doubt that some characteristics of the BFP such as favorable anatomical position, perfect epithelialization outcome, simple dissection for harvesting, and low rate of failure make it a desirable alternative [9]. Dolanmaz et al. claimed that using the BFP flap for the management of OAC is a reliable alternative, and this method probably is the best treatment choice for recurrent OAF [32].

The choice of the BFP versus a buccal advancement flap closure must weigh the advantages and disadvantages, and other available techniques, in regard to location, height of alveolus, sinus membrane status, and obliteration of the vestibule. Using the BFP eliminates the needs for removal of additional alveolar bone and mobilizes a buccal advancement flap, which may obliterate the buccal vestibule. It is also helpful when traumatized surrounding attached gingiva or mucosa precludes the use of a buccal advancement flap for primary closure [33]. It has a favorable healing course after the operation, and the wounds become successfully epithelialized in 3–4 weeks after surgery [7].

There is the minimal obliteration of the vestibule in the closure of OAF with the BFP as compared to closure with buccal advancement flap. There are no differences in the level or color of the mucosa [37]. The majority of reports point out a perfect success rate of the BFP in the treatment of OAC or fistula. Most studies state a high success rate of BFP in the closure of

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OAC/OAF [7]. Nevertheless, 7.5% complications were reported, for example, the elimination of vestibule and recurrence of OAF. The vestibular depth became normal in the due course of time resulting in no postoperative prosthodontics complications [8] (**Figure 7**).

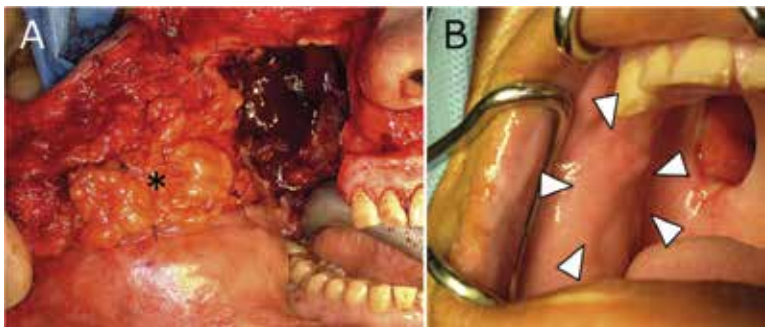

Figure 7. Reconstruction of the inner surface of a facial flap in a patient following resection of an ameloblastoma of the right upper gingiva. (A) BFP covers the inner surface of the facial flap (*). (B) At 1 year and 7 months postoperatively, cicatricial contracture is slight (arrowheads) (Toshihiro et al. [57]).

5.2. Regional defects

The other major use of the BFP is the closure of post-excision defects [9–11, 14, 29, 31, 39, 41, 44–48].

Different kinds of pathologies can cause a defect in the maxilla when resected. The applications of the BFP have been reported with a noted range of usage from the angle of the mouth to the retromolar trigone and palate [49]. The most used is for the reconstruction of the hard palate [44]. The most important consideration of using the BFP for reconstruction is the size of the defect. Most of the studies show a desirable result for closing defects up to 6 × 5 × 3 cm [8]. The authors have had successful experience in the treatment of nine patients with large hard palate defects as large as 7 × 5 cm.

The use of BFP in the reconstruction of defects is highly successful; however, some complications have been reported [7, 8, 29, 41, 44–48].

The application of the BFP for covering mucosal defects following ablation of the buccal cancer has been reported [50]. The result of epithelialization is acceptable after 4–6 weeks. The capability of the BFP in the treatment of mucosal defects is compared with radial free forearm flap and free split-thickness graft. Although the BFP epithelializes easily, due to the lack of lamina propria and submucosa in the dense fibrous connective tissue, the BFP restricts mouth opening [46].

Mehrotra et al. [51] performed a retrospective study of 100 patients and compared the BFP with nasolabial flap, tongue flap, and split-skin graft for the coverage of post-fibrotic band incision in oral submucous fibrosis with 25 patients in each group. They claimed that the BFP serves as the best substitute, providing excellent function without deteriorating esthetics. It offered the ease of surgery, little postoperative morbidity, and good patient acceptance [51].

5.3. Cleft palate

The use of BFP to repair primary cleft palate was first described by Zhao et al. [52] in 1998. Most researchers agree that the ease of harvesting and mobilization of the graft, an excellent blood supply, and minimal donor-site complications make the pedicle BFP graft a convenient and reliable method in cleft palate surgery [53] (**Figure 8**).

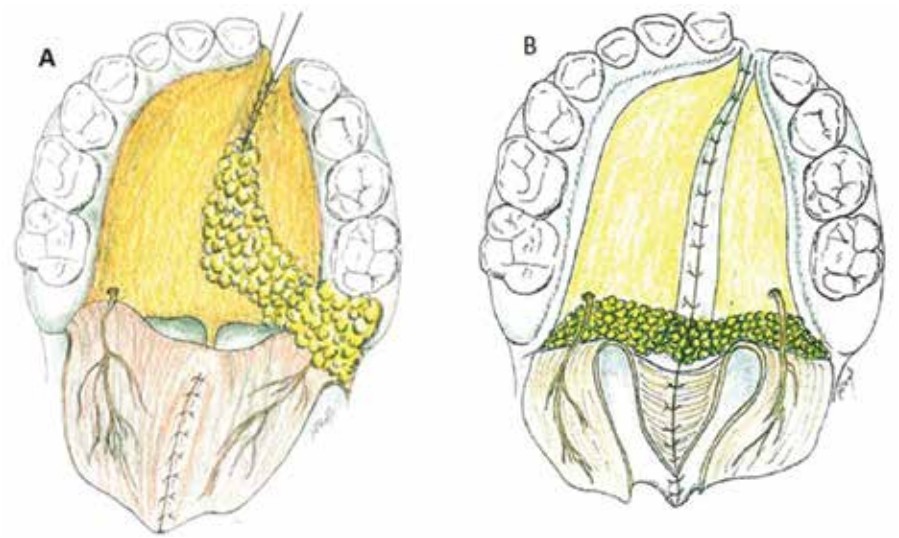

Figure 8. (A) The use of BFP for the closure of palatal fistulas. (B) The use of BFP to prevent type III fistulas between the hard and soft palate, minimizing scarring tension and obstructing the space of Ernst (Gröbe et al. [53]).

The transferred BFP was fully epithelialized with healthy-looking oral mucosa within 4 weeks, regardless of graft coverage with palatal mucosa or not. There is no significant impairment of palatal movement or any prevention of growth disturbances [54]. Levi et al. [54] suggests that the scar contraction and subsequent transverse maxillary growth restriction induced by the lateral hard palatal tissue defect decrease in this technique. Also, they believe that the hollowness of the child's cheek is unaffected.

Large, unlined, denuded palatal shelves serve as a key nidus of scar contraction as the palatal tissues attempt to fill the dead space [54]. Levi et al. state that adding the BFP to fill this open space causes an increase of vascularity in this area. Also, they believe that adding a layer of the BFP over the buccal mucosal flap decreases the time of surgery and needs less donor-site dissection [54, 55].

The combination of these two techniques, the BFP with pedicle mucosal flap, has some advantages: (1) the length of the soft palate increases without causing tension from the nasal side; (2) if the oral layer has failed and a perforation occurs, the graft serves as a bed for secondary granulation; (3) the flap also fills the secondary lateral defect; and (4) unlike buccal myomucosal flap, which is generated from another site, the BFP is easily accessible from the lateral incision [56].

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5.4. Temporomandibular joint

Rattan used the BFP as a useful adjunct to autogenous or alloplastic temporomandibular joint (TMJ) reconstruction after TMJ ankylosis release. He claimed that the BFP can be used for TMJ reconstruction because of its local availability [16]. Toshihiro et al. used BFP graft in the TMJ region to repair the postoperative defect left by a synovial chondromatosis resected from the left condylar head in a 58-year-old female. The size of the defect was 20 × 25 mm and the size of the BFP was 30 × 30 mm. Although the tumor was resected via an extraoral approach, BFP grafting was prepared intraorally and tunneled to the TMJ region (**Figure 9**). There was no contraction of soft tissues or functional disorder of the TMJ during follow-up [57].

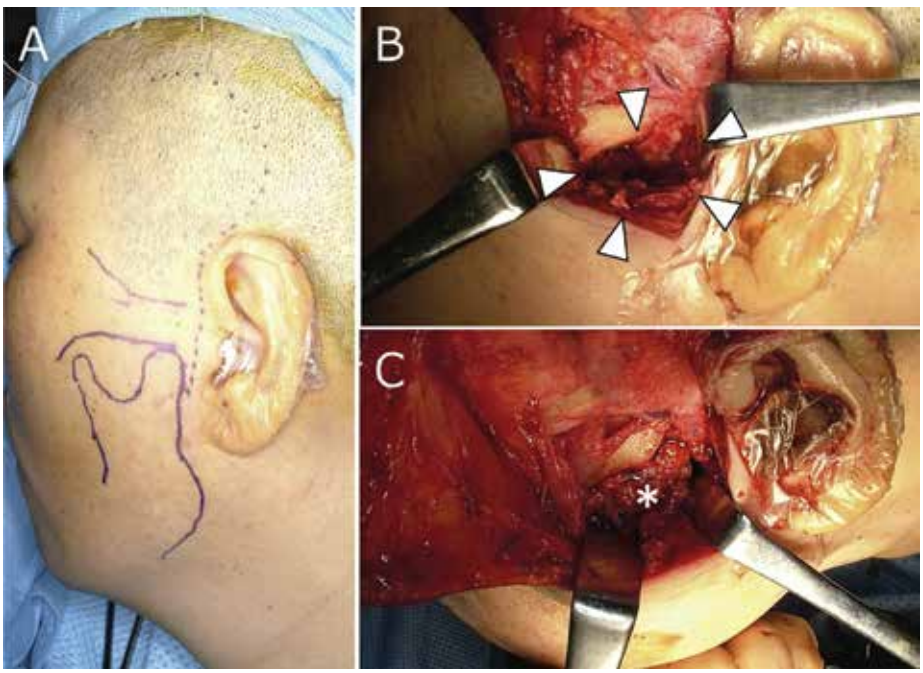

Figure 9. Reconstruction of a defect in the temporomandibular joint (TMJ) region in a patient following resection of a synovial chondromatosis of the left TMJ. (A) Preoperative view. (B) Resection of the mandibular condyle with the tumor (arrowheads). (C) Extension of the BFP to the surgical defect (*) (Toshihiro et al. [57]).

Singh et al. evaluated the feasibility and usefulness of BFP as an interposition graft in the treatment of TMJ ankylosis. Their findings showed the successful management of TMJ ankylosis using the BFP as an interposition graft. They assert that the mean of the maximum interincisal opening is 35.1 mm. Furthermore, the mean deviation to the affected side during opening the mouth is 1.6 mm. They claim that chewing function after this surgery satisfies the patients. Also, they believe that no major occlusal changes occur after this surgery and the intra-articular space is maintained well. Finally, they showed that using the BFP as an interposition graft is a desirable alternative to manage TMJ ankylosis, particularly in the short term [58].

Elimination of dead space is the main goal of using the BFP around the TMJ; the BFP prevents the hematoma around the joint. Also, due to the isolation of the joint by the BFP, the chance of the formation of fibrosis and bone decreases in the area [7].

5.5. Miscellaneous uses

Hassani et al. [59] reported the use of the BPF with a mixture of autogenous bone graft in sinus lifting procedure and covering the lateral wall of sinus for the first time. They believed that the BFP serves as both a physical barrier and a high vascularized bed for the bone graft. Tamura et al. used the BFP for augmentation of the vocal cord [60].

Khouw et al. reported the use of the BFP for palatal reconstruction when it is combined with a superiorly based pharyngeal flap. They used this technique to lengthen the soft palate in patients with extensive necrotizing defects [61].

El Haddad et al. reported the use of the pedicled BFP for covering of class IV Miller gingival defects. The BFP provides a significant amount of keratinized tissue for the gingival recession of the maxillary molars [62].

Also, some experts believe that the BFP can be used as a biologic membrane to cover bone grafts and in maxillary sinus lifting for implant placement. As mentioned before, the BFP can serve as a physical barrier. Also, it is well vascularized and contains adipose stem cells (ASCs), which have great potential to help bone regeneration in operation sites [59, 63, 64]. For these reasons and because the BFP is a source of stem cells, the BFP can be a great biologic membrane for covering the bone grafts.

Recently, researchers increased their focus of interest on adipose tissue-derived stem cells, and the BFP was introduced as a source of stem cells. Farré-Guasch et al. had claimed that the BFP is a source of stem cells. ASCs present in adipose tissue are able to differentiate into several lineages and express multiple growth factors, which makes them suitable for clinical application. The BFP represents an easy access source for dentists and oral surgeons. The stromal vascular fraction obtained from fresh BFP-derived adipose tissue and passaged ASCs were analyzed to detect and quantify the percentage of ASCs in this tissue. The BFP contains a huge amount of stem cells that has the capability to differentiate into the chondrogenic, adipogenic, and osteogenic lineages [65, 66].

6. BFP pathological conditions and complications

6.1. Pathological conditions

Kahn et al. explained that the continuity of fat tissue within the deep face makes it prone to pathological conditions such as cellulitis and abscess. The anaerobic organisms within the fat pad are responsible for it [67].

Although hemangioma in BFP is rare, some studies have reported the incidence of hemangioma with/without phleboliths inside the BFP mass [68] (**Figure 10**).

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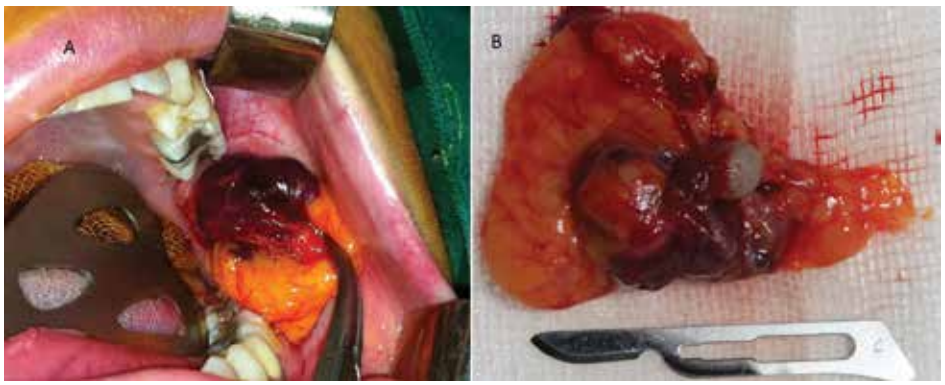

Figure 10. Hemangioma of the BFP. (A) Intraoperative view of the lesion. (B) View of the totally excised lesion showing hemangioma with phleboliths (Hassani et al. [68]).

BFP herniation is a common occurrence, particularly in infants and children. The BFP can pierce the oral mucosa and buccinators to the oral cavity [12]. Also, it may enter into the maxillary sinus after herniation [10].

A review of the literature shows that most cases of the BFP herniation involve children less than 5 years of age [28]. This fact can be due to some reasons. First, the BFP prominency is more in children. Second, because children put foreign objects into their mouth, they are more prone to the BFP herniation via rupturing the oral mucosa. Third, neonates and infant have a suckling activity which makes them prone to the BFP herniation [69].

6.2. Complications

Complications due to the mobilization of BFP are rare, and the BFP in the reconstruction of defects is highly successful [7, 19].

Partial necrosis accounted for the majority of failures involving the use of the BFP. A small dehiscence can be treated conservatively to see if spontaneous closure occurs. Reattempts at closure involve contralateral buccal fat flaps, palatal flaps, or buccal flaps. Rarely can the same flap be mobilized again, unless the defect was small and the reason for failure is easily identified. Trismus from scarring has been reported mainly when the BFP is used for the reconstruction of retromolar trigone or buccal mucosa defects. The range of motion should be noted in the few weeks after the use of the flap so that physical therapy, if necessary, is activated as soon as possible. A rarely visible change in facial contour has been reported in patients only when the BFP is used for the reconstruction of large defects. A surgeon might consider a contralateral buccal lipectomy to correct this alteration. The low morbidity and failure rate associated with the use of the BFP in maxillary reconstruction allows this simple reconstructive option to be used in carefully selected defects [33].

Different complications following application of the BFP have been reported. Although the complications are usually rare, it is a fact that it could be partial or complete loss of flap, limitation in mouth opening [44], hematoma, hemorrhage [45], postoperative infection [29,

47], and depressed cheek [8, 29, 46]. If a clinician harvests a large amount of the BFP for reconstruction purpose, the cheek may be depressed.

7. Summary

Generally, extraction of the BFP from the deep facial region is a safe procedure with minimal risk of unhazardous complications [19].

Due to the unique features of the BFP, such as its location, easy accessibility, rich blood supply, a rich source of ASCs, and high rate of epithelialization, using the term "versatile flap" is truly fitting. The BFP can be used in different directions. It can displace anteriorly up to the canine region, not beyond the midline, posteriorly in the hard palate tuberosity region, retromolar region, the soft palate, and to the anterior tonsillar pillar (**Figure 11**) [45].

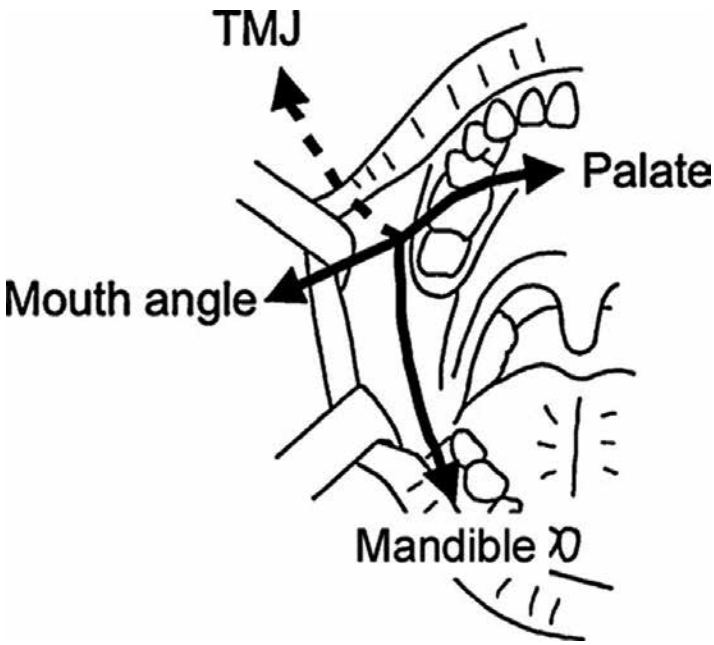

Figure 11. Applicability of the BFP. The graft could be extended in four directions to the palate via the maxilla, mandible, mouth angle, and TMJ region (Toshihiro et al. [57]).

The BFP has a variety of applications in oral and maxillofacial surgery. Among different applications, using it for the closure of OAC is the most common application reported. Although most of the time the BFP flap is used solely, it can be used in conjunction with other flaps, such as the pedicle temporalis muscle myocutaneous flap [31]. The success of the BFP has been attributed to its rich vascular supply, less donor-site morbidity, ease of harvest, and a lower rate of complications [39].

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Section 10

Surgical and Nonsurgical Treatment of Skeletal Malocclusion

Chapter 19

Treatment Protocol for Skeletal Class III Malocclusion in Growing Patients

Jamilian Abdolreza, Khosravi Saeed and
Darnahal Alireza

Additional information is available at the end of the chapter

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Abstract

Maxillary deficiency in growing patients with skeletal Class III malocclusion can be treated by either extraoral or intraoral appliances. Extraoral appliances include face mask, reverse chin cup, reverse headgear, and protraction headgear. Intraoral appliances include tongue appliance, fixed tongue appliance, tongue plate, Frankel III, miniplate in combination with Class III elastics, and miniscrew in combination with Class III elastics. Herein, we demonstrate our experience and treatment results in these patients.

Keywords: skeletal Class III malocclusion, maxillary deficiency, orthodontic treatment, growing patients, maxillary retrusion

1. Introduction

Skeletal Class III malocclusion is characterized by mandibular prognathism, maxillary deficiency, or some combination of these two features. The prevalence of Class III malocclusion varies among different ethnic groups. The prevalence in Caucasians ranges between 1% and 4%. A high prevalence has been reported in Asians. Various studies have reported that 4–12% of Chinese and 9–19% of Koreans suffer from Class III malocclusion which is relatively higher than 0.6–1.2% reported for African Americans and 6% reported for the Swedish population [1].

Approximately half of all skeletal Class III malocclusions are reported to result from maxillary deficiency. More precisely, the incidence of Class III malocclusions suffering from maxillary deficiency was reported to be 65–67% [2]. If the mandible of the patients is markedly affected, then the most common treatment would be orthodontics in combination with orthognathic surgery. In this chapter, the main focus of attention will be on maxillary deficiency in growing patients (pseudo-Class III).

In view of the high frequency of maxillary deficiency, maxillary advancement by orthopedic force is considered to be a viable treatment option in growing patients [3, 4]. A number of techniques have been described, including the use of a face mask [5–7], reverse chin cup [8], and direct force application through implants placed in the zygomatic processes [9]. It was also suggested that intentionally ankylosed teeth may be used as abutments for extraoral traction in patients with a severe disturbance in maxillary growth [10]. Miniscrew implants and miniplates have also been used to provide the necessary orthodontic anchorage in these cases [11–14]. The tongue plate and tongue appliance have also been used for the correction of maxillary deficiency in growing patients [15–17]. The mechanism of action associated with these appliances relies upon forward pressure from the tongue, which is transmitted via the appliance to the maxillary dentition and maxilla.

2. Treatment of maxillary deficiency in growing patients

Growing patients with skeletal Class III malocclusion characterized by maxillary deficiency can be treated by either extraoral or intraoral appliances. Extraoral appliances include face mask, reverse chin cup, reverse headgear, and protraction headgear and intraoral appliances include tongue appliance, fixed tongue appliance, tongue plate, Frankel III, miniplate in combination with Class III elastics, and miniscrew in combination with Class III elastics.

2.1. Extraoral appliances

2.1.1. Face mask

Face mask therapy has become a common technique used to correct the developing Class III malocclusion. A literature search will reveal extensive research on face masks and their effects on the nasomaxillary complex. In addition, the experimental studies constantly demonstrate pronounced forward movement of the maxilla due to heavy and continuous protraction forces of face masks [18]. Face masks were first described more than a century ago [19]. Delaire et al.'s [19] face mask promotes midface orthopedic expansion with slight inferior and anterior movement of the maxilla. The protraction face mask provides a direct constant anterior force to the maxilla with downward and backward rotation of the mandible [20]. Nanda introduced a modified protraction headgear that aimed to control the point and direction of force application [21] (**Figure 1**). Similar appliances to the face mask have been proposed by various clinicians and vary slightly from each other but their mechanisms are almost the same. Some

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of these appliances are reverse headgear, front pull headgear, and protraction headgear among others.

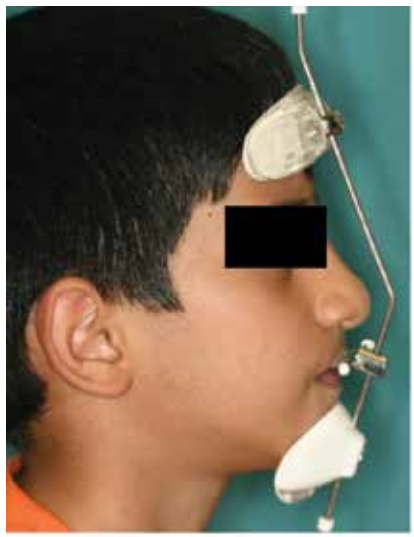

Figure 1. Face mask in situ; note forehead and chin pads, main bar, crossbar, and elastics connecting the crossbar to the maxilla.

2.1.1.1. Limitations

However, one of the problems with face masks is their bulky size and shape, which make it a discouraging choice for children. Patients who wear glasses will be especially more susceptible to discomfort. This discomfort along with the embarrassment caused by the large size, especially for children at school in front of other, may reduce patient compliance. The forehead and the chin are used as areas that support the face mask. Nanda reported that in face mask therapy although the maxilla will translate forward, downward and backward rotations of mandible are unavoidable [21]. The backward and downward rotations of the mandible are unfavorable in patients with vertical growth pattern. On the contrary, this effect may be favorable in patients with a horizontal growth pattern. Face mask would also cause forward movement of the maxillary dentition and lingual movement of the mandibular incisors [8].

2.1.2. Reverse chin cup

The chin cup is an extraoral appliance first introduced by Showkatbakhsh et al. [8, 22]. The reverse chin cup is composed of an upper removable appliance and a custom made porous acrylic chin cup with two vertical arms. The upper removable appliance consists of two Adams clasps on the permanent first molars, two C clasps on the primary canines, and two C clasps on the permanent central incisors. If necessary, the number of C clasps and Adams clasps can be increased for anchorage reinforcement. The end of each arm of the chin cup is bent to form

a hook. Two orthodontic latex elastics (recommended: 5/16, heavy elastics) connect the hooks of the palatal canine area of the upper removable appliance to the hooks of reverse chin cup in order to deliver approximately 500 g of force on each side. A high pull head cup is used to hold the reverse chin cup. The patients are instructed to wear the appliance full time except for eating, contact sports, and toothbrushing (**Figure 2**).

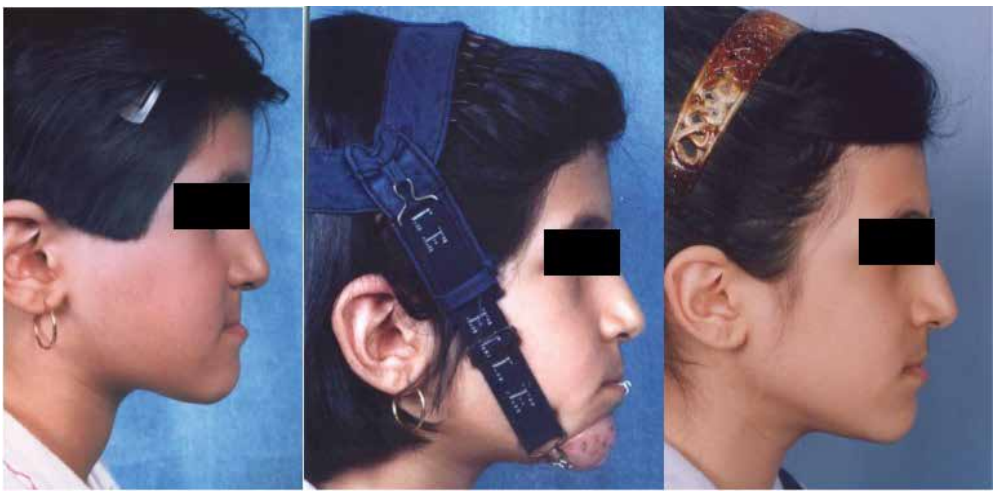

Figure 2. A 6-year-old patient in the mixed dentition with Class III malocclusion and maxillary deficiency. Concave profile was obvious. She had a reverse overjet and underbite. She was treated via reverse chin cup. After 18 months of treatment, her profile improved and a positive overjet was achieved.

The reverse chin cup is very similar to the face mask and is able to produce forward movement of the maxilla in growing patients; however, chin cup may be more favorable for patients due to its smaller size.

2.1.2.1. Limitations

Similar to face masks reverse chin cup is also associated with lingual tipping of the lower incisors and labial tipping of the uppers. Another drawback of the reverse chic cup is backward and downward rotation of the mandible.

2.2. Intraoral appliances

2.2.1. Removable tongue appliance

The tongue appliance is a habit breaker which is constructed via Adams clasps in the first upper molars and C clasps in the anterior teeth in order to increase retention. Three to five separate tongue cribs are placed in the palatal area from canine to canine. These cribs are long enough to cage the tongue and are adjusted to prevent traumatizing the floor of the mouth. A screw is mounted in the midpalatal area to correct bilateral posterior cross bite. The patients are instructed to tighten the screw once per week [15] (**Figure 3**).

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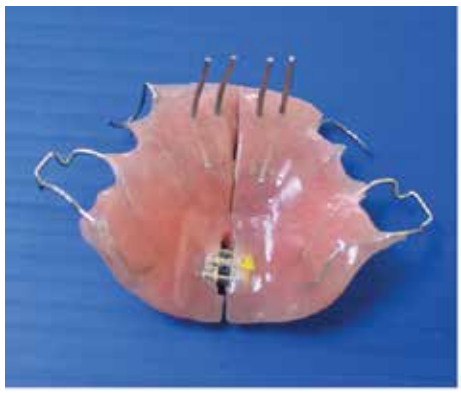

Figure 3. Tongue appliance.

When the tongue appliance is in the mouth, a considerable amount of pressure is transmitted to the deficient maxilla. The mechanism of this force is provided in two ways, namely:

The intermittent force is transferred through the tongue appliance to the deficient nasomaxillary complex via the pressure of the tongue during swallowing which is estimated to be about 5 pounds in each swallow. The frequency of swallowing is about 500–1200 times in 24 h.

Pressure to the tongue appliance transmits considerable force while it is in the rest position. This continuous force of the tongue pushes the maxilla into a forward position.

Physiological position and functional activity of tongue generate these forces. These forces are transmitted by the tongue through the palatal cribs and finally to the nasomaxillary complex. The more anterior the tongue is, the greater the force will be; the more posterior the crib is, the greater the force will be (**Figure 4**).

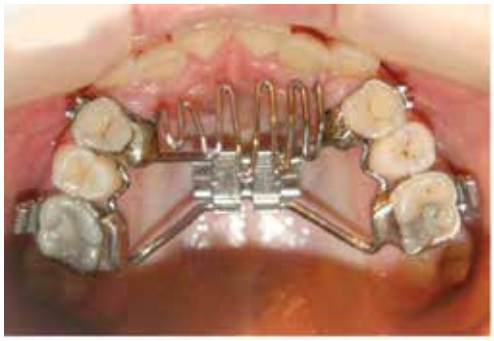

Figure 4. Fixed tongue appliance in situ.

Unlike extraoral appliances such as the face mask and reverse chin cup, the removable tongue appliance has no adverse effects on the mandible and would not cause its backward and

downward rotation. Another advantage of this appliance over the other extraoral appliances is that it is less conspicuous and needs less patient compliance.

2.2.1.1. Limitations

The removable tongue appliance will lingualize the lower incisors due to elimination of tongue pressure. In other words, after discontinuing the appliance, the IMPA will be increased and the overjet will be decreased [23]. Another disadvantage of removable tongue appliance is the need for patient cooperation and lack of compliance of which would have negative effects on the final result.

2.2.2. Fixed tongue appliance

In order to remove the need for patient compliance in removable tongue appliances, Showkatbakhsh et al. designed a new appliance called the "fixed tongue appliance" [24]. Fixed tongue appliances consist of a Hyrax® mounted on the first maxillary molars and premolars; a few curved cribs are soldered to the anterior side of the Hyrax® (**Figure 4**). The patient is instructed to activate the screw of the Hyrax® by making 1/4 of a turn at the beginning of each week. Fixed tongue appliance is a habit breaker used in conjunction with the Hyrax® for a different purpose other than its common application. The Hyrax® screw is for the purpose of loosening the maxillary sutures and extending the width of the maxillary arch and thus creating a better intermaxillary relationship. This expansion facilitates anterior displacement of the maxilla. When the fixed tongue appliance is in the mouth, a considerable amount of pressure is transmitted to the deficient maxilla through the cribs of the appliance. The mechanism of this force is similar to the removable tongue appliance (**Figures 5** and **6**). The fixed tongue appliance is used for the correction of skeletal problems and further treatment by fixed orthodontics is required for dental problems (**Figure 7**).

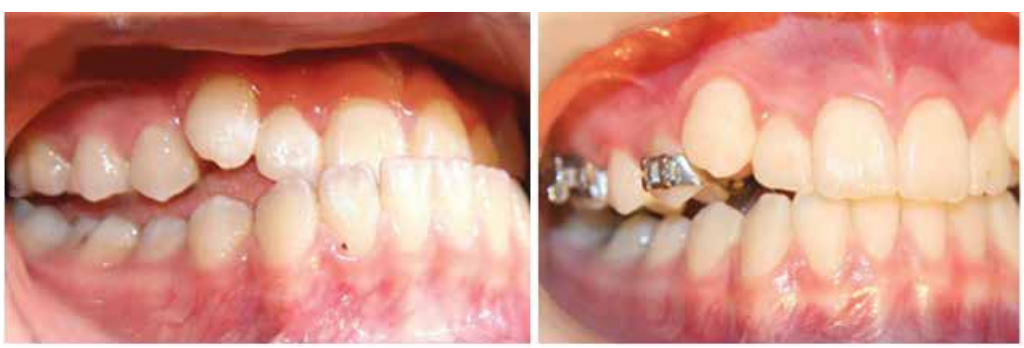

Figure 5. A 12-year-old girl with maxillary deficiency in the late mixed dentition and Class III molar and canine relationships. Skeletal problems of the patient were corrected by means of a fixed tongue appliance

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Figure 6. Pre- and post-treatment lateral cephalograms of the same patient.

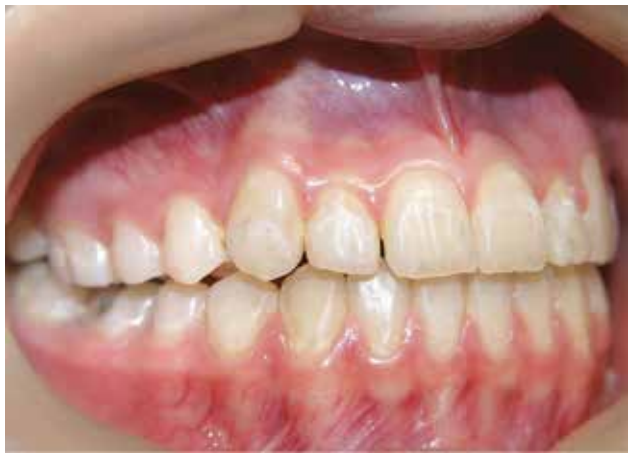

Figure 7. The occlusion of the same patient treated by fixed orthodontics.

One of the advantages of the fixed tongue appliance is that patient's cooperation is not needed. The vertical length of the cribs should be designed and adjusted in a way to avoid traumatizing the floor of the mouth. The main advantage of the fixed tongue appliance over the face mask is that the fixed tongue appliance does not cause backward rotation of the mandible; thus, it can be used in long-face patients, while the cup of the face mask results in backward rotation of the mandible and can have unfavorable effects in long-face patients [25].

2.2.2.1. Limitations

The fixed tongue appliance has one disadvantage. It will lingualize the lower incisors due to elimination of pressure of the tongue on them. However, removal of the fixed tongue appliance

will restore the pressure of the tongue on the lower incisors and will consequently result in the increase of the IMPA.

2.2.3. Tongue plate

The tongue plate is a tightly fitting and well-retained upper removable appliance fabricated with Adams clasps on the upper first permanent molars and C clasps placed on the upper primary canines [17]. Additional C clasps can be added if more retention is needed. An acrylic plate was mounted posterior to the upper incisors. The patients were instructed to wear the appliance full time except for eating, contact sports, and toothbrushing (**Figure 8**).

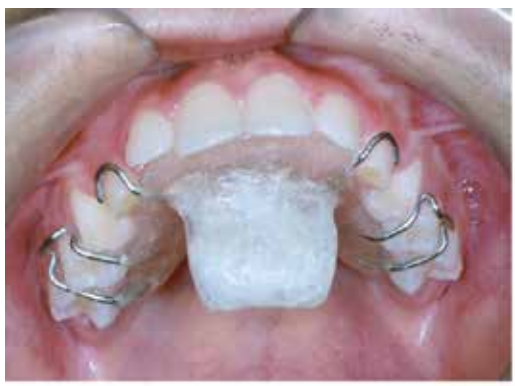

Figure 8. Tongue plate in situ.

The mechanism of action of the tongue plate is very similar to the fixed and removable tongue appliance. The force of the tongue during swallowing and resting is transferred through the tongue plate to the deficient nasomaxillary complex. The force of the tongue which is considerable is caged behind the acrylic plate and moves the maxilla in a forward position. The rounded surface of the plate and its softened edges make it undamaging for the tongue. In addition, it is designed and adjusted in a way to avoid traumatizing the floor of the mouth.

The disadvantages of the tongue plate are similar to those of fixed and removable tongue appliances in that it also lingualizes the lower incisors.

2.2.4. Frankel III appliance

The Frankel III appliance is a removable appliance used to stimulate the growth of the upper jaw and move it forward. The appliance was first designed by Professor Frankel and is composed of wire and four acrylic parts: two vestibular shields and two upper labial pads [26]. The vestibular shields extend from the depth of the mandibular vestibule to the height of the maxillary vestibule. These shields act to remove the restrictive forces created by the buccinator and associated facial muscles against the lateral surfaces of the alveoli and the buccal dentition. The appliance allows the maxillary molars to erupt and move mesially while holding the lower molars in place vertically and anteroposteriorly; it also tips the maxillary anterior teeth facially

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and retracts the anterior mandibular teeth. Vertical movement of the maxillary molar will help rotate the chin down and back to improve facial appearance.

2.2.4.1. Limitations

The Frankel III appliance requires a lengthy treatment time and excellent patient cooperation.

2.3. Skeletal anchorage

Recently dental implants, miniplates, and modified fixation screws have become popular for bone anchorage in orthodontics. These temporary skeletal anchorage devices (TAD) are smaller than extraoral appliances and require short healing periods [27]. Various techniques have been developed to use miniplates and miniscrews as temporary anchorage devices. De Clerck et al. treated a series of Class III cases with orthopedic traction on miniplates [12].

2.3.1. Miniplate in combination with Class III elastics

Showkatbakhsh et al. [13] used Class III elastics connected from two mandibular miniplates to an upper removable appliance to treat an 11-year-old boy with maxillary deficiency. Plates for orthodontic anchorage were placed under local anesthesia in the canine areas of the mandible by a maxillofacial surgeon. The ideal position for miniplate insertion was evaluated by using a panoramic radiograph in order to avoid damage to the roots of the adjacent teeth and mental foramen. A tightly fitting and well-retained upper removable appliance was fabricated with two Adams clasps on the upper first permanent molars. Each of the Adams clasps had a loop which was used for retaining the elastics. A labial bow was also used on the anterior teeth for retention. A maxillary posterior bite plate was used to disocclude the upper and lower jaws. Orthodontic latex elastics (3/16″ heavy size) were connected from the hooks of the miniplates to the Adams clasps of the removable appliance to generate approximately 500 g of anterior retraction. The patient was instructed to wear the appliance full time except for eating, contact sports, and toothbrushing; he was also told to change the elastics every day (**Figure 9**). After 10 months of active treatment, a positive overjet and Class I buccal segments were achieved and the anterior cross bite of the patient was corrected (**Figures 10** and **11**).

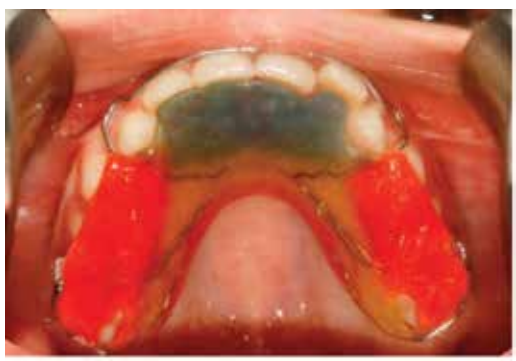

Figure 9. Miniplate in situ.

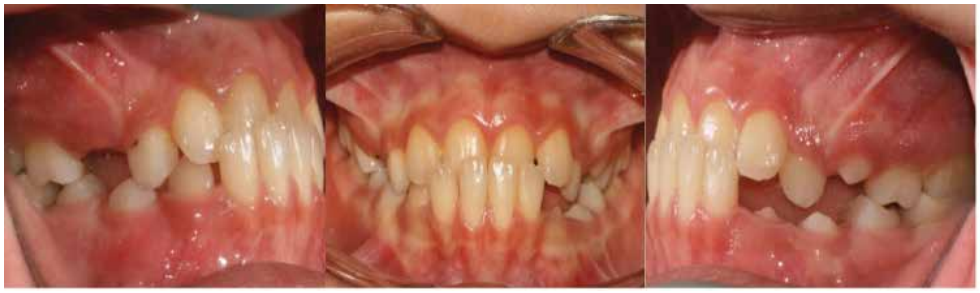

Figure 10. Pretreatment photos of an 11-year-old boy with pseudoprognathism (maxillary deficiency).

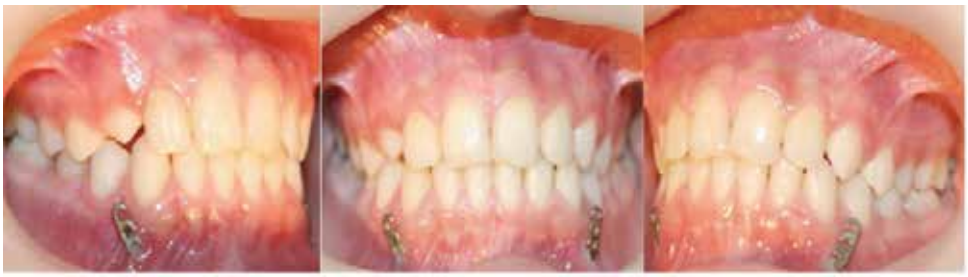

Figure 11. Posttreatment photos of the same patient treated by miniplates and Class III elastics.

2.3.1.1. Limitations

The need for minor surgery for inserting and removing the miniplates is their biggest disadvantage. Moreover, since the surgery involves flap elevation, it must be done by a maxillofacial surgeon under local anesthesia. Difficult oral hygiene around the appliance is another disadvantage of miniplates.

2.3.2. Miniscrews in combination with Class III elastics

Ease of placement, often by orthodontists themselves, has made miniscrews very popular. When used as orthodontic anchorage, they also have the advantage of fewer adverse effects and lower operational costs than tooth implants. Recently, Jamilian et al. used titanium alloy miniscrews along with Class III elastics for forward positioning of the maxilla of a patient with maxillary deficiency. In order to do so, self-drilling titanium alloy Jeil™ miniscrews (Jeil Medical Corp., Seoul, Korea; 1.6 mm diameter, 8 mm length) were placed under local anesthesia into the buccal alveolar bone between the mandibular canine and first premolar roots on both sides. The ideal position for screw insertion was evaluated by using a panoramic radiograph in order to avoid damage to the roots of the adjacent teeth and mental foramen. A tightly fitting and well-retained upper removable appliance was fabricated with Adams clasps on the upper first permanent molars and premolars. C clasps were placed on the upper permanent canines and central incisors. Orthodontic latex elastics (5/16″ medium size) were

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connected from the miniscrews to the Adams clasps of the removable appliance to generate about 450 g of anterior retraction. The patient was instructed to wear the elastics all the time, except for eating and to change the elastics every day. In order to retain these elastics, the Adams clasps on the molars and premolars were bent to form four loops; however in order to achieve optimal traction, the elastics were only connected to the loops adjacent to the molars (**Figure 12**).

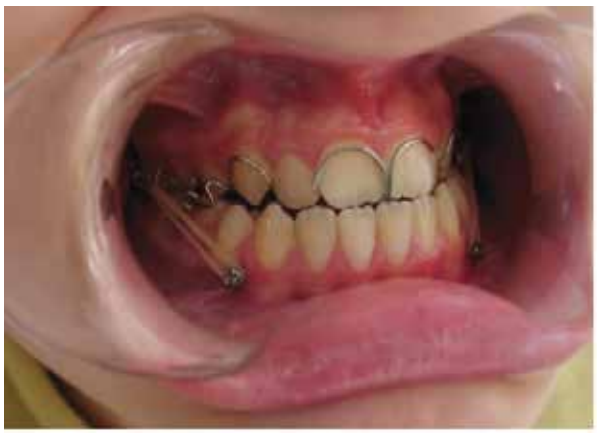

Figure 12. Miniscrews and Class III elastics.

An expansion screw was placed in the midpalatal area of the upper removable appliance and the patient was instructed to turn the screw once a week in order to correct the posterior cross bites. Two Z-springs were inserted in the upper removable appliance to correct the cross bite on the lateral incisors (**Figure 13**).

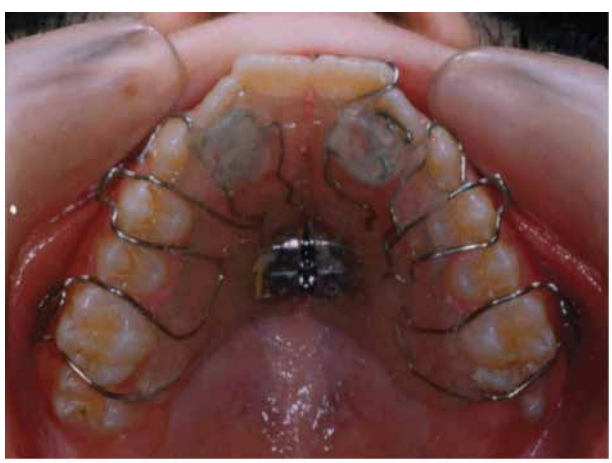

Figure 13. Expansion of the maxillary arch.

After 8 months of active treatment, a positive overjet and Class I buccal segments were achieved and the cross bites were corrected (**Figures 14** and **15**).

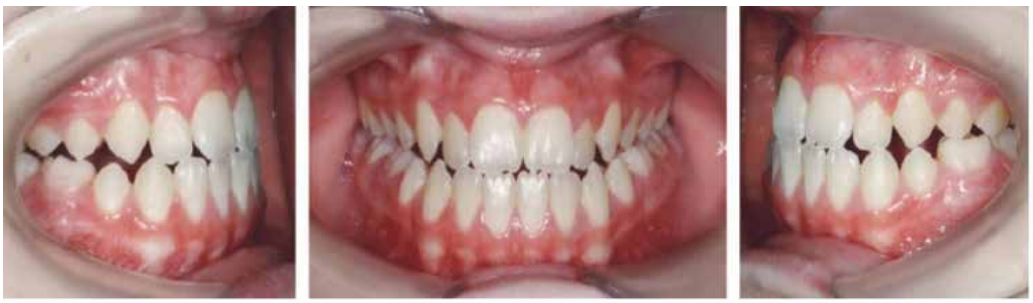

Figure 14. Pretreatment photographs of a 12-year-old boy with maxillary deficiency.

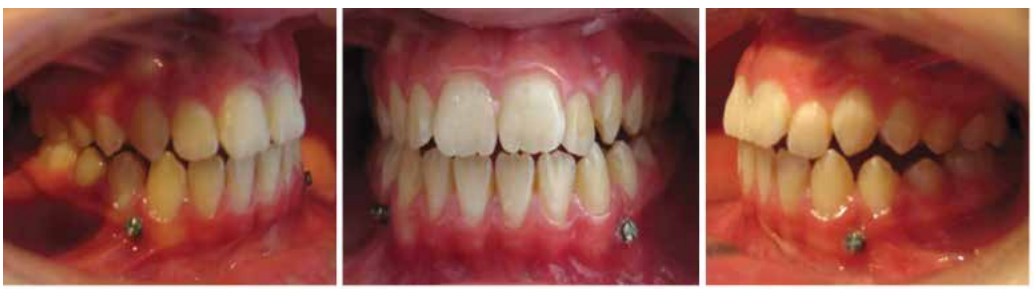

Figure 15. Post-treatment photographs of the same patient.

2.3.2.1. Limitations

The limitations of miniscrews include a high risk of failure when placed in unattached gingiva, screw loosening, tooth root injury when placed in keratinized mucosa, and limited amount and direction of tooth movement depending on the position of the miniscrews.

3. Conclusion

In growing patients with maxillary deficiency, maxillary advancement by orthopedic forces may be considered to be a viable treatment option. A number of techniques have been described, both intraoral and extraoral as well as direct force application through implants placed in the zygomatic processes with good results.

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Chapter 20

Advances in Management of Class II Malocclusions

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Farnaz Younessian and Sahar Hadadpour

Additional information is available at the end of the chapter

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Abstract

Although mandibular advancement by bilateral sagittal split osteotomy seems to be a good mandibular treatment option to treat skeletal class II malocclusion, it is less stable than setback; relapse depends on a wide range of patient-centered and surgeon-centered factors relating to the skill and experience of the surgeon, proper seating of the condyles, the exact amount of mandibular advancement, the tension of the muscles and soft tissues, the mandibular plane angle, and the patient's age. In fact, patients with low and high mandibular plane angles have increased vertical and horizontal relapses, respectively. Nonsurgical management of class II malocclusion may be an option by which to effectively manage such cases. The present chapter discusses different treatment modalities for clinical management of class II malocclusion in growing and non-growing patients.

Keywords: class II malocclusion, diagnosis, treatment, management, advances

1. Introduction

Class II malocclusion is among the most common developmental anomalies with a prevalence ranging from 15 to 30% in most populations [1, 2]. This malocclusion is likely to produce significant negative esthetic, psychological, and social effects [3–6]. This dentofacial anomaly can be divided into two different categories based on the involved arch to maxillary excess or mandibular deficiency [7, 8]. The resulting anomaly may demonstrate various severities of class II malocclusion in different ages, which dictates the preferred approach to clinical management.

2. Etiology and pathogenesis of class II malocclusion

Like other types of malocclusions, the etiology of class II malocclusion has been linked to hereditary and environmental factors [9].

2.1. Class II division 1

Proclination of upper incisors and/or retroinclination of the lower incisors by a habit or the soft tissues can result in an increased overjet in any type of skeletal pattern [10]. In class II division 1, the lips of the parents are usually incompetent and they try to compensate it via circumoral muscular activity, rolling the lower lip behind the upper incisors, or moving the tongue forward between the incisors, or a combination of all these items [11]. Finger-sucking or other oral habits may also lead to the development of this malocclusion, mostly following imbalances of the buccinator muscles and tongue force, and narrowing the maxillary arch. In addition, habits usually procline the upper incisors and retrocline the lower incisors (**Figure 1**).

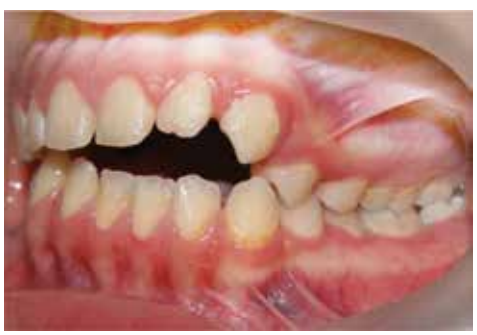

Figure 1. Prolonged thumb-sucking habit creating asymmetric open bite and class II malocclusion.

Dental features such as tooth size arch length discrepancies could be involved in developing class II malocclusion, which might be the reason for the labial movement of the upper incisors resulting in exacerbation of the overjet (**Figure 2**).

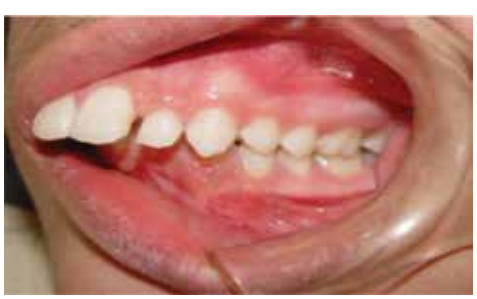

Figure 2. Class II div 1 malocclusion with class II molar and canine relationship and increased overjet and overbite.

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2.2. Class II division 2

Vertical dimension of class II division 2 patients is usually decreased in comparison to other types, which may result in the absence of an occlusal stop on lower incisors and consequently an increase in the overbite [11]. Dental crowding also, in contrast to the div 1 category, is exacerbated by retroinclination of the upper incisors [11, 12]. Active muscular lips are responsible for upper and lower retroinclination in this type (**Figure 3**).

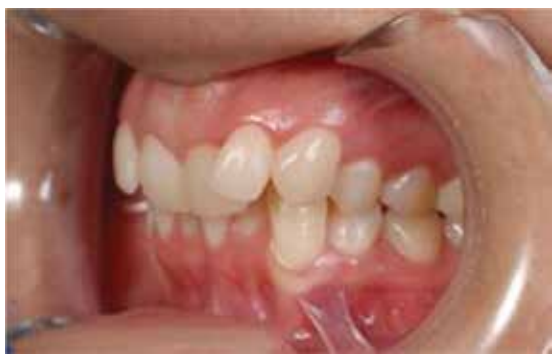

Figure 3. Retroclined upper central incisors, proclined laterals, and increased overbite in a class II div 2 case.

3. Diagnosis and clinical features of class II malocclusion

As in other types of malocclusions, class II malocclusion could be identified based on precise clinical evaluation (extra- and intra-oral features), diagnostic aids (history, photographic analysis, radiographic analysis, and cast analysis), and functional analysis (examination of postural rest position and maximum intercuspation, examination of the temporomandibular joint and orofacial dysfunction) of the patients [11–13]. The angle defined class II malocclusion as characterized by a distal relation of the lower to the upper permanent first molars to the extent of more than one-half the width of one cusp and the maxillary incisors being protrusive [14]. Class II division 1 patients demonstrate convex profile, dolichocephalic shape of the head, shallow/deep mentolabial sulcus, hyperactive mentalis, and upper lip. Class II division 2 patients present straight to convex profile, mesocephalic or dolichocephalic head shape, normal or hyperactive mentolabial sulcus, and normal or hyperactive upper lip [11, 12].

The presence of distal step molar relation, tooth size discrepancy, and/or excessive overjet may lead the clinicians to a false interpretation of skeletal class II malocclusion [9]. Skeletal class II malocclusion components may be classified by maxillomandibular relationship (mandibular retrognathism, midface protrusion or both), the cranial base length (increased length of the anterior cranial base: midface protrusion, while lengthening of the posterior cranial base: more retruded position of the temporomandibular articulation), vertical discrepancy (anterior upper face height often greater than normal), and steep occlusal plane (**Figure 4**) [9].

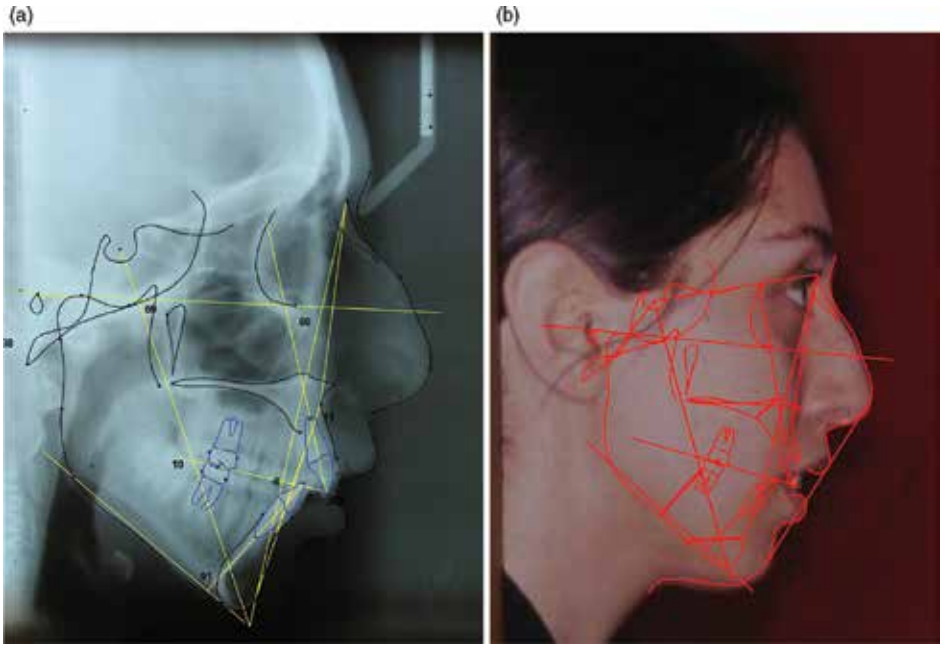

Figure 4. (a) Lateral cephalometric analysis of a patient with class II malocclusion and vertical growth pattern. (b) Superimposition of lateral cephalometric analysis on the soft-tissue profile of the patient (overlay tracing).

4. Treatment of class II malocclusion

Treatment strategies of class II malocclusion are categorized based on the growing and non-growing status of patients. Treatment timing of class II malocclusion has long been a topic of controversy for decades [15–17]. The literature is replete with research aimed at answering most clinical challenges of this type of malocclusion [18]. The existing evidence suggests that providing early orthodontic treatment for children with class II malocclusion and prominent upper front teeth is more effective in reducing the incidence of incisal trauma than providing one course of orthodontic treatment when the child is in early adolescence [19].

4.1. Early management in the mixed dentition

The best treatment modalities for class II malocclusion in growing patients include using functional appliances either removable (Activator, Bionator, Frankel, and Twin-block) or fixed appliances (MARA, cemented Twin-block, or Herbst appliance) that mostly enhance further mandibular growth via mandibular advancement and also headgear (Cervical, Highpull, and combination type), which provides extra oral force to restrict further maxillary growth [20–22] (**Figures 5** and **6**).

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Figure 5. (a) Patient at age 11 years: frontal and profile photographs of the patient before treatment. (b) Intraoral photographs of the patient showing class II div 2 malocclusion. (c) Patient at age 13 years: photographs of the patient after treatment with cervical headgear and fixed orthodontic treatment. (d) Intraoral photographs of the patient after treatment.

Figure 6. (a) Frontal and profile photographs of the patient at age 12 years prior to treatment. (b) Intraoral photographs of the patient showing class II div 1 malocclusion with increased overjet and overbite before treatment. (c) Photographs of the patient at age 14 years after an 8-month treatment with Twin-block, followed by fixed orthodontic treatment. (d) Intraoral photograph of the patient after treatment. (e) Pretreatment and posttreatment lateral cephalograms.

Both removable functional appliances and headgear therapy depend on the cooperation of the patients. However, in contrast to the theory, there would not be a clear cut between clinical indications of these two broad clinical interventions of class II malocclusions [23]. Among the different removable appliances, Twin-block is used more often [18], which can efficiently promote mandibular growth, restrict further forward growth of the maxilla, and improve skeletal relationships in growing skeletal class II individuals with mandibular retrusion [24, 25].

Figure 7 demonstrates a 14-year-old boy with class II malocclusion and bilateral buccal crossbite (Brodie syndrome). His mandible was totally locked and could not grow normally. Treatment began with a removable anterior bite plate, an open midpalatal screw in the acrylic portion for the upper arch in order to constrict the expanded ridge, and a Quad-helix appliance for the lower arch to expand the ridge. After 3 months, treatment was continued with a Twin-block appliance and an open screw in the maxilla. Fixed orthodontic treatment was performed for only 6 months.

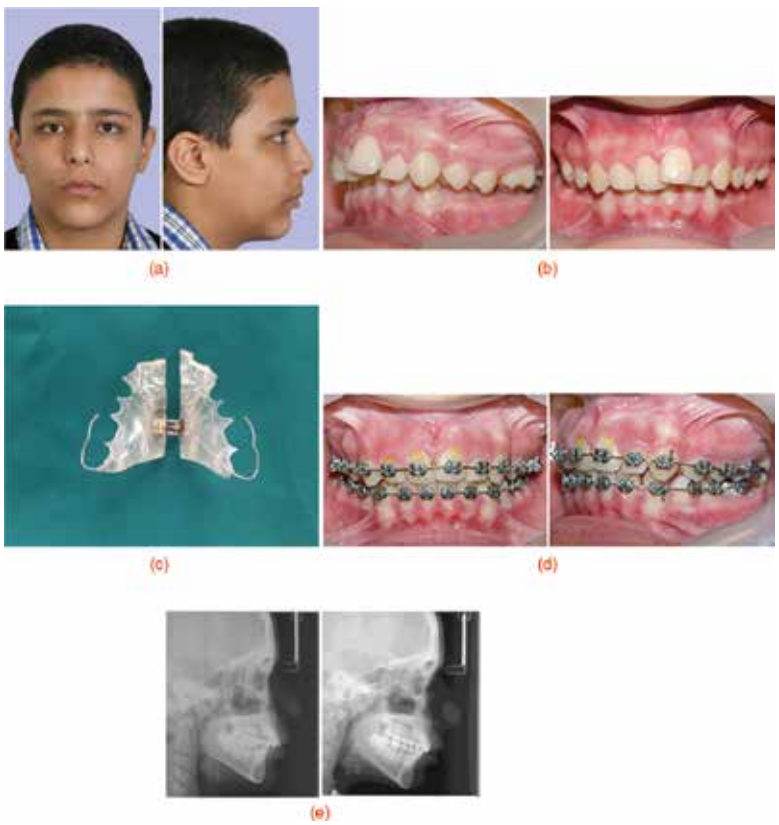

Figure 7. (a) Frontal and profile photographs of the patient before treatment. (b) Intraoral photograph before treatment. (c) Anterior bite plate and open screw in midpalatal portion. (d) Intraoral photograph of the patient 6 months after beginning the treatment. (e) Pretreatment and posttreatment lateral cephalograms.

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Several systematic review studies have investigated the present literature on the effect of treatment with functional appliances in comparison with untreated controls and demonstrated that skeletal changes were statistically significant, but unlikely to be clinically significant [26]. The limited quality and heterogeneity of the present studies in this field restrict the power of pure clinical judgment. However, in two recent systematic review articles, removable functional appliances were effective in improving class II malocclusion in short term, although their effects are mainly dentoalveolar, rather than skeletal [27]. On the other hand, more long-term skeletal effects following removable functional appliances were seen in patients during their pubertal growth phase, compared to prepubertal phase [18, 25]. However, their soft-tissue changes were minimal from the clinical standpoint [28].

Fixed functional appliances were introduced first by Emil Herbst to overcome the cooperation obstacle of removable appliances [29]. The key differences between removable and fixed appliances are different working hours (intermittent vs. continuous), and also optimal treatment timing (before puberty growth vs. at or after puberty spurt) and direction of further growth [30]. To date, there are a limited number of studies evaluating clinical effectiveness and patient's experience and perceptions of these fixed functional appliances [23]. As it is stated in the literature, fixed functional treatment is effective when performed during the pubertal growth phase, and very little data are available on postpubertal patients [31]. Various types of fixed functional appliances (rigid, semirigid, and flexible) have been developed and used in clinical settings [13] (**Figure 8**). However, dental changes including mesial movement of lower molars and proclination of lower incisors were proven more significant than skeletal changes following their implication, compared to removable appliances [18, 32], which can negatively affect the long-term stability of the results. Many treatment modalities have been introduced to minimize the aforementioned side effects of these appliances including the application of increased-dimension arch wire, negative torque arch wire, and the use of lower incisor brackets with increased lingual crown torque [33, 34].

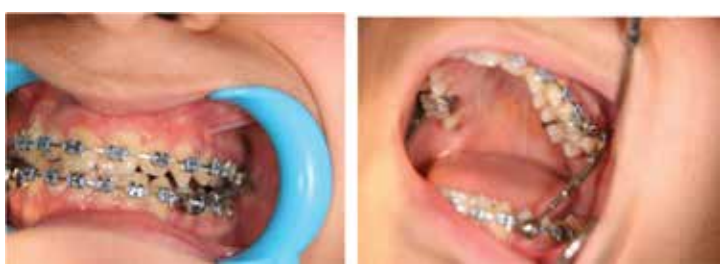

Figure 8. Fixed functional appliance.

Recently, clinicians tried to control the dentoalveolar side effects of fixed functional appliances by means of bone anchorage such as miniscrews and miniplates [35–37]. The results of the studies investigating the efficacy of skeletal anchorage were controversial and need further investigation [1, 38–40].

4.2. Late management of class II malocclusion

Currently, the number of adult patients seeking orthodontic treatment has gradually increased which focus mostly on camouflaging the malocclusion [41]. In contrast to growing patients, limited range of treatment modalities could be served for adult cases with class II skeletal and dental malocclusions. Depending on the severity of malocclusion, class II elastics, compensatory extraction (maxillary premolars and/or mandibular premolars) or even orthognathic surgical modalities may be used to alleviate the functional and esthetic problems associated with this type of malocclusion [42] (**Figures 9–11**).

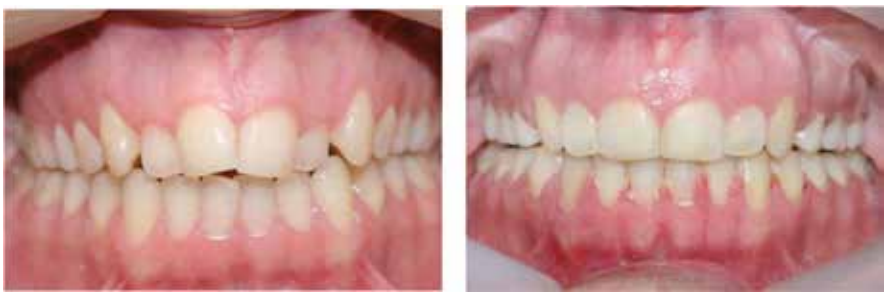

Figure 9. Pre- and posttreatment intraoral photographs of a patient using cervical headgear non-extraction treatment.

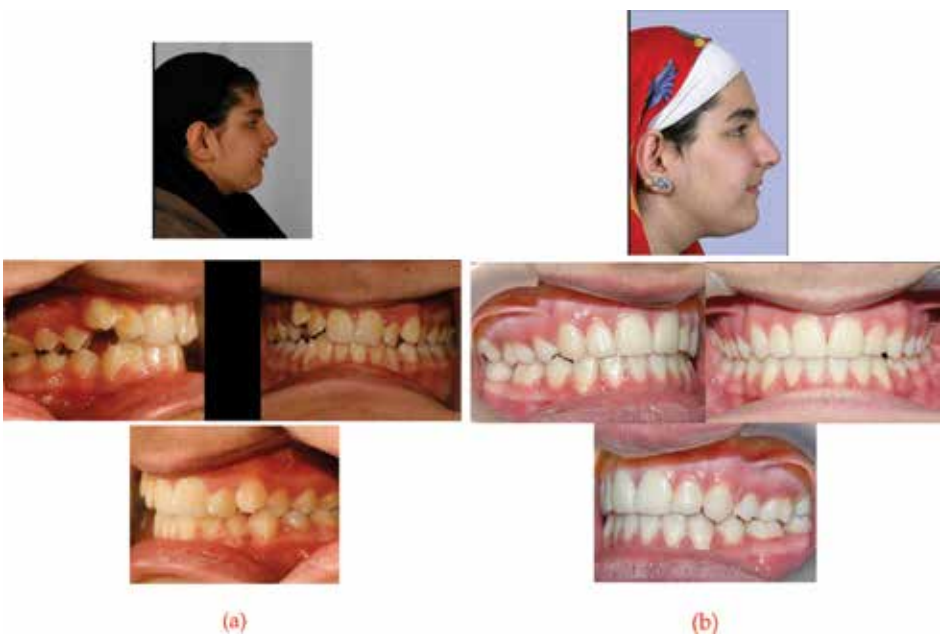

Figure 10. (a) Profile and intraoral photographs of the patient at age 13 years. Treatment plan was to extract upper first premolars and lower second premolars. (b) Photographs of the patient after treatment at age 15 years.

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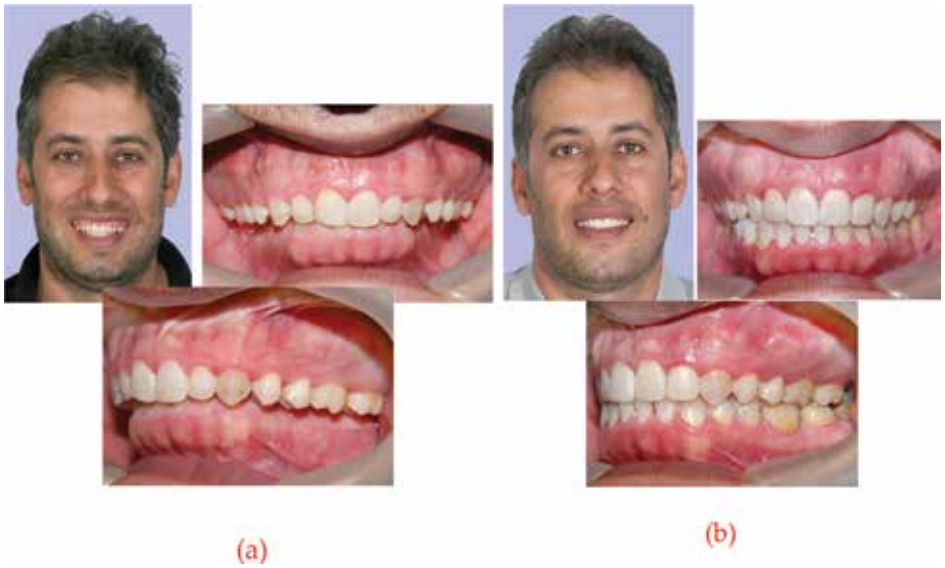

Figure 11. (a) Frontal and intraoral photographs of the patient with bilateral buccal crossbite. (b) Profile and intraoral photographs of the patient at the end of treatment.

The patient presented in **Figure 11** is another case of Brodie syndrome but at the age of 34 years. Fixed orthodontic treatment in combination with upper removable constriction plate and Quad-helix appliance in the lower arch was performed for 12 months, and then the patient underwent Lefort I (two-piece constriction and impaction) and mandibular advancement surgery. Postsurgical orthodontic treatment was continued for 5 months. Prevention of such complex orthognathic bimaxillary surgery could have easily been achieved in growing patients (**Figure 7**).

Class II elastics with non-extraction treatment plan is a typical interarch approach for managing mild class II malocclusion [43]. The effects of class II elastics include mesial movements of the mandibular molars, tipping of the mandibular incisors, distal movements and tipping of the maxillary incisors, extrusion of the mandibular molars and maxillary incisors, and consequently clockwise rotation of the mandibular plane [44]. As success of treatments based on interarch elastics depends heavily on patient compliance for their effectiveness, poor cooperation can lead to poor treatment outcomes and increased treatment time [45].

In many non-extraction cases, the pendulum appliance is the most effective and commonly used device for distalizing maxillary molars. Its significant clinical advantages include minimal dependence on patient compliance, allows for correction of minor transverse and vertical molar positions by incorporation of u-loop in adjustment springs (which further enhance additional space achievement), and laboratory-friendly fabrication. Palatal coverage concomitant to pendulum appliance mediated to reduce the moderate anchorage loss effect causing upper incisor proclination [46]. The expected distal movement of the first molars appears to be more significant if it could be used before the eruption of the upper second

molars. To achieve proper distal movement of dentition after second molar eruption, clinicians may need to distalize the second molars first, followed by using a palatal arch bar (PAB) or Nance holding arch for retention. Then, the first molars are distalized. The extraction of erupted second molars can be done in case of great demand of distalizing first molars and the presence of erupting third molars, which may totally replace the second molar position [47] (**Figures 12** and **13**).

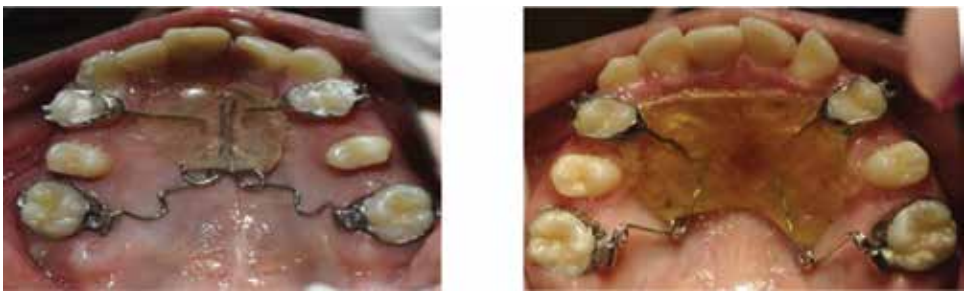

Figure 12. Distalizing maxillary molars by pendulum appliance, palatal coverage for anchorage control.

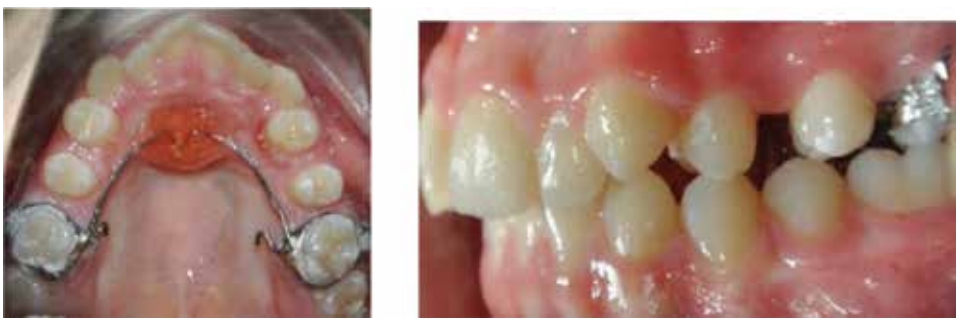

Figure 13. Nance holding arch for retention after achieving angle class I for the first permanent molars.

In a very recent study, both pendulum and distal screw seem to be equally effective in distalizing maxillary molars; however, greater distal molar tipping and premolar anchorage loss can be expected using the pendulum appliance [46].

Extractions of only upper premolars are indicated for some special patients. According to a current soft-tissue paradigm, clinicians must pay attention to several factors such as soft-tissue thickness, amount of pretreatment crowding or cephalometric discrepancy, when deciding their extraction regimens for adult patients [48, 49]. As it is stated in a very recent systematic review, when class II division 1 malocclusion is treated with maxillary and mandibular premolar extractions, the nasolabial angle increases and the lips are retracted. However, there is less retraction of the lower lip in the only upper premolar extraction protocol [50]. A delicate adjustment and trade-off between the amount of anterior retraction and the mesial movement of the posterior segment following extraction regimens in each vulnerable adult class II patient

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have to be considered to maintain the profile and the position of the upper lip at its most appropriate state. In order to reduce anchorage loss and space management obtained in extraction and non-extraction cases (distalizing appliances), temporary anchorage devices have been introduced in clinical orthodontic situations [51]. These devices serve considerable advantages including the ease of insertion and the removal in addition to the possibility of immediate loading [52, 53]. The only distinct factors predicting temporary anchorage device failures were soft-tissue inflammation surrounding a temporary anchorage device and early loading (within 3 weeks after insertion) [54].

In rare and very severe cases, distraction osteogenesis (DO) with or without further orthognathic surgery can be done to promote the situation [55, 56]. This procedure can be applied for very severe class II malocclusions following mandibular deficiencies with wide age range such as infants with Pierre Robbins syndrome, growing children with severe class II malocclusion (**Figures 14** and **15**), or even adult patients with the history of bilateral condylar ankylosis (**Figure 16**).

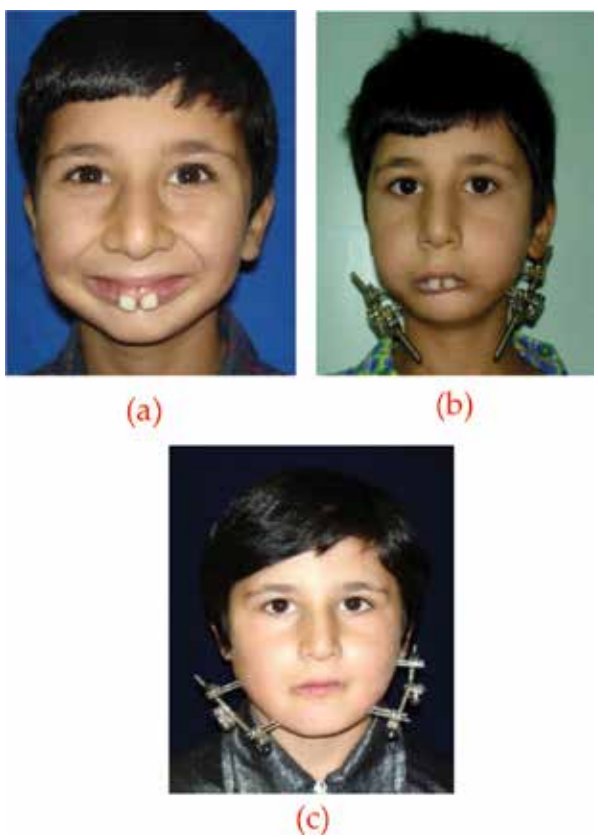

Figure 14. (a) Frontal photograph of the patient before distraction. (b) Bilateral extraoral distractors in place. (c) Post-distraction photograph after 30-mm activation.

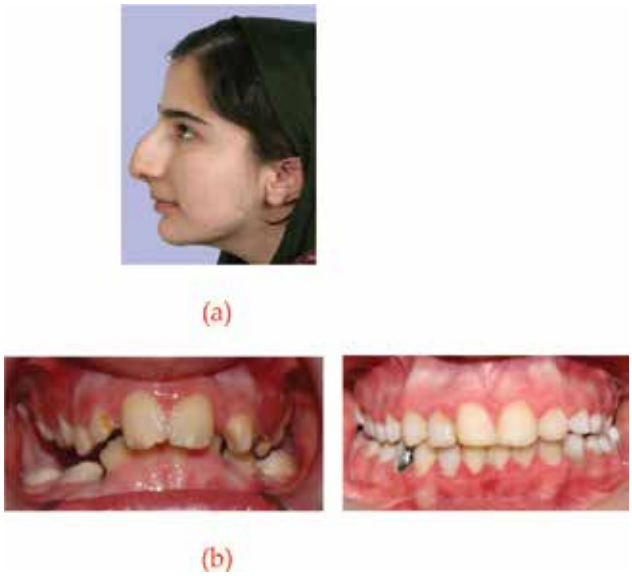

Figure 15. (a) Pre- and postdistraction photographs of patient's profile. (b) Intraoral photographs of the patient before and after bilateral DO.

Figure 16. (a) A 29-year-old patient with bilateral condylar ankylosis. (b) CBCT scans of the patient. (c) At age 33 years after bilateral distraction osteogenesis, orthognathic surgery, and genioplasty.

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In severe class II malocclusion cases, orthognathic surgery (mandibular advancement with or without maxillary impaction) can be done to enhance soft-tissue esthetic [57, 58]. The proper presurgical orthodontic tooth movements and alignment of arches are essential to maximize the amount of discrepancy correction during surgery [59]. Many class II patients present with proper mandible size, which is located downward and backward secondary to vertical maxillary excess. Superior impaction of the maxilla with proper center of rotation allows the mandible to rotate upwards and forwards, which enhance the facial height and increase chin prominence [59]. Although orthognathic surgery could be an efficient treatment modality in severe class II patients, both the cost of the surgery and the fear of undergoing surgery normally prevent patients from choosing this treatment option [60]. Furthermore, most of the studies on surgery-first approach are done on class III malocclusion cases, which significantly reduced treatment time with equal dentoalveolar short- and long-term results [61] (**Figures 17–20**).

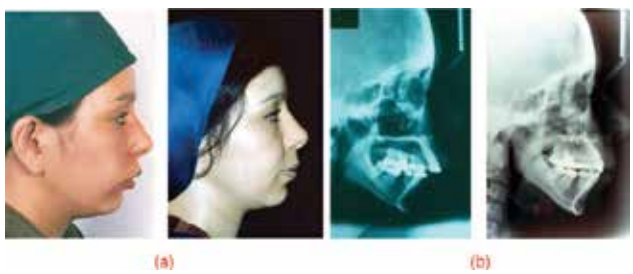

Figure 17. (a) Pre- and postsurgical (maxillary narrowing and mandibular advancement) photographs of the patient. (b) Pre- and postsurgical lateral cephalograms.

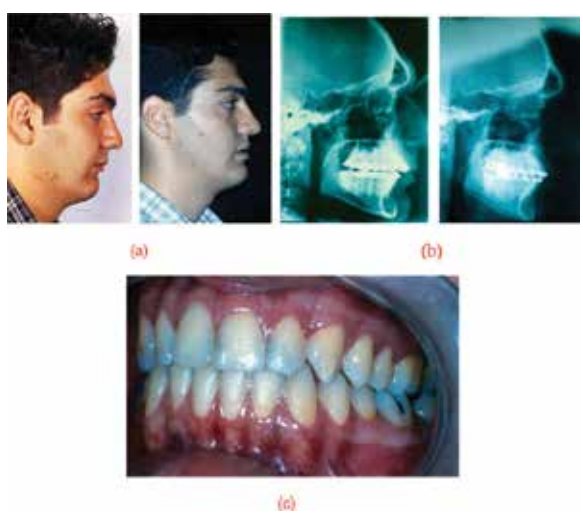

Figure 18. (a) Pre- and postsurgical (mandibular advancement) photographs of the patient. (b) Pre- and postsurgical lateral cephalograms. (c) Posttreatment occlusion.

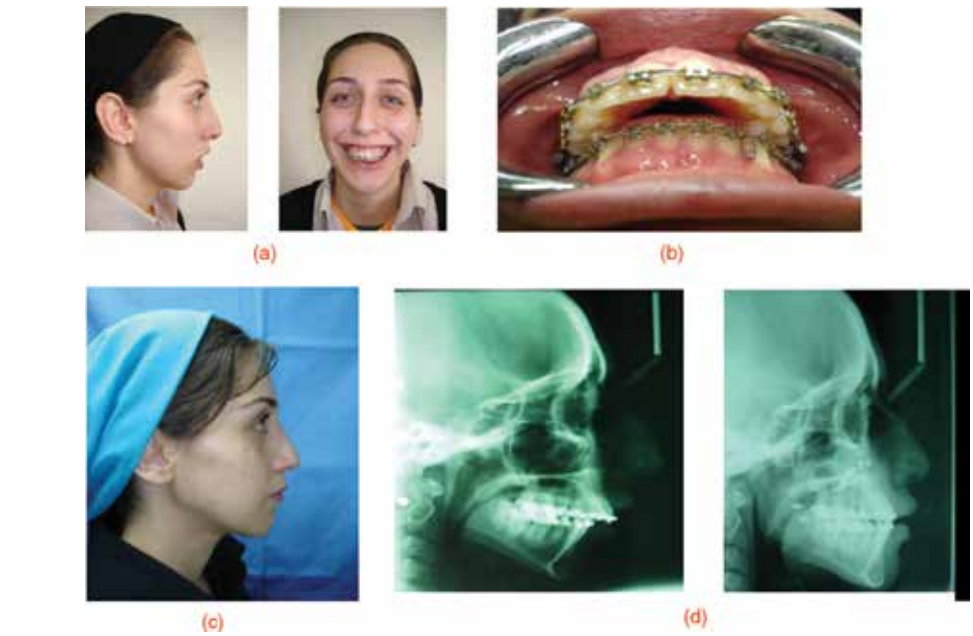

Figure 19. (a) Profile and frontal photographs of the patient before surgery. (b) Intraoral view of the patient prior to surgery. (c) Profile photograph of the patient after maxillary impaction and mandibular advancement surgery. (d) Lateral cephalograms of the patient before and after surgery.

Figure 20. (a)Frontal photograph of an adult patient with major thalassemia, severe class II malocclusion 9-mm overjet, and 8-mm overbite before surgery. (b) Frontal photograph after 12-mm maxillary impaction and 8-mm setback plus genioplasty.

The clinical efficacy of orthognathic surgery on preexisting temporomandibular disorder (TMD) in class II patients is controversial [62, 63]. There are some reports of postsurgical

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condylar resorption in class II adult patients [64]. This could be the result of direct changes in the position of condyle, which may take place by inappropriate application of rigid fixation during surgery, worsening the TMD [65]. On the other hand, the improvement of clinical symptoms after orthognathic surgery can be explained by the better occlusal stability following surgery [66] (**Figure 21**).

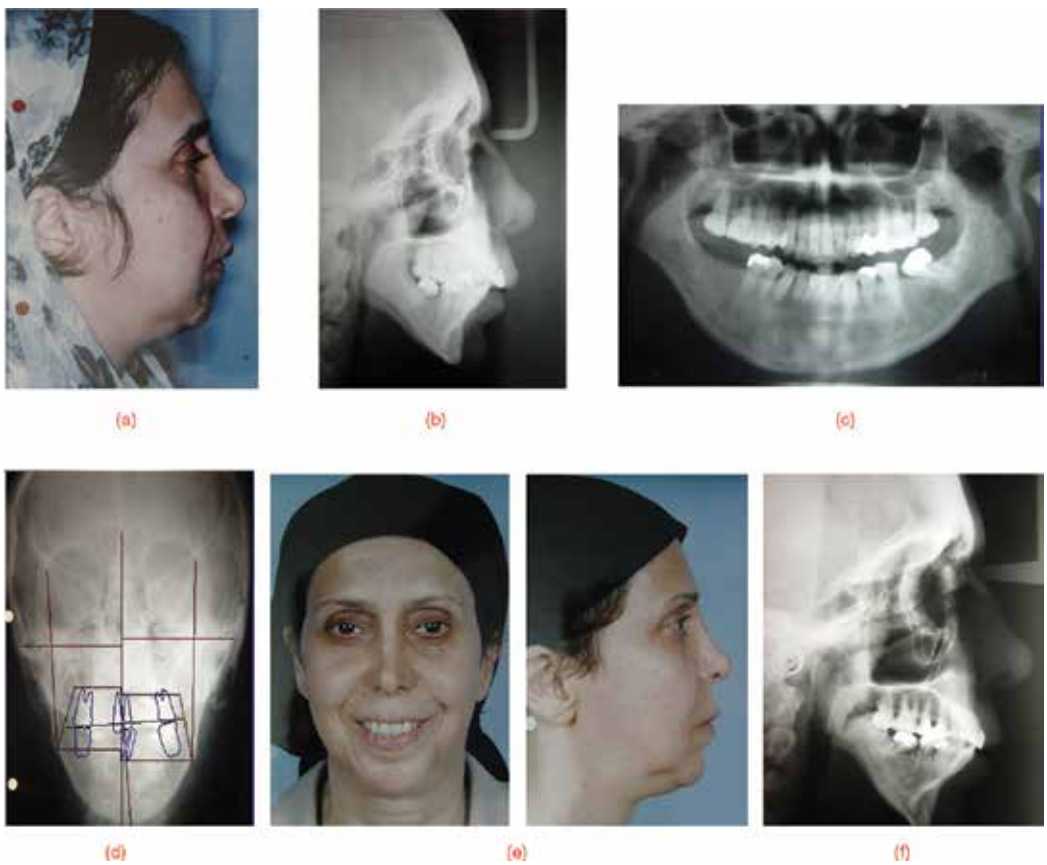

Figure 21. (a) Profile photograph of a patient with class II malocclusion and TMD. (b) Lateral cephalogram of the patient before treatment. (c) Panoramic view of the patient before treatment. (d) PA cephalogram showing cant of the maxilla and deviation of the mandible. (e) Frontal and profile photographs of the patient after mandibular advancement (nonrigid fixation). (f) Lateral cephalogram of the patient after surgery.

Mandibular DO has been introduced to correct severe skeletal discrepancies in class II adult patients [67]. This technique was first developed by Ilizarov for the long bones in the 1950s [68] and was ultimately applied for the facial skeleton [55, 69, 70]. At first, clinicians thought this method might end up in less neurosensory disturbances and a more stable result compared to the routine bilateral sagittal split osteotomies. However, these findings were not verified later by more controlled studies as they reported no considerable differences regarding neurosensory disturbances and short- or long-term skeletal stability [71] (**Figure 22**).

Figure 22. (a) Predistraction profile photograph and lateral cephalogram of an adult patient. (b) Postdistraction profile photograph and lateral cephalogram. (Bilateral intraoral distractors were used.)

5. Relapse

Despite the correction of a class II malocclusion, a considerable number of class II patients experience some level of unpredictable relapses in following years after treatment [28]. Reported relapse rates following these treatments range from 20 to 52% [72]. The only available evidence on stability of treatment regards the Herbst appliance [72]. Several factors including gender, muscular functions and pretreatment habits, different treatment modalities, and posttreatment occlusion have been considered as potential factors affecting stability of the result. However, a very recent systematic review concluded that currently, there is very limited evidence to support the influence of predictive factors on relapse or stability of treatment outcomes [73].

Although mandibular advancement by bilateral sagittal split osteotomy seems to be a good treatment option for skeletal class II, it is less stable than setback in the short and long terms [74]. Miniplates demonstrated better long-term results than bicortical screws of titanium, stainless steel, or bioresorbable material. However, their short-term relapse rate was approximately comparable in class II malocclusion patients. This observed relapse depends on a wide range of patient-centered and surgeon-centered characteristics involving the skill and experience of the surgeon in the proper seating of the condyles, the exact amount of mandibular advancement, the tension of muscles and soft tissue, the mandibular plane angle, and the patient's age. Patients with low and high mandibular plane angles have increased vertical and horizontal relapses, respectively [74].

6. Diagram

Class II Malocclusion Treatment

- Growing
  - Functional

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        - Removable
            - Activator
            - Bionator
            - Frankel
            - Twin-block
        - Fixed
            - MARA
            - Cemented Twin-block
            - Herbst
    - Headgear (skeletal effect)
        - Cervical
        - High pull
        - Combination
- Non-growing
    - Camouflage
        - Non-extraction regimen with class II elastics
        - Distal movement of upper teeth ± second molar extraction
            - Pendulum
            - Headgear (dental effect)
            - Miniscrew-assisted distalizations
        - Extraction of maxillary premolars
    - Orthognathic surgery
        - Mandibular advancement
        - Bimax surgery
    - DO
- Relapse

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Section 11

Computer-Aided Surgery

Chapter 21

Computer-Aided Designed/Computer-Aided Manufactured and Conventional Techniques in Maxillofacial Reconstruction with Free Fibula Flaps

Jan Rustemeyer, Aynur Sari-Rieger,
Alexander Busch, Alex Melenberg and Lutz Günther

Additional information is available at the end of the chapter

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Abstract

We treated 26 patients via vascularized osteocutaneous fibula flaps for maxillofacial osseous reconstruction between September 2012 and October 2015. The CAD/CAM technique was attempted for all patients needing bony maxillofacial reconstructions. The time interval from deciding to use the CAD/CAM technique and receiving the hardware depended on the capacity of the CAD/CAM providing companies. It usually takes between 3 and 4 weeks. Hence, the CAD/CAM technique was not used for patients with rapid tumor growth or pathologic fractures of the mandible. In these urgent cases, surgery could not be delayed and the conventional technique was used. In the abovementioned time period, 11 patients underwent osseous reconstruction using CAD/CAM and 15 patients using the conventional technique. Data were collected and evaluated according to demographics, medical history, number of bone segments, and complications. Time measurements of virtual planning sessions, flap harvesting, flap ischemia, tourniquet inflation, total reconstruction, and overall operating times were additionally recorded.

Keywords: CAD/CAM technique, maxillofacial reconstruction, free fibula flaps, flap ischemia time, virtual planning session

1. Introduction

Computer-aided designed/computer-aided manufactured (CAD/CAM) techniques have received increasing attention in maxillofacial reconstruction. Virtual simulation and three-

dimensional (3-D) hardware such as cutting guides and stereolithographic models to avoid error during intraoperative hand-setting can be used in CAD/CAM surgery [1].

There are three basic steps of surgical treatment in computer-aided osseous reconstruction, namely:

1. Virtual planning

2. CAD/CAM rapid prototyping of the customized surgical devices and

3. Surgery [2].

The clinical indications for virtual surgical planning include the following:

1. Need for multiple free tissue transfer

2. Reconstruction of multiple mandible or midface defects

3. Multiple osteotomies in reconstructive flaps [3–5].

The advantages of virtually planned surgery over conventional surgery include the following:

a. Enhanced accuracy

b. Less deviation of reconstructed areas

c. Improved aesthetic contour and

d. better functional outcomes [6–10].

Use of CAD/CAM techniques can eliminate the need for intraoperative measurement, provide bony segments with excellent apposition, accurately duplicate the preoperative plan, and minimize adjustments upon inset of the osseous transplant [11–13].

However, whether CAD/CAM techniques accelerate the time-consuming intraoperative steps or reduce overall operative times remains controversial [14, 15].

In this chapter, the description of bony maxillofacial defects followed international classification systems. The HLC applied classification of mandibular defects refers to the classification given by Boyd et al. [16]. The capital letter "H" stands for a defect involving a lateral mandibular segment with a condyle without crossing the midline; "L" represents the same defect but without a condyle; and "C" describes a defect of the anterior mandible between the incisor foramina. The classification of defects of the maxilla referred to the classification of Okay et al. [17]. Class Ia comprises defects with no involvement of the maxillary alveolus; Class Ib describes defects with preservation of both canines; Class II stands for the resection of one canine or less than 50% of the hard palate; and Class III cases comprises the resection of both canines or greater than 50% of the hard palate.

1.1. CAD/CAM technique

High-resolution, helical computed tomography (CT) scans (0.5 mm fine cuts) of the maxillofacial area and the respective fibula donor site were performed. Data including digital imaging

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and communications in medicine (DICOM) formats were transmitted to one of two CAD/CAM device-providing companies (Xilloc, Maastricht, Netherlands; Materialise, Leuven, Belgium). Virtual planning starts with using web-based meetings or e-mail services between the company, the biomedical engineers, and the surgical team. The biomedical engineers use the geometry of the virtually resected mandible or maxilla, or mirror of the contralateral disease-free bone to create the ideal orthognathic relationship. In defects involving both sides of the mandible or maxilla, the mirroring technique was not possible. Therefore, in such cases, we have to have a database with segmented atraumatic mandibles and maxillae from other patients that can be imported as a reference (**Figure 1**).

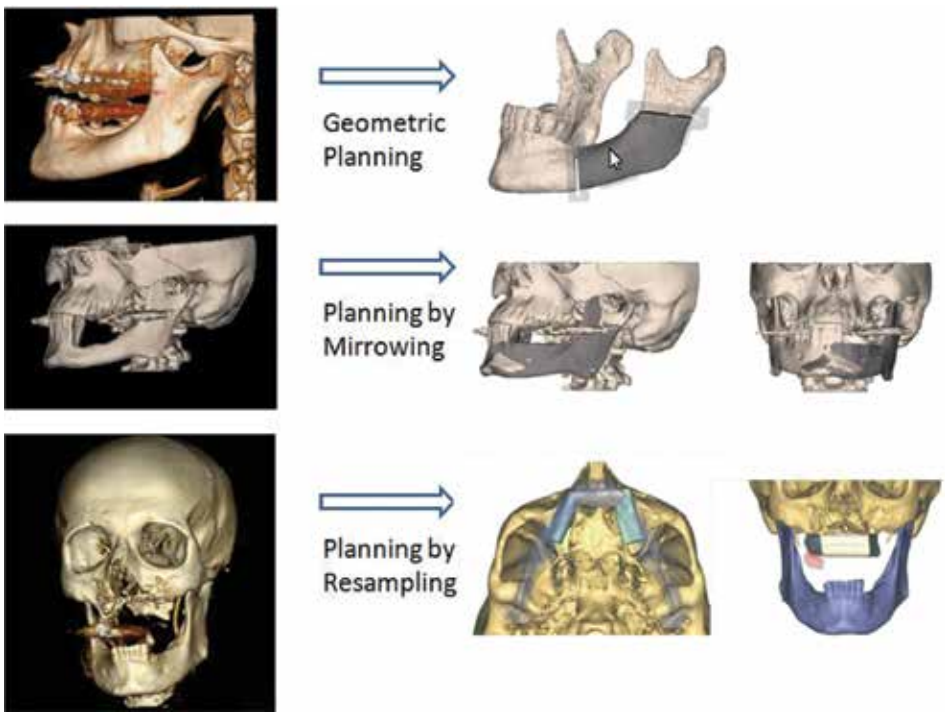

Figure 1. Virtual planning sessions.

The surgeon directs the virtual defect repair by superimposing the patient's own 3-D virtual fibula onto the mandibular or maxillary defect placing osteotomies to recreate the original mandibular or maxillary contour via a trial-and-error process until the number and cutting sites of the osteotomies, bone-to-bone contact, and segment lengths are optimized. A linearized patient-specific cutting guide designed from the cut segments of a virtual fibula with cutting slots or flanges located at appropriate lengths along the osseous transplant with proper angles is rendered to recreate the desired shape without any intraoperative measurements. Additional cutting guides for definite resection borders of the maxillary or mandibular region were created as well. Using a laser-sintering 3-D printer virtual cutting guides were converted to hardware. Stereolithographic models were manufactured similarly for the craniomaxillofacial

skeleton intended. A reconstruction plate or a 3-D bending template was manufactured. **Figure 2** displays the workflow of computer-assisted planning for reconstruction of the mandible.

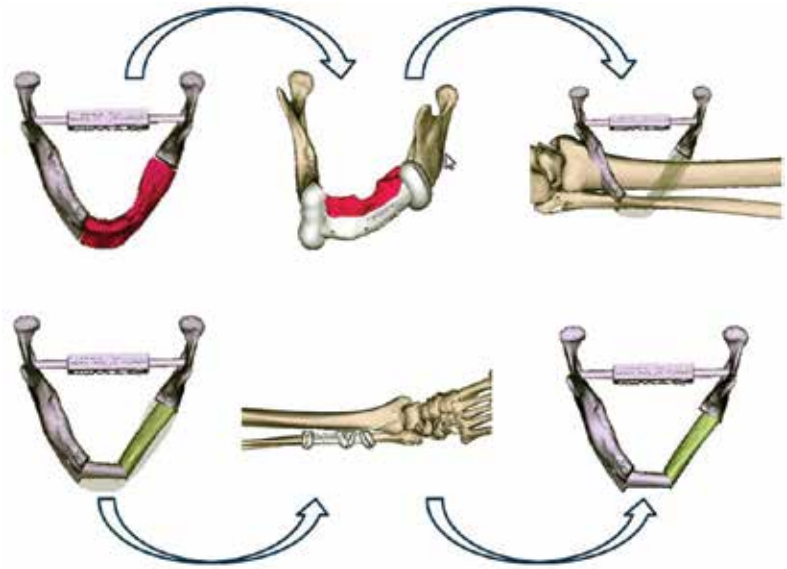

Figure 2. Workflow from virtual planning to 3-D cutting guides for intraoperative use.

1.2. Surgical technique

In order to reduce overall operation time, surgery was performed using two teams; a resection team to prepare the recipient site and a reconstruction team to harvest the fibula flap. The latter team harvested the flap according to the principles described by Hidalgo [18]. A senior surgeon did the planning, flap harvesting, modeling, inset, and microvascular anastomosis. The osteocutaneous fibula flap was dissected and isolated on the vascular pedicle under an inflated pneumatic tourniquet (350 mmHg). Strict adherence to scientifically based guidelines for tourniquet width, pressure, and duration of use is imperative [19]. After complete dissection, the tourniquet was released and meticulous hemostasis was done. In cases of using CAD/CAM technique, the cutting guides were fixed to the bone with lateral unicortical screws and osteotomies were performed with an oscillating saw placing in the cutting slots or along the flanges in order to effectively replicating the virtually planned osteotomies at the harvesting site. Fixation of the osseous segments was realized either via titanium miniplates or a pre-bent reconstruction plate. It was also possible to partially bend and fix the osteosynthesis plate to the transplant before transection of the pedicle using a sterilized defect model during surgery and also check the overall accuracy of osseous modeling (**Figure 3**). After the vascular pedicle was severed, the osseous reconstruction was transferred as a composite unit and secured to the mandibular or maxillary remnant at its optimal predetermined position.

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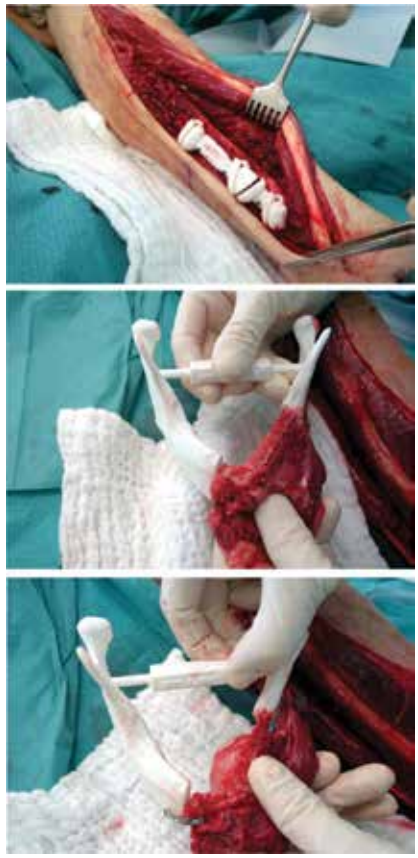

Figure 3. Sterilized defect model during surgery facilitates bending and fixing the osteosynthesis plate to the transplant to check the overall accuracy of osseous modeling before transection of the pedicle in the CAD/CAM technique group.

2. Conventional technique

When using the conventional technique, the lengths of the osseous defect and the desired fibula bone were measured with a metric ruler. Then, the fibula was harvested and the pedicle divided before segmental osteotomies and osteosynthesis were done. These procedures were performed on the back table. In contrast to the CAD/CAM technique, accuracy could only achieved by repetitive inset and trimming of the transplant, making necessary earlier transection of the pedicle (**Figure 4**).

After inset at the recipient site and fixation of the transplant, two microvascular anastomoses between the recipient neck vessels and the peroneal artery and its accompanying dominant vein are carried out in both techniques (**Figure 5**). For the arterial and venous anastomoses, interrupted sutures were used.

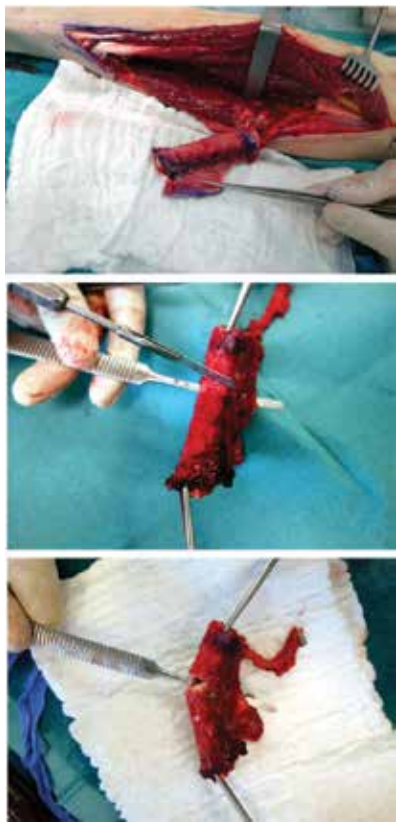

Figure 4. In the conventional technique group, accuracy could only be achieved by repetitive trimming of the transplant after transection of the pedicle on the back table.

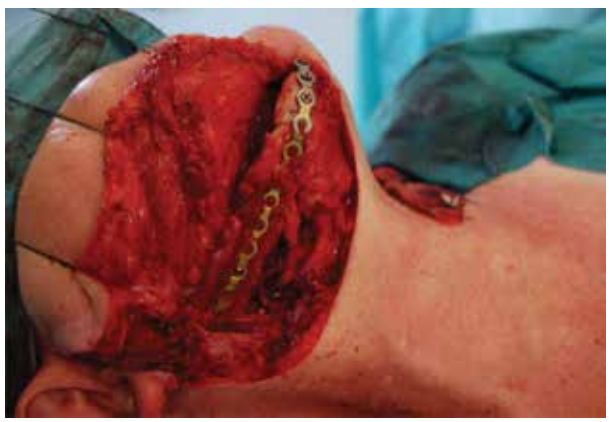

Figure 5. Inset and fixation of the transplant before microvascular anastomosis.

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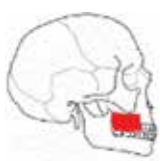
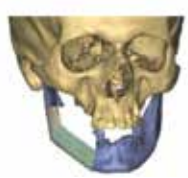
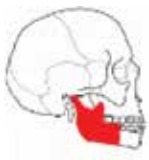
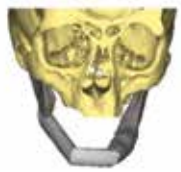
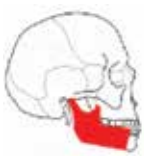
3. Outcomes

3.1. CAD/CAM group

Clinical data for all cases are shown in **Table 1** (CAD/CAM fibula flaps) and **Table 2** (conventional fibula flaps). The CAD/CAM group consisted of three patients suffering from osteoradionecrosis (ORN), two patients with squamous cell carcinoma (SCC), two patients with adenoid cystic carcinoma (ACC), and one patient with osteonecrosis of the jaw (ONJ), one patient with osteomyelitis (OM), one patient with melanotic neuroectodermal tumor of infancy (MNT), and one patient with posttraumatic defect (TRA). Immediate reconstruction was performed in only two patients undergoing the CAD/CAM technique.

Case	Age/ gender	History	Classification	Scheme	Virtual plan	Post-OP CT-scan	Osseous segments (n)
1	59/F	ORN RX SR	LCL				3
2	45/M	ONJ SR	III				3
3	38/F	ACC RX SR	Ib				1
4	64/M	ORN					2

Case	Age/ gender	History	Classification	Scheme	Virtual plan	Post-OP CT-scan	Osseous segments (n)
5	43/M	SCC RX SR	H				2
6	72/F	ORN RX SR					
7	44/F	ACC RX SR	III				2
8	57/M	SCC PR	CL				2
9	56/F	OM PR	H				2
10	36/M	TRA SR	C				2

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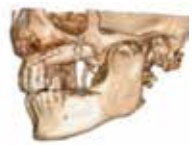
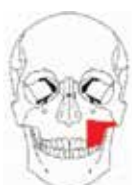
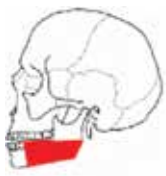
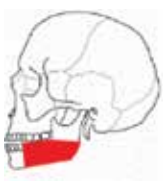
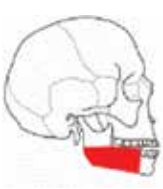
Case	Age/ gender	History	Classification	Scheme	Virtual plan	Post-OP CT-scan	Osseous segments (n)
11	17/M	MNT SR	II				1

ORN = osteoradionecrosis; ONJ = osteonecrosis of the jaw; ACC = adenoid cystic carcinoma; SCC = squamous cell carcinoma; OM = osteomyelitis; TRA = trauma; MNT = melanotic neuroectodermal tumor of infancy; RX = pre-operative radiation; PR = primary (immediate) reconstruction; SR = secondary reconstruction.

Table 1. CAD/CAM fibula flaps.

Case	Age/ gender	History	Classification	Scheme	Post-OP CT-scan	Osseous segments (n)
1	53/F	ONJ PR	LC			2
2	38/F	rACC RX PR	II			2
3	50/M	ONJ PR	CL			2
4	55/F	SCC PR	II			1

Case	Age/ gender	History	Classification	Scheme	Post-OP CT-scan	Osseous segments (n)
5	54/F	ONJ PR	CL			2
6	66/M	SCC PR	L			1
7	80/F	SCC PR	L			2
8	71/M	OM PR	L			1
9	27/M	rSCC RX PR	III			2
10	63/M	SCC PR	L			1

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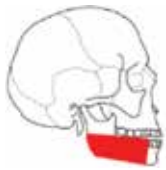
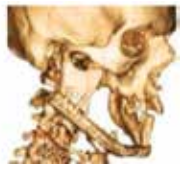
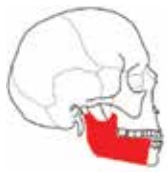
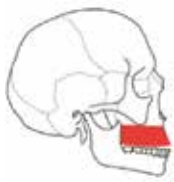
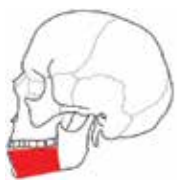
Case	Age/ gender	History	Classification	Scheme	Post-OP CT-scan	Osseous segments (n)
11	54/M	ORN RX PR	L			2
12	47/M	SCC PR	LC			3
13	63/M	SCC PR	L			2
14	58/M	OC PR	II			1
15	75/M	SCC RX PR	L			1

ONJ = osteonecrosis of the jaw; rACC = recurrent adenoid cystic carcinoma; SCC = squamous cell carcinoma; OM = osteomyelitis; rSCC = recurrent squamous cell carcinoma; ORN = osteoradionecrosis; OC = odontogenic cyst RX = pre-operative radiation; PR = primary (immediate) reconstruction.

Table 2. Conventional fibula flaps.

3.2. Conventional group

The conventional technique was used in eight patients with SCC, in three patients with ONJ, in one patient with ACC, one patient with OM, one patient with ORN, and one patient with

odontogenic cyst (OC). In all patients who underwent the conventional technique, osseous reconstruction was performed immediately after resection.

4. Complications

In the CAD/CAM group, one fibular flap failed completely after 1 week and one skin paddle showed ischemic necrosis on postoperative day 6 and had to be excised. In the conventional technique group, one fibular flap was lost after 8 days and one patient required operative revision following an episode of severe bleeding on postoperative day 3, with consecutive skin paddle loss. In the CAD/CAM group, six patients underwent neoadjuvant radiation (54.5%), as opposed to only three patients undergoing conventional reconstructive surgery (26.7%).

	Technique		
	CAD/CAM	**Conventional**	
	Mean ± SD	**Mean ± SD**	**p-value**
Age (years)	48.3 ± 14.6	56.9 ± 13.3	0.152
Segments (n)	1.9 ± 0.7	1.7 ± 0.6	0.371
Time (min)			
Virtual planning	43.1 ± 5.1	*N.A.*	
Torniquet inflation	102.9 ± 7.9	97.3 ± 8.9	0.121
Flap harvesting	141.4 ± 14.8	108.4 ± 7.7	<0.001*
Flap ischemia	72.9 ± 10.3	106.9 ± 23.7	<0.001*
Total ischemia	175.8 ± 7.5	204.2 ± 23.1	<0.001*
Total reconstruction[a]	214.1 ± 14.4	215.3 ± 24.1	0.893
Overall operating[b]	257.2 ± 17.5	215.3 ± 24.1	<0.001*

SD = standard deviation; *N.A.* = not applied.
[a] Total amount of Flap harvesting and flap ischemia time.
[b] Total amount of virtual planning time and total reconstruction time in the CAD/CAM group, similar to total reconstruction time in the conventional group.
* Highly significant at the level $p < 0.01$ (two-tailed).

Table 3. Comparison of demographics, intraoperative factors, and time measurements between the CAD/CAM and the conventional technique groups.

With regards to mean age, number of osseous segments, and tourniquet inflation times, there were no significant differences between groups (**Table 3**). However, flap harvesting time was significantly shorter in the conventional technique group; flap ischemia and total ischemia times were shorter in the CAD/CAM group. Total reconstruction time did not vary significantly among groups, although overall operating time (amount of virtual planning time plus total reconstruction time) in the CAD/CAM group was significantly higher, given the fact that overall operating time in the conventional group included only the reconstruction time.

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5. Discussion

The primary issues in conventional osseous reconstruction are that the whole volume of resection at the recipient site can vary and the definite anatomic shape of the osseous transplant can only be determined at the moment of surgery. This results in prolonged intraoperative time and flap ischemia time, with the risk of suboptimal reconstruction of a region which requires a high degree of precision for optimal orthognathic functional and aesthetic outcomes [12]. To avoid these drawbacks, some authors promote as a suitable alternative, a silastic sheeting, which can be cut intraoperatively to shape relying on the mandible segment removed and can be used as a template for fibula harvesting and shaping. In the hands of an experienced surgeon, the final result should not be different from that of applying CAD/CAM technique [24].

5.1. Flap ischemia times

Recent studies have already investigated osteocutaneous fibula flap ischemia times. However, study designs vary, as do mean ischemia times for either the CAD/CAM or conventional technique with or without adding tourniquet inflation times; different time periods in a surgeon's career also render differences in flap ischemia time between both techniques attributable to the surgeon's learning curve [14, 25–27]. Mean flap ischemia times vary widely, between 75 and 216 min, with differences of up to 30 and 50 min between both techniques (**Table 4**).

	Technique		
	CAD/CAM (min)[a]	**Conventional (min)[a]**	**p-value**
Succo et al. [27]	75	*N.A.*	*N.A.*
Modabber et al. [26]	105	132	0.014
Chang et al. [25]	*N.A.*	216[b]	*N.A.*
Seruya et al. [14]	120	170	0.004
Current study	73	107	<0.001
	176[b]	204[b]	<0.001

N.A. = not applied.
[a] Rounded up to the next full minute.
[b] Tourniquet inflatiogn time included, *N.A.* = not applied

Table 4. Mean flap ischemia times upon applying CAD/CAM and conventional techniques as provided by recent literature and this study.

In contrast to previous studies, this survey provides a more comparable setup. The CAD/CAM and the conventional techniques were used concurrently, not consecutively. Hence, the predicted bias was reduced to minimum with respect to a learning curve. Our results showed that flap ischemia time could be significantly reduced by 34 min in the CAD/CAM group

compared to the conventional group. The reduction in flap ischemia time was in accordance with the data given by Modabber et al. [26]. Nevertheless, flap ischemia times were definitively longer in the latter study.

However, in this study, it can be recognized that the decrease of ischemia time in the CAD/CAM group did not decrease the total reconstruction time as well. The reduced ischemia time in the CAD/CAM group was the result of shaping and modeling of the fibular parts prior to severing the vascular pedicle. Indeed, this procedure led to a longer flap harvesting time compared with that in the conventional group. But this time lost was regained, since in turn, ischemia time in the conventional group was significantly longer because shaping and trimming of the devascularized fibula flap was carried out on the back table and accuracy could only be achieved by repetitive and time-consuming in- and out-setting of the transplant.

There were no differences found between groups, however, with respect to partial or total flap loss and rate of soft tissue or bony tissue revisions, in this or in previous studies [14, 22]. Chang et al. [25] found that an ischemia time of up to 5hours (comprising tourniquet inflation and flap ischemia time) did not detrimentally affect fibula flap success or increase complication rates. In most cases, an ischemia time greater than 5 hours was attributable to time-consuming flap inset procedures as mentioned earlier or compromised septocutaneous perforators. In accordance with these findings, in our survey, partial and complete flap losses were not associated with prolonged ischemia times, since total ischemia times in both groups did not approach by far the 5hour limit. The total number of losses was equal between groups; flap failures were attributed to venous congestion, bleeding, and hematoma which compromised the anastomosed sites.

6. Conclusion

Results are comparable with findings in other studies evaluating the CAD/CAM technique. We showed again that CAD/CAM technology has several advantages compared with the conventional technique, comprising the potency to repair more accurately massive craniofacial defects, the possibilities to plan segmental osteotomies, to perform osteotomies by custom-made cutting guides with the flap pedicle still in continuity, to use a stereolithographic model to confirm proper configuration of osseous flaps, to effectively perform condylar positioning, and to operate with greater convenience and ease [1, 20–22]. In the same way, we experienced the disadvantages of increased preoperative time for planning and the considerable time delay between planning and receiving the hardware for the CAD/CAM technique not appropriate for urgent cases, and the costs incurred by applying this technique [23]. However, in addition to all the advantages of the CAD/CAM over the conventional technique given above, including reduced ischemia time of fibula free flaps, there was no clinically significant impact on total reconstruction time and flap survival at all, since ischemia times obtained with the conventional technique did not exceed critical time levels.

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Chapter 22

Three-Dimensional Printing: A Novel Technology for Use in Oral and Maxillofacial Operations

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Mohammad Hosein Amirzade Iranaq

Additional information is available at the end of the chapter

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Abstract

Three-dimensional (3D) printing is cited as "a novel, fascinating, future builder technology" in many papers and articles. Use of this technology in the field of medicine and especially oral and maxillofacial surgery is expanding. The type of manufacturing systems, materials, cost-effectiveness, and also bio-printing, with studies from around the world today, make this field a "hot-topic" in reconstructive and regenerative surgery. This chapter evaluates the latest updates and scientific uses of 3D printing.

Keywords: Rapid prototyping, three-dimensional printing, reconstructive surgery, oral, maxillofacial surgery

1. Introduction

Three-dimensional printing (3D), also known as rapid prototyping (RP), was first introduced in the 1980s. During the past three decades, enormous changes and developments have been made by scientists modifying this technology, materials, and accuracy. Within the field of craniofacial surgery, 3D surgical models have been used as templates to harvest bone grafts, tailoring bioprosthetic implants, plate bending, cutting guides for osteotomies, and intraoperative oral splints. Using 3D models and guides has been shown to shorten the operative time and reduce the complications associated with it. The ultimate goal of any surgical procedure is to improve peri-operative form and function and to minimize operative and postoperative morbidity. Many exciting and new technological advances have opened a new

era in the field of oral and maxillofacial surgery over the last years, and 3D printing is among the most novel. The aim of this chapter is to introduce 3D printing method and its role in contemporary oral and maxillofacial surgery and to review different applications and benefits of 3D printing-assisted surgeries in the oral and maxillofacial region.

2. History and benefits

Three-dimensional printing has been utilized in diverse aspects of manufacturing to produce different objects from guns, boats, and food to models of unborn babies. From over 1450 articles related to 3D printing listed in PubMed, nearly a third of them were published in the last 2 years [1].

3D printing is a manufacturing process wherein objects are fabricated in a layering method during fusing or depositing different materials such as plastic, metal, ceramics, powders, liquids, or even living cells to build a 3D structure [2, 3]. It is a process of generating physical models from digital layouts [4, 5]. This technology demonstrates a technique where a product designed via a computer-aided scheme is manufactured in a layer-by-layer system [6]. This process is also known as RP, solid freeform technology (SFF), or additive manufacturing (AM) [7].

3D printing techniques are not new and have existed since 30 years ago [8–10]. This technology was first introduced and invented by Charles Hull in 1986, and at first it was utilized in the engineering and automobile industry for manufacturing polyurethane frameworks for different models, pieces, and instruments [11]. Originally, Hull employed the phrase "Stereolithography" in his US Patent 4,575,330, termed "Apparatus for Production of Three – Dimensional Objects by Stereolithography" published in 1986. Stereolithography (SL) technique included subjoining layers over the top of each other, by curing photopolymers with UV lasers [12, 13].

Since then, 3D models have been used for a diversity of different objectives. Since 1986, this process has started to accelerate and has honored recognition globally and has influenced different arenas, such as medicine. The developing agora for 3D desktop printers encourages wide-ranging experimentations in all fields. Generally, medical indications of these printers are treatment planning, prosthesis implant fabrications, medical training, and other usages [4]. Having being used in the military, food industry, and arts, RP has received much attention in the field of surgery in the last 10 years [6, 14]. The pioneering usage of SL in oral and maxillofacial surgery was by Brix and Lambrecht in 1985. Later, this technique was used by them for treatment planning in craniofacial surgery [15]. In 1990, SL was used by Mankovich et al. for treating patients having craniofacial deformities [16, 17]. They used it to simulate bony anatomy of the cranium using computed tomography (CT) with complete internal components [17, 18].

By aiding in complex craniofacial reconstructions, 3D printing has recently earned reputation in medicine and surgical fields [19–21]. Today, maxillofacial surgery can benefit from additive

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manufacturing in various aspects and different clinical cases [22]. This technique can help with bending plates, manufacturing templates for bone grafts, tailoring implants, osteotomy guides, and intraoperative occlusal splints [23–27]. RP can shorten surgery duration and simplify pre- and intraoperative decisions. It has enhanced efficacy and preciseness of surgeries (**Table 1**) [10].

Diagnosis and treatment planning
Direct visualization of anatomic structures
Surgical guides/templates
Surgical practice/rehearsal
Designing incisions
Surgical resections
Assessment of bony defects for grafting
Adaptation/pre-bending of reconstruction plates
Fabrication of custom prostheses
TMJ prostheses, distraction devices, fixation devices
Decreased surgical time, anesthesia time, wound exposure duration
More predictable results
Improved colleague communication
Educational tool for patients

Table 1. Uses of 3D models [22].

3. Manufacturing process and types of models

There are different technologies introduced for 3D printing. Binder jetting (BJ), electron beam melting (EBM), fused deposition modeling (FDM), indirect processes, laser melting (LM), laser sintering (LS), material jetting (MJ), photopolymer jetting (PJ), and SL are well-known technologies of 3D printing [14, 28, 29]. There are many different 3D printing techniques. Benefits and disadvantages are factors inherent to each technology system [14]. Among this variety of different techniques, there is a huge demand for oral and maxillofacial surgery for SL, FDM, and PJ [1, 28, 30]. **Table 2** summarizes some different three-dimensional printing technologies.

3.1. Stereolithography (SL)

The initial 3D printing technique SL began in the late 1980s [31]. The original SL uses a laser beam for resin polymerization in two-dimensional patterns [32]. Being the pioneering additive manufacturing method, SL produces 3D objects by curing layers of liquid photopolymer or

epoxy resin with a low-power UV laser [13]. SL projects a UV laser to a cross section of a single layer of the resin onto a photopolymer resulting in the setting of the layer. This is repeated until fabricating all zones of the product [1]. This technique utilizes a mirror to guide the laser to the surface in a layer-by-layer manner. Furthermore, the 3D device projects it on the surface resins. This procedure is done from the base to the surface (**Figure 1**) [14, 33].

Techniques	Advantages	Disadvantages
	Light cured resin	
1. Stereolithography (SL) —Light-sensitive polymer cured layer by layer by a scanning laser in a vat of liquid polymer	Rapid fabrication. Able to create complex shapes with high feature resolution. Lower cost materials if used in bulk	Only available with light curable liquid polymers. Support materials must be removed. Resin is messy and can cause skin sensitization and may be irritant by contact and inhalation. Limited shelf life and vat life. Cannot be heat sterilized. High-cost technology
2. Photojet—Light-sensitive polymer is jetted onto a build platform from an inkjet-type print head and cured layer by layer on an incrementally descending platform	Relatively fast. High-resolution, high-quality finish possible. Multiple materials are available with various colors and physical properties including elastic materials. Lower cost technology	Tenacious support material can be difficult to remove completely. Support material may cause skin irritation. Cannot be heat sterilized. High- cost materials
3. DLP (digital light processing)—Liquid resin is cured layer by layer by a projector light source. The object is built upside down on an incrementally elevating platform	Good accuracy, smooth surfaces, relatively fast. Lower cost technology	Light curable liquid polymers and wax-like materials for casting. Support materials must be removed. Resins are messy, can cause skin sensitization, and may be irritant by contact. Limited shelf life and vat life. Cannot be heat sterilized. Higher cost materials
	Powder binder	
Plaster or cementaceous material set by drops of (colored) water from "inkjet" print head. Object built layer by layer in a powder bed, on an incrementally descending platform	Lower cost materials and technology. Can print in color. Unset material provides support. Relatively fast process. Safe materials	Low resolution. Messy powder. Low strength. Cannot be soaked or heat sterilized
	Sintered powder	
Selective laser sintering (SLS) for polymers —Object built layer by layer in powder bed. Heated build chamber raises temperature of material to just below melting point. Scanning laser then sinters powder layer by layer in a descending bed	Range of polymeric materials including nylon, elastomers, and composites. Strong and accurate parts. Self-supported process. Polymeric materials—commonly nylon may be autoclaved. Printed object may	Significant infrastructure required, e.g., compressed air, climate control. Messy powders. Lower cost in bulk. Inhalation risk. High-cost technology. Rough surface

Techniques	Advantages	Disadvantages
	have full mechanical functionality. Lower cost materials if used in large volume	
Selective laser sintering (SLS) —for metals and metal alloys. Also described as selective laser melting (SLM) or direct metal laser sintering (DMLS). Scanning laser sinters metal powder layer by layer in a cold build chamber as the build platform descends. Support structure used to tether objects to build platform	High-strength objects can control porosity. Variety of materials including titanium, titanium alloys, cobalt chrome, stainless steel. Metal alloy may be recycled. Fine detail possible	Elaborate infrastructure requirements. Extremely costly technology. Moderately costly materials. Dust and nanoparticle condensate may be hazardous to health. Explosive risk. Rough surface. Elaborate post-processing is required: Heat treatment to relieve internal stresses in printed objects. Hard to remove support materials. Relatively slow process
Electron beam melting (EBM, Arcam). Heated build chamber. Powder sintered layer by layer by scanning electron beam on descending build platform	High-temperature process, so no support or heat treatment needed afterward. High speed. Dense parts with controlled porosity	Extremely costly technology moderately costly materials. Dust may be hazardous to health. Explosive risk. Rough surface. Less post -processing required. Lower resolution
	Thermoplastic	
Fused deposition modeling (FDM) First 3DP technology, most used in "home" printers. Thermoplastic material extruded through nozzle onto build platform	High porosity. Variable mechanical strength. Low-to-mid-range cost materials and equipment . Low accuracy in low-cost equipment. Some materials may be heat sterilized	Low cost but limited materials— only thermoplastics. Limited shape complexity for biological materials. Support material must be removed

Table 2. 3D printing modalities and materials [14].

It is necessary to extract waste materials manually from the eventual outcome [34–36]. Nowadays, SL is known as the gold standard in 3D manufacturing with yield resolutions up to 0.025 mm. SL is reliable in reconstruction of internal frameworks and is more efficient in fabricating larger objects [37]. SL is largely accepted to have the best surfacing and the most accuracy of any 3D technology. Materials used in this system must be to some degree brittle and light [38, 39]. Acrylics and epoxies are commonly used for this method [40]. However, SL still requires manual handling after fabrication, and the process lasts more than a day to be completed. SL is more expensive than other techniques due to materials used, and the printer is considered more expensive due to the high cost of the raw materials and device maintenance [23, 41]. SL is largely utilized for producing implant drill guides [14]. The ability to build complex and detailed structures, extraction of waste resin without difficulty, and extremely high resolution (~1.2 um) are considered main advantages of SL [42] feature.

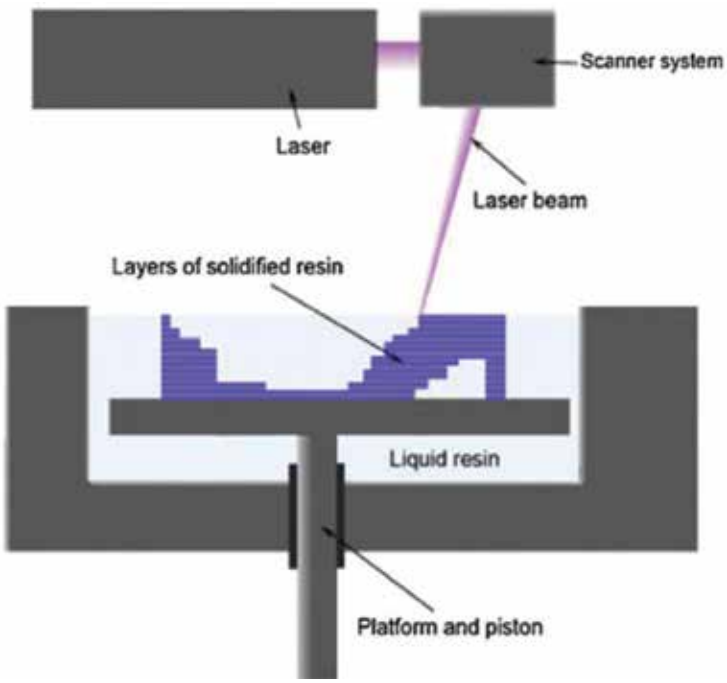

Figure 1. Schematic view of SL [115].

3.2. Fused deposition modeling

FDM uses a similar principle to SL in that it builds models on a layer-by-layer basis. When there is a discussion about cost-effectiveness, FDM is considered among the most utilized consumer 3D printing methods [16, 43, 44]. In FDM, a melted filament of thermoplastic material is extruded from a nozzle moving in the x-y plane and solidifies upon deposition on a build plate [45]. The build plate is lowered by 0.1 mm after each layer reappears. The process is repeated until the final product is produced. The most frequently used raw materials in FDM printers are acrylonitrile-butadiene-styrene (ABS) and polylactic acid (PLA) materials known for being key components of scaffold structures used for "bioprinting" [40].

Notable disadvantage and shortcoming for FDM is disability to form complex structures and most anatomical structures with complex shapes. For manufacturing a clean product, hollow internal structures or blind-ended openings are especially troublesome. Almost all household FDM printers are currently limited in mono-color and mono-material for manufacturing. However, this can be overcome by recently developed dual-extruder technology. In this technology, two filaments of different colors or materials can be extruded from a common printer head. MakerBot Replicator 2X Experimental (MakerBot Industries, New York, NY, USA), Cube 3 (3D Systems, Rock Hill, SC, USA), and Creatr x1 (Leapfrog, Emeryville, CA, USA) are known for this ability. Even more, the second extruder can be configured to build

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support structures using MakerBot Dissolvable Filament (MakerBot Industries), made of high-impact polystyrene (HIPS) [6, 46].

Support structures are required for FDM models such as SL as thermoplastic needs time to harden and also the layers to bond together [47]. Since multiple extrusion nozzles can be used in FDM, each with a different material, there is no theoretical restriction on compositional gradients in all three dimensions for FDM. High porosity due to the laydown pattern and good mechanical strength are notable and key advantages of FDM (**Figure 2**).

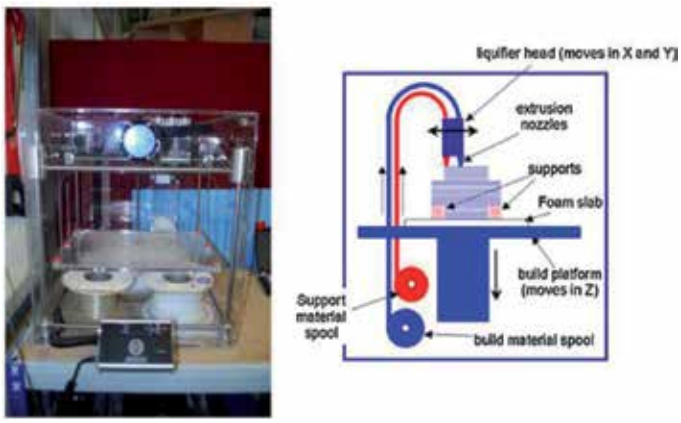

Figure 2. Schematic view of FDM [40].

3.3. PolyJet modeling

Multijet modeling printing, also known as MultiJet Printing (3D Systems, Rock Hill, SC, USA) or PolyJet Technology (Stratasys, Edina, MN, USA), is similar to SL; the difference is that the liquid photopolymer is immediately cured by UV light [48]. Multijet modeling printing can manufacture prototypes with high resolution (16 μ) that is comparable to or even better than SL. The advantage is the capacity to print in multiple materials for the desired degree of tensile strength and durability. An MJM printer is easier to maintain than an SL system. On the contrary, a disadvantage is the high price of these printers which makes MJM(Multi Jet Modeling) more suitable for large-scale productions rather than for office-based applications (**Figure 3**) [6].

The drawback is that the equipment and materials are costly to purchase and run, and the support materials can be tenacious and rather unpleasant to remove. They are useful for printing dental or anatomical study models, but these are expensive when produced. A particular advantage of this technology is that the use of multiple print heads allows simultaneous printing with different materials, and graduated mixtures of materials, makes it possible to vary the properties of the printed object, which may for example have flexible and rigid parts, for the production of indirect orthodontic bracket splints [14].

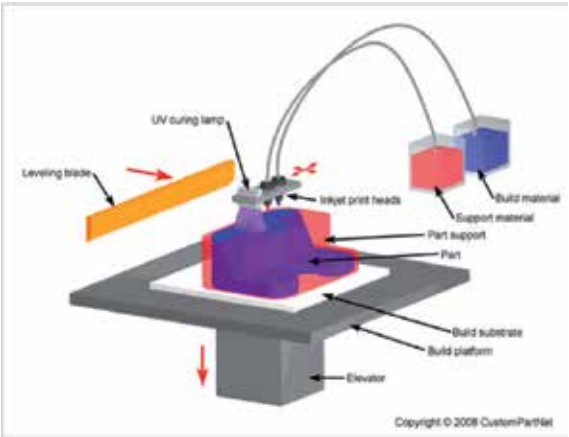

Figure 3. Schematic view of PolyJet [116].

4. Accuracy of 3D printing

Additive manufacturing plays a critical role in craniomaxillofacial surgery [49].

3D models simulate anatomy of the human body and can be extensively useful in oral and maxillofacial surgery. These models are of great value in decision making [50]. 3D models must be precise and extremely accurate in simulating head and neck anatomy to be beneficial in maxillofacial surgery. Faulty and inexact models can jeopardize diagnosis and treatment planning [16, 51]. There is limited data available about evaluation of the accuracy of 3D printed models. Inaccurate models can cause dramatic errors in treatment planning and simulations [49]. 3D printer accuracy generally depends on the accuracy of CT scans. CT is modality of choice for 3D printing purposes. While obtaining CT images, each slice thickness must be as thin as possible (1–2 mm) [30]. At present, no gold standard is introduced for measuring the accuracy of medical 3D models [49]. The accuracy of different additive manufacturing technologies is examined by researchers in maxillofacial surgery globally. The literature indicates that different techniques have different accuracy levels in reconstructing maxillofacial structures using 3D printing. As mentioned before, experiences have pointed out that SL creates 3D models with great accuracy. Average deviation of SL models varies from 0.20– 0.85 mm. Error percentage in these models is between 0.6 and 6% [17, 30, 52–54]. Peter Shih-Hsin Chang et al. investigated the accuracy of SL for modeling midface irregularities. This was done comparing distances between key landmarks on the skulls and 3D models. Average overall difference between replicas and cadaver samples was between 0.8 and 2.5 mm in all locations. They stated that SL preciseness is affected by variants in different stages of manufacturing such as data collection and transfer, product fabrication, and maintenance [38]. Preciseness and accuracy is critical in orthognathic surgery for gaining better results both esthetically and functionally. In a recent study, Shqaidef et al. evaluated the accuracy of 3D printed wafers of 10 orthognathic patients. After aligning with dental models, the absolute mean error of the

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wafers was 0.94 (0.09) mm. In this research, they showed error in 3D printed models is up to 1.73 mm which is considerable and will distort skeletal movements [55]. In another study, the PolyJet technique had the most precise fabrication in simulating mandibular architecture [50].

Salmi et al. assessed the accuracy of different 3D printing techniques by measuring balls attached to each 3D model. It was concluded that the PolyJet technique had the least inaccuracies [49].

Table 3 demonstrates results of different studies with accuracy measurement of 3D printed models.

Authors	Comparisons	Mean difference (%)	Measuring equipment
Salmi et al. (2013)	SLS e 3D CT (original 1. & 2. model) 3DP e 3D CT (original 1. & 2. measurement) 3DP e 3D CT (moderate) 3DP e 3D CT (worse)PolyJet e 3D CT (original 1. & 2. measurement)	0.79 0.26 & 0.80 0.320.67 0.43 & 0.69 0.440.38 0.220.55 0.370.18 0.12 & 0.18 0.13	Coordinate measuring machine and measuring balls & Pro Engineer software for 3D models
El-Katatny et al. (2010)	FDM e 3D CT skullFDM e 3D CT mandible	0.24 0.160.22 0.11	Digital caliper
Ibrahim et al. (2009)	SLS e dry mandible3DP e dry mandiblePolyJet e dry mandible	1.793.142.14	Digital caliper and test indicator attached to electric milling machine
Silva et al. (2008)	SLS e dry skull3DP e dry skull	2.102.67	Digital caliper
Nizam et al.(2006)	SL e dry skull	0.08 1.25	Digital caliper
Chang et al. (2003)	3DP e fresh skull	2.1e4.7	Dial caliper
Choi et al. (2002)	SL e dry skullSL e 3D CT skull	0.56 0.390.82 0.52	Caliper & MagicsviewSoftware for 3D model
Asaumi et al. (2001)	3D CT e dry skullSL e dry skull	2.160.63	Caliper & 3DCT images
Berry et al. (1997)	SLS e 3D CT	0.64	None reported
Barker et al. (1994)	SL e dry skull	0.6e3.6	
Ono et al. (1994)	SL e dry skull	3	
Waitzman et al. (1992)	3D CT e dry skull	0.9 (0.1e3.0)	CT images & caliper

Dawood, A., B. M. Marti, V. Sauret-Jackson and A. Darwood (2015). "3D printing in dentistry." *British dental journal* **219**(11): 521-529.
Mehra, P., J. Miner, R. D'Innocenzo and M. Nadershah (2011). "Use of 3-d stereolithographic models in oral and maxillofacial surgery." *Journal of maxillofacial and oral surgery* **10**(1): 6-13.
Salmi, M., K.-S. Paloheimo, J. Tuomi, J. Wolff and A. Mäkitie (2013). "Accuracy of medical models made by additive manufacturing (rapid manufacturing)." *Journal of Cranio-Maxillofacial Surgery* **41**(7): 603-609.

Table 3. Studies with accuracy measurement of AM models [49].

5. Clinical applications

Three-dimensional printing has been available for over three decades. Despite that, medicine has benefitted from its application recently [23–25]. As mentioned before, 3D printed models can be useful in different aspects of maxillofacial surgery such as templates, splints, tailored implants, and others [23–27]. These models can reduce surgery duration and enhance the results [10]. RP technology can become very useful for both doctor and patients in treatment planning for each patient individually [56]. Medical applications of 3D printers have expanded after recent advancements of these systems. In oral and maxillofacial surgery, 3D printing methods have been utilized for different purposes including distraction osteogenesis and treatment of craniofacial deformities [57, 58]. The following are the main applications of 3D printing technology in oral and maxillofacial surgery:

5.1. Surgical planning

Since 3D printing can distinguish traumatic and pathologic defects more effectively, it has proven to enhance diagnosis and treatment in the maxillofacial region. This feature results in precise decision making. In the aspect of pathologic lesions, 3D printing is capable of presenting spatial relationships to surrounding components [52–54, 58–63]. These important visualizations can minimize operative complications [26].

By 3D printing, surgeons can visualize the procedure and forecast the challenges to gain better results before they even start. Three-dimensional printing can produce models rapidly with acceptable accuracy and structural details to allow for better outcomes and reduced operating durations [64].

5.2. Trauma surgery

3D printers can facilitate the treatment of trauma patients with recent or delayed fractures and defects. Different fractures of maxillofacial structures can benefit from 3D printing but orbital wall fractures are the best targets for these methods [65–67]. These patients can be treated by 3D customized reconstruction of orbital wall defects with titanium mesh or sheet [68]. Before the surgery begins, titanium mesh or plate is adapted precisely on the 3D printed replica to help shortening the duration of general anesthesia [69, 70].

Complicated and detailed anatomy of the orbit makes it difficult to reconstruct orbital defects. Postoperative enophthalmos or diplopia always happens without accurate and proper reconstruction of orbital walls. Surgeons can solve these complications by using 3D printed titanium mesh using the contralateral orbital anatomy [30, 71].

Sasˇa et al. evaluated the application of custom-made implants using 3D printing system to reconstruct in blowout fractures of the orbital floor. After the surgery, average orbital volume (OV) of the affected side noticeably decreased, and OV of corrected orbit was not different compared to the unaffected side [72].

Chandan Jadhav et al. treated three patients with medial orbital wall fractures using 3D models. They used the 3D model as a template to measure and harvest bone graft from iliac

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crest easily and precisely, resulting in perfect adaptation and reduced operation time (**Figures 4** and **5**) [56].

Figure 4. The rapid prototype metal orbital floor reconstruction in the orbit of the stereolithic skull reconstructed from the original CT scans [71].

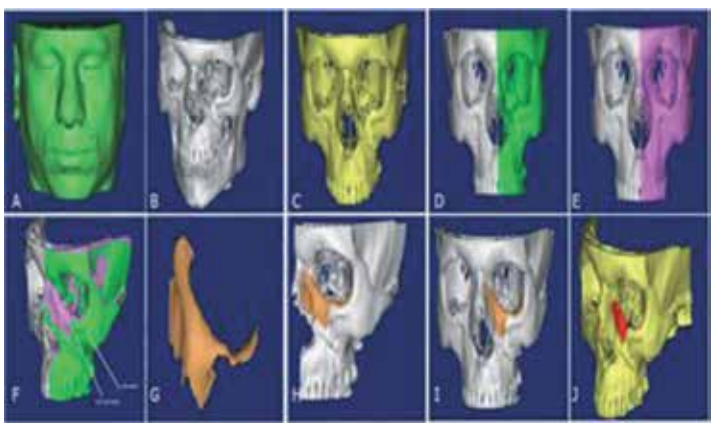

Figure 5. Treatment of orbital floor defect in a trauma patient using 3D printing technology. (a) 3D model designed based on CT scan images; (b) removal of soft tissue on differences between soft and hard tissue density; (c) removal of excess bone; (d) dividing the face into two halves from symmetry line; (e) mirroring the uninjured side on the other side; (f) comparison of the injured half and the mirrored half and finding their differences; (g) differentiation of the ideal design; (h) precise adaption on injured half; (i) correction of the design by removal of excess components; (j) final model.

5.3. Orthognathic surgery

Precise planning and decision making based on exact diagnosis is critical in the success of orthognathic surgeries [73]. As mentioned earlier, 3D printing technology shows some clinically noticeable inaccuracies for orthognathic surgery which is troublesome for ideal dental occlusion [30].

5.4. Facial prosthetics

There are reports of fabricating prosthetic nose [74, 75], ears [76, 77], eyes [78, 79], and face [80, 81], in the last 10 years. Literature indicates that better esthetic and functional outcomes are accomplished with the application of 3D printing in comparison to the traditional prosthetics (**Figure 6**) [76, 82].

Facial prosthetics fabricated with RP methods are being utilized successfully. Ancient Egyptians were the first people to apply facial prosthetics in 500 B.C [83].

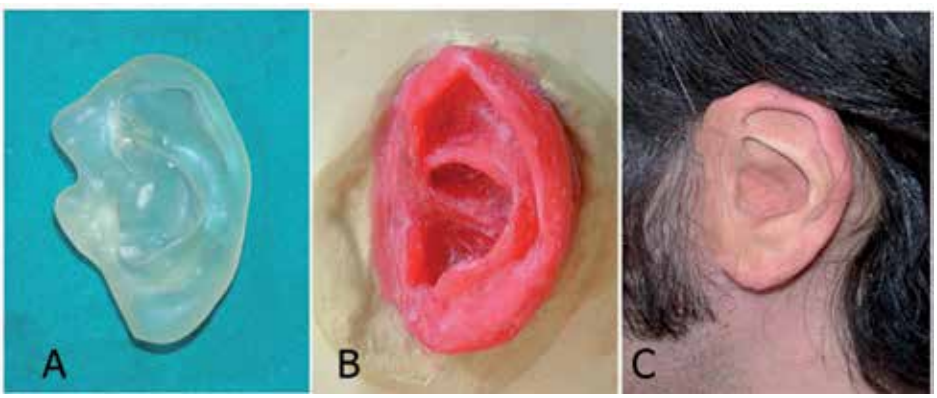

Figure 6. (a) 3D model obtained by stereolithography; (b) stereolithographic model turned into wax; (c) finished auricular prosthesis [85].

Figure 7. Application of 3D printing in lateral nasal osteotomy. (a) Planned osteotomy lines of lateral nasal osteotomy are drawn with a skin marker on the 3D model; (b) compensate the thickness of the soft tissue lining of the nose with thick wax; (c) trimming the custom-made splint on the 3D model; (d) performing the lateral nasal osteotomy in line with the surgical plan; (e) pre- and postoperative views [117].

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Facial prosthetics have evolved extensively with the application of 3D printing technology. This technique allows producing replicas of facial structure within just hours [84].

Impression procedures are the common method to manufacture facial prosthetics. Longer duration of production, soft tissue distortion, and patient discomfort are the main limitations of this process. Lately, 3D printing has been utilized to produce facial prosthetics to reduce limitations of traditional procedures. Additive manufacturing technology can simplify the procedure, shorten laboratory procedures by excluding impression procedures, and model wax-ups. No doubt, 3D printing will become the modality of choice to manufacture facial prosthetics [85]. Additive manufacturing is mainly used for hard tissue reconstruction. However, it is useful in soft tissue contouring [5, 86] such as auricular reconstruction in patients using the contralateral ear (**Figure 7**) [87].

Auricular prosthesis production consists of multiple time-consuming processes demanding patient presence. These procedures are (1) impression making, (2) fabricating a wax replica, (3) manufacturing a mold, and (4) creating the prosthetic object with a suitable color. 3D printing technique simplifies and shrinks the first three steps. The process can be completed in 24–48 hours instead of a week [88].

5.5. Customized TMJ reconstruction

In the field of TMJ(Temporomandibular Joint) reconstruction, sufficient exposure and access is critical to prevent damaging many vital structures in this area. Alloplasts and allografts must be accurately placed to regain correct function of the jaw [89]. 3D printing can become useful in the treatment of TMD(Temporomandibular Joint Disorders) patients with total condylar resorption [18]. Mehra et al. treated a patient by bone grafting and TMJ prostheses using additive manufacturing. 3D printing aided in measuring exact proportions of the bone needs to be harvested [22].

5.6. Dental implants

Creation of new dental implants has benefitted from 3D printing technology [90, 91].

3D printing acts as a tool to create dental implants with complicated geometries [14].

Drilling guides are of great value to transfer implants from their planned positions. Manufacturing a drilling guide by conventional methods is time-consuming and requires multiple patient visits and extensive laboratory work. RP facilitates this with solely a single consultation prior to operation. In this session, data are gathered, and the guide is virtually built and later will be manufactured by the 3D device [92].

5.7. Complex facial reconstruction

Pathologic lesions, traumatic events, and infections are main etiologies of mandibular defects needing partial resection and bone reconstruction [93, 94]. Maintaining acceptable esthetic and functional outcomes and facial symmetry are the main goals of mandibular reconstructions. Titanium reconstruction plates are biocompatible and adaptable alloplasts for temporary

reconstructions [95]. For more reliable reconstruction, autogenous bone grafts are commonly used. Complex mandibular morphology and muscular attachments moving the jaw in unfavorable positions are challenging to oral and maxillofacial surgeons in mandibular reconstructions [23]. 3D printing technology can be used in different aspects of facial reconstruction. This technology is widely used for mandibular reconstruction [96]. Better anatomical understanding, proper plate adaptation, plate pre-bending, precise bone harvesting by utilizing negative templates of the defect, reduced bone-plate distance, decreased duration of surgery, less blood loss, and shortened duration of general anesthesia are the main advantages of using additive manufacturing in mandibular reconstruction (**Figure 8**) [23, 96].

Hanasono and Skorackil indicated that 3D printing can reduce surgery duration up to 1.4 hour [97].

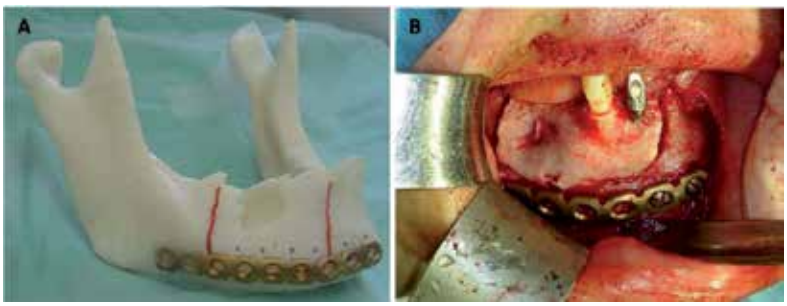

Figure 8. (a) Precontoured reconstruction plate before marginal mandibulectomy aiming to reinforce the remaining thin mandibular lower border; (b) note the anatomic alignment of the precontoured plate to the lower mandibular border [23].

6. Improvements in learning, training, and practice

6.1. Surgical education

Medical training can reform with enhancements of 3D printing technology [84].

As oral and maxillofacial surgeons, we are expected to master detailed morphology of the head and neck region and their spatial relationship. Patients and medical trainees and residents can benefit from 3D printed models [26, 98]. High maintenance charges, cultural and social complications, and formalin-related safety issues are making cadavers a limited source for medical education [99, 100].

Medical trainees can have better understanding of anatomical structure with 3D printed models.

These models allow a thorough and complete training before a surgery even begins [101, 102]. Operators can perform complicated surgeries on 3D models without any concerns and complications [103]. 3D printing also can aid in better understanding of patients' medical

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situation rather than a flat 2D screen [12]. Kah Heng Alexander et al. conducted a double blind randomized controlled trial to compare the success of 3D printing with human cadavers for distinguishing external cardiac anatomy. 3D printed models had significantly higher scores in comparison to the cadavers or combined groups [98]. With the enhancement of new materials, 3D printed models will be more accurate in the future [104–106].

6.2. Patient education

Fulfilling patient expectations is critical to have successful surgical outcomes. Surgeon-patient professional relationship can be simplified using 3D printing. In preoperative consultations, patients can understand surgical details, different results, and potential obstacles. Therefore, 3D printed models can aid gaining informed consent. [103]. CT/MRI scans that we use today to explain the procedure for the patients are usually hard to understand for uneducated patients. Patients mostly do not comprehend the situation.

Literature has shown that 3D printed models result in better training of both patients and medical trainees [26, 107, 108]. Also having in-office preoperative and postoperative 3D printed models of specific surgeries can help patients justify their expectations [26].

Patients' families can also benefit from additive manufacturing since they might have positive impacts on patient satisfaction. These models could be utilized to form a library for future educational goals [109].

7. Prospective visions

Three-dimensional printers are a new and emerging technology with the ability to manufacture physical objects from digital files. Decreasing hardware costs have made this technology affordable for use in the office setting [26]. 3D printing technology enables more effective patient consultations, increases diagnostic quality, improves surgical planning, acts as an orientation aid during surgical procedures, and manufactures guiding template segmental resections. In the future, additive manufacturing might be capable of organ bio-printing [30]. Surgery is a practical art! The surgeon often uses direct physical intervention in the treatment of patients. Surgical procedures must be accurately planned for each patient individually to minimize complications and increase benefits. In oral and maxillofacial surgery, potential uses extend to surgical planning, education, and prosthetic device design and development. RP is not utilized in conventional clinical applications but can revolutionize oral and maxillofacial surgery in the future [26]. To clarify and understand what is the best prediction for the future of the technology itself, production time of objects and costs should also be considered. Different researchers have indicated that they have found 3D printing a cost-effective technology [110–112]. However, some other investigators have doubted efficiency and price of RP [113]. 3D printed replicas are considered to be more precise and cost-effective for patients and trainee education compared to other techniques [114]. This method also eliminates the need for animal studies [64]. 3D printing technology is here to improve our lifestyle and health care in the twenty-first century [103].

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Section 12

Advanced Craniomaxillofacial and TMJ Reconstruction

Chapter 23

Concepts in Management of Advanced Craniomaxillofacial Injuries

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Additional information is available at the end of the chapter

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Abstract

The authors present a sequencing assessment of patients who were victims of traumatic deformities of the craniomaxillofacial complex. To that end, the authors highlight the eight steps worthy of particular attention, namely (1) clinical history and photographic documentation; (2) clinical assessment; (3) assessment through image and diagnostic exams; (4) planning of the treatment; (5) bases for the three-dimensional reconstruction of the face; (6) reconstruction sequence of multiple facial fractures; (7) support measures; and (8) complications. The proposed assessment sequence allows the oral and maxillofacial surgeon or craniomaxillofacial surgeon to assess the degree of impairment of traumatic deformity, which contributes in a significant way to the decision-making process of the treatment.

Keywords: craniomaxillofacial, trauma, treatment, facial injuries, reconstructive surgical procedures

1. Introduction

The treatment of craniofacial or maxillofacial trauma, from here on referred to as craniomaxillofacial trauma (CMF Trauma), is a challenging endeavor, as it involves the individual's so-called command and control center, including their face and skull. It is life-threatening and may lead to facial motor and sensory sequelae such as alterations of functions related to sight, speech, swallowing, and breathing, as well as facial aesthetics [1] and possible sequelae related to the central nervous system (CNS) and other parts of the body. CMF Trauma patients need to be initially assessed according to the Advanced Trauma Life Support (ATLS) protocol: (A) airways; (B) breathing; (C) circulation; (D) disability; and (E) exposure.

The main goal of the initial systematic assessment of CMF Trauma patients is to identify patients whose serious injuries are life-threatening and to set treatment priorities so that it is possible to manage them in an efficient and aggressive manner [2].

Therefore, patients who have gone through ATLS and are now stable can and should be specifically assessed from the craniomaxillofacial point of view. The stratification of trauma is then carried out, which requires a routine, which contains a number of issues. The proposed assessment sequence allows for the Oral & Maxillofacial Surgeon or Craniomaxillofacial Surgeon, from here on referred to as Maxillofacial Surgeon, to reach important conclusions about the degree of impairment of traumatic deformity, which contributes in a significant way to the decision-making process of the treatment. To that end, the authors highlight the following eight points.

2. Eight highlight points

2.1. Clinical history and photographic documentation

At this stage, the clinical history of the patient is established. It is then possible to determine the history of the current injury (history and understanding of the dynamics of the trauma), previous injury history, medical history, family history, social history, and physical examination. Photographic documentation is an important tool for recording the facial features and alterations prior to the proposed treatment (**Figure 1**).

It is also valuable information from a legal standpoint. Extraoral photographic shots should include front and side views of the patient, always aiming at a good positioning of the head whenever possible. Intraoral views should reveal pre-surgery dental occlusion and the presence of puncture or penetration wounds. Fractures involving the orbital content may be associated with the incarceration of the extrinsic muscles of the eyeball or even nerve damage, causing ophthalmoplegia, dystopia, diplopia, and sometimes enophthalmos because of the increase in the orbit perimeter (**Figure 2**).

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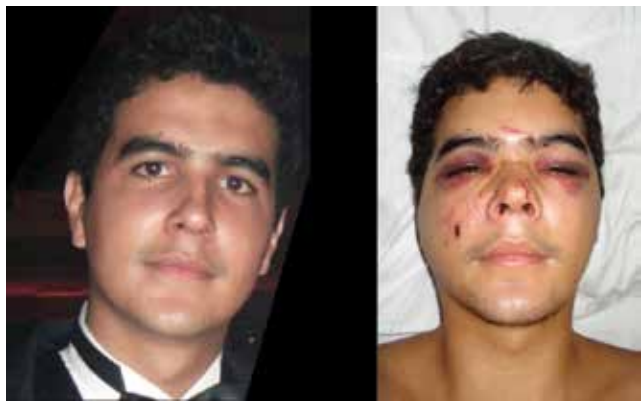

Figure 1. (A) and (B)—Photographic analysis.

Figure 2. Left eye—enophthalmos and hypophthalmos.

The photographic recording of those alterations is extremely relevant for the comparison of pre- and post-surgery parameters [3]. The combination of the anamnesis, physical and radiographic examinations, and photographic analysis allows for the initial dimensioning of the trauma.

2.2. Clinical assessment

When ATLS has been concluded, attention is directed to the following parameters:

2.2.1. Visual acuity

The evaluation of the pupils and the eyeball is carried out in accordance with the Glasgow Coma Scale (GCS) during the neurological examination of the patient [4]. When the patient is stable, the examination of the face, carried out by the maxillofacial surgeon, should focus on the optic pathways in search of alterations, which might point to possible direct or indirect lesions of the CNS. The examination also allows for an initial assessment of the integrity of the eyeball. Such measures are important as part of the basic neurological and ophthalmological

examinations and could contribute to the identification of possible lesions that have a risk of leading to visual loss or amaurosis. In CMF trauma, the initial ocular evaluation carried out by the maxillofacial surgeon is essential for patients with fractures on the midface [4–7].

It is worth keeping in mind that the specialized ocular evaluation for patients who have open or closed lesions of the eyeball is to be carried out by an expert ophthalmologist. Early diagnosis of the cause of amaurosis is essential for the treatment of patients [5, 7], and its assessment includes the following: detailed clinical history, physical examinations, and imaging [7]. All CMF trauma patients need to be examined, as apparently mild lesions or ones which have not been noticed, may lead to complications which could lead to amaurosis, even in the absence of facial fractures [5]. The initial assessment of the optic pathways and cranial nerves (CN) of the superior orbital fissure (SOF) consists of the following: (a) assessment of pupil diameter; (b) response to light—through photomotor and consensual reflex; and (c) assessment of ocular movements. The assessment of eyeball tension by means of gentle touching [5] could help in the examination of the eyeball structure, as a decrease in tension could point to rupture of the eyeball.

Figure 3. Right eye pupil dilated and alterations related to visual acuity after CMF trauma.

According to the literature [5, 8], the presence of relative afferent pupil defect (RAPD) is considered to be a sensitive clinical sign of visual deficiency. The second CN is assessed by means of visual acuity tests, pupil reactivity, fundoscopy, perception of color, and visual field [5, 7]. The assessment of the optic pathways depends on the clinical conditions of the patient [7, 8]. It is carried out on patients who are awake and cooperative and difficult in patients who are unconscious [5, 6], but every effort should be made to evaluate the visual function in the initial examination [7, 8]. Studies show that amaurosis may occur as a result of optical ischemia which occurs 90–120 min after the trauma. Some authors state a longer time interval, however, the best results in treatment are observed in early approaches [6] (**Figure 3**).

2.2.2. Cerebrospinal rhinorrhea

Patients with trauma in the central region of the face or those who present signs of disjunction in the frontal-ethmoid-maxillary region, and, therefore, an impairment of the cribriform plate

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should be assessed with the hypothesis of cerebrospinal fluid leak, known as cerebrospinal rhinorrhea borne in mind (**Figure 4**).

Figure 4. Patients with baso-ethmoid-orbital fracture and cerebrospinal rhinorrhea.

2.2.3. Cervical spinal cord trauma

This situation is evaluated during the "A" phase of ATLS, in which patients normally wear a cervical collar. Possible manipulations that are deemed unavoidable should be carried out with fixation devices that prevent head and spinal cord movement (**Figure 5**).

Figure 5. Fixation devices that prevent head and spinal cord movement.

2.2.4. Myocutaneous injuries

Assessment of previous tetanus immunization should be done. Patients who have been immunized and have received a booster shot within the last 10 years and who have wounds with no risk of tetanus **do not** require prophylaxis. The wounds, which present tetanus risk, include those which are highly contaminated by dirt or fertilizer, slough, and deep puncture wounds. Patients with wounds that are a tetanus risk and who have not received a booster shot within the last 5 years should be treated with 0.5 mL of tetanus toxoid. If patients have not received a booster shot within the last 10 years, it is possible to choose to give them 250 IU of homologous tetanus immunoglobulin, and a booster shot, followed by the complete immunization cycle [9]. However, it is important to emphasize that generally the health systems of each country recommends immunization according to their own criteria. The wounds should be treated as quickly as possible so as to ensure the covering of hard and soft tissue avoid infection and healing by secondary intention, which has considerable potential for forming scars that result in aesthetic and functional damage. If necessary, it is possible to use regional flaps for the covering defects [9] (**Figure 6**).

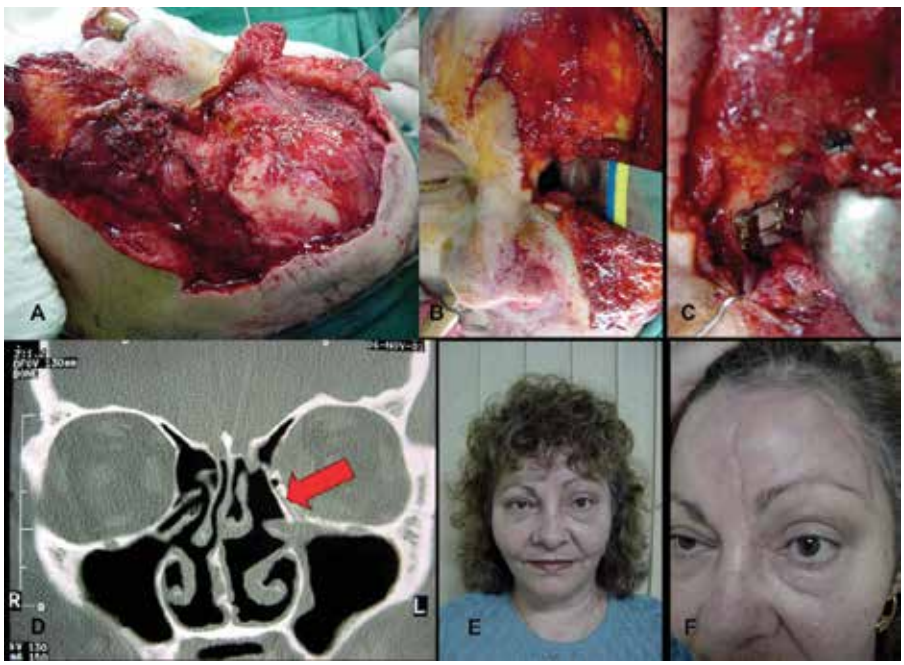

Figure 6. (A)–(F) – Patient with severe soft tissue injury and medial orbital wall fracture. Immediate reconstruction of the skeletal and soft tissues.

2.2.5. Other trauma

The maxillofacial surgeon should keep in mind that the dynamics of trauma, which is directly related to the kinetic energy, could lead to other associated fractures and concomitant other

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musculoskeletal and visceral injuries which should be sought. Thus, combining the initial dimensioning of the injury and the initial clinical evaluation, the surgeon must quantify the "*degree of apparent impairment*" of the trauma.

2.3. Imaging and diagnostic assessment

Imaging obtained through helical computed tomography scanning (CT scans) is important in the assessment of CMF Trauma; as the facial skeleton amounts to one of the most complex anatomical relationships and three-dimensional combinations of bone anatomy. It may still be pointed out that in polytrauma patients the sensitivity of contrast of the various densities on the CT can identify a wide variety of foreign bodies which may be present, depending on the nature of the trauma (such as fragments of wood, plastic, glass, and other materials). CT is considered to be a primary diagnostic tool, especially in the field of traumatology. It is important that the surgical and radiology teams collaborate on the needs of the surgical team and the technical possibilities of every piece of equipment that the radiology team may offer, which should be exploited via the installed software at hand to optimize the standards of patient evaluation (**Figure 7**).

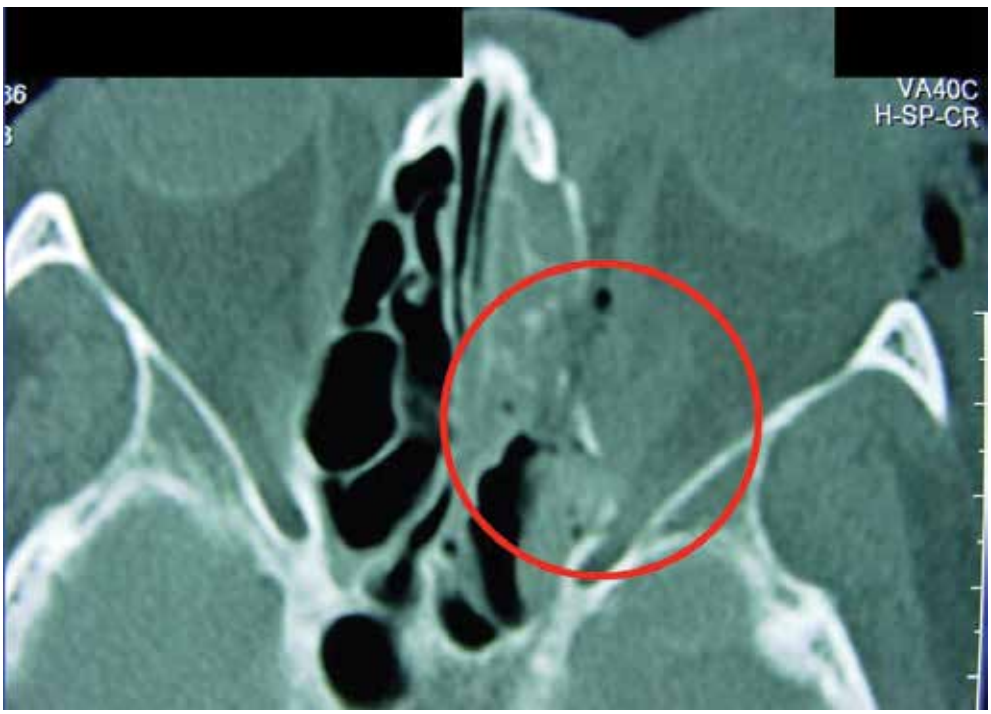

Figure 7. CT scan axial section showing fracture of the medial wall and orbital apex.

The main advantages of CT, which the authors call the "*Decalogue of Helical Computed Tomography*," include the following:

1. Being non-invasive;
2. Minimum discomfort for the patient;
3. Low exposure to radiation;
4. Greater speed in the execution;
5. Maximized details;
6. Allows for multidisciplinary evaluations;
7. Allows for the reconstruction of images;
8. Allows for the establishment of investigation protocols;
9. Guides viable surgical approaches; and
10. Facilitates the analysis of results.

2.3.1. Technical possibilities of CT scan

CT scan acquisition of images is possible with the patient lying down or the patient sitting up. In patients that are trauma victims, the "lying down" position is frequently used. CT scan allows for the acquisition of images of the head (skull, maxilla, and mandible) in a few seconds, with the patient lying down (supine position). Hospital tomography scans are of the helical or spiral type, and are fourth generation devices and have a significant reduction of the image-acquisition time, which has enabled the complete study of the head in less than one minute. Spiral-CT allows for high-quality multidisciplinary and three-dimensional (3D) reconstructions (**Figure 8**).

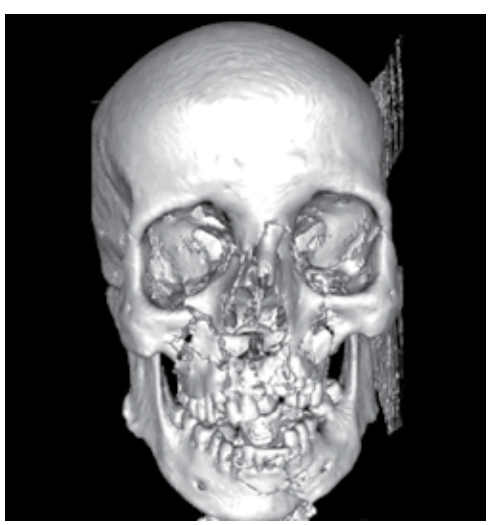

Figure 8. CT scan 3D reconstruction in a patient with panfacial fracture.

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Zimmerman et al. [10] stated that spiral-CT is the diagnostic method of choice for assessment of severe brain trauma in pediatric patients. As a routine, the authors recommend to delimit in scout view the *axial sections* between the vertex of the skull and the submandibular region, and the *coronal sections* between the nasal and occipital points. With those limits and the programming of thin slices (equal to or smaller than 1 mm) and extension of the Digital Imaging and Communications in Medicine (DICOM), it is possible to evaluate with relative precision the totality of the craniofacial skeleton. It is important to note that in patients with cervical spinal cord trauma the study of the cervical spine during the screening must be included. It is possible to evaluate bone thickness, to obtain linear, angular, and volumetric measurements. The acquisition of images enables skeleton reconstructions with the use of virtual surgical planning applications, through which it is possible to plan the spatial position of the mandibulomaxillary relation to the skull with precision, evaluating three dimensions (**Figure 9**).

1. Yaw axis or "**Y**" axis;
2. Lateral axis, pitch axis or "**X**" axis; and
3. Roll axis, longitudinal axis or "**Z**" axis.

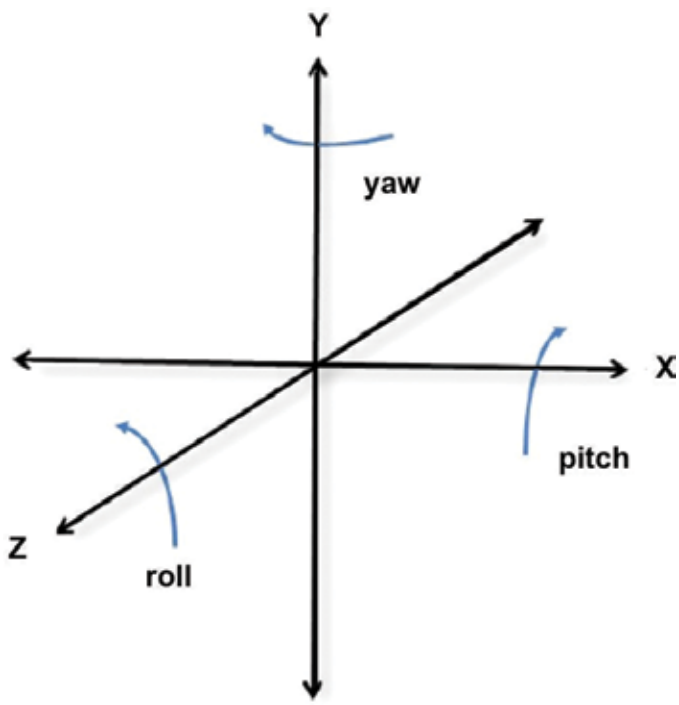

Figure 9. The three axes: yaw axis or "**Y**" axis, pitch axis or "**X**" axis, and roll axis or "**Z**" axis.

It is also possible to plan the surgical sequence and the kinds of fixation materials, the anatomical contours and the size of screws to be used. Therefore, it is possible to quantify and

to qualify the skeleton fixation material to be used in the surgery. If the surgeon does not have the software to make a complete virtual surgical plan, the quality of the obtained image allows for the printing of biomodels with 3D printers. It is then possible to plan the surgical procedure by repositioning fractured segments, bending the plates, and choosing the size of the screws that are to be used for skeleton fixation (**Figure 10**).

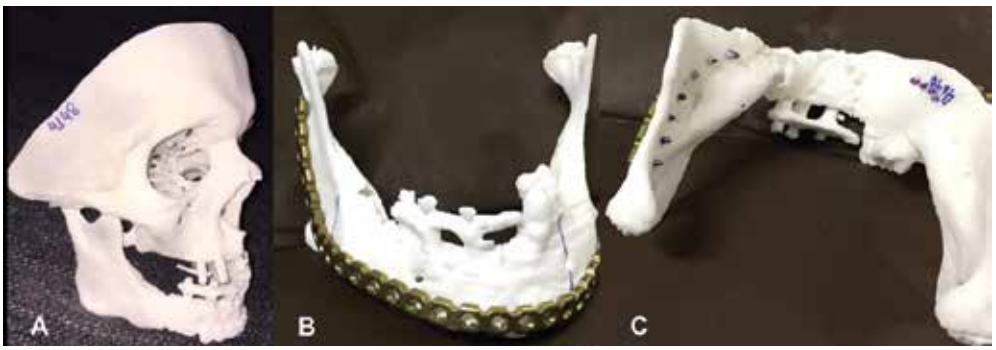

Figure 10. Biomodel obtained by 3D printer for surgical planning.

From those images, it is possible to carry-out a high-quality two-dimensional multiplanar evaluation of the craniomaxillofacial region, with the *axial, coronal*, and *sagittal* sections. The 3D reconstruction of the images illustrates the trauma from the point of view of general assessment. It is, therefore, important for the 3D evaluation. It should be pointed out that 3D reconstruction by itself is not yet the ideal reconstruction for pre-surgery assessment of the orbital cavities, as the low thickness of the medial or ethmoidal walls of the orbit and of the orbital floors do not enable the viewing of good-resolution, irregularity-free images. However, it is of particular importance for the treatment of sequelae of trauma and congenital deformities, for the planning and guidance of osteotomies. The 3D reconstruction helps the maxillofacial surgeon more than it does the radiologist. However, one should keep in mind that in order to obtain a good-quality 3D reconstruction the slices must be of low thickness, so as to avoid the so-called stacking artifacts.

CT scan images that can be combined in a two-dimensional or in a 3D way make the diagnosis easier and provide more effective guidance for treatment. The use of CT scan must be preceded by the mental incorporation of the sectional anatomy of the craniomaxillofacial skeleton, enabling the clear and precise identification of the structures that are involved in the object of the evaluation. It is a diagnostic instrument that offers advantages which make its use more than just an imaging resource.

The presence of metallic components in the teeth or bones may present problems for the acquisition of images. The use of titanium plates and screws causes interference less frequently. Considering the highlighted points, the evaluation of the patient with traumatic deformity by

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imagery allows the maxillofacial surgeon to quantify the "*degree of anatomical impairment*" of the trauma and to establish the diagnosis for the planning of treatment.

2.4. Planning of the treatment

For the treatment of complex facial trauma, it is important that the maxillofacial surgeon and team have core knowledge of craniofacial anatomy, of its pathophysiology, principles of individualized treatment of each fracture, the biomechanical basis of the craniomaxillofacial skeleton, and the facial reconstruction sequence. In the past, when imaging resources were limited to conventional two-dimensional radiographs and the absence of functionally stable internal fixation (SIF), complex traumas were often treated in a conservative manner with limited surgical approaches and frontal skeleton wire suspensions and intermaxillary fixation (IMF) with steel wires. The diagnosis and consequent treatment of those fractures sometimes were not satisfactory. Important complications, including **dental malocclusion, alterations in ocular motility and visual acuity** (dystopia, ophthalmoplegia, and diplopia), were relatively common, and numerous **aesthetic deformities** such as **severe asymmetry, enophthalmos and hypophthalmos, elongations or facial retrusions persisted** [11–13] (**Figure 11**).

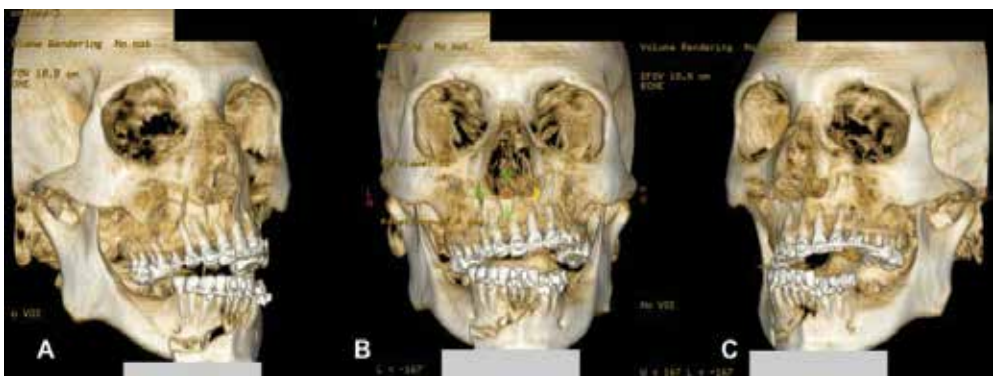

Figure 11. (A)–(C)—CT scan 3D reconstruction showing complex fracture and retrusion of the maxilla.

The gold standard for treatment is early diagnosis by means of CT, with a three-dimensional and volumetric evaluation of the entire facial skeleton, which makes it possible to plan adequate surgical exposure and the use of SIF.

It is important to know the "*degree of anatomical impairment*" to classify complex trauma. Follmar et al. [14] divides the face into four segments (**Figure 12**):

a. **Frontal Region** (frontal bone, frontal sinus, supraorbital ridges, and orbital roof)—Physiognomically constitutes the **Upper Face**;

b. **Upper Midface**—composed of the orbital floors, lateral and medial orbit walls, naso-orbital-ethmoid region (NOE), nasal bones, nasal septum, and the zygomaticomaxillary complexes or malar eminences;

c. **Lower Midface**—composed of teeth-supporting portions of the jaw and hard palate; for containing those structures, it is also called the "occlusal Unit" by some authors [15]; and

d. **Mandible** or **Lower Face**—the movable third of the facial skeleton.

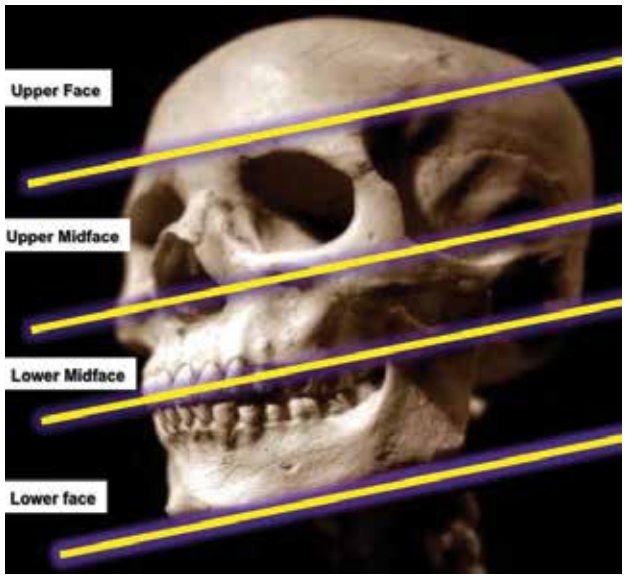

Figure 12. The face in four segments.

According to Follmar's classification [14], it can be said that the so-called Panfacial fractures are those that affect at least three of the four axial segments of the facial skeleton. To clarify the frontier between the Upper Midface and the Lower Midface, it is represented by the imaginary line of the LeFort I fracture line [14, 16]. The surgical treatment for facial reconstruction is challenging because it is complex. The treatment plan is related to the existing fractures and also to the access routes for the fixation of the fractures, choosing of the best areas for the use of bone fixation (plates, mesh, and screws). It is important to highlight the fact that craniomaxillofacial trauma is complex, panfacial with loss of soft and/or hard tissue that may lead to difficulty in the application of osteosynthesis material in the areas that are ideal for support of physical load. Besides, high-energy trauma, which sometimes presents with comminution, may also present increased difficulty for the placing with miniplates and screws, especially because of the impairment of bone vascularization [17].

It is important to point out that a complex craniomaxillofacial trauma patient should not be treated as if they have "some isolated fractures"; because traumatic brain injury (TBI), spinal cord injury of various levels, acute or in-progress impairment of airways, pulmonary contusion and eventual restriction of thoracic expansibility (fractured ribs, pneumothorax), or abdominal trauma and loss of intravascular volume may be associated with it may be missed in the first evaluation [16].

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Treatment will involve:

1. Choosing of surgical approaches;
2. Initial selection of fixation systems;
3. Planning of the reconstruction sequence

    3.1. Reconstruction of the craniofacial unit and/or

    3.2. Reconstruction of the central segment and/or

    3.3. Reconstruction of the maxillomandibular unit.

The first described surgical approaches for treatment of facial fractures were small, limited approaches, with direct access to the fracture areas. It is currently known that the correct 3D reconstruction of the face can only be accomplished by means of wide surgical exposition, which allows for the reduction and fixation of fractures [13, 18, 19], by reconstructing the jaw horizontally and vertically at the zygomatic and naso-orbital-ethmoid (NOE) area, the LeFort, palate, frontal region and the frontal sinus [15]. For those reasons, complex facial fractures must be treated by means of wide surgical access, via coronal approach for exposure of the frontal, frontozygomatic, frontoethmoidal, and fronto-orbital regions [20], with or without preauricular extension subciliary and subtarsal approaches which can sometimes be replaced by transconjunctival approaches; full maxillary surgical approach for exposure of the entire jaw, as well as approaches pertinent to jaw fractures, which can usually be intraoral, extraoral or both, depending on the topography of the fractures.

Other surgical approach should be considered, such as the use of pre-existing lacerations. Sometimes, the lacerations that are a consequence of trauma are closely associated with the fracture areas. The use of those lacerations as surgical approaches should be considered when they offer adequate exposure for the reduction and fixation of fractures. The advantage of those approaches is avoiding new surgical incisions. Surgical approaches should address the safety of noble structures and attention to cosmetic considerations in order to permit an esthetic scar [21]. Extraoral approach to the jaw should be made carefully, considering the branches of CN VII branches, responsible for the motility of facial muscles [21]. When the surgical approach has been made, the maxillofacial surgeon can expose the fractures, which will let the team know what the "*degree of real impairment*" is.

2.5. Basis for the three-dimensional reconstruction of the face

2.5.1. Zones of greater resistance in the craniofacial skeleton

The Midface human skeleton has evolved to resist the vertical forces of mastication. It protects the face and the base of the skull against various kinds of trauma. Those zones of greater resistance are known in the upper face, midface and lower face or mandible as vertical, horizontal, arch or sagittal buttresses, and platforms (**Figure 13**).

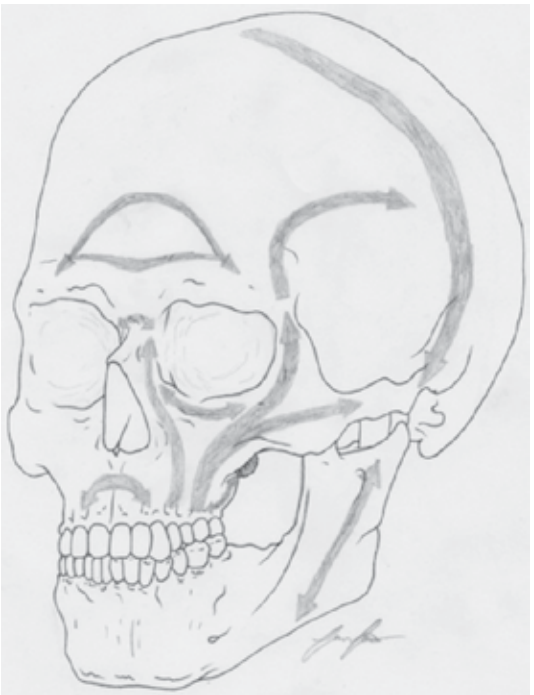

Figure 13. Zones of greater resistance in the craniofacial skeleton.

Facial reconstruction consists of 3D reconstruction in *vertical, horizontal, and sagittal buttresses* and the *platforms*.

The **vertical buttresses** include:

(a) *Nasomaxillary or canines* which are located in the canine fossa and extend to the orbits;

(b) *Zygomaticomaxillary* which include the zygomatic bones up to the orbital rims and zygomatic arches; and the

(c) *Pterygomaxillary* which include the pterygoid processes of the sphenoid bone and the maxillary tuberosities. Those buttresses are not reconstructed because of the difficulty of access [13].

Vertical buttresses in the Lower Face include the following:

(d) *Condyles of the mandible*;

(e) *Angle of the mandible*; and

(f) *Mandibular ramus* [15].

The condyles and ramus of the mandible establish the posterior vertical height of the face [13] and are important anatomical structures which should be considered at the time of facial reconstruction, so that there are no alterations in facial height.

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The **horizontal buttresses** are as follows:

A. *Frontal bar* which is a key area in the reconstruction of Joseph Gruss's Outer Facial Frame [15];

B. *Arches*:

1. *Interorbital* or *supranasal* which unites the nasomaxillary or canine buttresses, in the upper part;

2. *Infranasal* which unites the nasomaxillary or canine buttresses, at the base;

3. *Supraorbital* which unite the nasomaxillary or canine buttresses to the zygomatic buttress;

4. *Infraorbital* which unite the nasomaxillary or canine buttresses and zygomatic buttresses in their medial portion; and

5. The *malars* which unite the zygomatic and pterygoid buttresses.

Horizontal buttresses in the Lower Face include:

The mandible *body*;

The *parasymphysis*; and

The *symphysis*.

The **sagittal buttresses** are represented by the *zygomatic arch*, the *maxilla*, and the *mandibular body* [15].

The so-called **platforms** are references of the Upper Face and Midface which correspond to imaginary ramps from the auditory meatus which represent the facial projection from the *anterior cranial fossa*, the *orbital floors*, and the *floor of the nasal cavities* (**Figure 14**).

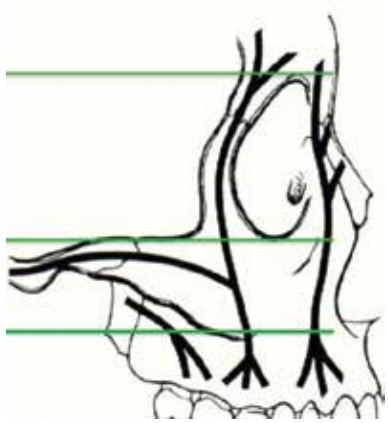

Figure 14. The craniofacial platforms as references of the upper face and midface.

The reconstruction of those vertical, horizontal, and sagittal buttresses and, consequently, the platforms is the basis for reestablishing the **projection, height, and width of the face** [13, 16]. They are essential triad for the three-dimensional reconstruction of the face. Nowadays, what is used, as a parameter for the three-dimensional reconstruction of the face is the intervention in the craniofacial and maxillomandibular units, which will be detailed further on, in the surgical approach sequence. The technique for reconstruction of the Midface has evolved from orthopedic and craniofacial reconstructive surgery with skeleton fixation and immediate bone grafting [22].

For the execution of the reconstruction of the craniomaxillofacial skeleton, one should take into account that in the upper midface and lower midface there is variable bone thickness and a factor in choosing the region that is more or less favorable to osteosynthesis; regions such as that of the body of the zygomatic bone, zygomaticomaxillary buttress, orbital rims, nasal bone, and the frontal bone are favorable to the placement of plates and screws for osteosynthesis, because they are regions of suitable bone thickness. On the other hand, regions of lower bone thickness such as the anterior wall of the maxillary sinus and orbital walls do not provide solid anchorage for the application of SIF, except for the lateral wall and roof, because they are respectively thicker.

The thickness of the frontal bone varies from 4 to 9 mm [22], so in some cases it is possible to use screws of that length without risk of damage to the Dura mater; it is important to pay attention to the frontal sinus, where the thickness is usually less. According to the AO Manual [15], the SIF material to be used for the reduction of Midface Fractures is neutralization plates (adaptation plates) or the Locking® System, in the regions of the above-mentioned buttresses. Regarding the SIF material to be used for the reduction of Lower Face fractures, it is possible to choose a number of systems for load sharing or load-bearing osteosynthesis.

2.6. Reconstruction sequence in multiple facial fractures

In the past, the starting point for the treatment of facial fractures used to be dental occlusion, with or without the use of surgical guides obtained by means of plaster models from complex, low-precision castings. In any case, occlusion is still an important reference for the reconstruction of facial buttresses during the procedure, not only because of the necessity of good occlusion but also because of the relation of the occlusal plane to the fixed facial skeleton; occlusion still occupies an important place in the treatment of facial fractures. However, guiding the reconstruction primarily by the occlusion leads to results which were faulty in some cases, regarding height, width, and facial projection. A good occlusion without the standards of correct skeleton positioning resulted in failures in reconstruction and residual facial deformities below the functional and aesthetic expectations of the treatment.

With this concept, 3D reconstruction has had significant progress in terms of results for patients who are victims of facial multiple trauma [23]. Several reconstruction sequences have been described [23–25] including the "top-down," "bottom-up," "inside-out," and "outside-in" steps, with an emphasis on the zygomatic arches [11, 13, 26] ending up in the reconstruction of the naso-orbital-ethmoid (NOE) complex and establishing the upper midface and lower midface connection or on a "LeFort I imaginary line." The reconstruction order is not more

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important than the surgical planning. A prime factor for the good sequencing of the reconstruction is the identification of stable points of reference from which it is possible to initiate the sequence [16] of fixations that make up the facial skeleton. Simplifying and reconstructing the distribution buttresses of masticatory forces could be the secret to the treatment of extensive facial trauma patients. In order to accomplish the three-dimensional reconstruction of the face, most authors [27] recommend the management of the two primary facial units: the **craniofacial unit** and the **maxillomandibular unit**, from the so-called key areas to the three-dimensional reconstruction of the face; we can summarize these in the following manner: **Projection:** zygomatic arches and anteroposterior mandibulomaxillary position (**Figure 15**);

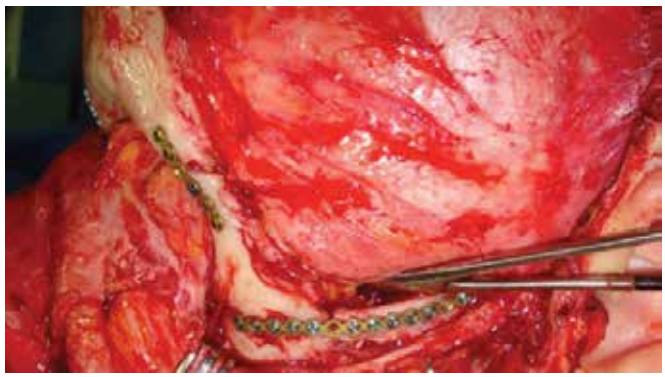

Figure 15. 3D facial reconstruction—projection—key area: zygomatic arches and anteroposterior mandibulomaxillary position.

Height: Frontozygomatic suture and zygomaticomaxillary complexes, buttresses of the maxilla and mandible, especially the mandibular ramus and the condylar process (relation of connection between the Upper Midface and Lower Midface and Lower Face or Mandible (**Figure 16**).

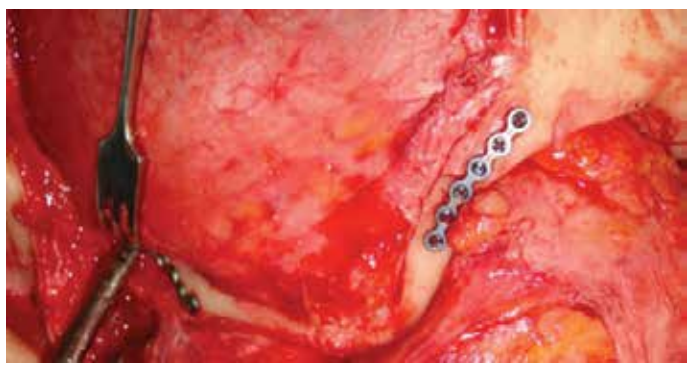

Figure 16. 3D facial reconstruction—height—key area: frontozygomatic suture and zygomaticomaxillary complexes and buttresses of the maxilla and mandible.

Width: Outer facial frame: frontal bar, internal orbits, zygomaticomaxillary complexes, (**Figure 17**) central segment of the face, and the correct arcuate contour of the jaw.

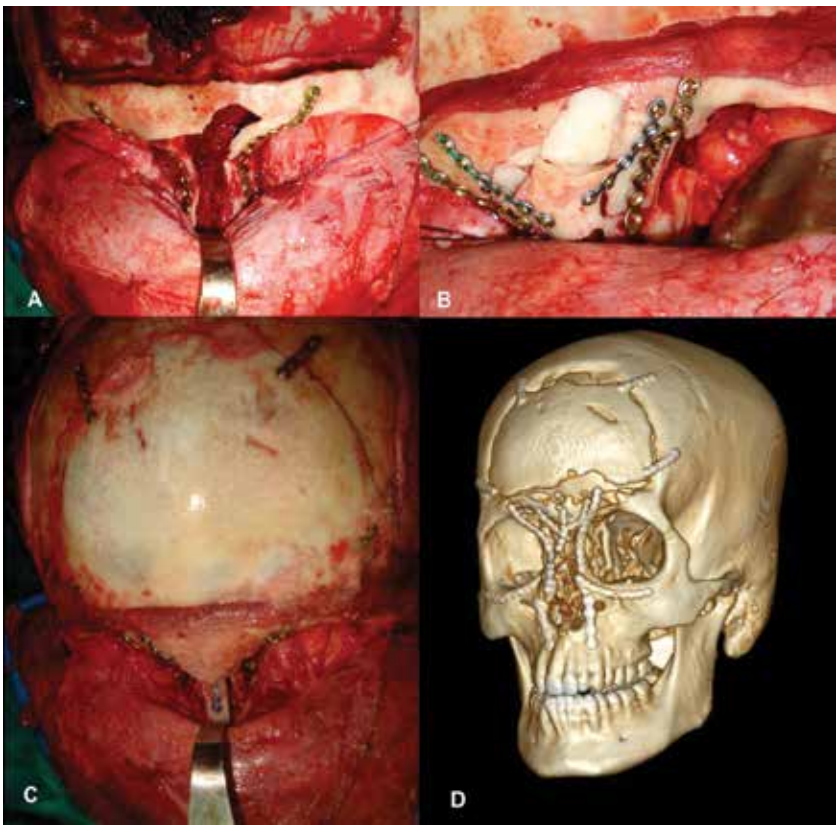

Figure 17. (A)–(D)—3D facial reconstruction—width—key area: outer facial frame—frontal bar, internal orbits, zygomaticomaxillary complexes, central segment of the face and the contour of the jaw. Patient with extensive frontal-nasal-baso-ethmoid-orbital fracture, subjected to three-dimensional reconstruction including the anterior cranial fossa and the "central midface.".

As a rule of the entire facial skeleton, the treatment goes along a very simple concept of *exposing the fractures, identification of the anatomical references, and fixation of the buttresses*. Those fixations should begin with the simplification of the fracture lines, whenever possible, with Erich bars and/or plates and screws of lighter systems and monocortical screws. Interfragmentary screws can also be used, as they are simple, low profile materials. Screws for IMF are useful in the cases of fractures without much fragmentation of the alveolar processes because of the impossibility of ensuring adequate mandibulomaxillary "arcuate contour." The execution sequence of the reconstruction may vary according to the extension of the fractures and, in general, should be initiated at the mandible through the intervention in the **maxillomandibular unit** made up of: (a) maxilla in the *lower midface*; (b) *buttresses of the mandible* (**Figure 18**); and (c) *dental occlusion* [13].

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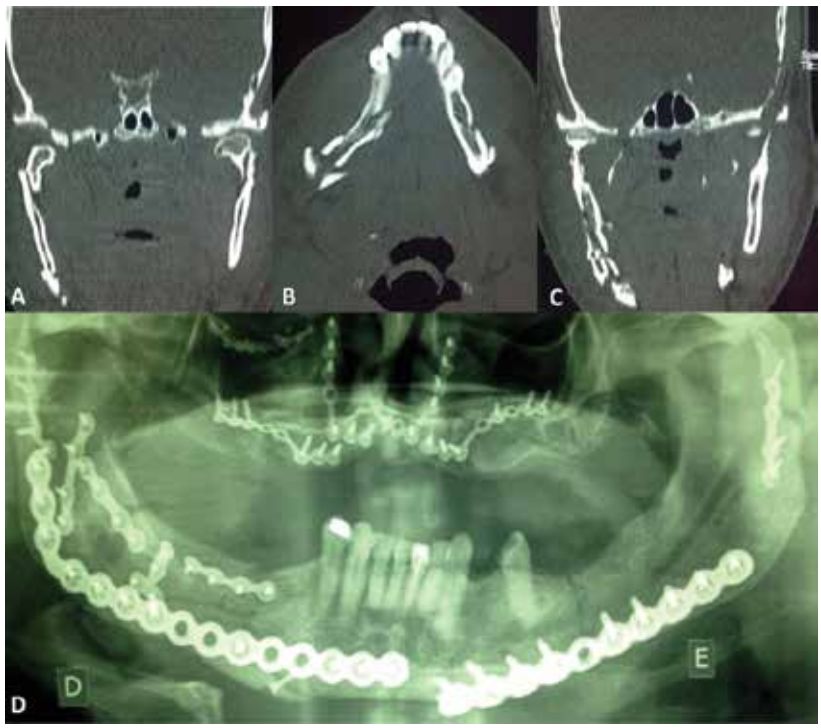

Figure 18. (A)–(D)—maxillomandibular unit—(a) maxilla in the lower midface; (b) buttresses of the mandible (complex fracture), and (c) final result.

The reconstruction of the mandible can be used for rehabilitation of the occlusion reestablishment of facial height and width, as well as of the posterior vertical height [11, 13, 14]. In fractures that reach the maxilla and the mandible, the hard palate region should be considered a guide for mandibular reconstruction; thus, the palate needs to be reconstructed so that it can be used as a reference for the latero-medial relation of the mandible.

However, it is important to pay close attention in the reductions of symphyseal fractures (especially when associated with bilateral condylar of subcondylar fractures) so that there is no enlargement of the mandibular arch, a fact which would lead to an erroneous reconstruction of the entire lower midface and upper midface, causing complete facial enlargement which would be difficult to correct later on. In that situation, the extraoral approach of the symphyseal fracture is justified for the perfect evaluation of the internal face of the mandible.

When there is a low subcondylar fracture without comminution and with good bone interface, it is possible to ensure the repairing of posterior facial height and then proceeds to the reduction of the other fractures in the mandibular arch [13].

From there, one carries out the reductions of the fractures of the mandibular arch (symphyseal and/or parasymphyseal and/or body and/or mandibular angle fractures), paying attention to the correct reduction and alignment of the internal cortex in order to avoid facial enlargement. To that end, digital compression in the region of the mandible angles contributes to an adequate

outline of the mandibular arch. When one uses a plate in the mandible that has sufficient strength and uses the fixation system of compression of the stumps promoted by the eccentric relation of the screws relative to plate (Dynamic Compression Plate – DCP®), the overbending maneuver which contributes to the correct alignment of the internal mandibular cortex is recommended.

The chosen material for the fixation of the mandible should prioritize plates with intermediate segments for the fracture lines. One should avoid leaving instability orifices, which may represent areas of fragility of the fixation system. The choice of plates also includes the construction of a whole that promotes as much stability as possible without interfering with mandibular function and aesthetics. Plates of security to plate system, or Locking® System should be preferred, as they cause less compression of the cortical bone, lessening local osteolysis and lowering infections from failure in the fixation system.

The reconstruction of the **craniofacial unit** is made up of: (a) *Gruss's Outer Facial Frame* (**Figure 19**), which includes the frontal bar, zygomatic arches, and orbital rings [26], where the zygomatic arch is related to the reestablishment of width and facial projection; and (b) *Upper Midface*, known as "*Paul Manson's Upper Midface"* (**Figure 20**), where it is necessary to control facial width, taking into consideration the NOE region [28].

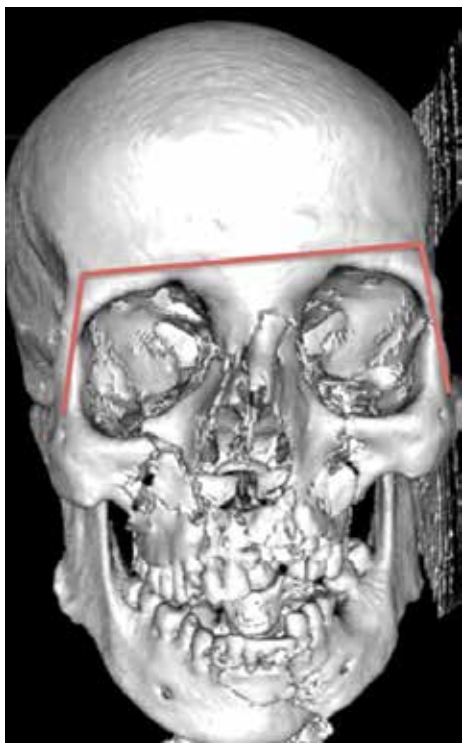

Figure 19. Frontal view, "Gruss' Outer Facial Frame.".

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Figure 20. (A) and (B)—Reconstruction of "Paul Manson's upper midface.".

The coronal surgical approach (**Figure 21**) should be made on the supragaleal plane, that is, above the galea aponeurotica and of the subtarsal (**Figure 22**) or transconjunctival approaches (**Figure 23**), depending on the type and extension of the orbit fractures, or fragmentation of NOE fractures.

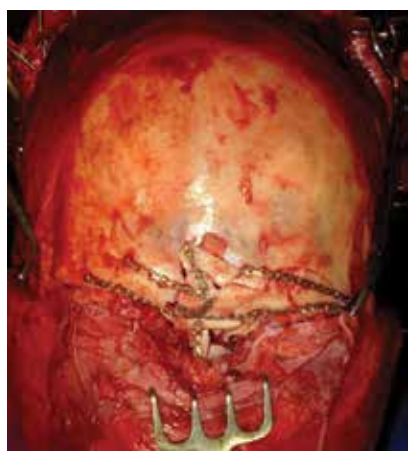

Figure 21. Coronal approach showing the reconstruction of the extensive frontal-nasal-ethmoid-orbital fracture.

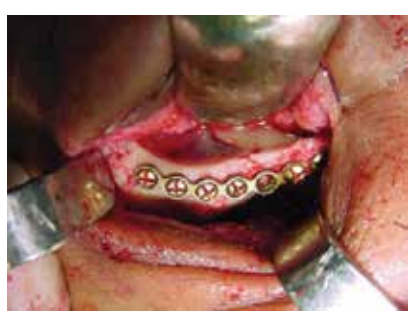

Figure 22. Subtarsal approach.

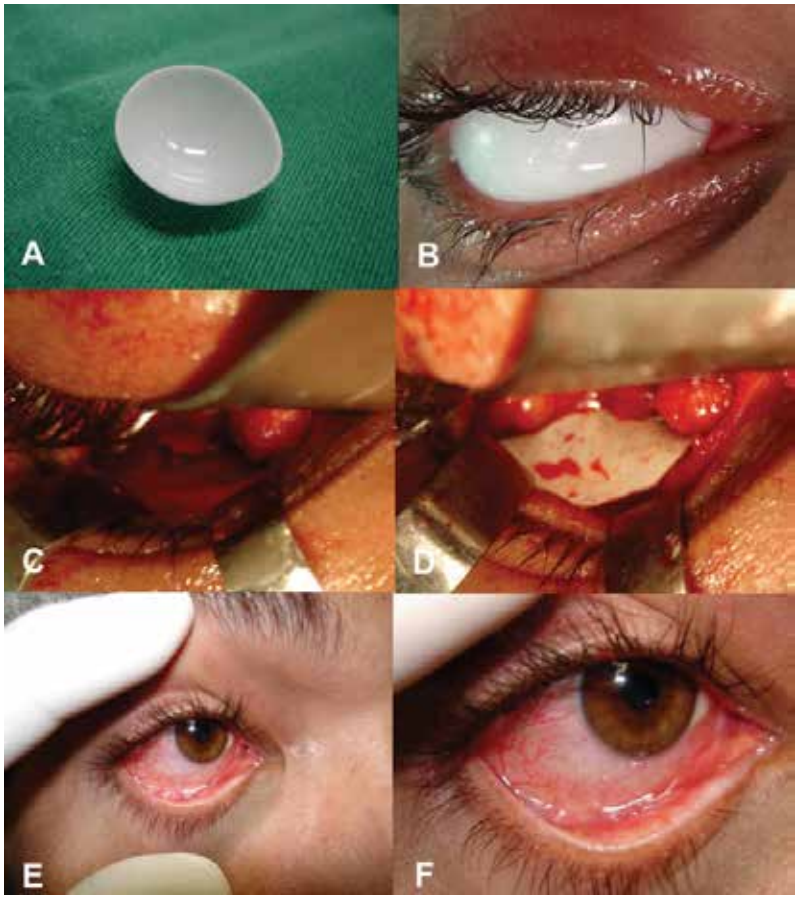

Figure 23. (A)–(F)—A patient with orbital fracture treated by transconjunctival approach. (A)–(B)—protective lenses; (C)–(D)—approach and use of polytetrafluoroethylene and (E)–(F)—follow-up of 07 days with excellent result.

One initiates the reconstruction of a unit, with the reconstruction of the outer facial frame and the reduction of the linear or fragmented fracture(s) of the anterior wall of the frontal sinus. For that stage, we can employ plates and screws of the 1.0 or 1.2 mm system, with or without bone grafts, titanium mesh, or other biomaterials depending on the degree of comminution and/or loss of substance at the fracture site. However, if there is a misaligned and/or fragmented fracture, a neurosurgical approach should be carried out.

If the fracture of the frontal sinus extends into the cribriform plate, associated with ACF fracture or not, the frontal sinus should be carefully curetted so that there is no remaining mucosa that is vascularized by small diploic valveless veins, the so-called Breschet veins [15]. Cranialization or obliteration should be carried out. In that case, the obliteration of the frontonasal ducts should be done and bone graft in the ACF should be used when necessary, associated with a pericranium flap (**Figure 24**) for repair of dura mater or use of other biomaterials for repair, such as polytetrafluorethylene.

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Figure 24. Pericranium flap.

With the exposition of the frontozygomatic region and zygomatic arches, it is possible to reposition the zygomas by fixating them to the frontal bone and to the zygomatic arches. The initial positioning from the zygomas to the frontal bone can be done with a "pivot" steel thread that enables some rotation of the zygomaticomaxillary complex until the final reduction [16] with SIF. The SIF used in those areas is of the stable kind, with the necessary strength to support buttresses of distribution of force and muscle insertions. At this point, the lateral limits of the upper midface will be reestablished. At that stage, the maxillary fractures should be reconstituted and the maxillary buttresses repaired. IMF is again imperative and fixation materials need to be sufficient to support the masticatory load and compensate possible spaces without bone support. The fixation of those plates should be carried out with short monocortical screws so as to impair the upper airways as little as possible. The next step is the reconstruction of the infraorbital rims, when the zygoma and the maxilla are fixed upwards using delicate SIF, which will also provide the fixation of the central region of the face, the NOE region. SIF in the frontonasal region can also be used for the fixation of occasional nasal dorsum grafts. For that, it is possible to use systems of remarkable flexibility and low profile, avoiding touch sensitivity of the material that is employed. At this point, the reconstruction of the upper face and of the upper midface is finished, and the mandible is integrated to the lower midface with the use of IMF.

In order to "connect" the upper midface to the maxillomandibular unit one performs the reconstruction of the vertical buttresses, in the following manner: (a) nasomaxillary buttresses reconstruction that fixates the central segment of the face to the maxilla downward, using SIF and (b) zygomaticomaxillary buttresses reconstruction which fixates the zygoma and the maxilla downwards, also using SIF. Completing the reconstruction of the vertical and horizontal buttresses, the next stage regards bone grafting or the employment of biomaterials for the reconstruction of the orbital walls, which usually do not withstand the use of screws, except

for the areas next to the orbital rims or in the region of the lateral wall and the ceiling, which are naturally thicker.

It is important to point out that in cases of fracture of the orbits, with extensive fragmentation of the walls and therefore an alteration in the "orbital continent," it becomes necessary to reconstruct the orbital walls with bone grafts, malleable or preformed titanium plates, and other biomaterials to reestablish the contour of the internal orbit. In general, traumatic deformities of the orbital cavity may require contour correction or volumetric reconstruction, which will determine the kind of material that can be used in the reconstruction. However, that is a truly complex situation, as lesions of the periorbita, occasional escapes of intraconal fat or post-traumatic lipolysis are factors that lead to the evolution of late enophtalmos.

Figure 25. (A)–(F)—NOE fracture treated by expanded approach. (A)–(B)—subtarsal approach, (C)–(D)—coronal approach and (E)–(F)—pre and postoperative photos, 06 months follow-up.

When that kind of fracture reaches one of the orbits, it is possible to use the contralateral orbit as a parameter for the reconstruction and the projection of the eyeball as a guide to the reconstruction of the key area of the projection of the eyeball. Neuronavigation has been used as an adjuvant to treatment to obtain, among others, that parameter of the contralateral orbit and also adequate anteroposterior position of bone grafts and/or titanium mesh without damage to the optic nerve. Finalizing the reconstruction of the NOE region, with the reestablishment of the intercanthal segment [13, 24], one performs the reinsertions of the eyelid medial ligaments, in the posterosuperior region of the posterior lacrimal crests. After the grafting or inclusion of other biomaterials, one proceeds to the reinsertion, when necessary, of the lateral eyelid ligaments and to the bilateral facial resuspension before the synthesis of coronal access.

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Adequate sequencing and, whenever possible, surgical approaches that are barely or not at all visible lead to results that are stable and aesthetically well accepted (**Figure 25**).

2.7. Support measures

Although some of the stages that are listed are not necessarily steps related to the surgical procedure to be carried out, they are important items which contribute in a significant way to the result of the definitive surgical treatment.

2.7.1. General support measures

1. Tetanus prophylaxis: human hyperimmune immunoglobulin;
2. Antibiotic prophylaxis;
3. Volume replacement;
4. Use of diuretics;
5. Steroids;
6. Analgesia;
7. Cryotherapy;
8. Headboard elevated to 30°;
9. Others medications routinely used by the patient;
10. Permeability of tracheal tube and/or tracheal cannulas;
11. Urinary catheter;
12. Venous puncture or venous dissection;
13. Hydro balance;
14. Vital signs; and
15. Oximetry.

2.7.2. Support measures for soft tissue

1. Preserve the integrity of soft tissue and noble structures;
2. Protection with dressings;
3. Protection of eyeballs;
4. Neurovascular structures;
5. Consider grafting and/or inclusions; and
6. Final reconstruction of soft tissue.

All alterations that have been identified in the clinical history, physical examination, and complementary examinations must be in the medical records and preferably photographed so that possible preexisting alterations are attributed to the treatment (**Figure 26**).

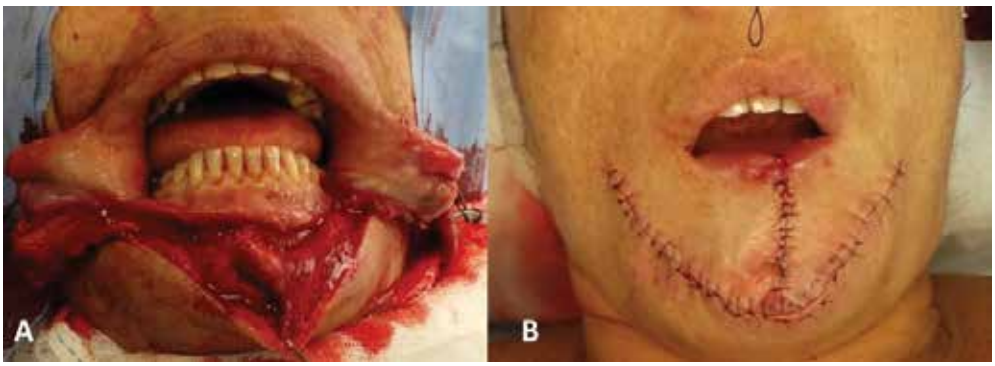

Figure 26. (A) and (B)—Immediate reconstruction, by Gilles flap, extensive lower lip injury caused by dog bite.

2.8. Complications

The authors divide complications to general and specific; they are subdivided as immediate and late; according to the moment they arise.

2.8.1. General complications

A. Immediate:

1. Reconstruction failure;
2. Dental malocclusion;
3. Edema;
4. Bruises;
5. Hematoma;
6. Rhinorrhagia;
7. Cerebrospinal rhinorrhea: rare and normally associated with fractures of the cribriform plate or posterior wall of the frontal sinus associated with meningeal lesion;
8. Partial or complete neurogenic lesion: CN III, IV, and VI (ptosis, mydriasis and ophthalmoplegia), CN II (amaurosis);
9. Diplopia may have a neurogenic or mechanical origin (incarceration in fracture line) (**Figure 27**); and
10. Inadequate aesthetics.

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B. Late:

1. Meningitis: most common intracranial complication;
2. Secondary mucocele: the average time interval between the trauma and diagnostic confirmation of the presence of secondary mucocele is about 7.5 years. (However, secondary mucocele has been reported from a period of two months up to 42 years after the trauma);
3. Frontal headache: most common complication after frontal sinus trauma;
4. Lesions of the lacrimal system which must be treated by a simple survey of the nasolacrimal duct or by dacryocystorhinostomy according to the severity of the lesion;
5. Infection;
6. Visibility of the implantable material: One must use titanium plates of low profile with adequate screws because they lead to a better aesthetic result and do not need to be removed; and
7. Eye dystopia and enophthalmos: inaccurate position because of inadequate correction of the orbital walls.

Figure 27. Mechanical incarceration extrinsic muscle of the left eyeball (superior rectus muscle) in fracture line (orbital roof fracture).

For a didactical dissertation, the authors divide the complications by anatomic topography of the affected facial thirds.

2.8.2. Upper face fractures

Among the immediate complications, we can mention infection, which rarely takes place thanks to great local vascularization; and CSF leak, which occurs to more than 10% of patients with frontobasal fractures. Treatment consists of lumbar drainage, rest, and antibiotic prophylaxis (third-generation cephalosporin) for the prevention of meningitis. If after one week there is no remission of symptoms, it will be necessary to study a possible surgical reapproach to repair the dura mater [29]. Intermediate complications are rarer and normally associated with an obstruction of the patency of the frontonasal duct. When that occurs, there may be the development of frontal mucocele, which should be surgically treated immediately [30].

2.8.3. Upper midface and lower midface fractures

Hematoma and hemorrhage are the most common complications in the fractures of the midface. Among kinds of hemorrhage, those resulting from extensive blunt cut injuries are treated with local hemostasis and suture of the wounds. Rhinorrhagias are controlled with anterior nasal packing, associated with or without posterior nasal packing, for 48 h. In some situations of epistaxis refractory to the initial treatment, it is possible to use selective electrocauterization helped by nasofibroscopy or endovascular embolization. When hematoma is associated with orbit fractures, it can lead to serious complications. Retrobulbar hematoma is characterized by intense orbital pain, exophthalmia/proptosis, diplopia or reduction in visual acuity associated with mydriasis. In the presence of those signs and symptoms, tomography evaluation and emergency orbital decompression are mandatory [27]. Intermediate complications are normally associated with facial deformities caused by bad repositioning of the fractured bone segments or by failure in facial reconstructions.

Among late complications, we can mention:

enophthalmos, hypophthalmos, ophthalmoplegia, traumatic telecanthus, dacryocystitis, epiphora, lagophthalmos, diplopia, amaurosis, paresthesia, and nasal synechiae [30].

2.8.4. Lower face or mandible fractures

Obstruction of the superior airways and hemorrhage is the most common immediate complications of the lower face. Obstruction of the airways may occur in patients with bilateral fracture of the parasymphysis, with glossoptosis; or patients who are victims of gunshot wounds that cause more damage to bone tissue and cervical soft tissue, with the formation of extensive swelling and bruising, evolving to acute respiratory failure [30].

Among late complications, we can mention infection, pseudarthrosis, nonunion, malunion, and ankylosis of the temporomandibular joint (TMJ) [27].

Infections are normally associated with the presence of foreign bodies in the interior of soft tissue, contamination of the osteosynthesis material, devitalized bone fragments, or non-vital teeth. Treatment is based on the removal of the focus of infection and antibiotic therapy.

Pseudarthroses, nonunions, and malunions are usually related to failure in the stabilization of the osteosynthesis material or to failure in the anatomic reduction of the fractured segments. The treatment requires surgical reapproach [27]. TMJ ankylosis is one of the complications of intracapsular fracture of the mandibular condyle, associated with failure in postoperative physiotherapy. The treatment is surgical resection of the ankylosed mass and articular reconstruction with the use of autogenous bone graft or prosthetic joints [27, 30].

3. Conclusion

The management of CMF trauma should be understood as a continuing learning. Knowledge of anatomy and other basic sciences, the understanding of the pathophysiology of trauma, the

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correct triage of the traumatized patient stratification sequence combined with good specialized training are factors that will determine the outcome and yield the best chance for a correct diagnosis and the more precise and safe treatment result. Finally, it should be kept in mind that "the best chance of the patient is the first." For this reason, the well-conducted initial care, for all who participate in treatment, is an important step toward successful outcomes.

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Chapter 24

Reconstruction of TMJ with Prosthesis Joint

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Paulo Hemerson de Moraes and
Francisco de Sousa Neves Filho

Additional information is available at the end of the chapter

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Abstract

Temporomandibular joint (TMJ) and the associated muscles turn possible mandibular movements as a complex engineering appliance that may be affected by signs and symptoms such as pain, including in head and neck areas, abnormal jaw movement and clicking or crepitus sounds, classified as temporomandibular disorders (TMD). Some procedures such as discopexy, eminectomy, or arthroplasties, which we consider conservative, can result in ankylosis, even resorption and joint degeneration, limiting surgical options to treat TMJ. The alloplastic prosthesis becomes an option. Total joint reconstruction using prosthesis becomes the treatment choice during the following conditions: previous surgeries including autogenous grafts fail; presence of arthritic diseases; fibrous or bony ankylosis; tumors involving the TMJ; loss of vertical posterior mandible dimension by other TMJ pathologies; and previous prosthetic joint fail. The use of TMJ prosthesis, when compared to other reconstructive procedures, provides immediate function, reducing the duration of surgery and hospitalization time. Disadvantages of the TMJ prosthesis include high cost, prosthesis failure, functional mandibular movements loss, such as protrusion and laterality, and limited fit of stock prosthesis.

Keywords: temporomandibular joint, customized temporomandibular joint prosthesis, prosthesis, prosthetic reconstruction, temporomandibular disorders

1. Introduction

The temporomandibular joint (TMJ) is responsible for the mandibular movements and consists a set of bones, muscles and ligaments. It is subject to various diseases such as congenital, acquired (traumatic), local and systemic diseases and can lead to signs and symptoms such as pain, including in head and neck areas, abnormal jaw movement and clicking or crepitus sounds, classified as temporomandibular disorders (TMD). The complex etiopathogenesis and the variability of symptoms complicate the adoption of standardized diagnostic and therapeutic approaches, as suggested by the number of treatment modalities that have been proposed, such as occlusal splints, physiotherapy, behavioral and physical treatments, drugs and surgery. A surgical approach to the disorders of the TMJ is reserved to a minority of cases who do not respond to traditional and conservative therapies. For these situations, joint reconstructive surgery becomes necessary [1] with autogenous graft bone or alloplastic joint reconstruction, which is a challenge for the maxillo-facial surgeon. We can use autogenous bone for the reconstruction of TMJ and the preferred donor region would be the costal arch. The costochondral graft rib is obtained with an inframammary incision, where it removes part of the 5th, 6th or 7th rib, with about 3–4 cm bone tissue and 5 mm to 1 cm chondral cartilage. These patients may present some complications such as perforation or pleural laceration, resulting in pneumothorax, hemothorax, infection and chronic pain in the donor area. There is also the disadvantage of not having growth potential of the control of this type of graft, occurring overgrowth with mandibular deviation after a few years [2].

TMJ prostheses do not have many complications such as autografts, what qualifies as an alternative to the joint reconstruction. The prostheses are primarily indicated for [3, 4] the following:

- patients who have undergone multiple surgeries TMJ unsuccessfully
- infections with destruction of the mandibular condyle
- chronic inflammation or pathological resorption of TMJ
- autoimmune diseases and collagen diseases (rheumatoid arthritis, psoriatic arthritis, Sjogren's syndrome, lupus, ankylosing spondylitis)
- TMJ ankylosis
- trauma sequelae with severe functional changes
- congenital deformities (hemifacial microsomia)
- tumors in the TMJ area

The advantages for using the TMJ prosthesis are the reduction of surgical time (because there is no need for donor site), shorter hospital stay and immediate function, there is no need for each-jaw blockade postoperatively. As for the disadvantages we can mention the lack of predictability for a revision surgery, the prosthesis size limit (in the case of prefabricated

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prosthesis or stock), the loss of translational movement causing loss of laterality and protrusion due to detachment of the pterygoid lateral muscle and the high cost [5].

The following are desired characteristics in a joint prosthesis [6]:

- low level of wear and corrosion of materials
- biocompatibility
- low flow and material fatigue
- adaptability anatomical structures and their functions
- stability of the components
- absence of hypersensitivity to materials
- lightness
- functionality

These features do not stop being researched by companies Materials in order to physiologically rebuild the TMJ. Due to the low clinical longevity of these types of prosthesis, a strict follow-up still is needed, for evaluating the anatomical and functional status of patients undergoing this type of treatment. Regardless of whether the TMJ is reconstructed using alloplastic, allogenic or autogenous materials, the following should be the management goals [1]: (1) to improve mandibular function and form; (2) to reduce suffering and disability; (3) to contain excessive treatment and cost; and (4) to prevent morbidity.

2. History

The surgery for TMJ reconstruction began with Risdon, in 1933, inserting gold foil in the articular fossa in an attempt to prevent ankylosis relapse. Eggers in 1946 positioned one tantalum sheet in the pit on the mandibular head after treatment for ankylosis arthroplasty.

In subsequent years, different types of materials and techniques have been developed to repair the TMJ. The first consideration for the use of alloplastic materials has been for treating fibrous and bony ankylosis. Subsequently, they have also been used in attempts to treat osteoarthritis, disc degeneration and loss of articular severe vertical dimension [7].

The history of aloplásticas prostheses has been characterized by failures due to inappropriate designs, inattention to biomechanical principles and ignorance of the already described in the orthopedic literature. Because TMJ is a ginglymus-artrodial articulation and its function is closely associated with occlusion, ATM prosthesis requires features not seen in a conventional orthopedic prosthesis [5].

Nowadays, TMJ prostheses are designed to minimize these failures, using different materials in such different parts or prosthesis components.

3. Indications of prostheses total TMJ [5, 6, 8–10]

- Ankylosis with excessive heterotopic bone formation
- Revision procedures where other treatments have failed (eg. alloplastic reconstruction with Teflon or silastic and autografts)
- Avascular necrosis
- Joints subjected to several previous unsuccessful attempts
- Fractures with extensive destruction
- Important functional deformities
- Benign neoplasms
- Reconstructions post-malignant tumor excision
- Degenerate or resorbed joints with severe anatomical discrepancies
- Development anomalies
- Inflammatory or resorptive disorders locations (osteoarthrosis)
- Autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, systemic lupus erythematosus, Sjogren syndrome, scleroderma)
- Severe chronic pain without clinical and surgical resolution of possibilities
- Severe restriction of mouth opening

TMJ prosthesis has special role in bone ankylosis where surgical outcomes cannot be predicted when using other techniques such as autogenous grafts, leading to heterotopic bone growth [11].

4. Advantages of the TMJ implants [12, 13]

- Functionality immediately after surgery
- Symmetry and occlusal stability
- Simpler surgical technique
- Less morbidity (does not require donor area)

5. Contraindications of the prosthesis TMJ [5, 9, 10, 13]

The following are contraindications to placement of ATM protheses:

- Active or chronic infections.

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- Patient conditions in which there is no sufficient bone quality or quantity to support the components.
- Systemic diseases with increased susceptibility to infections.
- Patients with extensive drilling on the glenoid fossa or bone defects in the articular eminence or zygomatic arch that could seriously compromise the support of artificial tank.
- Only partial reconstruction of TMJ.
- Allergic reaction to any material used in the prosthesis. Cr-Co-Mo devices should not be used in patients with sensitivity to nickel, as this is also a component of the material.
- Patients with neurological and mental problems who cannot or refuse to follow optimal postoperative care
- Patients with immature skeleton. Do not use in children.
- Patients with marked hyperfunctional habits (ex. dental clenching).
- Patients with foreign body reaction caused by previous implants.
- Patients with high expectation of decreased pain and improved functional activity complete articular.

There is a technical limitation of custom-made prosthesis model on esterolitografia when the patient has a pre-metal prosthesis, as this would need to be removed by additional surgery before the CT scan in order to avoid artifacts produced.

6. Disadvantages of TMJ prosthesis [13, 14]

- The main disadvantage of prostheses is the TMJ loss of translational movement. However, the new biomechanical concept of placing the pivot point inferior to the center of the natural condyle leads to a better translation mouth opening [15], even in patients unable to perform natural protrusive movements. This concept further enhances the mandibular function and would prevent overloads on the natural TMJ contralateral side unilateral prosthesis (**Figure 1**) [16].
- High cost, although the decrease in associated costs, with shorter hospital stay and faster recovery of the patient [13].
- Doubt as the durability of the prosthesis and its possible shortcomings, because among all models of prostheses known there is no giving this predictability. There is much attention as the fixation of the prosthesis to the remaining bone, because over time some screws used to attach can lose efficiency which would lead loss adjustment and lack of component stability [5, 17, 18].

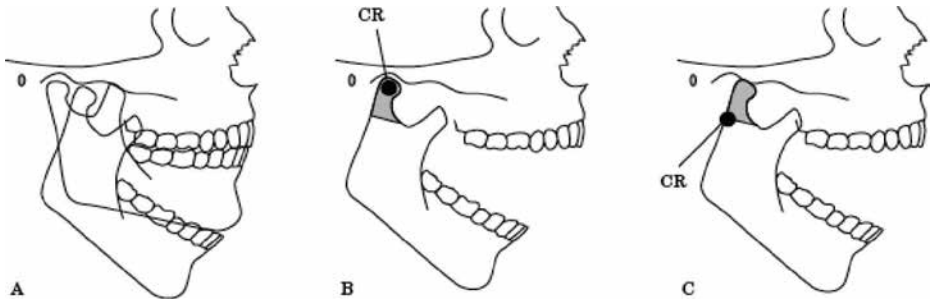

Figure 1. Center of rotation of modern TMJ prosthesis according to concepts of Falkestron (1993). (A) Normal mouth opening; (B) opening mouth rotation center located in the area of the condyle; (C) opening mouth rotation center located 15 mm below the condylar center, imitating the condylar translation [16].

7. Considerations as prothetic TMJ

The success and longevity of the TMJ alloplastic reconstruction are directly attributable to the stability of the prosthesis deployment location, biocompatibility, design, resistance to loads during function over time and correct and aseptic surgical technique [12, 18, 19].

Although the customized prosthesis is considered optimal, the accuracy of computed tomography (CT) used to make the model of the TMJ is of the order of 0.5 mm, resulting in a close fit of the prosthesis. It should also be still considered the dose of radiation while performing the CT scan, the high cost in the manufacture of three-dimensional prototype and the individual adjustment of this type of prosthesis that can consume more time [14].

The stock prosthetics require large number of different anatomical forms because of individual variability of bone structures shapes, mainly for the component of the glenoid fossa. This may hinder a little fit of the prosthesis and choosing the best component [14].

The prostheses of W. Lorenz™ and TMJ™ concepts have similar concepts, but different designs. The materials used in the two prostheses are nowadays the gold standard in orthopedic joint deployment with respect to wear resistance properties and structural stability, showing be reliable materials in prosthetic reconstructions [20, 21].

A major difficulty is knowing the best time to use a denture TMJ, and reconstruction with prosthetic joint should be considered as the final surgical stage and not be used for minor problems [18].

Autogenous grafts have shown better results than the aloplásticas aids in TMJ reconstructions for some authors. This does not mean that autologous grafts and flaps are exempt from complications and sequelae, but these are less frequent and more recoverable than those caused by dentures [22]. On the other hand, it is known that autografts (costochondral, sternoclavicular, myofascial temporal, ear cartilage, dermis or vertical osteotomy of mandibular branch) are used for TMJ reconstruction in similar conditions to the use of hearing aids, which may

occur also adverse response and possible failures in its use. There are known factors that contribute to the failure of dentures TMJ, as stated earlier, and success depends on an attempt to minimize these factors [6].

7.1. Stock prostheses

The stock prosthesis, compared to the customized one, requires less time for preoperative preparation. However the disadvantages is need a surgeon with experience because the anatomical variations still a challenge to the prostheses stability. Also the Stock prostheses is not appropriate for some patients with extensive tumors or severe deformities, intraoperative time consume to prepare the mandibular the fossa and mandibular ramus fit with the prosthesis. In contrast, the custom-made prosthesis is more expensive, but it is highly accurate, and it is also considered the prosthesis of choice in patients with major TMJ and mandibular defects [23, 24].

Some stock prostheses are relatively complex and unsuitable with fit and shape. The eminence area irregularities and the fossa bottom with complex depressions result in the instability of the prostheses. Surgeons must take care when removing irregularities by a bone bur and then place the fossa component directly because they got to preserve enough bone to retain the screws on zygomatic arch [24].

The latest inventory prostheses (W. Lorenz™) used nowadays have two components: a condylar composed of cobalt-chromium-molybdenum alloy (Cr-Co-Mo) and titanium alloy coating (Ti-6Al-4V), and a component of the composite cavity of ultra–high molecular weight polyethylene (PUAPM) (**Figure 2**). It also presents evidence of fixtures, with the compound condyle Aluminum and Radel™ plastic tank. Both components are available in various sizes as well as in specific designs for the right and left sides, being fixed to bone by titanium screws [9–21].

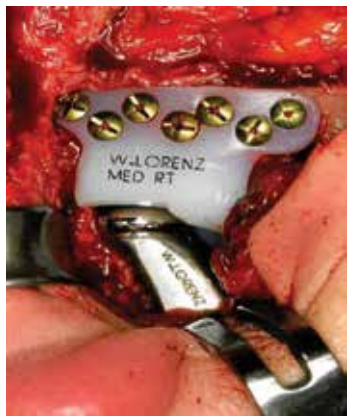

Figure 2. Installed stock prosthesis W. Lorenz. The metallic component of condylar articulating against PUAPM pit fixed with titanium screws is observed [21].

The fossa PUAPM has a minimum of 4 mm thickness in the central region and has a cavity with larger walls to protect the condyle of the heterotopic bone invasion and to prevent its displacement or dislocation. The neck condylar appears as swan neck, avoiding the obstruction problem at the implant-bone interface inherent to the drawing at right angles other condylar prosthesis and is based on the innovation of Falkestrom and Van Loon designs with rotation point lower than that of natural TMJs, resulting in an imitation of translational movement when the mouth opening, which results in 15% interincisal aperture gain [1–21].

The system does not replace normal healthy bone, and chronic pain can continue to exist even after the placement of the prosthesis. The system can also loosen or break due to stress, activity or trauma. The presence of mandibular screws or prior zygomatic arch placement or pre-existing holes may compromise the fixation. Placing the unilateral prosthesis can result in detrimental effects on the contralateral joint. It should also be noted that there may be occlusal changes over time after installation of the prosthesis [9, 10].

The following are cited as adverse effects that may occur after placement of the prosthesis [9, 10]:

1. removal components due to changes caused by overloading or wearing, degenerative changes in the joint surfaces arising from disease or prior implants and corrosion or produce particles of implant material
2. loosening or displacement with or without removal of the implant
3. systemic or superficial infection
4. allergic reaction or foreign body implant components
5. wear fossa
6. edema or facial pain
7. dysfunction of the facial nerve
8. tissue excision
9. heterotopic bone formation
10. training neuroma
11. problems headset
12. dislocation of the prosthesis

The maximum inter-incisor opening ranges from 24.9 mm in the first postoperative month moving up to 36 mm [25], for the second postoperative year, on average, in monitored patients. They are recommended post-surgical care and local measures (surgical wound care and physical therapy), proper diet and medication as well as regular visits to follow-up. The technical scheme of placement of TMJ prostheses can be seen in sequence in **Figure 3** [9, 10].

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Figure 3. Scheme of surgery and placement of the prosthesis W. Lorenz [9, 10].

The surgical technique for this type of procedure follows the sequence described [25]:

- naso-tracheal intubation directly or assisted by video
- local anesthetic infiltration with vasoconstrictor in pre-auricular region
- pre-auricular incision and dilatation of the tissues in layers
- osteotomy for the removal of the head of ankylosed jaw or mass (in the case of TMJ ankylosis) and realization of the ceiling planing of joint cavity with surgical drills and bone files to adapt the temporal feedback

- feedback fixing the pit/articular eminence with titanium screws, checking the stability and parallel to the zygomatic arch
- conducting submandibular incision (Risdon) with dilatation of the tissue plans for communicating the two surgical approaches
- blocking of patients using screws trans-gingival maxillo-mandibular intercuspidation during surgery not exist occlusal changes
- the condylar component is fixed and the lock to open maxilomandibular mobility check
- if the patient presents the restriction opening movement is carried out a second osteotomy, the coronoidectomy in order to eliminate interference with movement
- the time template is then replaced by the prosthetic fossa component
- sutures were made by planes of the two accesses with vicryl and nylon 5.0 yarn type and curative were kept locally for 48 h
- conducting physiotherapy with isometric exercises and occlusal rehabilitation

7.2. Customized temporomandibular joint prosthesis

Most patients presenting with indications for total TMJ alloplastic reconstruction have distorted anatomy caused by either numerous failed prior surgical interventions/materials or primary or secondary joint disease that compounds the stability problems in the TMJ area. This finding makes it extremely difficult to reconstruct these cases with an off-the-shelf or so-called "stock" device [26]. More recently, with the advent of CT scans with three-dimensional reconstruction (3D-CT) and esterolitografia, it was possible the manufacture of ATM-individualized dentures. This prosthesis (Bioconect Temporomandibular prosthesis design and principles and materials) uses a powerful 3D printing technology to shape the desired metal geometry by melting metal powder layer by layer. The metal used in the creation of the customized implant (temporomandibular joint) is Titanium Ti – 6% Al – 4%, wt% (Ti64 degree 23) with a low oxygen content. An ideal combination is achieved by having a biocompatible metal, titanium, designed at any desired geometric shape for a perfect customized fit. With the advances in heath technology, the work of the Direct Metal Laser Sintering (DMLS) has allowed treatment of clinical cases that were previously practically impossible to treat due to their complexity. With the use of the DMLS technology, the use of various materials and a high range of complexity on the customizations, reduced manufacture time is possible [27].

The fossa component is constructed from two basic materials – Ti64 degree 23 and ultra–high molecular weight polyethylene (UHMWPE). The UHMWPE have a relatively flat functional surface and had a posterior stop to provide a centric relation position for the condylar head of the prosthesis. The customized surgical guides are used specifically for each planning and cutting rails specific to each type of drill, saw or ultrasonic nozzle. Thus, it allows the surgeon to accurately replicate the trans-surgical what was accomplished in planning (**Figure 4**), while other prostheses that are made using plastic prototypes and conventional machining (computer numerical control, CNC) do not allow this essential advantage, thereby causing poor adaptations and failures.

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Figure 4. Customized cutting guide; fossa component; mandibular component.

8. Discussion

Treatment with denture TMJ is still a matter of controversy. It is evident that a variety of etiologies and different treatments may be used in the reconstruction, as autogenous and alloplastic grafts, with the indication of TMJ prosthesis based on the surgeon's experience and results described in the literature [5, 6, 8–22, 28].

Previous surgery can be tried, but some patients do not respond satisfactorily to the prosthesis, being an excellent alternative for resolving these cases. One should be aware that the TMJ prosthesis is the final stage in joint reconstruction and should be proposed only for cases where there is no evidence for the possibility of other techniques [16, 29].

The occlusal stability has lead to placement and longevity of the prosthesis. Changes of the occlusal plane, the Z-axis (lateral-lateral), II severe classes, spee curve inversions, overbites or accentuated overjet and multiple missing teeth could compromise the lock stability in trans-operative and post-operative functional balance, causing occlusal and adapting prosthesis overloads, interfering in the right condyle-fossa relationship, which on the long run could interfere with the functional outcome [5, 25].

The commitment of mandibular movements is extremely variable and dependent on the etiology and clinical condition presented. Patients with ankylosis have greater functional impairment mainly due to their severe functional limitation. Also in these patients, both placed prostheses—unilateral and bilateral form—best functional gains are achieved. In cases of patients with idiopathic resorption, trauma sequels and arthrosis of TMJ, the gains are more related to the stability of movement and decrease in symptoms such as headaches, muscle fatigue and local pain [25].

In some cases, there is loss of movement quality, especially the translation of Caused by damage of the lateral pterygoid muscle that was detachment of the site [15, 16]. Furthermore,

adaptation and gradient component with respect to the condylar fossa prosthesis cause greater amplitude during translational motion, thereby reducing the limitation of movement that occurred earlier. Note that the maximum opening and also the best efficiency of this type of prosthesis can be achieved by performing coronoidectomy, enabling the mouth opening without interference [5]. Even with the modifications proposed in the most modern prostheses, there are still significant functional loss and functional movement restriction and in particular lateral protrusion, which cannot be measured, and in most cases, values above 6 and 6 mm respectively. In older cases, where the prostheses have not had the spin axis changes, the conditions of laterality and protrusion were even more restricted [16].

Symptomatic conditions such as headaches, muscle fatigue, local pain, swelling and asymmetries can be improved after placement of the prosthesis. However, for all cases there will be some degree of limitation of the excursion of mandible head compared to a normal ATM. Also note that the prosthetic condyle-sump movement occurs across length and the surface thereof, so there is a certain rotation and translation that in cases of Of patients with bony ankylosis can be improved after surgery, since they have no moving none or very limited pre operatively [25].

The movement of the prosthesis occurs because of one's jaw movement, Realized other muscle muscle groups, supra-hyoid, contralateral mandibular elevators, temporal, masseter and medial pterygoid (which keeps some degree functional even after detachment for prosthetic installation). The ability of functional adaptation of the jaw is a decisive factor in the prosthesis-jaw system [5, 11].

Dislocations of the metal component of the polyethylene tank, fixing losses of the prosthesis system to fracture and locoregional bone formation could occur, but there are frequent complications. Some case reports of these complication It has been caused to failure of the surgical technique, both the component adjustment, in osteotomies and wear bone, the choice of location of bone resection, the lack of stability of the components and their attachment to the bone and also in Setup component in improper angles [5, 6, 8–25, 30].

A good surgical technique combined with postoperative physiotherapy and functional with adequate maintenance, proper fixation and favorable angle means that there is clinical success [25]. Modern custom-made prostheses have a pit format that allows great adaptation to the temporal bone and are placed parallel to the zygomatic arch Restricting several movements. The component thickness is a decisive factor that hinders exaggerated bone formations and local ankylosis [21].

The behavior of the TMJ contralateral to the prosthesis, in cases of execution of unilateral prosthesis, requires particular attention, because the functional balance achieved in short time is great, but the behavior of the anatomical structures is somewhat uncertain way, and condylar resorption, disc dislocations, muscle aches, some functional restriction by anatomical limitation of the contra-lateral prosthesis, chewing functional changes, periodontal and progressive joint degeneration may occur [25].

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9. Conclusion

In conclusion, the TMJ prostheses have the reconstruction order to articulate and fulfill this role satisfactorily. Due to developments over time, Their biomechanical principles and biocompatibility have made TMJ prostheses reliable and a safe alternative for the reconstruction of the joint. Long-term studies are needed, because clinical longevity of patients undergoing this type of prosthesis is still less [5, 12–25, 30].

10. Case report of alloplastic temporomandibular joint W. Lorenz

Case report orthognatic with alloplastic temporomandibular joint W. Lorenz.

Patient with mandibular defect after remove Aneurysmal bone cyst deviation of the mandible.

Provide adequate stability of occlusal bite. Decrease the deviation of the mandible.

Patient with condylar resorption after trauma Occlusal plane alteration facial symmetry occlusal relationship before treatment.

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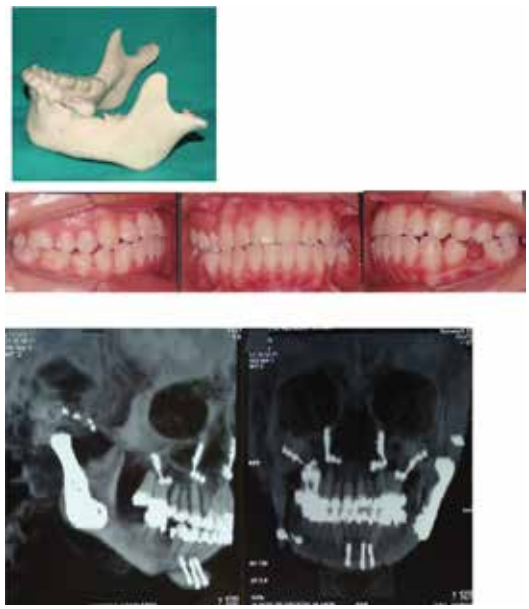
Concomitant Temporomandibular Joint and Orthognathic Surgery.



Correction of Facial Asymmetry and occlusal bite.

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Chapter 25

Use of Intra-Oral Osmotic Self-Inflating Tissue Expanders for Bone Reconstruction and Rehabilitation of the Jaws

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Rouzbeh Kahali and
Mohammad Hosein Kalantar Motamedi

Additional information is available at the end of the chapter

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Abstract

Reconstruction of oral and maxillofacial defects is challenging. Insufficient soft tissues may render hard tissue reconstruction problematic. Several surgical techniques have been used over time to address this issue; these techniques are usually complicated and unpredictable. Soft tissue expansion is a physiological process that leads to the formation of new cells and growth of tissue and allows for soft tissue with similar color, texture and function to that of the adjacent tissues. In this article we present the applications of osmotic tissue expanders in facilitating bone graft augmentation. OSMED (Ilmenau, Germany) self-inflating tissue expanders were used prior to bone augmentation in our patients. After making a 1.5 cm full thickness incision, a sub-periosteal tunnel was prepared and the tissue expander was implanted sub-periosteally. The tissue expanders were removed approximately 6–10 weeks later in the course of augmentation surgery. In all patients after the use of the tissue expander, sufficient soft tissue was available for primary, tension-free, wound closure and there was no need for local or regional flap techniques. No complications such as infection, necrosis, or graft loss occurred and the functional and esthetic outcomes were acceptable. Use of this tissue expander prior to bone augmentation was effective in facilitating bone graft augmentation.

Keywords: Soft tissue expander, bone augmentation, reconstruction, soft tissue management, osmotic-tissue expanders

1. Introduction

Reconstruction of oral and maxillofacial defects is challenging. These defects may be congenital malformations, defects caused by severe atrophy, trauma or oncologic ablation. Such cases can cause considerable esthetics and/or functional problems and may require augmentation, grafting, and implantation procedures that may significantly affect the quality of life of the patients [1].

Insufficient hard and soft tissues may present esthetics or functional problems. Bone grafts, bone substitutes and guided tissue regeneration (GTR) techniques have been used for many years to rebuild the alveolar ridge [2]. Reconstructing large and complex defects are more complicated. One of the common problems is inadequate soft tissue for coverage of the graft. Several surgical techniques such as rotational flaps, pedicle flaps, free flaps and composite flaps have been used over time to address this issue [3, 4]; these techniques are usually complicated and they have limitations, such as donor site morbidity, necrosis and infection [4]. Another problem is the unpleasant functional and esthetics results due to the differences of the grafted tissues from the original tissue. One of the most common problems during reconstruction of bony defects of the jaws is soft tissue dehiscence which leads to the exposure of the bone grafts into the oral cavity and may result in loss of the bone graft [5–9]. Adequate soft tissue coverage of grafted bone is important to avoid graft exposure; thus, primary tension-free closure of the flap without compromising the vascularization is important [10–12]. When a large amount of bone augmentation is required, it is usually hard to achieve tension free soft tissue coverage. A periosteal incision is often used to make it possible to mobilize and stretch the mucoperiosteal flap. This, however, reduces the perfusion of the mucoperiosteal flap [11, 13–16]. Sufficient blood flow is important for tissue survival [17]. Even simple flap elevation can disturb flap perfusion and causes ischemia [18]. Extensive flap preparation and elevation can result in impaired perfusion and increased incidence of necrosis and tissue dehiscence [19, 20]. Inadequate perfusion and dehiscence of the soft tissue can jeopardize the success of bone augmentation.

One possible solution is soft tissue expansion. Tissue expansion was first described by Radovan [21, 22] as a method of creating soft tissue with similar color, texture, thickness, and sensation as the adjacent tissue with minimal scarring and little donor site morbidity. Neumann was the first who mentioned the potential to use tissue expansion for reconstructive surgery [22, 23]. Nowadays tissue expansion is a well-known technique for head and neck reconstructive surgery [24–27]. Soft tissue expansion is a physiological process that leads to the formation of new cells and growth of tissue [28] and allows us to gain extra soft tissue with similar color, texture and function to that of the adjacent tissues for covering grafts [29].

After the tissue expander is inserted, during the expansion process the tissue is under a persistent tensile stress; traction of the surrounding soft tissue leads to extra soft tissue volume [30–32]. Sub-periosteal implantation of the expander is usually preferred over extra-periosteal implantation because of its optimum soft tissue increase [33]. However, sub-periosteal implantation of the expander limits the nutritional supply to the bone [34].

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Traditional tissue expanders are silicone envelopes with self-sealing injection ports. They are filled by serial saline injections through the ports at weekly intervals. Volume expansion of the expander puts tension on the overlying tissue [35]. These traditional tissue expanders are now known to be associated with complications because of their intermittent sudden expansion [36]; this lead to the development of osmotic tissue expanders (OTEs). The OTE was first described by Austad and Rose [37]. It was made of a semi-permeable membrane filled with hypertonic saline which leads to the entrance of the water by osmotic forces from the surrounding tissues into the expander. Wiese developed an osmotic self-inflating expander [38], which has been used successfully to expand the orbit in the management of enophthalmos, microphthalmos, and cryptophthalmos [39–41].

The osmotic self-filling expander is made of polymeric methyl methacrylate–vinylpyrrolidone which gains volume by absorbing body fluids [42, 43]. The purpose of this chapter is to present some examples of the application of this expander before bone graft augmentation.

2. Technique

We used OTE in various patients. In our study, we used OSMED (Ilmenau, Germany) self-inflating tissue expanders (**Figure 1**) prior to bone augmentation and evaluated its complications and problems.

Figure 1. Osmed tissue expander.

2.1. Surgical technique

After making a full thickness incision, a sub-periosteal tunnel was prepared (**Figure 2**). After completion of the tunnel preparation, the tissue expander was placed under the tunnel flap while keeping the surgical field as dry as possible to reduce the risk of contamination with oral fluids. Wound closure was performed to minimize the leakage and contamination. The sutures were removed after 2 weeks. The tissue expanders were removed approximately 6–10 weeks later in the course of augmentation surgery; 1 g of intravenous cefazolin antibiotic was administered pre-operatively and continued every 6 h post-operatively for 24 h then it was replaced by 500 mg of oral cephalexin antibiotic taken every 6 h for the next 7 days. Chlorhexidine mouth-wash was used every 8 h post-operatively and was continued for 14 days.

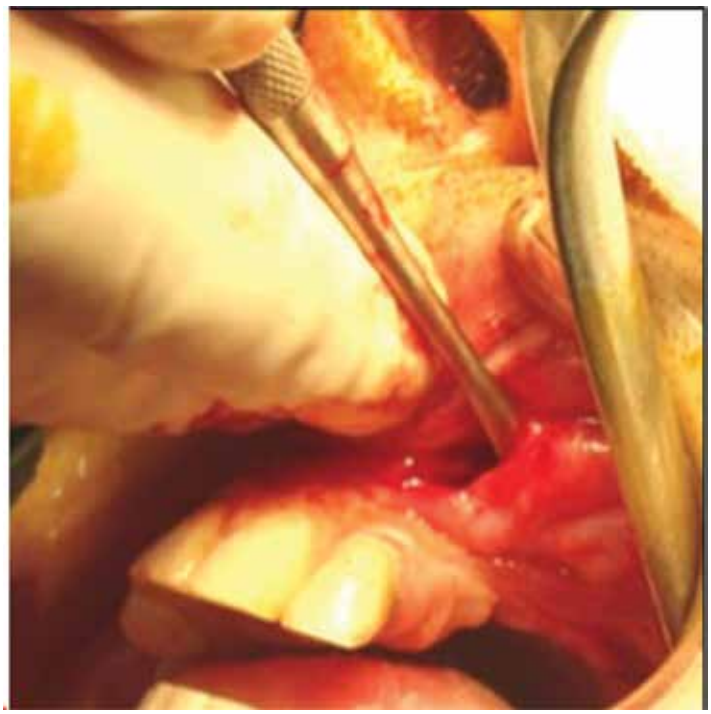

Figure 2. Subperiostal tunnel preparation.

3. Cases

3.1. Patient 1

A 23-year-old male had partial maxillectomy surgery on the left side due to central giant cell granuloma 12 years ago (**Figure 3**).

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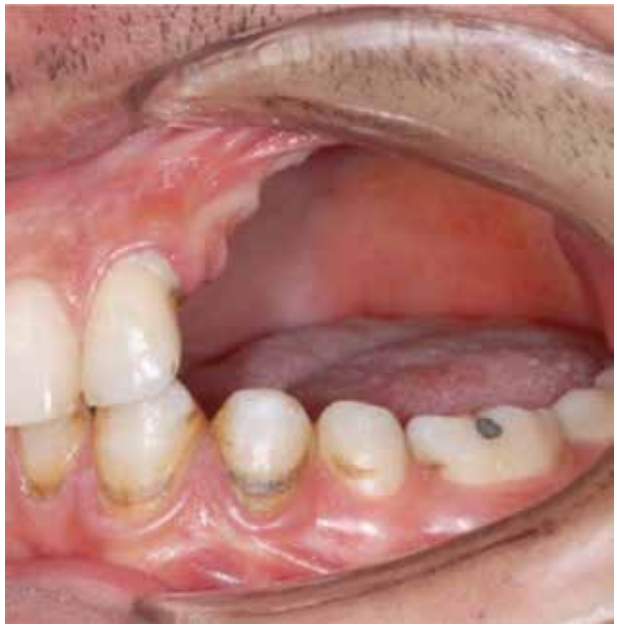

Figure 3. Partial maxillectomy of the left side.

In the first operation, an OSMED tissue expander cylinder 2.1 ml, with initial volume of 0.42 ml and final volume of 2.1 ml was placed sub-periosteally in the defect (**Figure 4**).

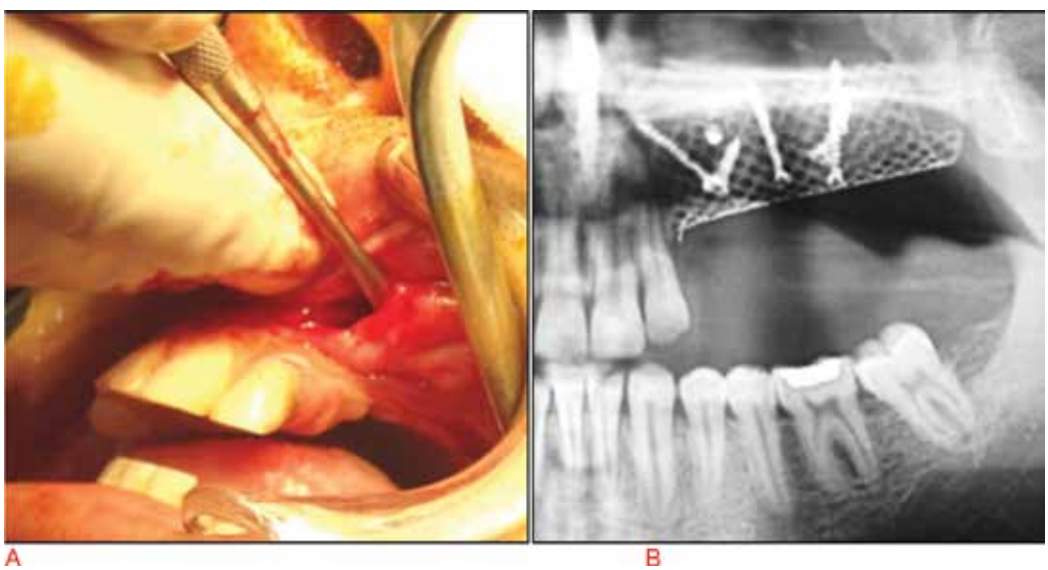

Figure 4. (A) OSMED tissue expander was placed sub-periosteally. (B) 10 weeks later, the tissue expander was removed and the bone was augmented.

In the second operation, done 10 weeks later, the tissue expander was removed and the bone was augmented by iliac bone graft (**Figure 5**).

Figure 5. The tissue expander was removed and the bone augmented by iliac bone graft.

In the third operation, done 5 months later, the titanium mesh and fixation screws were removed and three dental implants were inserted (**Figure 6**). No post-operative complications were observed.

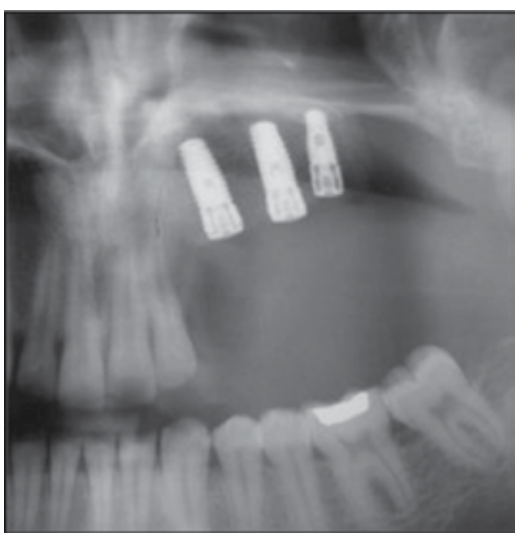

Figure 6. The titanium mesh and fixation screws removed and three dental implants were inserted.

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3.2. Patient 2

A 54-year-old woman had severe mandibular atrophy. She had been edentulous for 30 years and had bone augmentation with iliac bone graft on the right side of the mandible 20 years ago. In the first operation, because of the lack of enough soft tissue and the presence of scar tissues from previous surgery, we used an OSMED tissue expander cylinder 1.3 ml, with initial volume of 0.25 ml and final volume of 1.3 ml (**Figure 7**).

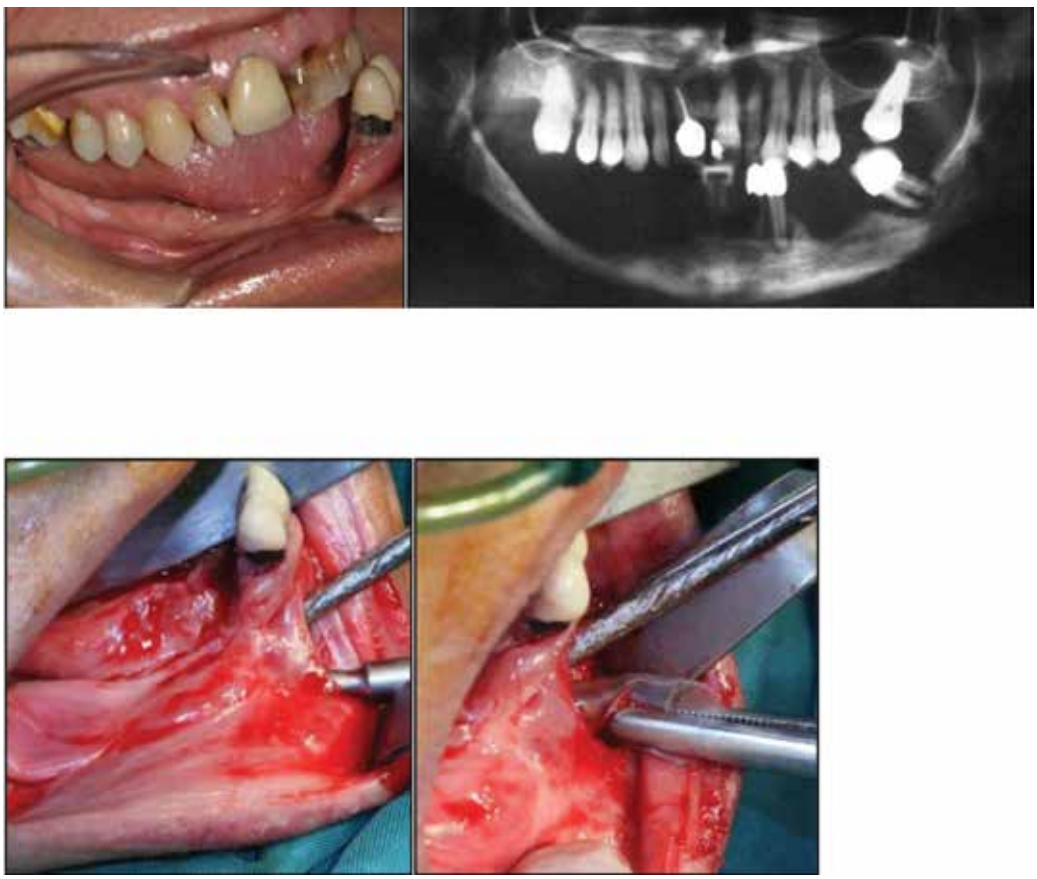

Figure 7. Severe mandibular atrophy. OSMED tissue expander cylinder placed in a sub-periosteal tunnel.

In the second operation, done 6 weeks later, the tissue expander was removed and the bone was augmented with iliac bone graft (**Figure 8**) and later dental implants were inserted (**Figure 9**). In this case, despite of the lack of enough soft tissue and the presence of scar tissues, the hard tissue was augmented vertically and desirable outcome and adequate bone volume for implant placement was achieved.

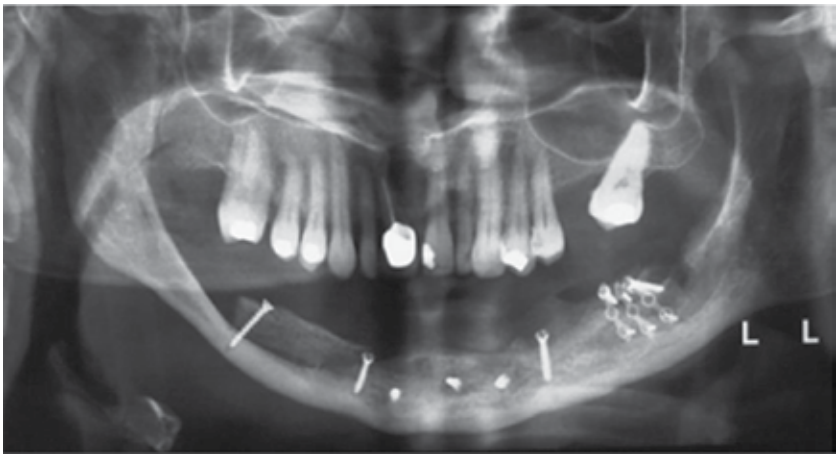

Figure 8. The bone was augmented with iliac bone graft.

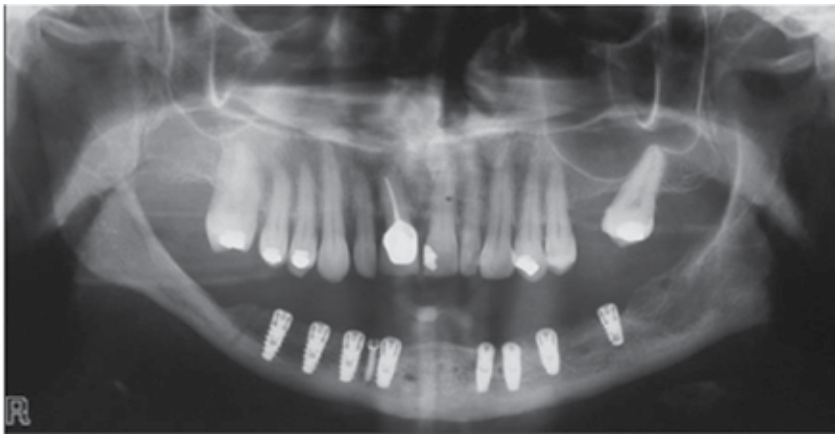

Figure 9. Later dental implants were inserted.

3.3. Patient 3

A 41-year-old woman had previous partial mandibular resection surgery due to an ameloblastoma (**Figure 10**).

In the first operation, an OSMED tissue expander cylinder 2.1 ml was used. In the second operation, done 8 weeks later, the tissue expander was removed and the bone was augmented by iliac bone graft prior to dental implant insertion (**Figure 11**). In this case, due to the tension free closure of the soft tissue overlying the bone graft, postoperative complications were reduced and good results obtained.

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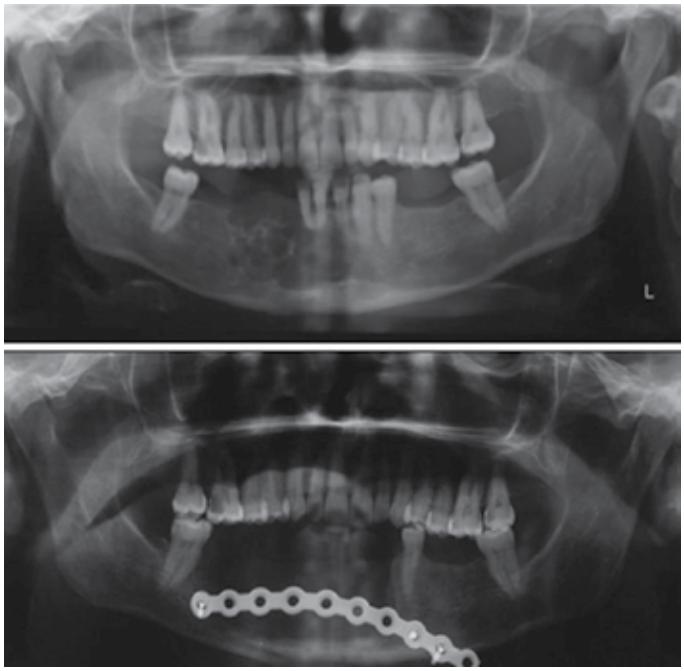

Figure 10. Ameloblastoma of the lower jaw. Resected.

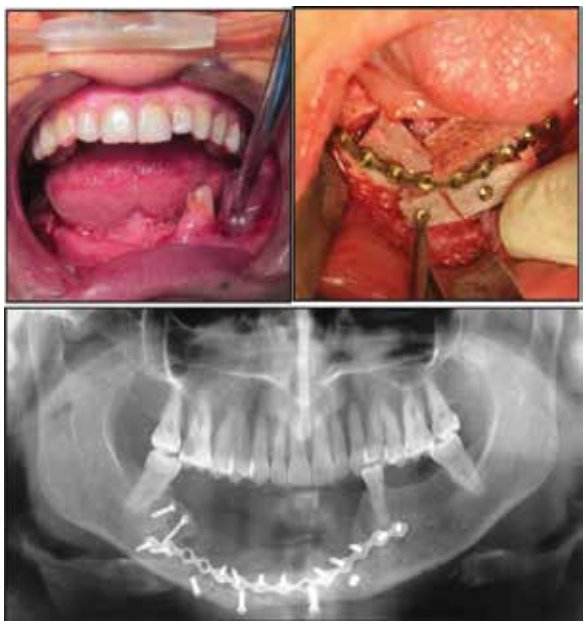

Figure 11. Left, Sub-periosteal tunnel preparation for tissue expander implantation Right, Bone augmentation was performed 8 weeks later Bottom, Panoramic view of the patient after bone augmentation.

4. Discussion

Soft tissue expansion has been used successfully for the reconstruction of soft tissue defects [44–47]. In case of inadequate normal soft tissue, new tissue should be created with the same color, texture and function as the adjacent tissue, which was first described by Neumann [48] for auricular reconstruction. In the head and neck area, tissue expansion has been used successfully for scalp, nose and ears [29, 30, 49, 50]. Intraoral soft tissue expanders have also been used prior to the bone augmentation in the case of inadequate soft tissue for primary tension free wound closure [51–56]. In their study they used classic forms of tissue expanders which were inflatable expanders inflated by weekly injections of saline. However, because of their sudden and intermittent volume increase, tissue hypoxia due to decreased blood flow to the area was reported [57]. Two types of expansion regimens are used clinically for classic tissue expansion namely 'conventional, prolonged expansion' for 1–3 months and 'intraoperative sustained limited expansion' [58, 59]. Some studies suggest that 'conventional, prolonged tissue expansion' can also be performed for 1–2 weeks without complications [60, 61]. The most common complications of soft tissue expansion are infection, dehiscence, hematoma, necrosis and failure [46, 47, 62–64]. When infection occurs, the expanders are usually removed to control the infection. Although several methods have been reported to salvage tissue expanders [65–67], usually substitution of the infected tissue expander with a new one is required.

By making a small incision as far as possible from the intended site for tissue expander insertion, the risk of dehiscence and failure is minimized [22, 29, 45]. Generally, in the same conditions, the smaller tissue expander is preferred over the larger one. Larger tissue expander usually require larger incisions with wider dissection and more undermining, which may increase the risk of dehiscence and also may cause scar expansion instead of normal tissue expansion [68]. As mentioned earlier, the expansion rate is important. Use of self-inflatable osmotic expander, has a gradual rate of expansion [43]. The early osmotic implants were made of a semi-permeable envelopes containing hypertonic liquid. Their expansion rates were rapid and were completed within the first 24–48 h following insertion and they were associated with more complications such as tissue ischemia and failure. Subsequent tissue expanders were made of dehydrated hydrogel in a silicone envelope with a more gradual expansion rate and lower complications [43, 69]. The OSMED self-inflating tissue expanders are made of a specially developed hydrogel that use the osmotic principle to gain volume. The hydrogel is made of co-polymers based on methyl methacrylate and N-vinyl pyrrolidone. Pre-operatively they are in their pre-expanded state and therefore are small, hard and easy to handle. After implantation, they start to absorb body fluid and grow consistently to a predefined shape and size. Their final volume depends on the product type and is between 3 and 12 fold their initial volume. The increase volume of the implant leads to an increase of soft tissue. Their expansion speed also differs by the product type. In some the tissue expander is delivered in a silicone shell, with an exact number and size of holes to assure gradual and consistent swelling of the device.

In this study, we used OSMED self-inflating tissue expander cylinder which is delivered in a silicone shell. The tissue expanders were placed sub-periosteally. It is reported that sub-periosteal implantation causes significant resorption of the underlying bone by impairing the micro-circulation of the underlying bone [33, 70–72], which was not observed in our patients. Periosteal-releasing incisions may reduce the blood supply to soft tissue flaps and increase the risk of dehiscence. The periosteal expansion facilitates a tension-free wound closure without the need to use any periosteal-releasing incisions [16]. Another strategy for minimizing the risk of intraoral dehiscence and infection [29] is keeping the incision small and away from the tissue expander, which may explain the low incidence of complications in our study and other reports [43]. It has been reported that slow and continuous expansion results in safe and effective generation of soft tissue and decreased incidence of intraoral dehiscence [38, 73]. In our study, the rate of expansion was slow enough not to cause any perforation of the soft tissue [74]. After expansion, the quality and quantity of expanded soft tissue was good enough to permit easy primary tension-free wound closure after major bone augmentation. The slow expansion will lead to slow and proper formation of new tissues over the time period [73].

5. Conclusion

In conclusion, our cases demonstrate that the use of tissue expander prior to bone augmentation can reduce the complications associated with non-OTE and lead to more predictable results.

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Section 13

Osteotomies of the Jaws and Complications

Chapter 26

Complications of Orthognathic Surgery

Reza Tabrizi and Hassan Mir Mohammad Sadeghi

Additional information is available at the end of the chapter

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Abstract

Orthognathic surgery is a common approach for treatment of maxillofacial deformities. Sagittal split ramus osteotomy (SSRO) is one of the most common techniques used to treat various mandibular deformities. A LeFort I osteotomy is suggested in deformities of the maxilla and can be used along with SSRO or intra-oral vertical ramus osteotomy (IVRO).The aim of orthognathic surgery is to improve function and facial appearance; this benefits the patient psychologically and socially. Common complications which may occur in orthognathic surgery include vascular disease, temporomandibular joints (TMJ) problems, nerve damage, infection, bone necrosis, periodontal disease, vision impairment, hearing problems, hair loss, and neuropsychiatric problems. Rarely complications could be fatal. Because of the wide range of complications the surgeon should keep prevention protocols in mind and be prepared to treat them should they occur. In this chapter, common complications of various osteotomies in the mandible and maxilla are discussed.

Keywords: osteotomies, complications

1. Introduction

1.1. LeFort osteotomies

Midface osteotomies have been used to correct maxillary-zygomatic deformities, and historically have been classified anatomically based on the Guerin-LeFort fracture classification [1]. The first total LeFort I osteotomy was performed by Wassmund in 1927 for correction of the skeletal open bite [2]. In spite of all the advancements made in the field of orthognathic surgery, a variety of complications are documented [3]. These include maxillary sinusitis, loss of tooth vitality, sensory nerve morbidity, aseptic necrosis, vascular complications (i.e., arteriovenous fistulae or hemorrhage) nasal septum deviation, unfavorable fractures of the skull base and

pterygoid plates, ophthalmic complications (including blindness) malpositioning, nonunion, maxilla instability, and relapse [4].

1.2. Hemorrhage

Excessive bleeding has been reported as a common complication of LeFort osteotomies. The incidence of life-threatening hemorrhage in maxillary osteotomies is reported in approximately 1% [5]. The descending palatine artery is the most common source for mild to moderate bleeding during LeFort I osteotomy and delayed bleeding afterward. The descending palatine artery damage may occur during the medial wall osteotomy. Injury to the descending palatine artery during LeFort I osteotomy can be minimized by limiting the osteotomy to 30 mm posterior to the piriform rim in females and to 35 mm in males[6]. In maxillary superior repositioning, bone removal around the descending palatine artery is a common cause of vascular injury. If the surgeon encounters the descending palatine artery, it should be cauterized. The internal maxillary artery is the most frequently cited source of massive hemorrhage [7]. Meticulous placement of the curved osteotome in the pterygomaxillary junction is important to avoid injury to the internal maxillary artery and its branches. Turvey and Fonseca reported that the main trunk of the maxillary artery was most vulnerable to the damage within the pterygopalatine fossa in the lateral position and they recommended angling the posterior lateral maxillary osteotomy downward to avoid damaging the artery [8]. Packing is suggested as the first attempt to tamponade the hemorrhage. In delayed bleeding after LeFort I osteotomy, the surgeon should reopen surgical site and move the maxilla downward to find the bleeding source (**Figure 1**). In many cases, direct visualization of the bleeding source and cauterization of injured vessels stops the hemorrhage (**Figure 2**). Several techniques have been suggested to control bleeding from the internal maxillary artery such as ligation of the external carotid artery and angiographic embolization. Emergency access to vascular embolization is crucial. If a patient has severe bleeding, the surgeon should not waste time and intervene immediately. The collateral arteries and the anastomoses between circulations lead to the limited success of surgical ligation of the external carotid artery [9]. A recent study recommended use of tranexamic acid irrigation in obviating perioperative blood loss during orthognathic surgery [10].

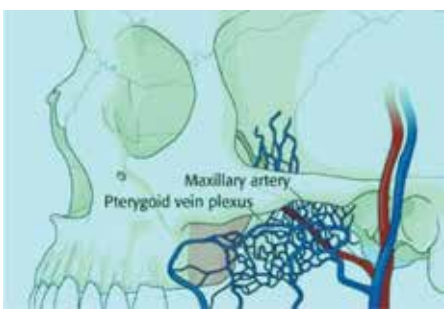

Figure 1. Possible bleeding sources during LeFort I osteotomy.

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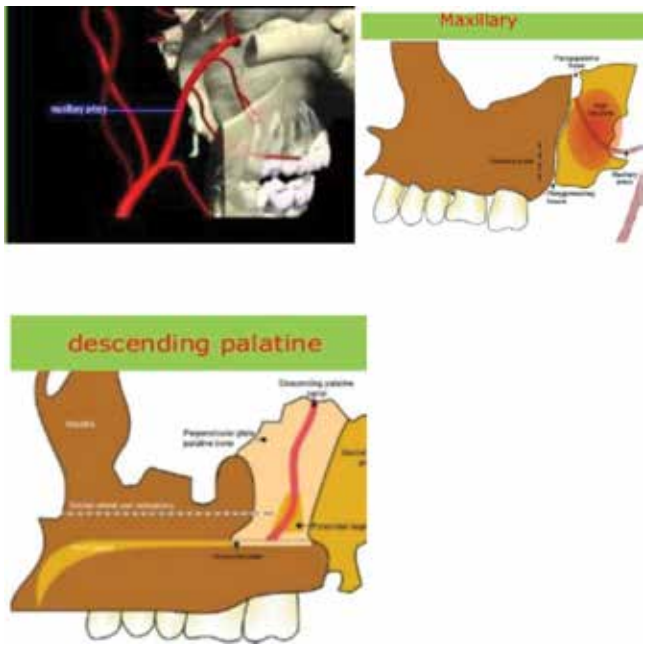

Figure 2. Relationship of osteotomy sites and major hemorrhage sources during LeFort I osteotomy.

1.3. Neurosensory deficit

The infraorbital nerve may be compressed, retracted or transected inadvertently during subperiosteal dissection.

Infraorbital nerve injury may have resulted from incorrect separation during disimpaction.

As are the cases with bilateral sagittal ramus osteotomy, nerve sensitivity may return within 6–12 months [11].

The absence of post-operatory sensitivity after a LeFort I procedure was documented in a study that applied both objective and subjective tests. The results showed a greater incidence of insensitivity in the region above the upper lip, followed by the lower lip and the chin, as was observed in bimaxillary procedures [12]. Neurosensory alterations are normally immediately perceived in the post-operatory period. They are the result of traction of the infraorbital nerve and direct trauma to the anterior, medial, and posterior superior alveolar nerves, as well as to the nasopalatine nerve and the descending palatal nerve [13]. A study performed at the University of North Carolina on patients undergoing bilateral Sagittal split ramus osteotomy (SSRO) reported that 98% of the patients presented altered sensitivity of the chin 1 month after the operation; with 81% of these patients still presenting with this alteration 6 months after the operation [14]. It is recommended that the patient be advised of possible neurosensory alterations in pre-operatory visits, thus reducing the patient's post-operatory anxiety [15]. Many studies confirm the return of neurosensory function up to 1 year after surgery [11].

1.4. Tooth sensitivity

An osteotomy closer than 5 mm of the apices of the teeth has risk of root injuries[16]. In superior repositioning of the maxilla by more than 6 mm, saving of 5 mm margin is not always possible because of the infraorbital foramen position [4]. After orthognathic surgery, loss of vascularity of the dentition is rare, but initial loss of response to pulpal stimulation is common. Long-term suppressed response to stimulation can occur, but does not necessarily mean a tooth requires endodontic therapy. Although some teeth may eventually become necrotic and require endodontic treatment, many teeth recover without treatment and return to normal coloration and respond to pulp testing [17]. De Jongh et al. studied electric and thermal pulp testing of 10 patients after LeFort I osteotomy in compared to 10 control patients without osteotomy. Their study showed that 71% of 128 teeth were responsive to electric and thermal pulp stimulation and 93% of 136 teeth in the controls [18].

1.5. Maxillary sinusitis

Sinusitis after LeFort I osteotomy is uncommon, with a reported incidence of septic complications of 0.5–4.8% [19]. Possible explanations for postoperative maxillary sinusitis following LeFort I osteotomy were pre-existing sinus disease or non-viable bone fragments left in the maxillary sinus (**Figure 3**) [20]. A recent study by Valestar et al. showed LeFort I procedure did not influence already existing physical or mental complaints, and nasal ventilation was not negatively affected. However, evaluation of sino-nasal pathology should be emphasized in the preoperative work-up [19]. A recent study by Nocini et al. suggested that LeFort I osteotomies can affect the maxillary sinus. The postoperative radiologic views of the maxillary sinus showed inflammation and rhinosinusitis symptoms after LeFort osteotomies. Larger long-term studies are warranted to clarify the postoperative outcomes and complications (**Figure 4**) [21].

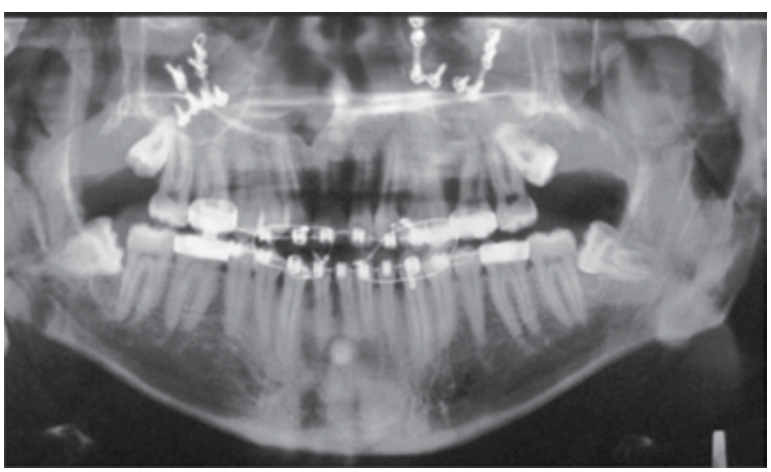

Figure 3. Maxillary sinusitis after LeFort I osteotomy.

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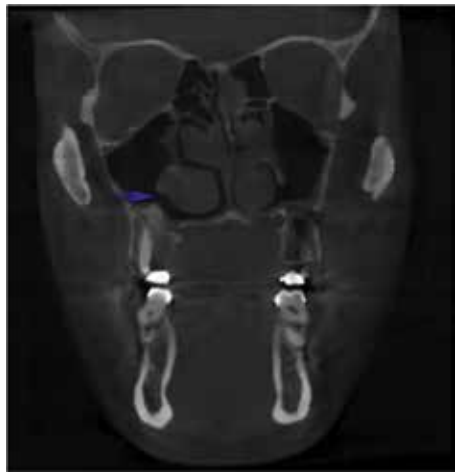

Figure 4. Radiologic findings: postoperative computed tomography scan displaying interruption of the medial walls [21].

1.6. Nose deformity

Septal malposition may occur during LeFort osteotomy and cause nasal deviation. A possible reason for a cartilagenous septum deviation after a maxillary osteotomy is dislocation by a partially deflated cuff during extubation. Manual inspection of the nares after extubation is important, yet often forgotten [22]. Nasal ventilation generally improves after orthognathic surgery [19]. The most common reason for postoperative nasal-septal deviation is compression or displacement from inadequate bone removal of the nasal crest of the maxilla or inadequate trimming of the cartilagenous septum (**Figure 5**) [9].

Figure 5. Severe nasal deviation after LeFort I osteotomy.

1.7. Aseptic necrosis

Avascular necrosis of the maxilla after LeFort I osteotomy has been reported [23]. Usually, these complications relate to the degree of vascular compromise and occur in less than 1% of cases. Rupture of the descending palatine artery during surgery, postoperative vascular thrombosis, perforation of palatal mucosa when splitting the maxilla into segments, or partial stripping of palatal soft tissues to increase maxillary expansion may impair blood supply to the maxillary segments. Sequelae of compromised vasculature include loss of tooth vitality, development of periodontal defects, tooth loss, or loss of major segments of alveolar bone or the entire maxilla (**Figure 6**) [24]. The risk is increased in patients with anatomical irregularities, such as craniofacial dysplasia's, orofacial clefts, or vascular anomalies [5]. The treatment of avascular necrosis of the maxilla is not easily manageable [25]. Regarding no treatment protocol has been established, aseptic necrosis of the maxilla should be treated by maintenance of optimal hygiene, antibiotic therapy to prevent secondary infection, heparinization, and hyperbaric oxygenation [24]. In such cases, it is evident that there is a serious problem with the tissue perfusion immediately postoperatively and the patient must be taken back to the theatre immediately to reposition the segment; delay only makes it worse [26].

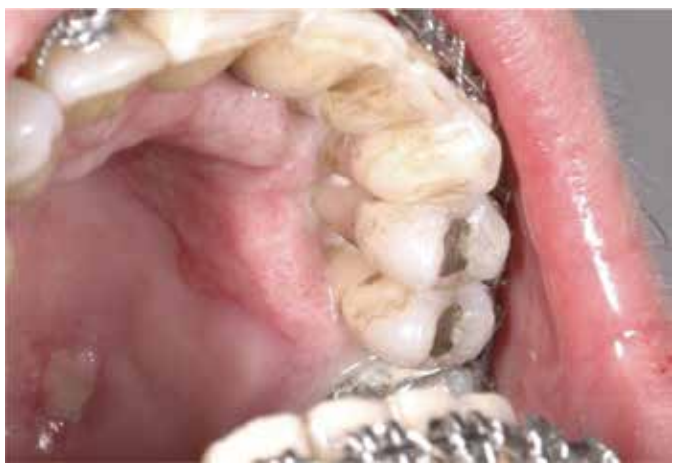

Figure 6. Initial aspect of the aseptic maxillary necrosis on the seventh postoperative day [24].

1.8. Unfavorable fractures

Unfavorable fractures may consist of pterygoid plate, sphenoid bone, and middle cranial fossa fractures. Lanigan and Guest demonstrated pterygomaxillary dysjunction using a curved osteotome and described high-level fractures of the pterygoid plates with disruption of the pterygopalatine fossa which could extend to the skull base [27]. Unfavorable pterygoid plate fracture is well studied and documented (**Figure 7**) [28]. Postoperative CT scans indicated that the prevalence of unfavorable fractures of the pterygomaxillary region may be more than previous expectations. Many of these unfavorable fractures are unobserved as there was no

CSF leak because of a local soft tissue seal [29]. Renicke et al. reported the incidence of pterygoid plate fracture was 58% following LeFort I osteotomy using postoperative CT scans [30].

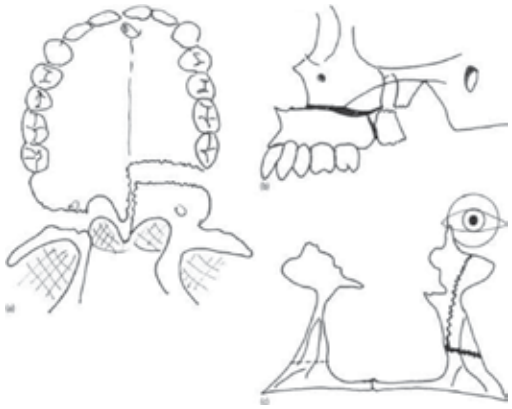

Figure 7. Possible lines of bad split during LeFort I osteotomy.

1.9. Improper maxillary repositioning

Several factors are responsible for improper maxillary repositioning such as missing a centric relation-centric occlusion discrepancy preoperatively; failure to achieve the desired maxillary position during isolated maxillary surgery, failure to seat the condyle because of inadequate removal of posterior bony interference and inaccurate vertical positioning [9]. Improper maxillary positioning may occur in correction of vertical maxillary excess. In a study by the first author, the incidence of under-correction (25%) was more than over-correction (7.5%)

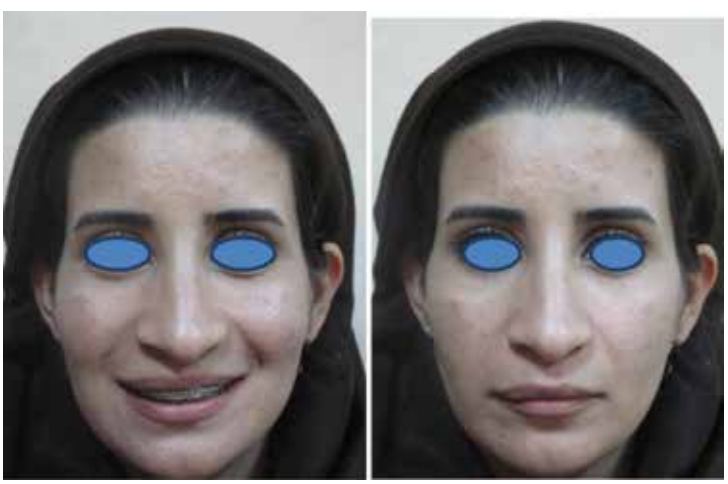

Figure 8. Over-correction after maxillary superior repositioning.

(**Figure 8**). Five millimeter was considered as a cutoff point for tooth shows at rest and 15 mm at the maximum smile. When tooth show at rest was more than 5 mm presurgically, 50.5% of clinical predictions did not follow the clinical results, and 75% of clinical predictions revealed the same results when the tooth show was less than 5 mm. When the amount of tooth shown in the maximum smile was more than 15 mm presurgically, 75% of clinical predictions did not follow clinical results, and 25% of the predictions met the same results in the maximum smile was less than. Clinical predictions based on the tooth show at rest and at the maximum smile did not have a reliable correlation with clinical results in maxillary superior repositioning. The risk of errors in predictions raised when the amount of superior repositioning of the maxilla increased. Generally, surgeons had a tendency to under-correct rather than over-correct. Also clinical prediction is used as a guideline by many surgeons, and it may be associated with variable clinical results [31].

1.10. Trigemino-cardiac reflex

Trigemino-cardiac reflex (TCR) is characterized by cardiac arrhythmia, ectopic beats, atrioventricular block, bradycardia, syncope, vomiting, and asystole. This life-threatening condition has been documented during simple zygomatic arch elevations, repositioning of blowout and maxillary fractures, orthognathic surgery, and nasoethmoidal fractures [32]. Besides evaluation of at-risk patients (e.g., children and patients with a medical history of cardiac disease) and high-risk surgeries (e.g., strabismus), some authors suggested using ketamine for anesthetic induction to decrease the oculocardiac reflex in children undergoing strabismus surgery [32]. Predisposing factors besides cardiac disease are hypoxia and hypercarbia, and use of opioids and β-blockers. TCR has been identified with a sudden onset of parasympathetic hypotension, apnea, or gastric hypermotility during stimulation of any of the sensory branches of the trigeminal nerve. In some cases, stopping the surgery has resulted in recovery of a normal rhythm; in other cases, anticholinergic drugs and cardiac massage have been mentioned. It is recommended that the anesthesiology team be informed that they may be prepared for mobilization in case of adverse effects. In every high-risk case presented in the classification, prophylactic administration of, for example, 0.5 mg atropine IV, right before any surgical manipulation known to be risky for TCR is mandatory [32].

1.11. Ophthalmic complications

Potential ophthalmic complications following LeFort I osteotomy includes decrease in visual acuity, extraocular muscle dysfunction, neuroparalytic keratitis, and lacrimal apparatus problems including epiphora [33]. Visual impairment after LeFort I osteotomy may be due to inappropriate separation of the pterygomaxillary junction and resulting fractures extending to the pterygoid plates, sphenoid bone, orbital floor, optic canal, or the skull base. It may damage the optic nerve or its vascular supply. Hemorrhage from the descending palatine artery or sphenopalatine artery in LeFort I osteotomy may be considered as a reason for systemic hypotension. Hemorrhage from the pterygopalatine fossa may leak the orbital cavity through the inferior orbital fissure and increase intraocular pressure (IOP). Hypotensive anesthesia is useful during a maxillofacial operation for blood loss control and enhancing the

visibility in the surgical field. The blood flow to the globes may be changed by elevated IOP or dropped systemic blood pressure. Hypotensive anesthesia may potentially reduce the blood supply to the retina and choroid and may cause embolism of the vessels or infarction of the optic nerve. The effect of hypotensive anesthesia on visual impairment has not been clarified yet [34].

1.12. Nasolacrimal duct obstruction

Nasolacrimal duct obstruction (NLDO) after maxillary orthognathic surgery is rare. The absence of an NLDO after LeFort I osteotomy is reasonable because the distance from the nasal opening of the NLD to the levels of osteotomy should be at least 5 mm. The normal distance between the NLD nasal opening and the nasal floor is 11–17 mm. LeFort I osteotomy should be performed 5 mm above the nasal floor. The distal to the proximal part of the NLD is vulnerable to be obstructed after maxillary osteotomy. Secondary inflammatory changes associated with an indirect injury of the NLD lead to obstruction. So surgeons should be aware of the risk of NLDO after orthognathic surgery (**Figures 9–11**); this can be managed by dacryocystorhinostomy with high success rate [35].

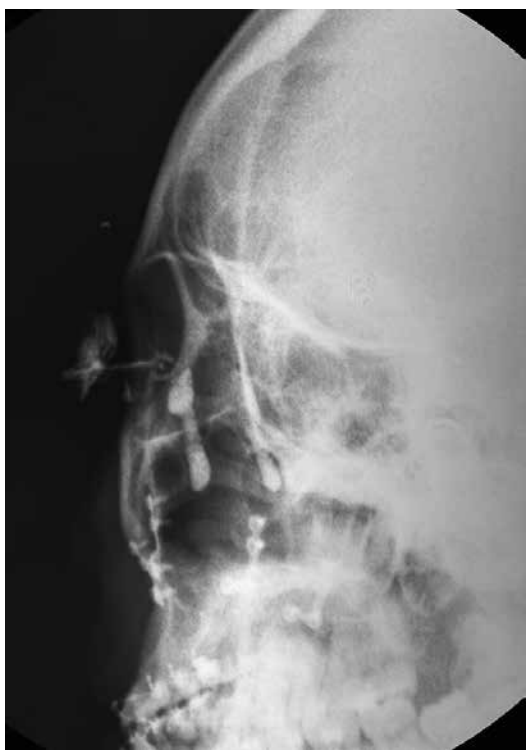

Figure 9. Representative dacryocystograms showing obstruction of the nasolacrimal duct in a patient who underwent orthognathic surgery and complained of permanent epiphora [35].

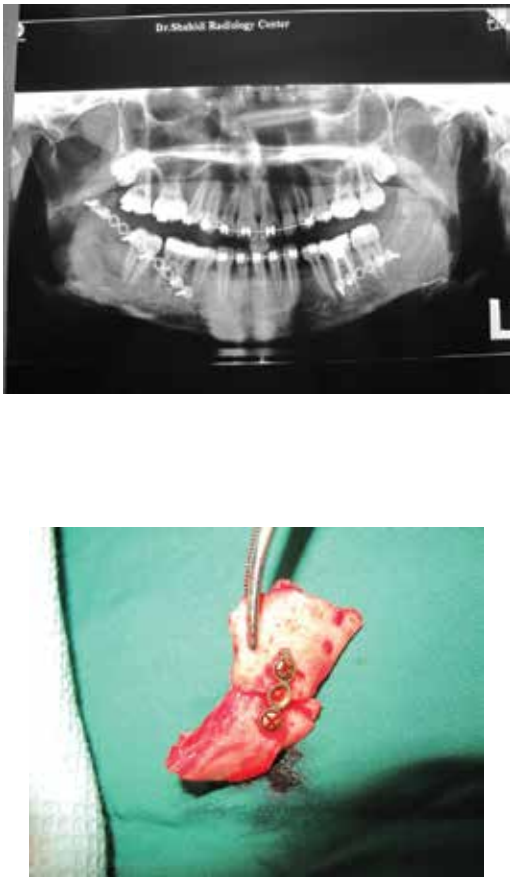

Figure 10. (A) Bad split occurred on the right side. (B) Fixation of bone fragment was done and replaced.

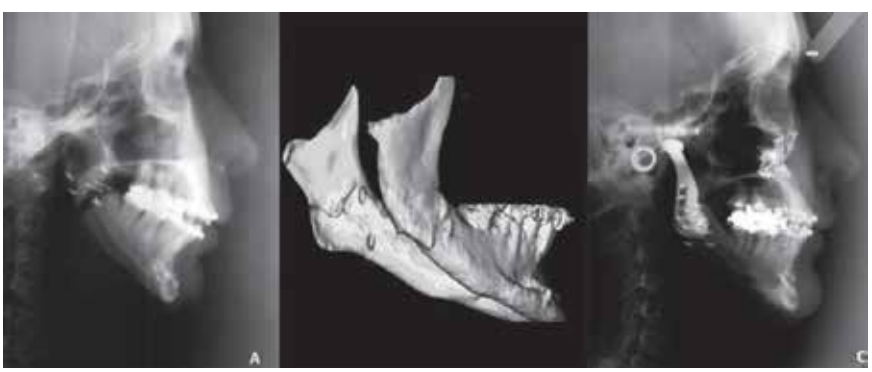

Figure 11. Complete destruction of condyle in a patient, who had undergone orthognathic surgery, was re-treated with the aid of temporomandibular joint prostheses. Before surgery (A), 3D image of the mandible showing bilateral absence of condyles (B), and after surgery (C) [53].

1.13. Nonunion of segments

Nonunion of segments in conventional LeFort I osteotomy is rare. In segmental osteotomy the risk of nonunion is higher. A good vascular pedicle and bone grafts are crucial. Additional stability of the maxillary segments after fixation with miniplates was suggested by the use of palatal dressing plates. Use of split with intermaxillary fixation may be useful. Three-dimensional fixation or immobilization can therefore be gained by using miniplates superiorly on the bony aspect, a dressing plate on the palatal aspect, and a wired-in final surgical wafer on the occlusal aspect of the dentoalveolar segments [36]. If nonunion occurs the surgical site should be reopened, fibrous tissue removed and proper rigid fixation be used for predictable union of segments.

1.14. Tooth damage

Tooth damage in segmental osteotomy is not uncommon. In LeFort I, the risk of damage to the teeth roots increases when the horizontal osteotomy line is 5 mm or less. Close proximity to interdental osteotomy cuts or to screws may cause tooth damage, and pulp necrosis [36]. The pulpal blood flow of teeth adjacent to vertical osteotomies of LeFort I segmental maxillary osteotomies has been reported to be decreased significantly at 4 days after surgeries for lateral incisors, canines, and premolars. However, recovery was seen 56 days after operations. The central incisors and teeth that are distant from the vertical osteotomy have blood flow without significant change [37]. It is advocated that presurgical orthodontic separation of the roots by at least 2 mm at the cementoenamel junction and 4 mm at the apical third be maintained to avoid vascular compromise or damage to the roots adjacent to interdental osteotomies [36].

2. Sagittal split osteotomy

Sagittal split osteotomy (SSO) is a conventional technique to correct mandibular excess or retrognathia. Since its introduction by Trauner and Obwegeser, SSO has undergone numerous modifications and improvements [38].

2.1. Neurosensory disturbance

In SSO, the inferior alveolar nerve (IAN) may be injured and cause neurosensory disturbance (NSD) in the lower lip. The NSD caused by damage to the IAN is reportedly 9–84.6% [39, 40]. Even with careful surgery, injury to the IAN appears unpredictable. Multiple factors are considered responsible for the development of NSD after SSO, including fixation methods, patient age and surgical procedures, improper splinting, magnitude of mandibular movement, experience of the surgeon, and timing of the postoperative neurosensory evaluation [40]. Injury to the IAN may happen with direct and indirect intraoperative trauma and results in change of sensibility or altered sensation of the lower lip and/or mental region. It may lead the negative effect on patients' normal functions such as eating, drinking, speech, and social interaction. NSD may affect patients' everyday lives and can have social or psychological problems [41].

The position of the canal is important in NSD following SSO because the canal position is impacted by osteotomy design and fixation techniques. Nowadays, technologies and software help to evaluate the canal by using CBCT data. An increased distance between the canal and cortical bone presurgically decreased the incidence of postoperative NSD, and high bone density increased of the risk of postoperative NSD. A short post-operation assessment comparing monocortical and bicortical fixation in a monkey model, showed that IAN function was better with plate fixation than screw fixation [42].

2.2. Unfavorable split

An unfavorable fracture, called a "bad split" although infrequent in the hands of an experienced operator, occasionally develop and can lead to intraoperative difficulties as well as postoperative relapse [43]. Frequently cited reasons for bad split include incomplete osteotomies, using osteotomes that are too large, attempting to split the segments too rapidly presence of impacted third molars, misdirecting the medial osteotomy upward toward the condyle and placement of the medial osteotomy too far superior to the lingula [44].

Synonyms used for bad split include "buccal cortical plate fracture" (proximal segment) and "lingual cortical plate fracture" (distal segment) [45]. A bad split can occur during SSO of the mandible regarding precautions. The incidence of bad split is low (0.7% of all SSOs) and patients sometimes have uneventful healing. A significant decrease in incidence did not report during the 20-year period, and neither technical progress nor the surgeon's experience further decreased the frequency of bad splits [45]. It was reported that older patients experienced more bad splits than younger patients [46]. The length of the medial osteotomy line—short or long—did not alter the prevalence of a bad split. The bone thickness of the ramus may affect the type of fracture pattern on the medial side of the ramus [47]. It is clear that certain mandibular anatomic differences can increase the risk of a bad split during SSO [44]. Use of splitters and separators instead of chisels does not increase the risk of a bad split and is therefore safe with predictable results [48].

2.3. Infection

Postoperative infection was reported in studies of patients undergoing bilateral sagittal ramus osteotomy in a period ranging from 5 days to up to a year after surgery. Infections required antibiotic therapy, and in some cases, the patients underwent surgical drainage. osteomyelitis in bilateral sagittal ramus osteotomy was reported [11]. The rate of infection after SSO is up to 11.3%. Infection after SSO is within normal range for a clean-contaminated procedure. Rigid fixation of the osteotomy may decrease the need for hardware removal [49].

2.4. Excessive bleeding

In the literature, there were no uniform criteria defining bleeding complications. Incidence varied between 0.39 and 38% ranging from slight to a life-threatening hemorrhage.

Minor bleeding in SSOs can usually be easily managed by using local anesthetics containing 1:100,000 adrenalines injected before the operation, electrocautery or compression. Excessive

blood loss may due to surgical injury of larger vessels. It was reported that excessive blood loss happen mainly to maxillary surgery and the need for blood transfusion in mandibular operations is rarely necessary [50].

2.5. Condylar resorption

Condylar resorption (CR) or condylysis can be defined as progressive change of condylar shape with a reduction in mass. Most patients have a decrease in posterior face height, retrognathism, and progressive anterior open bite with clockwise rotation of the mandible. CR may be defined as osteoarthrosis and can be categorized as primary (idiopathic) and secondary. Current evidence on CR is not clear but seen more in female with mandibular deficiency and high mandibular plane angle after bimaxillary surgery; a change in occlusal plane (counterclockwise rotation) may be associated with condylar resorption after orthognathic surgery [51]. It was hypothesized that condylar remodeling is due to an imbalance between mechanical stress applied to the temporomandibular joints (TMJ) and patient' adaptive capacities. It mainly occurs in 14 to 50-years-old women with pre-existing TMJ dysfunction, estrogen deficiency, and class II malocclusion with a high mandibular plane angle, a diminished posterior facial height and posteriorly inclined condylar neck. Mandibular advancement superior to 10 mm, counterclockwise rotation of the mandible, and posterior condylar repositioning were associated with an increased risk of CROS. Treatment consists of re-operation in case of degradation after an inactivity period of at least 6 months [52].

2.6. Temporomandibular dysfunction

The effect of orthognathic surgeries on temporomandibular dysfunction(TMD) is controversial. Some studies support degrees of improvement of TMD [5, 54]. Patients with preexisting TMJ dysfunction undergoing orthognathic surgery, particularly mandibular advancement, are likely to have significant worsening of the TMJ dysfunction postsurgery. TMJ dysfunction must be closely evaluated, treated if necessary and monitored in the orthognathic surgery patients [55]. Use of lag screws, improper control of the proximal segments, and advancement more than 10 mm increases the risk of post-orthognathic TMD. Orthognathic surgery should not be used solely for management of TMD; patients having orthognathic treatment for correction of their dentofacial deformities with TMD problem had more improvement in their signs and symptoms than deterioration [56].

2.7. Postoperative airway problem

It is clear that mandibular set back can affect upper airway patency [57]. The amount of narrowing of the pharyngeal airway is smaller in patients undergoing bimaxillary surgery than in patients undergoing mandibular setback surgery [58]. Bimaxillary orthognathic surgery for correction of Class III malocclusion caused an increase of the total airway volume and improvement of polysomnography parameters [59]. Bimaxillary surgery rather than mandibular setback surgery should be used to correct a class III deformity and reduce the risk of obstructive sleep apnea; in fact, bimaxillary surgery may have less effect on the pharyngeal airway patency than mandibular setback surgery alone [60]. A recent study suggested that

BSSO presents less change in the pharyngeal airway space after mandibular setback surgery compared to intraoral vertical ramus osteotomy. Furthermore, bimaxillary surgery is superior to mandibular setback surgery alone for the correction of the prognathic mandible, particularly in patients with factors predisposing them to the development of breathing problems [61].

3. Intraoral vertical ramus osteotomy

Intraoral vertical ramus osteotomy (IVRO) is another approach for the correction of mandibular prognathism. It is very simple and rapid. The inherent anatomic architecture of the mandible poses little interference on the cut surface of the IVRO osteotomy site during mandibular setback, even in cases of severe asymmetry. In addition, because the segments are not fixed, no stress occurs while the distal segment is positioned with the condylar head during and after the osteotomy procedure. Moreover, IVRO has less chance of nerve damage during the osteotomy procedure than SSRO. In addition to advantages provided during the operation, this procedure has various postoperative advantages. It seems to have curable effects on most patients with preoperative TMD [9].

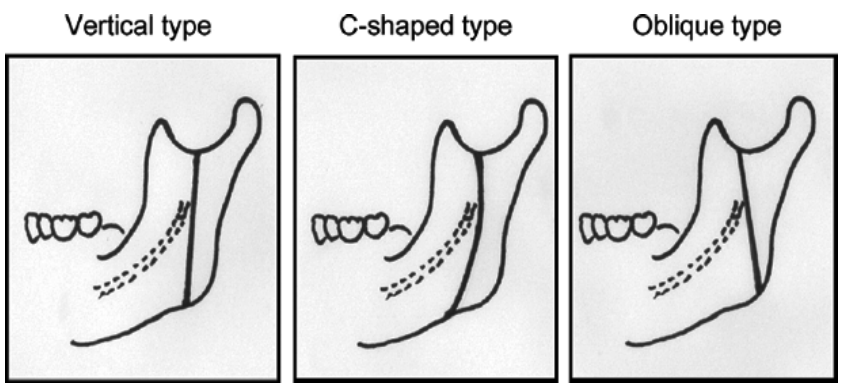

Figure 12. Classification of the shape of the osteotomy line [62].

During IVRO, inferior alveolar nerve (IAN) damage may occur due to the proximity of the vertical osteotomy to the IAN. Preoperatively, the surgeon should evaluate the lingula on radiographic views. The antilingular eminence on the lateral surface of the ramus should be detected. This small protuberance is located at the posterior one third from the posterior border of the ramus and about 10 mm above the occlusal plane of the lower molars in the vertical aspect, which corresponds to the opposite side of the mandibular foramen. The cut should begin 6–7 mm from the posterior border of the ramus. Kawase-Koga et al. classified the osteotomy line into three types, namely vertical, C-shaped, and oblique. The most complications occurred in the vertical type cases, and no complications were found in oblique type cases. Condylar luxation was found mainly in unilateral IVRO cases, and bony interference was found in bilateral IVRO cases. These results suggest that the oblique type of osteotomy line has the advantage of avoiding complications (**Figure 12**) [62].

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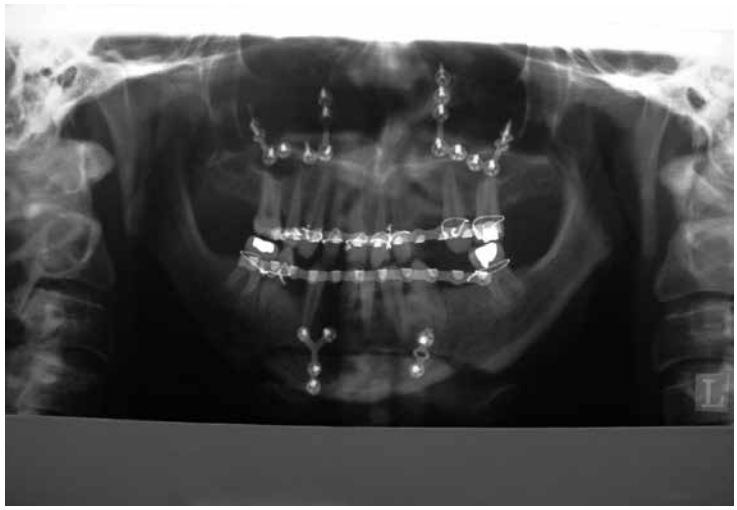

Figure 13. Condylar sagging at the (left side) after IVRO.

Condylar luxation and bony interference are major complications of IVRO [62]. The most troublesome sequelae are skeletal instability and antero-inferior condylar displacement (sag), with resultant unpredictability of postoperative mandibular position [63]. Condylar luxation is considered to be related to condylar sag, which occurs with the antero-inferior postoperative displacement of the proximal segment [62]. When the attachments of the masseter and medial pterygoid muscles to the proximal segment are removed extensively, large condylar sag occurs as a complication of IVRO. Condylar luxation is also related to forward force on the condyle from the lateral pterygoid muscle. Normally, the condyle is located in the anterior and inferior position within the glenoid fossa immediately after IVRO. It is gradually reseated into the original position after surgery with the application of intermaxillary elastics [64]. Several techniques have been reported to avoid condylar luxation and interference of the proximal segment. Suturing the periosteum of the segments around the incision with3–0 Vicryl to prevent sagging against the mandibular fossa has been suggested [64]. Rigid fixation is not recommended in IVRO and increases risk of post-operation open bite. Elastic therapy after osteotomy effectively decreases open bite due to the muscle tension (**Figure 13**).

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Chapter 27

Osteotomies in Orthognathic Surgery

Hossein Kashani and Lars Rasmusson

Additional information is available at the end of the chapter

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Abstract

Orthognathic surgery is mostly performed to correct developmental or acquired oral and maxillofacial skeletal deformities (OMSDs). During the past three decades, significant advances in surgical osteotomy techniques and instrumentation have been developed and carried out in orthognathic surgery. However, the basic surgical principles have more or less remained unchanged. At the same time, numerous surgical techniques have been developed and refined and used by surgeons in the field of oral and maxillofacial surgery. These techniques have treatment of the most complex dentofacial deformities with confidence. Additionally, it has been possible to predict the results of the treatment. Although the initial surgical techniques for correction of anterior mandibular open bite were reported as early as the late 1800s, widespread use of currently acceptable techniques began in the middle of the last century. Detailed surgical planning is essential for a successful outcome. The treatment involves an accurate treatment plan, correct type of instruments for a specific procedure, a thorough surgical routine, and adherence to the guidelines for each routine. Although similar orthognathic surgical techniques are used, there are multiple important differences related to each osteotomy. It is essential for the surgeon to understand these differences in order to provide an effective and safe surgical care for the patient with facial anomalies. Choosing an optimal method of osteotomy depends on many factors, including the indication for treatment, the goal of therapy, patient profile, underlying medical conditions, and the magnitude of surgical movement. The major objective of this chapter is to provide practical guidelines and principles of osteotomies and commonly used techniques. These guidelines are based on a review of the current literature and the author's personal experience. The chapter focuses on the history of orthognathic surgery, anatomical considerations, indications for different osteotomies, and the surgical technique for each osteotomy. Techniques such as the Le Fort I, II, III osteotomies, segmental osteotomies of the maxilla, bilateral sagittal split osteotomy (BSSO), bilateral vertical osteotomy (BVO) genioplasty, segmental osteotomy of the mandible, and the chin wing osteotomy are described.

Keywords: osteotomy, maxilla, mandible, chin, segmentation

1. Introduction

During the last three decades, remarkable advances have been made in surgical techniques and instrumentation for dentofacial surgery. Our knowledge and understanding of all aspects of orthognathic surgery have also grown over time. However, the basic surgical principles have more or less remained unchanged, despite technical innovations. Oral and maxillofacial surgery plays a central role in many aesthetic and functional procedures affecting the face and oral cavity. Since the first reported osteotomy performed on the mandible in the USA in 1849 [1], a large number of improvements have been published in the fields of orthognathic surgery. A well-defined treatment plan is required to ensure a successful treatment outcome. The surgeon should develop and adopt a proper technique for each procedure; using the same surgical sequence enables assisting residents to anticipate each step, thus adopting skills and developing a routine. The leading surgeon should have explicit knowledge on each surgical step. The most common surgical techniques currently used for the correction of dentofacial deformities, with various modifications, are the bilateral sagittal split osteotomy (BSSO) of the mandible, the oblique ramus osteotomy of the mandible, genioplasty, and the Le Fort I osteotomy of the maxilla. Osteotomies of jaw must be performed in a safe way and preferably intraorally to avoid scars on the face and at the same time provide adequate exposure to the skeleton. Essential structures must be preserved, and provision for appropriate nutrition postoperatively should be considered.

2. History

The first reported operation to correct malocclusion was performed in the USA in 1849 by Simon P. Hullihen [1] (**Figure 1**), in a patient with an open-bite deformity secondary to scar contractures of the neck and chest.

Figure 1. Simon P. Hullihen [1] first reported an operation to correct the malocclusion.

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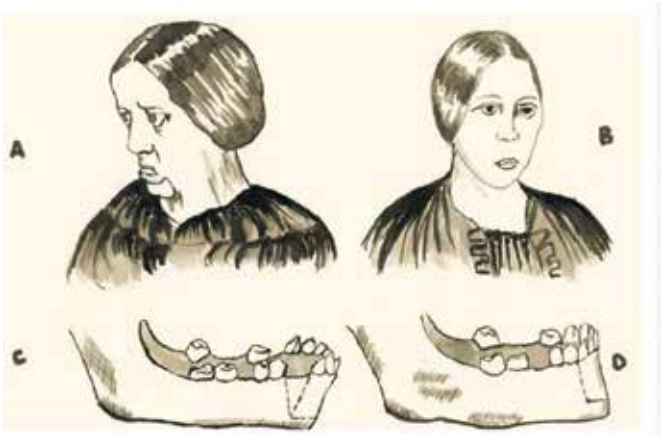

Figure 2. A 20-year-old woman severely burned on the neck at the age of 5 years operated by Hullihen [1] in 1849.

The cicatrix caused a deformity, and her head was drawn forward and downward with the chin frowsy close to the chest. Hullihen [1] performed an operation on the front section of the mandible and removed a wedge-shaped section from the anterior portion of the mandible, by sawing out a V-shaped segment, repositioned it, and fixed it with wire ligatures (**Figure 2**). Although the operation was performed primarily to correct the grotesque facial deformity, Hullihen [1], without formal dental training, had enough vision to reduce the class III malocclusion with bilateral subapical osteotomies. This was performed without having access to anaesthesia, antibiotics, or sophisticated instruments [2]. The development of orthognathic surgery continued in the USA when Steinhäuser and Berger 1897 described osteotomy of the condyle for the correction of prognathism.

Vilray Blair performed the first osteotomy of the mandibular body for the correction of horizontal mandibular excess, in 1907 [3]. He described three distinct problems: (1) cutting of the bone, (2) replacing the segment to a new position, and (3) fixation of the segments. This chapter was written more than 100 years ago but is still of great value.

In 1925, Limberg reported the first subcondylar osteotomy as an extraoral technique; later it was modified into the intraoral vertical subcondylar osteotomy. In the 1950s, mandibular osteotomies were routinely used with more or less predictable results, and publications came subsequently by Blair, Bruhn, Ascher, Obwegeser, Caldwell, and Letterman [4, 5]. Wassmund 1927 suggested a variation of the different subcondylar cuts similar to what is now known as the inverted L osteotomy. An anterior mandibular alveolar osteotomy was proposed by Hofer in 1963 to advance anterior teeth to correct mandibular dentoalveolar retrusion. Caldwell and Letterman developed a vertical ramus osteotomy technique that had the advantage of minimizing traumatic injury to the inferior alveolar neurovascular bundle [6].

A tremendous improvement in cutting the vertical ramus was the sagittal split osteotomy, described by Obwegeser in 1955 [7]. Trauner and Obwegeser published a modification of the same technique in 1957 [8]. Delpont made significant changes in osteotomy design in 1961 [9]. Later, Hunsuck 1968 [10] suggested a minor modification, which decreased trauma to

overlying soft tissues. In 1965, Obwegeser [11] performed complete mobilization of the maxilla for the first time. Relocating the maxilla could be done without tension. Until 1960, a pedicle of the soft tissue of buccal side was still preserved. Bell in 1970 published a paper and stressed that as long as the maxilla is attached to the palatal mucosa, the down fracture of the maxilla including the labial gingiva with complete mobilization can be done with adequate vascular supply [12].

Kent and Hinds, in 1971, presented the use of single tooth osteotomies of the mandible. Macintosh followed this technique with his description of total mandibular alveolar osteotomy in 1974 [13].

David Cheever reported the very first maxillary osteotomy in the USA in 1867 [14], for the treatment of complete nasal obstruction due to a sinus tumour for which a right hemimaxillary downfracture was used. The first time that an entire Le Fort I osteotomy was used for surgical correction of a facial deformity was by Wassmund in 1927. Wassmund introduced Le Fort I, or total maxillary osteotomy, for the treatment of an open bite. The early maxillary osteotomies that were performed in the 1950s were regarded with scepticism because of unpredictable results. After the successful mobilization and repositioning of the maxilla, presented by Wassmund, surgical correction of the maxilla appeared to be accepted from the early 1960s.

Schuchardt advocated the separation of pterygomaxillary junction in 1942. Bell 1975 stated that Le Fort I osteotomy has become a routine procedure in orthognathic surgery. Its simplicity, its broad application to resolve many functional and aesthetic problems, and the dependability of its results support this evolution. The applicability of the osteotomy makes it possible to reposition the maxilla in several directions; however, the setback of the maxilla is difficult because of the pterygoid plates. In the case where elongation of the maxilla is desired, a bone graft is often needed since bone contact will be lost. In modern protocols this can, however, be avoided if a pyramidal osteotomy is performed in the lateral walls of the maxillary complex, making the maxilla slide inferio-anteriorly. In 1949, Moore and Ward [15] recommended horizontal transection of the pterygoid plates for maxillary advancement. However, this technique was abandoned due to the incidence of severe bleeding in most cases. In 1959, Köle [16] suggested interproximal bone segmentation to expedite mobility between tooth bearing segments. He suggested that teeth could be segmented and moved as 'small boxes' through bone remodelling without involving the periodontal ligament. In the 1960s, Obwegeser suggested that the maxilla/maxillary segments should be fully mobilized so that they could be brought into the desired position without tissue resistance. This proved to be a significant advancement in stabilization, as documented by Hogemann and Willmar, De Haller, and Perko, respectively [17].

3. Anatomical considerations

3.1. Blood supply

Blood supply is essential for the healing of osteotomies. Bell and Levey 1969 18] and 1970 have shown in a study that periosteum is necessary for maintaining the blood supply to the teeth

of a mobile jaw segment [12, 18]. Even when the labial periosteum is raised, care should be taken not to cause any tension or tears. A subapical osteotomy needs to be carefully planned to ensure as large a vascular pedicle as possible. In the lower jaw, the proximal segment of the vertical osteotomy is attached by the lateral pterygoid muscle and temporomandibular joint capsule. In some recent studies, stripping of the muscle attached to the medial segment has been suggested. However, in older literature, it was recommended to keep this muscle attachment intact. Apparently, either approach when used does not show any significant differences in clinical outcomes. However, it is important that the distance between the osteotomy and apices of the teeth is at least 5 mm. Keeping this distance minimizes tooth and pulpal injury, and a mobile segment will have greater vitality to survive by increased vascular supply.

It is advised to handle the soft tissues with care so that adequate collateral blood supply to the osteotomized segment is maintained and injury to other vital structures is avoided.

Prominent vessels to consider when planning orthognathic surgery are the posterior superior alveolar (PSA) artery, greater palatine artery, maxillary artery, pterygoid venous plexus, inferior alveolar artery, and buccal artery (**Figure 3**).

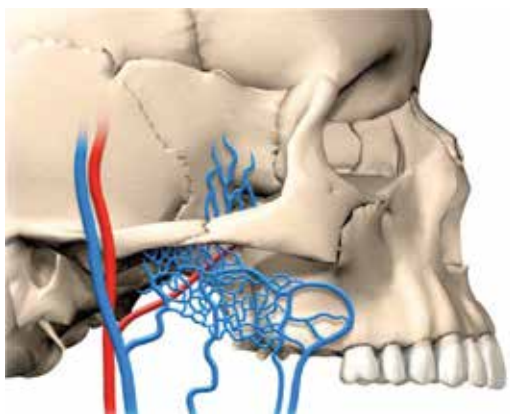

Figure 3. Prominent vessels to consider in orthognathic surgery are the posterior superior alveolar (PSA) artery, greater palatine artery, maxillary artery, pterygoid venous plexus, inferior alveolar artery, and buccal artery.

3.2. Nerves

Facial nerve branches are rarely damaged in orthognathic surgery, but great care should be taken when, for example, an extraoral vertical ramus osteotomy is performed. The course of the inferior alveolar nerve through the mandibular canal is at increased risk of injury when any osteotomy is carried out in the mandible. Bradycardia and asystole may occur during downfracture or mobilization of the maxilla due to the trigeminal-cardiac reflex. This can happen as a result of manipulation of the central or peripheral portions of the trigeminal nerve during mobilization of the maxilla [19]. All patients can experience varying degrees of dysesthesia some months postoperatively such as numbness, hypaesthesia, or tingling, most

commonly after BSSO [20]. Patients who undergo Le Fort II and III osteotomies may experience infraorbital nerve sensory dysfunction.

3.3. Muscles

Muscles are, as mentioned earlier, important in orthognathic surgery. On the one hand, they are essential for blood supply to the segments, and on the other, they have an impact on relapse. Surgery can affect muscles in two different ways; they can change the length and direction of function. The muscles that can be affected by orthognathic surgery are the suprahyoid group of muscles and the masticatory muscles.

4. Osteotomies in the maxilla

4.1. Le Fort I

Wassmund 1927 [21] described this osteotomy. In 1969, Obwegeser reviewed and modified the technique [22]. An intraoral incision, 3–4 mm above the attached gingiva at maxillary vestibular fornix, is made from the second premolar of one side to the opposite side. A mucoperiosteal flap is raised exposing maxillary walls. Modern protocols [23–26], however, advocate a less extended incision with an opening in the incisor region only. The infraorbital nerve must be identified, and the dissection will then extend to the level of infraorbital nerve to simplify the following osteotomies and to achieve direct control of periorbital tissues. During the exposure, great care should be taken not to expose the buccal fat pad. Before the bone osteotomy, a nasal mucosa mobilization is performed from the wall of the nasal cavity. The osteotomy is carried out with a burr, saw, or piezo machine, starting from the lateral aspect of the piriform aperture and extended to the posterior aspect of the maxilla towards the zygomatic buttress as backwards as possible and inferiorly (**Figures 4** and **5**).

Figure 4. Schematic picture of a Le fort I Osteotomy

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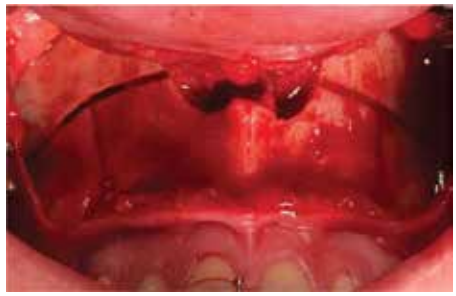

Figure 5. Frontal view of a Le Fort I osteotomy performed by a piezo saw with a nice cut.

The same is done on the opposite side. These osteotomies are completed with a chisel, to detach the nasal septum and lateral wall of the nasal cavity. The osteotomy of the nasal septum and separation of septal cartilage from the anterior nasal spine is usually made by chisel. Finally, it is important to separate the pterygomaxillary junction by using a curved chisel lateromedially to simplify the mobilization of the maxilla. After the last detachment of the maxilla is done, downfracture can be performed. The advantages of this osteotomy are full mobilization, speed, simplicity, direct vision, the safety of segmentation, and reduced risk for relapse. An alternative to the separation of the pterygomaxillary junction is a vertical osteotomy in the tuber region of the alveolar crest. This method will, however, not enable the same degree of mobility. It is fixated using miniplates.

Over many years, the precision of the operative technique and establishment of a scientific and biological basis for the procedure has been established. The Le Fort I osteotomy has become an essential procedure in the surgical armamentarium for correction of dentofacial deformities.

4.2. Segmented Le Fort I osteotomy

In cases of open bite or when a transversal expansion is required in the maxilla, a Le Fort I osteotomy approach can be combined with a multiple-piece osteotomy to correct an unfavourable curve of Spee or a transverse discrepancy. The maxilla can be sectioned into 2, 3, 4, 5, or 6 segments depending on the indications (**Figures 6–8**).

Figure 6. Segmentation of maxilla into 4 pieces.

Figure 7. Segmentation of maxilla into 6 pieces.

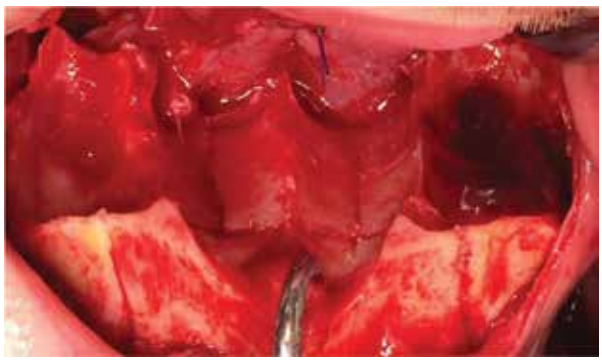

Figure 8. Clinical view of segmented maxilla.

A median osteotomy is made by a Lindeman burr or piezo at the lateral aspect of the median palatal suture. When a two-segment osteotomy is planned, one median cut is performed only on the side of the palatal suture. This cut will be connected consequently to a vertical interdental osteotomy that will be placed between the canine and first bicuspid teeth on the same side (**Figure 9**).

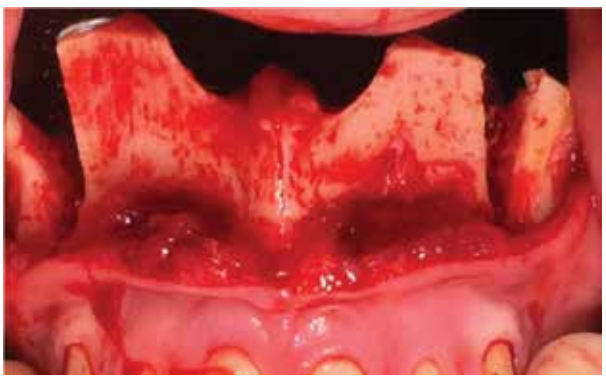

Figure 9. A vertical interdental osteotomy placed between the canine and first bicuspid teeth on the same side.

Another option of vertical osteotomy is to place the vertical interdental osteotomy between the lateral incisor and canine [23-30]. In both cases, the interdental osteotomies are combined with palatal osteotomies but from a superior angle without raising a palatal flap. When a four-piece segmentation is required, two parallel osteotomies are performed on each side (**Figure 6**). These osteotomies will consequently be connected to each other by an oblique osteotomy and subsequently to the vertical interdental osteotomy placed between the canine and first bicuspid or between the lateral incisor and canine. It is essential to keep the palatal mucosa intact. Careful sectioning when performing the interdental osteotomies is mandatory to avoid injury to the tooth roots and their blood supply. This approach allows placement of the maxillary segments in different directions since they are detached.

In some cases, a high Le Fort I osteotomy is required for advancement of the entire midface to improve the extraoral profile of the facial skeleton (**Figure 10**).

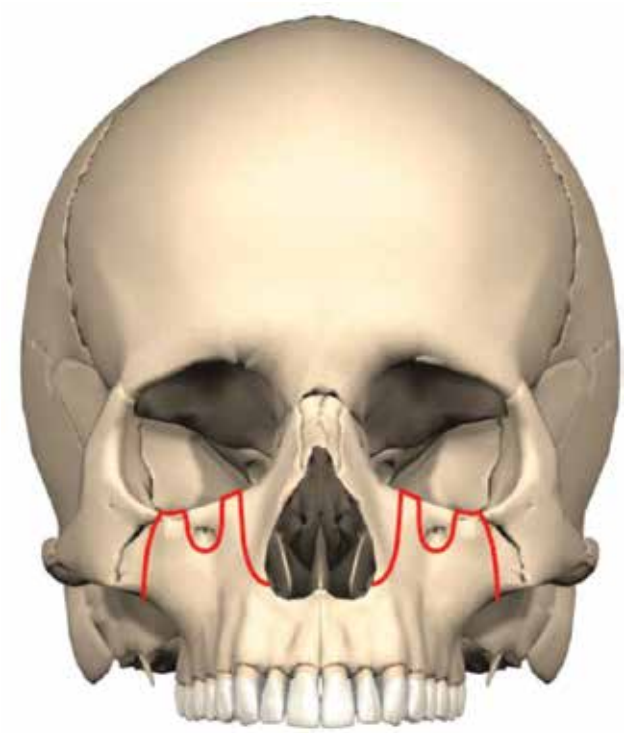

Figure 10. In some cases, a high Le Fort I osteotomy is required for advancement of the entire midface to improve the extraoral profile.

4.3. Le Fort II

The indication for this osteotomy is when a forward, downward movement of the nasal and maxillary complex is necessary for correction of the midface. This osteotomy is performed in the upper midface, between the frontal facial unit and above Le Fort I (**Figure 11**).

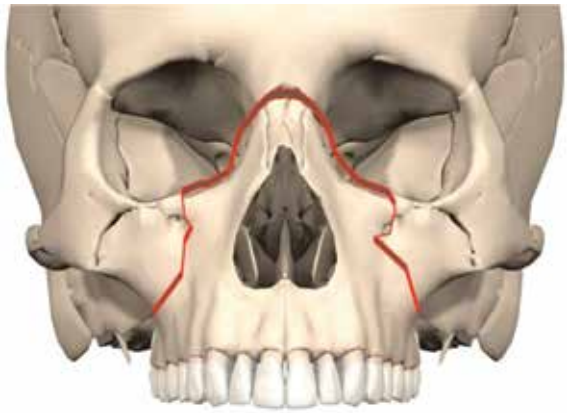

Figure 11. Le Fort II osteotomy is performed in the upper midface, between the frontal facial unit and above Le Fort I.

The approach has its place where there is a need for the correction of nasomaxillary hypoplasia [31, 32]. This osteotomy is also called a pyramidal naso-orbital maxillary osteotomy. The Le Fort II osteotomy includes the naso-orbital ethmoidal (NOE) fracture line, the zygoma laterally, and internal part of the orbit. This osteotomy was first presented by Henderson and Jackson in 1973. Surgically, an incision is performed obliquely to the paranasal region extending to the infraorbital rim to the medial canthus and over the nasal bone. The Le Fort II osteotomy is relatively rare because it is not required as often (only in 2% of dentofacial anomalies cases, such as in Apert, Crouzon Treacher Collins syndromes). Other indications are a skeletal class III malocclusion in combination with maxillary-zygomatic deficiency, maxillary-alveolar-palatal cleft deformity, and nasomaxillary deficiency [28]. The osteotomy allows lengthening of the nose along with the movement of the upper jaw in selected cases where this effect is desired.

Steinhauser, 1980, described three different surgical approaches namely anterio-, pyramidal, and quadrangular osteotomies [33].

To get surgical access for the Le Fort II osteotomy, a V-shaped incision with the apex at the glabella is made to extend bilaterally along both sides of the nose to reach just above the alar base. The columella of the nose is pulled down, and the cartilaginous and bony part is separated. Osteotomy starts at the bottom of the nasal bone towards the medial wall of orbit towards the floor of orbit posterior to the nasolacrimal apparatus. Then it continues to the infraorbital margin medial to the infraorbital nerve and extends to the alveolar bone posterior to the second premolar. A flap in the posterior buccal area is raised. The osteotomy is completed through the intra oral incision towards the pterygoid plates. In cases with deficiency in the infraorbital area, the cut can be continued to the zygomatic buttress before going down towards the pterygoid plates. Downfracture of the midface can be done. The segment can be advanced after mobilization. Fixation can be done either by an acrylic splint or by fixation plates. In this approach, bone grafts should be used to restore the bone deficiencies. It is crucial to have skin coverage, and nasal lining must be provided. The nasolacrimal apparatus must not be damaged.

4.4. Le Fort III

Sir Harold Gillies and colleagues presented the Le Fort III osteotomy for the first time in 1951. The technique was improved by Paul Tessier in 1967 making five different variations mainly regarding the osteotomy of the lateral wall of the orbit [34]. The Le Fort III procedure is designed to move the entire midface forward including the portions of the eye sockets to get a more balanced appearance in whom facial disharmony results from panfacial hypoplasia. This technique is used in various craniofacial syndromes such as Apert, Crouzon, Treacher Collins, etc.

Those patients who have a total retrusion of the midface often have a retrusion of the nose, cheeks, inferior orbital rims, and upper lip. Patients with Crouzon, Apert's, and Pfeiffer's syndrome often have a hypoplastic nose. In some cases, it will be necessary to complete a Le Fort III with a Le Fort I osteotomy to make the appropriate adjustment for optimal aesthetics and occlusion. One more detail to keep in mind is the intercanthal distance and level of attachment of the medial and lateral canthal tendons. Epker et al. 1980 [35] suggested that this method is more aesthetic, and function of the lacrimal sac is better when dystopia of the medial canthal tendons or telecantism does not exist.

The bicoronal approach is preferred and often utilized in Le Fort III osteotomies. The incision is a coronal flap to lift the full-face skin combined with subciliary, subtarsal or transconjunctival incision, and intraoral vestibular incisions. The dissection of the supraorbital rim includes decompression of the supraorbital nerve by an osteotomy on the supraorbital rim to release the nerve (**Figure 12**).

Figure 12. The dissection of the supraorbital rim includes decompression of the supraorbital nerve by an osteotomy on the supraorbital rim to release the nerve. The incision extended to the lateral orbital rim, nasion, and through the zygomatic arch via a coronal incision.

After releasing the nerve, nasal bone, medial canthal tendons, and superior part of the lacrimal sac, the lateral and inferior orbital rims are exposed.

The osteotomies start at the glabella using a horizontal cut (**Figure 12**). The medial canthal tendons should be either left intact or reflected off or reached with a suture. The lacrimal fossa is exposed below this area with the accompanying lacrimal sac. Care should be taken not to interfere with the ethmoidal artery that is located about 25 mm back in the orbit. Thus, the cut can be applied only 12–15 mm posteriorly avoiding the ethmoidal artery. If the medial canthal distance is average, the cut can be placed anterior to the medial canthal tendon, leaving the

tendon untouched. If any subciliary or subconjunctival incision is made, the cut of the medial wall can be done via a chisel. A horizontal cut is then performed across the orbital floor extending to the lateral orbital rim. At the lateral orbital rim, the cut of the lateral wall can be carried out in the middle, but depending on the deficiency of the lateral rim it can be more superior or inferiorly placed according to Tessier I, II, and III. By elevating the anterior part of the temporal muscle, direct access to the retro-orbital and infratemporal space is gained. To detach the pterygomaxillary junction, an intraoral gingivobuccal incision as described for Le Fort I is used. It is also possible to separate the junction via bicoronal approach.

In some cases, a glabella incision together with bilateral subciliary incisions and oral vestibular incisions is utilized. With that approach, the osteotomies start at the glabella section through a horizontal incision in the skin. This cut continues to the middle part of the orbital rim with the same care mentioned earlier at the medial section of the orbit, downwards to the inferior orbital rim through the subciliary incision. The incision is then extended to the lateral orbital rim and finally through the zygomatic arch through an intraoral incision back to the pterygoidomaxillary junction that is detached by a chisel (**Figure 13**).

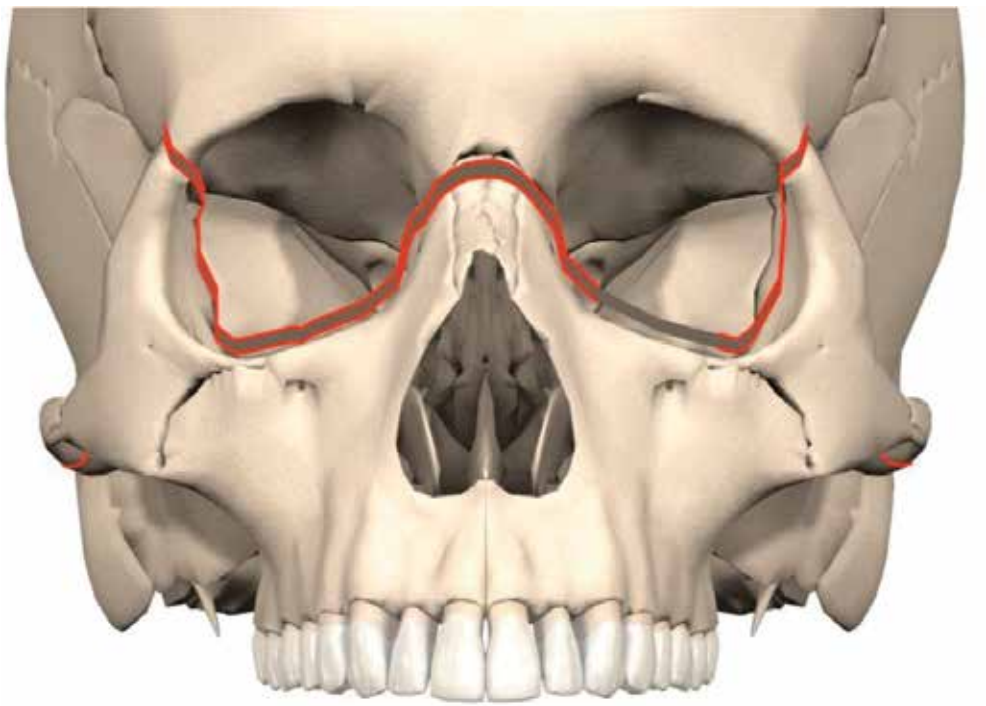

Figure 13. *Le Fort III* The incision extended to the lateral orbital rim, nasion, and through the zygomatic arch via a coronal incision, through an intraoral incision back to the pterygoidomaxillary junction that is detached using a chisel.

Rowe's forceps are then used to mobilize Le Fort III. Garcia and colleagues recently suggested some changes in this technique [36]. This method can be used in combination with distraction osteogenesis resulting in a very good outcome (**Figures 14–16**).

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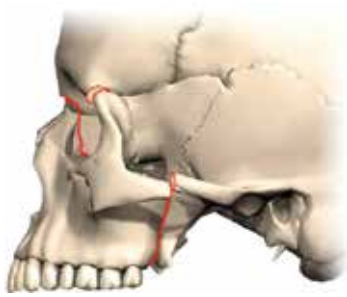

Figure 14. Le Fort I osteotomy cab be used in combination with distraction osteogenesis resulting in a very good outcome. The mobilized midface is at the zygomatic region and paranasal bony anchored to the distractor. At the end of distraction, the midface is advanced. Note the increase of pharyngeal volume compared with the preoperative situation.

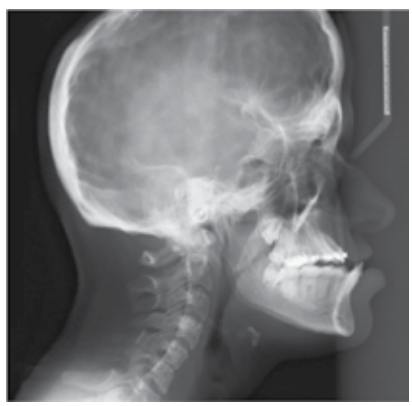

Figure 15. Lateral radiographic projection showing the preoperative view

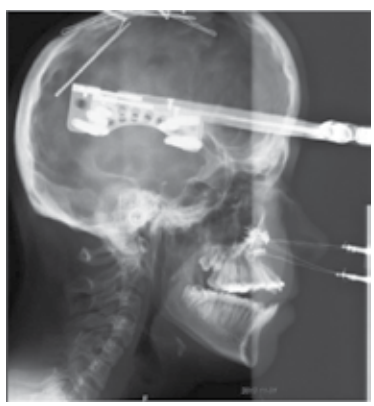

Figure 16. Lateral view after surgical correction with large anterior movement of the maxilla with distraction

4.5. Monobloc

The so-called monobloc craniofacial surgery is used for craniofacial advancement in combination with distraction osteogenesis and is used for children with complex craniosynostosis syndromes. A bicoronal incision will be used, following a standard fronto-orbital osteotomy. After separating the frontal bone flap, a forceful forward protrusion of the frontal lobe is noticed suggesting high intracranial pressure from the craniosynostosis. After that, the orbital bandeau is separated by the aid of a piezo saw. A Le Fort III osteotomy should then be performed. The osteotomy line should pass the arch of zygomatic, from the spheno-zygomatic suture across the floor of the orbit, continuing behind the nasolacrimal duct. After that, it should continue along the lacrimomaxillary suture to the nasal bone (**Figures 17** and **18**). The nasal septum must be separated from the perpendicular plate of the ethmoid bone with a chisel or straight osteotome. Next, the pterygoid plates must be separated with a chisel as described in Le Fort I osteotomy at pterygomaxillary fissure. The viscerocranium can then be mobilized. Rowe's forceps can be used for mobilization of the viscerocranium for rotation downwards.

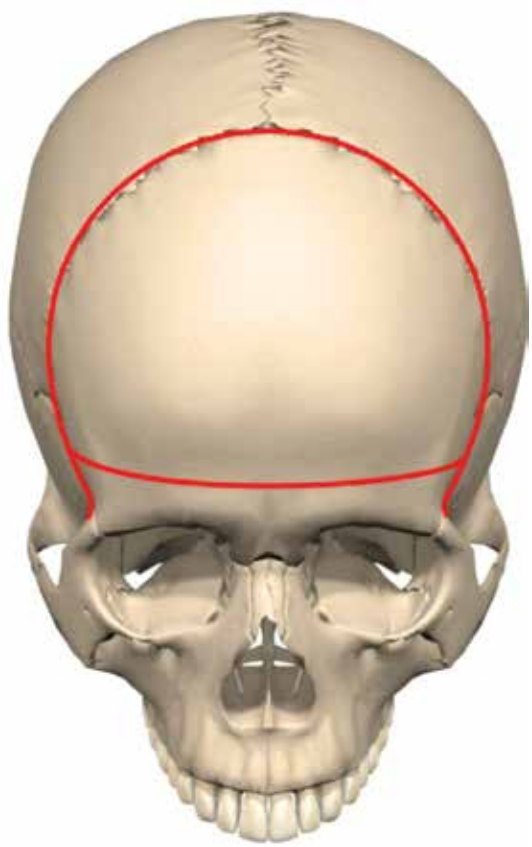

Figure 17. *Monobloc* The forehead, superior orbital rims when a monobloc approach is performed from a frontal point of view.

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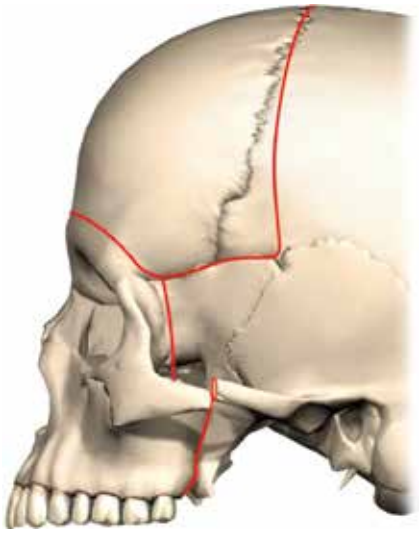

Figure 18. The monobloc approach seen from a sagittal point of view.

4.6. SARME

Surgical assisted rapid maxillary expansion osteotomy (SARME) or surgical assisted rapid palatal expansion osteotomy (SARPE) (SARME/SARPE expressions are used interchangeably) is one of the most commonly performed orthognathic techniques. The terminology is somehow confusing since this approach includes both maxillary and palatal expansions. The terminology includes only one part and is, therefore, inaccurate [37]. It was used and described first by

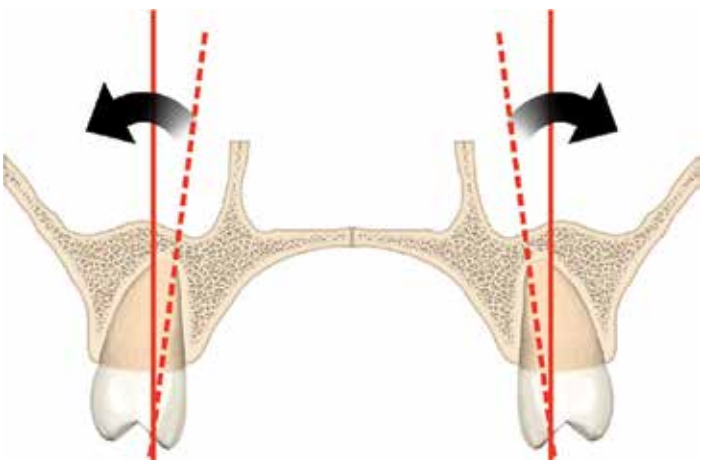

Figure 19. Important to avoid orthodontic tilting of molar teeth. When the median suture is fused, attempting to widen the palatal suture by orthodontic treatment only cause buccal displacement of teeth with a very high risk of relapse. A widening of the dental arch without tilting of the teeth is only possible by a surgery.

Brown in 1938. The most common indications for SARME are a transverse discrepancy in the maxilla, failed orthodontic expansion, significant nasal stenosis, and widening of the arch following collapse associated with the cleft palate deformity. This procedure is often used for patients between 16–20 years when the median sutures of the palate are fused. When the median suture is fused, attempting to widen the palatal suture by orthodontic treatment only causes buccal displacement of teeth with a very high risk of relapse (**Figure 19**). Therefore, in those patients, a widening of the dental arch without tilting of the teeth is only possible by a surgically assisted osteotomy together with orthodontic expansion.

The approach is similar to Le Fort I osteotomy as described above. A medial osteotomy is performed carefully with an osteotome following the suture. The activation of the expansion device is preferably done so the expansion can occur quickly. Proper care must be taken not to perforate the soft tissue in the gum with a chisel and not to damage the central incisor roots. Once the separation is done, the expansion device deactivates again. The activation of the device for expansion of the palatal can first be started one week post-operatively. In some cases, an anterior expansion is needed, only then the pterygoid-maxilla junction can be kept untouched. If posterior expansion is planned, a similar detachment between the posterior maxilla and pterygoid plate is done as described previously for a traditional Le Fort I osteotomy (**Figure 20**).

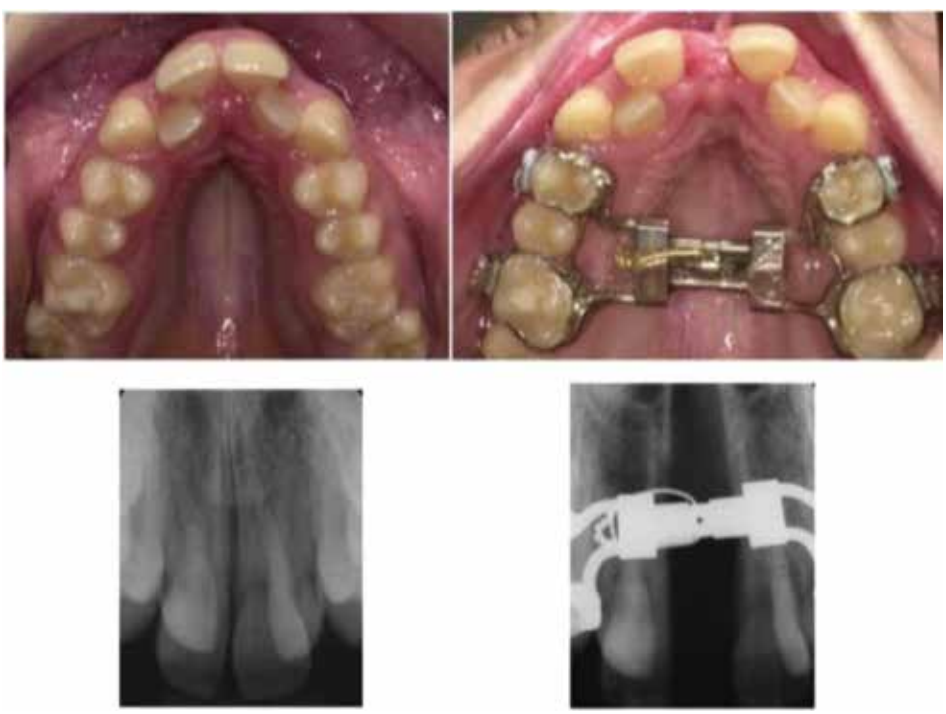

Figure 20. If the posterior expansion is planned, a similar detachment between the posterior maxilla and pterygoid plate is done as described previously for a traditional Le Fort I osteotomy.

The expansion device extends over the palate with an attachment, and by the use of a screwdriver it can spread the bony segments (**Figure 20**). The expansion of the maxilla may take some weeks depending on how far the plate needs to be expanded. The expansion is 1 mm per day. Transversal expansion of the mandible is possible in the same way but is a very unusual approach.

4.7. Anterior segmental maxillary osteotomy

This technique is applied when repositioning of the premaxilla in a vertical plan is required such as for frontal open bite, to retract the anterior teeth, when orthodontic treatment cannot accomplish the desired movement (e.g., when teeth are ankylotic or when a deep bite is present). Cohn-stock (1921) [38] was the first surgeon who reported this technique. A mucosal incision is applied in the buccal side of the maxilla above the roots of the incisors. This incision is extended to the distal section of the first bicuspid bilaterally. It is common to use a micro saw or piezoelectric device, followed by chisel since a high risk of injury to tooth roots exists. Consequently, osteotomies are performed after extraction of first bicuspids. After that, a transverse palatal incision is made following a wedge-shaped osteotomy to provide a green stick fracture. This osteotomy can be done either by performing a Le Fort I osteotomy or by a restricted buccal vestibular incision, allowing direct access to the anterior lateral maxillary walls, piriform aperture, nasal floor, and septum (**Figure 21**).

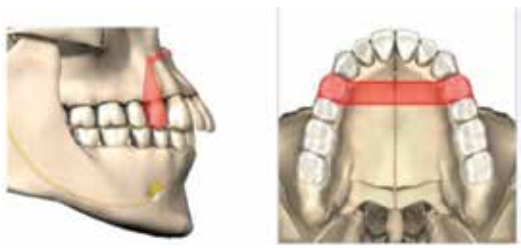

Figure 21. Anterior segmental maxillary osteotomy can be done either by performing a Le Fort I osteotomy or by a restricted buccal vestibular incision, allowing direct access to the anterior lateral maxillary walls, piriform aperture, nasal floor, and septum.

The anterior segmental maxillary osteotomy can cause some complications such as oronasal or oroantral fistula, damage to the teeth, loss of vitality of teeth, complication with the maxillary sinus and nasal cavity, unfavourable nasolabial aesthetics, and nasal septal deviation. The most common complication with anterior segmentation is a retraction of gingiva in the anterior segment and relapse during the early healing phase. This method has been revised and discussed widely in the literature by Epker 1977 [39], Epker and Wolford 1980 [35], and Wunderer 1985 [40].

4.8. Posterior maxillary segmental osteotomy

The technical difficulties concerning approaches to the posterior maxillary segmental osteotomy have been emphasized. The indications are mainly uni- or bilateral posterior open bite.

The cut is performed at the buccal vestibular section of the posterior maxilla 5 mm above the root apices (**Figure 22**).

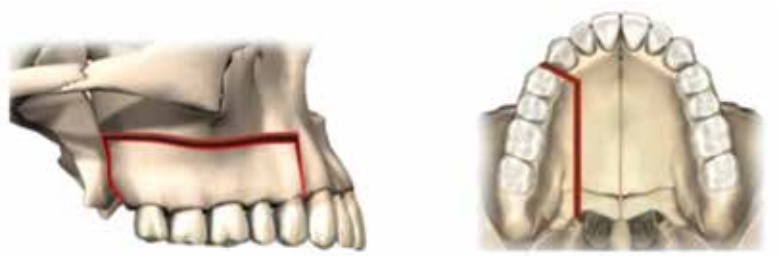

Figure 22. The cut is performed at the buccal vestibular section of the posterior maxilla 5 mm above the root apices.

The access to the bone is made through a horizontal cut in the buccal vestibule extending from the second molar to the distal aspect of the canine. The incision continues vertically to the papillae at the distal aspect of canine and distal aspect of the second molar. It is preferable to extract the molar in advance some months before this approach. After a horizontal cut, if an interdental vertical osteotomy through the extraction sites (in cases extraction is needed) and also a posterior vertical osteotomy at the pterygomaxillary junction is done, the palate will remain in original position, but the dentoalveolar complex will be separated and moved to the planned position. After a buccal vestibular incision, a parasagittal palatal incision is performed without any vertical interdental incisions (**Figure 22**).

The method is somewhat complicated since multiple areas of bony contacts may interfere. A Le Fort I osteotomy is more often used for correction of the posterior maxillary deficiency. There are, however, a number of indications for this approach namely maxillary hyperplasia, distal replacement of the posterior maxillary alveolar fragment to provide space for proper eruption of an impacted canine or bicuspid posterior open bite, posterior cross bite or scissors bite, and anterior open bite correction through bilateral impaction of the posterior parts.

Complications related to this approach are the loss of teeth vitality, relapse, necrosis of segment, and periodontal defects.

4.9. Combination of anterior and posterior maxillary osteotomy (Horseshoe osteotomy)

Paul Tessier in 1969 [34] reported this procedure for midface hypoplasia. It has also been described and further developed by West and Epker 1972, Hall and Roddy 1975, Wolford and Epker 1975, West and McNeil 1975, Hall and West 1976, and Maloney 1982. Palatal parasagittal osteotomies are performed with a piezoelectric device. The hard palate is untouched staying in position. The method creates a three-piece maxilla with the central nasal portion left undisturbed. This is a complicated technique since multiple areas of bone contacts exist. The indication is maxillary alveolar hyperplasia or transverse hypoplasia without a vertical component. The method has more or less been replaced by the traditional Le Fort I osteotomy (**Figure 23**).

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Figure 23. The horseshoe osteotomy; this method has more or less been replaced by the traditional Le Fort I osteotomy.

5. Osteotomies of mandible

5.1. Bilateral sagittal split osteotomy (BSSO)

The original bilateral ramus osteotomy by Trauner and Obwegeser [41] is performed in the ramus above the mandibular foramen. Dal Pont et al. [42] in 1961 modified this to the vertical osteotomy of the body of the mandible combined with lower horizontal osteotomy with an advantage of easy splitting. Hunsuck [10] in 1968 recommended the shorter horizontal cut that should only extend to the mandibular foramen at the medial ramus (**Figure 24**).

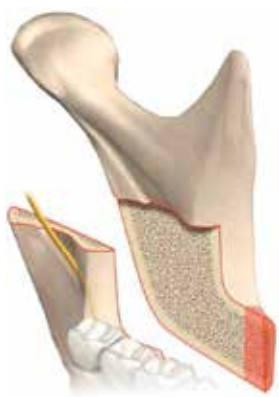

Figure 24. Hunsuck's shorter horizontal cut only extends to the mandibular foramen in the medial ramus.

This procedure is used to correct retrognathism and mandibular prognathism. Mandible advancement, setback, rotation, and in some cases closing of the an open bite is possible. The incision is made through the mucosa, muscle, and periosteum, down to the bone on the lateral aspect of the anterior border of the ramus midway up to the ascending ramus and downwards

into the depth of the vestibule ending mesial to the second molar. It is advisable to leave 7–8 mm of non-keratinized buccal epithelium for ease of suturing [10, 43].

Dissection of the periosteum starts subperiosteally along the anterior border of the ramus upwards the coronoid process. Dissection should be limited only to areas where the osteotomies will be performed and muscle attachments that need to be separated from the bone. No lateral dissection of the ascending ramus is needed. By using a coronoid notch retractor, soft tissue over the ascending ramus can be elevated. At medial section, the soft tissue is retracted gently to avoid damaging the inferior alveolar nerve. The inferior alveolar neurovascular bundle as it enters the mandibular foramen should be identified and supported by a medial retractor. The stylomandibular ligament and the medial pterygoid muscle can be stripped from the angle of the medial aspect.

The sagittal osteotomies can then be started by using a Lindeman fissure bur through only the medial cortex and extended just posterior and superior to the lingual about 2 mm above the inferior alveolar neurovascular bundle. It is advised that the horizontal cut at the medial section of the mandible is made through the whole length of the lingual cortex to avoid an unfortunate split (**Figure 24**). But it is still possible to extend the horizontal cut in the medial section of the mandible just some mm behind the inferior alveolar neurovascular bundle.

When the osteotomy is completed on the medial aspect of the mandible, the next cut is performed on the lateral aspect of the anterior ramus posterior to the second molar. This cut is made parallel and directly adjacent to the lateral cortex. Finally, the osteotomy is extended from approximately the first to second molar downwards vertically just inside the buccal cortex and ends at the base of the mandible [10, 43, 44]

The medial section of the mandible base should be included in the osteotomy. Chisels are then used to control the cut through all osteotomies. Usually, two osteotomes are used as levers to separate the segments: one of the osteotomes places in the vertical osteotomy and the other one in the horizontal osteotomy site behind the second molar. It is important to keep in mind that in cases where the separation does not proceed favourably, it is better to stop the procedure and identify the problem. The problem should be diagnosed and solved to avoid an unfortunate split. It is important that when the split is done, it will in effect separate the lateral proximal section from the cancellous bone, and the inferior alveolar nerve will remain in the distal segment, and the nerve should not be injured.

If the alveolar canal (including the nerve) is attached to the proximal segment during the splitting procedure, the canal should be carefully dissected from the proximal part, but this will increase the sensory morbidity of the inferior alveolar nerve. The separation of nerve from proximal section of the ramus is debated in the literature. In our experience, the nerve can be left in the proximal segment if the fixation material does not pinch it, and if the movement of the fragments is not too much. Thus, the nerve must be easily moveable in the mandibular canal. As soon as the separation of the layers is done, the surgeon should check that the osteotomy is done accurately, and the neurovascular bundle is intact and separate from the proximal segment (**Figure 25**).

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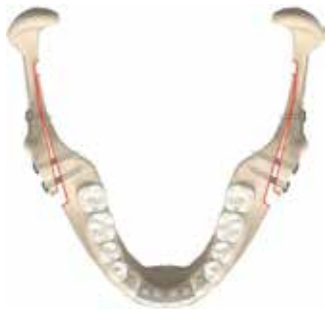

Figure 25. Rigid fixation of the segments by lag screws or plating.

5.2. Vertical ramus osteotomy

5.2.1. Extraoral

In the early 1950s, Caldwell and Letterman [6] popularized an osteotomy performed in the ramus of the mandible for the correction of mandibular excess. This technique is mainly used for the correction of asymmetry of the mandible [37, 45-47]. In this procedure, the lateral aspect of the ramus is exposed through a submandibular incision. The incision is marked about 2 cm below the inferior border of the mandible base, in the angle region. The length of the skin incision is about 4 cm long. Dissection is made through the skin and all the covering soft tissues over the platysma are carefully undermined. An incision is then performed on the platysma to the next layer as deep as to the superficial layer of the deep cervical facia. The marginal mandibular branch of the facial nerve passes through this layer. Thus, extreme care should be taken. As soon as this layer is dissected, the masseter muscle will be exposed which can be cut

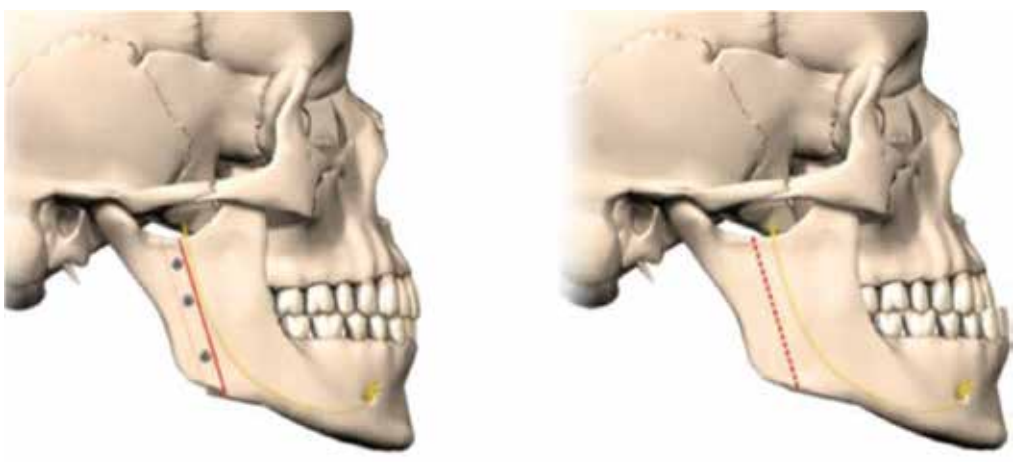

Figure 26. Vertical ramus osteotomy is suitable for posterior repositioning of the mandible.

with a knife. From here, dissection can be continued posteriorly to the gonial notch and superiorly subperiosteally to expose the ascending ramus laterally. Before starting the osteotomy, the medial pterygoid muscle should be released from the medial part of the angle. The ramus is osteotomized in a vertical direction, posterior to the foramen where the mandibular inferior nerve enters. The cut can be done superiorly from the sigmoid notch to the angle of the mandible. This osteotomy is suitable for posterior repositioning of the mandible (**Figure 26**).

It is also possible to perform an inverted L osteotomy, where a horizontal cut from the anterior section of the ascending ramus is made just below the coronoid process extending to the vertical osteotomy from the angle of the mandible. The entire body and anterior ramus section of the mandible are moved posteriorly, which places the teeth in proper occlusion. The proximal segment of the ramus that is attached to the condyle will overlap the anterior part of the jaw that includes the teeth and will be stabilized during the healing phase with wiring or plating of the bone segments combined with using elastic mandibulomaxillary fixation.

5.2.2. Intraoral

A similar technique can be done through an intraoral incision and an angulated oscillating saw or piezo saw. The design of the osteotomy is identical to that performed through an extraoral incision. The incision is performed via an intraoral entrance. This procedure has, at least, two advantages namely elimination of the risk of damage to the facial nerve and elimination of the risk of a visible scar postoperatively. The main disadvantage with the intraoral approach is that it is difficult to perform since visibility is limited (Hall et al. 1975) [48]. Additionally, fixation of the fragments is difficult.

Previously, it was common to use mandibulomaxillary fixation (MMF) for 5–7 weeks postoperatively when this approach was used. A rigid, internal fixation can be used but MMF must be considered for a short period.

5.3. Genioplasty

The chin is a critical part of the face. A disharmony in the chin is very noticeable and should be corrected in an artistic way [49]. Each of the different skeletal deficiencies (e.g., class II and III deep bite or open bite) can cause a morphology change of the chin that is very different between individuals even if the dentofacial deformities are similar.

Correction of a chin deficiency can be performed by reducing or augmenting in three different dimensions namely vertically, transversely, and sagittally. This correction can be combined with any operation in both maxilla and mandible. Augmentation genioplasty, reduction genioplasty, straightening genioplasty, and lengthening genioplasty are some procedures that can be used (**Figures 27–30**).

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Figure 27. It is highly important to mark the midline of the chin before any osteotomy is performed.

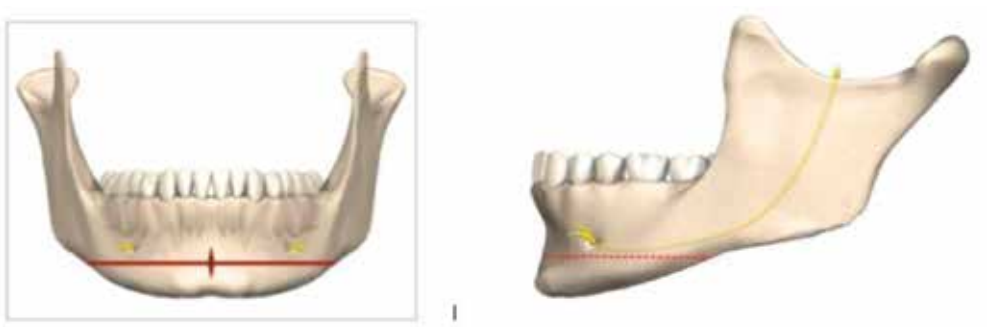

Figure 28. The midline can be marked as a reference point using a burr or saw. A plus (+) sign can be used to mark the bone in the centre of the buccal cortex.

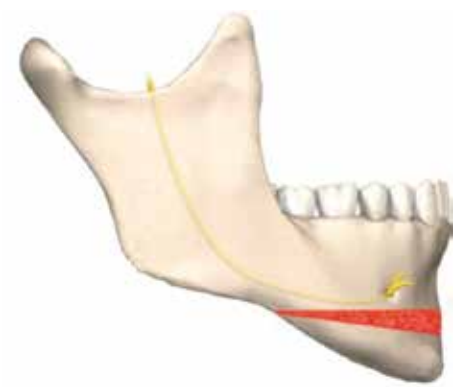

Figure 29. Lengthening or reduction of the chin by the so-called sliding osteotomy. In the case of reduction, a slice of the bone is removed and in the event of augmentation, the chin is pulled forward and sometimes downwards. Additional bonegraft material may be used to improve the augmentation.

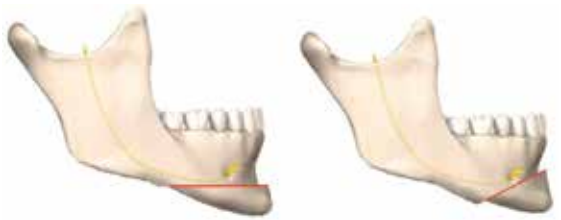

Figure 30. Augmentation genioplasty, reduction genioplasty, straightening genioplasty, and lengthening genioplasty are some procedures commonly used.

The most common osteotomy is sliding horizontal osteotomy [49, 50]. However, double horizontal osteotomy, hinge sliding osteotomy, oblique osteotomy for advancement, jumping genioplasty, wedge osteotomy, propeller genioplasty, triple osteotomy, quadruple osteotomy, and genioplasty using grafts or implants are also used.

A transoral incision is performed in the mucosa from the canine to canine with a good margin from the attached gingiva to make suturing easier. The mental muscles must be exposed and dissected to expose the bone. The second incision is made through the periosteum on to the bone. The periosteal attachment will be released, but the inferior anterior border should be untouched to keep the soft tissue contour unchanged and also keep the blood circulation intact. It is crucial to identify the mental foramen bilaterally. Then, the midline should be marked as a reference point, e.g., by using a burr or saw. A plus (+) sign can be used to mark the bone in the centre of the buccal cortex (**Figure 28**).

The osteotomy starts below the apical level of the roots (**Figure 28**), with a piezo ultrasonic or reciprocating saw. The osteotomy should be well planned with regard to chin shape and type of deficiency. Posteriorly, the angulation of the osteotomy can be altered depending on the treatment demands. This angulation results in the changes in vertical dimension of the anterior mandible. The posterior osteotomy must end at least 7–8 mm below the mental foramen (**Figure 30**) to avoid injury to the nerve bundle. The nerve canal is at about 5 mm below the mental foramen. When increasing the vertical dimension of the chin, bone can be applied to the gap. When reduction of the vertical dimension is planned, a parallel osteotomy to the first one can be performed and the segment in the middle can be pulled out (**Figure 29**).

The transverse dimension of the chin can be altered by segmentation of the symphysis area (**Figure 27**). If reducing the transverse dimension of the chin is planned, two parallel vertical osteotomies are performed laterally to the midline. The wound should be sutured in two layers. It is important to ensure the accurate position of the mental muscles before suturing the mucosa [49, 50].

5.4. Chin-wing osteotomy

In 2009, Albino Triaca described a different osteotomy, called chin wing osteotomy, for the correction of aesthetic dislocation of the lower face, either in the anterior part of the mandible

or for the entire border of the mandible base [51]. The name of the approach was coined due to the fact that the shape of the mandible base is like a wing (**Figure 31**).

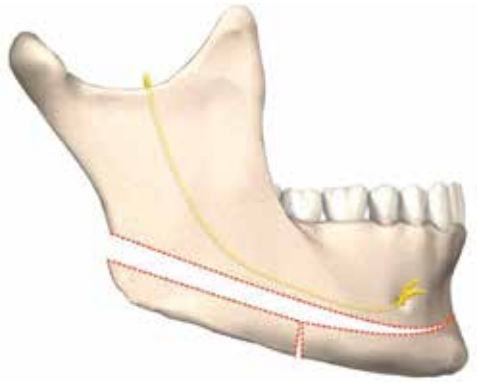

Figure 31 . Chin-wing osteotomy.

The incision is always intraoral and along the entire border of the mandible from the mandibular ramus to the opposite site below the dental arch. The mucoperiosteum will be raised to the same level of the cortex where the Chin-wing osteotomy is planned. It is important not to strip the periosteum caudally to allow a new blood circulation to the mandible. Particular care is taken near the mental foramen. Before performing this osteotomy, careful examination and identification of the location of the nerve bundle and canal is required by CBCT examination. The inferior mandibular nerve should not be placed buccally because the osteotomy is performed from the buccal cortex, and angulation of the osteotomy is in a somewhat sloping direction from superior to inferior below the nerve canal. A horizontal bicortical mandibular cut is then done with piezo-ultrasonic, reciprocating saw or a Mayfair bur (Maillefer Instruments, Ballaigues, Switzerland). The anterior region of the mandible can be cut in one or two segments. After osteotomy of the entire mandible, mobilization should be carried out very carefully not to fracture the mandible. The most dangerous place for fracture is around the mental foramen. Using this method, a change of the base of the mandible is possible, and the shape of the chin prominence can be adjusted sagittally and transversely without changing the tooth-bearing mandible and without influence on the Temporomandibular joint (TMJ). The method can also be combined with other osteotomies of the face [52, 53].

5.5. Lateral body osteotomy of the mandible

This osteotomy is widely used in selected cases of mandibular prognathism. This method is used especially when first or second premolars are missing or are planned to be extracted, and by using this method, a prosthetic reparation of intact teeth can be avoided. It is also desirable to use this method in the case of an anterior open bite, excess growth of the mandible with negative overjet located in the anterior dentoalveolar area of the mandible, to treat mandibular dental arch asymmetry.

This method can be used to reposition the anterior section of the mandible in every desirable direction, such as for posterior and superior repositioning. The method can be used for a block osteotomy or segmental or total alveolar osteotomy (**Figure 32**).

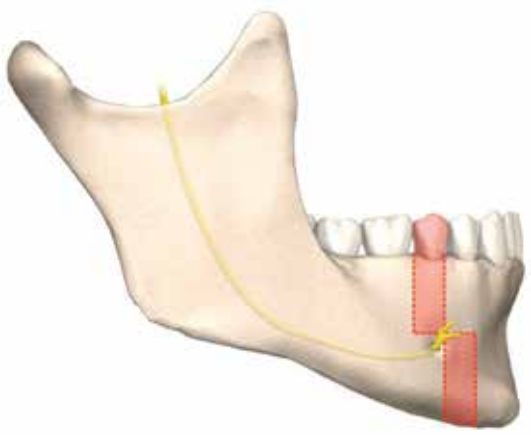

Figure 32. Lateral body osteotomy can be used for a block or segmental osteotomy or total alveolar osteotomy.

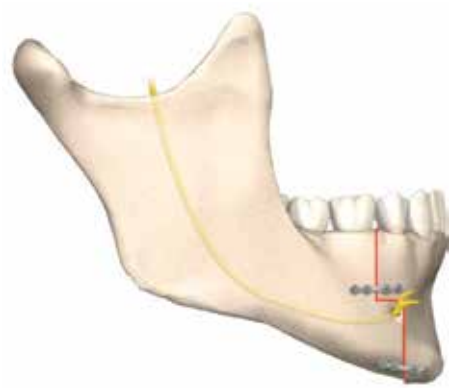

Figure 33. Fixation is performed with miniplates.

A transoral circumvestibular incision is performed following the extraction of the first premolars. The periosteal attachment will be released, but the inferior anterior border should be untouched to keep the soft tissue contour unchanged, and also keep the blood circulation undisturbed. An incision is made distally to the second premolar. The flap should be extended behind the second premolar to give sufficient access to the area. Care should be taken not to cause any unnecessary soft tissue stripping. The subapical area will then be exposed enough to achieve proper exposure for osteotomy. The osteotomy is horizontally placed subapical about 5 mm from the root apices and then will be connected with two vertical osteotomies at

the extracted first premolars. The horizontal osteotomy ends about 2–3 mm anteriorly to the mental foramen. The vertical osteotomies are preferably positioned at the extraction sites. Often, the vertical incision is performed with an anterior step osteotomy to avoid the inferior alveolar neurovascular bundle (**Figure 33**).

In this osteotomy, removal of premolar teeth and bone in the area of extraction sites is desired. After downfracture and separation, the anterior segment is repositioned posteriorly, at the same time extraction sites are closed. If no extraction is planned, the anterior section can be repositioned upwards to close an anterior open bite. The bone graft should be placed into the gap. It is important to remember to keep the excessive interdental bone to avoid periodontal problems.

5.6. Anterior subapical osteotomy

Anterior subapical osteotomy is suggested when the skeletal class I relation exists, and deformities in the front part of the mandible cannot be treated by orthodontic treatment. Some of the indications are as follows:

– Excess growth of the mandible with negative overjet located in the anterior dentoalveolar process of the mandible,

– The negative curve of Spee

– Some particular types of open bite

– Mandibular dental arch asymmetry

– When a lateral body osteotomy is planned, but the position of the chin is satisfactory

Figure 34. The subapical area is exposed far enough to provide sufficient access for the osteotomy.

Anterior subapical osteotomy method can be used to reposition the anterior section of the mandible in every desirable direction, such as posterior and superior repositioning.

A transoral circumvestibular incision is performed in the mucosa from canine to the canine with a good margin of attached gingiva. The periosteal attachment will be released, but the inferior anterior border should be untouched to keep the soft tissue contour unchanged, and also to keep the blood circulation undisturbed. After identifying the neurovascular bundle, the incision is extended carefully in the posterior direction to the premolar area. The flap should

be extended behind the first premolar to give sufficient access to the area. The mental muscles are identified and dissected to expose the bone. Care should be taken not to cause unnecessary soft tissue stripping. The subapical area will then be exposed far enough to provide sufficient access for the osteotomy (**Figure 34**).

The osteotomy is horizontally placed subapical, about 5 mm from the root apices and then connected with two vertical osteotomies between the canines and first premolars. Interdental osteotomy is performed with care to avoid injury to the roots. The anterior segment is subsequently repositioned superiorly to close the anterior open bite, and a bone graft is placed into the gap area. It should be kept in mind that interdental bone is essential to avoid periodontal problems.

5.7. Posterior subapical osteotomy

This method can be used for the correction of supereruption of mandibular posterior teeth or ankylosis of the posterior teeth.

A transoral incision is performed at the anterior border of the vertical ramus and is carried forward to the canine area. The incision is made around the margins of the teeth with starts one tooth behind the proposed osteotomy anteriorly and posteriorly. Two vertical, oblique incisions are connected to the horizontal. The periosteal attachment is released, but the inferior border is untouched to keep the soft tissue contour unchanged, and also to keep the blood circulation undisturbed. Again, the neurovascular bundle is identified and the incision is extended carefully in an anterior direction to the premolar area (**Figure 35**).

Figure 35. The neurovascular bundle is identified and preserved.

The osteotomy is horizontally placed subapical, about 5 mm from the root apices, and special care must be taken to preserve the mandibular canal. The horizontal osteotomy is connected with two vertical osteotomies between the first molar and second premolars. Interdental cuts should as always be done carefully with a chisel to avoid injury to the roots. The vertical

interdental cut is to be made from the buccal after downfracture and separation. The posterior segment can then be repositioned superiorly.

5.8. Inverted L and C ramus osteotomies

Trauner and Obwegeser presented inverted L and C ramus osteotomies in 1957 [35]. Indications for this osteotomy are horizontal mandibular deficiencies. This approach can be performed extraorally in the same way as vertical ramus osteotomy (**Figure 36**).

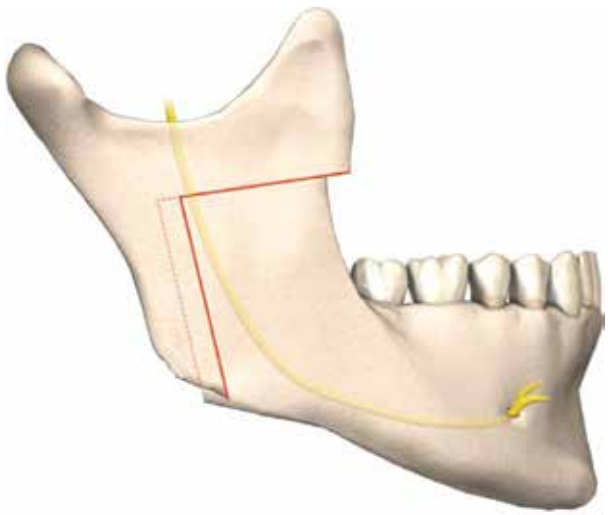

Figure 36. Extraoral inverted L ramus osteotomy.

The incision is very much like bilateral vertical ramus osteotomy. It starts with a 6 cm submandibular cut 2 cm below the angle of the mandible in the inferior border. Exposure of the entire ramus is done very carefully by dissection through the different layers of soft tissues.

A vertical osteotomy is placed behind the mandibular foramen to avoid nerve damage. This vertical osteotomy starts at the base of the mandible and is connected to a horizontal osteotomy that is placed above the mandibular foramen and below the sigmoid notch. For setback of the mandible, the proximal segment is placed laterally. The segments can be fixed rigidly by plates, or left without fixation, but then maxillomandibular fixation (MMF) for 6 weeks will be needed.

If an increasing of the vertical height or horizontal direction is planned, a bone graft can be placed in the osteotomy.

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Facial Lifting

Chapter 28

Facelift: Current Concepts, Techniques, and Principles

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Mohammad Esmaeelinejad,
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Additional information is available at the end of the chapter

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Abstract

The effects of aging on skin, including thinning and loss of muscle tone, result in a flabby or drooping appearance of the face. The demands of an attractive appearance and smooth skin are wanted all around the world. There are a lot of factors which influence the choice of rejuvenation techniques, including anatomy of the facial skeleton, the severity of aging changes, social and economic status of the patient, and structure of the skin. Facelifting is a facial rejuvenation procedure in which by dissection of subcutaneous layers and different suturing techniques we are able to stretch the skin and make the patient look younger. This chapter presents the technique, current concepts, complications, and indications of facelift surgery.

Keywords: aging, lifting, rhytidectomy, rhytidoplasty

1. Introduction

Facelifting, also known as a **rhytidectomy,** technically means removal of wrinkles by surgery to give a more youthful appearance to the face. Although the history of this surgery goes back to more than one hundred years ago, in recent decades it has become more popular because demands of being youthful in middle and senile ages have increased among people. Due to contemporary improvements in medical care and increased common knowledge about the importance of healthcare, the life-span of people all around the world, especially in the first world countries, has been significantly increased. As a result, the common problems associated with senility have gained more attention.

One of the main concerns is facial rejuvenation of wrinkles.

A wrinkle or **rhytide** is a crease in the skin. Skin wrinkles typically appear as a result of aging processes such as glycation [1]. There are other factors such as age spots, sun ray effects, tissue sagging, and volume loss, which may also lead to an aged face. The major role of each factor depends on the skin type of the patient. Sagging or drooping is more prominent in patients with thick skin whereas patients with thin skin usually manifest aging with wrinkles and volume loss.

Asian people have thicker skins than Caucasians; therefore, their chief problem is tissue drooping and have less wrinkles in their face. Due to their relatively thick skin, the weight of their tissue is considerably more than other groups and performing facelift surgery is more difficult. Wrinkles begin to form in the early 30s. They usually start in anatomic regions with the thinnest skin such as the periorbital area. As the body gets older, skin and subcutaneous fat loses its volume and the collagen and elastic fibers lose their elasticity, which results in superficial wrinkles.

This chapter briefly explains different approaches of facelifting as well as indications, advantages, and disadvantages of various modifications of facelift surgery, complications, and postoperative care.

2. History of facelift surgery

In early 1900, Hollander introduced the basic facelift surgery which only involved removal of excessive tissue along the hairline. In 1920, surgeons undermined the subcutaneous layer, which became the preferred technique. This method improved skin laxity, but it was unable to address the underlying soft tissues ptosis. Surgeons found that increased skin redundancy is not the only factor involved in aging processes and there are other factors such as ptosis of the deep soft tissues, skeletal deformities, and changes in skin texture which play a significant role.

In 1974, Skoog developed a technique which elevated a subdermal flap in continuity with the subplatysmal plane in the neck in order to address the deeper tissues. The skin and platysma muscle were elevated together as a unit to develop a more youthful jawline for the patient. Although Skoog's technique did not gain acceptance, it was a turning point in facelift surgery.

In 1976, Mitz and Peyronie defined the superficial musculoaponeurotic system (SMAS) [1]. In the late 1980s and early 1990s, based on Skoog's technique, Hamra introduced the deep plane rhytidectomy followed by composite facelift in order to improve the periorbital and nasolabial regions [2]. Owsley made this technique even better by describing the malar fat pad dissection and suspension to improve the nasolabial crease [3]. Ramirez introduced the subperiosteal rhytidectomy technique to improve the cheek, forehead, jowls, lateral canthus, and eyebrows [4].

[1] Non-enzymatic glycosylation is the result of typically covalent bonding of a protein or lipid molecule with a sugar molecule, such as glucose, without the controlling action of an enzyme.

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There have been a lot of comparisons between the risks and benefits of these methods. Less invasive methods which only included the superficial plane dissection showed decreased risk, reduced complications, lower morbidity, decreased convalescence, and more patient satisfaction.

More invasive methods, which included deeper plane dissections, showed more stable long-term results, better control of the midface and similar risks and complication rates as less invasive techniques. During the past decade, surgeons tend to reduce the complexity of facelift procedure and patients demanded less invasive and less complicated surgeries. Nowadays, due to younger age of facelift procedure, less invasive methods such as endoscopic technique, minimal incision facelift surgery and suspension sutures have gained popularity.

3. Facelift anatomy

Any surgeon who wants to perform a facelift procedure must know the anatomy of the face. The first layer in facelift anatomy is the skin. The dermal plexus of blood vessels is responsible for the skin and facelift flap blood supply. Usually, fat is left adherent to the dermal under surface of the flap to enhance its viability.

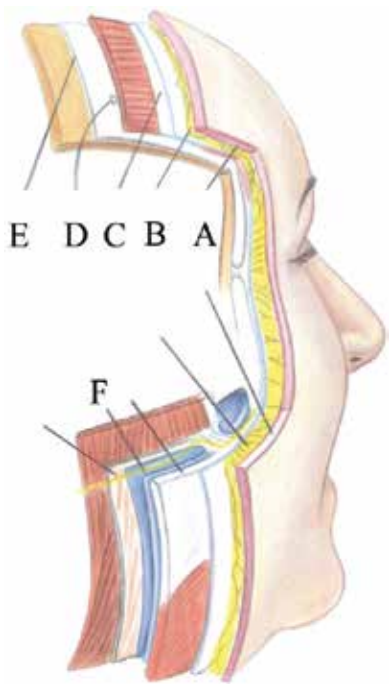

Figure 1. Anatomy of layers of the face. (A) Skin; (B) subcutaneous; (C) SMAS; (D) retaining ligaments; (E) deep fascia; (F) nerve.

The next layer is the subcutaneous layer. The fat in this layer is in close contact with deeper SMAS and superficial dermis. This layer can be safely undermined without damaging the anatomic structures. The subcutaneous layer has different thicknesses based on the location and patient. It becomes thickened over the malar region and is attached to it by ligaments running from the underlying periosteum through the malar pad and insert into the dermis. This area, also referred to as McGregor's patch, provides resistance when dissecting because of its fibrous nature.

The third layer is the SMAS layer. This layer separates the subcutaneous fat from the parotid-masseteric fascia and facial nerve branches. The SMAS layer is continuous with the galea in the scalp, the temporoparietal fascia in the temples, and the superior cervical fascia in the neck. SMAS is continuous with the platysma and separates two layers of fat in the face into superficial and deep layers. All of the facial muscle motor nerves are deep to this plane (**Figure 1**). When this layer is stretched or pulled, it moves the entire lateral face in the desired vector. In theory, this would allow the face to move more as a unit, thus making expression more efficient.

The fourth surgical plane is the sub-SMAS plane. It contains the facial nerve motor branches and the parotid duct. The parotidomasseteric fascia is the layer over the parotid gland and masseter muscle. By operating superior to this layer, the facial nerve branches are protected. Just as the SMAS is an extension of the superficial cervical fascia, parotidomasseteric fascia is also an extension of the superficial layer of the deep cervical fascia into the face and the deep temporal fascia above the zygomatic arch. By deeper and more anterior dissection beneath this layer, the chance of injury to the facial nerve branches increases.

There is a sub-SMAS loose areolar tissue plane extending from the anterior border of the parotid to the anterior border of the masseter. Blunt dissection in this plane gives the deep plane facelift (DPFL) dissection the ability to proceed safely even though it is almost intimate with the underlying facial nerve branches.

As the facial nerve branches move further anteriorly, they pass over the buccal fat pad and innervate the mimetic muscles. Facial nerve branches, parotid duct, buccal fat pad, and facial artery and vein are all part of the plane under the parotidomasseteric fascia. Dissection over the parotid gland must be done with great caution because although it is a safe plane, it may damage the facial nerve branches as they course out of the parotid gland and cross the masseter muscle.

Several other structures may be damaged in a routine facelift procedure. The greater auricular nerve and external jugular vein are in close contact with sternocleidomastoid muscle. The greater auricular nerve innervates the earlobe and cheek. These two are always superficial to the SMAS layer; hence, dissecting in the subcutaneous layer may preserve these structures.

4. Patient selection and evaluation

As any other cosmetic procedure, patient evaluation and selection are very important in the whole treatment plan. The surgeon should keep in mind that failing to plan is planning to fail.

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During the asking of chief complaint and taking case history, evaluation of psychological aspect of the patient must be done carefully. Never treat a SIMON[2] patient.

At first, the surgeon and the patient must have complete understanding of the procedure and the risk and benefits. Second of all, the surgeon must know the chief complaint of the patient. Next, a thorough medical and habitual history must be taken from the patient. Some drugs such as isotretinoin and vitamin E have adverse effects on healing and must be noted in the patient's history. Vitamin E supplements and NSAIDs or aspirin should be avoided at least 2 weeks before the surgery. Smoking and alcohol consumption can further delay the healing period and increase the skin flap necrosis. The patient must be persuaded to quit smoking 2 months before surgery.

Areas such as the jowls, prominent bands in the platysma, and a collection of submental fat are the most improved areas in facelift procedure. Thorough examination of these regions gives valuable clues about the treatment plan.

The face is divided into thirds. The upper third consists of the forehead and upper and lower eyelids, which are not typically addressed in superficial plane rhytidectomy. The middle third includes ears and cheeks. The surgeon must assess the amount of skin laxity in this region. The initial position of the earlobe must be noted because there may be a displacement after closure. The lower third includes chin, jawline, and neck [5].

Dedo classified neck profiles into the following subtypes [6]:

- Class 1: No submental fat, good muscle tone, and a well-defined cervicomental angle.
- Class 2: Cervical skin laxity and an obtuse cervicomental angle.
- Class 3: Submental fat accumulation; may require submental lipectomy.
- Class 4: Platysmal muscle banding.
- Class 5: Retrognathia and/or microgenia.
- Class 6: Demonstrating a low hyoid.

Based on this classification, the surgeon chooses the best treatment modality possible. In some cases, facelift surgery alone is not enough for attaining proper results, so other resurfacing procedures must be discussed with the patient that might be needed in future. Good marking of the patient's face and neck in upright position before scheduling for anesthesia has an important role in facelift surgery.

4.1. Indications for facelift surgery

The appearance of wrinkles, folds, and creases on an individual's face is the primary basis for a surgeon to agree to the operation. Skin drooping of the cheeks and jowls are among the factors indicating a person as a prime candidate for the facelift procedure. Other factors include

[2] Single, immature, male, overly expectant, narcissistic is a patient with excessive concern of their surgery and usually exaggerates a minor physical defect.

predominant eye bags, folds in the eye area (crow's feet and laugh lines), and a permanent crease above the bridge of the nasal region and folds in the forehead. Ideally, the patient should be around the age of fifty or below. Above this age may not be ideal anymore, because the work may be more extensive than for younger individuals. This means that more surgeries may be needed.

Another indication for rhytidectomy is the state of skin in the surgical site. Sun exposure is one of the main reasons of wrinkles. The sun basically makes the skin look older and constant exposure of skin to sun exacerbates this matter. Facelift can rejuvenate patients. It is important to remember that normal looking appearance is one of the primary goals after this kind of surgery.

4.2. Contraindications of facelift surgery

Relative contraindications are poor medical health, patients who continuously consume blood-thinning medications, patients with unrealistic expectations, and heavy smokers. Fine wrinkles which can be managed by nonsurgical or conservative treatment very well are contraindications of facelift surgery. Secondary facelifts should also be done with caution because the scar from the primary procedure may disrupt the original tissue planes and increase the risk of facial nerve damage.

5. Facelift techniques

5.1. Subcutaneous facelift

5.1.1. Procedure

Subcutaneous facelift or skin-only facelift was initially the major concept of the facelift procedure. Lexer presented skin-only facelift as a procedure in which the dissection is in a subcutaneous plane [7]. Subcutaneous dissection is needed in this technique so that muscular structure and SMAS remain intact. Facelift in this technique is consisted mainly of skin excision with primary closure. This method was the most popular modification of facelift for a long time. Although the role of subcutaneous facelift has diminished after deep layer (i.e., SMAS layer) was presented, the skin-only facelift is still suggested in selected patients.

This procedure is indicated in thin women with good facial skeleton as well as appropriate skin tone. Actually, this technique is suitable when the surgeon needs to only reduce the facial skin excess. Previous facelift surgery with SMAS plication is an indication for subcutaneous facelift procedure. The results of skin-only facelift are limited because of not addressing other senile facial structures. This technique is contraindicated in obese patients, especially with a non-ideal facial skeleton. Besides, this procedure is not appropriate in elderlies with severe aging changes and sagging of deep facial structures [8]. It is also important to consider that excessive subcutaneous dissection medially especially in smokers make the skin flap at the risk of ischemia [9].

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5.1.2. Advantages

This procedure is very simple and suitable for beginners. The dissection plane is above the SMAS layer which contains the facial nerve, so it decreases the risk of nerve injury in this technique. This procedure is associated with good recovery and is an appropriate technique in secondary facelift and after that [10]. The complications of this method are not significantly higher than other DPFL [10, 11].

5.1.3. Disadvantages

The long-term results of skin-only facelifts are not very good. This is a major concern for surgeons. This issue results from two reasons. First, skin viscoelasticity property causes loosening of tightened skin after a while [12]. Second, intact subcutaneous tissues are susceptible to ptosis after a period of time because they are not manipulated in this technique.

5.2. SMAS plication facelift

5.2.1. Procedure

Introducing and describing SMAS by Mitz changed the concepts of facelift [1]. This technique was suggested as a new method to manipulate the subcutaneous tissues to solve the senile changes of the face including skin wrinkles and deep soft tissue sagging simultaneously. The fibro-fatty composition of SMAS layer gives it greater strength against gravity than skin. The concept of SMAS plication technique was manipulating a stronger layer which can bear more loads than skin.

The dissection plane in this technique is supra-SMAS. After dissecting in the subcutaneous plane, SMAS layer is exposed. The mobile segment of SMAS layer is fixed to the posterior relatively immobile layer (i.e., parotidomasseteric fascia) by mainly three sutures in a vertical direction. The excess of SMAS layer could be trimmed after suturing to prevent bulging. This technique is indicated in middle-aged patients with thin skins and moderate to severe laxity. Obese patients with thick skin types are not candidates for this technique.

5.2.2. Advantages

SMAS plication seems to be an easy procedure with little risk for facial nerve damage. Despite manipulation of SMAS layer, the dissection plane is above this layer and the facial nerve plane which let this method to be a relatively safe procedure. The surgery time is short and the recovery would be good in this technique. This technique may have a better esthetic result in midface area than DPFL [13]. On the other hand, the surgeon may be able to manipulate skin movements by SMAS plication procedure comparing to MACS lift and less invasive than sub-SMAS procedures [14, 15].

5.2.3. Disadvantages

Resolving neck aging is more difficult by this technique than DPFL. This issue is related to the inadequate release of platysma facial attachments [16]. SMAS plication is more invasive than some other lifting methods such as MACS lift [14]. The surgeon is not able to manipulate deeply positioned soft tissues under SMAS layer, which results in relatively short-term outcomes comparing to DPFLs.

5.3. Minimal access cranial suspension (MACS) lift

5.3.1. Procedure

The main concept of MACS lift was the difference in vector of traction. The skin is re-draped in an oblique direction in traditional face lifting. In MACS procedure, the horizontal vector of traction is avoided and skins simultaneously with under soft tissues are moved vertically [17] (**Figure 2**). MACS procedure is mainly divided into two types: simple and extended. The simple variation of MACS technique is used to correct the lower third of the face and aging appearance of the neck including jowling and the cervicomental angle by using two purse-string sutures. Extended MACS lift was presented to correct nasolabial groove and midface and lower eyelid senile changes [18]. The incision in the latter form of MACS technique is

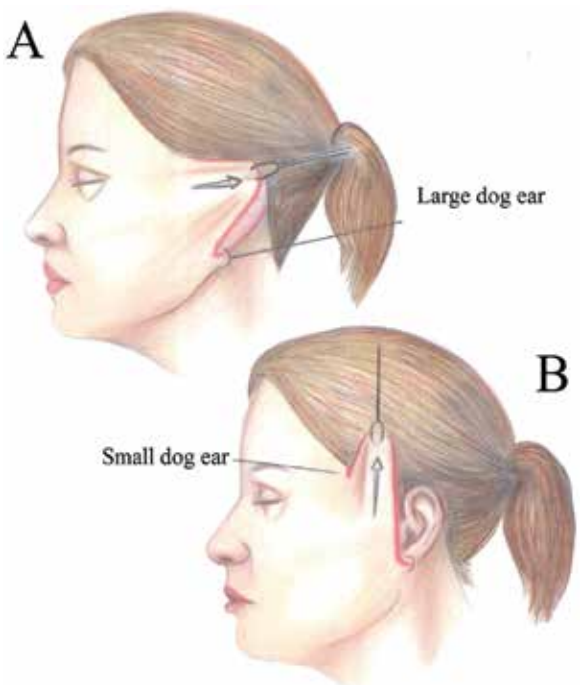

Figure 2. (A) The wrong direction of facelifting forms a large dog ear under the ear lobe. (B) The correct direction of lifting in MACS technique omits the dog ear.

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extended along the temporal hairline and a third purse-string suture is used to suspend the malar fat pad (**Figure 3**).

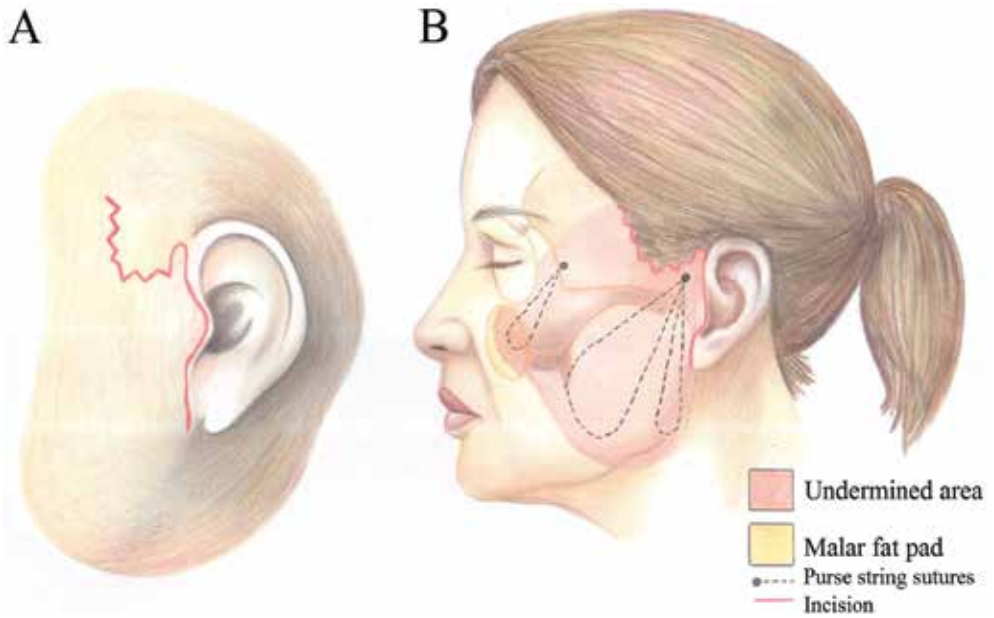

Figure 3. (A) Incision line in MACS technique. (B) Undermining area in MACS technique.

Submental liposuction is performed before starting MACS lift. The incision is made from lower limit of the lobule going through the pre-auricular crease upwards. The upper limits of the incisions in simple and extended variations are at the level of the lateral canthus and the level of the tail of the eyebrow, respectively. This procedure is performed in the pre-SMAS plane above the plane of facial nerve path. Dissection is performed two fingers below the angle of mandible. The purse-string sutures are used to fix the deep temporal fascia in the simple variation. In the extended variation, the third u-shaped purse-string suture is placed between the anterior part of the deep temporal fascia and the malar fat pad. The skin is excised after re-draping in a vertical direction.

5.3.2. Advantages

There are several advantages of MACS procedure suggested in the literature. Small skin incisions and limited subcutaneous dissection are the major advantages of this technique. The risk of facial nerve damage is low due to supra-SMAS dissection. The results are good and the recovery is rapid in this technique. The surgeon is able to re-drape the skin of the lower third of the face, correct the senile changes of the neck, and correct the cervicomental angle [19].

The MACS lift is a shorter procedure than SMAS imbrication with high patient satisfaction and low morbidity. The short incision in MACS lift is a major advantage in this technique,

especially in young patients. Avoiding the postauricualr incision in this method makes this procedure acceptable in young patients who usually pull their hair up. The risk of hematoma is low in this technique. Besides, hematoma is easily evacuated and usually does not track into the neck. The dog ear formation under the ear lobe is prevented in this technique, owing to the vector of traction [20].

5.3.3. Disadvantages

The limitations of MACS lift procedure are mainly associated with the anatomy of the patient. The results of this technique are not very good in patients with a bulky neck and significant skin laxity [21]. The final neck contour is unsatisfactory in bulky neck patients due to limited skin excision and pure vertical vector of skin re-draping. The improvement would be less optimal in the latter group. There is a chance of skin flap irregularity regarding to the excessive bunching of the purse-string sutures. Avoiding the ligamentous lysis in this technique prevents the long-term results of MACS lift, especially if the sutures pull through. The cheese wiring effect is also more probable in this facelift modification.

5.4. Deep plane facelift (DPFL)

5.4.1. Procedure

Deep plane rhytidectomy was suggested in place of traditional face lifting to correct aging changes of midface (i.e., malar fat pad) and nasolabial grooves. The deep plane modification was presented by Hamra for the first time [2]. The main concept of this technique was based on reversing gravity's effect by manipulating deep soft tissues to make more satisfying changes in older patients.

In the beginning of the procedure, subcutaneous dissection is performed 2 to 3 mm anterior to the tragus. SMAS layer is then incised after a few millimeters exposure. The dissection plane is the sub-SMAS plane. There are three main reference points during dissection of DPFL (**Figure 4**). Orbicularis oris is the first reference point which should not considered as a part of the flap in deep plane dissection. Good esthetic results would be achieved by incorporating most of the soft tissue into the flap. The zygomatic major muscle is the second important reference point. Deep plane dissection is continued superiorly to the border of this muscle. The last reference point is the zygomatic minor muscle. Zygomatic cutaneous ligament as a major facial retaining ligament is lysed directly. It is necessary to release this ligament to mobilize the midface completely. The final flap consists of skin, subcutaneous tissue, and malar fat pad [22].

Patients with significant aging changes of midface and mentolabial fold are good candidates for this procedure. This method is not suggested for patients with irrational expectations and with poor medical health. This procedure is not suitable in secondary facelift unless the first one was not a sub-SMAS procedure. Although DPFL is indicated for smokers in some investigations [23], the surgeon should be aware of increased risk of wound-healing complications.

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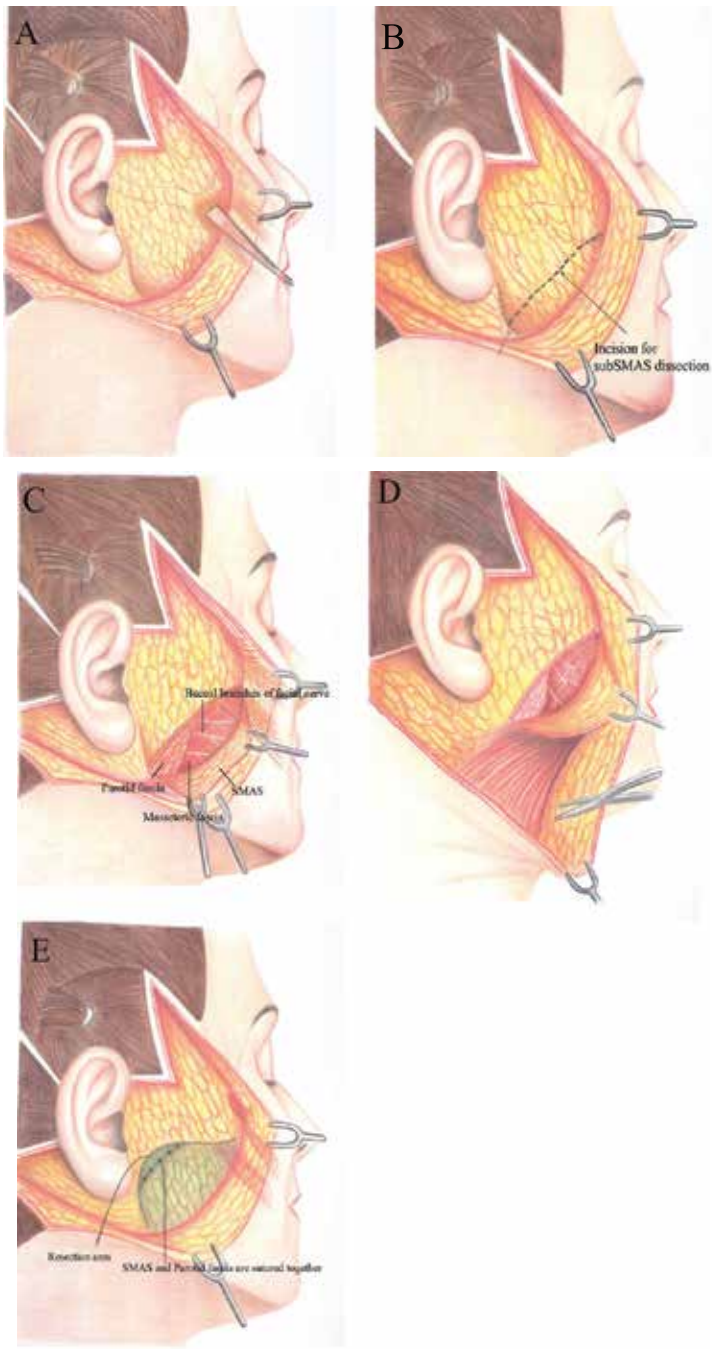

Figure 4. Deep plane rhytidectomy. (A) Subcutaneous dissection is performed 2–3 mm anterior to the tragus. (B) SMAS layer is then incised after a few millimeters exposure. (C) The dissection plane is the sub-SMAS plane. (D) Dissected SMAS layer is obvious. (E) The SMAS layer is sutured to the parotid fascia at the end.

5.4.2. Advantages

This procedure is performed to gain good results in improvement of nasolabial folds. The results of this technique are relatively longer than other supra-SMAS techniques [24]. The surgeon is able to lyse the major facial retaining ligament (i.e., zygomatic cutaneous ligament) and assess the herniation of buccal fat pad directly. Dissecting in sub-SMAS layer and manipulating deep soft tissues of the face give rise to major changes and improvements of senile faces.

5.4.3. Disadvantages

This facelift modification is associated with higher risk of facial nerve damage. Mono-plane dissection in this procedure does not give the surgeon the ability to move different layers including skin, subcutaneous, and SMAS layers in various directions.

5.5. Extended SMAS lift

5.5.1. Procedure

Presenting sub-SMAS dissection by Lemmon was rapidly accepted by cosmetic surgeons [25]. Supporting the overlying skin by manipulating deeper soft tissues (i.e., SMAS layer) is the key concept of sub-SMAS modifications. Although SMAS plication seems to provide better results where the SMAS layer is thin, dissection of thick SMAS layer obtains more satisfactory outcomes.

This technique was presented by Stuzin et al. in 1995 [26]. The main procedure protocol in this method is dissecting and drawing skin and SMAS flaps separately. At first, the skin flap is dissected in the subcutaneous plane. The SMAS layer is incised, after which dissection is continued in sub-SMAS plane.

There are five critical landmarks during performing extended SMAS facelifting [27]:

The first point is 1 cm inferior to the zygomatic arch, which is the origin of the frontal branch of the facial nerve. The incision to start sub-SMAS dissection is from this point.

The second important landmark is the beginning point of releasing and dissecting the platysmal auricular ligament. This second landmark is 3 cm below the earlobe.

The third point is 5 cm below the mandibular angle, which is the inferior extent of sub-platysmal dissection.

Fourth landmark is the anterior border of the sub-platysmal dissection, which is identified by the facial vein where it crosses the inferior border of the mandible.

The last landmark is the zygomaticus major muscle, which is the anterior limit of sub-SMAS dissection in the cheek.

The vector of stretching the SMAS layer is different from the skin's [28]. The vector of retracting the SMAS layer is more vertical than the skin flap. The SMAS and platysma flaps can be rotated

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in the postauricular area to improve the jowl and cervical contour. The SMAS flap is advanced superolaterally, perpendicular to the nasolabial fold in the malar fat pad area.

5.5.2. Advantages

The surgeon is more able to reverse the effects of the aging process by manipulating skin and SMAS flaps separately. The outcomes of this technique are long lasting due to releasing the facial ligaments and repositioning of the malar fat pad. As it was mentioned before, we are capable of replacing the malar fat pad by this technique. Maximum effects on lower face and neck can be achieved by creating a continuous SMAS-platysmal flap. The unnatural appearance of skin, which sometimes is seen in other facelift techniques, is prevented by reducing the tension of the skin flap due to separating the skin and SMAS flaps.

5.5.3. Disadvantages

The operation time of this technique is relatively longer than other modifications. This procedure is technically sensitive and needs a lot of experience to dissect the soft tissue of the face in two separate parts. The risk of facial nerve damage is relatively high is this method. Extensive dissection of the skin places is at a higher risk of necrosis. The compromised viability of the skin flap is a major concern in this technique. This procedure is not indicated in younger patients with mild aging changes and youthful lower face and neck. Less invasive procedures such as short scar facelift techniques are preferred in these patients.

5.6. Lateral SMASectomy

5.6.1. Procedure

Lateral SMASectomy was first described by Baker [29]. Lateral SMASectomy or limited SMAS procedure is a facelift modification in which the lateral portion of the SMAS located between the mobile and the fixed SMAS is removed.

Classical facelift procedure is begun at first until the SMAS layer is exposed. Superficial fascia covering the anterior border of parotid gland is excised and discarded. The anterior SMAS layer which is mobile is stretched in a superoposterior direction and fixed to the posterior fixed SMAS layer. The vector of tracing the SMAS layer is perpendicular to the nasolabial fold. Manipulating the SMAS layer is the key concept in determining the stability for satisfactory results (**Figure 5**).

This facelift method is indicated in patients younger than 50 with moderate skin laxity and moderate jowls. There should not be medial platysma bands present on normal animation although submental fat may be observed [30]. This technique can be performed in microgenia patients. This procedure is not indicated in the patients over 60 with severe skin laxity in the neck area.

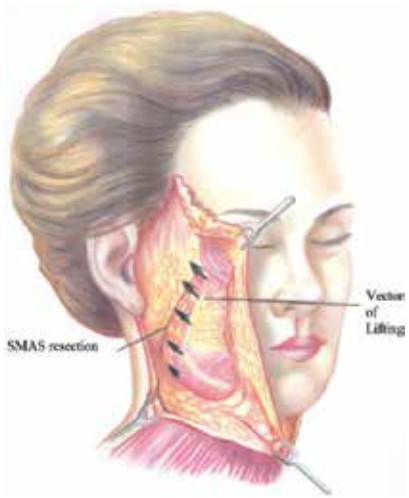

Figure 5. Vector of elevation in SMASectomy technique.

5.6.2. Advantages

The outcomes of this procedure continue much longer than SMAS plication technique due to the stronger fixation of SMAS layer. This technique is relatively easier than complicated procedures such as DPFL and composite facelift. It is a simple technique with minimal SMAS dissection and predictable postoperative results [31]. The postoperative pain may be more tolerable than MACS lift with similar short-term results [19].

5.6.3. Disadvantages

Manipulation of deep soft tissue is limited in this technique as in SMAS plication method. The intact facial ligaments after performing this surgery and limited advancement of deep facial tissues make the results less satisfactory [28]. The risk of facial nerve injury is relatively high in the current method. Preserving the integrity of SMAS layer after removing the indicated part is sensitive and needs experience [31]. The visible scar in this technique is a drawback compared to the short scar facelift modifications; the operation time is longer than MACS lift procedure [19].

5.7. Subperiosteal facelift

5.7.1. Procedure

Tessier proposed the subperiosteal facelift technique for the first time [32]. It is possible to lift the soft tissues of the face vertically and reposition them at the level of their bony origin. This technique rapidly developed and was accepted as a suitable procedure for lifting the upper two thirds of the face.

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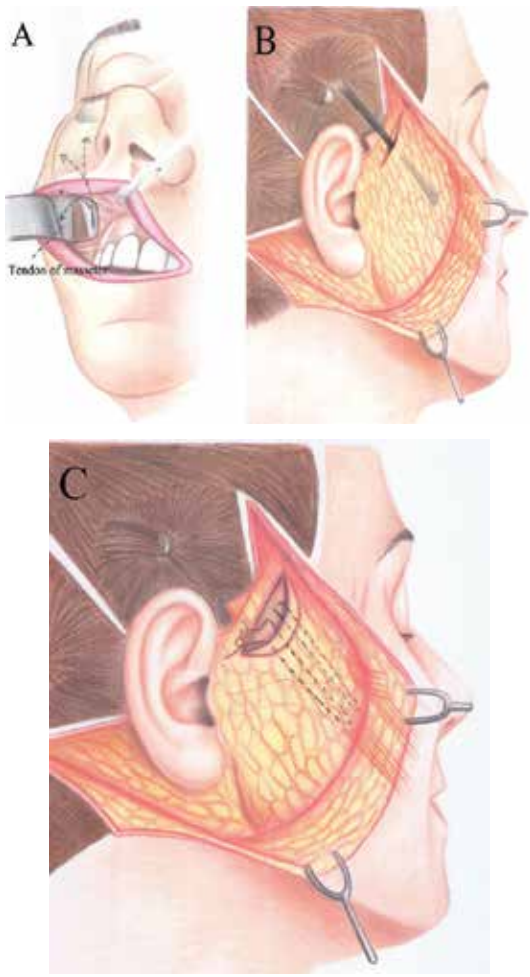

Figure 6. (A) Intraoral dissection to provide direct exposure of subperiosteal dissection. (B) Temporal incision to dissect zygomatic area subperiosteally. (C) Suturing the midface soft tissue to the temporalis fascia.

There are three main landmarks in subperiosteal facelift [33]:

The first is the SOOF [3]. This landmark is located at the cross point of two imaginary lines which pass through the lateral of the eyebrows and inferior orbital rims.

The malar fat pad is the second important landmark in this procedure. The location of this point is at the cross of a vertical line passing through the lateral canthus and the horizontal line passing through the superior margin of the nasal alae.

The last point is Bichat's fat pad, which is located at the cross point of the vertical line passing through the lateral canthus and the horizontal line passing through the nasal base.

[3] Suborbicularis oculi fat.

Subperiosteal dissection is performed through the incision in the temporal area (**Figure 6**). The three mentioned points are lifted and sutured to the deep temporalis fascia. The SOOF, malar fat pad, and Bichat's fat pad are sutured and suspended to the deep temporalis fascia laterally, centrally, and medially, respectively. Nowadays, intra-oral subperiosteal dissection is more popular due to decreased operation time and reduced nerve damage risk [34].

This procedure is indicated in the patients with significant aging changes. Endoscopic subperiosteal facelift is an appropriate approach in patients with good skin tone. The other indication of this technique is in the patient who needs other simultaneous cosmetic procedures like skin resurfacing and implant or fat transfer. This method is suitable in raising the eyebrows, eyelid lateral corners, forehead, glabella, cheeks, and nasolabial fold.

5.7.2. Advantages

This technique includes less incisions, use of endoscope, better fixation and allows for repositioning of the buccal and malar fat pads. Satisfactory results in correcting orbital festoons and brow ptosis are possible by this method. The risk of facial nerve damage is very low in this technique. Long lasting results of this method are expected due to manipulating deeper tissues and good fixation. The vascularity of the flap is maintained by minimal dissection and keeping whole layers together, which is an important advantage of this procedure in smokers. The face appears more natural comparing to SMAS lifting methods.

5.7.3. Disadvantages

This facelift technique is not suitable to use as the second facelift surgery. This procedure is relatively contraindicated in patients with a history of facial bone fractures. Irregularities of the face make the subperiosteal dissection much harder.

Prolonged operation time and recovery period are the major drawbacks of this technique. This technique is not suitable for correcting the aging changes of the lower third of the face and neck.

6. Post-operative care after facelift surgery

Facelift surgery is one of the most dramatic procedures for rejuvenation. The success rate of the surgery relies on the surgeon and the patient as well. The surgeon cannot gain satisfactory results unless the patients follow the post-operative care properly.

6.1. Immediately after surgery

The patient should be in complete bed rest for the first 24 hours after surgery. The patients will be wrapped in dressings that will not be removed until 24 hours later. The patient's head must be elevated for at least the first week after surgery. They should not sleep on the side of their face but rather sleep supine with the back of the head on the pillow for about 2 weeks. The

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surgeon should prescribe pain medications to prevent pain. The activities of the patient should be restricted the day of surgery and up to a week afterwards. The patient should place ice packs over the surgical site.

6.2. Bleeding

Mild bleeding from the surgical site is not unusual. Head elevation and applying an ice compress with mild pressure about the face and neck usually decrease the bleeding. Elevation of the patients' blood pressure by bending, sneezing, lifting, coughing, straining, straining on the toilet, and other strenuous activities are the main causes of bleeding. The patient should refrain absolutely from activities that may increase blood pressure for 10 days after the surgery to avoid complications from bleeding.

6.3. Swelling

Edema is a routine finding of any surgery. The amount of swelling is dependent on the looseness of the tissues and the amount of manipulation varies from person to person. Swelling around the eyes, cheeks, face, and down into the neck and chest are not uncommon. Swelling starts immediately following surgery and will reach its maximum 2 to 3 days post-operatively. Edema will decrease after the third day. The swelling will cause the skin of the face feel tight for a while. It may interfere with smiling before disappearing within a few weeks.

6.4. Pain

Acetaminophen may be taken every 4 hours for mild pain. NSAIDs are not recommended for the first several days after surgery because of the increased risk of bleeding and/or bruising. Narcotics are indicated in severe pain. The patients should avoid alcoholic beverages since it enhances the effect of the narcotics. Pain and discomfort usually decreased after the first 2 to 3 days. Persistent pain may need attention.

6.5. Diet

Clear liquids should be initially taken after general anesthesia or I.V. sedation. Over the next several days, a high calorie, high protein intake is very important. Supplements should be taken regularly. The patient should not be dehydrated by taking fluids regularly. Keeping well hydrated also prevents nausea and vomiting.

6.6. Wound care

The patients should start cleaning the skin incisions the day after surgery with soap and water three times per day very gently and pat dried (do not wipe). The incisions should be dried and cleaned with a 50% solution of 3% hydrogen peroxide. The hydrogen peroxide should be mixed with an equal amount of warm tap water and a Q-tip should be used to clean the incisions. The incisions should be covered with antibiotic ointment after that. Incisions should not be allowed to become dry or crust over.

6.7. Discoloration

Discoloration of the skin following swelling occurs in some cases. Blood spreading beneath the tissues leads to development of discoloration. This is a normal occurrence in most patients which occurs 2 to 3 days post-operatively. Applying moist heat to the area could speed up the removal of the discoloration. Bruising is rare in younger patients, and sometimes yields as a slight yellow discoloration. In older patients, bruising can be quite significant and is represented as black and blue discoloration. Bruising of large degree may take approximately 2 weeks to resolve.

6.8. Antibiotics

The patient should be prescribed the antibiotics on-time to prevent postoperative infection.

6.9. Nausea and vomiting

In the event of nausea and/or vomiting following surgery, do not give anything by mouth to the patient for at least an hour including the prescribed medicine. Anti-emetic drugs are useful to prevent nausea.

7. Complications of the facelift procedure

Some of the complications of facelift surgery are hematoma (the most common complication), pre- and postauricular scar hypertrophy, facial telangiectasia, stitch abscess, neck hyperpigmentation, pre- and postauricular skin necrosis, nerve damage, temporal alopecia cutaneous sloughing or necrosis, seroma, wound dehiscence, hypertrophic scarring, contour irregularities, dimpling, and infection [35–42].

The most dangerous complications include hematoma (rates 1.0–15%), infection (0.05–0.18%), nerve injury (0.07–2.5%), skin sloughing (1.0–1.85%), and systemic vascular complications like venous thromboembolism (VTE 0.1%) [37, 41, 43, 44]. It has been reported that the complication rate in patients with a high body mass index (BMI) over 25 was 9.5%, compared to 4.7% in normal weight patients undergoing a facelift [43].

7.1. Hematoma

Hematoma formation remains the most common major complication after facelift surgery [45–47]. Common themes in patients who may experience hematoma following facelift include male sex, hypertension, preoperative medications that affect coagulation such as aspirin use, smoking, BMI, pre- and post-surgical blood pressure spikes, retching vomiting, post-surgical activity, and nausea [46, 47].

Hematomas in face can cause tissue ischemia, long-term edema, hyperpigmentation, and patient complaint. The incidence of hematoma reported 0.2–8.1% (needs a space between reported and 0.2) in articles [35]. Studies that document the occurrence of hematoma formation

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following facelift surgery includes the use of drains in the surgical site which have some problems such as introducing infection into the wound, leakage, and being displaced [48, 49]. They create tracts at the site of removal, necessitate painful extraction, and risk injury to vessels on removal.

The incidence of hematoma following male rhytidectomy is lower than facelift in females although the incidence of hematoma in men remains higher than that in women in 30-year-old patients [49]. Meticulous perioperative blood pressure control significantly reduces the rate of postoperative hematoma formation [45]. Large hematomas can cause skin necrosis and need to be promptly evacuated.

7.2. Infection

Infection is the second most common major complication occurring in 0.3% facelifts. Combined procedures and high BMI are risk factors for developing major infection. A post-facelift infection is most commonly caused by *Staphylococcus aureus* [37, 38].

7.3. Nerve injury

Injury to the facial nerve during a face lift is a relatively rare but serious complication. Understanding of the anatomical course of the facial nerve and the relative danger zones can prevent this complication [50].

Two of the most feared complications of facelift surgery are motor and sensory nerve damage and flap necrosis [51]. Different injuries can result in frontal, buccal, zygomatic, marginal mandibular, and cervical nerve damage, including direct injury, neurapraxia, thermal injury from cautery, compression injury from sutures, edema, or hematoma. The greater auricular nerve is the most common sensory nerve that may be damaged during the facelift procedure.

7.4. Edema and ecchymosis

Although some degree of postsurgical edema can be seen in all patients undergoing a facelift procedure, some of them show impressive swelling. Patients undergoing multiple procedures, including brow lift, midface implantinsertion, lip implants, and simultaneous laser resurfacing can swell to alarming proportions [52].

7.5. Skin slough

Skin slough is a rare occurrence following face lift. The skin flaps are monitored closely during the postoperative course. Usually, vascular compromise is noted in the preauricular region and may appear as a distinct area of ecchymosis [41].

7.6. Scarring

With a well-designed and well-executed facelift, noticeable scars are unusual, following a face lift procedure.

7.7. Alopecia

There is very little information associated with development of dermatological conditions after cosmetic surgical procedures, including hair transplantation and facelift surgery. Alopecia occurs following damage to the hair follicles from electrocautery, excess traction or tension on the skin flaps, and involuntary elevation or elimination of the temporal hair tuft [41].

7.8. Contour deformities

These temporary deformities are common immediately after rhytidectomy. The preauricular and submental regions are the usual regions of these deformities occurrence which are related to post-surgical edema or ecchymosis [41].

7.9. Flap necrosis

Flap necrosis following facial rhytidectomy is an irritating complication, both to the patient and to the surgeon [53]. Necrosis of the lipocutaneous flap may result in permanent scars and prolonged recovery. Causes vary from bandage compression, sleeping position of the patient, flap sutures under tension, inherent healing difficulties, and no detectable cause. Although smokers or patients with compromised health are more common to encounter this complication, flap necrosis may happen in the best conditions [52].

7.10. Systemic complications

Major complications included deep vein thrombosis (DVT), pulmonary embolism, blood transfusions, stroke, important anesthetic complications, and death [41].

8. New trends in non-surgical rejuvenation

Understanding the facial anatomy and its changes through aging has led to development of different facelift techniques that focus on being less invasive and less traumatic and also providing long-lasting results [54]. Numerous non-invasive face rejuvenation techniques have been investigated over the past decade to improve the results of the procedure and to avoid incisional surgery. Some of the treatment options are as follows: radiofrequency (RF) and ultrasound therapy that are useful in skin tightening/laxity. Also, there are numerous liposuction techniques/devices and injectable cytolytic drugs for submental fat reduction. Fractional lasers and RF devices, chemical peels, micro-needling, intense pulsed light (IPL), injectable fillers, pigment and vascular lasers, liquid nitrogen therapy are useful in superficial dyschromias and rhytides/crepe skin. Moreover, neuromodulators may enhance platysmal banding. Various types of fillers and volumizers including autologous fat, hyaluronic acid (HA), and injectable poly-L-lactic acid (PLLA) calcium or hydroxylapatite (CaHA) are used. A novel bimodal technique to restore volume loss facial structures for panfacial lipo-atrophy with PLLA has been introduced [55, 56].

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A novel, minimally invasive, RF device employing a bipolar micro-needle electrode system is introduced, varying the pulse length allowed for fractional sparing of dermal tissue. In some studies, bipolar mode delivering energy directly within the dermis using five micro-needle electrode pairs is used with real-time feedback of tissue temperature for treatment control. Superficial cooling is achieved with a Peltier device [57].

The thermaCool TC (Thermage Inc.) is a RF device to induce tightening of the addressed skin problem via a uniform volumetric heating into the deep dermis tightening, resulting in a "nonsurgical facelift". RF produces a uniform volumetric heating into the deep dermis. Gradual tightening is produced by this technique in most patients with no adverse effects [58, 59].

Laser, light, and RF energy sources have succeeded in treating the second category of skin aging; however, the surgical facelift is still the gold standard in treatment of laxity associated with intrinsic aging [60].

Laser resurfacing was presented in the 1980s with continuous wave carbon dioxide (CO_2) lasers; however, because of many side effects, including scarring, short-pulse, high-peak power, and rapidly scanned, normal-mode erbium-doped yttrium aluminium garnet lasers and focused-beam CO_2 lasers were developed to remove skin in a precisely controlled manner [61]. Laser skin tightening is an FDA-approved method for the reduction of fine wrinkles and skin laxity. Laser skin tightening is a non-surgical, minimally invasive technique that uses an infrared light source to tighten skin through collagen heating under the skin's surface, causing the skin to contract [62]. Facial rejuvenation using polydioxanone (PDO) thread is a safe and effective procedure associated with only minor complications in cases of fine wrinkles, face sagging, and marked facial pores [63].

One important advance in facial rejuvenation is the use of fiber endoscopic video-assisted technique in aesthetic plastic surgery of the face. It substitutes the coronal incision with no skin resection and leads to a vertical reposition of the mobile soft tissue of the midface in indicated cases. It needs only a small incision of the scalp just behind the coronal incision and in the temporal area [64].

Pak et al. introduced a nonabsorbable polypropylene mesh as a newface lifting instrument, with the nasolabial fold as the main target area. Face lifting using a nonabsorbable mesh can improve nasolabial folds without serious adverse effects. So, this is a safe and effective technique in midface rejuvenation [65].

Incorporation of selective fat compartment volume restoration through SMAS manipulation allows for improved control in recontouring while addressing the problem of volume deflation in facial aging. Facial rejuvenation is described through merging two key important points based on lift-and-fill face lift: (1) lifting and tightening tissues in differential vectors according to original facial asymmetry and shape; and (2) precious facial contouring through selective fat compartment filling of malar locations (deep and high) and graft of nasolabial fold fat [66].

9. Summary

Cosmetic surgeries including facelift operation are becoming increasingly popular, and facial rejuvenation remains one of the most commonly requested aesthetic procedures. Many lifting procedures can be used in order to reduce sagging of skin and subcutaneous tissues and create a more youthful face. In the forehead and eyebrow region, the direct brow lift, temporal brow lift, transferable pharoplastic brow lift, coronal brow lift, and the endoscopic brow lift can be identified. The facelift is considered in the mid-face. Classic facelifts can be divided into the one layer, two layers, and the deep plane facelift (DPFL). The incidence of postoperative complications associated with lifting procedures is rare, but clinically important. Hematoma, skin necrosis of the wound edges, infection, nerve injuries are some of these complications. Today, the tendency toward minimally invasive procedures with smaller risk of complications and shorter recovery period are desired.

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Facial Transplantation

Chapter 29

Basics of Facial Transplantation: Surgical Principles and Management of Risks

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Additional information is available at the end of the chapter

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Abstract

Facial transplantation offers an alternative approach towards restoring gross facial disfigurement. Since its advent in 2005, the surgical principles have become continually refined depending on the nature of the injury and anatomical requirements posed by the recipients. Owing to the complex nature of the procedure, it bears a number of different risks. These have included graft rejection from alloimmune responses, complications from the effects of immunosuppression and risk of mortality; in addition, there is an inherent predisposition for the development of psychological complications. This chapter outlines the stepwise process of conducting a facial transplantation with emphasis on key surgical principles. It also provides details with case examples of how to minimize complications associated with the procedure.

Keywords: risks, facial transplant, surgical principles, complications, composite tissue allograft

1. Introduction

Facial transplantation has revolutionized complex forms of reconstruction where conventional procedures have produced suboptimum results [1–3]. Originally conducted in 2005 [4], it has redefined the technical boundaries of plastic surgery with many more having been conducted globally. However, performing a facial composite tissue allotransplantation (CTA) poses a significant number of challenges, which were anticipated early on [5]. Psychological complications can be profound [1] and therefore pre-operative mental assessment is vital [6, 7] to ensure engagement with the long-term multidisciplinary team therapy. Failure to do so has resulted

in mortality in one case due to lack of compliance with the immunosuppressive regime [1]. Acute rejection episodes have affected all allograft recipients [1, 8, 9] with one patient having had sustained a chronic rejection of the CTA [10]. The adverse effects of immunosuppression have been depicted within the literature, most notably an increased predisposition towards acquiring infections, which have affected a significant proportion of recipients [1]. Functional outcomes have so far exceeded expectations with all patients having demonstrated good motor and sensory development [4, 8, 11]. Motor recovery has, however, been slightly lagging in comparison to neurosensory restoration [1, 3, 12]. There have been three post-operative mortalities associated with facial CTAs so far [1]. Miscellaneous complications including renal insufficiency, blood loss and neoplasia development have been encountered too [1]. This chapter aims to draw focus towards the management of risks in facial transplantation and offers an insight into revising existing protocols. In addition, an overview concerning the principles of surgical approach in performing the procedure is addressed.

1.1. Ethical aspects

Ethical debates raised in the case of facial transplantation emphasize on the significance of the risks associated with the procedure taking into account that is not considered life saving but life changing [13]. In addition, the face unlike other forms of organ transplantation is unique to each person and represents one's individuality; the ethical dilemma, therefore, of a transfer of identity is an issue debated by many. So far, however, many of these concerns have been answered with the promising results of transplanted CTAs. No psychological complications of an identity crisis have yet been reported in the literature. All individuals have shown great functional improvement thus justifying the importance of the procedure [1]. Despite this, the associated risks have still meant that clinical and public opinion remains divided regarding the ethics of the surgery.

1.2. Malformations

Severe facial malformations not amenable to routine reconstructive methods serve as ideal indications for facial transplantation. So far, reports have included injuries sustained from shot-gun injuries, animal attacks, carcinomas and burns [1]. Such is often the severity of these defects that it would require countless surgeries over many years and still this would only be expected to produce suboptimum results. The unique ability of facial composite tissue allografts to correct gross disfigurement successfully in a single procedure has made it an ideal option.

1.3. Donor and recipient matching

It is important to identify the correct donor and recipient match for the surgery to be successful. Age, race, skin colour and blood type are some of the important considerations to take into account. This will lead to a more aesthetic outcome in keeping with the rest of the recipient's physical makeup. Also, a closer anatomical match will allow for an easier apposition of the procured CTA on to the donor.

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1.4. The surgical experience

1.4.1. Pre-operative workup

1.4.1.1. Imaging

Prior to transplanting a facial CTA, thorough pre-operative imaging is necessary in order to outline the anatomical characteristics of the recipient [14]. This will help to guide the surgery in accordance with an individualized protocol. Computerized tomography (CT) scanning of the head and neck will delineate the bony structure of the recipient and can produce accurate specifications of the disfigurement. Three-dimensional (3D) reconstruction of the CT images can then help guide osteosynthesis of the recipient's bony framework to allow for finer anatomical apposition with the donor CTA.

Detailed venous and arterial assessment of the recipient has so far been best achieved by CT angiography. This has allowed for identifying inflow and outflow vessels aided by spatial resolution. It has shown to be more superior than magnetic resonance imaging (MRI) angiography as it has a greater potential to detect smaller vessels and with less artefacts. CT angiograms have therefore been identified as the first-line modality for delineating the recipient's vascular makeup [15] (**Figure 1**).

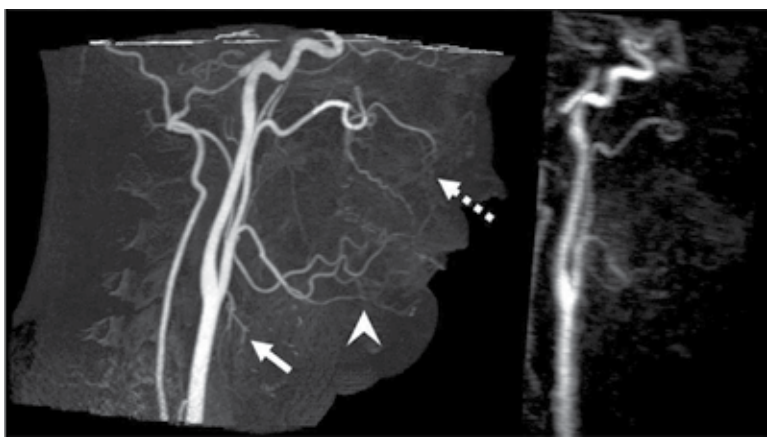

Figure 1. CT angiogram (left) demonstrating fine anatomical outline of internal maxillary, lingual and superior thyroid arteries in contrast to MR angiography which offers less resolution (right). Image reproduced from Shigeyoshi et al. [15].

1.4.1.2. Nerve function

Sensory-motor status of the recipient is assessed through electromyographic (EMG) studies. This helps evaluate the current neurological status and guides microscopic anastomosis of the nerves. This form of mapping is essential towards the success of the surgery. In addition, post-operative EMG results can be later compared to assess recovery and guide rehabilitation.

1.4.1.3. Oropharyngeal assessment

This is important so as to identify any underlying dental abscesses or periodontal disease which may require treatment prior to surgery. Such conditions can reduce the rate of post-operative recovery as it leads to immunomodulation, which could manifest in acute graft rejection.

1.4.1.4. Screening for carcinomas

The detection of underlying carcinomas in recipients is important as it can result in significant complications. In addition, it may also lead to reconsideration as to whether the recipient is at all a suitable candidate for the procedure. Immunocompromised states such as carcinomas would predispose individuals to a greater risk of opportunistic infections; also, immunomodulation due to reducing the immunosuppression regime can result in acute graft rejection. Recipients need to undergo screening for any oropharyngeal carcinomas, women over the age of 40 should be up to date with mammography and all patients above the age of 40 should undergo upper as well as lower endoscopy to detect underlying undiagnosed carcinomas [14]. The literature has depicted the severity of carcinomatous conditions on recipients of facial transplantation. A recurrent squamous cell carcinoma in one individual resulted in a mortality [3], which ultimately undermined the indication for performing the procedure in the first instance.

1.4.1.5. Anaesthetic assessment

The anaesthetic workup for performing facial CTAs just like other forms of solid organ transplantation begins with the routine evaluation of cardiovascular and respiratory status. This is aided by transthoracic echo and lung function tests, respectively. These tests although routinely conducted in those aged greater than 50 years should also be considered for younger patients if they possess risk factors for cardiopulmonary disease. Routine bloods to identify pre-existing coagulopathies or biochemical deficiencies are an important step in any pre-surgical workup [14].

An essential aspect of the anaesthetic assessment is delineating the airway anatomy in recipients of facial CTAs and this can be a complex process due to the severe nature of the injuries sustained. Often, there is gross disfigurement of the normal anatomy not only from the physical injury itself but also from numerous failed reconstructive attempts, which poses greater challenges in airway management. Pre-planning can be aided by reviewing the relevant imaging including both CT and MRI scans to obtain greater detail. Intraoperative management often involves the use of a tracheostomy; this not only avoids the difficulties in obtaining a definite airway as is a problem in recipients of facial CTAs but also keeps the facial-operating field clear for the surgeon.

Owing to the complexity of facial transplantation surgery as well as the haemorrhagic risk, obtaining adequate vascular access is an important element that requires careful consideration. Femoral lines not only provide a good mode of intraoperative monitoring but also abide in keeping the surgical field clear [16]. This is an important anatomical consideration.

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1.4.1.6. Donor prosthesis

Procurement of the facial CTA is known to create significant disfigurement at the donor site. In abiding to transplantation principles, which have previously stated that a sufficient aesthetic appearance should be obtained post organ retrieval [17], it is therefore important to take this factor into account. The process of producing a suitable prosthesis can be initiated pre-operatively whilst the donor is in ITU, an alginate material can be employed to obtain an impression of the donor's face, which is converted to a plaster of Paris (POP) cast in the laboratory. After this stage, a silicone putty material can be poured over this cast and a facial plaster of Paris structure can be obtained. Adhesive dental carding wax can be applied to reproduce the dimensions of skin and subcutaneous tissues over the POP prosthesis. A silicone elastomer can be finally mixed with it in the last stage. Artificial hair and eyebrows can be fabricated on to the prosthesis [18]. This can then be used post-operatively to cover the donor's facial defect.

1.4.2. Intraoperative period

The intraoperative period involves two surgical teams working simultaneously with one group involved in the procurement of the donor CTA and the other concerned with the preparation of the recipient to undergo implantation of the donor allograft.

1.4.2.1. Retrieval of the donor allograft

A major aim of transplant teams in the procurement of facial CTAs is to limit the ischaemia time. Heart-beating donors offer a greater period in which to arrange for the retrieval of the allograft and transfer it to the recipient [19]. The process of procurement begins after the anaesthetic teams perform a tracheostomy of the donor.

The next stage involves marking the boundaries of the CTA to be dissected as displayed in **Figure 2**:

Figure 2. Marking the boundaries for dissection on the donor. Note the extension of margins into the neck to provide additional tissue as part of the allograft. The extra section allows for adjustments to be conducted during transplantation on to the recipient as well as providing tissue for obtaining grafts to aid reconstructing residual defects.

A silastic sheet can be employed as a template to delineate the margins that need to be incised. This template is produced based on the specifications of the defect of the recipient and is then placed on to the donor to guide the surgeons of the retrieval margins. Models produced by 3D printers specifying the exact dimensions of the recipient's defect can help guide the depth of dissection on the donor. Depending on the structural and functional needs of the recipient, discretion is advocated as to what facial component and nerve structure is required for preservation.

After the initial incisions, the facial flap is elevated and the major vessels are identified including the facial arteries and external jugular veins. Vascular loops can be employed in labelling them. The facial artery is often preserved and dissection involves separating it from its point of attachment with the external carotid artery. A bi-coronal incision is often employed in removing the donor CTA; this is extended along the subperiosteum up towards the level of the orbits. It is then extended laterally and may include the ears if they are needed; however, if not, then a rhytidectomy incision can be employed. A deep plane is usually required for the incision so that when undermining of the facial CTA is being performed, skin, soft tissues and muscles can all be obtained. Nerves that require transection can be tested by stimulators to assess their functional status before deciding whether to transfer them with the facial CTA [14, 19, 20] (**Figure 3**).

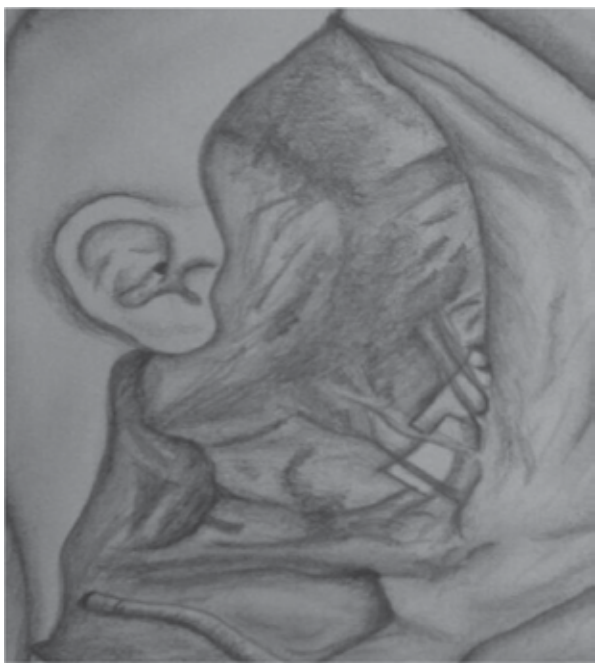

Figure 3. Elevation of flap after creating a bi-coronal incision. Arrow heads depicting incision trajectory.

In procurement of the craniofacial skeleton, superior osteotomies can be employed just above the lateral canthi bilaterally [20, 21]. These can be advanced forward to include variable sections

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of the maxilla, zygoma and orbits depending on the anatomical requirements of the recipient. These structures can be elevated by pressure underneath after having been transected at the appropriate points. Haemostatic control is important when the facial CTA is being removed from the donor. The facial arteries and veins are clamped bilaterally and transected. The defect produced within the donor can be covered up with a silicone prosthesis as aforementioned.

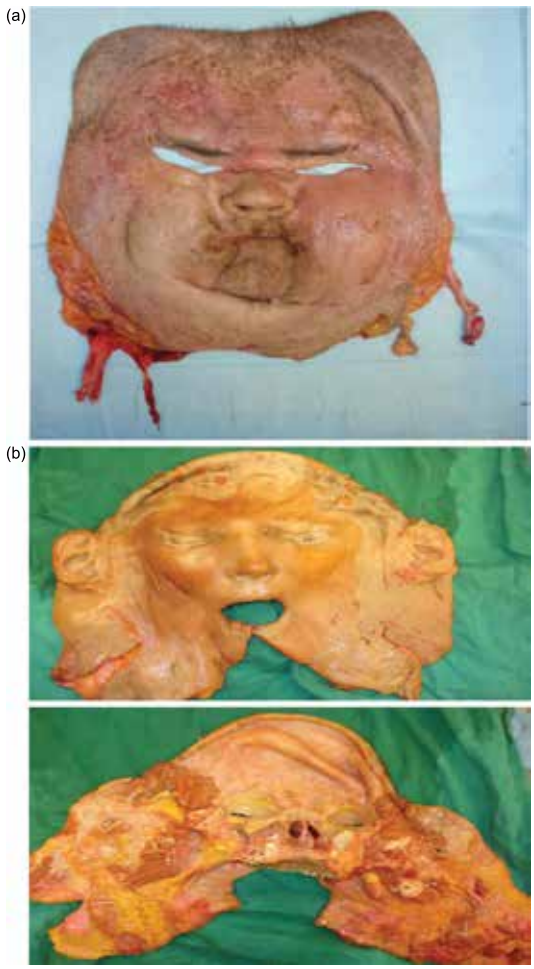

Figure 4. (a) Example of a sub-SMAS (subsuperficial muscular aponeurotic system) facial allograft in a cadaveric model after procurement containing skin and soft tissues. (b) Example of a subperiosteal Le Fort III graft. Image reproduced from Baccarani et al. [21].

The type of flap needed to be harvested and the structures required for preservation is dependent on the anatomical dimensions of the defect to be repaired. If only soft tissues are required, then a sub-SMAS (subsuperficial muscular aponeurotic system) graft can be obtained, which involves dissection from the vertex down towards the subplatysmal plane. If bony structures are necessary for procurement, then a subperiosteal Le Fort III harvest can be

conducted. This involves dissection down from the vertex towards the subperiosteal plane instead followed by a Le Fort III osteotomy to obtain sections of the facial skeleton in addition to soft tissues (**Figure 4**).

1.4.2.2. Preparation of the recipient

Often when bony reconstruction is required it commences with osteosynthesis of the donor's facial bones most notably the maxilla, zygomatic arch, orbital rim and mandible depending on the nature of the injury. The dimensions are surgically modified to match those of the donor allograft so as to allow for a more natural apposition. This in addition to offering a more aesthetic result bares an important physiological benefit because closer anatomical alignment of the sinuses reduces the risk of sinusitis from poor aeration. Conventional wires, plates and screws aid this phase of the reconstructive process. Initially, a temporary osteosynthetic method may be employed so as to proceed much earlier to microvascular anastomosis, which would reduce the duration of ischaemic insult to the facial CTA. When the risk of ischaemia has been alleviated, the completion of bony realignment can be carried through.

The next phase of the facial transplantation procedure will include coaptation of both motor and sensory nerves. This technique involves meticulous microsurgical reattachment of the nerves to enable functionalisation of the donor allograft. If recipient nerves have been damaged by previous deformities, then they can be reconstructed through the aid of donor cable grafts for which a number of host nerves can be employed. These include the facial, infraorbital, supraorbital, inferior alveolar nerves and mental nerves. A mastoidectomy can often be employed to obtain additional facial nerve length within the host. This enables for extrusion outside of the bony facial canal and allows for easier attachment during cable grafting. A similar method in the form of an orbital osteotomy can be conducted to provide the release of the infraorbital nerve. This technique will allow for a more tension-free attachment. Points of skin attachment of the facial CTA to that of the recipient should ideally be performed along natural lines of cleavage such as the nasolabial folds. This will allow for a more tension-free closure offering a better aesthetic outcome [22, 23]. The original surgical technique in full facial CTAs involved bilateral inclusion of superficial temporal and facial arteries often with the parotid gland, which gave poor aesthetic outcomes. This method became revised in 2012 when it was shown that the inclusion of the facial arteries alone was sufficient to produce desirable outcomes thus simplifying the surgery [23]. In addition, the exclusion of the parotids allowed for more distal nerve coaptation. Recently, there has been an increase in revision surgeries post transplantation [24]. Results have been favourable [1, 23, 24] without major complications, thus offering an additional option towards enhancing both aesthetic and functional outcomes of the CTA.

1.4.3. Revision surgeries

Secondary procedures post transplantation can be employed in order to revise residual functional and aesthetic defects. These have included bony realignment, soft-tissue resuspension, dermabrasion, skin grafting and fat injection [1].

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Dermabrasion is a method of surgical planning that can be conducted under local anaesthetic. The epidermis is abraded to a variable extent; however, this certainly carries the risk of bleeding as well as acquiring infections. Refined techniques including CO_2 laser resurfacing as well as electrobrasion have become more renowned and carry less risks [25]. These can help eliminate scars post transplantation as well as remove abnormal pigmentation of the CTA giving enhanced skin texture and appearance.

Both skin grafts and fat injections can be employed to correct residual anatomical defects within the hybrid facial structure. Skin grafts, however, expose the patient to the added risk of anaesthesia as well as post-surgical infections which may provide a challenge to eliminate especially in the presence of immunosuppressant medications.

Bony realignment post-transplantation is one of the more invasive revision procedures and carries a greater risk of complications since it involves the resection of the facial CTA to obtain access to the craniofacial skeleton. For this reason, effective pre-operative surgical planning is vital to avoid this clinical scenario.

1.4.4. Pre- and post-operative outcomes

In the subsequent text, we provide example cases of pre- and post-operative outcomes (**Figure 5**).

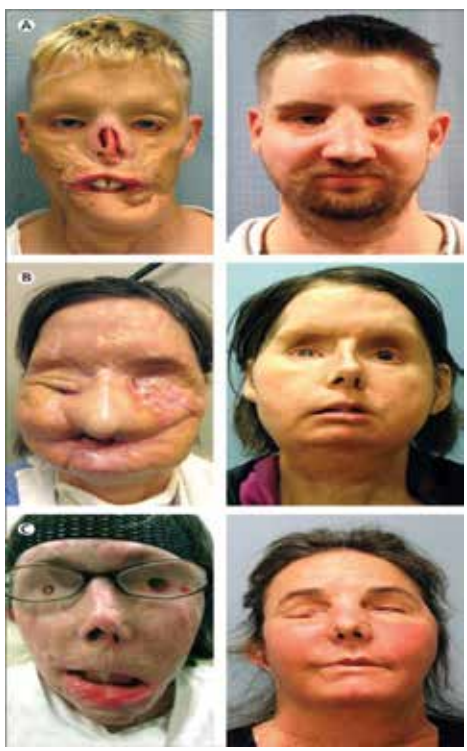

Figure 5. Pre- and post-operative outcomes for facial transplantation, adapted from Khalifian et al. [1].

1.4.5. Post-operative management

1.4.5.1. Rehabilitation

The post-operative period is an essential time when effective multidisciplinary team rehabilitation can help maximize function of the allograft. This process includes a host of different teams constituted by speech and language therapists, occupational as well as physical therapists. In addition, engagement with psychological teams and dietary teams is crucial too.

The patient needs to cognitively recognize the new facial structures he/she has been transplanted with. Research has shown that early and extensive rehabilitation of facial musculature is important in aiding cerebral recognition [26]. The recipient needs to learn how to make the newly acquired musculature functional. Exercises with physical therapists can help achieve this process by practising different facial expressions. Speech therapy is essential in order for the patient to not only be able to regain full vocal ability but also be able to safely swallow.

It is important to assess nerve innervation post transplantation to not only establish the technical success of the microsurgical reattachment but also ensure that rehabilitation will be a success. Nerve function is best assessed with EMG studies.

Occupational therapists can help ensure that patients are able to cope with activities of daily living at home prior to discharge and clinical psychologists are able to address any concerns regarding the development of identity issues. Ultimately, the post-operative period involves a strong multidisciplinary approach to allow for the functional success of the transplanted CTA.

1.5. Management of risks

Minimizing risk in the case of facial transplantation requires effective pre-operative planning as well as robust measures to tackle any post-operative complications. Over the years as the transposition of facial CTAs has increased, important lessons have been learnt about avoiding adversities. This has helped to continually refine protocols to minimize risks.

1.5.1. Graft rejection

1.5.1.1. Acute rejection

Graft rejection is a universal drawback to all forms of transplantation [27, 28] and was considered a definite risk to recipients of facial allografts in 2006 [5]. Despite advancements in immunosuppressant therapy, acute graft rejection has been evidenced in the literature [29, 30]. All current documented cases of facial transplants have sustained episodes of acute rejection [8, 9]. However, they have been well controlled with changes in immunosuppressive therapy preventing graft loss. An incidence of 50% [31] (in reference to hand transplants) was predicted initially [5]; however, until present 100% of reported cases in the literature have succumbed to modes of acute rejection [1, 8, 9].

Facial transplant	Acute rejection – Time Period	Treatment	Outcome
November, 2005 Amiens, France, performed by Devauchelle and Dubernard[32]	Acute rejection episode sustained on post op day 24	Prednisolone was used at a higher dose from 25 to 60 mg/kg daily. Tacrolimus and clobetazol ointments were employed. The dose of mycophenolate mofetil was increased	Normal outcome
April, 2006 Xi'an, China Guo[33]	Episodes of acute graft rejections occurred in months 3, 5, and 17 after transplantation	Tacrolimus dose adjustment and methylprednisone therapy for 5 days. The steroid regime was tapered subsequently by a gradual reduction of the dose	Normal outcome
January, 2007 Paris, France Lantieri[1]	Two episodes of rejection occurred on days 28 and 64.	Prednisolone was increased to 60mg for 3 days along with 3 daily 500mg IV boluses which were administered	Resolution of the rejection episode clinically however biopsies still demonstrated evidence of graft rejection
December, 2008 Cleveland, OH, USA Siemionow[1]	On day 47, biopsy revealed Banff III/IV). rejection of the graft	A single dose of IV corticosteroids	Normal outcome shown by negative biopsy
March, 2009 Paris, France Lantieri[1], [34]	Biopsies showed a grade 1 acute T cell mediated acute rejection	Intravenous methyrlprednisolone for 3 consecutive days with ATG therapy	Normal resolution
April, 2009 Boston, MA, USA Pomahac[35]	On post-op day 17, the patient developed facial redness. Flap biopsies showed a grade 1 rejection	A methylprednisolone bolus was given. And MMF was switched to mycophenolic acid At day 74 and 107, topical treatment included clobetazol cream. This was given between days 27-35 and 37-45 as well. Tacrolimus cream was used on day 107-113. Metronidazole cream was given on day 115 for rosacea infection	Normal outcome (An undiagnosed case of rosacea infection went undetected in the donor allograft tissue which delayed treatment)
August, 2009 Paris, France Lantieri[2]	One episode at day 5 of acute rejection	Intravenous methylprednisolone doses on 3 consecutive days as well as administration of ATG	Normal outcome
August, 2009 Valencia, Spain[36]	Two acute rejection episodes occurred on postoperative days 14 and 350 (Banff l, grade III)	Methylprednisolone 500 mg/24 hrs for 5 days.	Normal outcome
November, 2009 Amiens, France Devauchelle [9]	5 episodes of acute rejection on day 41, day 103, month 6, 16 and 18th	Antithymocyte globulin, tacrolimus and prednisolone were all employed	Normal outcome

Table 1. Example cases of acute rejection episodes with treatments and outcomes.

Analysing all current documented cases of facial transplants, they have all sustained episodes of acute rejection [1], which contrasts to the initial predicted incidence of 50% based on hand transplants [5]. However, all episodes have been well controlled with changes in immunosuppressive therapy therefore preventing graft loss in the acute stage. **Table 1** demonstrates some cases where the timelines of acute rejection episodes have been reported along with the treatment method and outcome. Currently, no graft loss from acute rejection has been reported [1, 8, 9]; however, detailed explanation of the nature of all acute rejections in the literature is still pending.

Although the majority of acute rejection episodes have been well controlled, greater clinical research is needed to reduce the incidence when performing facial transplantation as it hinders post-operative recovery. For now, strict early recognition protocols should be adapted to allow for timely detection and treatment.

1.5.1.2. Chronic rejection

Chronic graft rejection can result in progressive fibrosis of skin with ultimate graft failure [37]. So far, there has been one case reported within the literature. This occurred subsequent to the minimization of immunosuppressive therapy due to an Epstein-Barr virus (EBV)-positive B-cell lymphoma [10]. The chronic rejection ultimately compromised graft function with evidence of reduced mouth opening [10]. Such a rejection event can be avoided if better donor and recipient matching for EBV is conducted. Also, strict management protocols of acute rejection episodes should be adapted for the prevention of any potential progression towards a chronic mode of rejection.

1.5.2. Infections

Immunosuppression causes an increased predisposition to acquiring infections and Butler had collectively referred to all the adverse effects that could potentially surface from immunosuppressive agents [5]. Infective complications have affected 11 patients of transplanted allografts so far [1, 38]. Lack of pre-transplantation detection of cytomegalovirus has led to six recipients acquiring the infection [2, 38]. Bacterial infection has been reported in eight cases with five patients developing sepsis [3]. Leukopenia has also been experienced amongst two recipients who had their medication regime altered to lower doses [39, 40]. With respect to the high proportions of infections developing in the recipients of facial allografts, it is fair to say that we should employ better pre-op screening techniques to reduce the incidence of transmission. Certainly, viral screening of the allografts could have prevented cytomegalovirus transmission and reduced the incidence of infections encountered. Such a protocol should be considered for future transplantations. Also, early recognition is key as in one case an underlying Candida infection was misdiagnosed [3] as an acute rejection episode and this can lead to a delay in treatment. Maintenance immunosuppression certainly poses significant risks for facial CTAs and this like other forms of allotransplantation is dependent on the success of tolerance regimes to provide better functional outcomes. So far, clinical trials have included Tregs, which are regulatory T cells and are believed will be able to induce tolerance enabling graft survival. Recent evidence also points to focusing research on the role of effector cells such as T cells as

well as B cells as they are believed to possess key roles in regulating inflammatory responses [41, 42]. Tolerance would allow for better outcomes in facial CTAs as it would eliminate the need for long-term immunosuppression.

1.5.3. Mortality

There have so far been three reported mortalities in the case of facial transplantation [1]. The Chinese case failed in complying with long-term immunosuppressive therapy ultimately resulting in multi-organ failure [1]. A second case who received bilateral simultaneous below elbow upper limb transplants in conjunction with a facial transplant sustained a cardiac arrest in the post-operative period whilst in ITU after being treated for septic shock and pneumonia [2, 43]. Another patient who also underwent simultaneous hand and facial transplantation sustained upper limb ischaemia subsequent to septic shock and the hand transplants were removed with salvage of the facial allograft [2]. This indicates that perhaps concomitant limb and facial transplantation should not be conducted due to increased risk of post-operative complications. The third patient mortality stemmed from a squamous carcinoma development of the tongue in a human immunodeficiency virus (HIV)-positive patient [36, 43]. This indicates that patients with severe co-morbidities should not be considered as recipients particularly in those with immunocompromised states.

1.5.4. Functional outcome

Results concerning functional improvement have been positive with increased ability to perform basic facial functions [2, 4, 8]. Regression of normal motor function has been encouraging although slightly slower than sensory restoration [2, 12]. Despite this, the first case in France regaining the ability to eat and drink after 1 week [10] has displayed great promise. Equally, results have been paralleled globally with a case in Spain regaining full swallowing ability at 16 months [36, 44]. This demonstrates that motor function restoration can be just as swift as that of sensory. Gross return of lip motion has been reported too at 3 months [3]. Pomahac has reported restoration of olfaction as early as the third post-operative day and a return to facial sensation at 3–4 months time for the three cases he has addressed [3]. Chronic pain induced by skin contractures has also been obliterated and offered an additional mode of function improvement [1]. Fischer et al. have demonstrated significant improvement in numerous facial functions including speaking, breathing, eating, smelling, improved facial expression as well as sensation in the vicinity of a single study [45]. They report that between 20 days and 1 year, all patients were capable of oral food intake with removal of all feeding tubes, after 9 months all patients at their centre had regained intelligible speech, which correlated with other studies within the literature, olfactory sensation was recovered in 100% of cases where it was previously impaired, significant improvements in breathing were reported too, facial expression was, however, only reported to increase in 76% of reported cases. A unique finding that has been deduced from facial transplants is the efficiency of sensory nerve reinnervation even when they have not been directly opposed in terms of microvascular restoration. Restoration of sensory function has still been very good [2, 11]. This, however, has not been the case in terms of motor function where poor anastomotic recon-

struction has been reflected by lack of motor improvement [45]. Therefore, a standardized level of microvascular reconstruction should be aimed for so as to obtain both satisfactory motor and sensory reinnervation. Early rehabilitation of facial musculature is important in facilitating a normal outcome and therefore a multidisciplinary approach including speech and language therapy is important as it aids cerebral recognition of newly transplanted facial musculature [4].

1.5.5. Psychological risks

Psychiatric evaluation of patients for the receipt of donor facial CTAs is essential in order to minimize risk. Patients who are considered for selection must acknowledge the pros and cons of the procedure, be highly motivated as well as appreciate the importance of engagement with long-term multidisciplinary team therapy [32]. Some of the contraindications include active psychotic disorders, severe personality disorders as well as previous suicide attempts [32]. Viewing an altered facial structure can induce emotional stress as an individual fails to recognize his/her own identity [28]. However, until now there has been no documented psychological complications due to altered identity with recipients having had accepted their new appearance [5, 19, 25]. Recipients have also been shown to not possess donor resemblance [29, 30] as was initially predicted by Butler [16], thus nullifying these perceived risks. Results overall have shown positive outcomes with reports of reduced depression and a sense of greater social integration amongst patients treated with the facial CTAs [14].

Despite thorough psychological assessment for the selection of patients, there has been one case in China where lack of motivation in compliance with long-term immunosuppressive therapy has contributed to a mortality [14]. This emphasizes the importance of maintaining a robust pre-operative psychological workup as well as the need for post-operative psychological follow-up.

It is important to appreciate maintaining a quantitative method of assessing psychological changes. Coffman et al. have emphasized the use of various psychological scales in order to achieve this [46]. They followed outcomes for up to 3 years in a recipient of a facial CTA and quantified their findings. Scaling systems were used every 3 months for the first 2 years and then every 6 months. The Psychosocial Adjustment to Illness Scale (PAIS-SR) scoring system was employed in order to assess social reintegration and psychological distress. The patient's Perception of Teasing FACES scores decreased from 25 to 9 at the last follow-up. PASTAS-State (Physical Appearance State and Trait Anxiety Scale: State) was utilized in order to evaluate the patient's mental state in accordance to their body and facial image. Overall, it showed an improvement during the course of the 3 years. Other scales that were used included the Beck Depression Inventory, which decreased from 16 to 6 by 3 months, and the PAIN thermometer, which showed a reduction in the degree of pain post-surgery.

Quantifying the psychological outcomes will most certainly reduce risks as it will enable for timely recognition of mental problems that could develop post-operatively. Early detection and treatment will therefore allow for a quicker recovery, which will also maintain patient motivation in complying with the post-op multidisciplinary therapy.

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1.5.6. Miscellaneous risks

1.5.6.1. Blood loss

Significant intraoperative blood loss was a complication that was initially overlooked in 2006 [16]; however, it was a concern amongst the initial transplants [2, 3] conducted and the associated indirect risks posed from subsequent transfusions. However, as surgical techniques have become more refined, the incidence of significant intraoperative blood loss has been reduced.

1.5.6.2. Chronic renal insufficiency

This has so far developed in two patients subsequent to immunosuppressive therapy [4, 39]. Such problems had been predicted [26] in relation to long-term immunosuppression; however, the incidence has so far been low [43]. Unless tolerance regimes become developed, the risk of this complication will persist.

1.5.6.3. Malignancy

Neoplasia has been evidenced in three cases so far with one patient sustaining mortality subsequent to a squamous cell carcinoma of the tongue [43]. This was due to the effects of immunomodulation from an underlying HIV infection in the recipient. Another patient developed a monoclonal B-cell lymphoma at 4 months [43] due to Epstein-Barr virus mismatch implicating that stricter viral screening measures of donors need to be adapted. Cervical dysplasia has also been reported in the first partial facial allograft in France for which the patient underwent hysterectomy [47].

1.6. Conclusion

In conclusion, we can see that acute rejections have shown to affect almost all patients. Although they have been well controlled with no graft loss, it should still draw focus towards more research in this field and how to limit its incidence as there has been a report of one case that has progressed towards chronic rejection impairing graft function. Infective complications have affected 11 patients. Almost half of these could have been avoided if stricter protocols were practised in terms of pre-operative viral screening of donor grafts. Six cases of cytomegalovirus and one case of EBV were acquired. These could have been prevented. Significant complications can arise as a result of infections as was evidenced in the case of Epstein-Barr virus acquisition from a donor graft causing monoclonal B-cell lymphoma. The risk of unpredictability in functional improvement has certainly been disproved. All reported cases so far excluding the three mortalities have demonstrated improved facial function to some degree apart from one case of reduced graft function due to chronic rejection. Psychological complications have been negligible apart from one case in China not complying to his immunosuppressive therapy. This can be avoided by better patient selection and a more thorough psychological assessment in terms of choosing transplant recipients. Also, it is important to quantify the psychological outcome as it will help to improve the post-op follow-

up and recognize mental problems that may develop. Concomitant limb and facial transplants should be avoided as it has shown to increase mortality and morbidity in the two cases where it has been attempted. Recipient co-morbidity status should therefore be considered pre-operatively as it can increase the complication incidence. This has been further highlighted by mortality in relation to one recipient with HIV succumbing to a malignant complication of the tongue again emphasizing the importance of considering co-morbid state.

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Section 16

Management of Common Complications in Rhinoplasty

Chapter 30

Management of Common Complications in Rhinoplasty and Medical Rhinoplasty

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Additional information is available at the end of the chapter

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Abstract

Rhinoplasty is considered among the most challenging aesthetic operations because many variables have to be taken into consideration to achieve an optimal aesthetic and functional result. This implies that complications are always waiting around the corner. It is of prime importance to know the main minor and major complications related to the procedure to be able to prevent and treat them promptly when required. Septorhinoplasty is a delicate and difficult procedure, which requires accurate anatomical knowledge and important clinical experience. Nevertheless, complications can affect both inexperienced and expert surgeons. Thus, the most frequent complications of rhinoplasty should be known and adequately prevented when possible.

Keywords: Adverse events, rhinoplasty, complications, rhinofiller, Medical Rhinoplasty

1. Introduction

Some post-operative complications are easily treated, whereas others require multiple reconstructive surgeries and sometimes *restituito ad integrum* (a flawless result) is impossible to obtain. Therefore, the best therapy for complications is prevention. The most frequent complications in rhinoplasty are classified according to their nature as traumatic, respiratory, aesthetic, infective or vascular.

2. Traumatic complications

2.1. L-structure or K-area fracture

During septorhinoplasty, whatever approach is used, two fundamental rules must be kept in mind:

1. Respect the Cottle K area, which is anatomically defined as the intersection of the nasal bones, septum and triangular cartilages.
2. Preserve an adequate dorsal-caudal L structure for support.

Damage to these structures causes an inadequate support of the nasal pyramid and with time causes nasal dorsum collapse and dorsum sill deformity spontaneously or after minor trauma. An adequate dorsal-caudal L structure of at least 1 cm is necessary for structural support to prevent this type of complication. The K area should be addressed with extreme care upon dorsal hump removal. Precise subperiosteal dissection is done above the nasal bones with a Joseph dissector. Incremental dorsal hump reduction with a rasp or osteotomes allows for maneuver control and removes the hard tissue while avoiding damage to the triangular cartilages or nasal bones.

Treatment of L-structure fractures of the septum includes the use of robust reconstructive spreader grafts on the dorsal segment and columellar strut grafts on the caudal segment. Septal cartilage grafts are preferred when available; otherwise, conchae or costal cartilage grafts are necessary.

Repair of K-area damage and triangular cartilage detachment from the nasal bones is more complex. If a small residue of cephalic cartilage remains, reattachment of the triangular cartilages is possible with non-resorbable sutures. Otherwise, holes are drilled in the nasal bone to anchor stitches of the triangular cartilages. Permanent surgical sutures (Nylon 4.0) are preferred over Kirchner metal wire, as proposed by other authors, given the fact that the skin is extremely thin in this area and a greater incidence of infection, irregularities and transcutaneous translucency can be expected with the latter technique.

2.2. Dental trauma

Hypoanesthesia of the superior central incisors and palatal premaxilla is frequently noted in the post-operative period after septorhinoplasty. This is due to the fact that the incisive nerve, before exiting in the oral cavity through the homonymous canal, lies on the maxillary crest at the base of the nasal septum. This complication frequently arises when septal dislocations close to the anterior nasal spine, nasal septum cartilage resections or anterior nasal spine remodeling procedures are done. Spontaneous resolution of the hypoesthesia is expected for the majority, and sensitivity is reestablished in a variable period between 1 week and 6 months. In the case of abnormal vascular support of superior anterior incisors or long teeth roots, a direct damage to the superior central incisors is possible; this can cause pulpitis or abnormal pigmentation. Prompt dental evaluation and endodontic therapy are advised, if necessary, before intrinsic pigmentation occurs or more complex and expensive prosthetic therapies are needed.

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2.3. Intracranial complications

Intracranial complications include rhino-liquoral fistulas and anosmia. **Rhino-liquoral fistulas** are among the major post-rhinoplasty complications.

Given the fact that the superior portion of the septal cartilage is directly abutting the cribriform lamina of the ethmoid and is the direct continuation of this structure, an understanding of why this severe complication is not that uncommon is apparent.

Septoplasty is a delicate phase of the procedure. Very often, surgeons treat the septum aggressively by grabbing the bony portion with Weil forceps and attempting to break or remove the tissue through rotatory movements. Prevention of rhino-liquoral fistulas consists of an accurate and delicate septum dissection, particularly with regard to the superior bone portion. Before pulling a fragment, adequate dissection and freeing is necessary. The clinical symptomatology of rhino-liquoral fistulas includes rhinorrhea and positional cephalus. Diagnosis is confirmed through beta-2 transferrin presence in the fluid, specifically the cerebrospinal fluid.

Such complication requires hospitalization, lumbar drainage positioning by a neurosurgeon and eventual multilayer nasal endoscopic fistula repair.

Anosmia is fortunately very seldom observed due to the damage of the olfactory bulb. Most frequently, this condition is secondary to a persistent respiratory nasal obstructive pathology.

2.4. Orbital complications

Orbital complications related to septorhinoplasty are extremely rare and include blindness and epiphora. Blindness has been reported in some cases and is related to turbinate or nasal dorsum steroid injections. The etiopathogenesis described involves an embolic occlusion of the central retinal artery. Other cases due to vasoconstrictor injections in the septum and turbinates, being the etiology of a spastic response on the central retinal artery, have been described [1–3].

These unfortunate complications are hard to predict and impossible to resolve. For this reason, prevention is done by avoiding steroid infiltration in the turbinates and aspiration prior to injection and injecting a small quantity when treating the dorsum. Epiphora is an extremely rare complication after rhinoplasty. Lateral osteotomies are generally safe if executed in a standard manner. Damage to the lacrimal ducts is possible when the osteotomy direction is incorrect or when motorized instruments or saws are used. It is frequently clinically confused with paralateronasal edema. Spontaneous resolution is often verified, although sporadic cases require dacryocystorhinostomy for complete resolution [4, 5].

3. Respiratory complications

3.1. Internal nasal valve dysfunction

Internal nasal valve dysfunction is a frequent complication secondary to old school destructive rhinoplasty. The principal cause is over-resection of the lateral cartilages during hump

removal. The internal nasal valve angle is formed by the confluence of the nasal septum medially and lateral cartilages externally; its normal value is around 15° [6].

A reduction in this value determines impairment in airway flow. More severe than an excessive resection of the triangular cartilages is scarring in the internal valve area due to transmucosal disjunction of the septum from the triangular cartilages; fortunately, this is an old and discarded technique. Patients with a non-deviated septum are referred for treatment of severe nasal respiratory problems. Moreover, in addition to this severe functional defect, a dorsal inverted V deformity appears after the resolution of the surgical edema due to inferomedial collapse of the triangular cartilages [7].

The remedy for this type of complication is the placement of a spreader graft, whatever the type (auto, mini or classic) and source (septum, concha or rib). The important technical detail is to place the graft so as to raise and reposition the collapsed triangular cartilages and return internal nasal valve function, augmenting the cross-sectional area.

Classic spreader grafts are longitudinal grafts placed in a subperichondrial pocket and fixed to the triangular cartilages and the septum through non-resorbable sutures.

Spreader grafts also allow straightening of a cephalic deviated septum, reconstruction of an open roof deformity or improvement of dorsal aesthetic lines [8].

Auto-spreader grafts are obtained from the triangular cartilages after mucosal dissection and then partially cut and folded medially over themselves; this maneuver is very difficult to perform in secondary cases due to prior over-resection of the cartilages. On the other hand, mini-spreader grafts are obtained from the cephalic portion of the alar cartilages but due to their reduced dimensions are seldom useful for severe reconstruction [9].

3.2. Nasal septal perforation

The etiology of septal perforation is diverse and may be iatrogenic, which is most often the case, due to cocaine abuse, infections, trauma and granulomatous diseases. With subperichondrial septum dissection, caution should be taken not to trespass the mucoperichondrial flaps. It is advisable to start with the easier side to grant integrity in at least one side. When both mucosal flaps are damaged bilaterally, an iatrogenic septal perforation will be produced.

The symptomatology of septal perforation includes crusts, recurrent bleeding, whistling or inspiratory rumors and nasal respiratory obstruction. The more anterior the perforation is, the greater the associated disturbance.

The most ancient solution for the problem was the use of silicone septal buttons, which are less popular among patients nowadays.

Diverse septal perforation repair techniques have been described, with the most effective ones being from Kridel and Castelnuovo [10, 11]. Kridel described an open approach for the provision of sliding superior (from the internal nasal valve region) and inferior (from the nasal floor and inferior turbinate) mucoperichondrial flaps. Castelnuovo reported an endoscopic approach for an intranasal septal mucosal pedunculated flap to the ethmoidal arteries, which is rotated to obtain defect closure. Both techniques grant a high success rate.

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Whatever the case, it is proper to prevent septal perforation and if verified to take time to repair the mucoperichondrial flaps properly. Allotting an additional 10 minutes at the primary surgery is better than performing 3 hours of revision surgery for perforation closure.

3.3. External nasal valve dysfunction

The external nasal valve is an area defined three-dimensionally by the inferior turbinate head, caudal portion of the triangular cartilages, cephalic portion of the alar cartilages and septum. The most common source of post-rhinoplasty dysfunction is related to an excessive resection of lateral crura of the alar cartilages.

This condition is occasionally seen when an attempt to reduce nose tip dimensions is sought at all costs, not leaving enough alar cartilage to support the nasal ala.

Nasal alar collapse can be dynamic if it manifests only during inspiration (forced or not) or static in more severe cases if it is verified at rest. The minimum alar cartilage dimension to preserve varies according to the intrinsic consistency of the cartilage and it is not the same for all patients. Nevertheless, a minimum of 4–5 mm should be kept and old risky, interruptive approaches should be avoided.

Multiple techniques have been described to treat this complication, namely, alar spreader grafts, lateral crura repositioning, alar spanning grafts, barrel roll technique, lateral crura strut grafts and alar batten grafts. Alar batten grafts are the most frequently used, but every case should be analyzed individually and treated accordingly with the most indicated technique [12].

External nasal valve compromise is also verified after maneuvers that cause narinal stenosis. This condition is seen, for example, when a sloppy adaptation of the vestibular skin occurs after rhinoplasty due to a lack of closing sutures in the area, infection or abnormal scarring. Another cause is represented by excessive alar base wedge resection.

Corrections in these cases are complex and foresee the use of local flaps and Z-plasties, but in the majority of cases, auricular composite grafts are necessary to replenish the lack of previously excised tissue.

Residual anterior septal deviations and turbinate hypertrophy can cause external nasal valve dysfunction. Residual anterior septal deviations require surgical revision with a more precise septoplasty. Inferior turbinate hypertrophy is very frequent, especially in allergic patients. In these cases, medical therapy is advised with local steroids and systemic antihistamines, discouraging continuous surgical retouching [13].

Turbinoseptal synechiae (adherences) can also produce external nasal valve stenosis, although they can appear even more posteriorly in the nasal fossae. Silicone splints should be used and kept in place long enough to allow re-epithelization of the turbinate and septum to prevent turbinoseptal synechiae when mucosal lacerations occur.

3.4. Sinusitis

Sinusitis is rare as a post-rhinoplasty complication, but it can become apparent if unrecognized predisposing conditions are present.

The medial meatus protected by the middle turbinate represents the common drainage path for the ducts of paranasal sinuses. Ethmoidal anterior, frontal and maxillary sinuses all drain at this level.

Medial turbinate lateralization maneuvers are extremely dangerous as they may cause rhino-liquoral fistulas and compromise normal paranasal sinus function.

If predisposing conditions are present, the presence of concha bullosa may predispose a patient to post-rhinoplasty sinusitis. It is advisable to assess pre-operative nasal and paranasal sinus CT scans that will give valuable information regarding septal deviation and turbinate hypertrophy and identify sinusal alterations suitable to be treated during the surgery through functional endoscopic sinus surgery (FESS) to avoid this complication.

4. Aesthetic complications

4.1. Supratip deformity (polly beak)

Post-operative deformity of the supratip nasal area that assumes a convex shape in relation to the nasal dorsum can have two sources: cartilaginous tissue or scar tissue. Cartilaginous polly beaks are caused by an insufficient resection of the inferior third of the dorsal septum in proximity to the septal angle. Scar tissue polly beaks, on the other hand, are more frequent in cases with sebaceous skin and are due to hypertrophic scarring of the subcutaneous tissue of the supratip region.

Prevention of cartilaginous supratips relies on meticulous assessment of an adequate relation between the dorsum and nasal tip. Normally, the distance between the level of tip-defining points and septal angle is about 6–8 mm, but it is based on the surgeon's experience to define the magnitude [14].

Supratip scarring is more difficult to prevent. Supratip empty spaces that may fill with blood and further scar tissue should be avoided.

Compressive bandaging of the supratip area for 4–5 weeks is of prime importance to reduce the dead space and prevent polly beak deformity from scarring.

The remedy for supratip scarring is based on local steroid injections; they are very effective if done properly with regard to timing and modality. Triamcinolone acetonide (Kenacort, 40 mg/ml injectable suspension) is the steroid of choice. Dosage should be triamcinolone 1–2 mg applied early (2–3 weeks after the surgery) if a tendency for supratip deformity is perceived and not repeated before a 2-month interval. The effect of the therapy is seen in the following 2 months post injection. The injections should be in a deep plane and never intradermal.

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Superficial injection causes cutaneous atrophy, telangiectasia, depressions, color modifications and underlying cartilage visibility [15].

Cartilaginous supratips and non-responders with scar-based supratips are treated with revision surgery. An in-depth analysis of tip-dorsum relation and the use of tip-defining grafts (onlays and shields) are useful to avoid recidivism.

4.2. Dorsal irregularities

The nasal dorsum is the region more prone to unexpected and unwanted surprises after a rhinoplasty. It is very difficult for the surgeon to ensure that no dorsum unevenness remains at the end of surgery and that the end result is smooth and with no imperfections in the majority. Nevertheless, months or years after the surgery, it is difficult to find an operated nose that does not show some dorsal irregularities at least upon palpation. The reason for this is that surgical edema will hide small irregularities and mask an adequate palpation evaluation of dorsum smoothness. With time, as nasal tissue swelling disappears, irregularities start to show [16].

Dorsal deformities are among the most common causes of revision rhinoplasty. They are mostly due to excessive or inadequate hump removal, remnant fragments after removal, asymmetric resections, inadequate graft modeling or fixation and dislocation.

Open rhinoplasty can reduce the frequency of these imperfections as it allows for direct vision of the dorsum. Another tip to reduce the percentage of these complications is to perform dorsal index palpation with the surgical gloves wetted with normal saline, augmenting sensitivity for the surgeon. Profuse cleansing and washing of the dorsal area under the skin envelope before suturing is imperative as it eliminates small cartilage residues and bony fragments, avoiding future irregularities.

Avoiding dorsal irregularities in patients with thin skin is still very difficult. In these cases, it may be advisable to use dorsal augmenting materials. These can be autologous (temporal fascia, perichondrium graft), heterologous (equine or bovine pericardium membranes) or alloplastic (Gore-Tex). Autologous materials are preferable due to the lower incidence of infections associated with them; however, at the dorsum level, the risk of infection or extrusion is very small even for non-autologous materials [17].

4.3. Tip deviations and irregularities

Tip deviations and irregularities are among the most common causes of revision rhinoplasty and are more prevalent in the closed approach. They include depressions, irregularities, asymmetries and lateral crura collapse. They can appear due to faulty techniques, excessive or asymmetric lateral crura resections, incorrect graft positioning or scarring [18, 19].

Another particularly anti-aesthetic condition is an altered tip projection, either hyperprojection or hypoprojection. Nose tip deformities often manifest a long time after the surgery (1 or 2 years after). In fact, the nose tip is the last region to swell down in the post-operative period.

Prevention of this complication relies on knowledge of tip supportive mechanics and the tripod theory as well as attention to avoid disruptive or destructive techniques. Nevertheless, the most important factors are still expertise and respecting aesthetic proportions that will grant good results in the long term. Revision rhinoplasty is surely easier and predictable if done via an open approach, but this also depends on the skills and experience of the surgeon [20].

4.4. Skin necrosis

Nasal skin necrosis is among the worst complications that can occur during a septorhinoplasty. It is mainly caused by vascular damage in the vessels that supply the nose tip. Rarely, it can present due to excessive dressing compression. Most frequently, it appears after damage in the lateral nasal arteries due to an incorrect plane of dissection or following excessive nose tip fat tissue reduction, in an attempt to reduce its size.

A new source of skin necrosis of increasing prevalence is the post-operative use of dermal fillers at the nasal pyramid, nasolabial folds or paranasal region to camouflage irregularities. This outcome is more frequently verified when the filler is delivered with needles that may cause direct vessel damage and intravascular occlusion or indirect vascular compression, jeopardizing tip vascularity.

Some rules should be respected to prevent this complication:

1. Avoid injecting fillers with sharp needles (preferably blunt tip cannulas) in paranasal areas.
2. Dissect the nasal tissues attached to the cartilaginous framework without getting superficial.
3. Avoid defatting techniques of the nose tip or reduce it to a minimum.
4. Avoid firm and tight dressings, especially in revision cases.
5. Limit alar wedge resections under the alar crease.

Treatment of skin necrosis is very complex and ranges from conservative approaches (such as second-intention wound healing) to complex reconstruction procedures with local, regional or free flaps. Whatever the approach, skin tropism and elasticity are a primary goal before intending more complex repair. The latter procedure can be achieved through platelet-rich plasma and micro-lipofilling sessions.

5. Infective complications

Rhinoplasty infections are not frequent, probably due to the natural protective mechanisms of the nasal mucosa. Nevertheless, the myriad of infective cases can be very vast and go from small subcutaneous cellulitis due to infected sutures to severe cavernous sinus thrombosis.

Local skin or mucosal infections are treated with local and systemic antibiotics. Abscesses may affect the dorsum, tip or septum, with septal abscess being the most dangerous, and they

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should be promptly drained; septal abscess can appear from an undiagnosed septal hematoma that can evolve to a septal perforation if not treated promptly.

High fever, meningeal signs, nausea, vomiting and hypotension are suggestive signs of a severe infection, such as cavernous sinus thrombosis. If the diagnosis is suspected, nasal tampons should be removed immediately (especially if placed several days before) and secretions should be sent for cultural and bacteriological analysis, with the most frequent germ involved being *Staphylococcus aureus*. Patients should be hospitalized and systemic antibiotics should be initiated promptly.

Prophylactic antibiotics in rhinoplasty are a controversial topic but nonetheless highly indicated by the majority of surgeons.

6. Vascular complications

Vascular complications include septal hematoma and epistaxis.

6.1. Septal hematoma

Septal hematoma can occur secondary to trauma or surgery and is a serious complication. Its symptomatology includes nasal obstruction, pain and, occasionally, fever. Anterior rhinoscopy reveals a septal mass that occludes one or both nasal fossae. Immediate therapy is indicated and consists of hematoma drainage, nasal tampons to impede recidivism and proper antibiotic therapy to avoid abscess transformation.

Septal abscesses can evolve to mucosal and/or cartilage necrosis and septal perforation varying in dimension and location according to the underlying infection [21].

6.2. Epistaxis

Bleeding in rhinoplasty patients post-operatively is normal if limited, whereas it can become a complication if profuse or continuous. The condition is more frequent in at-risk patients on anticoagulants or platelet anti-aggregating agents. In these cases, prior consultation with a hematologist and a cardiologist is advisable, and oral clot-altering drugs should be discontinued and subcutaneous LMW heparin initiated several days before the surgery. All patients should be advised to discontinue NSAID or aspirin intake at least 2 weeks prior to operation.

A precise and delicate technique during surgery is desirable to avoid vascular problems. During septoplasty, for example, it is important to avoid mucosal flap lacerations to minimize bleeding. A nasal septum mattress suture can be useful to prevent bleeding and septal hematoma. Turbinate cautery should be gentle. An open technique allows for direct vision and hemostasis of bleeding vessels during the procedure. Epistaxis therapy includes 60° head elevation, nasal packing and gentle nares pressure for 10–15 minutes. Severe epistaxis can require an emergency endoscopic procedure to coagulate the sphenopalatine septal and lateral branches.

7. Medical rhinoplasty

Medical rhinoplasty was first described by Braccini and Dohan Ehrenfest [22] in 2008. The concept, although highly polemical and refused by rhinoplasty surgeons at its onset, developed popularity among aesthetic patients due to its minimally invasive characteristics, with minimal or no downtime and pleasing aesthetic improvements.

The term *medical rhinoplasty* (particularly, *rhinofiller*) is defined as the application of dermal fillers in the external or internal nasal area to modify or improve aesthetics or functionality. It is especially suitable for patients with minor aesthetic or functional concerns that are refractory to surgery [23–26]. It may be combined with the use of botulinum toxin injections around the nose to enhance the results. The procedure is currently a frequent request in aesthetic practice, and many physicians perform it systematically. Nevertheless, it should be considered that it is an advanced technique and should only be attempted by expert practitioners due to the potential for devastating vascular complications [27]. Local anatomical knowledge and advanced technical skills are required to achieve successful and safe corrections.

7.1. Rhinofiller

Rhinofiller specifically involves the infiltration of a dermal filler to modify external or internal nasal structures for aesthetic or functional purposes. Since its introduction in 2008, many temporary and permanent substances have been used to achieve the desired corrections. Successful application mandates adequate anatomical knowledge of the related structures.

Proper patient selection is important to achieve good results. Exclusion criteria include severe nasal airway impairment, permanent filler in the area, history of ischemic/thrombotic events or known hypercoagulability, local infection and recent trauma.

Before the procedure, nasal analysis should be performed clinically and photographically to define needed corrections.

Areas of potential correction include dorsal aesthetic lines, the dorsum, minor hump camouflage, radix enhancement, tip rotation and projection and base augmentation. Details are shown in **Figure 11**.

Functionally, in selected cases, the use of fillers can be useful to augment the aperture of the internal nasal valve as a volumetric spreader graft.

Morphing simulations are advisable before treatment in order to give patients an indication of the post-treatment outcomes, explain the procedure and establish common goals. In addition, specific, informed consent should be properly discussed and obtained.

7.1.1. Technique

Treatments are typically performed with medium-viscosity hyaluronic acid (HA) fillers under local anesthetic (lidocaine intradermal vesicles applied using a 0.3 ml syringe with a 32G needle) with the aid of a 25G (0.5 mm) × 4 cm blunt-tip disposable cannula, manually bent,

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maintaining sterility at all times, in order to obtain better compliance of the shapes and silhouette within the nasal area. The distribution of material should be performed as required to follow the treatment plan. Tip refinements can be sporadically carried out through needle infiltration with extreme care.

The specific pattern of anesthetic peripheral blocks and filler infiltration is shown in **Figure 12**.

Generally, the patient satisfaction rate with this correction is very high and, due to the scarce muscular activity in the nose, corrections with Hyaluronic acid dermal fillers last more than 1 year and in many cases even 2 years. A clinical case of rhinofiller is described in **Figures 13** and **14**.

8. Discussion

The nasal area is composed of different interacting tissues, such as the skin, subcutaneous tissue, muscle, bone, cartilage and mucosa, which come together to form a normal, functional and aesthetically pleasing nose. To make things more complicated, there is also a vascular anatomy formed by two main circuits, namely, the supratrochlear and dorsal arteries and the facial circuit that includes the superior labial and angular arteries, all of which are anastomosed in the tip. This has been the subject of recent interest and study because it is believed that a proper technique and anatomical knowledge are of prime importance in order to avoid vascular complications [28–30]. Facial vascular complications were first described in 1991 after collagen injections in the glabellar area [31]. The reported incidence of Nicolau syndrome or embolia cutis medicamentosa (ECM) following glabellar treatments is 9/10,000 procedures (0.09%). The known risk factors associated with this catastrophic event are a high syringe piston pressure, a highly vascularized territory and previously traumatized tissue. The first of these factors can be mitigated using fluid materials of low viscosity. Unfortunately, the entire facial region, especially the nasal area, is considered highly vascularized and many reports of paranasal vascular complications, which vary from mild symptoms of pain and skin color changes to necrosis and even bilateral blindness, have been published [32–41]. The pathophysiology of ECM is an intravascular injection that advances in a retrograde mode to a distant area and, through changes in blood pressure, arrives at a distant vessel and causes a vascular complication. The resulting symptoms vary according to the physiology of the vessel that is compromised; affliction of arteries leads to pallor, whereas occlusion of veins manifests as livedo reticularis. According to the author's experience, there is a second mechanism of vascular compromise in the nose known as *compartmental syndrome*. Due to the low elasticity of the nasal skin (especially after surgical rhinoplasty), there is a chance of producing indirect vascular compromise due to mechanical obstruction when large amounts of filler are positioned, even in the absence of intravascular injection. The former, together with the altered anatomy and possible iatrogenic vascular damage, makes these corrections particularly tricky in this patient setting. Vascular complications can range from mild to severe and therefore prompt recognition and treatment are crucial. Oral aspirin, nitrate cream 2%, heat, massages and intralesional hyaluronidase have all been proven to be beneficial. The author has also used

intralesional heparin mesotherapy with good results (unpublished observations). In severe, unresponsive cases, prostaglandin E_1 (alprostadil) treatment can sometimes limit the extent of the damage. For the remaining scar tissue, occasionally complex reconstruction procedures are necessary [42, 43], although the recent use of stem cells has shown promising results [44]. All of the above have determined nasal augmentation with dermal fillers to be particularly challenging, and mastery of the correct technique is of utmost importance in order to achieve good results and reduce the incidence of adverse reactions. Important factors to consider include the following:

- **Patient selection:** Proper patient selection is vital in order to achieve a good outcome. Rule out individuals with unrealistic expectations and treat post-rhinoplasty patients with extreme care.
- **Materials:** A good technique begins with selection of the correct materials. Only temporary or autologous materials (fat) should be used in the nose. Among temporary materials, HA is the best option because it causes no fibrotic changes in the subcutaneous tissue, such as those that can occur with calcium hydroxyapatite. Moderate-viscosity HA is preferred due to the lower piston pressure in the syringe associated with it.
- **Correct amount of material:** Never exceed the correct quantity of filler used in the nose. It is always better to undercorrect and then repeat as needed. A good safety measure is to stay within 1 ml of filler per session. Remember that the pressure of the material can induce vascular problems even without being intravascular. Place the fingers to position and maintain the product in the target area to avoid migration. Small amounts of material should be placed using low infiltrative pressure and few passes in a retrograde infiltration fashion.
- **Cryotherapy:** It is always wise to favor vasoconstriction in order to limit bruising and edema and reduce intravascular compromise.
- **Cannula, manually curved:** The use of atraumatic cannulas permits gentle dissection of the tissues, reduces the trauma and risks of intravascular injection and delivers the material through a laminar flux that guarantees evenness. The manually curved feature allows for perfect shape compatibility with the nasal dorsum. The use of local anesthetic vesicles and needle skin penetration prior to cannula entry limits pain, trauma and vascular compromise.
- **Needles:** Extreme caution should be used when injecting with needles around the nose; their use should be limited to retouches or refinements and only by very experienced physicians. Perform tunnels (visible entry and exit points created with the needle being used) and allow material to exit if needed. The most risky areas are the tip, glabella, canine fossa and columellar base. Avoid bolus techniques in these regions and inject only when *coming out*. It is preferable to use medium-sized needles and inject into the deep or intermediate plane. Prior aspiration is not useful.
- **Improve; do not attempt a perfect outcome:** This technique should be considered part of the armamentarium of every aesthetic surgeon but not used as a single instrument. Whenever we want to completely correct a surgical deformity with fillers, we get into possible complications.

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- **Planning and discussion of potential complications:** It is essential to obtain proper informed consent. Frequently, patients are ill-informed about this procedure and have often read that it is extremely easy and free of risks. Establish a good relationship based on truth and trust with your patient. Morphing software can be of great help in this phase to help communicate with patients and establish common goals; underpromise and overdeliver.
- **Analyze the columellar labial angle:** Analysis of this feature allows for objectivity of the outcome and even the most critical patients will be able to appreciate the improvement.
- **Available kit for potential ECM:** If you intend to treat the nose with dermal fillers, you should be prepared to handle the complications as well.

9. Conclusions

The use of dermal fillers around the nose, although an advanced technique with potentially severe adverse events, is a powerful tool that can be used with a great deal of satisfaction and safety for the benefit of patients who wish to achieve aesthetic or functional improvements without a surgical procedure. The risks and benefits should always be considered and discussed, and complications should be prevented and promptly treated if necessary.

9.1. Nasal botulinum toxin

The onset of the neurotoxin in aesthetics revolutionized the treatment of dynamic facial dynamic wrinkles, producing a reversible paralysis that allows overlying tissues to relax and aesthetically to be flattened and raised. The use of botulinum toxin around the nose differs from the typically recommended indications of the superior facial third, being considered an advanced and off-label technique.

The use of botulinum toxin in the nose is useful in hypermotile noses that typically move with mimic expression. The complications related to this technique are not as severe as those associated with the use of rhinofiller as they are reversible and do not affect nose vascularity. Complications include pain, bruising, swelling, asymmetries, short-lasting effect and resistance. The duration of the corrections is limited (3–4 months) and action takes 2–10 days to establish, but it may enhance the results obtained with a rhinofiller as it removes muscular action and tension over the nasal region. Deep punctures at a muscular level are necessary.

The following muscles suitable for treatment around the nose are as follows:

- The **nasalis transverse muscle** is responsible for the wrinkling in the radix paranasal region known as *bunny lines*. Treatment typically requires 1–2 U per side 1 mm above the angular vessels at the lateral aspect of the radix.
- The **levator anguli oris alaeque nasi muscle** is responsible for gummy smiles. Treatment requires 2–5 U per side at the intersection of the nasolabial fold and the alar region.
- The **depressor septi nasi muscle** is responsible for hypermotile nose tips and an acute columellar labial angle. Treatment requires 1–2 U at the base of the columella.

- The **alar nasalis muscle** acts together with the depressor septi nasi muscle to lower the tip projection and restrict the nasal aperture. Treatment requires 1–2 U per side at the midpoint of the alar area.

A summary of these muscles and their corresponding treatment doses is given in **Figures 15**.

10. Clinical case patients

10.1. Clinical case patient 1

A 28-year-old female patient who previously underwent destructive septorhinoplasty with excessive resection of the alar and triangular cartilages presented to us with an inverted V deformity, right nasal alar collapse, tip asymmetry and a deformed dorsum sill.

Revision rhinoplasty was done using an open approach and harvesting right concha cartilage grafts. Tip de-projection, right lateral reconstruction and bilateral spreader graft positioning were performed (**Figures 1–4**).

Figure 1. Clinical case 1: Before (right) and after (left) images.

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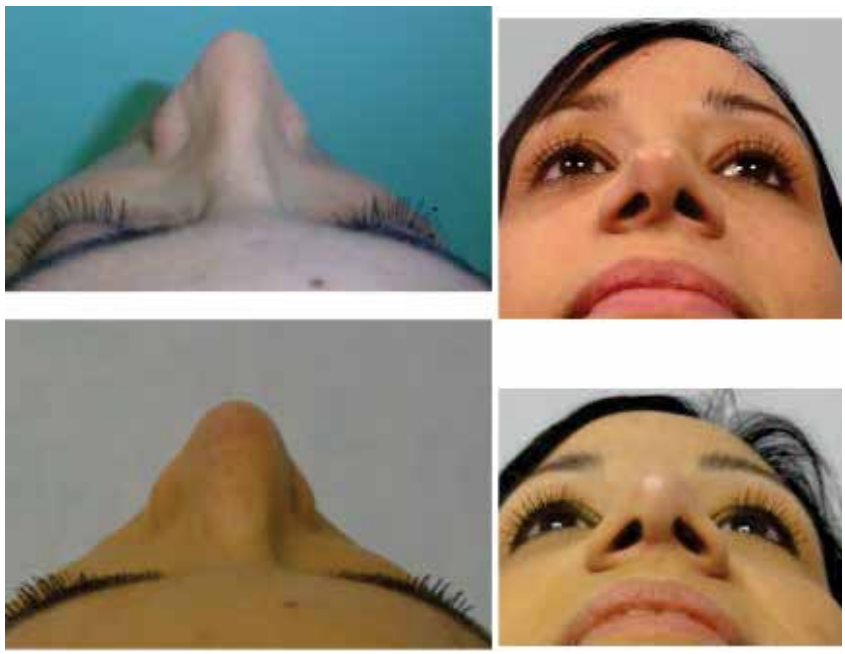

Figure 2. Clinical case 1: Before (upper) and after (below) images.

Figure 3. Clinical case 1: Before (left) and after (right) images, lateral view.

Figure 4. Clinical case 1: Before (left) and after (right) images, oblique view.

10.2. Clinical case patient 2

A 42-year-old female patient who previously underwent septorhinoplasty presented to us with dorsal irregularity, tip asymmetry and a 3 cm diameter anterior septal perforation.

Reconstructive procedure was performed using an open approach and the Kridel septal perforation closure technique. Regularization of the dorsum and tip symmetrization was done (**Figures 5–8**).

Figure 5. Clinical case 2: Septal perforation.

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Figure 6. Clinical case 2: Before (right) and after (left) images.

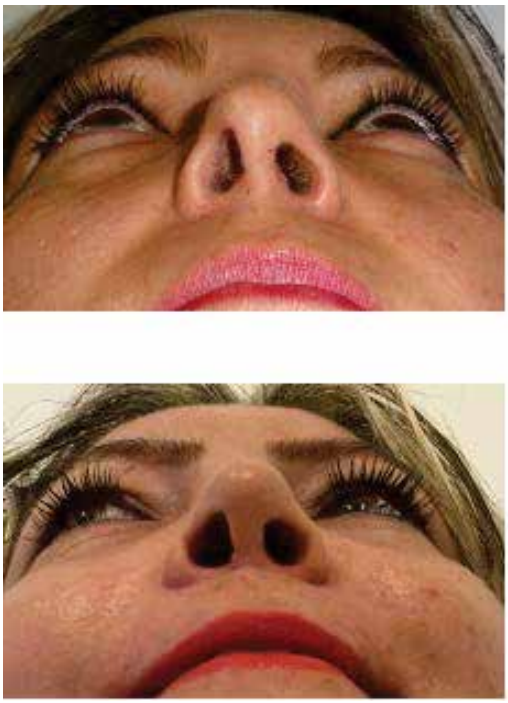

Figure 7. Clinical case 2: Before (upper) and after (lower) images, basal view.

Figure 8. Clinical case 2: Before (right) and after (left) images, lateral view.

10.3. Clinical case patient 3

We also report the case of nasal lipofilling for iatrogenic skin necrosis post-rhinoplasty and filler use in a 22-year-old female patient who previously underwent open rhinoplasty and received several steroids and filler (HA) treatments in the post-operative period until the nose tip, alar cartilages, caudal septum and anterior nasal spine vascularity were jeopardized. The patient was referred with severe scarring and low skin elasticity. She refused reconstruction with a forehead flap. Our treatment plan was initiated with PRP mesotherapy to the nasal region through a dermic pen device. Successive nasal micro-lipofilling sessions (×4) enhanced with a 20% mix of PRP significantly improved skin quality and elasticity for further reconstructive steps (**Figure 9**).

Figure 9. Clinical case 3: Dramatic ischemic progression due to fillers and steroid injections post-rhinoplasty courtesy of Dr Sebastian Torres.

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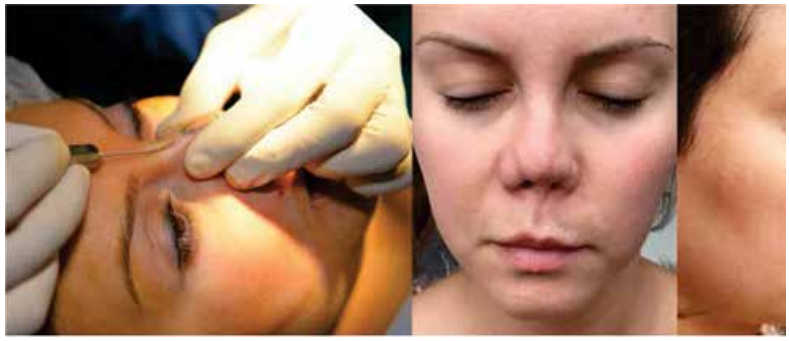

Figure 10. Clinical case 3: Micro-lipofilling technique (left) and post-operative (12 months) reconstructive procedures (center and right) courtesy of Dr Sebastian Torres.

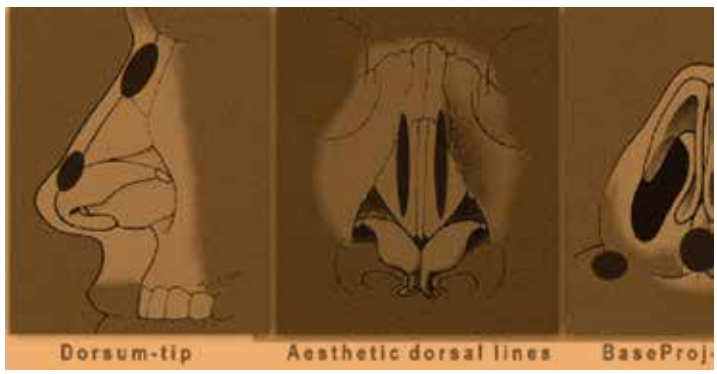

Figure 11. Rhinofiller main treatment areas.

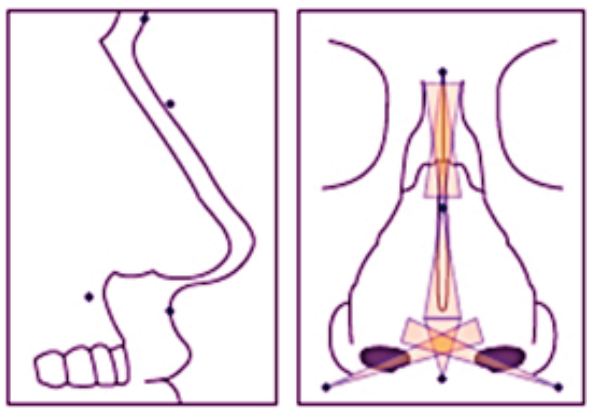

Figure 12. Rhinofiller injection technique. Spots indicate the entry point for cannula; orange triangles indicate material distribution.

Figures 13-14. Rhinofiller pre-operative (upper) and post-operative (lower) immediate results, lateral view.

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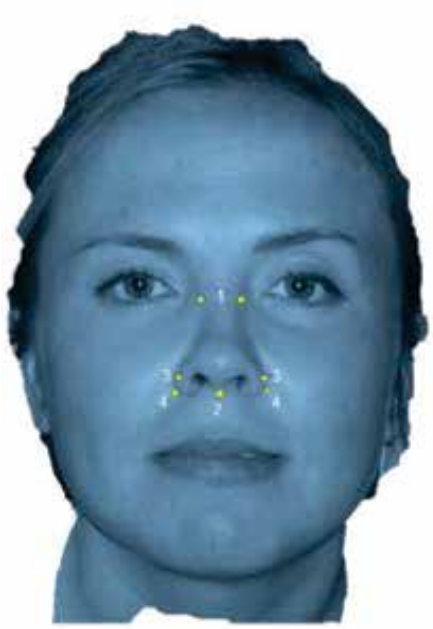

MUSCLE	ACTION	DOSE
1) Transverse Nasalis	Shortens Nose, Bunny lines	1-2 U per side
2) Depressor septi Nasi	Lowers tip, decrease projection	1-2 U
3) Dilator Naris	Dilates Narines, lowers tip	1-2U per side
4) Levator angulis oris alaeque nasi	Raises Upper lip, Gummy smile	5U per side

Figure 15. Summary of paranasal muscles and botulinum toxin doses.

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Section 17

Complications in Esthetic Surgery

Chapter 31

Complications in Esthetic Surgery

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Arash Khojasteh and M. Hosein Amirzade Iranaq

Additional information is available at the end of the chapter

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Abstract

Facial plastic and reconstructive surgery is a remarkably diverse specialty, ranging from maxillofacial trauma and reconstruction to facial rejuvenation, rhinoplasty, cleft surgery, microvascular surgery, facial cosmetic procedures, and pain control. It is unique among surgical specialties due to changing trends, racial, and regional ethnic preferences that influence what is considered an esthetic result.

A growing trend of popularity is seen for facial cosmetic surgery recently. One reason is the consumer's increased accessibility to information through television, the Internet, and other media sources. Also, the development of safe and effective surgical techniques, with reduced "downtime" and long-lasting, natural–appearing results, has popularized this field. Although some patients seek to rejuvenate their appearance to "turn back" the clock, others are interested in altering their appearance to a more desirable social norm.

As a result of this huge interest for cosmetic procedures, variable complications may also arise. Complications are important, and they play a critical role in developing practice guidelines, identifying gaps in knowledge, defining surgical quality metrics, and allocating resources. This chapter reviews both early, often transient, complications as well as delayed, often prolonged or permanent, complications with special attention to prevention and management.

Keywords: complication, aesthetic, management, plastic surgery, facial surgery

1. Introduction

In this chapter, we address;

- Complications in the periorbital area and midface
  - **Table 1**: periorbital and midface complication
- Complications in cosmetic rhinoplasty
  - **Table 2**: summary of complications
  - **Table 3**: comparative incidence of complications with grafts implants
- Complications in aesthetic blepharoplasty
- Complications in rhytidectomy (facelift)
- Complications in hair restoration surgery
- Complications in otoplastic surgery
  - **Table 4**: complications in otoplastic surgery
- Complications in forehead and brow lift surgery
- Complications in skin resurfacing
  - **Table 5**: summary of common laser complications and their management
  - **Table 6**: the most common long-term complications specific to certain skin resurfacing modalities
- Complications in facial suction lipectomy and fat transfer
  - **Table 7**: complication of fat grafting
  - **Table 8**: complications involving contour problems
- Complications in filler injections in cosmetic facial surgery
  - Box 1-1: presentation and management of common filler complications
  - Box 1-2: vascular occlusive events: presentation, treatment, and prevention
- Complications in botulinum toxin A (botax) injections
  - **Table 9**: complications of botox treatment
- Complications in facial implants in cosmetic surgery

2. Periorbital area and midface

2.1. Periorbital area

The eyes play a central role in what we consider beautiful face. The goal of periorbital rejuvenation surgery is to restore youthful proportions and focus attention on the eyes. This

is the reason made blepharoplasty as the third most common cosmetic procedure performed today, and for the foreseeable future. [1, 2, 3].

Patients with systemic diseases such as Sjogren syndrome, rheumatoid arthritis, Grave's disease, or neuromuscular diseases should be evaluated appropriately and counseled regarding the increased risks (**Table 1**).

Keratoconjunctivitis sicca or dry eye syndrome (DES) is a common condition that has a wide range of etiologies. Symptoms of dry eyes (redness, soreness, mucoid discharge changes) must be asked from patients, because blepharoplasty can cause DES, or worsen the condition if present preoperatively [4].

Preoperative DES, transcutaneous approaches, preoperative skin laxity, simultaneous upper and lower blepharoplasty, hormone therapy, and male sex can also increase the incidence of both DES and chemosis. To reduce the risk of this complication, adjunctive lid-tightening procedures should be done in potential risky patients.

During the preoperative evaluation, it is important to identity patients with Grave's disease. This condition is owing to autoimmune activity against thyroid-stimulating hormone receptors and is associated with orbital disease in 40% of patients [5]. It is characterized by glycosaminoglycan deposition, fibrosis of extraocular muscles, and adipogenesis in the orbit [6]. Although blepharoplasty is often required in the surgical management of this disease, there are often multiple stages and varying techniques to address the proptosis and lid retraction that are associated with this condition [5, 7].

Critical to maximizing outcomes after upper blepharoplasty is proper preoperative evaluation of the brow. Excessive contraction of the frontalis muscle occurs to compensate for significant upper lid dermatochalasia. If blepharoplasty is performed alone, relaxation of the brow will occur after surgery, which reduces the effectiveness of the operation [8]. Relaxed gaze is preferred to identify brow ptosis. Another method is to manually fixate the brow while assessing for excess skin.

Unusually high creases can be a sign of levator dehiscence that, if present, should be addressed at the time of surgery. Prolapse of lacrimal gland can be mistaken for excess fat, and injury to this structure can lead to postoperative complications such as DES (**Figure 1**). Proper evaluation of the lower lid helps to prevent complications from lower blepharoplasty such as ectropion/entropion, lid malposition, DES, and chemosis [9].

Excessive lid laxity should be addressed by either lid tightening or shortening techniques. Malposition of the lower lid should also be assessed by placing upward traction on the lower lid. A normal lid should elevate to at least the mid-pupillary level (**Table 1**).

Anterior lamellar shortening can be prevented by preoperative evaluation of excess skin in the lower eyelid. This is evaluated by having the patient open the mouth widely while pinching the lower eyelid skin. If there is no excess in this position, removal of skin will put the patient as risk for lower lid malposition and ectropion. A negative vector eyelid is described as a prominent globe with a recessed orbital rim/maxilla [10]. Blepharoplasty in these patients is associated with higher complication rates, particularly lid malposition [11].

For patients with significant exophthalmos, operative intervention should be modified by performing minimal fat excision or using spacer grafts to reduce the incidence of lid malposition. In addition, canthal-tightening procedures can exacerbate the malposition, as increased tension along the prominent globe will force the lid to retract further [13].

Periorbital complications	Cause	Prevention	Management
Dry eye syndrome	Missed preoperative, exposure, irritation	Preoperative history/ examination, eye protection	Lubrication, lacrimal puncta ducts
Chemosis	Conjunctival irritation, disruption of lymphatics	Temporary tarsorrhaphy	Topical dexamethasone, topical phefrylephrine, lubricants, severe cases
Ptosis	Missed preoperative, mechanical factors, levator injury	Limited deep cautery in lateral fat pad, muscle preservation	If persistent after 3 months, surgical ptosis repair
Diplopia/ strabismus	Scar tissue, muscle injury	Preoperative history/ examination	Local steroid injections, corrective strabismus surgery
Lower lid retraction/ lagophthalmos	Missed brow ptosis, under resection	Preoperative history/ examination, Chantal tightening procedures	Canthopexy/plasty, spacer graft, skin brow lift
Corneal abrasion	Muscle injury, preoperative lid laxity, overzealous skin excision	Corneal protector	Lubrication, topical antibiotics
Hemorrhage	Corneal exposure during surgery	Meticulous homeostasis	Surgical exploration, lateral canthotomy lubrication
Lacrimal gland injury	Anticoagulant use, vascular injury	Proper identification intraoperatively	Lubrication
Infection.	Improper diagnosis, missed preoperative	Preoperative antibiotics	Oral antibiotics, surgical decompression for abscess formation
Overcorrection	Surgical wound contamination, unsterile technique	Thorough preoperative assessment, conservative fat removal	Postoperative fat grafting, fillers
Under correction	Inappropriate preoperative assessment	Thorough preoperative assessment, marking	Revision surgery

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Periorbital complications	Cause	Prevention	Management
Midface complications			
Sensory nerve damage	Surgical error	Subperiosteal dissection	Expectant management
Facial nerve damage	Cautery, wrong plane of dissection	Subperiosteal dissection	Expectant management
Infection	Oral contamination	Copious irrigation, possibly avoiding	Antibiotics, surgical drainage as indication
Asymmetry	Suture fixation		Revision surgery
Implant malposition	Improper placement, shiftin	Tight subperiosteal pocket, implant fixation	Revision surgery.

Table 1. Periorbital and midface complications.

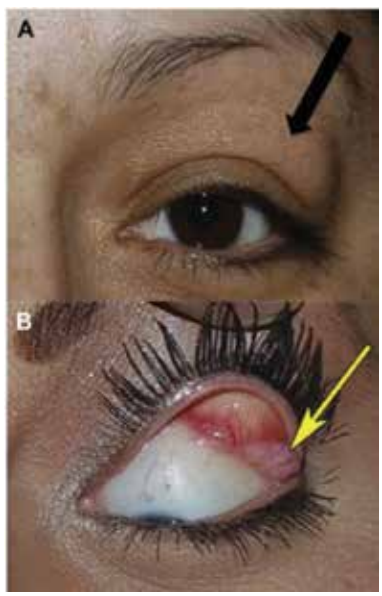

Figure 1. (A) Prolapsed lacrimal gland causing temporal fullness in the left upper eyelid (black arrow). (B) On eversion of the upper eyelid, the prolapsed gland can be seen beneath the conjunctiva (yellow arrow) [12].

2.1.1. Intraoperative complications

Corneal abrasions are a potential perioperative complication. Oculotoxic sterilization chemicals, surgical instruments, gauze, or desiccation of the ocular surface predispose to inadvertent injury to corneal epithelium. By using corneal shields, which can be placed after applying tetracaine drops to the eye and a generous amount of oil-based lubricant, it is completely

preventable. When corneal abrasions occur, patients often complain of pain, foreign body sensation, burning, tearing, and blurry vision. Evaluation with a fluorescein stain and a slit lamp seems to be necessary. Most can be managed with 48 h use of topical erythromycin or bacitracin [14]. The surface can also be protected with application of contact lens [15].

Thermal injuries have been reported after cosmetic blepharoplasty, and complications have resulted in postoperative astigmatism [16].

Topical antimicrobials followed by topical steroids to reduce scar tissue formation are mentioned for treatment. **Hemorrhage** is a potentially devastating complication with high risk of the potential blindness. Retrobulbar hematoma presents symptoms like rock hard proptosis, chemosis, severe pain, and visual changes. Ophthalmic consultation is requested early on in the course of therapy. Intraocular pressure is also elevated; however, surgical management is more dependent on the presence of visual changes. For patients with intact vision, conservative measures of cold compresses, intravenous osmotic agents, topicalb-blocker drops, and acetazolamide are initiated. For patients with visual loss, aggressive management is required beginning with a lateral canthotomy. Persistent visual should be evaluated with an orbital CT. If a posterior hematoma is present, bony decompression is warranted [17].

2.1.1.1. Postoperative complications

Postoperative DES is a common complication after blepharoplasty, as mentioned. Postoperative lagophthalmos, orbicularis injury, and lacrimal gland injury can have increasing effect on the risk of developing DES. Irritation, blurry vision, or foreign body sensation are some of the patient's common complains. Diagnosis is confirmed with a positive Schirmer test [18].

The management generally entails usage of ocular lubricants such as artificial tears and a petroleum-based ointment. If symptoms persist, blockage of the lacrimal outflow via a punctal plug can be useful. Chemosis often accompanies DES after blepharoplasty and is defined as swelling of the conjunctiva. It can be incited by inflammatory factors such as allergy or infection, as well as traumatic causes. After blepharoplasty, chemosis has been attributed to disruption of the lymphatic channels [19] or canthal disruption [20].

Temporary tarsorrhaphy should be performed if significant chemosis is encountered intraoperatively, to limit propagation of the chemosis and protect the conjunctiva. Conservative measures include topical phenylephrine, dexamethasone, and lubrication. Severe cases are managed with a conjunctivotomy and patching to apply pressure to the eye. There are several causes for ptosis after upper blepharoplasty. The most common is likely failure to properly identify ptosis before surgery. Injection of anesthetic agents causes a temporary ptosis if the levator superioris innervation is affected. Ptosis in the immediate postoperative period is usually dependent on mechanical forces and increased weight of the lid from edema. This edema resolves by 1 week after surgery as it is resorbed.

The levator is more susceptible to injury at the inferior aspect of the lid where it attaches to the orbital septum and muscle to form the upper eyelid crease. To avoid injury, access to the orbital fat pads should be performed at the superior aspect of the lid through the orbital septum. The medial fat pad serves as an important landmark because it rests on top of the levator aponeu-

rosis, preventing its injury. Correction of ptosis requires operative exploration of the wound through an anterior approach. If a tear in the aponeurosis is identified, direct repair is performed. If the aponeurosis is disarticulated from the tarsal plate, it must be reattached using interrupted sutures [21].

Lagophthalmos can occur owing to anterior lamellar deficiency (aggressive skin excision), incorporation of septal fibers into the skin during closure, or significant injury to the orbicularis muscle. Anterior lamellar shortening can often be treated with full-thickness skin grafts. Septal adhesions should be explored early and lysed. A new technique that is gaining popularity is the application of fillers to correct lagophthalmos [22, 23]. The technique mentioned has been used for patients with paralytic lagophthalmos [23] and for patients with superior sulcus syndrome [22] with excellent results.

Infections after blepharoplasty are extremely rare. Infections typically occur 5–7 days after surgery and present with increasing edema, erythema, and pain.

Orbital cellulitis involves the orbit and is associated with proptosis, restricted extraocular muscle movement, and visual changes. Organisms involved in periorbital infections include beta-hemolytic streptococcus and staphylococcus aureus and require more aggressive treatment [24].

Necrotizing fasciitis has been reported after blepharoplasty [25, 26].

Diplopia is thought to relate to direct trauma to the extraocular muscles during the procedure [25] or scar tissue formation, which limits extraocular muscle movement [27].

Strabismus in which superior oblique injury or inferior rectus injury is diagnosed can be treated successfully with systemic steroids and triamcinolone injections.

Diplopia has also been reported directly owing to lower lid fat repositioning [28].

Canthal webbing can occur both medially and laterally after blepharoplasty. The usual error is incision placement too medial or lateral, or too close to the lid margin. It can also occur from excessive anterior lamellar shortening. Managements ranging from gentle massage, steroid injections up to surgical correction with V–Y advancement, or multiple Z-plasties are performed.

Poor scarring is a potential complication anytime the skin is incised. Joshi and colleagues [29] looked at various closure techniques and found that a running 6-0 plain gut with several interrupted prolenes resulting in the lowest rates of standing cone deformities and milia formation. Running locking 6-0 prolene was associated with the highest rate of complications. For patients with track formation, subcuticular closure reduces the risk of recurrence. Fat repositioning can be performed in the subperiosteal or preperiosteal plane [30].

If hollowing does occur in the lower lid, this can be corrected with autologous fat grafting or placement of fillers. Owing to the delicate quality of the lower lid, softer hyaluronic acid fillers are preferred to prevent palpable or visible abnormalities. Hollowing in the upper lid is also a potential complication not only does it result in a cosmetic deformity, severe cases can result

in lagophthalmos [22]. Recent techniques such as limited removal of the central fat pad and repositioning of the nasal fat into the orbitoglabeller groove are developed [30].

Lower eyelid retraction can be caused by inadequate vertical laxity from lamellar shortening in 1 or a combination of the 3 lamella. To diagnose which of the 3 has the deficiency, cheek skin is pushed up to artificially recreate the anterior lamella. If the deformity is corrected, then the issue is from anterior lamellar shortening. If the retraction persists, middle or posterior lamellar shortening is more likely. Vertical inadequacy results in ectropion with anterior lamellar shortening, entropion with posterior lamellar shortening, and lower lid retraction with middle lamellar shortening.

Ectropion most commonly occurs from excessive skin excision. A transcutaneous approach alone, without skin excisions leads to 2–3 mm of anterior lamellar shortening [31].

Correction of anterior lamellar shortening is usually done with full thickness skin grafts. The ideal skin donor is the upper eyelid skin owing to the thinness and color match. If patients have had recent upper eyelid surgery and this skin is not available, supraclavicular skin or postaurical skin is an option. Another option to correct lower lid malposition from anterior lamellar shortening is the midface lift. Repositioning of the suborbicularis oculi fat pad supports the lower lid, recruits skin and muscle, and rejuvenates the midface. Multiple approaches have been described, including a transconjunctival, temporal approach, and subcilliary with subperiosteal or preperiosteal dissections. Marshak et al. [40] described a lateral canthal incision that allows for release of scar tissue and adequate access to the subperiosteal plane of the midface. Middle and posterior lamellar shortening is managed with scar lysis and placement of spacer grafts. Various autogenous and allogenic materials have been used with varied results. Common autogenous grafts include palate grafts, conchal cartilage, septal cartilage, temporalis fascia, and fascia lata [32].

Allogenic grafts, such as acellular dermis, palate grafts [33] dermis fat grafting [34], have also been used with variable results. Another significant factor in lower eyelid malposition is horizontal lid laxity, which is assessed preoperatively with snap and distraction tests. If this laxity is present preoperatively, a prophylactic canthal tightening procedure can prevent lid malposition. Multiple techniques can be used to resuspend the canthus, including canthoplasty, tarsal strip removal, and canthal suspension.

2.2. Midface

Midface rejuvenation can be performed using a multitude of different techniques. Preventable complications include improper implant choice, migration, and improper placement. The proper size is one that is slightly smaller than the desired projection, because soft tissue over the implant increases the fullness [35].

Implant migration is a preventable complication. Creating a limited subperiosteal pocket to reduce mobility, placement of a temporary stay suture, or screw fixation of the implant can prevent this complication. There have been several reports of severe orbital complications from implant migration, including conjunctival extrusion, scleral erosion [36], and intraorbital erosion [37].

Nerve injury can occur, and the most common is the infraorbital nerve which occurred during malar augmentation with implants, owing to its close proximity of the dissection. These injuries are commonly transient [38] and resolve without intervention. **Infection** is also potential complication, as with any other surgical implants. These complications were reported in proplast implants and often occurred as a late sequela owing to maxillary sinus erosion [39].

The transtemporal approach has been shown to be an effective technique to rejuvenate the midface. Because the lateral canthus and other orbital structures are not manipulated in this approach, lower lid malposition is not encountered [40].

The incision in the temporal tuft of hair carries a risk of **Alopecia**, which can be limited by beveling the incisions to limit disruption of hair follicles. **Bleeding** and **infection** are not common complications. Abscess formation has been reported, which led to malar wasting requiring malar implants for correction [41].

3. Rhinoplasty

Rhinoplasty is one of the most difficult cosmetic operative procedures performed today. Surgeons must develop skills for a three-dimensional manipulation of various tissues, often performed with limited access. Like all other surgeries, occurrence of complications is inevitable but must be managed properly. Early complications in rhinoplasty can be avoided through very careful and precise techniques during or at the end of the operative procedure. Late complications may occur due to failure to understand the consequences of surgical manipulation of the underling tissues, or from the idiosyncrasies of the various anatomic tissues healing (**Table 2**).

Complication	Cause	Avoidance	Correction
Asymmetry of the bony vault	Asymmetric osteotomies	Meticulous attention to osteotomies	Percutaneous osteotomies
Asymmetry of the middle vault	Unmasked dorsal septal deviation after dorsal reduction	Recognition of septal deviation	Crushed cartilage camouflage grafts
Tip asymmetry	Asymmetric tip sutures unmasked caudal septal deviation	Meticulous attention to suture technique Meticulous inspection	Revision Possible placement of septal extension graft Possible repositioning of caudal septum with swinging door, secure to nasal spine with suture
Over resection of nasal bones	Overaggressive resection	Judicious bony dorsal reduction	Placement of dorsal onlay graft

Complication	Cause	Avoidance	Correction
Open roof deformity	Bony dorsal reduction	Judicious bony dorsal reduction when no osteotomies are planned, but unavoidable when narrowing of the bony base is planned	Lateral osteotomies to close open roof
Rocker deformity	Continuation of osteotomies into frontal bone	Meticulous planning of o steotomies and continuous palpation/inspection	Percutaneous osteotomies
Stair step deformity	Improper placement of lateral osteotomy anterior to the ascending process of the maxilla	Meticulous planning of dorsal reduction, both bony and cartilaginous dorsum	Percutaneous osteotomies
Polly beak deformity	Over resection of nasal bones under resection of dorsal septum (anterior septal angle) Postoperative soft tissue scar formation	Meticulous planning of reduction both bony and cartilaginous dorsum Avoid overaggressive dossal reduction in\ thick-skinned patients	Dorsal onlay camouflage graft Appropriately match cartilaginous dorsal reduction to that of bony dorsal reduction May require revision Kenalog injections postoperatively
Inverted V deformity	Upper lateral cartilages drop inferior and posterior, causing show of the nasal bones and dorsal septum This results from failure to repair the upper laterals to the dorsal septum after dorsal reduction	Repair upper lateral cartilages to dorsal septum after dorsal reduction use of spreader grafts or auto spreader grafts	Revision with use of spreader grafts (if upper lateral cartilage present), possible onlay crushed cartilage camouflage grafts, consider osteotomies to narrow the bony base if this is a contributing factor
Saddle nose deformity (**Figure 2**)	Overaggressive dorsal reduction with septoplasty, resulting in a dorsal strut that is inadequate to support cartilaginous dorsum	Maintain 1.5-cm dorsal strut	Revision with dorsal onlay camouflage graft (minor cosmetic deformity) and rib cartilage graft reconstruction (severe cases)
Bossae	Overaggressive cephalic trim of lateral	Note predisposing factors for bossae formation (see below),	Revision with structural grafting of lateral crura (strut grafts). crushed

Complication	Cause	Avoidance	Correction
	crura	avoid over aggressive resection	cartilage, and/or temporal is fascia camouflage grafts
Visible grafts (**Figure 3**)	Thin skin	Note thin skin preoperatively and place temporalis fascia overlay grafts to camouflage	Revision with possible graft removal and/or placement of temporal is fascia for contour smoothing and camouflage
Pinched tip (**Figure 4**)	Over resection of lateral crura during cephalic trim malpositioning of lateral crura Contracture from wound healing	Spare 6- to 7-mm rim strip Ensure appropriate orientation and patient about this risk and document having done so	Lateral crural strut grafts, possible crushed cartilage grafts for camouflage Removal/revision of any offending tip sutures, possible lateral crural strut grafting, possible repositioning of lateral crura Revision surgery with one or more of the above maneuvers
Poorly defined tip	Overaggressive tip deprojection in thick- skinned patient	Avoid overaggressive deprojection	Judicious superficial nasalis aponeurotic system (SNAS) excision intra operatively, ken log injections postoperatively
Nostril asymmetry	Altered caudal septum, medial, intermediate, and lateral crura dynamics from intra-operative sture technique or alteration	Meticulous attention to symmetric placement of sutures, such as tip and tongue in groove sutures	Revision, with correction of underlying offending cause
Alar retraction	Overly tight closure of marginal incision Over resection of lateral crura during cephalic trim Malpositioning of the lateral crura Overly tight lateral crural spanning sutures Contracture from wound healing		Remove/revise offending sutures Lateral crural strut grafts, possible alar rim grafts (minor cases), auricular composite grafts (severe cases) Repositioning of the lateral crura, lateral crural strut grafts, possible alar rime Grafts (minor cases),

Complication	Cause	Avoidance	Correction
			auricular composite grafts (severe cases) Removal/ revision of any offending tip sutures Revision surgery with one or more of the above maneuvers
Columellar retraction	Over resection of the caudal septum Excessive setback of the medial crura during tongue-in-groove	Avoid over resection Avoid excessive setback	Caudal septal extension graft, columellar strut graft, columellar plumping graft Revise tongue-in-groove, consider columellar plumping graft Septocolumellar suture can be used to help prevent contracture during wound healing
Columellar and alar base scar formation	Wound healing	Meticulous wound closure	Kenalog injections with revision reserved for severe cases
Nasal obstruction	External nasal valve collapse Internal nasal valve collapse Septal deviation intranasal synechia Recurvature of the lateral crura	Maintain integrity and appropriate position of lateral crura, avoid overaggressive narrowing of the alar base Avoid overaggressive narrowing of the bony base, use spreader grafts or auto spreader grafts to maintain patency Appropriately address any septal deviation careful soft tissue handling and fastidious wound closure Recognize contribution to the patency of the nasal airway	Lateral crural strut grafts, possible alar rim grafts Spreader or autospreader grafts Septoplasty Lysis of synechia Lateral crural strut grafts
Septal perforation	Opposing mucoperichondrial	Meticulous elevation of mucoperichondrial	Place fascia or crushed cartilage

Complication	Cause	Avoidance	Correction
	lacerations Septal hematoma	flaps to prevent opposing lacerations Placement of septal whip sutures and use of removable soft silastic intranasal splints, prophylactic mucoperichondrial flap incision to allow drainage of any accumulated blood	graft interposed between lacerations Incision and drainage
Costal cartilage (autograft and homograft) warping	Intrinsic property of cartilage	Concentric carving	Revision
Pneumothorax after costal cartilage harvest	Injury to the pleura	Harvest cartilage in subperichondrial plane	Close wound under water with positive pressure ventilation

Table 2. Summary of complications [42].

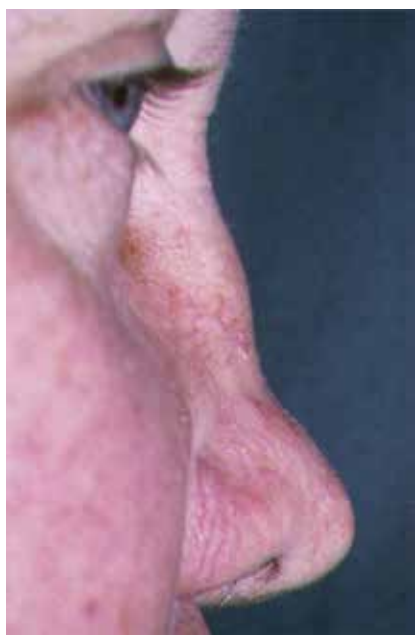

Figure 2. A saddle deformity caused by excessive loss of the bony and cartilaginous dorsum [1].

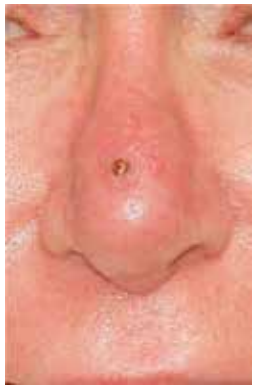

Figure 3. Erosion of a dorsal Gore-Tex implant through the skin of the nasal dorsum [2].

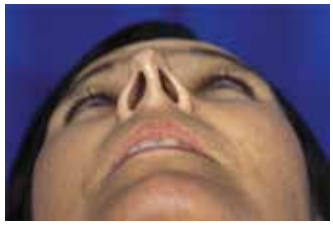

Figure 4. A pinched tip due to over-resection of the tip cartilages and insufficient tip framework [43].

The focus of rhinoplasty is to achieve nasal balance and maintain harmony with the face while keeping the nasal airway functional. Understanding the use of autologous, homologous, and alloplast materials for grafting and implantation purposes has become a necessity (**Table 3**; **Figures 5** and **6**).

	Resorption	**Warping**	**Infection**	**Extrusion**	**Skin changes**	**Support**
Cartilages	+	+	Low	–	–	Good
Bone	++	+	Low	–	–	Rigid
Homograft	+++	+	+++	–	–	Good
Alloderm	++++	NA	Low	Low	–	None
Silicone	–	–	+	+++	+	Rigid
Medpor	–	–	Low	–	–	Rigid
Gore-Tex	–	–	++	Low	+	Mesh
Mersilene	–	–	++	–	–	Mesh
Prolene	–	–	Low	–	–	Mesh

Table 3. Comparative incidence of complications with grafts and implants [44].

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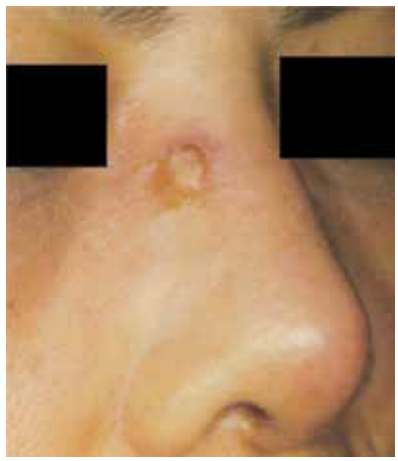

Figure 5. Extruding silastic implant 14 years postoperatively [45].

Figure 6. (A) Patient at surgery to remove an infected alloplastic dorsal graft that had been in place for 5 years. The patient was a heavy smoker. (B) No incision was made, as the graft had begun extruding through the columella. The material appeared to be porous, high-density polyethylene [46].

4. Midface lifting and blepharoplasty

4.1. Complications of midface lifting and the related surgical technique

Various complications may be encountered in the transeyelid approach, including temporary complaints of dry eyes, and lateral periorbital skin excess may occur in the early postoperative period, but these typically resolve with time. In the subciliary approach, a visible scar may remain. In the transconjunctival approach, conjunctival edema (chemosis) may be seen in up to 20% of patients [47].

In addition, there is a potential for middle lamellar scarring, leading to vertical shortening of the eyelid, which could present as a cicatricial ectropion or entropion or even permanent

changes in the shape of the eyes. There could also be zygomatic branch injury, leading to forms of lagophthalmos (**Figure 7**).

Figure 7. Patient referred with bilateral lagophthalmos resulting from overzealous skin excision during prior blepharoplasty [12].

4.2. Endoscopic temporal approach

Several complications may be encountered in this approach. Injury to the frontal branch of the facial nerve may occur. Injury may occur when approaching the zygomaticotemporal nerve and vein [48].

Injury to the vascular structures without adequate hemostasis results in hematoma formation. Aggressive medial dissection through the temporal incision may lead to lateral canthal distortion [41]. When beginning this temporal approach, if the plane is dissected too superficially, injury to hair follicles can lead to permanent hair loss. The use of the sublabial incision carries risks, given the potential exposure to oral flora. These patients may be at greater risk for developing malar subperiosteal abscesses [41]. Therefore, it is of the utmost importance for patients to receive postoperative antibiotics to cover oral flora for 7–10 days [48].

4.3. Preauricular deep plane approach

Complications include parotid duct fistulas if the parotid duct is invaded [49]. These complications are addressed by recannulizing the duct after locating the stensen duct intra-orally. If not a full cut, this complication could be addressed with warm compresses and aspiration. Another complication is earlobe deformity, including pixie ears. There could also be complications of the buccal branch or marginal branch nerve injury. There is also the risk for hematomas, leading to possible necrosis of the skin flap.

4.4. Complications of lower eyelid blepharoplasty and the related surgical technique

Lower eyelid blepharoplasty is generally performed through a transconjunctival or transcutaneous route. Both approaches can be complicated by lower eyelid retraction, DES, retrobulbar hemorrhage, diplopia, and volume depletion.

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4.4.1. Lower eyelid retraction

The transconjunctival approach has a lower incidence of retraction, because it avoids the orbital septum [50].

Patients can present with an inferior scleral show chemosis, rounded lateral canthus, tearing, and a postsurgical look. A forced upward traction test can show tethering to the orbital rim or an overall tight feel. During the first 3 months, it is customary to encourage lower eyelid pushups and, if needed, injections of fluorouracil 50 mg/mL directly into the cicatrical region once per month. If, after 3 months, lower eyelid retraction remains, a surgical approach is planned. Depending on the severity of the lower eyelid retraction, a plan is formulated accordingly.

- First, it must be established whether the problem is anterior or middle lamella. If there is vertical inadequacy of the anterior lamella, a full-thickness skin graft is generally the treatment of choice.
    - More commonly, a middle lamellar problem is encountered. In this case, because of cicatrical contraction of the middle lamella, a spacer graft is the treatment of choice.
        - A cantholysis is performed, a transconjunctival incision is made with tenotomy scissors, and the tether is released.
        - If needed, a SOOF lift can be performed, and the orbitomalar ligament disinserted at this point.
            - A spacer graft, whether hard palate graft or acellular human or animal product, is secured, essentially extending the lower eyelid retractors to the conjunctiva.
            - The canthus is closed with a standard tarsal strip procedure, and the lower eyelid is placed up on a frost lower eyelid suspension suture for 5–7 days.

4.4.2. Diplopia

If the medial and central fat pads are injured during a lower eyelid blepharoplasty, torsional diplopia can result. If injury results from scarring to the inferior rectus or its attachments, hypotropia can result.

4.4.3. Dry eye syndrome

Most eyelid surgery can result in temporary dry eye symptoms or can be subclinical, which is evident only in the tear film breakup time or consistency of the tear film itself. Artificial tears can be prescribed, and, if more significant symptoms present, punctual plugs can be used.

4.4.4. Volume depletion

Excessive fat removal during a lower eyelid blepharoplasty will present the patient with complaints of a sunken appearance or darkened lower eyelids from a shadow effect and looking more tired than before surgery. The orbital rim can be seen with increased definition,

especially in patients with a less prominent orbicularis or thinner skin. A more prominent tear trough deformity can also be seen. This complication can be corrected with fat grafting to the newly hollowed area or a transeyelid midface lift. The best option is to avoid this complication by conservative fat reduction or performing a fat transposition.

5. Rhytidectomy (face lift)

A thorough preoperative evaluation will result in fewer complications after surgery. Patients are instructed to avoid the use of aspirin and nonsteroidal anti-inflammatory drugs for at least 2 weeks before surgery. Smoking must be stopped for at least 1 month before surgery. All other medications should also be avoided for 2 weeks prior to surgery because of the risk of postoperative bleeding and intraoperative anesthetic complications, including arrhythmias [51].

Chemotherapeutic agents and oral steroid use can alter the wound. Facial nerve paresis or paralysis must be documented preoperatively. Complete documentations for possible submalar hollowing, microgenia, facial asymmetry, submandibular gland ptosis, low-riding hyoid, and platysmal bands need to be done and discussed with the patient. Patients must be aware that perioral rhytids, deep neck rhytids, and nasolabial folds are unaffected by this surgery so alternative treatment plans must be discussed. It is important to evaluate the patient's position of the frontal and temporal hairline and look for evidence of alopecia. The present position of the temporal and mastoid hairlines needs to be respected in the design of any rhytidectomy incision. The temporal hairline must not be elevated or narrowed as the result of a poorly designed incision. The upper end of the rhytidectomy incision should be placed along and parallel to the lower end of the temporal hairline and should not extend above the upper edge of the pinna. If it does, the temporal hairline is raised and narrowed, compromising the final aesthetic result and making reconstruction of this valuable landmark difficult. Hairline incisions in the mastoid and post-auricular area should be avoided because they often result in hypopigmented and quite obvious scars that prevent the patient from wearing her hair up, which might expose them. If it is necessary to extend the incision behind the ear, then it is prudent to continue it into the hair-bearing scalp.

5.1. Intraoperative complications

5.1.1. Positioning and preparation

Careful patient positioning following anesthesia and before surgery improves patient visibility and outcome and reduces complications. Surgical lights should shone on the outer surface of the skin flaps and not directly into the surgical field for transillumination and to achieve the so-called peau d'orange effect in order to make necessary adjustments to avoid perforation of the SMAS and possibility of parotid fistula.

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5.1.2. Parotid duct injury

It may occur along the anterior border of the masseter on a line from the external auditory canal to the upper lip. If it is injured, the distal end of the duct is cannulated with a small catheter and passed retrograde into the field and then passed into the proximal severed end. It is left in place for about 2 weeks.

5.1.3. Facial nerve branch injury

Too deep dissection might result in injury to branches of the facial nerve. If recognized during the surgery, the nerve must be repaired. The temporal branch is most vulnerable anterior to the temporal hairline so dissection here must be superficial with observation of the overlying hair follicles in the skin flap. Marginal mandibular and cervical branch injuries are possible if the dissection below the mandibular border extends beneath the platysma.

5.1.4. Auricular nerve and jugular vein injury

The posterior neck flap dissection must be done superficially but without buttonholing the skin flap. Care is taken to avoid exposing the fascia overlying the sternocleidomastoid muscle and risking injury to the great auricular nerve and accompanying external jugular vein. If injured, direct repair of nerve and suture ligature of vein should be undertaken.

5.1.5. Spinal accessory nerve injury

More posteriorly, injury to the spinal accessory nerve can occur if the dissection becomes too deep. A good superficial landmark to keep in mind is Erb's point (**Figure 8**).

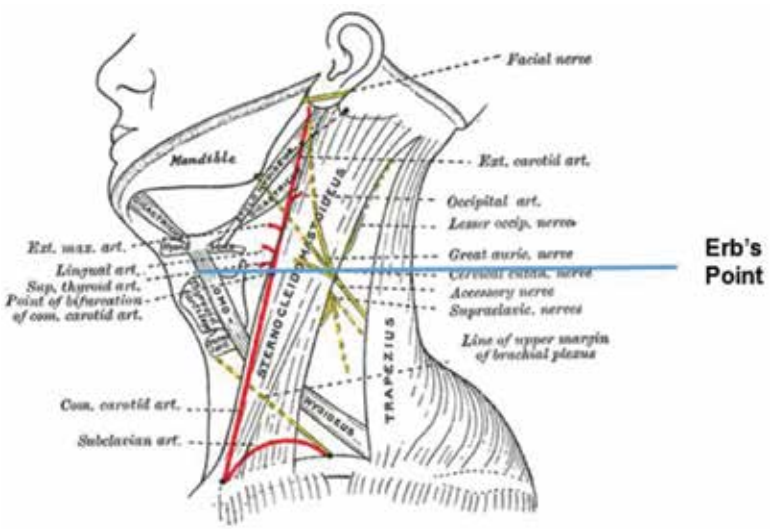

Figure 8. Erb's point [51].

5.2. Postoperative complications

5.2.1. Hematoma

Hematoma formation the most common postoperative complication typically occurs within the first 24 h following surgery, ranging from 3 to 8% of cases according to multiple studies [52–56]. Before discharge, the dressings are inspected and flaps viewed with a flashlight while lifting up the Kerlix wrap from each cheek. In the presence of significant pain or asymmetric swelling, flaps inspection is done. If a hematoma is discovered, the patient is returned to the operating room to prevent further complication to an already compromised flap. The incision is opened, clots evacuated, bleeding controlled, and the incisions closed over an active drain.

5.2.2. Infection

Infection is unusual following rhytidectomy but may occur as the result of a stitch abscess or, more rarely, a suture passed through the tragal cartilage. The offending suture(s) should be removed, and local wound care with an antimicrobial ointment often clears the problem. Significant erythema and tenderness to the auricular cartilage warrants oral antibiotics to cover *Staphylococcus*, *Streptococcus*, and *Pseudomonas* to prevent permanent cartilage damage.

5.2.3. Nerve injury

If noted during surgery, primary repair results in the best outcome. Mild facial paresis is usually temporary but may persist for 12 h after surgery, caused by the prolonged duration of local anesthetic agents or edema of the nerve. The great auricular nerve is the most frequently injured sensory nerve and results in numbness. If the nerve is repaired during surgery, return of sensation is common but may be delayed for 12–18 months and result in localized areas of persistent anesthesia. The temporal branch is the most frequently injured motor nerve and may resolve within 18–24 months of onset, but the resultant asymmetric brow can be improved with careful use of paralytic agents like Botox or Dysport on the nonparalyzed side. If the forehead paralysis is permanent, treatment is dictated by the extent of the subsequent deformity and disability. Mild asymmetry is best managed by the paralytic agents mentioned earlier, whereas significant brow ptosis may require a brow lift on the affected side.

Other nerve injuries may include marginal mandibular, zygomatic, buccal, or cervical branches of the facial nerve, and permanent damage was <1% in a large study [57].

5.2.4. Systemic complications

Major systemic complications are unusual in patients undergoing facelift surgery and may include deep vein thrombosis (DVT), pulmonary embolism, stroke, blood transfusions, major anesthetic complications, and death [58].

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5.2.5. Skin slough

Skin slough is a rare occurrence following rhytidectomy (**Figure 9**). Vascular compromise is usually noted in the periauricular region and may appear as a distinct area of ecchymosis. Local application of nitropaste or DMSO 2–3 times daily may be beneficial to reduce the chance of full-thickness skin loss. Nevertheless, the area of concern is allowed to demarcate fully into an eschar before conservative debridement is done in the office. Excision of scars and closure are delayed until full maturation of the wound and scars has occurred to prevent further compromise of the flaps and ultimate aesthetic result.

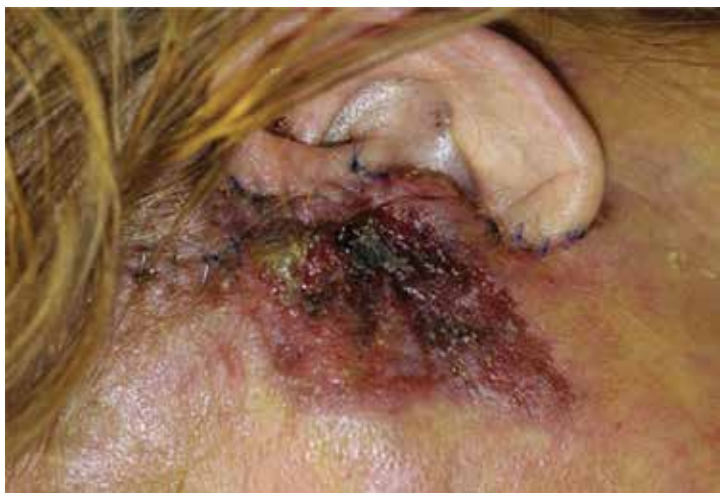

Figure 9. Preauricular skin slough. The preauricular and postauricular regions represent the most distal segments of the facelift skin flap. These sites are prone to skin loss in smokers and in other instances where flap vascularity is compromised [59].

5.2.6. Scarring

Hypertrophic scars are injected with a dilute concentration of Kenalog 2–5% every 6 weeks once noted, along with the use of silicone sheeting or gels. Persistent scars may respond to pulsed dye laser therapy if resistant to the aforementioned measures and usually require multiple treatments. Hypopigmented scars are most common along the posterior hairline when incisions have been placed along the hairline instead of behind it.

5.2.7. Alopecia

Alopecia occurs following damage to the hair follicles from electrocautery, excess traction of tension on the skin flaps, and inadvertent elevation or elimination of the temporal hair tuft and temporal hairline. Temporary loss may be shortened with the use of topical minoxidil. Permanent alopecia requires the insertion of single-hair follicular units into the areas of alopecia or the replacement or lowering of the temporal hairline.

5.2.8. Contour deformities

Contour deformities are common immediately after rhytidectomy. Most of these are temporary and related to postoperative edema and ecchymosis and occur in the preauricular and submental regions (**Figure 10**). As the swelling subsides, most of these resolve, and resolution may be hastened with gentle local digital massage. Persistent contour deformities may be seen for several months and require no further treatment. If localized areas of depression persist after 6–12 months, they can be improved by injections of dermal fillers or fat.

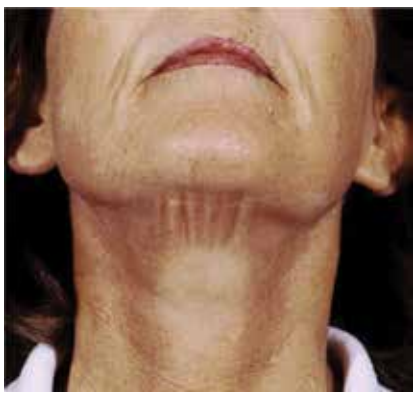

Figure 10. Submental banding following overaggressive liposuction. Excessive fat removal or aggressive liposuction with scarification of the dermis may result in banding and an unnatural contour. This deformity is difficult to correct. Early in the postoperative period, massage and the judicious use of triamcinolone injections may help to minimize such irregularities. In the long run, the juxtaposition of soft tissue or fat grafting may diminish the appearance of banding. Avoidance of overaggressive lipocontouring is an important tenet [59].

Another problem with facelift skin adjustment is an unnatural-appearing earlobe. Although this seems like a straightforward part of the lift, failure to address the earlobe properly can lead to the most telltale sign of a poor technique, which is a "pixie" earlobe (**Figure 11**). The pixie or "elfin" earlobe is a result of lack of attention to the skin cutback to deliver the earlobe from under the excess pulled skin.

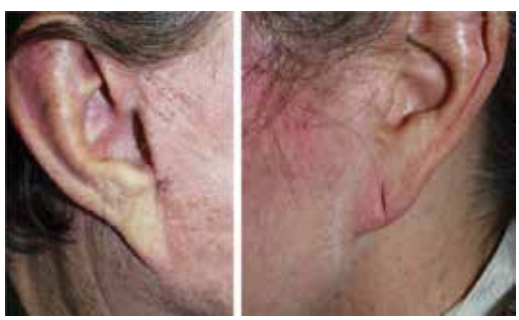

Figure 11. The pixie ear lobe deformity can occur with improper technique in facelift surgery [60].

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6. Hair restoration surgery

6.1. Donor site

6.1.1. Complications

- Poor wound healing/scarring (atrophic, widened, hypertrophic, hypopigmented)
- Necrosis (**Figure 12**)
- Chronic pain

Cause: Improper donor harvesting (too wide a scar, too much tension, poor location, transection of hair follicles, transection of blood and nerve supply, improper undermining).

Avoidance: Surgical complications can be avoided by paying attention to the depth and angle of one's harvest (staying within the subcutaneous plane and above the galea), avoiding transection of the underlying blood supply, nerves, galea, and surrounding hairs. It should be ascertained that there is sufficient laxity (preoperative scalp relaxation exercises in a tense scalp), sufficient time between operative harvesting cases so that the scalp has had time to relax, and only 1 cm or less in width should be harvested when removing a donor strip. Use of tumescent solution to help straighten follicles and to limit injury to the underlying nerve and blood supply is critical. A careful two-layered closure is helpful to minimize scarring. Use of platelet-rich plasma (PRP) can help with good wound healing. If a wound is under tension, the wound should be closed in a delayed fashion rather than undermined or forcefully drawn close, both of which can lead to necrosis, unpredictable hair loss in the donor area, and additional scarring.

Correction: Albeit tempting, surgical excision of a scar tends to lead to the reappearance of the same scar over time. Placing grafts into the scar can be helpful but sometimes the blood

Figure 12. Donor-site necrosis resulting from a high-tension suture closure. Eschar is identified over the necrotic site in this 2-week postoperative photo. Early postoperative effluvium surrounds the devitalized incision site [61].

supply is poor and may not be entirely beneficial. Use of micropigmentation (tattooing) can also help cover the previous scarring. Chronic nerve pain (or conversely permanent anesthesia) that can arise from inadvertent transection of occipital nerves can be addressed with targeted botulinum-toxin injections into the specific area of discomfort. After 1–2 sessions of neurotoxin (2–5 units), the patient can be afforded lasting relief.

6.2. Recipient site

6.2.1. Complications

- **Pitting** (**Figure 13**)

  Cause: The graft was placed too deep relative to the surrounding tissue.

  Avoidance: The graft should fit the site correctly, and test grafts should always be undertaken first to ensure that the graft-to-site fit is appropriate before major graft dissection is undertaken. The graft should fit so that it rests approximately 1 mm above the surrounding skin because when the edema resolves, the graft settles to be flush with the surrounding skin. If placed flush or lower than the surrounding skin, the site has a greater likelihood of eventual pitting.

  Correction: It is very hard to correct pitting. In sensitive areas like the hairline, if the hairline is at the appropriate position or too low, then the grafts can be removed through punch excision. Otherwise, additional grafts can be placed around the bad grafts to camouflage them in an approach known as "de-emphasis grafting."

- **Cobblestoning** (**Figure 13**)

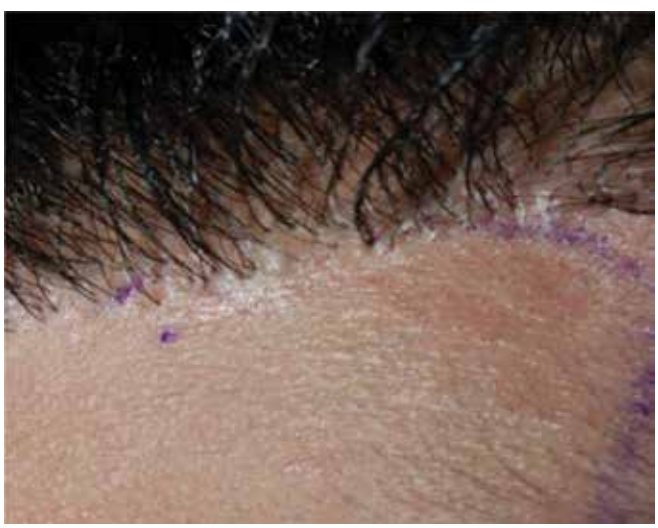

Figure 13. Graft height error. Careless graft placement resulted in a combination of cobblestoning (too high) and pitting (too low) [61].

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Cause: Cobblestoning is the opposite problem of pitting. When grafts are placed too high to the surrounding scalp, they can create a cobblestoned appearance (i.e., raised vis-a`-vis the surrounding scalp).

Avoidance: Grafts must be placed that fit the site correctly. If the grafts are too large, they may not settle into the site correctly and thereby leave a cobblestoned appearance after wound healing.

Correction: Cobblestoning is very hard to correct. The cobblestoned area can be transected flush to the scalp, or more grafts can be used to be placed around the existing bad grafts through "de-emphasis grafting."

- **Compression**

  Cause: Grafts with numerous hairs and that are too large for a particular site can be squeezed together to appear as a central tuft of hair, almost like a plug of yesteryear.

  Avoidance: Ensure that grafts fit the site appropriately.

  Correction: Similar to the correction stated above in "pitting."

- **Kinky hair**

  Cause: The hair shaft is overly manipulated or crushed during insertion by the grasping forceps leading to a wiry hair growth.

  Avoidance: The graft should be held only by the surrounding fat cuff and never on the hair shaft itself.

  Correction: Correction is similar to the correction stated above in "pitting."

- **Poor growth**

  Avoidance: Patients must understand that sometimes, despite a surgeon's best efforts, growth can be underwhelming based on a patient's growth characteristics. However, certain factors can predispose toward poor growth including not using recipient tumescent solution (0.01% lidocaine with 1:500,000 epinephrine) to protect the underlying neurovasculature, implanting grafts into too dense a distribution, and poor handling and manipulation of grafts (as mentioned above in pitting and kinky hair). Use of PRP during a procedure can improve a patient's chance of success with hair growth in the author's experience.

  Correction: A second hair transplant may need to be performed with better technique.

- **Unnatural hairline**

  Cause: An unnatural hairline can arise from a host of problems that involve a badly positioned hairline (too low, too high, improper slope, too wide, too narrow, and does not match a natural Norwood pattern of hair loss), too straight or harsh [use of grafts that are too large in the frontal hairline, not angling the grafts correctly (see **Figure 4**), not creating a natural micro-undulating hairline, not putting "sentinel" one-hair grafts to soften the hairline], or having any of the problems like pitting, kinky hair, and so on, mentioned above.

Avoidance: The macro-hairline (the line drawn on the head) should be undertaken only after a surgeon understands the natural Norwood patterns and can construct a hairline based on accepted principles that mimic nature. The micro-hairline (the actual recipient sites and grafts placed) must be constructed with utmost care so that the angles are low and straightforward and appear to look like a cragged coastline (i.e., without appearing too straight and harsh). The assistants who place grafts must adhere to careful attention to avoid previously enumerated problems, including pitting, kinky hair, placement of inappropriate graft sizes for a particular location, poor growth, and similar problems.

Correction: If the hairline is too high, the hairline can be redrawn lower and a better designed and constructed hairline can be placed in front of the bad grafts to camouflage them ("de-emphasis grafting"). If the hairline is too low to be acceptable or natural in appearance, then grafts can be punched out that reside in front of the proposed new hairline (**Figure 13**). Alternatively, a strip of grafts can be excised from the hairline to raise the hairline upward, after which time when the wound is well healed, a new hairline can be constructed according to the meticulous principles of good hairline design and execution.

- **Necrosis/poor scalp healing. Poor scalp healing can manifest as a hypopigmented scalp, a chronically discolored scalp, or frank necrosis**.

  Cause: Besides a patient's predisposing factors, such as smoking, chronic sun damage, and diabetes, a surgeon can inflict this outcome when the underlying vasculature is carelessly transected during recipient-site creation.

  Avoidance: Use of proper recipient-tumescent fluid is important to increase the distance between the recipient-site creating instrument (e.g., needle, blade) and the underlying neurovasculature. Also, avoiding overdense packing (>50 sites per cm^2) may help to minimize this problem. For signs of venous congestion or incipient necrosis, using nitropaste can be an immeasurably important rescue tactic. As mentioned earlier, use of PRP injected into the scalp an hour or so before site creation can help improve wound-healing capacity and minimize this risk. In patients who are very bald and have signs of poor vascularization, use of topical minoxidil for several months may anecdotally improve blood supply to the target recipient area but no conclusive studies have been undertaken to demonstrate that benefit.

  Correction: If the scalp looks discolored or hypopigmented in some way, additional grafts (placed in a more careful manner explained above and only undertaken a year or more later to allow for wound healing) may camouflage the scalp appearance. However, clearly the concern is compromising the blood supply further from additional transplantation. Use of minoxidil postoperatively may also help revitalize the scalp. In cases of frank necrosis, the eschar should be left in place (not debrided for fear that the tenuous blood supply is further compromised) and kept moistened with an antibiotic solution. When the eschar sloughs, the surgeon can consider excision of the necrosis or grafting into the area preferably many months to a year later. As an alternative, micropigmentation of the scalp can be performed to camouflage the area of baldness.

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7. Otoplastic surgery

	Complication	Importance	Cause	Treatment	Note
Early complications	*Hematoma*	Can lead to infectious chondritis and necrosis Lead to cauliflower ear deformity	Improper plane of dissection Inadequate hemostasis before closure Poor auricle protection with dressing Postoperative trauma	Release sutures and milk out clotted blood Passive closure over a passive Penrose drain Apply fresh dressing Prescribe broad-spectrum antibiotics	Pay attention to extreme or asymmetric pain Bent ear and pressure necrosis can cause unilateral pain
	Infection	Chonritis	Non aseptic operative technique Ischemia Pressure necrosis Untreated hematoma	Irrigate with antibiotics before closure Incision and drainage Wound irrigation with clindamycin or gentamycin Postoperative antistaphylococcus and antipseudomonas antibiotics	Uncommon Associated with pain and focal erythema Purulence may be seen
	Skin and cartilage necrosis	Cartilage necrosis	Technical error Violation of subdermal plexus during dissection Excessive cautery use An overly compressive dressing causing compartment syndrome, and placement over a bent ear	Similar to that of infection Possible skin grafting or flap advancement to cover exposed cartilage	Rare Necrotic tissue must be debrided before coverage
Late complications	*Patient dissatisfaction*	Most common	Technical error Unrealistic expectation of patient and family	Revision	Preoperative discussion with the patient and family must establish realistic expectations Slight overcorrection

	Complication	Importance	Cause	Treatment	Note
					is likely to be more accepted than slight undercorrection
	Suture complications	Surface irregularities Erosion of the sutures through the skin Contour irregularities of the ear Narrowing of the external Auditory meatus Bowstringing Granuloma formation	Monofilament nonabsorbable sutures, such as nylon or polypropylene, can erode through the thin postauricular skin causing suture fistulae or granuloma formation Polyfilament nonabsorbable sutures, such as silk or polyester, may cause less erosion through the skin, but tend to have a higher infection risk placing sutures under tension across a gap spanning an area with little to no subcutaneous tissue	No treatment Suture removal using 4–0 mersilene suture for the mustarde technique Postauricular skin incision is closed with 4–0 plain gut suture	Sutures can safely be removed after 6 months without fear of relapse
	Loss of correction		Elastic recoil of the auricular cartilage Technical error such as improper suture location or placement Too few sutures, resulting in excess tension and subsequent pull-through of the sutures Inadequate weakening of the cartilage with adjunctive techniques	Proper placement of the suture through the anterior perichondrium	Slight overcorrection is advisable to account for the expected loss of correction
	Pathologic scarring	Patients at risk are younger or darkly pigmented or	Pathologic scarring occurs almost exclusively in Asians, Africans,	Particularly following postauricular incision Careful surveillance for infection	Particularly following postauricular incision

	Complication	Importance	Cause	Treatment	Note
		those with either a personal or family history	and Scandinavians		
	Hypesthesia		Technical error	Resolves spontaneously over several months During the winter months patients must cover their ears when outside for prolonged periods to help avoid frostbite	Quite rare Patients may be at increased risk of frostbite following otoplasty because of disruption in blood supply and/or transient sensory changes
Esthetic complications	*Telephone ear deformity*	Protruding superior and inferior poles	Overcorrection in the mid-third, such as overzealous conchal setback or excessive skin removal in the mid-portion of the auricle under correction of the superior and inferior poles	Careful preoperative planning and proper intraoperative technique Positioning the patient during surgery to be able to evaluate the ear from the frontal view	
	Reverse telephone ear deformity	Protruding middle pole	Prominence in the mid-third persists, and the superior and inferior poles are relatively overcorrected under correction of the middle third occur in the absence of conchal setback sutures when indicated overutilization of Mustarde-type sutures	Careful preoperative planning and proper intraoperative technique Positioning the patient during surgery to be able to evaluate the ear from the frontal view	
	Vertical post-deformity	Shows exaggerated vertical scaphal folding	Mustarde-type sutures placed in a vertical, rather than oblique, fashion	Placement of sutures along the natural arc of the antihelix	

Complication	Importance	Cause	Treatment	Note
Overcorrection and hidden helix deformity	"stuck down" appearance of the auricle	Excessive reduction of cartilage in the concha bowl is performed excess flattening if overcorrection of the antihelix is applied Helix that sits medial to (and hidden by) the antihelix on frontal view	Can be circumvented by initial placement of conchal setback sutures to avoid over tightening the antihelical sutures	
Antihelix creasing and puckering		Mustarde sutures that are too closely placed will cause notches or creases to form within the antihelix, rather than the desired gentle curvature overly large bites of more than 6 mm may cause puckering within the scapha	Careful preoperative planning and proper intraoperative technique	
Tragal prominence		When a considerable degree of conchal setback is attempted without adequate excision of postauricular soft tissue	Careful preoperative planning and proper intraoperative technique	
Auricular ridges		Cartilage-cutting techniques tend to destabilize the auricular cartilage	Cutting techniques should be confined to finely feathered abrasions or scoring of the anterior antihelical surface	
Interaural asymmetry		Technical error	Precise replication of both the sites for suture placement Frequent reevaluation and comparisons of both ears throughout the procedure	When prominauris is present only unilaterally, the patient should be advised of the possibility of achieving greater

Complication	Importance	Cause	Treatment	Note
				balance if both ears are operated on despite the relative normalcy of the uninvolved side

Table 4. Complications in otoplastic surgery [62].

8. Forehead and brow lift

Although the nonendoscopic approaches (coronal or trichophytic) have been the standard, there has been a trend toward, and wider acceptance of, the endoscopic brow lift as a preferred method for surgical rejuvenation of the brow.

8.1. Trichophytic forehead and brow lift

8.1.1. Bleeding

Bleeding complications may occur with any approach. Avoidance of injury to the superficial temporal or zygomaticotemporal arteries, supraorbital or supratrochlear vascular bundles, and sentinel vein improves outcomes.

8.1.2. Nerve injury

The supratrochlear and supraorbital neurovascular bundles should be identified and preserved to minimize additional forehead hypoesthesia medially up to the vertex. Direct injury is uncommon; however, traction neuropraxia may occur secondary to suspension [63].

Temporally, dissection in a plane superficial to the superficial layer of the deep temporal fascia minimizes injury to the zygomaticotemporal and auriculotemporal branches of the second division of the trigeminal nerve and avoids temporal and lateral frontal paresthesias [64].

Additionally, in the temporal region, great care must be taken to avoid injury to the temporal branch of the facial nerve because this results in paralysis and asymmetry of the forehead.

8.1.3. Scarring and alopecia

This complication may be minimized in open approaches by making an irregular incision with an extreme bevel 4–5 mm posterior to the hairline in an area of consistent follicular density to avoid dermal appendages and allow for postoperative hair follicle growth through and around the forming scar [65].

8.1.4. Asymmetry

Brow asymmetry and over/under elevation: Postoperative brow asymmetries may cause poor patient satisfaction. Asymmetries must be documented preoperatively and discussed with patients. Postoperative asymmetry may be caused by unrecognized preoperative asymmetries or blepharoptosis with failure [66].

Overelevation or underelevation of the brow may occur with any approach to forehead rejuvenation [66].

Overresection of skin in any variation of the coronal lift or excessive suspension with any technique may result in overelevation of brow with possible lagophthalmos. This may resolve with time or uncommonly may be permanent and difficult to manage. Concomitant upper blepharoplasty can increase the risk. The forehead lift should always be done before eyelid surgery and overexcision of eyelid skin must be avoided. Lagophthalmos with symptoms of dryness or irritation should be treated with lubricating eye drops and ointments. Limiting postoperative lagophthalmos to <2 mm is advised to decrease the risk of DES [4].

8.2. Endoscopic brow lift

Despite noticeable advantages over coronal approach, like short incisions which limit scarring, direct endoscopic visualization, that enables a safer and more complete dissection in endoscopic brow lifting, there remain complications inherent to endoscopic brow lifting such as asymmetry, irregular facial expressions, lagaophthalmos, visible scars, alopecia, infection/abscess, bleeding and hematoma, temporary hypesthesia of forehead, permanent anesthesia of forehead, brow paresis, wound dehiscence, skin sloughs or perforations, eyelid ptosis, corneal abrasions, DES, relapse and contour irregularities.

When bleeding occurs, the superficial temporal and/or zygomaticotemporal vessels are often the source. A head wrap with Kerlix, placed for the first 24 h, helps eliminate dead space within the optical pockets. The risk of bleeding or infection is similar for all techniques (endoscopic, trichophytic or coronal approach).

Lagophthalmos must be considered a risk of brow lifting. Once complete release of the arcus marginalis has been achieved, considerable elevation of the upper eyelid will occur with brow elevation. Patients who have undergone a previous upper blepharoplasty are most at risk. The authors attempt to limit this risk by performing the brow lift procedure before performing the upper blepharoplasty.

The risk of alopecia is significantly less with the endoscopic technique than in the coronal approach brow lifting. However, hair follicle damage can occur at any of the 5 incision sites, resulting in transient or permanent alopecia. The risk of alopecia with trichophytic technique is extremely lower in comparison with other techniques.

There is inherent risk of temporary hypesthesia or even permanent anesthesia of the forehead. The authors think that the temporary hypesthesia commonly seen after an endoscopic brow lift is secondary to a traction neuropraxia of the supratrochlear and supraorbital neurovascular bundles that occurs during elevation and release of the arcus marginalis. Lastly, injury to the

temporal branch should not occur during endoscopic brow lifting to avoid brow paresis. If paresis is noted in the immediate postoperative period, one must consider the possible temporary effect of local anesthetic. Sensation typically returns over the course of months, with improvements in sensation starting near the brow and extending toward the vertex, typically with full return of sensation by 12 months. Rarely, but occasionally, a patient may have some dysesthesia along the incision line or in the caudad scalp after sensation returns. It can be successfully treated with complete resolution through injection of the incision or with the use of supraorbital nerve blocks consisting of 0.5% marcaine with 1:200,000 epinephrines.

Postoperative brow asymmetry can result from failure to elevate either brow adequately by inadequate release of the orbital rim tissues.

We routinely place our patients in a standard facelift dressing for the first 2 postoperative days. The forehead component places pressure on the operative field, whereas the portion going around the head prevents displacement of the forehead dressing. The patient is instructed to keep the incision sites dry until sutures are removed on postoperative day 7.

9. Complications in skin resurfacing

Complication	Risk factors	Prevention and management
Erythema	Sensitive and thin skin Excessive sun damage	Icing, rigorous sun precautions Masking with makeup Treat with topical biafine (Valeant, Montreal, QC) and 590-nm LED photomodulation Consider a mild topical corticosteroid if condition persists
Blistering and burns	High-energy/penetration lasers Improper pulse stacking or high-density passes Insufficient cooling of the dermis Loss of pain feedback with heavy sedation or general anesthesia	Implement standard device safety and review of laser settings Allow the dermis to cool between passes and after treatment Burn care for severe thermal injuries
Infection (**Figure 14**) *and herpetic eruption*	Closed facial dressing left >48 h Insufficient facial hygiene/care History of herpetic rash	Adherent to posttreatment facial care with topical disinfectant with hypochlorous acid 0.01% (NeutroPhase, NovaBay, Emeryville, CA) or acetic acid 0.25–0.0125% (vinegar solution) Prophylactic antibiotic (cephalosporin), and a 1–2 weeks anti viral course (valacyclovir) started 24–48 h before treatment
Acne and milia	Closed facial dressings Oil-based creams	Daily facial rinses and noncomedogenic moisturizer Course of oral tetracycline for persistent acne Milia can benefit from topical tretinoin, gentle epidermabrasion, or extraction

Complication	Risk factors	Prevention and management
Postinflammatory hyperpigmentation	Fitzpatrick skin type III–VI Recent sun exposure/tanning History of hyperpigmented healing	Careful skin type selection with appropriate laser type setting Sun precaution 2–4 weeks before treatment and continued for 2–4 months Prophylactic or therapeutic 2–4% hydroquinone, 2–4% kojic acid or Kligman formula (5% hydroquinone, 0.1% tretinoin, and 0.1% dexamethasone). This should be started 2–4 weeks before treatment and continued for 2–4 months
Scarring and hypertrophic healing	Secondary to infections or burns Poor healing capacity History of keloid formation The periorbital region, the neck, and off-face areas	Scar-prone areas require lower fluence and density Apply silicon gel dressing to healing scars and hypertrophic bands Intralesion corticosteroid or 5-fluorouracil

Table 5. Summary of common laser complications and their management [67].

Resurfacing modality	Complications
Phenol based peels	Cardiac arrhythmias Laryngeal edema and stridor
Baker-Gordon solution	Prolonged erythema Permanent hypopigmentation Cardiac arrhythmias Laryngeal edema and stridor
Medium-depth peels	Scarring and permanent hypopigmentation (rare)
CO_2lasers	Scarring, permanent hypopigmentation (higher incidence in older lasers)
Infrared lasers	Dermal blisters, heals with depressed scars
Microdermabrasion	Streaks of hyperpigmentation
Visible light lasers and broadband light sources	Epidermal blisters; may heal with scarring and permanent hypopigmentation
Monopolar capacitive radiofrequency	Skin blisters Permanent fat atrophy when delivered in very high energy
Plasma skin regeneration	Burns, scarring
Fractional resurfacing	Scarring Recalcitrant hyperpigmentation
Photodynamic therapy	Intra- and postoperative pain, burning sensation, edema

Table 6. Resurfacing modality and complications.

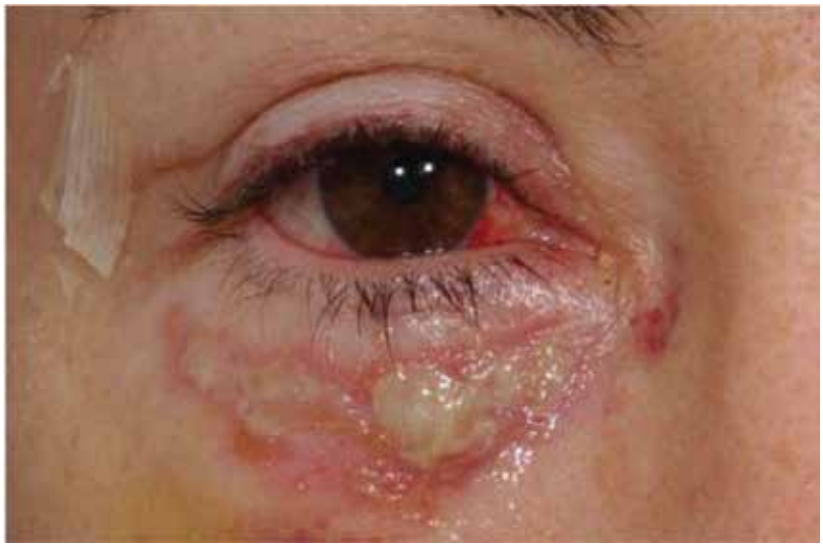

Figure 14. The crusting of a bacterial infection that developed after resurfacing [68].

10. Facial suction lipectomy and fat transfer

	Complication	How occurs	How avoid	How treat	Note
Other complications	*Embolization: blindness, stroke and skin/ tissue necrosis*	Permanent blindness usually results by tiny amount of the filler slipping into the retinal artery which can precipitate a central retinal artery blockage It is also possible to force the column back into the internal carotid a rtery and embolize into any area supplied by the internal carotid area, and this may result in a stroke	-Do not use sharpneedles. Additionally, one should limit bolus size, limit syringe size (only 1 mL syringe to the face), and avoid using ratcheting guns -The volume placed with each pass of the cannula should also be limited. Infiltration of less than 0.1 mL with each pass of the cannula is		Use only 1 ml Luer-Lok syringes for subcutaneous infiltration into the face

	Complication	How occurs	How avoid	How treat	Note
			recommended in the face		
	Fat necrosis: calcifications and oil cysts	Dead adipocytes become oil droplets and are first surrounded by infiltrated M1-type (inflammatory) macrophages for phagocytosis At a later stage, stratified layers of M2-type (anti-inflammatory) macrophages surround the M1 macrophages and form a fibrous cyst wall	-Fat particles with a more than 2–3 mm diameter cannot been grafted at 100%. - Use smaller injection syringes such as 1 mL syringe for the face and 3 mL syringe for the body	not easy totreat without surgical resection. Another option is to partially cut the cystic wall with an 14–18G needle and squeeze it, leading to leakage and phagocytosis of oil or necrotic tissue	Ultrasound assessment at 1 month after lipoinjection is particularly valuable
	Infection	As the grafted fat is not vascularized, it can be a focus of infection once severely contaminated by bacteria	Sterile technique should be observedat all times. Intraoperative antibiotics are recommended to use, but perioperative use of antibioticsis not recommended unless there is a specific indication	In cases of delayed infection, a high index of suspicion should be maintained for mycobacterialor other unusual infections	
	Damage to underlying structures	Even a blunt cannula, when inserted for removal and placement of fat, can damage underlying structures			Permanent injuries are extremely rare
	Pneumonia	Induced by damaging the pleura with an injection cannula/needle	Great care should be taken to avoid when introducing fat into the bottom layer close to the rib	It can be treated by a conservative treatment such as waiting with careful monitor of X-ray and symptoms	

Complication	How occurs	How avoid	How treat	Note
Aesthetic problems and complications	The presence of irregularities, which can be caused by the intrinsic nature of the patient's body, from the technique used for placement, and from migration after placement, is also noted	Irregularities after fat grafting diminish significantly as the surgeon gains experience with the technique		
Swelling and downtime	The placement of fatty tissue may create remarkable swelling in the recipient tissues	Elevation, cold therapy, and external pressure with elastic tape or Tegaderm (3 M, Maplewood, MN, USA) help prevent swelling. Certain medications (Arnica montana and bromelain) may also speed recovery. The patient is asked to avoid heavy pressure on the grafted areas for 7–10 days to avoid migration of the grafted fat		A slight staining of the skin, possibly hemosiderin deposits or other pigment changes, can remain for months in some patients after minimal fat grafting to the lower eyelid
Donor site problems	Some patients simply do not have adequate donor sites, especially if they have previously undergone liposuction	Complications of the donor sites are rare, but irregularity of the surface could occur, particularly when an excessive volume liposuction is performed in verythin patients		

Table 7. Complications of fat grafting.

	Complication	Cause	Treatment	Caution
Complications involving contour problems	*Lumps* (**Figure 15**)	-May arise if too large a bolus of fat is placed in a sensitive region like the lower eyelid. -The fat may have been placed too superficially so that it becomes visible as a contour deformity	Steroid injections may be a reasonable first step, these lumps may need to be excised to achieve complete resolution	If excision is required in the lower lid region, the most discreet placement for an incision is in the tear trough at the junction of the thin lower lid skin and thicker sebaceous cheek skin
	Bulges	-Arise from imprecise placement of fat along the inferior orbital rim, usually from a lateral entry point. -Arise in the lateral aspect of the malar region and may be caused by overcorrection. -May develop when the patient gains excessive weight	-Readily responds to injectable agents that can reduce the element of scarring, such as 5-fluoruouracil and dilute triamcinalone acetonide. -Focused microliposuction to reduce the bulk of fat	A bulge may develop when the patient gains excessive weight. The best way to mitigate this problem is through weight loss
	Persistent malar mound edema (**Figure 16**)	Generally occurs only in patients who have a visibly defined malar mound preoperatively, especially if they have a history of cyclical malar mound edema	The condition may resolve independently over time, if it persists, dilute steroid (kenalog) injections repeated every 4–6 weeks as necessary may hasten this process	The most important step in avoiding this complication is to identify the presence of a malar mound preoperatively and determine whether the patient has a history of cyclical swelling
	Overcorrection		Waiting a minimum of 6 months before	Overcorrection is best avoided through

Complication	Cause	Treatment	Caution
		intervention is advisable to allow for resolution of edema or resorption of fat over time. If this fails, then microliposuction of the overcorrected area may be required	a conservative fat transfer. "Hitting doubles" should underscore every fat-grafting endeavor
Undercorrection		Pre-operative counsel and description on the likely chance that a second fat transfer procedure will be needed to obtain the ideal result	The need for secondary fat transfer is seen more frequently in patients requiring large volume augmentation, those who smoke, and those who are extreme exercisers

Table 8. Complications involving contour problems.

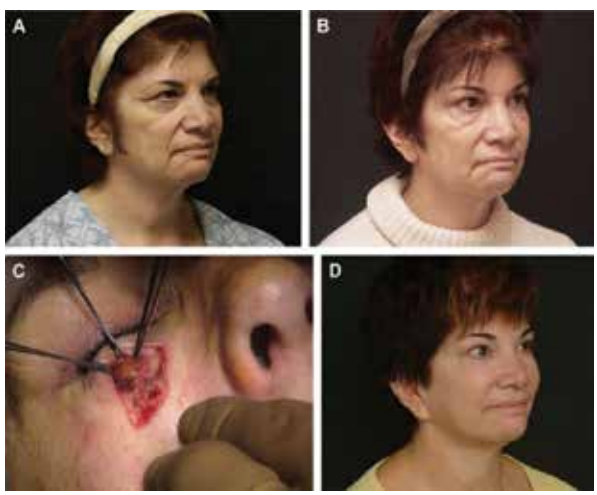

Figure 15. (A) Patient before fat transfer to the inferior orbital rim and cheek. (B) At 6 months postoperatively, patient had a lump in the central inferior orbital rim and was also unhappy with the residual lateral fat pad. (C) Intraoperative photograph showing removal of the lump of transplanted fat that was causing the contour irregularity. This incision, at the junction of the lower lid and cheek skin, allowed for removal of redundant lower-lid skin. At the same setting, the lateral fat pad was reduced through a transconjunctival approach. (D) Postoperative photograph, after correction of the contour irregularity [69].

Figure 16. The malar mound is a triangular-shaped elevation (large arrow), anatomically delineated by the orbital septal–periosteal adhesion superiorly and the malar septum inferiorly (small arrow) [70].

11. Filler injections

Although HA fillers have been touted to be safer and thus more widespread than the other filler types, all have been associated with adverse outcomes. These complications range from localized bruising, erythema, edema, migration, allergic response, the formation of small bumps underneath the skin, to more serious sequelae, such as permanent visual loss and nerve paralysis (**Tables 5**–**8**).

The importance of hyaluronidase is due to its value in treating a variety of the complications of facial fillers. Hyaluronidase has the ability to dissolve HA. Approximately 30 U of hyaluronidase are needed to dissolve 0.1 mL of HA. Restylane may resolve the fastest and Belotero the slowest relative to more cross-linking in the latter [71].

Chronic prolonged edema can also be related to a type 4 hypersensitivity reaction. If it is unresponsive to antihistamines, it may need to be dissolved with hyaluronidase (**Figure 17**). Angioedema is an immediate allergic response that can last for several weeks. It may respond to antihistamines or prednisone [72].

Bruising is a complication of any procedure that involves the use of a needle or cannula. There is debate as to whether or not one should stop anticoagulants for patients receiving fillers [74].

For patients at low risk for cardiac disease or cerebrovascular disease, discontinuation of aspirin, nonsteroidal anti-inflammatory drugs, or herbal supplements, such as vitamin E, fish oil, ginseng, and ginkgo, is generally suggested. If a patient is at risk of thrombotic disease,

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the anticoagulants may be continued and the patient must be made aware of the increased risk of bruising [72]. Some physicians believe that cannulas are safer and have less chance of causing bruising than needles [75].

Figure 17. This patient was injected with hyaluronic acid filler for tear trough correction and the filler was injected too superficially (top image). The same patient is shown 24 h later (lower image) after injecting 70 units of hyaluronidase (diluted with local anesthetic) in each lower lid in the area of the filler excess [73].

Arnica montanais a herbal supplement that inhibits transcription factor nuclear factor-kB2 has been promoted for its ability to minimize bruising. Some dermatologists fear contact dermatitis from the topical form. Oral Arnica demonstrated no improvement with blepharoplasty and hand surgery [76, 77]; however, it did improve postoperative bruising associated with facelift procedures [78].

Patients can also suffer from vasovagal responses or seizures because of the stress of the injection procedure. Close supervision of the patient at all times is recommended. Asymmetry is always a consideration in filler injections (**Figure 18**).

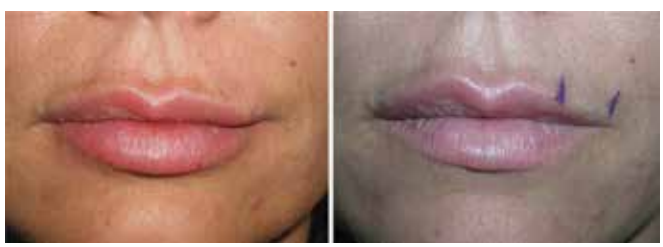

Figure 18. This patient exhibited asymmetry from under treatment of her left side. The marked area indicates where the touch up filler was needed [73].

11.1. Infection: biofilms

Proper topical preparation of the skin is inherently critical for prevention of infection. Topical alcohol 70% is inexpensive, readily available, and has quick onset. Topical chlorhexidine, available by swab or surgical scrub, is gaining popularity because it demonstrates a longer frame of action and tends to be nonirritating [79].

Immediate bacterial infections are thought to be caused by introduction of bacteria from the surface of the skin though the injection portal sites. Such infections can often be treated with broad-spectrum oral antibiotics, such as clarithromycin, because of its activity against atypical mycobacteria [80].

Makeup application should be delayed until 4 h after injection. Reactivation of a herpetic infection is also possible and can be treated with oral valcyclovir, 2–3 g/day.

Delayed infections caused by biofilms can be more difficult to treat. An inflamed nodule with a delayed presentation of 2 or more weeks can be caused by a biofilm.

They can contain bacteria, protozoa, or fungi in a low-grade infection that chronically seeds the local area and can even trigger a systemic infection [81]. Biofilms can be associated with foreign body granulomas (discussed in next section). Antibiotics should be started before any attempts to remove the granuloma with hyaluronidase (for HA); steroid, 40 mg/mL or fluorouracil (5-FU), 50 mg/mL injections; laser lysis; or surgical excision [72].

11.2. Granulomas

Granulomatous reactions are rare and can present months to years after an injection. Intralesional steroids and 5-FU are the therapeutic mainstay to inhibit fibroblast activity. If the nodules are associated with an abscess, the infectious component is often sterile. Granulomas may occur more commonly with long-lasting or permanent fillers, such as silicone, polyacrylamide, poly-(L)-lactic acid (PLLA), and Poly(methyl methacrylate) (PMMA) [72].

Granuloma can be localized or present as a global systemic response (Box 1). All can be treated with use of hyaluronidase and oral or intravenous steroids.

(Box 1) Presentation and management of common filler complications.

Nodules (early presentation)

- HA: extrusion, hyaluronidase
- Non-HA: intraregional steroids with lidocaine and or 5-FU, micro-focused ultrasound or fractional lasers, surgical excision

Inflammatory nodules

- Biofilm: antibiotics (biaxin, ciprofloxacin, or clarithromycin) for 4–6 weeks.
- 5-FU 50 me/mL, 0.1- to 0.5-mL injections
- Consider biopsy and infectious consultation for atypical mycobacterium of fungus.

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Foreign body granulomas

- Localized; hyaluronidase if HA and intraregional steroids and/or 5-FU injections, then excision
- Global: hyaluronidase if HA, test spot on arm, biopsy, intralesional, or intravenous systemic steroids

11.3. Vascular occlusion

It is one of the most devastating complications arising from facial filler injections. Arterial embolization is more commonly direct anterograde with occlusion of an artery causing ischemia distal to the injection point. This direct form of occlusion usually occurs with injections to the glabellar region [82].

Clinically, patients manifest with significant pain and ischemic pallor, eventually leading to necrosis and atrophic changes. Hot compresses, massage, hyaluronidase, aspirin, and possibly oral steroids should be immediately considered. A venous occlusion is also possible during cosmetic injections. Instead of immediate pain and blanching, this presents with venous mottling termed livido. Livido from venous occlusion should be distinguished from bruising. Patient can be treated with heat, massage, hyaluronidase, and prednisone (Box 2).

(Box 2) Vascular occlusive events: presentation, treatment, and prevention.

venous

- Presentation: livido, lack of significant pain
- Treatment: heat, massage, oral prednisone, hyaluronidase if HA
- Prevention: awareness of anatomy danger zones, consider injection with cannulas, aspiration before injection, slow retrograde injections, avoid bolus injections >0.1 mL

Arterial

Anterograde

- Presentation: Pain, blanching distal to site of injection
- Treatment: heat, massage, aspirin, hyaluronidase, dase, oxyent infusion cream, hyperbaric oxygen
- Prevention; awareness of anatomy danger zones, consider injection with cannulas, aspiration before injection, slow retrograde injections, avoid bolus injections >0.1 mL

Retrograde followed by anterograde

- Presentation: dizziness, blindness, cerebrovascular accident, pain
- Treatment: heat, massage, acetylsalicylic acid (aspirin), hyaluronidase, hyperbaric oxygen

- Prevention: awareness of anatomy danger zones, consider injection with cannulas, aspiration before injection, slow retrograde injections, avoid bolus injections >0.1 mL

The literature has described devastating permanent visual loss from injections of steroids in the head and neck region for various benign lesions (i.e., chalazion, capillary hemangioma) [83, 84].

The substance must be injected against the systemic arterial pressure to fill the entire vessel retrograde past the bifurcation before it flows anterograde into the central retinal artery or its distal tributaries. Egbert and colleagues [85] approximated as little as 0.01 mL as the minimum required volume to cause vascular occlusion in the setting of intralesional corticosteroid injections to eyelid lesions. Numerous case reports describe this retrograde occlusive event clinically arising from filler injections in the nasal dorsum, nasolabial folds, and lips [86–89].

When such a vascular event occurs, patients can immediately experience significant pain, skin blanching, loss of vision, and decreased extraocular motility. Rapid recognition of these symptoms can allow the injector to promptly manage the evolving vaso-occlusion with the following measures: applying pressure to the injection site in an effort to dislodge the embolus, injecting hyaluronidase (if an HA filler was used) to dissolve the filler particles, and applying nitroglycerin paste and topical oxygen therapy to allow for vasodilatation and spontaneous release of the occlusive bolus. Some sources, however, indicate that nitroglycerin paste may worsen the impending ischemia by propagating the filler substance into other portions of the arterial tree [90].

Additionally, fat is more likely to cause an embolus, whereas HA filler attracts water, which may prevent further particle migration. The method of injection also contributes to the overall result. Slower injection of smaller volumes generally <0.1 mL in any given location allows for more controlled filling. Injection by blunt cannula may minimize the risk of perforating a vessel and facilitates remodeling of facial ligaments with gentle manipulation of the cannula tip.

12. Botulinum toxin A (Botox) injections

	Complications	Cause	Treatment	Note
Complications of Botox treatment	*Under treatment*	A past subclinical botulinum infection from food poisoning that did not require hospitalization could cause an immunity to botulinum toxin type A. Secondary to that, some patients simply	Use of botulinum toxin type B	It is important for patients to realize that some patients are sensitive to Botox and some are resistant or immune

Complications	Cause	Treatment	Note
	do not respond to any amount of the toxin		
Overtreatment	If the frontalis is heavily treated (especially the lateral areas) the main brow elevator is deactivated. When this happens, patients who usually lift their lids no longer can, making the brow and lid feel heavy and, because the brow is not elevated, the excess upper lid skin is more apparent	treat the lateral frontalis conservatively in older patients who have dermatochalasis and protect with informed consent and preinjection consultation	
True eyelid ptosis	Eyelid opening is controlled by the levator palpebrae superioris muscle, which in turn inserts into the levator aponeurosis of the upper eyelid. If Botox is injected (or more commonly diffuses) into this muscle, the eyelid does not open	This complication can be avoided by keeping all injections at least 1 cm above the bony orbital rim.	It's recommended that inject just beneath the brow. This is acceptable if patients have normal positioned brows, but in patients who have ptotic brows, the injection may be close to the levator muscle
Asymmetry	Injector placement or patient anatomic variation	This is easily corrected by placing some additional Botox at the active area	One of the most common asymmetries is the Spock eyebrow. This is a demonic curvature of the lateral brow that occurs when the central frontalis is deactivated but the lateral frontalis is active and only lifts the brow tail
Bruising	This occurs when	Using a 32-gauge	Screening patients

Complications	Cause	Treatment	Note
	a vessel is disrupted by the injection needle	needle and paying close attention to the superficial vasculature can limit this situation	for aspirin or other drugs that affect platelet aggregation also is important in preventing bruising
Perioral droop	Can cause or contribute to dysfunctional animation of the perioral region	Lower facial Botox treatment should be reserved for advanced injectors and conservative treatment should be a mantra	A patient who presents to a cosmetic office to look better but is left drooling, lisping, or with the inability to pucker will not be happy
Unrealistic patient expectations	Although not a complication, an unhappy patient is a problem	Preinjection discussion and informed consent should cover this	

Table 9. Complications of Botox treatment.

13. Facial implants in cosmetic surgery

13.1. Improper selection or placement

Generally speaking, improper placement of the implant is the most common complication followed by improper implant selection. The implant should be slightly smaller than the desired increase in fullness to take the contribution of the soft tissue into account. Appropriate implant selection is also important [38] (**Table 9**).

13.2. Neuropraxia

The malar neuropraxias had a slightly higher ratio of motor nerve injuries than sensory. Neuropraxia can be incurred from impingement by the implant because a size selection that is too large, migration, improper placement, a traction injury, a thermal injury, or a direct traumatic injury from dissection. Most patients regain sensation and function within 3 weeks. Anesthesia postimplant placement probably indicates the implant is resting on the nerve. Dissection for malar implants can also involve instrumentation around the facial nerve branches. Weakness of the zygomaticus, orbicularis oculi, or the frontalis muscles can be induced by the disturbance of the temporofrontal branch of the facial nerve while dissecting posteriorly over the middle third of the zygomatic arch.

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During dissection of the chin for genial alloplast placement, it is important to avoid the mental nerve. The marginal mandibular branch of the facial nerve, which supplies muscles of the lower lip and chin, is above the periosteum over the inferior border of the mandible and is difficult to injure unless there is a severe traction injury or perforation of the periosteum.

13.3. Edema and ecchymosis

Typically the majority of postoperative edema and ecchymosis resolves in 2 weeks, but edema can persist for 6 months and even up to a year [91].

Implant fixation is important because excessive continuing movement can cause tissue injury, chronic inflammation, and suboptimal soft tissue acceptance with prolonged edema. This could also be due to a nonspecific immune reaction to the implant material.

13.4. Hematoma and seroma

Smaller hematomas (<5 cc) resolve without treatment in 10–14 days. Large hematomas need to be recognized and evacuated with the implant removed as necessary. Seromas usually present around 2 weeks after surgery. The presence of liquefied hematomas or seromas 2–4 weeks postoperatively may be drained percutaneously. Hematomas and seromas are best prevented with control of blood pressure during the procedure with general anesthesia and adequate local anesthesia, postoperatively with antihypertensive prophylaxis, and gentle handling of the tissues, maintaining a subperiosteal plane, and consideration for a drain in secondary procedures [92].

13.5. Infection

There are many different factors that determine whether an infection will be propagated after an implant is contaminated. Some of these factors include the bacterial load of contamination, host factors such as immune function, the method of contamination and age of the implant, and the perioperative prophylactic interventions by the surgeon to prevent infection. Implants can be contaminated by hematogenous, contiguous spread, or direct inoculation.

Implants decrease the amount of bacterial innoculum required to produce an infection. Foreign bodies have been shown to reduce the number of bacteria required to produce an infection by 10^4–10^6 power [93].

Zimerli found that decreased overall bactericidal activity was seen, including opsonization, bacterial ingestion, and intracellular killing of bacteria in neutrophils exposed to a foreign body [94].

Scalfani and colleagues studied the infection susceptibility of implants with different pore sizes. They found that the PTFE with an average pore size of 22 microns became infected at lower innoculum counts and sooner than polyethylene with a pore size of 150 microns. Most infections in the early postoperative time phase are more likely to occur with porous implants because of increased surface area, irregularity, and surface energy, which facilitates glycolax formation and bacterial adherence. Late infections are less likely to occur with porous implants

because of incorporation of host tissue and improved immune response. Late infection associated with malar implants has been associated with dental injections as reported by Cohen and Kawamoto [23]. In Wilkinson's retrospective review of 35 malar implant found that infections were associated with an old hematoma and subsequently cultured *Staphylococcus aureaus* [95].

Some authors hypothesize that exposure to saliva confers enough risk for development of infection that the intra-oral route should be avoided. In a study by Deva and colleagues, 422 patients had silastic nasal augmentation consisting of primarily columellar struts using an intraoral approach without prophylactic antibiotics and no postoperative infections occurred. Karras and Wolford [96] reported on 18 patients who had hard tissue replacement polymer (HTR) chin implants placed intra-orally with perioperative and postoperative antibiotics and reported no incidence of infection. These studies support the idea that patients with an intact immune system and healthy wound bed do not need additional antibiotics.

If salvage is selected in the setting of a purulent infection, the implant should be removed and scrubbed and/or sterilized to remove the biofilm. In addition, debridement and copious irrigation of the implant pocket, and finally, a prolonged postoperative antibiotic course are advocated. If rapid improvement does not occur and the implant needs to be removed, it should not be replaced for 6–8 weeks to allow for resolution of the infection and inflammation [97].

13.6. Migration and contour changes

There is a hypothesis that this is highly influenced by implant shape and method of fixation. Migration is usually the result of overdissection, selection of the wrong-sized implant, and lack of fixation. Supraperiosteal placement can also predispose the implant to mobility especially without adequate fixation (**Figure 19**).

13.7. Extrusion

Factors which are critical to preventing extrusion include adequate soft tissue bulk with quality tissue for coverage and insertion in the correct plane without tension. Decreased tissue perfusion decreases the potential for successful wound healing. Factors such as prior surgery and history of radiation will decrease the local vascular supply and result in fibrosis and stiffening of the tissues [98].

Excessive tension is usually the result of using too large an implant for too small a dissection. In addition to tensionless closure, subperiosteal placement helps to prevent exposure.

Some biomaterials can be treated symptomatically if exposure occurs without the need for removal. Frodel and Lee report secondary healing over polyethylene implant exposure and believe that if there is adequate vascularity, the implant will do well [98].

Other authors report intra-oral exposure of silastic implants that go on to cover secondarily with local wound care. Typically, however, if extrusion occurs, the implant must be removed and the site allowed to heal for multiple weeks before replacement.

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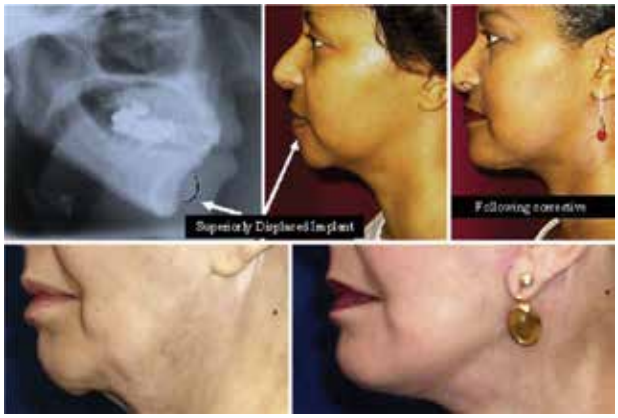

Figure 19. The top figure demonstrations a superiorly displaced chin implant corrected by repositioning and placement of a larger anatomic implant with screw fixation. The lower figure shows on inferiorly displaced chin implant beneath the jaw requiring removal and replacement using screw fixation [99].

13.8. Palpability

Even the most perfect augmentation will be a failure if the patient can feel the implant and does not like it. This can be the result of improper size selection or contour, improper positioning, improperly placed fixation, or capsular contracture. It is important to make sure the implants are intimately adapted before fixation. Patient factors such as a thin amount of overlying tissue also predispose to palpability. In malar augmentation, Whitaker recommends limiting the thickness of the implant to no >4–5 mm and tapering the ends thinly to avoid palpability [100].

13.9. Lip dysfunction

Altered lip function is primarily associated with malar implants. This problem occurs because dissection can interfere with the muscles responsible for smiling mimetics, more so than for mandibular augmentation. Other factors could include edema, interposition of a solid implant which stretches the muscles of the midface, or interference with the facial nerve during dissection over the zygomatic arch. The edema can cause dysfunction in the muscles of the upper lip resembling facial nerve dysfunction. When dysfunction is due to muscle displacement, it usually takes 1–3 months for the muscles to reattach and the capsule to become soft and distensible. In malar augmentation, upper lip weakness can be minimized by a small, vertical mucosal incision, and dissection parallel to and in between the zygomaticus major and minor.

13.10. Bone resorption

Bone erosion under alloplastic implants have occurred to a significant extent with early implants (**Figure 20**) [101].

The bone resorption was often attributed to foreign body giant cell reaction between the implant and the bone or to pressure from the mentalis muscle against the implant. Other factors that were considered were improper implant positioning, pressure due to an oversized implant, subperiosteal placement, and hardness of the implant. Significant resorption poses not only an obvious problem associated with the creation of a bony defect and potential damage to underlying structures like tooth roots, but it also leads to loss of chin projection. Bony erosion probably occurs less with anatomic extended implants because of greater distribution of the pressure forces over a broader anatomic area [102].

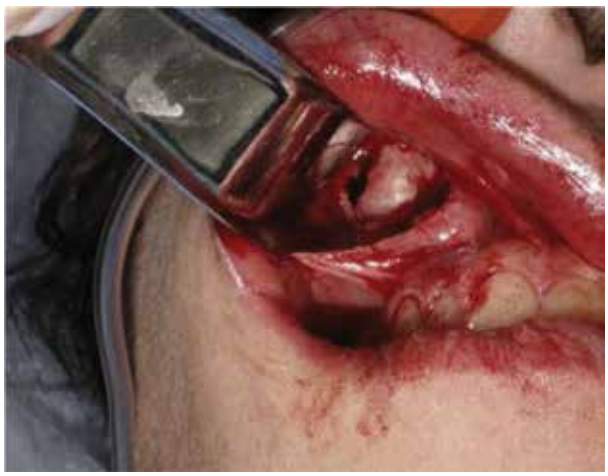

Figure 20. Erosion of cheek implant into the maxillary sinus. Fortunately, this is a rare occurrence and most often a result of inadvertent entry during placement over a thin bony sinus wall [99].

13.11. Postoperative asymmetry

Asymmetry has many causes, but it is usually caused by initial malposition or by creation of asymmetric bilaterally dissected spaces. It can also be the result of unrecognized preoperative skeletal or soft tissue deficiencies. Although major asymmetries require a second surgery, minor asymmetries have a natural tendency to adjust and correct themselves over a 6-month postoperative period as healing progresses and the tissue around the implant relaxes and softens.

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Section 18

Advanced Craniofacial Surgery

Chapter 32

Advances in Craniofacial Surgery

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Additional information is available at the end of the chapter

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Abstract

Calvaria development initiates by growth from primary ossification centers meeting each other to form suture sites. The term craniosynostosis describes premature fusion of one or more of the calvarial sutures. Deformities are usually observable during the first few months of the newborn's life. The premature fusion of sutures could produce intracranial pressure elevation and consequently lead to abnormal neurocognitive = neurologic development. Patients with craniosynostosis require surgical plans containing multiple surgical staging. In the following chapter, we present our experience in surgical treatment of children with various craniosynostosis syndromes.

Keywords: craniosynostosis, craniofacial surgery, syndrome, surgical operation, frontal advancement

1. Congenital craniofacial abnormalities

The term craniofacial anomaly describes all congenital deformities of the cranium and the face [1]. A deformity is an alteration in shape due to unusual pressure or positioning in the uterus during late pregnancy. Some deformities resolve spontaneously without any interference within a few days after the newborn's birth, but others persist and require surgical treatment (**Figure 1**) [1, 2].

Figure 1. Congenital craniofacial abnormalities.

A malformation describes as an error in normal development of the organs or tissues. Malformations may arise from chromosomal abnormalities, teratogenic agents, single-gene defects, or a combination of genetic and environmental factors; albeit few cases are idiopathic [1, 2].

2. Craniofacial abnormalities (CFA)

Various craniofacial abnormalities result from mal-development of the first and the second visceral arches, which form the facial bones and ears during the second month of gestation. Causes include several thousand genetic syndromes as well as prenatal environmental factors [3]. Each specific congenital anomaly may be associated with several different genetic syndromes. The patients should be evaluated for other probable associated physical anomalies and delayed development that may require treatment and involvement.

3. Craniosynostosis

Craniosynostosis describes as early fusion of one or more of the cranial sutures of infant's head. **Figures 2** and **3** show the different sutures, which could be involved in craniosynostosis syndromes [3].

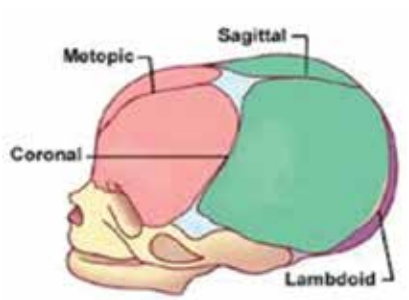

Figure 2. Different sutures which could be involved in craniosynostosis syndromes.

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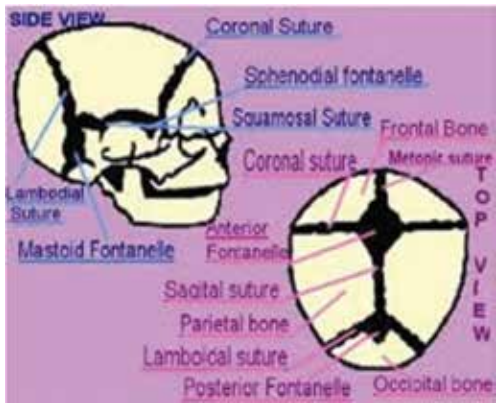

Figure 3. Sutures which could be involved in craniosynostosis.

During brain growth, open sutures allow the skull to expand and develop a normal head shape. If one or more of the sutures closes early, it causes the skull to expand in the direction of the open sutures lead to an abnormal head shape and may cause increased pressure on the growing brain in severe cases (**Figure 4**) [3, 4].

Figure 4. Abnormal head shape from early suture closure.

3.1. Types of craniosynostoses

In sagittal synostosis also named scaphocephaly, the sagittal suture is prematurely closed. So the head does not expand in width and grows long and narrow to accommodate the growing brain. [In Greek, the word skaphe means "light boat or skiff" and kephale means "Head" which resembles an inverted boat]. The sagittal suture is statistically the most common single suture involved in craniosynostosis.

Metopism is known as a condition of having a persistent metopic suture or persistence of the frontal metopic suture in the adult human calvarium. The main factor of metopic synostosis is to increase the volume of the anterior cranial fossa (**Figure 5**) [5, 6].

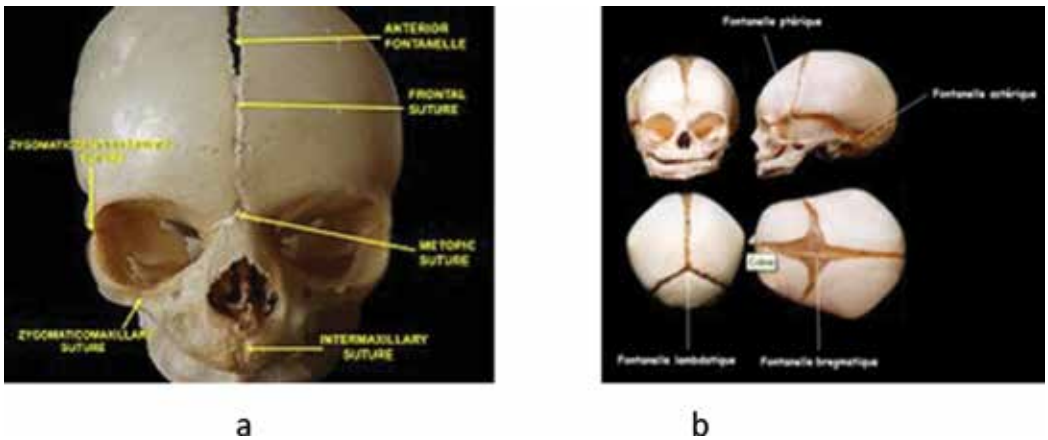

Figure 5. (a, b) Baby skull and the metopic (frontal) suture.

During the embryonic period at the frontal region, there is a membranous tissue between the right and the left halves. On each half, a primary ossification center manifests about the end of the second month of the fetus. At birth, the frontal bone contains two portions, separated by the metopic or frontal suture. Normally, the frontal suture is obliterated, except at its lower part until the 8th year, but rarely persists during the entire lifetime (**Figure 6**) [5, 6].

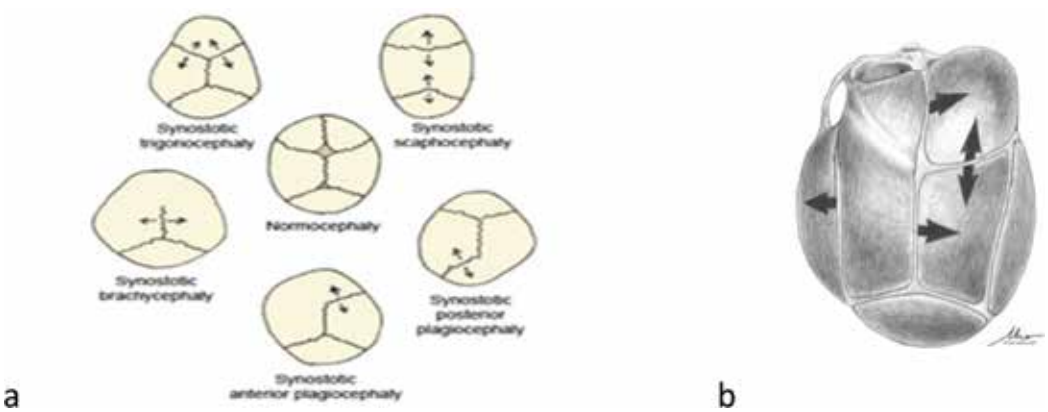

Figure 6. Various craniosynostoses. (a) Various types of craniosynostoses. (b) Possible directions of craniosynostosis in calvarium sutures

Plagiocephaly, also known as flat head syndrome, is a condition with asymmetrical distortion and flattening of one side of the skull. The coronal suture goes from ear to ear on the top of the head. Early closure of one side, unilateral coronal synostosis creates a flattened appearance on that side at forehead and orbital rim areas and causes the "winking" effect. It divides into two groups, namely synostotic plagiocephaly, with one or more fused cranial sutures, and nonsynostotic (deformational) plagiocephaly [7, 8].

Brachycephaly [7, 8] describes a very wide head shape with a flattening across the whole back of the head. In brachycephaly, both sides are fused. The patient may have a very flat and recessed forehead. Flat spot on the back or one side of the head may be caused by remaining in a supine position for a long time [5–8].

3.2. Confirmation of diagnosis of craniosynostosis

The first clue is a misshaped head. The anterior fontanel or soft spot may be open or fused. Diagnosis is confirmed by x-rays like CT scan evaluation to make sure there are no underlying brain abnormalities [5, 8].

Eye anomalies may include the following:

- Hypertelorism [9]
- Hypotelorism [9]
- Coloboma [10, 11]
- Microphthalmia [9–12]
- Anophthalmia [9–12]

3.3. Classification of craniofacial anomalies

Craniofacial anomalies are divided into three main subgroups [5]:

- Craniosynostoses [13–15]
- Craniofacial clefts
- Miscellaneous craniofacial anomalies

Types of craniosynostosis include the following:

(1) Primary craniosynostosis

This is an idiopathic developmental error occurring in otherwise normal conditions with no previous familial incidence.

(2) Secondary craniosynostosis

Premature fusion of the cranial sutures could result from failure of brain growth as in microcephaly or an encephaloclastic process which occurs during the first years of the newborn's life. When severe hydrocephalus has been treated with a low-pressure shunta, similar process occurs.

(3) Metabolic craniosynostosis

Premature fusion of the sutures may arise due to the obvious biochemical disorders (mucopolysaccharidoses, rickets, hypophosphatasia, or hypercalcemia) (**Table 1**).

Affected suture	Sagittal	Metopic	Unicoronal	Bicoronal	Multiple sutures	Oxycephaly	Kleeblattschädel
Traditional name	Scaphocephaly	Trigono cephaly	Plagio cephaly	Brachy cephaly	Turricephaly	Sharp skull	Clover-leaf skull
Literal translation	Boat skull	Triangle skull	Oblique skull	Short skull	Acrocephaly	Decreased	Decreased
Skull length	Increased	Normal	Decrease	Decreased	Tower skull	Increased	Increased
Skull width	Decreased	Increased	normal	Increased	Decreased	Increased	Increased
Skull height	Normal or increased	Increased	Increased		Increased		

Table 1. The various types of calvarial deformity.

Side problems due to the calvarial synostosis could be as follows: [16–18]

- Raised intracranial pressure
- Exorbitism and orbitostenosis
- Orbital hypertelorism
- Orbital dystopia
- Airway restriction
- Speech problems
- Mastication problems

Syndromic craniofacial synostosis usually has autosomal dominant genetic causes; these syndromes affect growth of the midface and the skull base. These conditions lead to insufficient space for the growing brain so intracranial pressure rises. Also they cause airway restriction and various ophthalmologic problems.

3.3.1. Apert syndrome

Apert syndrome is an autosomal dominant disorder and is a congenital disorder characterized. Acrocephalosyndactyly is an autosomal dominant disorder. Males and females are affected equally [19]. In Greek, "acro" means "peak," referring to the "peaked" head and "Cephalo" means "head." Almost certainly, all cases are sporadic and have de novo mutations or environmental insult to the genome [20–25]. It is caused by a defect on the fibroblast growth factor receptor 2 gene on chromosome number 10; usually due to a C to G mutation at the 755 position on the FGFR2 gene that causes a Ser to Trp change in the protein [15].

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3.3.1.1. Apert syndrome characteristics

- Unusual headshape
- Wide-set eyes with shallow sockets and poorly closing eyelids
- Recessed midface
- Beak-shaped nose
- Underdeveloped jaws with under bite and crowded dentition
- Cleft palate
- Impaired hearing capabilities
- Atypical spine development
- Fused fingers and toes
- Limited intellectual development
- Gastrointestinal malfunctions
- Cardiac malformations
- Hyperhydrosis and heavy sweetening
- Severe acne
- Patches of lost hair (**Figure 7**)

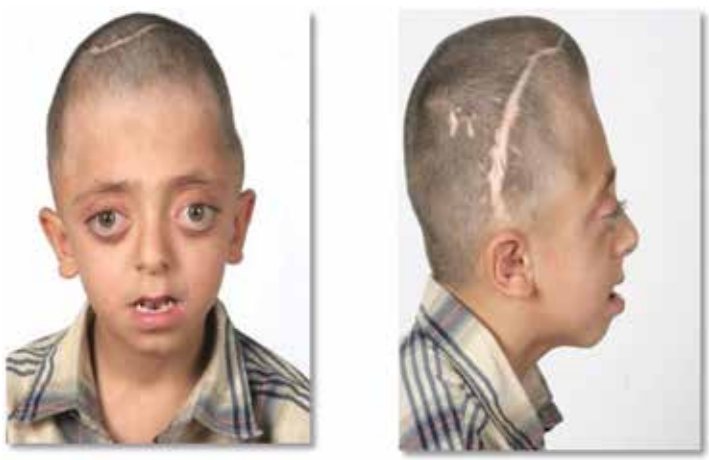

Figure 7. Photograph of a 9-year-old patient with history of cranioplastic surgery at the age of 1 year. Preoperative photograph of the patient, above. Photograph of the patient during the corrective surgery: the frontofacial monobloc advancement surgery, middle. Note the globs in both sides of the calvaruim vault are exposed in the superior view. Postoperative photograph of the patient: The same patient 8 months after the frontofacial monobloc advancement surgery, above.

3.3.2. Carpenter syndrome

For the first time, George Carpenter (1859–1910) described this condition and its related features [24–28].

Its features contain as follows:

- Tower-shaped skull because of craniosynostosis
- Additional or fused fingers and toes
- Obesity
- Reduced height

Patients may have average intellectual capacity and intellectual disability [29–32].

Malformation of the skull is the primary diagnostic factor. The two most common types of craniosynostosis in this syndrome are the sagittal and the bicoronal sutures. Mutations in the RAB23 gene located on chromosome 6 are responsible for these features. Also three key SNPs in theMEGF8 gene, located on chromosome number 19 at 19q13.2, have been identified as primary causes [33].

3.3.2.1. Carpenter syndrome surgical treatment

Surgical operations to correct the malformations of the skull should be done during the first year of infancy because modifying the bones is so much easier when the skull is in the growing stage; therefore, performing surgery at a young age increases the chance of obtaining good results. The fused sutures should be broken to allow for brain growth. The cranial plates are removed, reshaped, and replaced back on the skull. Despite the broken sutures, they will quickly refuse, and sometimes holes form in the plates allowing cerebral spinal fluid to escape into cyst-like structures on the external surface of the head (**Figure 8**).

Figure 8. A 3-year-old boy with carpenter syndrome: Preoperative photographs of the patient, above. Photographs during the monobloc frontofacial advancement surgery, middle. Postoperative photographs of the same patient: 6 month after the monobloc frontofacial advancement surgery, above.

3.3.3. Crouzon syndrome's surgical treatment

3.3.3.1. Crouzon syndrome

Crouzon syndrome also known as a branchial arch syndrome is an autosomal dominant genetic disorder that affects the first branchial (pharyngeal) arch. Mutation in the FGFR2 and FGFR3, located on chromosome 10, is responsible for it. For the first time, Octave Crouzon, a French physician, described the mentioned condition [34–39]. He noted that the affected patients were a mother and her daughter, implying a genetic basis. Low-set ears are a typical characteristics in all branchial arch syndromes. It usually presents as brachycephaly resulting in an appearance of a short and broad head. Exophthalmos and psittichorhina could be accompanied. External strabismus is a common feature. Hypoplastic maxilla and insufficient growth of the midface result in relative mandibular prognathism appearance so give the patient having a concave face. Typically, surgery is used to prevent the closure of skull sutures around the developing brain. Otherwise, blindness and mental retardation are typical outcomes of premature suture fusion (**Figure 9**).

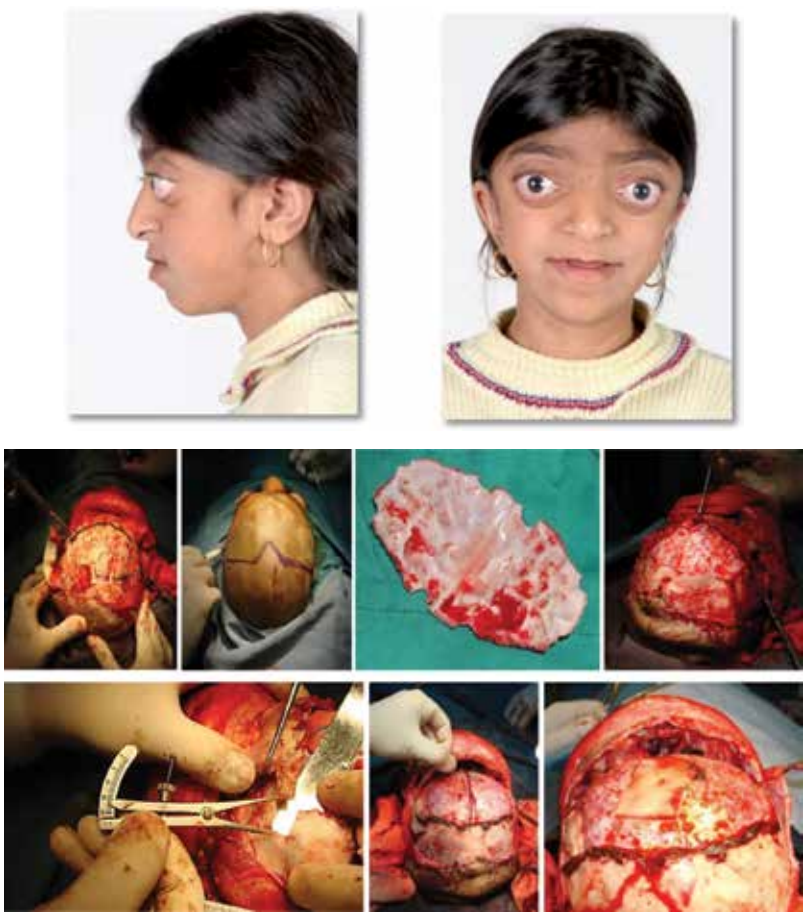

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Figure 9. Photograph of the patient an 8-year-old girl with the Crouzon syndrome: Preoperative photographs of the patient, above. Exposure the calvaria by the Bicoronal Flap, middle. Note: pressure effect of brain on the inner table of the frontal bone segment is obvious. Monobloc advancement: 17 mm advancement is obvious in zygomatic arch region. Note: Creating frontal intracranial volume by the surgery, below. The same patient 8 years later before and after orthognathic surgery, last.

3.3.4. Goldenhar syndrome

Goldenhar syndrome is defined as congenital defects due to involvement of the first arches during intrauterine development and includes incomplete development of the ear, lip, nose, mandible, and soft palate [40–45]. It is also known as oculo-auriculo-vertebral (OAV) syn-

drome. In 1952, this condition was documented by the Belgian ophthalmologist Maurice Goldenhar for the first time.

3.3.4.1. Signs and symptoms

Incomplete development of the ear, nose, soft palate, lip, and mandible on usually one side of the body is the main hallmarks. Some patients will show growing problems with internal organs, especially the lungs, heart, and kidneys [47, 48].

3.3.4.2. Cause

The cause is unknown but involves the branchial arch development in the first trimester and probably is multifactorial with genetic components which would account for certain familial patterns [45, 46].

3.3.5. Treatment

Surgical intervention is essential to help the patient continue natural development, for example, jaw distraction; bone grafts; ocular dermoid debulking; repairing palatal or lipclefts; repairing heart malformations or spinal surgery. Patients may require assistance of hearing aids or eye glasses as they grow.

3.3.6. Muenke syndrome

Muenke syndrome also known as FGFR3-related craniosynostosis is distinguished by the premature closure of certain bones of the skull during development. It was first described by Maximilian Muenke [50–57].

3.3.6.1. Signs and symptoms

Affected patients have premature fusion of skull bones especially along the coronal suture leading to abnormally shaped head, wide-set eyes, low-set ears, and flattened cheekbones and sometimes have macrocephaly and hearing loss.

Most affected patients have normal intellect with no mental retardation, but developmental delay and learning disabilities are possible problems. The condition is caused by a FGFR3 gene mutation with an autosomal dominant pattern. This mutation causes the overexpression and overactive FGFR3 protein, so this protein interferes with normal bone growth leading to premature fusion of the skull bones. Strabismus is the most common ocular finding [49].

3.3.6.2. Treatment

Surgical correction of the abnormal skull shape and coronal craniosynostosis is planned although abnormal growth patterns continue during the growing years.

3.3.7. Parry-Romberg syndrome

Parry–Romberg syndrome is a neurocutaneous syndrome distinguished by progressive shrinkage and degeneration of the tissues beneath the superficial skin, usually on only one side of the face as hemifacial atrophy but occasionally extending to other parts of the body known as progressive hemifacial atrophy. It probably has an autoimmune background; the syndrome could be considered a variant of localized scleroderma and a type of connective tissue disease. The condition is usually accompanied by significant neurological, ocular, and oral signs and symptoms [58–64].

During the first or early second decade of life, symptoms and physical findings usually become apparent. The average age of onset is 9 years of age, and the majority of individuals experience symptoms before 20 years of age. The disease may progress for several years before eventually going into remission.

Neurological abnormalities might be afflicted with trigeminal neuralgia. Some patients develop seizures. The type of the seizure is typically Jacksonian and occurs on the side contralateral to the affected side of the face. Enophthalmos is the most common eye abnormality.

Oral tissues are commonly involved in Parry-Romberg syndrome. Affected individuals develop dental abnormalities on the affected side include resorption of the dental roots, dental root exposure, or delayed tooth eruption. Patients may have difficulty or inability in normal mouth opening or other jaw symptoms, including temporomandibular joint disorder and spasm of the muscles of mastication on the affected side. Patients may experience atrophy of one side of the upper lip and tongue.

Diagnosis could be made by history and physical examination according to the facial asymmetry. In patients with neurological symptoms like migraine or seizures, brain MRI scan is the choice imaging modality. Detection of autoantibodies by diagnostic lumbar puncture and sera tests may be indicated for those whom present seizures of recent onset. Immunosuppressive drugs might be indicated to control the course of the disease. Autologous fat transfer or fat grafts could be useful for of a more acceptable facial contour. Larger defects require microsurgical reconstructive surgeries.

3.3.8. Pfeiffer syndrome

For the first time, in 1964, Rudolf Arthur Pfeiffer described a list of features included a coronal synostosis, turribrachycephaly, and maxillary hypoplasia (**Figure 10**). Pfeiffer syndrome, a genetic disorder, distinguished by premature craniosynostosis also affects the hands and feet bones. The patients usually have hearing loss and dental problems. Extracranial features include broad thumbs and toes of the hands and feet. The thumbs and first big toes are wide and bend away from the other digits. Short fingers and toes (brachydactyly) and webbing or syndactyly may be seen [65–72].

Figure 10. Photograph of a Pfeiffer syndrome patient before and after the corrective surgery.

Pfeiffer syndrome has three subtypes:

- **Type 1:** Classic type has symptoms as described above. Usually, they have normal intelligence and a normal life span.
- **Types 2 and 3** are more severe forms that often accompany nervous system involvements. The premature fusion of skull bones provides limitation for brain growth leading to delayed development and more neurological problems.

Type 2 is differentiated from type 3 by a cloverleaf-shaped head, caused by more extensive fusion of bones of the skull.

3.3.9. Saethre-Chotzen syndrome

Saethre-Chotzen syndrome (SCS) or Acrocephalosyndactyly type III is a congenital disorder accompanying cranio synostosis and affects the craniofacial shape resulting in a cone-shaped head and an asymmetrical face [73–77]. Patients have ptosis, hypertelorism, and syndactyly. In severe cases, mild-to-moderate mental retardation or learning disabilities can be noted. Depending on the level of severity of the condition, medical or surgical intervention may be needed (**Figure 11**).

http://dx.doi.org/10.5772/63739

Figure 11. Photograph of the patient with the Saethre-Chotzen syndrome before and after the corrective surgery.

Even within the family, affected individuals have different features. The majority of individuals with SCS are moderately affected, with uneven facial features and a relatively flat face due to underdeveloped eye sockets, malar bones, and the mandible. Growth delays like relatively short stature also are noted. Albeit most individuals with SCS are of normal intelligence, some individuals may have mild-to-moderate mental retardation (IQ levels 50–70).

3.3.9.1. Cranial defects:

- Flat and asymmetric head and face
- Acrocephaly and/or brachycephaly and/or dolichocephaly
- Short head from front to the back
- Lopsided face
- Low-set hairline causing forehead to appear tall and wide

3.3.9.2. Defects of the hands and feet

- Syndactyly between the second and third fingers and between the second and third toes
- Short fingers and toes (brachydactyly)
- Broad thumb and/or a broad hallux (big toe) with a valgus deformity (outward angulation of the distal segment of a bone/joint)
- Hands have a single palmer flexion crease

3.3.9.3. Ocular defects

- Strabismus
- Hypertelorism
- Tear duct stenosis

- Ptosis
- Nearsightedness
- Epicanthal folds
- Blepharophimosis
- Optic atrophy
- Refractory errors

3.3.9.4. Ear, nose, and mouth defects

- Small, low-set ears may be rotated somewhat backward and has a bulging pinna.
- Beaked nose; slightly bent downward at tip, that is, slightly off center and contains a deviated septum.
- Malocclusion associated with dental abnormalities, including enamel hypoplasia and hyperdontia and peg teeth.
- Cleft palate with high arch.

3.3.9.5. Less common defects

- Short stature
- Vertebral fusions
- Congenital heart problems
- Speech problems
- Malformed rectum
- Cryptorchidism
- Renal abnormalities
- Personality disorders

3.3.10. Treacher Collins syndrome (TCS)

Treacher Collins-Franceschetti syndrome [78–84] or mandibulofacial dysostosis is distinguished by craniofacial deformities such as absence of malar bones and has an autosomal dominant pattern. The typical accompanying features include downward-slanting eyes, micrognathia, conductive hearing loss, underdeveloped zygoma, drooping part of the lateral lower eyelids, and malformed or absent ears (**Figure 12**).

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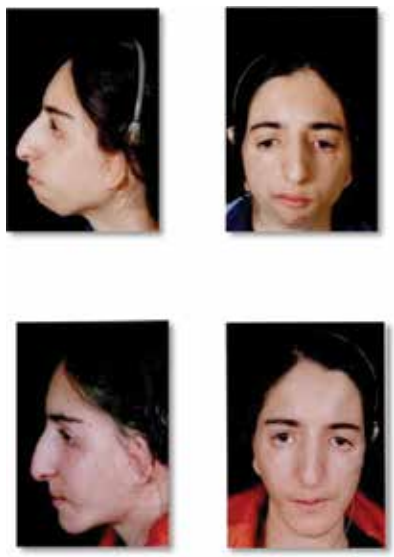

Figure 12. Photograph of a patient with Treacher Collins syndrome before and after corrective surgical treatment.

The presentation of symptoms varies. Some individuals may be so mildly affected and remain undiagnosed; others may show severe facial involvement and life-threatening airway compromises. Most of the features are bilateral and are already recognizable at birth.

3.3.10.1. Accompanying abnormalities:

- Facial bones hypoplasia
- Ear anomalies
- Eye problems
- Cleft palate
- Airway problems

Dental anomalies include tooth agenesis, enamel deformities, and misplacement of the maxillary first molars could be noted and usually in combination with mandible hypoplasia results in a malocclusion with problems in food intake and the ability of chewing.

3.3.10.2. Less frequent features:

- Nasal deformity
- High-arched palate
- Coloboma of the upper lid
- Ocular hypertelorism

- Choanal atresia
- Macrostomia
- Preauricular hair displacement

Intelligence of TCS patients is generally normal. The psychological and social problems associated with facial deformity may affect the quality of life in a number of patients.

3.3.10.3. Mandible:

- M0: Normal mandible.
- M1: Small mandible and glenoid fossa with short ramus.
- M2: Short and abnormally shaped ramus.
  1. 2A: Glenoid fossa in anatomical acceptable position.
  2. 2B: Temperomandibular joint inferiorly, medially, anteriorly displaced with severely hypoplastic condyle.
- M3: Complete absence of ramus, glenoid fossa, and TMJ.

3.3.10.4. Ears

- E0: Normal ear.
- E1: Minor hypoplasia and cupping with all structures present.
- E2: Absence of external auditory cannel with variable hypoplasia of the auricle.
- E3: Malposition of the lobule with absent auricle, lobular remnant usually inferior anteriorly displaced.

The treatment requires a multidisciplinary approach. Imaging evaluation consists of X-rays, CT scans, MRI, and ultrasound.

The primary concerns are breathing and feeding problems. Some when even atracheostomy is requisite to adequate airway preservation. Sometimes during the protection of the airway a gastrostomy can be done to provide an adequate caloric intake. Depending on the development state, surgical treatment is done for restitution of a normal facial contour and the structure of the face at certain times. Hearing loss is caused by deformed structures in the outer and middle ear. The hearing loss is generally bilateral with a conductive loss of about 50–70 dB. The ossicular chain is often malformed even in cases with normal auricles and open external auditory canals.

Surgical treatment can be done early during the first year of life or later. For psychological and social support, every effort is made as soon as possible [80–84].

3.4. Surgical treatment of craniosynostosis

Early: (Before 1 year of age)

1. Strip craniectomies
   - Limited
   - Extended
2. Frontal bone advancement with or without strip craniectomies
3. Cranial vault remodeling
4. Monobloc or craniofacial advancement
5. Shunt surgery for hydrocephalus

Late (After 1 year of age)

1. Frontal bone advancement
2. Le fort III and frontal bone advancement
4. Monobloc or craniofacial advancement
5. Le fort II advancement
6. Maxillary/mandibular/zygomatic surgery

Early surgical treatment of craniosynostosis

3.4.1. Before 1 year of age

The goals of surgery for newborn with a craniosnostosis are twofold:

(1) Decompression of the intracranial space to reduce intracranial pressure, prevent visual problems, and permit normal mental development.

(2) Achievement of satisfactory craniofacial form.

In this chapter, we discuss the late surgical treatment of craniosynostosis.

3.4.2. Late surgery

Late surgery is defined as surgical procedures performed on the patient with craniofacial synostosis after 1 year of age.

3.5. Le fort III advancement osteotomy

Gillies and Harrison reported the first high maxillary (modified Le fort III) osteotomy for craniofacial dysostosis. Through external incision, they performed transverse osteotomies that separate the nasal bones from the frontal bones. The osteotomy of the orbital floor was placed immediately within the infraorbital margin and extended across the floor of the orbit to the

medial orbital wall anterior to the lacrimal groove. Intermaxillary fixation was placed. Although no bone grafting was done, a satisfactory result was reported. Seven and one half years after this operation, the patient underwent further surgery to correct persistent exorbitism by removal of the medial portion of the orbital floor, and ox cartilage was also placed over the zygoma for contour improvement. The fate of the ox cartilage was not reported. Techniques of the Le fort III advancement osteotomy through a subcranial (Extracranial) route. Anesthesia is achieved through a transnasal endotracheal tube if the Le fort III advancement is to be performed without a tracheostomy [85–90].

The exposure of the facial skeleton is obtained through three incisions:

(1) Scalp (Bicoronal)

(2) Conjunctival or subciliary cutaneous

(3) Buccal vestibular

The eyelid incisions can be avoided, but the operation is technically more difficult. The bicoronal incision and the raised scalp flap provide access in a subperiosteal plane to the lateral wall and floor of the orbit, to the root of the nose, and to the medial orbital wall. The subperiosteally raised area can then communicate with the area, which will be exposed through the conjunctival or eyelid incision (optional). After the scalp flap is raised, the periorbita is elevated from the roof, the floor, and the lateral and medial orbital walls are exposed; the medial canthal tendon is left undisturbed, and the lacrimal sac is elevated from the lacrimal groove. A transverse cut is made across the orbital floor and joins the inferior orbital fissure to the lower end of the medial wall osteotomy.

The lateral wall of the orbit is sectioned transversely in the region of the frontozygomatic suture line or above it. After retraction of orbital contents medially and the temporal muscle laterally, the lateral orbital wall is divided in a full thickness fashion at its junction with the cranium. The zygomatic arch is likewise sectioned. After all lines of osteotomy are verified, the midfacial skeleton may be loosened with the Rowe disimpaction forceps. Autogenous bone grafts are placed in the defects of the nasofrontal junction, lateral orbital wall, and ptrygomaxillary fissure.

Le fort III osteotomy performed through a combined intracranial approach with advancement of the frontal bone.

After the neurosurgeon has removed the frontal bone segment, the supraorbital osteotomy is extended horizontally to the region of the temporal fossa and continued in a stepwise fashion inferiorly toward the base of the skull. A posterior extension is thus outlined, which guides the advancement and maintains bony contact. In a horizontal direction, osteotomy then transgresses the lateral orbital wall and follows a line through the orbital roof at about the junction of middle and posterior thirds of orbit. The procedure is then completed by performing the Le fort III osteotomy. In this way, a horizontal component is also advanced approximately 2 cm in height, containing the frontal bone, part of the roof, and the lateral wall of the orbit (**Figures 13** and **14**).

3.5.1. Monobloc advancement of orbits and midface [90–95]

To increase the orbital volume for the correction of the exorbitism, the subtotal orbits and midface could be advanced as a single skeletal segment. The lines of osteotomy are similar to the previously described for the combined Le fort III–frontal bone advancement except that the nasofrontal junction and frontozygomatic sutures are spared of osteotomies. The technique also has the advantage that a concomitant hypertelorism correction can be done; it suffers the disadvantages of an increased infection rate and limited orbital volume expansion.

3.5.2. Le fort III advancement

The most common indication for Le fort III advancement is the patient with midface hypoplasia and adequate zygomatic projection.

Figure 13. Photograph of a 24-year-old patient with midface deficiency and mandibular prognathism. Before the surgery, top. One week after the Le Fort III osteotomy and mandibular set back surgery, below.

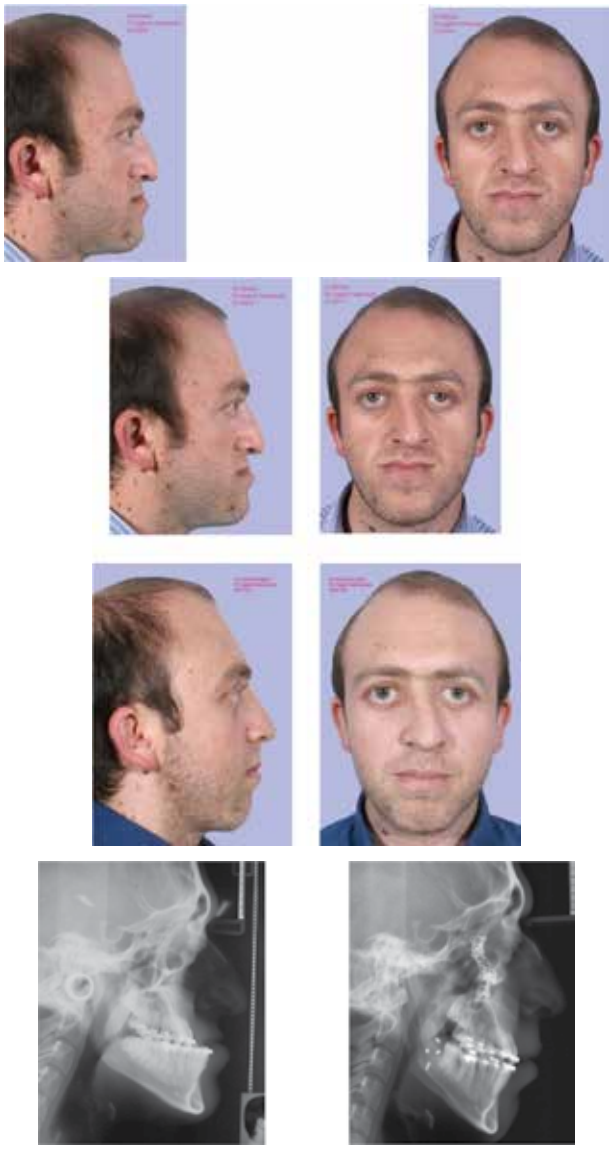

Figure 14. Photographs of a 32-year-old patient with midface deficiency and mandibular prognathism. Photographs of the patient before the orthognathic surgery, top. Photographs of the patient 1 year after the Le Fort III osteotomy and mandibular set back surgery, below.

3.6. Possible surgical complications

In the best of circumstances, surgical complications are inevitable but using theoretical knowledge and sufficient practical knowledge and requisite skills; complications can be reduced or be prevented. Despite all efforts in surgery in any surgery, including craniofacial surgeries, there are possible side effects and even a risk of death.

3.6.1. Some examples of problems during the surgery

- Anesthesia related
- Difficult airway
- Blood loss
- Electrolyte imbalance and hyponatremia
- Venous air or blood or fat embolism
- Intraoperative events
- Incision-related events

3.6.2. Miscellaneous events related by the surgery

- Periorbital or eye related events
- Bone wax granuloma formation
- Infection
- Neurological deficit
- Death

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Advanced oral and maxillofacial surgery encompasses a vast array of diseases, disorders, defects, and deformities as well as injuries of the mouth, head, face, and jaws. It relates not only to treatment of impacted teeth, facial pain, misaligned jaws, facial trauma, oral cancers, jaw cysts, and tumors but also to facial cosmetic surgery and placement of dental and facial implants. This specialty is evolving alongside advancements in technology and instrumentation. Volume 1 has topped 132,000 chapter downloads so far, and Volume 2 is being downloaded at the same pace! Volume 3 is basically the sequel to Volumes 1 and 2; 93 specialists from nine countries contributed to 32 chapters providing comprehensive coverage of advanced topics in OMF surgery.

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