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Rhinology Conditions

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Edited by Mohannad Al-Qudah

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Meet the editor

Professor Mohannad Al-Qudah obtained his medical degree from the University of Jordan in 1991. He started his otolaryngology residency in Jordan, then finished two years of clinical accredited fellowship programs in rhinology and endoscopic skull base surgery in the USA. He is a fellow of the American Academy of ORL-HNS, the American College of Surgeons, and the International College of Surgeons. Currently, he is a professor at JUST University and a senior consultant at KAUH Hospital, Irbid, Jordan. He has published more than 150 articles and abstracts in international journals. His research interests are sinusitis pathogenesis, new minimally invasive techniques, and indications in endoscopic sinus and skull base surgery. Professor Al-Qudah described many novel surgical techniques and pathological hypotheses in his specialty. In recognition of his medical achievements, he has been awarded the Royal Silver Jubilee medal.

Contents

Preface

Our fundamental understanding of rhinological disorders has improved substantially over the last three decades. Nowadays, the sinonasal region is considered as one physiological functionally separate unit that can be affected by disorders of different etiopathogenesis with variable structural histopathology manifestations.

This progression has been facilitated by advances in basic and clinical research, new methods of endoscopic visualization, high-resolution CT scans, the global exchange of experience, and the new guidelines agreed upon by various prestigious international scientific committees.

The umbrella of rhinology disorders is wide. It involves variations in anatomical structures, allergy, inflammation, cosmetic deformity, trauma, and tumors. These disorders have common indistinguishable and nonspecific presenting symptoms that require accurate knowledge and clinical skills to reach the correct diagnosis so the proper management plan can be set.

This book highlights certain topics concerning rhinological disorders that have been left unexplained by other literature. The first section of this book reviews the complex embryology and anatomy of the sinonasal region in a concise yet precise method covering all the essential clinical data that the reader needs to understand.

Nonallergic (intrinsic) rhinitis is a multifactorial common disorder that is usually misdiagnosed as allergic rhinitis because of the similarity between their symptoms. The peculiar aspect of this subject is thoroughly explained in the medical rhinology section. In another chapter in this section, the intricate relationship between rhinology disorders and neuropsychological health is unraveled, offering valuable insights and strategies to emphasize the importance of addressing both the physical and psychological aspects of rhinology disorders.

Effective management of refractory chronic rhinosinusitis and other complex sinonasal conditions by various extended sinus surgical approaches and techniques is explained in the surgical rhinology section. A separate chapter in this section discusses the application of medical lasers in rhinology and provides inspiration for exploring new ideas of medical lasers in this field.

Pathology in the sinonasal region is common, and its manifestations can present in different medical specialties. The present book covers certain rhinology disorders that are often neglected elsewhere.

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Section 1

Basic Rhinology

Chapter 1

Surgical Anatomy of the Nose and Paranasal Sinuses

Basma S. Almaadani

Abstract

This chapter delves into the intricate surgical anatomy of the nasal cavity and paranasal sinuses, highlighting their relevance in otolaryngological procedures. Understanding these anatomical details is crucial for performing safe and effective surgical procedures, minimizing complications, and enhancing patient outcomes. By integrating anatomical knowledge with clinical insights, this chapter aims to equip surgeons with a comprehensive understanding necessary for successful surgical intervention of nasal and sinus pathologies.

Keywords: anatomy, nasal cavity, paranasal sinuses, skull base, surgery

1. Introduction

The anatomical complexity of nasal cavity and paranasal sinuses is heightened by the proximity of significant surrounding structures, including the orbits and skull base which demand meticulous surgical navigation.

This chapter elucidates the basic anatomy of the nasal cavity and paranasal sinuses, emphasizing their clinical significance and the intricate relationships with adjacent critical structures. Mastery of this anatomical knowledge is imperative for the otolaryngologist to perform precise and safe surgical interventions, thereby optimizing patient outcomes and reducing intraoperative risks.

2. External nose anatomy

The external nose is composed of both bony and cartilaginous structures (osteocartiliginous framework), providing it with support and shape.

The bony part of the nose consists primarily of two nasal bones united in the midline by internasal suture. These nasal bones articulate with the frontal bone superiorly through the nasal process of the frontal bone and to the maxillary bones laterally through the frontonasal process of the maxilla (**Figure 1**).

The cartilaginous part of the nose consists of the nasal septum in the midline; in addition to the upper lateral cartilages and lower lateral cartilages (also known as allar cartilages).

The nasal septum divides the nasal cavity into two sides. It consists of the columellar septum which is the most anterior part of the septum, it is formed by the medial

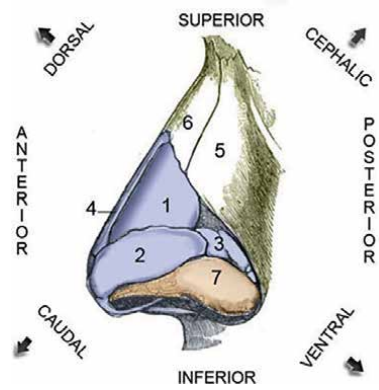

Figure 1.
Showing the terminology for nasal surgery topography and the external nasal osteocartilaginous framework. 1: upper lateral cartilage; 2: lower lateral cartilage; 3: accessory cartilage; 4: cartilaginous part of nasal septum; 5: frontonasal process of maxilla; 6: nasal bone; 7: fibroconnective tissue. Adapted from Ref. [1].

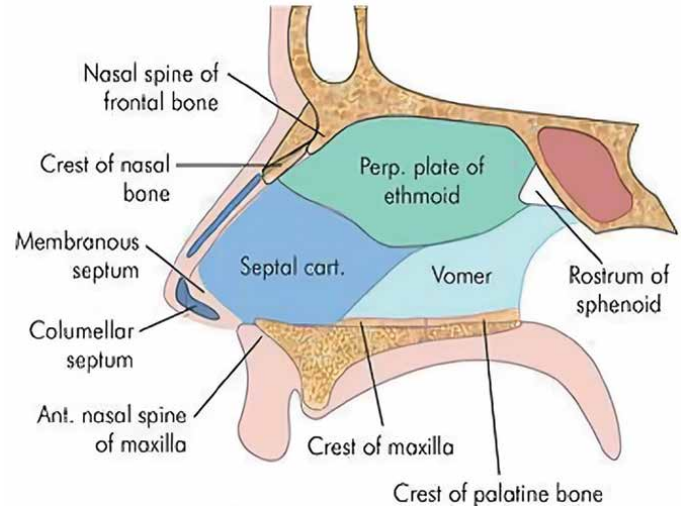

Figure 2.
Illustration of the nasal septum anatomy parts. Adapted from Ref. [2].

crura of alar cartilages which are connected by fibrous tissue and covered by skin. The membranous part of the septum, which lacks any bony or cartilaginous support, is situated between the columella and the lower edge of the septal cartilage. These two parts of the septum can be movable from side to side. The septum proper consists of an osteocartilaginous framework covered by nasal mucosa. The cartilaginous part is formed by the quadrangular septal cartilage anteriorly while the bony part is composed of the perpendicular plate of the ethmoid postero-superiorly and the vomer postero-inferiorly (**Figure 2**).

3. Blood supply and lymphatics

The nose is richly supplied with blood, with arterial contributions from both the internal carotid (including the anterior and posterior ethmoid arteries from the

ophthalmic artery) and the external carotid (including the sphenopalatine, greater palatine, superior labial, and angular arteries).

The dorsal nasal artery, a branch of the ophthalmic artery, traverses the medial palpebral ligament to reach the dorsum of the nose, primarily supplying the bony portion of the external nose. Meanwhile, the external carotid artery gives rise to the facial artery, which provides branches to the cartilaginous part of the external nose; however, these branches are not specifically described in anatomical terminology [3].

The superior part of the nasal septum is nourished by the anterior and posterior ethmoidal arteries, as well as the sphenopalatine artery. The anterior septum and nasal floor receive blood from terminal branches of the superior labial artery. Kiesselbach's plexus, also known as the Little area, is located in the lower anterior third of the nasal septum and is formed by the convergence of the superior labial, anterior ethmoidal, greater palatine, and sphenopalatine arteries.

The venous drainage of the nose, which mirrors the arterial pattern, is carried out by the anterior facial vein, the sphenopalatine vein, and the ethmoid veins. Notably, these veins directly communicate with the cavernous sinus and lack valves, facilitating the potential intracranial spread of infections. Lymphatic drainage from the nose flows anteriorly through the upper lip lymphatics and posteriorly through the deep cervical and retropharyngeal lymph nodes [4].

4. Nasal cavity

The nasal cavity is a complex structure comprising two cavities separated by the nasal septum, with each cavity having distinct anatomical features including the anterior nares, choana, roof, floor, medial, and lateral walls. The anterior nares are bounded by the columella medially and the ala laterally, while the choana is framed by the vomer medially and the medial pterygoid plate laterally. The cribriform plate of the ethmoid bone forms the roof of the nasal cavity, while the hard palate makes up the floor.

The medial wall of the nasal cavity is formed by the nasal septum which is comprised of cartilaginous and bony parts; the quadrangular cartilage being antero-inferiorly, the perpendicular plate of the ethmoid bone being postero-superiorly and the vomer is postero-inferiorly.

The lateral wall features three turbinates (conchae) and four corresponding spaces (meatuses), with the inferior turbinate being the largest and highly vascular, located above the inferior meatus where the nasolacrimal duct opens. The middle turbinate is of moderate size and is located centrally within the nasal cavity. Below it lies the middle meatus, which contains several notable structures: the bulla ethmoidalis, the largest cell of the anterior ethmoid sinus; the hiatus semilunaris, a semilunar groove below the bulla; and the uncinate process, a bone shelf medial to the bulla. The osteomeatal complex (OMC), crucial for drainage of the anterior group of sinuses, is bounded laterally by the lamina papyracea and medially by the middle turbinate. The superior turbinate is the smallest and highest, with the superior meatus below it, where the posterior ethmoid sinus opens. The sphenoethmoidal recess, located above the superior turbinate, drains the sphenoid sinus.

The nasal valve, the narrowest part of the nasal cavity, is located at the junction of the lower and upper lateral cartilages near the anterior end of the inferior turbinates.

The lateral nasal cavity, with its intricate anatomy, will be explored further in this chapter.

5. Ethmoid bulla

The ethmoid bulla is a prominent anterior ethmoid air cell originating from the lamina papyracea along the medial wall of the orbit. Despite the intricate nature of ethmoid bone anatomy, the ethmoid bulla remains the most recognizable and dependable ethmoid cell. It is located medial to the lamina papyracea, anterior to the vertical basal lamella of the middle turbinate, posterior to the uncinate process and postero-inferior to the frontal recess. Roughly 92% of patients exhibit well-pneumatized ethmoid bullae, making it a reliable landmark for anterior ethmoid sinuses during endoscopic procedures. In the remaining 8% of patients, the ethmoid bulla is either minimally pneumatized or completely absent, a condition referred to as torus lateralis [5].

6. Uncinate process, ethmoid infundibulum, and hiatus semilunaris

Uncinate process, a hook-shaped projection, is located anterior and inferior to the ethmoid bulla. Starting superiorly, near the agger nasi region at ethmoidal crest of the maxilla, the uncinate process extends downward and backward ending in a free edge with no bony attachment. This curving will result in both vertical and horizontal portions to the uncinate process (**Figure 3**).

The way the vertical portion of the uncinate process attaches superiorly is significant, since it can influence the layout of the frontal recess and the outflow pathway of the frontal sinus. Not recognizing this alignment can result in insufficient drainage of the frontal sinus after surgery.

Most often, the uncinate process attaches laterally to the lamina papyracea. In this alignment, the frontal sinus drains medially to the uncinate process insertion and directly into the middle meatus. In uncommon instances, the uncinate process attaches to the upper section of the middle turbinate or directly to the skull base. In these scenarios, the frontal sinus drainage route will be lateral to the uncinate process, flowing into the ethmoid infundibulum [6].

Hiatus semilunaris, a two-dimensional space between the posterior free margin of the uncinate process and the ethmoid bulla that serves as an "entrance" to the three-dimensional ethmoid infundibulum.

The *ethmoid infundibulum is a channel that is* bordered anteromedially by the uncinate process, posteriorly by the ethmoid bulla, and laterally by the lamina papyracea.

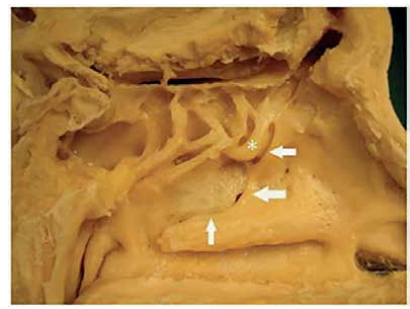

Figure 3.
Parasagittal cadaveric dissection of the lateral nasal wall. The arrows are demonstrating the hook-shaped uncinate process with its vertical and horizontal parts. (*) Ethmoid bulla [6].

This structure is important because it acts as an innate drainage channel for the maxillary sinuses and often the frontal sinuses.

7. Agger nasi region

Agger nasi is an area of ridge bone on the anterior region of lateral nasal wall, when pneumatized, it is identified as an agger nasi cells which are the most anterior ethmoid sinus cells. The agger nasi region is bordered superiorly by the frontal sinus, superiorly and posteriorly by the frontal recess, by nasal bones anteriorly and by anciante inferomedially. Recognizing and excising the agger nasi cell is essential in the surgical management of frontal sinus disease, as it often plays a major role in narrowing the frontal recess and sinus outflow tract [5].

8. Middle turbinate

The middle turbinate consists primarily of three sections, oriented in various planes and firmly attached to the lateral nasal wall, orbit, and skull base.

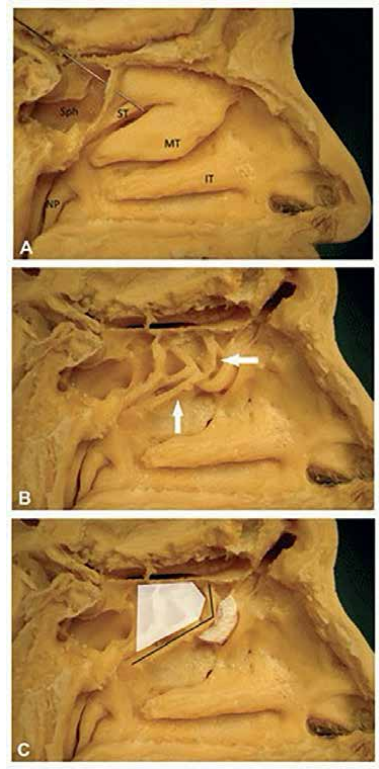

Figure 4.
Gross cadaveric dissections of the lateral nasal wall. (A) The three turbines are unbroken and in position. (IT) Inferior turbinate; (MT) middle turbinate; (ST) superior turbinate. (B) The vertical and horizontal portions of the MT basal lamella can be seen (arrows) after the parasagittal sections of the MT and ST have been excised. (C) The anterior ethmoid cavity is separated from the posterior ethmoid cavity by the vertical and horizontal parts of the MT basal lamella (demarcated in a black line) [6].

The anterior part of the middle turbinate, which is the first portion of the middle turbinate to be seen during anterior rhinoscopy or nasal endoscopy, is oriented in the sagittal plane. It is attached anterosuperiorly to the crista ethmoidalis of the maxilla, and base of the skull near the lateral lamella of cribriform plate of the ethmoid bone with a free edge anteroinferiorly.

The middle turbinate basal lamella has a vertical part which is aligned in the coronal plane and a horizontal part aligned in an axial plane (**Figure 4**).

The vertical part divides the anterior and posterior ethmoid complexes and attaches to the skull base superiorly and to the lamina papyracea laterally. The horizontal part, which forms posteriorly, can be used to locate the sphenopalatine foramen.

Pneumatization of the middle turbinate is possible and the nomenclature of these structures is determined by the location of the pneumatized portion. It is referred to as a concha bullosa if the anterior parasagittal-oriented portion is pneumatized and it is referred to as an interlamellar cell if the vertical section of the basal lamella is pneumatized [5].

9. Posterior ethmoid complex

The posterior ethmoid sinus is bounded anteriorly by the vertical portion of the middle turbinate basal lamella, posteriorly by an anterior wall of the sphenoid sinus, laterally by the laminia papyacea and superiorly by the skull base.

An Onodi cell, which is the term anatomical variant, is a highly pneumatized posterior ethmoid cell that has persisted in growing superolaterally in relation to the true sphenoid. Studies have shown that the incidence of sphenoethmoidal air cells in individuals ranges from 3.4 to 60%, a variation that is probably attributed to differences in definitions rather than actual rates of occurrence [7].

Since the term "sphenoethmoid cell" better describes the anatomy in this region, it is now preferred over "Onodi cell." sphenoethmoidal cell when present can be mistaken for a sphenoid sinus. Before sinus dissection, radiographic identification of sphenoethmoid cells is crucial to avoid incomplete dissection that may result from not identifying them beforehand.

The other primary reason for the significance of these air cells is that they are situated in close proximity to the internal carotid artery and optic nerve, with a mere 0.03 mm (median 0.08 mm) of bone dividing them [7].

10. Ethmoid roof and skull base

The anterior skull base is divided by the middle turbinate vertical lamella into the cribriform plate medially and the roof of the ethmoid laterally. The ethmoid roof is made up of two parts: a thinner vertical portion, named the lateral cribriform plate lamella (LCPL), and the thicker horizontal portion named fovea ethmoidalis which an extension of the orbital plate of the frontal bone.

The skull base is thicker laterally and as it gets medially it becomes thinner reaching only (0.2 mm thickness) along the cribriform plate which represents the thinnest point in the anterior skull base and the most frequent location for iatrogenic cerebrospinal fluid leaks during sinus surgery [6].

Furthermore, there is a positive correlation between the depth of the olfactory cleft and the chance of iatrogenic injury during surgery. The ethmoid roof is classified

by Keros classification system into—shallow type I (1–3 mm), medium type II (4–7 mm), and deep type III (8–16 mm). As the depth increases the risk for complications increases during endoscopic endonasal surgery which can include CSF leak or intracranial hemorrhage [8].

10.1 Maxillary sinus

Out of all the paranasal sinuses, the maxillary sinus is the biggest and the first to develop. The maxillary sinus is positioned within the maxillary bone, it has a pyramid shape, with its base near the nasal cavity and its apex directed toward the zygomatic bone. The boundaries of the maxillary sinus include the floor, which is formed by the alveolar process of the maxilla housing the roots of the maxillary teeth; the roof is formed by the floor of the orbit; the medial wall is formed by the lateral nasal wall; and the lateral wall is facing the zygomatic process.

The usual opening of the maxillary sinus is through a single natural ostium positioned in the posterior part of the ethmoid infundibulum. Nonetheless, up to 23% of patients may develop accessory ostia through the anterior or posterior fontanelles. These fontanelles are situated in the lateral nasal wall and lack bone; in some instances, the mucosa and connective tissue covering them are insufficient, creating an alternative drainage route for the sinus [6].

The maxillary sinus can show different levels of pneumatization and occasionally, hypoplasticity. The orbital contents tend to fill a greater volume of the midface as the volume of the maxillary sinus decreases. Due to the increased orbital volume-to-maxillary sinus volume ratio in cases of maxillary sinus hypoplasia, paranasal sinus surgeons need to proceed with caution during surgery. The uncinate process is often shifted inferolaterally and positioned near the orbital wall in cases of the hypoplastic maxillary sinus. Furthermore, marked degrees of maxillary sinus hypoplasia may be associated with an underdeveloped uncinate process because of their shared developmental origins [5].

10.2 Sphenoid sinus

Positioned within the sphenoid bone at the central skull base, the sphenoid sinuses are a pair of large paranasal spaces found posterior to the ethmoid sinuses. The natural ostium of the sphenoid sinus connects the sphenoid sinus with the roof of the nasal cavity via the sphenoethmoidal recess.

The sphenoid ostium opens in the anterior superior wall of the sinus and it is situated approximately 1.0–1.5 cm above the superior edge of the posterior choana and it is typically situated approximately midway between the posterior insertion of the superior turbinate and the nasal septum [5].

Due to its variability, the sphenoid sinus is one of the most complex sinuses. Its proximity to critical neurovascular structures makes it challenging for endoscopic surgeons to navigate [9]. These relationships include the pituitary gland which is located posterior and superior to the sphenoid cavity. Above it lies the optic chiasm, with the optic nerves extending laterally toward the orbital apices. The internal carotid arteries are positioned lateral to the pituitary gland and clivus, often creating impressions in the sphenoid sinus walls and forming the opticocarotid recesses. The cavernous sinus, which houses oculomotor; trochlear; ophthalmic and maxillary divisions of trigeminal; and abducent cranial nerves, is situated lateral to the sphenoid sinus.

Additionally, the vidian nerve can be seen as an impression along the inferolateral aspect of the sinus floor. Understanding these anatomical relationships is vital to avoid damaging these structures during surgery.

The right and left sphenoid sinuses are separated by a sphenoid intersinus septum. It is common for these sinuses to develop unevenly, and demonstrate differences in size and pneumatization. When planning sphenoid sinus surgery, it is essential to thoroughly assess the sphenoid intersinus septum. This septum can deviate to one side and may attach near critical structures like the internal carotid artery or optic nerve [10].

Awareness of the anatomical layout and positioning of these neighboring structures can make interventions considerably safer, given the potentially devastating outcomes of damaging any of them.

10.3 Frontal sinus

The frontal sinus has a trapezoidal or triangular shape and it develops last among the paranasal sinuses. In newborns, the frontal sinus (FS) is barely noticeable, but it becomes detectable on radiographs around age 4. Its growth parallels that of the craniofacial area, attaining its maximum size approximately at age 18 [11].

The frontal sinus is bounded inferiorly by the orbital roof, anteriorly by the terminal frontal table of the frontal bone, and posteriorly by the posterior table dividing the sinus from the brain.

Despite the notable anatomical differences in the frontal sinus area, the right and left frontal sinuses are divided by a thin bone known as the frontal intersinus septum. The right and left frontal sinuses are often unequal in size, with the septum leaning toward one side. The frontal sinus is commonly bilateral; however, it might be unilateral in up to 15% of cases and absent in 8% of cases [12].

In some cases, the septum becomes pneumatized, resulting in an intersinus septal cell that can drain into the left or right frontal sinus. Surgeons may mistakenly think they have drained the opposite sinus by entering this cell.

Other pneumatized cells that should be taken into consideration in the frontal sinus region are the supraorbital ethmoid cells, which extend over the orbit, as they can also confuse without proper preoperative imaging.

Connecting the frontal sinus to the anterior ethmoid cells, the frontal recess is an inverted cone featuring a narrow upper end at the internal frontal ostium and a broader lower end that merges into the anterior ethmoid cells. Endoscopic surgeons need to have a comprehensive understanding of the frontal recess.

Despite that the drainage pathway can vary based on the superior insertion of the uncinate process, the frontal recess bony structures remain fairly the same. The frontal recess is bound medially by the anterior superior portion of the middle turbinate and laterally by the lamina papyracea. The frontal sinus forms its upper limit while the nasal cavity forms its lower limit. The agger nasi cells constitute the anterior border and the ethmoid bulla forms the posterior border [11].

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References

[1] Tu J, Inthavong K, Ahmadi G. The Human Respiratory System. 2012

[2] Sharma AR et al. Clinical outcome following septoplasty with or without inferior turbinate reduction. International Journal of Otorhinolaryngology and Head and Neck Surgery. 2020

[3] Pilsl U, Anderhuber F. The external nose: The nasal arteries and their course in relation to the nasolabial fold and groove. Plastic & Reconstructive Surgery. 2016;**138**(5):830e-835e. DOI: 10.1097/prs.0000000000002626

[4] Facs EWCMD. Nasal Anatomy: Embryology, Skin and Soft Tissues, Blood Supply and Lymphatics. n.d. Available from: https://emedicine.medscape.com/article/835134-overview

[5] Kennedy DW, Hwang PH. Sinonasal development and anatomy. In: Rhinology: Diseases of the Nose, Sinuses, and Skull Base. New York: Thieme; 2012c

[6] Villari RC, Wise SK. Surgical endoscopic anatomy of the nose, paranasal sinuses, and skull base. In: Devaiah AK, Marple BF, editors. Rhinology and Endoscopic Skull Base Surgery. Vol. 3. New York: Thieme; 2013

[7] KN, Gaillard F. Sphenoethmoidal Air Cell. Radiopaedia.org; 2008. DOI: 10.53347/rid-1776

[8] Fars ASM. Paranasal Sinus Anatomy: Overview, Gross Anatomy, Microscopic Anatomy. n.d. Available from: https://emedicine.medscape.com/article/1899145-overview

[9] Budu V, Mogoantă CA, Fănuţă B, Bulescu I. The anatomical relations of the sphenoid sinus and their implications in sphenoid endoscopic surgery. PubMed. 2013. Available from: https://pubmed.ncbi.nlm.nih.gov/23529304/

[10] Famurewa O, Ibitoye B, Ameye S, Asaleye C, Ayoola O, Onigbinde O. Sphenoid sinus pneumatization, septation, and the internal carotid artery: A computed tomography study. Nigerian Medical Journal/Nigerian Medical Journal. 2018;**59**(1):7. DOI: 10.4103/nmj.nmj_138_18

[11] Dassi CS, Demarco FR, Mangussi-Gomes J, Weber R, Balsalobre L, Stamm AC. The frontal sinus and frontal recess: Anatomical, radiological and surgical concepts. International Archives of Otorhinolaryngology. 2020;**24**(03):e364-e375. DOI: 10.1055/s-0040-1713923

[12] Ochs MW. Fractures of the Upper Facial and Midfacial Skeleton. Elsevier eBooks; 2008. pp. 905-933. DOI: 10.1016/b978-1-4160-2445-3.50097-2

Section 2

Medical Rhinology

Chapter 2

Nonallergic Rhinitis

Carlos Ríos-Deidán, Diana Villacrés-Silva, Daniela Saénz-Chávez and María Peña-Vásquez

Abstract

Non-allergic rhinitis (NAR) is a heterogeneous nasal disease with high global prevalence. While the specific factors contributing to the origin of NAR remain uncertain, there is indication that neurogenic factors play a significant role in the development of NAR. There are seven subtypes with overlapping presentations, including senile or geriatric rhinitis, gustatory rhinitis, drug-induced rhinitis, hormonal rhinitis, smokers' rhinitis, occupational rhinitis and idiopathic rhinitis. The approach to treatment is focused on alleviating symptoms and parallels the methods used for allergic rhinitis. Patients are advised to minimize exposure to identified triggers whenever feasible. Initial treatments involve the use of primary interventions such as intranasal corticosteroids, intranasal antihistamines, and intranasal ipratropium. Combination therapies may be considered if single interventions do not effectively manage symptoms. The surgery is considered in patients refractory to medical therapy, the reduction of inferior turbinate hypertrophy is a surgical procedure with an excellent outcome, besides the selective neurectomy of the vidian branches, has also proven to be effective.

Keywords: idiopathic rhinitis, endotypes, subtypes non allergic, intranasal corticosteroid, intranasal antihistamines, nasal surgical procedures

1. Introduction

Rhinitis constitutes an alteration of the nasal mucosa and stands out as one of the prevalent reasons for medical consultations globally. Its incidence has shown a rising trend over time. This condition is notably widespread in both Europe and America, with geographical variations possibly attributed to diverse environmental conditions, lifestyle factors, and host-related risk factors [1, 2].

The classification of rhinitis includes infectious rhinitis, allergic rhinitis, non-allergic rhinitis, and mixed rhinitis. Although non-allergic and allergic rhinitis exhibit certain overlapping symptoms, they diverge in terms of treatment approaches, affected demographic groups, and underlying pathophysiology [2]. **Figure 1** shows the phenotypes of chronic rhinitis.

Infectious rhinitis, as its name implies, is a condition triggered primarily by a virus, and to a lesser proportion, by bacteria, commonly recognized as the common cold. Symptoms encompass the presence of discolored nasal secretions, nasal obstruction or congestion, and the formation of crusts [3].

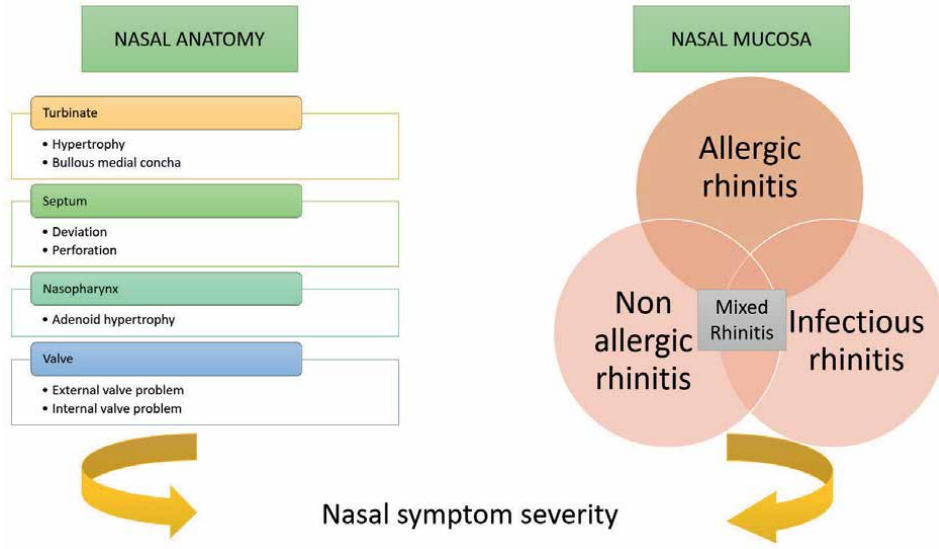

Figure 1.
Phenotypes of chronic rhinitis.

Allergic rhinitis is caused by IgE mediated reactions to inhaled allergens that trigger a type 2 immune reaction that starts in childhood and usually have seasonal exacerbation of symptoms. It is associated to asthma and conjunctivitis. Treatment included allergen avoidance, topic corticosteroid, antihistamines, and immunotherapy [2, 4].

Nonallergic rhinitis is a chronic condition that starts later in life which is defined as inflammation or dysfunction of the nasal mucosa present for at least 12 weeks per year without any indications of allergic sensitization. Diagnostic tests capable of detecting allergies include allergic skin tests, measurement of total immunoglobulin E (IgE), and specific serum IgE assays for certain allergens [1, 3, 5].

To establish a diagnosis of chronic rhinitis, it is necessary for two nasal symptoms to be consistently present for at least 1 hour each day. These symptoms include rhinorrhea (anterior or posterior), nasal obstruction or congestion, sneezing or nasal itch, cough, hyposmia, facial pressure, and eustachian tube dysfunction. These symptoms can be categorized as perennial/persistent, intermittent, or triggered by non-immunologic factors such as irritants, environmental humidity, or temperature variations [3, 5–7].

Mixed rhinitis has the characteristic of presenting several etiologic factors, whether known or not, that is why the diagnostic must be precise and a nasal endoscopy should be done to identify the presence of chronic rhinosinusitis with or without polyps and anatomic factors that may increase symptoms and are completely different pathologies [3].

2. Epidemiology

Limited data are available regarding the prevalence of general rhinitis, with even fewer statistics on Nonallergic rhinitis. However, estimates indicate that over 70 million individuals in the United States and 200 million globally are affected by chronic rhinitis. The European Community Respiratory Heath Survey (ECRHS), the most

extensive international multicenter study on prevalence, reported a median self-reported nasal allergy prevalence of 20.9% in 1995, focusing on Western European countries. Notably, it did not delineate the prevalence of Nonallergic or allergic rhinitis. The absence of prevalence data for nonallergic rhinitis is attributed to the lack of a standardized definition and diagnostic criteria, as highlighted by Hellings. Nonetheless, Greiwe et al. proposed mechanistic theories involving autonomic dysfunction, resulting in altered sympathetic activity or parasympathetic overactivity. These mechanisms also encompass changes in the expression of receptor potential channels on sensory nerves in the nasal mucosa, serving as irritant sensors, and the involvement of neuropeptides leading to vasodilation and transudation [3, 7, 8].

Savoure et al. perform a study of worldwide prevalence of rhinitis and described unspecified rhinitis prevalence at 29.4% (1.1 to 63.3%), allergic rhinitis with 18.1% (1 to 54.5%) and 12% for nonallergic rhinitis (4 to 31.4%). They classified the median prevalence based on symptoms at 16.4% and based on IgE definition at 31.4% for nonallergic rhinitis. Bernstein et al., reported prevalence of 23, 34 and 43% for nonallergic rhinitis, mixed rhinitis, and allergic rhinitis respectively [7].

Between the prevalence reported Savoure et al. found studies from Europe, Africa, Asia, Oceania and America for non-specific rhinitis and allergic rhinitis but there were no data from America, Africa, and Oceania for nonallergic rhinitis. For Asia reported prevalence were ranging from 4 to 31.4% and for Europe 5.5 to 23.5% [9].

Savoure et al. in another study reported general prevalence of rhinitis were 53.4%, allergic rhinitis 36.5% and nonallergic rhinitis 16.9% and the onset of allergic rhinitis were 10 years earlier compared with nonallergic rhinitis which is consistent with Dykewicz that explain a study perform by Rondon et al. in which compared nonallergic and allergic rhinitis and demonstrated that patients with nonallergic rhinitis tend to be older and have severe symptoms and unlikely association to asthma. Savoure et al. reported in their study that moderate to severe rhinitis was found in higher percentage in nonallergic rhinitis (40%) compared with allergic rhinitis (24%) [1, 2].

Dykewicz et al. estimated nonallergic rhinitis affect 17–52% of adults in the United States and 34% may have a mixed rhinitis [1].

An important difference between nonallergic and allergic rhinitis is the seasonality of symptoms. Savoure et al. referred allergic rhinitis increased from March to June (spring) and nonallergic rhinitis increased during winter and decreases from May to September which is demonstrated in **Figure 2** [2].

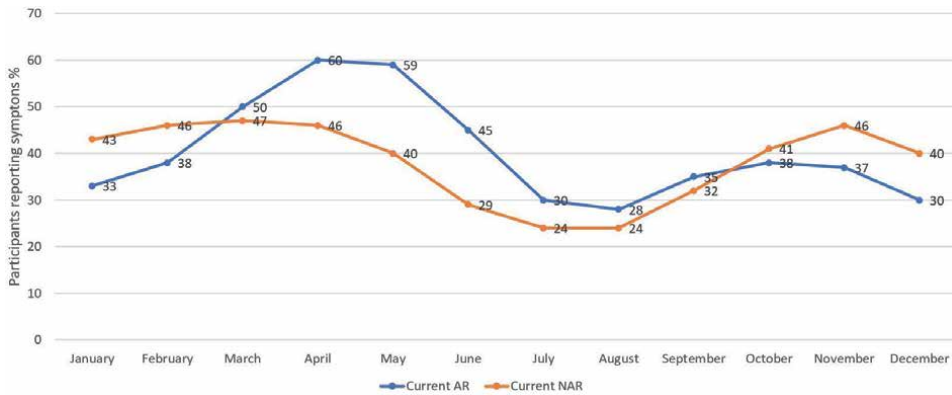

Figure 2.
Seasonality of symptoms of nonallergic rhinitis (NAR) and allergic rhinitis (AR) [2].

3. Histopathology of allergic rhinitis and non-allergic rhinitis

In the inflammatory process of rhinitis, the hair cells decrease and the number of goblet cells responsible for: rhinorrhea increased; capillary permeability causing edema and nasal obstruction [10], with stimulation of nerve endings responsible for sneezing and neuromodulators that recruit more inflammatory cells [11]. Chronic hypertrophic is characteristic with loss of cilia and a tendency to squamous metaplasia [12].

In their research, Ríos et al. discovered that histological examination of allergic rhinitis revealed a noteworthy increase in remodeling across all patterns, including epithelial markers and edema, except for fibrosis. Within the stromal marker, there was an elevated occurrence of subepithelial edema, and this was directly proportional to the presence of more than 10 eosinophils per field. This finding is clinically associated with heightened obstruction and severity of the condition [13].

Fibrosis was more frequently identified in the non-allergic variant, although this observation did not reach statistical significance. The collagen deposition in these cases is influenced by the upregulation of transforming growth factor beta [14].

3.1 Non-allergic rhinitis phenotypes

NAR needs to be differentiated from rhinitis patients experiencing an allergic response localized to the nasal mucosa, which is commonly referred to as local allergic rhinitis (LAR) [3]. NAR is characterized by rhinorrhea, blocked nose, sneezing, and/or itchy nose without clinical signs of infection or allergy. **Figure 3** shows the subtypes of non-allergic rhinitis [12].

Nonallergic noninfectious rhinitis (NANIR) encompasses a diverse set of patients experiencing rhinitis without apparent signs of infection, such as discolored secretions, and lacking systemic indications of allergic inflammation, such as allergen-specific IgE in the blood. Subcategories within NAR include drug-induced rhinitis, rhinitis associated with aging, hormonal rhinitis, including pregnancy-induced rhinitis, nonallergic occupational rhinitis, gustatory rhinitis, and idiopathic rhinitis [15–18]; its phenotyping is essential for choosing the best treatment option [19, 20].

3.1.1 Subgroups of NAR

3.1.1.1 Senile rhinitis or rhinitis

Senile rhinitis or rhinitis in elderly is characterized as rhinitis occurring in individuals aged 65 years and older, constituting an often-overlooked condition that impacts up to 29.8% of the population in this age group. The diagnosis of senile rhinitis typically pertains to individuals experiencing bilateral watery nasal secretions in the absence of endonasal mucosal or anatomical abnormalities. The symptoms are attributed to neurogenic dysregulation and are considered to arise late in onset [9].

3.1.1.2 Gustatory rhinitis

Is marked by a runny nose following the consumption of hot and spicy foods. This phenomenon is thought to be triggered by a gustatory reflex linked to an overactive neural system that is nonadrenergic, noncholinergic, or peptidergic [9].

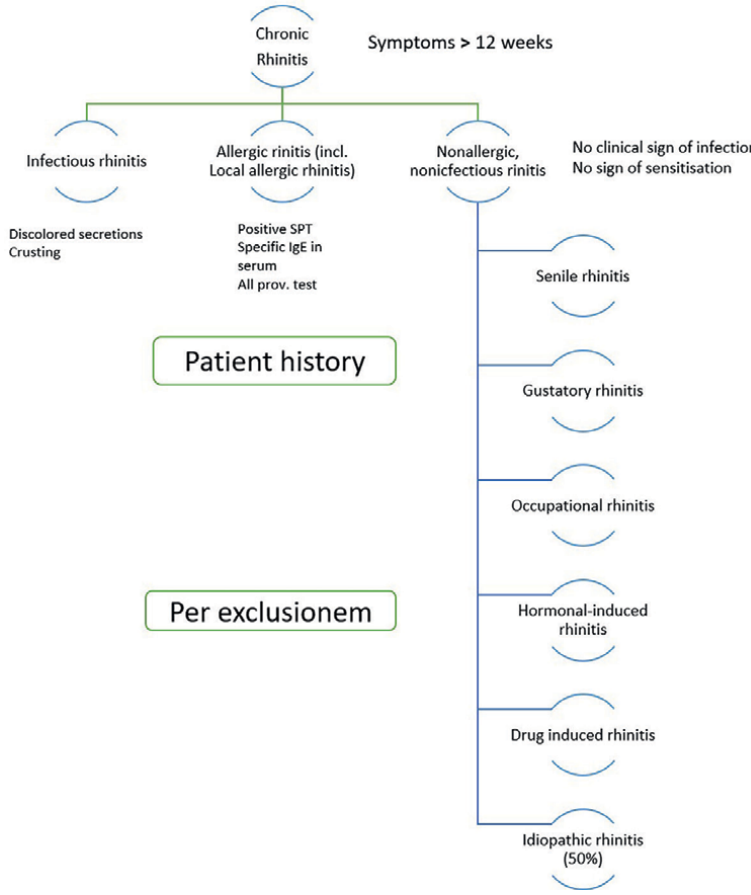

Figure 3.
Diagnosis of chronic rhinitis [3].

3.1.1.3 Occupational rhinitis

Is characterized as inflammation of the nasal mucosa resulting from exposure to a specific work environment and must be differentiated from "work-exacerbated" rhinitis [6]. Substances linked to occupational rhinitis include allergens of both high and low molecular weight (HMW and LMW) as well as irritants, according to reports. HMW agents could trigger a typical allergic inflammation mediated by IgE. The mechanisms behind chronic inflammation caused by LMW molecules are not clearly understood [9].

Prolonged exposure to occupational agents may lead to the development of asthma in patients. Recognizing occupational rhinitis is crucial for preventing occupational asthma. Rhinitis can emerge anew following prolonged exposure to airborne irritant chemicals in the occupational or environmental setting [20].

Nasal hyperreactivity to workplace triggers that are not specifically identified can also exist, with only about one-third of individuals experiencing relief during weekends or vacations. Individuals reported that their nasal issues were

linked to sensitivity to nonspecific workplace triggers like air conditioning, dust and dry air [9, 12].

3.1.1.4 Hormonal rhinitis

Hormonal imbalances occurring during various stages such as the menstrual cycle, puberty, pregnancy, menopause, and specific endocrine disorders like hypothyroidism and acromegaly are frequently linked to NAR. Estrogens, induce nasal vascular engorgement, potentially leading to nasal obstruction and/or increased nasal secretions. Both beta-estradiol and progesterone contribute to an elevated expression of histamine H1-receptors on the nasal epithelium. Although hormonal changes are believed to have a notable impact, especially in conditions such as gestational rhinitis or pregnancy-induced rhinitis, the exact pathophysiology of hormonal rhinitis remains uncertain.

Smoking emerges as the sole universally acknowledged risk factor in pregnancy-induced rhinitis [12]. Regarding instances of new-onset allergic rhinitis and asthma after puberty, studies suggest that girls undergoing a delayed onset of menarche (first menstruation) are less susceptible to developing allergic rhinitis compared to those experiencing menarche at the average age.

Late menarche (occurring after 13 years of age) is statistically inversely correlated with the development of allergic rhinitis [9].

Additionally, the use of hormonal contraceptives is inversely associated with the onset of allergic rhinitis, suggesting that, aside from endogenous hormones, these contraceptives might provide protection against allergies and asthma in young women post-puberty [20].

3.1.1.5 Drug-induced rhinitis

A variety of drugs may cause nasal symptoms, primarily nasal obstruction. 11 Nasal obstruction and post-nasal drip being the most prominent complaints. Drug-induced rhinitis can be divided into two subgroups:

- *adverse events of systemic treatment*: includes prolonged oral intake of aspirin, ibuprofen, and other NSAID, beta-blockers, sedatives, antidepressants, oral contraceptives, or drugs used to treat erectile dysfunction. Peptidergic drugs activate human mast cells through a G-protein coupled receptor, and this interaction could be responsible for some forms of drug-induced rhinitis

- *abuse of decongestive nasal* therapy, most commonly recognized as rhinitis medicamentosa (RM), this condition arises from the extended use of powerful decongestant sprays, and it is advised to discontinue the use of these sprays suddenly [14].

Rhinitis medicamentosa (RM) is a result of a particular medication with localized action, operating through a distinct pathophysiological mechanism and showing connections with psychiatric conditions like anxiety or opioid use disorders. Mehuys et al. have revealed concerning rates of nasal decongestant (ND) abuse. Approximately half of individuals with persistent rhinitis, obtaining over-the-counter medication for their nasal issues, were found to be overusing ND, despite being informed about the recommended duration of use [21].

3.1.1.6 Smokers' rhinitis

Current smokers exhibited a significantly higher likelihood of having NAR compared to non-smokers (chi-square p = .034, OR 1.7 (1.04–2.8); RR 1.6 (1.004–2.6)). Among the NAR group, current smokers had a notably higher number of pack-years of smoking in comparison to individuals who were currently smoking but did not have NAR (32 ± 29 vs. 14 ± 14; t-test p = .014; MWU test p = .04) [20].

In contrast, former smokers had a comparable likelihood of having NAR when compared to those who had never smoked. The pack/year of smoking among former smokers did not differ between those with NAR and the control group [20].

3.1.1.7 Idiopathic rhinitis

Approximately half of individuals with NAR lack a clearly defined cause for their symptoms and are referred to as idiopathic rhinitis patients. The defining characteristic of these patients is the presence of Nasal Hyperreactivity. Recently, research has demonstrated an upregulation of the nociceptive TRPV1-substance P (SP) signaling pathway in idiopathic rhinitis patients, suggesting its probable involvement in the pathophysiology [2].

In her research, Klementina et al. affirms that Idiopathic Rhinitis (IR) represented the highest prevalence among the phenotypes, accounting for 39% of the NAR group. IR is characterized as a purely neurogenic phenotype, and identifying the disease with NHR as its most prominent symptom holds significant implications for its treatment [2].

Additionally, Klementina notes that 20% of the Non-Allergic Rhinitis group defied classification into any of the defined phenotypes. In this subset, a discernible pattern explaining the nature of nasal complaints eluded identification. Without NHR as a defining criterion for IR, these individuals might have been categorized under IR. This subgroup potentially comprises participants with anatomical factors contributing to nasal symptoms, such as septal deviation and/or inferior turbinate hypertrophy, and/or phenotypes that are yet to be recognized [20].

3.2 Diagnosis

The diagnosis of NAR relies on a comprehensive medical history, which includes the exclusion of clinically relevant sensitization to airborne allergens and the absence of clinical signs of rhinosinusitis [22]. In addition to the medical history, anterior rhinoscopy is employed to examine for signs of infection, endonasal crust formation, and/or significant anatomical deformities.

Nasal endoscopy is strongly recommended, as it enables a comprehensive evaluation of the entire endonasal cavity, including the ostiomeatal complex. Emphasizing the significance of nasal endoscopy in diagnosing prolonged cases of rhinitis is crucial, as it can unveil the presence of chronic rhinosinusitis without nasal polyps (CRSsNP) or with nasal polyps (CRSwNP) [21, 22].

The following diagnostic tests are not recommended in NAR: allergen provocation testing, microbiological analysis of the nasal content, nasal cytology or biopsies, measurement of total IgE or allergen-specific IgE in nasal secretions, CT scans of the sinonasal cavities, measurement of nasal hyperreactivity, measurement of markers of cerebrospinal fluid leakage (b2- transferrin or b-trace [21]. **Figure 4** shows an algorithm for diagnosis between the subtypes [20].

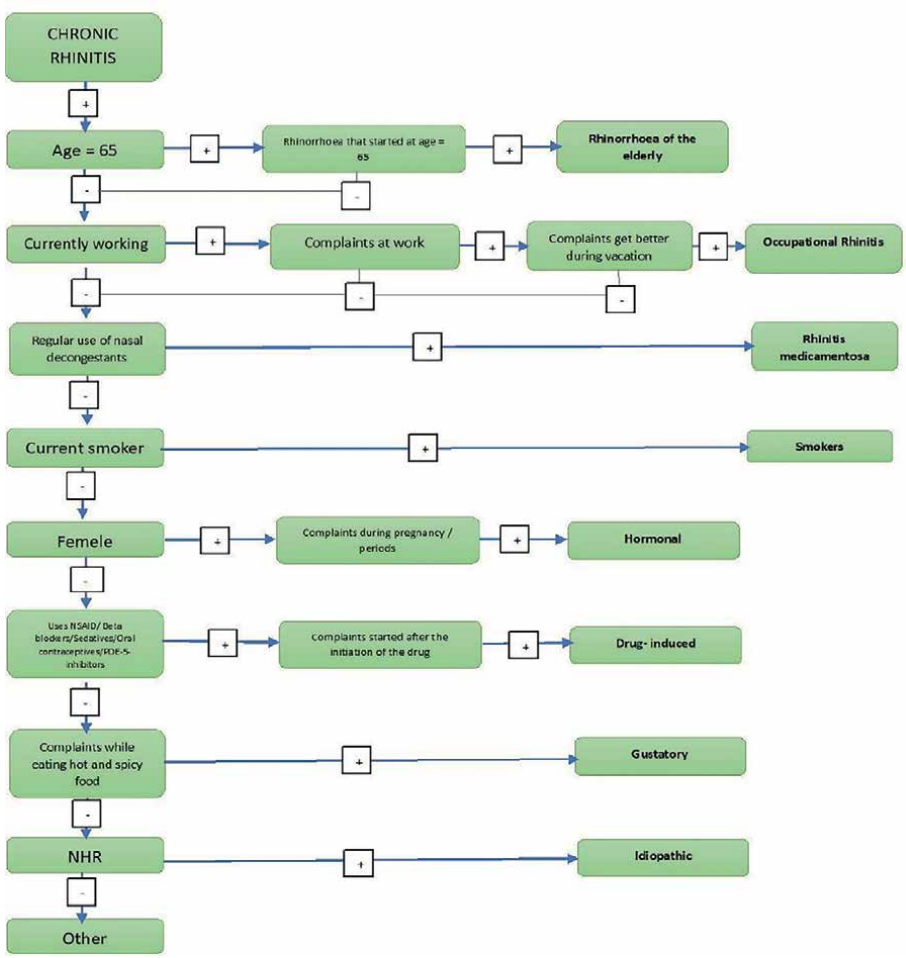

Figure 4.
Definitions of NAR phenotypes. NHR – Nasal hyper reactivity [20].

4. Endotypes of NAR

Varieties exist with diverse pathophysiological mechanisms, broadly categorized into a traditional inflammatory pathway, a neurogenic pathway, and other pathways that are predominantly unknown (**Figure 5**) [20].

The inflammatory pathway is present in a subset of NAR individuals. A Th2 cytokine inflammatory pattern, observed in patients with Allergic Rhinitis (AR) and those with work-related allergic rhinitis triggered by high molecular weight (HMW) allergens, characterizes this subgroup. Managing these patients typically poses no significant therapeutic challenges, as they generally respond favorably to nasal corticosteroid treatment, akin to individuals with Local Allergic Rhinitis (LAR) [20, 22].

Nevertheless, a portion of Non-Allergic Rhinitis (NAR) patients does not exhibit an infiltration of inflammatory cells in the nasal mucosa, suggesting involvement of a

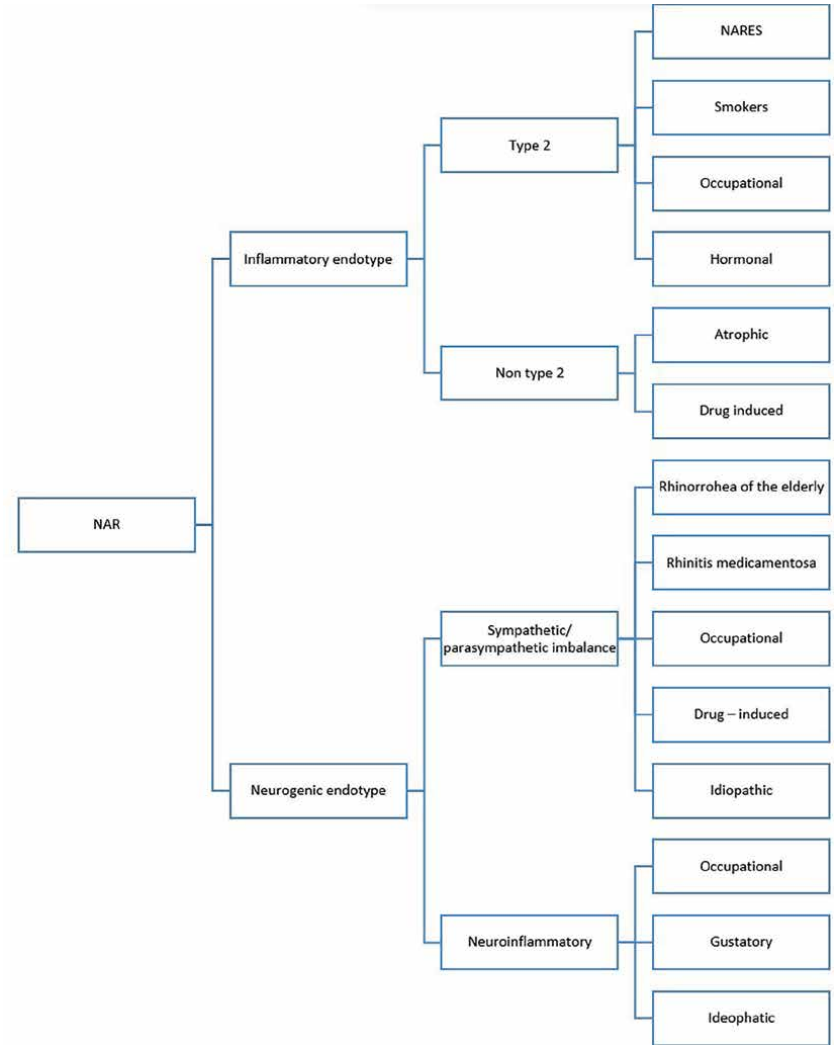

Figure 5.
Endotype and phenotype of NAR [20].

neurogenic mechanism. This includes conditions such as rhinitis of the elderly, gustatory rhinitis, certain types of occupational rhinitis, certain drug-induced rhinitis, and Idiopathic Rhinitis (IR). The intricate neural regulation of the upper airways involves various interacting nervous systems, where sensory, parasympathetic, and sympathetic nerves play roles in regulating processes in the nasal mucosa, including epithelial, vascular, and glandular functions [20–22].

Certain phenotypes appear to stem from a relatively straightforward regulatory disorder. For instance, rhinitis of the elderly primarily appears to involve a dysregulation in the balance between the parasympathetic and sympathetic neural systems. This can be addressed with the anticholinergic drug ipratropium bromide. Another example is rhinitis medicamentosa, where dysregulation of adrenergic receptors in the nasal mucosa results in a relative increase in parasympathetic drive, causing significant rhinorrhea and nasal obstruction [20].

Specialized epithelial chemosensors known as solitary chemosensory cells in the nasal cavity react to irritants via the canonical taste transduction cascade, activating peptidergic trigeminal nociceptive (pain) nerve fibers. The activation of these nasal cells can initiate comparable local inflammatory responses, including mast cell degranulation and plasma leakage. This response mirrors the effects of directly exciting trigeminal pain fibers using capsaicin. Importantly, this reaction is solely attributable to cholinergic neurotransmission and neural activity, without involving the release of local inflammatory mediators.

Idiopathic Rhinitis is believed to be a disorder affecting the nonadrenergic noncholinergic (NANC) or peptidergic neural system. Perivascular and intraepithelial nonadrenergic noncholinergic (NANC) sensory nerve fibers contain neuropeptides, including VIP, substance P (SP), and calcitonin gene-related peptide (CGRP). These neuropeptides are locally released from peptidergic neurons, mainly unmyelinated sensory C-fibers, in the nasal mucosa following activation by nonspecific stimuli. They can be responsible for the symptoms of IR. Stimulation may occur due to inflammatory mediators like histamine and bradykinin, as well as various inhaled irritants such as nicotine, chlorine, formaldehyde, and capsaicin, predominantly acting via the TRPA1 and TRPV1 receptors. Recent findings indicate an upregulation of the nociceptive TRPV1-SP signaling pathway in individuals with IR [18–20].

5. Treatment of NAR

Patients diagnosed with NAR are often offered different treatment modalities ranging from nasal topical medication to surgical [23].

The treatment modalities includes trigger avoidance, topical and systemic medications, and surgery [24–27].

There is little systematization in the protocols and there is little high-grade evidence regarding treatment, which causes difficult management with an impact on the quality of life and low patient satisfaction [23].

Intranasal corticosteroids are the first choice for NAR. Intranasal antihistamines have also been used in combination with the intranasal corticosteroids when monotherapy could not adequately control the symptoms of NAR [21].

5.1 Treatment modality

5.1.1 Intranasal corticosteroids

Act locally on the nasal mucosa, eliciting anti-inflammatory and immunosuppressant effects, modifying and reducing inflammation through suppression of the synthesis of pro-inflammatory cytokines and proinflammatory enzymes, inhibiting lymphocyte proliferation and chemotaxis [24, 25]. Avoid the systemic side effects of corticosteroids [25].

First-generation intranasal corticosteroids:

- Beclomethasone dipropionate
- Triamcinolone acetonide

- Flunisolide
- Budesonide

Second-generation intranasal corticosteroids:

- Fluticasone furoate
- Fluticasone propionate
- Mometasone furoate
- Betamethasone sodium phosphate
- Ciclesonide

Fluticasone propionate and beclomethasone dipropionate are the only topical nasal corticosteroids approved by the Food and Drug Administration for treatment of NAR [26, 27].

The adverse effects are [25]:

- Epistaxis (5–10%)
- Nasal irritation (5–10%, including dryness, burning and stinging)
- Headache
- Nasal septal perforation (<1%)
- Candida infection of the nose and pharynx
- Impaired wound healing after recent nasal surgery or trauma.

Intranasal corticosteroids are likely to work better for the inflammatory endotypes of non-allergic rhinitis [25].

The certainty of the evidence for most outcomes in this review was low or very low. Not all studies have shown these agents to be effective [25, 26].

It is unclear whether intranasal corticosteroids reduce patient-reported disease severity in non- allergic rhinitis patients compared with placebo when measured at up to 3 months. There is a lack of evidence comparing intranasal corticosteroids with other pharmacological treatments [23, 27].

It is unclear which is the best intranasal corticosteroid to use with respect to type, concentration, vehicle and how often to use it [25, 27].

5.1.2 Combination of intranasal corticosteroids antihistamines

Combination therapy of fluticasone propionate and azelastine hydrocholoride (AZE) – first-line therapies in seasonal allergic rhinitis – has been shown to be more effective compared against monotherapy with either class or placebo in seasonal allergic rhinitis [25, 27].

Combination therapy can be achieved either by using 2 separate nasal sprays or a combination product [27].

5.1.2.1 Topical antihistamine

Unclear mechanism(s) of action in since this is a non immunoglobulin E pathophysiology.

To diminish eosinophil activation and adhesion molecule expression and suppression of inflammatory cytokine generation [27].

Two topical antihistamine sprays have been studied in NAR, azelastine and olopatadine [23, 27].

Olopatadine and azelastine (0.1%) were compared for the treatment of NAR in a multicenter, randomized, both reduced congestion, rhinorrhea, postnasal drip, and sneezing; There were no statistically significant differences between their effects [23, 27].

In the review by Khoueir et al., all studies used Azelastine Hydrochloride (HCl) (137 mcg/aerosol) vs. olopatadine HCl 0.6% (665 mcg/spray). Both groups showed an importance decrease in TNSS after 14 days of treatment ($p < 0.001$) [23].

A statistically significant adverse effect reported was the sensation of bitter taste in patients who used azelastine. Another adverse effect reported in 3 studies was minor nasal bleeding [23].

5.1.2.2 Ipratropium bromide

The ipratropium bromide is the only topical anticholinergic approved in the treatment of NAR [24, 26]. In a study of 253 patients with perennial NAR the ipratropium nasal spray significantly reduced rhinorrhea versus placebo [16, 19]; dryness and epistaxis were uncommon [25].

5.1.2.3 Topical capsaicin

Reduced the density of the innervation of the nasal mucosa and the TRPV1-SP signaling pathway, without affecting the integrity and function of nasal epithelial cells or mast cells [24].

5.1.2.4 Oral decongestants

There is a lack of good evidence of effect, but theoretically it may be helpful for nasal stuffiness only [25].

5.1.2.5 Oral antihistamines

Limited data suggest that the newer nonsedating H1 antihistamines are not as effective in NAR, compared with allergic rhinitis.

5.1.2.6 Nasal saline lavage

The role is undefined. A 2007 Cochrane database review noted that nasal saline alone has not been demonstrated to be beneficial in CRS or more effective than an intranasal corticosteroid [26].

Intranasal saline sprays have been found effective in relieving postnasal drip, sneezing, and congestion [27].

5.2 Subgroups of NAR

- Senile rhinitis or rhinitis in elderly: ipratropium bromide is considered effective in reducing the severity and duration of the senile rhinitis (**Figure 6**) [24, 25, 27].
- Gustatory rhinitis: Ipratropium bromide is effective only for rhinorrhea.

  It is particular benefit in gustatory rhinitis [25, 27].
- Occupational rhinitis: The treatment is to avoid the trigger [27].
- Hormonal rhinitis: Nasal corticosteroids can be used to improve symptoms [27].
- Drug-induced rhinitis: Treatment is usually focused on cessation of the affecting agent, as well as support with intranasal corticosteroids [25].
- Smokers' rhinitis: the mainstay of treatment is triggering avoidance [25, 26].
- Idiopathic rhinitis: Intranasal capsaicin (8-methyl-N- vanillyl-6-nonenamide), the active component of chili peppers, appears to have a therapeutic effect in idiopathic rhinitis with long-lasting relief of symptoms from 6 to 9 month in 80% of well-selected IR patients ranging, based on several randomized controlled trials (**Figure 6**) [24, 25].

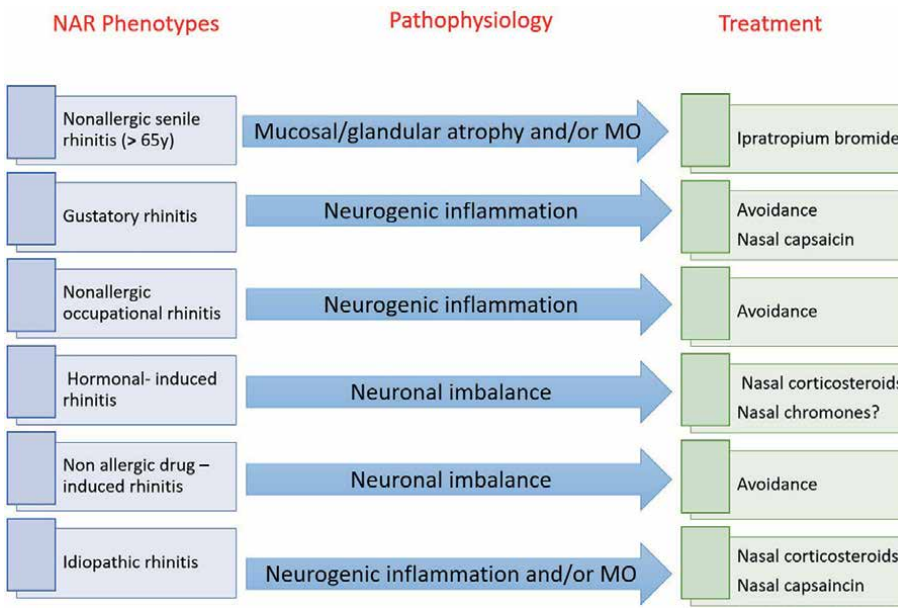

Figure 6.
Therapeutic strategy of nonallergic rhinitis.

5.3 Nonpharmacologic treatment

Surgical interventions are contemplated for patients with allergic rhinitis and non-allergic rhinitis (NAR) who do not respond adequately to medical therapy. A surgical procedure known for its favorable outcomes involves reducing the hypertrophy of the inferior turbinates. This intervention proves to be highly effective for individuals experiencing nasal obstruction that persists despite the clinical treatments described earlier [26].

The surgical techniques for inferior turbinate can be grouped into five groups [28]:

1. Turbinectomy is a procedure that removed turbinate: total, partial or by submucosal resection using cold steel instruments [SMR]

2. Microdebrider-assisted turbinoplasty [MAIT] which was defined by submucosal resection of the inferior turbinate with microdebrider.

3. Radiofrequency ablation [RFA] relying on the use of radio waves to create heat to cause tissue fibrosis and shrinkage.

4. Electrocautery techniques (monopolar/bipolar probe, diathermy electrode, straighttip electrode) which make use of an electrical current to destroy tissue.

5. Laser-assisted turbinoplasty (carbon dioxide, diode, potassium titanyl phosphate) that uses light energy to ablate tissue.

Irrespective of the method employed and the equipment utilized, the primary objectives remain to enhance air passage and minimize complications [29]. The selection of the most suitable technique depends on individual cases, taking into consideration factors such as the anatomy of the inferior turbinate (whether hypertrophy is more associated with bone or mucosa), the extent of hypertrophy (whether it is predominantly anterior or posterior), the availability of equipment, and the proficiency of the surgeon [29].

Another aspect to take into account is the preservation of nasal physiology. The fundamental physiological principles for this approach are [30]:

- The critical zone is the nasal valve region (inferior turbinate head);

- Small area increase = large increase in airflow (exponential correlation between area and airflow);

- Nasal sensation depends in part on the nasal mucosa of the inferior turbinate.

Hence, diminishing the volume of the inferior turbinate could result in a decrease in the quantity and/or activity of the responsive mucosa. This, in turn, could contribute to the amelioration of symptoms such as rhinorrhea, sneezing, and itching, all while maintaining the physiological functions of the mucosal epithelium [31]. Moreover, the alleviation of symptoms may be associated with the disruption of branches of the posterior nasal nerve, key in the mechanisms of sneezing and hypersecretion [31].

In a Systematic Review by Zhang et al. indicates that all techniques described above, significantly improved nasal obstruction post-operatively based on

patient-reported outcome measures. No statistical significance was observed when stratifying outcomes by AR and NAR groups, improving is similar for both populations [28], RFA and MAIT improved rhinorrhea significantly compared to baseline [28]. A systematic review by Acevedo et al. assessing outcomes on VAS nasal obstruction found similar results when comparing RFA and MAIT [32], in contrast, Mirza et al. concluded that MAIT resulted better [33].

In relation to alternative techniques, RFA demonstrated comparable enhancements in nasal obstruction compared to electrocautery and turbinectomy/Septoplasty with Mucosal Reduction (SMR) [28]. Improvements in all physiological indicators of nasal patency, encompassing active anterior rhinomanometry (nasal resistance), acoustic rhinometry (nasal cavity volume), and nasal airflow, were observed with RFA, MAIT and laser interventions [28, 32, 33].

RFA and MAIT initially improved, but after 1-year, VAS obstruction scores worsened when compared to 3–6 months postoperatively [28], these results suggest that peak effect following inferior turbinate reduction is achieved within the first year; however patients are still significantly improved relative to baseline; with improvement a favor MAIT at 5 years.

An alternative technique outlined is the endoscopic vidian neurectomy (EVN) and posterior nasal neurectomy (PNN), involving both surgical (SPNN) and cryoablative (CPNN) methods. The systematic review indicates that EVN, SPNN, and CPNN serve as effective and safe surgical options for patients with non-allergic rhinitis (NAR) unresponsive to medical management. Notably, SPNN and CPNN are linked to lower rates of complications, including dry eye and palatal/cheek numbness, in comparison to EVN [34]. Another systematic review reveals that both selective vidian neurectomy (SVN) and PNN result in significantly reduced symptoms in both short-term and long-term postoperative periods when compared to the preoperative phase [35].

Another noteworthy aspect to emphasize pertains to the choice between septoplasty alone or septoplasty combined with turbinoplasty, it is observed that patients undergoing the combined procedure experience more pronounced symptomatic improvement [36].

In summary, the surgical treatment of inferior turbinate hypertrophy should be personalized based on the patient's clinical condition, with a primary focus on enhancing air space and nasal function [29]. In this context, the importance of experience-based medicine appears to outweigh the reliance on evidence.

6. Conclusions

NAR is a diverse nasal condition characterized by a high global prevalence. Its etiology is related to neurogenic factors. NAR comprises seven subtypes with overlapping presentations. Treatment strategies should prioritize the avoidance of known triggers, and initial therapeutic approaches involve the use of intranasal corticosteroids, intranasal antihistamines and intranasal ipratropium. Combinations of these therapies may be considered if monotherapy fails to adequately manage symptoms. Surgical interventions are contemplated for patients resistant to medical therapy, with effective outcomes noted in procedures such as the reduction of inferior turbinate hypertrophy and selective neurectomy of the vidian branches.

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References

[1] Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, Craig TJ, et al. Rhinitis 2020: A practice parameter update. Journal of Allergy and Clinical Immunology. 2020;**146**(4):721-767

[2] Savouré M, Bousquet J, Leynaert B, Renuy A, Siroux V, Goldberg M, et al. Rhinitis phenotypes and multimorbidities in the general population: The CONSTANCES cohort. European Respiratory Journal. 2023;**61**(2):2200943

[3] Hellings PW, Klimek L, Cingi C, Agache I, Akdis C, Bachert C, et al. Non-allergic rhinitis: Position paper of the European academy of allergy and clinical immunology. Allergy. 2017;**72**(11):1657-1665

[4] Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Walter Canonica G, et al. Allergic rhinitis. Nature Reviews Disease Primers. 2020;**6**(1):95

[5] Rombaux P, Hellings PW. Rinitis crónica no alérgica. EMC - Otorrinolaringología. 2014;**43**(3):1-10

[6] Baroody FM. Nonallergic rhinitis: Mechanism of action. In: Immunology and Allergy Clinics of North America. Vol. 36. W.B. Saunders; 2016. pp. 279-287. DOI: 10.1016/j.iac.2015.12.005

[7] Bernstein JA, Singh U. Neural abnormalities in nonallergic rhinitis. Current Allergy and Asthma Reports. 2015;**15**(4):18

[8] Greiwe J, Bernstein JA. Nonallergic rhinitis: Diagnosis. In: Immunology and Allergy Clinics of North America. Vol. 36. W.B. Saunders; 2016. pp. 289-303. DOI: 10.1016/j.iac.2015.12.006

[9] Savouré M, Bousquet J, Jaakkola JJK, Jaakkola MS, Jacquemin B, Nadif R. Worldwide prevalence of rhinitis in adults: A review of definitions and temporal evolution. In: Clinical and Translational Allergy. Vol. 12. John Wiley and Sons Inc; 2022. DOI: 10.1002/clt2.12130

[10] Wheatley LM, Togias A. Allergic rhinitis. The New England Journal of Medicine. 2015;**372**(5):456-463. DOI: 10.1056/NEJMcp1412282

[11] Campo P, Salas M, Blanca-López N, Rondón C. Local allergic rhinitis. Immunology and Allergy Clinics of North America. 2016;**36**(2):321-332. DOI: 10.1016/j.iac.2015.12.008

[12] Rios-Deidan C, Reyes M, Acosta-Castillo T, Escalante-Fiallos E, Villacres-Silva D. Histological characteristics of chronic allergic rhinitis versus non-allergy: Is there a difference in the remodeling? Indian Journal of Otolaryngology and Head & Neck Surgery. 2023;**75**(4):3364-3372. DOI: 10.1007/s12070-023-03922-y

[13] Kuhar HN, Tajudeen BA, Mahdavinia M, Gattuso P, Ghai R, Batra PS. Infammatory infltrate and mucosal remodeling in chronic rhinosinusitis with and without polyps: Structured histopathologic analysis: Infammation and mucosal remodeling in CRS. International Forum of Allergy & Rhinology. 2017;**7**(7):679-689. DOI: 10.1002/alr.21943

[14] Serpero L, Petecchia L, Sabatini F, Giuliani M, Silvestri M, Diblasi P, et al. The efect of transforming growth factor (Tgf)-β1 and (Tgf)-β2 on nasal polyp fbroblast activities involved upper airway remodeling: Modulation by futicasone propionate. Immunology Letters. 2006;**105**(1):61-67. DOI: 10.1016/j.imlet.2006.01.003

[15] Morais-Almeida M, Pite H, Pereira AM, et al. Prevalence and classification of rhinitis in the elderly: A nationwide survey in Portugal. Allergy. 2013;**68**(1150-1157):10

[16] Orban N, Maughan E, Bleach N. Pregnancy-induced rhinitis. Rhinology. 2013;**51**:111-119

[17] Hox V, Steelant B, Fokkens W, Nemery B, Hellings PW. Occupational upper airway disease: How work affects the nose. Allergy. 2014;**69**(282-291):12

[18] Jovancevic L, Georgalas C, Savovic S, Janjevic D. Gustatory rhinitis. Rhinology. 2010;**48**(7-10):13

[19] Van Gerven L, Alpizar YA, Wouters MM, et al. Capsaicin treatment reduces nasal hyperreactivity and transient receptor potential cation channel subfamily V, receptor 1 (TRPV1) overexpression in patients with idiopathic rhinitis. The Journal of Allergy and Clinical Immunology. 2014;**133**:1332-1339

[20] Avdeeva KS, Fokkens WJ, Segboer CL, Reitsma S. The prevalence of non-allergic rhinitis phenotypes in the general population: A cross-sectional study. Allergy. 2022;**77**:2163-2174. DOI: 10.1111/all.15223

[21] Gomez E, Campo P, Rondon C, et al. Role of the basophil activation test in the diagnosis of local allergic rhinitis. The Journal of Allergy and Clinical Immunology. 2013;**132**:975-976

[22] Rondon C, Campo P, Galindo L, et al. Prevalence and clinical relevance of local allergic rhinitis. Allergy. 2012;**67**:1282-1288

[23] Khoueir N, Khalaf MG, Assily R, Rassi S, Hamad WA. Intranasal antihistamines in the treatment of idiopathic non-allergic rhinitis: A systematic review and meta-analysis. Rhinology. 2023;**61**(4):290-296. DOI: 10.4193/Rhin21.380

[24] Meng Y, Wang C, Zhang L. Diagnosis and treatment of non-allergic rhinitis: Focus on immunologic mechanisms. Expert Review of Clinical Immunology. 2020;**17**:51-62

[25] Segboer C, Gevorgyan A, Avdeeva K, Chusakul S, Kanjanaumporn J, Aeumjaturapat S, et al. Intranasal corticosteroids for non-allergic rhinitis. Cochrane Database of Systematic Reviews. 2019;**2019**(11):CD010592

[26] Daramola O, Kern R. An update regarding the treatment of nonallergic rhinitis. Current Opinion in Otolaryngology & Head and Neck Surgery. 2016;**24**:10-14

[27] Lieberman PL, Smith P. Nonallergic rhinitis treatment. Immunology and Allergy Clinics of North America. 2016;**36**:305-319

[28] Zhang K, Pipaliya R, Miglani A, Nguyen S, Schlosser R. Systematic review of surgical interventions for inferior turbinate hypertrophy. American Journal of Rhinology & Allergy. 2023;**37**(1):110-122. DOI: 10.1177/19458924221134555

[29] Roithmann R. Inferior turbinectomy: What is the best technique? Brazilian Journal of Otorhinolaryngology. 2018;**84**:133-134

[30] Sozansky J, Houser SM. The physiological mechanism for sensing nasal airflow: A literature review. International Forum of Allergy & Rhinology. 2014;**4**:834-838

[31] Maniaci A, Di Luca M, La Mantia I, et al. Surgical treatment for

the refractory allergic rhinitis: State of the art. Allergie. 2021;**1**(1):48-62. DOI: 10.3390/allergies1010005

[32] Acevedo JL, Camacho M, Brietzke SE. Radiofrequency ablation turbinoplasty versus microdebrider-assisted turbinoplasty: A systematic review and meta-analysis. Otolaryngology–Head and Neck Surgery. 2015;**153**(6):951-956. DOI: 10.1177/0194599815607211.)

[33] Mirza A, Alandejani T, Shawli H, Alsamel M, Albakrei M, Abdulazeem H. Outcomes of microdebrider-assisted versus radiofrequency-assisted inferior turbinate reduction surgery: A systematic review and meta-analysis of interventional randomised studies. Rhinology. 2020;**58**(6):530-537. DOI: 10.4193/Rhin19.350

[34] Senanayake P, Wong E, McBride K, Singh N. Efficacy of vidian neurectomy and posterior nasal neurectomy in the management of nonallergic rhinitis: A systematic review. American Journal of Rhinology & Allergy. 2022;**36**(6):849-871. DOI: 10.1177/19458924221105933

[35] Niu X, Chen Y, Zhou T, Xiao H. Endoscopic vidian and vidian-branch neurectomy for refractory allergic rhinitis: A systematic review. International Forum of Allergy & Rhinology. 2023;**14**(3):679-694. DOI: 10.1002/alr.23259

[36] Samarei R, Mabarian S. A randomised trial comparing the subjective outcomes following septoplasty with or without inferior turbinoplasty European annals of otorhinolaryngology. Head and Neck Diseases. 2020;**137**:277-283. DOI: 10.1016/j.anorl.2020.01.024

Chapter 3

Current Medical Management of Chronic Rhinosinusitis in Adults

Moath Abdulrahman Alfaleh

Abstract

Rhinosinusitis is a prevalent disorder that places a heavy financial strain on society in terms of medical expenses and lost productivity. It is characterized by discomfort and pressure in the face, sinus and nasal lining irritation, nasal obstruction, rhinorrhea, and loss of smell. It occurs with or without nasal polyps. This chapter aims to evaluate and review each medical intervention for chronic rhinosinusitis to provide analysis and medical management recommendations. It is known that medical management of chronic sinusitis is a complex subject with many options available with different advantages and disadvantages, and so during our literature review, we focused on reaching to recommendations based on the latest and most accurate available studies from double-blinded randomized controlled clinical trial and meta-analyses using Ovid Medline, CINAHL, Scopus, and Cochrane. We focused on studies that compared the different types of medical management options to a placebo and in some instances to other drugs regarding how the patient's quality of life and disease burden improved. Based on our literature review, medications that showed benefit and improved patient quality of life were intranasal/systemic steroids, saline irrigation, biologics Anti-IL-5 and Anti-IL4/IL13, antihistamine, and montelukast. Other mentioned medical interventions need larger and higher-quality studies.

Keywords: chronic rhinosinusitis, nasal polyps, topical steroid, biologics, quality of life

1. Introduction

In much of the world, rhinosinusitis is a prevalent disorder that places a heavy financial strain on society in terms of medical expenses and lost productivity. It is characterized by discomfort and pressure in the face, sinus and nasal lining irritation, nasal obstruction, rhinorrhea, and loss of smell. It can occur with or without nasal polyps. This chapter aims to evaluate and review each medical intervention for chronic rhinosinusitis to provide analysis and medical management recommendations. As it is known that medical management of chronic sinusitis is a complex subject with many options available with different advantages and disadvantages, and so, during our literature review we focused on reaching to our recommendations based on the latest and most accurate available studies from double-blinded randomized controlled clinical trial and meta-analyses through using Ovid Medline, CINAHL, Scopus, and Cochrane, in which we focused on studies that compared the different types of medical management options to a placebo and in some instances to other

drugs in regard to how the patient's quality of life disease burden improved. Based on our literature review, medications that showed benefit and improved patient quality of life were intranasal/systemic steroid, saline irrigation, biologics Anti-IL-5 and Anti-IL4/IL13, antihistamine, and montelukast. Other mentioned medical interventions need larger and higher-quality studies.

2. Short-term oral antibiotics for chronic rhinosinusitis (CRS)

In basic and secondary care settings, individuals with chronic rhinosinusitis (CRS) are frequently offered short-term regimens of antibiotics [1]. More proof is required to fully understand the function of antibiotics in the treatment of CRS. For this evaluation, 4 weeks or less is considered a short treatment period for antibiotics. Two published randomized clinical studies with a placebo control have examined the impact of short-term antibiotics in CRS [2, 3]. Thirty-two individuals with acute on chronic CRS exacerbations participated in a single-center, placebo-controlled trial [2]. In this study, an immediate worsening of sinonasal symptoms in the previous 4 weeks (nasal secretion, nasal obstruction/congestion, sense of smell, and/or face discomfort) in patients with underlying CRS was considered as an acute aggravation of the CRS condition. For 2 weeks, patients were randomly assigned to receive either a placebo or amoxicillin/clavulanate. Despite the fact that both groups' nasal secretions and nasal blockage significantly improved from baseline, on the Visual Analog Scale-Severity Scoring Assessment, there were no statistically significant changes between the groups [nasal secretion: mean difference (MD) -2 (−16.1, 12.1), $p = 0.44$; nasal obstruction: MD – 6.6(−10.6, 24), $p = 0.78$]. Nose endoscopic scores at day 14 did not differ between the groups (overall endoscopy score, $p = 0.88$; nasal polyps, $p = 0.58$; oedema, $p = 0.36$; nasal secretion, $p = 0.42$). After 3 months, the groups' improvements in quality of life (Sino-nasal Outcome Test, SNOT-22) were comparable [MD -2.7 (−20.36, 14), $p = 0.75$]. There was a notable observation of bacterial eradication in 29% of the amoxicillin/clavulanate group and 9% of the placebo group; nevertheless, there was no statistically significant difference seen between the groups ($p = 0.37$).

A double-blinded, placebo-controlled randomized controlled study (RCT) was carried out by Van Zele et al. [3] to evaluate the efficacy of doxycycline in the treatment of CRS with nasal polyps (CRSwNP) in 28 patients. After starting doxycycline therapy, there was a significant reduction in postnasal drip symptom ratings at week 2 ($p = 0.044$) and a tendency toward a decrease in rhinorrhea at week 8 ($p = 0.058$) (no adjustments were made for multiple testing). During the trial period, doxycycline did not significantly affect rhinorrhea, postnasal drip, or nasal congestion. It also did not significantly affect loss of smell. For 3 months, the doxycycline group showed a little but significant decrease in nasal polyp size (0,5 on an 8-point scale) in comparison to the placebo group ($p = 0.015$).

Ninety patients were included in the analysis of a single-blind, randomized, controlled trial that took place between 2018 and 2019 [4]. For 4 weeks, the patients in the clarithromycin group were given 500 mg pills twice a day. For 4 weeks, the second group took 500 mg pills of azithromycin every day. The group treated with azithromycin saw a considerably greater rate of complete symptom remission (71.1 vs. 24.4%, $P < 0.001$) than that treated with clarithromycin. There was no significant difference ($P = 0.120$) in the baseline Lund Mackay ratings between the groups. Nevertheless, both groups saw a substantial decrease in Lund Mackay scores following

the intervention; however, the azithromycin group experienced a significantly larger improvement ($P < 0.001$).

In a randomized controlled trial, the authors measured the levels of two frequently given antibiotics, roxithromycin and doxycycline, in the sinonasal mucus, serum, and sinonasal tissues of patients with CRS after a one-week treatment [5]. Two groups were randomly assigned to twenty patients after they undergone functional endoscopic sinus surgery (FESS) for chronic rhinosis (CRS): (1) 100 mg of doxycycline every day for 7 days and 2) 300 mg of roxithromycin per day for 7 days. Liquid chromatography-tandem mass spectrometry was used to detect drug levels in steady state in blood, sinonasal tissues, and mucus. The amounts of doxycycline in the mucus were found to be substantially lower than those in the tissue (mean mucus/tissue ratio ¼ 0.18, $p < 0.0001$) and serum (mean mucus/serum ratio ¼ 0.16, $p < 0.001$). The concentration of roxithromycin in the mucus was likewise considerably lower than that in the tissue (mean mucus/tissue ratio ¼ 0.60, $p < 0.001$) and serum (mean mucus/serum ratio ¼ 0.37, p¼0.002).

Because of the complexity of bacterial biofilm antimicrobial tolerance, the effectiveness of doxycycline and roxithromycin in sinonasal mucus *in vivo* cannot be predicted solely from reported minimum inhibitory concentrations. However, these results suggest that low mucosal penetration of antibiotics may be one of the factors contributing to the limited efficacy of these agents in the treatment of CRS.

2.1 Conclusion

It is unclear whether or not the administration of a brief course of antibiotics has an effect on patient outcomes in people with acute exacerbations of CRS when compared with placebo because of the extremely low quality of the available data.

Furthermore, it is unclear whether or not the administration of a brief course of antibiotics has an effect on patient outcomes in adults with CRS when compared to placebo because of the extremely low quality of the data. Larger, higher-quality trials are required, particularly to assess the efficacy of brief courses of antibiotics in cases of acute exacerbations of CRS.

3. Long-term oral antibiotics for chronic rhinosinusitis (CRS)

Long-term antibiotic therapy was defined for the purposes of this systematic review as any course of treatment lasting more than 4 weeks. A few placebo-controlled trials have examined the effects of treating acute rhinosinusitis with antibiotics, despite the fact that this approach is often used. Two such studies assess the results of prolonged administration of macrolide antibiotics. The effects of long-term macrolide treatment on signs, symptoms, and patient-reported quality of life outcomes have been examined in two completed placebo-controlled trials [6, 7]. Both trials assessed a 12-week course of therapy; however, Wallwork et al. assessed roxithromycin at 150 mg daily, while Videler et al. assessed azithromycin (AZM) at 500 mg per week. In terms of nasal endoscopy, saccharin transit time, and SNOT-20 scores, Wallwork and colleagues demonstrated a notable improvement. In Wallwork and colleagues, groups were separated into low and high IgE levels (less than 200 μg/L against more than 200 μg/L); the low IgE group showed a substantial improvement in endoscopy, saccharin transit time, and nasal lavage of IL-8. Nevertheless, Videler et al.'s results did not improve, and since IgE was not assessed, a subgroup analysis was

not feasible. By the time the study came to a close, Videler and colleagues had seen a nonsignificant improvement in 35% of the placebo group and 51% of patients on Azithromycin. Remarkably, 50% of the Azithromycin group claimed "improvement/cure" when the groups were reassessed by phone 12 weeks after the antibiotics ended, compared to 9% in the placebo group. This was statistically significant ($p = 0.017$). The response rate for Wallwork and colleagues was 67% in the roxithromycin group and 22% in the placebo group. Despite having comparable study numbers (60 vs. 64), the inclusion criteria of these research differed. Videler included individuals with and without nasal polyps, but Wallwork et al. exclusively included patients without nasal polyps. In the Wallwork et al. paper, patients were sub-analyzed according to their IgE levels, as previously mentioned. The majority of nonresponders were in the high IgE group. Another important difference was the dosing regimen, which in the study done by Videler et al. it was a once-weekly dosing compared to Wallwork et al.'s low-dose daily dosage.

A double-blind, randomized, placebo-controlled trial was conducted by de Oliveira et al. [8]. For 12 weeks, patients were given 500 mg of azithromycin orally three times a week. Sino-Nasal Outcome Test (SNOT-22), and nasal polyp biopsies were used to assess improvement. Data gathered 3 months after therapy and before treatment were compared. Evaluation of quality of life took place at the 1-year follow-up. For a duration of 12 weeks, treatment with 500 mg azithromycin three times a week resulted in a reduction in the amount of eosinophils in polyp biopsies, polyp staging, and a substantial clinical improvement based on subjective improvement as assessed by a quality-of-life questionnaire (the SNOT-22). On the other hand, the placebo group did not exhibit any noteworthy changes before or during the intervention. Furthermore, after the 1-year follow-up after therapy, the azithromycin group's improved quality of life persisted. Even though the current literature suggests that azithromycin therapy should be administered only to CRS patients with low polyposis and IgE, the outcomes that were seen in this particular patient group were unexpected.

Metanalysis conducted by Do Hyun Kim et al. to assess the efficacy of doxycycline (DOX) versus traditional therapy for individuals suffering from nasal polyps and refractory chronic rhinosinusitis (CRSwNP) [9, 10]. Up until September 2023, six databases were checked. Studies comparing improvements in refractory chronic sinusitis-related symptoms in groups treated with DOX and control groups were obtained. Lund-Kennedy (LK) score [−0.3670 (range - 0.6173; −0.1166); I2 = 92.8%], nasal polyposis score [−0.9484 (−1.2287; −0.6680); I2 = 92.5%], patient-reported sinonasal outcome test (SNOT) score [−0.3141 (−0.4622; −0.1660); I2 = 91.2%], and nasal obstruction score [−0.1813 (−0.3382; −0.0243); I2 = 86.2%] were all significantly decreased by DOX. The DOX group had considerably less nasal polyposis at the beginning of therapy, the completion of treatment, and 4 and 8 weeks later, according to subgroup analyses based on the measurement timepoints. Additionally, improvements were shown by the LK scores both during and after therapy. Over time, the therapy group's SNOT score tended to drop. The symptoms of nasal blockage improved both during and 4 weeks after therapy. In conclusion, by decreasing inflammation and recurring polyposis, DOX improves the postoperative endoscopic results for patients with CRSwNP who are resistant.

3.1 Risks of macrolide antibiotics

Patients having a history of congenital or documented acquired QT prolongation; ventricular cardiac arrhythmia, including torsades de pointe; or hypokalemia (risk of

prolonging QT-time) should not be administered macrolides. Because of the increased risk of myopathy, including rhabdomyolysis, macrolides should not be taken concurrently with HMG-CoA reductase inhibitors (statins) that are substantially metabolized by CYP3A4 (lovastatin or simvastatin). Colchicine users should not take macrolides antibiotic, just like they should not take other potent CYP3A4 inhibitors. Patients with severe liver failure combined with renal impairment should not use macrolides.

3.2 Conclusion

In the studies shown previously, there was some promising positive effect for macrolides and doxycycline in improving the quality of life for patients with chronic rhinosinusitis without polyps and with polyps, respectively, but due to the low quality of evidence and the danger of these antibiotics adverse, we prefer to steer away from use of long-term macrolides. In the future, we are in need for a larger high quality trials.

4. Topical antibiotics for chronic rhinosinusitis (CRS)

The possible existence of bacterial biofilm in sinuses provides justification for using local antibiotics to treat patients with resistant, hard-to-treat rhinosinusitis. The sinus mucosa in these individuals stays inflamed even after washing with saline, anti-inflammatory corticosteroid therapy, and/or systemic antibiotics. These patients usually have undergone sinus surgery and so have wide open sinuses that are easily accessible for local treatment.

Pseudomonas aeruginosa or *Staphylococcus aureus* are frequently grown from these sinuses (producing biofilms) [11].

Nebulization of a solution of 150 mg tobramycin every day for 7 days resulted in the elimination of bacteria based on posttreatment culture, which was considerably better than placebo; all of this according to research conducted by Bonfils et al. in which they recruited 59 patients with CRSwNP who still had symptoms following sinus surgery [12] Day 0 and Day 10 of the bacteriological examination were conducted in accordance with Day et al.'s [13] investigation of the existence of pathogenic strains in culture and their sensitivity to antibiotics, together with a cytological analysis of the quantity and presence of leukocytes (at Day 0 and Day 10). The bacterial isolates from day 10 posttreatment and pretreatment were compared.

Leukocyte counts and antibiotic sensitivity tests were also conducted. But there was no discernible difference in the symptoms [12].

Victoria et al. conducted a prospective randomized controlled trial that is single-blinded (doctors only). Acute exacerbations of chronic rhinosinusitis and gram-positive bacteria on culture were seen in the postsurgical subjects. Subjects were divided into 3 groups (saline group, povidoen-iodine group, and mupirocin group), and for 30 days, they had twice-daily sinus irrigations [14]. The Mupirocin (14/20, 70%) group of the 62 participants under analysis had a greater posttreatment culture-negative povidone-iodine rate than the povidone-idodine (9/21, 43%) and Saline (9/19, 47%) groups, although this difference was not statistically significant ($p = 0.28$). The Lund-Kennedy endoscopic score (povidone-iodine −3.5 [−7, −0.5] vs. mupirocin −2 [−4, 2] vs. saline −3 [−5, 0]; $p = 0.35$) and the Sinonasal Outcome Test-20 score (povidone-iodine −0.3 [−0.6, 0.05] vs. mupirocin −0.3 [−0.7, 0.05] vs. saline −0.4 [−0.8, 0.05]; $p = 0.74$) did not differ significantly. When compared to saline and povidone-iodine, mupirocin sinus irrigations produced a greater

posttreatment culture "control" rate in patients who had previously had sinus surgery and had acute exacerbations of CRS and gram-positive bacteria on culture.

4.1 Conclusion

Patients with CRS do not appear to benefit more from topical antibiotic treatment than a placebo in terms of symptom improvement.

It can, however, result in a clinically insignificant improvement in symptoms. We do not know for sure if topical antibiotic treatment affects patient outcomes in people with CRS since the evidence is of extremely low quality.

5. Intranasal corticosteroid for chronic rhinosinusitis (CRS)

In a double-blinded placebo-controlled trial conducted by Leopold et al. [15], 323 patients with CRSwNP 27% of whom previously had sinus surgery were randomized to receive either an exhalation delivery system (EDS)–placebo or twice-daily EDS-FLU (93, 186, or 372 mg) for a total of 24 weeks (16 double-blind plus 8 open-label when all got 372 mg). The coprimary end goals were the total bilateral polyp grade at 16 weeks and the change in nasal congestion/obstruction at 4 weeks. Functioning, polyp removal, and symptoms were secondary end goals. On both coprimary end points, EDS-FLU outperformed EDS-placebo ($P < .001$ across all dosages). The average polyp grade steadily increased through week 24 ($P < .009$, all comparisons), and at that point, 25% of patients had at least one side of the polyp removed, compared to 8.7% with the EDS-placebo ($P < .014$, all comparisons). Additionally, patients' SNOT scores increased considerably ($P < .05$ for all dosages) from those in patients receiving EDS-placebo (221.1 to 221.4 vs. 211.7 at week 16). All four of the defining illness symptoms were considerably improved by EDS-FLU (all dosages) at the end of the double-blind phase. 69% of the patients who received EDS-FLU experienced "much" or "very much" improvement. The percentage of patients who could have surgery dropped by 62–67%. The safety profile matched the information from earlier trials. In this study, they concluded that in individuals with chronic rhinosinusitis with nasal polyps, EDS-FLU results in a clinically and statistically significant improvement in all four diagnostically defined illness symptoms, polyp grade, and quality of life.

Japanese patients with chronic rhinosinusitis with nasal polyps have among them a common variant known as eosinophilic chronic rhinosinusitis (ECRS). Refractory eosinophilic airway inflammation, ECRS is strongly linked to asthma and necessitates comprehensive management as part of the unified airway concept [16, 17]. Kobayashi et al. in a double-blinded placebo-controlled trial reported a series of ECRS patients with asthma treated with fine-particle inhaled corticosteroid (ICS) exhalation through the nose (ETN). A double-blind randomization process was used to assign 23 patients with severe ECRS who were not responding to intranasal corticosteroid therapy to either the HFA-134a-beclomethasone dipropionate (HFA-BDP) metered-dose inhaler (MDI) ETN ($n = 11$) or the placebo MDI ETN ($n = 12$) over a 4-week period. Assessments were made of changes from the baseline in the nasal polyp score, smell test, computed tomographic (CT) score, and quality of life (QOL) score. Measurements of fractionated exhaled nitric oxide (FENO), a sign of eosinophilic airway inflammation, were made. Evaluation of the corticosteroid response was done both before and after therapy. Furthermore, a particle deposition model was used to illustrate the deposition of small particles. Purified eosinophils were co-incubated

with BEAS-2B human bronchial epithelial cells to assess corticosteroid sensitivity and investigate the function of eosinophils on airway inflammation. Treatment with HFA-BDP MDI ETN increased corticosteroid sensitivity, and all evaluated clinical endpoints without impairing pulmonary function. HFA-BDP MDI ETN therapy decreased FENO and blood eosinophil count. According to the visualization investigation, fine particle deposition in the middle meatus, including the sinus ostia, was caused by ETN at expiratory flow rates of 10–30 L/min. Corticosteroid resistance was produced when BEAS-2B cells and eosinophils were co-incubated.

A metanalysis conducted by Bognanni et al. looked for randomized controlled trials comparing INCS administered in any way to placebo or other INCS administration types in studies stored in Medline, Embase, and Central between September 1, 2021 and the creation of the database [18]. Sixty-one randomized controlled trials with 7176 individuals and 8 treatments were examined. In comparison to a placebo, the quality of life linked to sinusitis may be enhanced by INCS rinse (mean difference [MD] −6.83, 95% confidence interval [CI] −11.94 to −1.71) and exhalation delivery system (EDS) (MD −7.86, 95% CI −14.64 to −1.08). In comparison to placebo, nasal obstruction symptoms are probably lessened after receiving INCS by stent/dressing (MD −0.31, 95% CI −0.54 to −0.08), spray (MD −0.51, 95% CI −0.61 to −0.41), and EDS (MD −0.35, 95% CI −0.51 to −0.18). The unfavorable effects of the various therapies did not significantly differ from one another (moderate certainty for INCS spray, extremely low to medium certainty for others). For CRSwNP, there are several effective INCS delivery methods that can enhance patient important results. The broadest possible range of evaluated outcomes seems to benefit from INCS using stent, spray, and EDS.

5.1 Conclusion

There is strong evidence that treating CRS patients with nasal corticosteroids over the long term is both safe and effective. They affect nasal symptoms and enhance one's quality of life.

6. Systemic corticosteroid for chronic rhinosinusitis (CRS)

For chronic rhinosinusitis with nasal polyps, short doses of systemic corticosteroids (7–21 days) are commonly administered in conjunction with local corticosteroids. In addition to lowering inflammation, systemic corticosteroids may also shrink nasal polyps. It is interesting to note that, in particular, olfactory mucosal inflammation is frequently decreased, leading to a quick improvement in olfaction (days) without any discernible change in polyp volume.

Shen et al. conducted a double-blind, placebo-controlled, randomized clinical study in which patient who underwent ESS with bilateral CRSwNP were randomly assigned to take oral prednisolone (30 mg/day) or a placebo for 2 weeks following operation. As the subjective outcomes, the visual analog scale (VAS) and Sino-Nasal Outcome Test 22 (SNOT-22) scores were selected and assessed at preoperative baseline, as well as 1, 3, and 6 months after surgery. The objective result was measured using Lund-Kennedy Endoscopic Scores (LKESs), which were assessed preoperatively, at 2 weeks, 2, 3, and 6 months after surgery [19, 20]. Out of the 100 patients that were included, only 82 with bilateral CRSwNP finished the 6-month follow-up. At every follow-up point, there was no discernible variation in the subjective results. Six months after surgery, the corticosteroid group reported an improvement in

LKESs (p = 0.05) among the objective results. Only patients with NECRSwNP (<10 eosinophils/HPF) showed a significant improvement in LKESs at 3 months post-operatively (p = 0.03), after classification by tissue eosinophils. In conclusion, oral corticosteroids administered after surgery did not result in further improvements in VAS or SNOT-22 scores; however, at 6 months after surgery, there was a tendency of improving LKES. At the three-month follow-up, this impact was significant only among NECRSwNP patients after stratification by tissue eosinophils.

In a meta-analysis conducted by Zhang et al. [21], 7 RCTs with a total of 414 participants were included in the meta-analysis out of the 337 pertinent papers that were found. In contrast to nonsteroid treatments or placebos, systemic corticosteroids significantly increased peak nasal inspiratory flow (PNIF) (SMD 42.39; 95% CI, 28.95 to 55.84; P < .00001), decreased the size of nasal polyps (SMD ~4.76; 95% CI, ~6.99 to ~2.52; P < .0001), and improved nasal obstruction scores (standardized mean difference; SMD ~2.81; 95% confidence interval [CI], ~4.68 to ~0.95; P¼.003). The low-dose subgroup (less than 50 mg/day prednisone) and high-dose (greater than or equal to 50 mg/day prednisone) had comparable advantages. But individuals receiving large dosages of prednisone reported experiencing sleeplessness and gastrointestinal problems more frequently. No discernible variation was seen in the frequency of any adverse events among the groupings. In conclusion for individuals with CRSwNP, systemic corticosteroids significantly reduce the amount of nasal polyps and significantly improve PNIF and nasal symptoms. In CRSwNP, prednisone dosages under 50 mg/day were advised when the benefits of oral corticosteroids were weighed against possible side effects.

6.1 Conclusion

Both the nasal polyp score and the overall symptom score are significantly reduced after a brief course of systemic corticosteroid therapy, either with or without local corticosteroid treatment. Up to 3 months after the commencement of treatment, the effect on the nasal polyp score is still significant, but by then, the effect on the symptom score has vanished.

7. Saline

In order to effectively manage CRS, nasal saline irrigation is thought to be crucial. By disrupting and eliminating antigens, biofilms, and inflammatory mediators as well as improving mucus clearance and ciliary beat activity, saline nasal irrigation may improve the function of the nasal mucosa through a number of physiological effects. It may also increase the hydration of the sol layer. Saline may also act as a carrier to provide the necessary volume to deliver medication into the sinuses. That being said, there is not much agreement on the optimal irrigation technique, the tonicity (concentration) of the saline solution, or the appropriateness of the devices, head position, volume, pressure, and frequency of washing.

In a non-blinded randomized controlled trial Glotakis et al. evaluated 174 patients with CRSwNP (whom 154 were posteopratively), they were divided to 3 groups [22]. The first group used 250 ml of 1175% Emser Salt solution (EmsSalt) (n = 59) twice daily for 1 year, the second group used 250 ml of isosmotic mineral salt mixture (IsoMix) (n = 58) twice daily for 1 year, and in the third group they were on no irrigation (n = 57) for one year. Outcomes were measured at 3, 6, 9, and 12 months

including nasal symptoms, RQLQ, missed work days and postoperative condition of the mucosa. Results were significantly improved outcomes when comparing irrigation to no irrigation in terms of nasal symptoms and RQLQ. There is no discernible difference between mucosa and missed work days. There are no appreciable variations between the isosmotic mineral salt mixture and Emser Salt.

In a meta-analysis conducted by Lei Liu et al. [23, 24], in an effort to offer a guide for clinical nasal irrigation for the treatment of chronic rhinosinusitis, the authors compared the efficaciousness of hypertonic and isotonic saline in the management of rhinosinusitis. There were seven investigations in all. In four groupings, the effects of hypertonic saline on nasal symptoms were stronger. The patients with nasal secretion (SMD = 1.52; 95% CI: 1.04, 2.00; $p < 0.01$), congestion (SMD = 1.52; 95% CI: 1.04, 2.00; $p < 0.01$), headache (SMD = 0.82; 95% CI: 0.38, 1.26; $p < 0.01$), and overall symptomatic relief (SMD = 1.63; 95% CI: 0.83, 2.44; $p < 0.01$) were the first group of patients classified as (1). On the other hand, there was no difference in the improvement of radiologic scores (SMD = 2.44; 95% CI: −3.14, 8.02; $p < 0.01$) or scent (SMD = 0.47; 95% CI: −0.65, 1.59; $p = 0.41$). Furthermore, compared to the isotonic saline group, the hypertonic saline group had a higher improvement in mucociliary clearance time scores (SMD = 1.19; 95% CI: 0.78, 1.60; $p < 0.01$). Greater mild negative effects were observed with hypertonic saline. In conclusion, when treating chronic rhinosinusitis, hypertonic saline nasal irrigation is far more successful than isotonic saline and has less side effects. It also improves ciliary movement and nasal symptoms, but there is no discernible change in imaging results or improvement in smell.

7.1 Conclusion

Evidence provided showed that normal saline irrigation is effective in CRS in improving symptoms and quality of life compared to placebo but hypertonic saline is better than normal in regard to improving patients symptoms.

8. Anti-IgE

A substantial local IgE production that may contribute to chronic inflammation by persistently activating mast cells is a pathophysiological feature of CRSwNP [25]. Omalizumab is a recombinant humanized monoclonal antibody that has been studied for its potential use in the treatment of CRS in a randomized clinical study by Gevaert et al. [25]. Omalizumab works by selectively attaching to free circulating IgE, which inhibits the activation of effector cells such as mast cells, basophils, and dendritic cells and reduces the expression of IgE receptors on them. A subcutaneous dose of omalizumab (four to eight doses) or a placebo was administered to 24 individuals with CRSwNP with concomitant asthma for a period of more than 2 years. There were 20–700 kU/mL of total serum IgE. There was no discernible decrease in RSOM-31 or SF-36 following the subcutaneous delivery of four to eight doses of omalizumab. On the other hand, the omalizumab group showed a substantial improvement in the physical domain of the SF-36 and the Asthma Quality of Life Questionnaire (AQLQ), while the placebo group showed no meaningful changes. Comparing anti-IgE to baseline, there was a substantial reduction in the symptoms ratings for nasal congestion ($p = 0.003$), anterior rhinorrhoea ($p = 0.003$), loss of smell ($p = 0.004$), wheeze ($p = 0.02$), and dyspnea ($p = 0.02$). Anti-IgE medication did not help the patient's cough or spirometric findings. Over the course of the trial, a linear mixed model

showed that the omalizumab group had a lower total nasal polyp score (NPS) than the placebo group ($p = 0.2$). The omalizumab group showed significantly higher Lund-MacKay scores on radiologic imaging ($p = 0.04$) when compared to the placebo group. Anti-IgE therapy was used, and the improvements in radiography and clinical outcomes were observed regardless of serum IgE levels. Patients who were allergic (−2.57; $p = 0.03$) and nonallergic (−2.75; $p = 0.06$) showed a decrease in total NPS after 16 weeks. Compared to nonallergic patients (20.66, $p = 0.75$), allergic patients showed an improvement in their Lund-Mackay CT scan scores (22.61, $p = 0.04$). On the other hand, the nonallergic group's total AQLQ score showed improvement (259.4, $p = 0.03$), but the allergic group's score (212.3, $p = 0.12$) did not. Among the patients covered, 22 out of 23 (95.7%) had at least one adverse event. In the omalizumab group, the most often reported adverse event was a common cold, which happened more frequently in the treatment group than in the control group ($p = 0.02$). In the omalizumab group, one patient died of lymphoblastic lymphoma a year after the research began. It is noteworthy that the analysis did not include four out of eight patients (or 50%) in the control group.

A randomized, double-blind, placebo-controlled study of anti-IgE for CRS was carried out by Pinto et al. [26] in 14 patients (12 of 14 with CRSwNP) who were not responding to conventional therapy. It was necessary for participants to have serum total IgE levels between 30 and 700 IU/ml. For 6 months, all patients received subcutaneous injections of either placebo or omalizumab at a rate of 0.016 mg/kg per IU every 2 to 4 weeks. The SNOT- 20 scores did not significantly differ between the treatments (median omalizumab −5.5, placebo −2.3, $p < 0.60$). Over the course of the study, the omalizumab group showed a clinically significant improvement (defined as at least 0.8) in their median change in SNOT-20 scores, while the placebo group showed no clinically significant change (−1.05 vs. -0.20, $p < 0.78$). All domains showed no significant differences between treatments, with the exception of vitality ($p < 0.05$; omalizumab 9.4, placebo 12.5). Comparing the omalizumab and placebo groups, there were no statistically significant differences in the sinus opacity in the CT scan, the median change in the percentage of eosinophils in nasal lavage, the median PNIF, the total nasal symptom scores, or the results of nasal endoscopy. Omalizumab-using patients utilized less antibiotics (0 vs. 1, $p < 0.32$) and fewer doses of steroids (median 0 vs. 1, $p < 0.043$) during the trial than placebo-using patients. During the trial, no negative outcomes or side effects happened [26].

In a meta-analysis study conducted by Qingwu Wu et al. [27, 28], randomized controlled studies comparing placebo and omalizumab in adult patients with CRSwNP, administered for a minimum of 16 weeks. Four randomized controlled trials with a total of 303 participants were found. Nasal Polyps Score (MD = −1.20; 95% CI −1.48 to −0.92), Nasal Congestion Score (MD = −0.67; 95% CI −0.86 to −0.48), Sino-Nasal Outcome Test-22 (MD = −15.62; 95% CI −19.79 to −11.45), Total Nasal Symptom Score (MD = −1.84; 95% CI −2.43 to −1.25), and decreased surgical requirement (risk ratio (RR) = 5.61; 95% CI 1.99 to 15.81) were among the significantly different outcomes when omalizumab was compared to placebo. The probability of adverse events (RR = 0.83; 95% CI 0.60 to 1.15), significant adverse events (RR = 1.40; 95% CI 0.29 to 6.80), and rescue systemic corticosteroid (RR = 0.52; 95% CI 0.17 to 1.61) did not vary either. In conclusion, omalizumab was shown to be safe and well-tolerated, and it improved endoscopic, clinical, and patient-reported outcomes in people with moderate to severe CRSwNP. Regarding adverse effects, current research on anti-immunoglobulin-E (IgE) therapy indicates a very low risk of anaphylaxis [27];

however, there is some evidence linking the drug to venous and arterial thromboembolic events that result in cardiovascular and cerebrovascular accidents [29].

8.1 Conclusion

There is a need for and an ongoing demand for larger population studies because the current studies' sample populations were too small. The literature recommends that Anti-IgE usage in CRSwNP cannot currently be recommended due to a lack of accessible data.

9. Anti-IL5

In the past, systemic and topical corticosteroids, long-term antibiotics, and surgery have all been used to treat CRS. Even with the application of optimal practices, some patients continue to have recalcitrant disease. Final development into an eosinophil requires interleukin 5 (IL-5), which also increases the mature cell's survival time within the tissue [30]. The care of patients with nonallergic asthma and CRSwNP may involve IL-5 as a target due to its observed elevation in nasal polyp tissue [31].

Bachert et al. conducted a double-blind, randomized, placebo-controlled experiment; patients with recurrent nasal polyposis who needed surgery were enrolled if they were between the ages of 18 and 70. In addition to daily topical corticosteroid treatment, patients received 750 mg intravenous mepolizumab or placebo every 4 weeks for a total of six treatments [26]. The number of patients who were no longer in need of surgery at Week 25 was the main outcome, which was determined by combining the endoscopic nasal polyp score with the visual analogue scale (VAS) score for nasal polyposis severity. Patient-reported outcomes (PRO), safety, improvement in individual VAS symptoms (rhinorrhea, mucus in the throat, nasal blockage, and sense of smell), and change in the nasal polyposis severity VAS score were among the secondary objectives. Mepolizumab (n = 54) or a placebo (n = 51) was administered to 105 patients. When compared to the placebo group, a considerably higher percentage of patients in the mepolizumab group (16[30%] vs. 5[10%], respectively, P = 0.006) no longer needed surgery. The nasal polyposis severity VAS score, endoscopic nasal polyp score, individual VAS symptom ratings, and SNOT-22 PRO score significantly improved in the mepolizumab group as compared to the placebo group. In terms of safety, mepolizumab was similar to a placebo. In conclusion, mepolizumab medication resulted in a higher improvement in symptoms and a reduction in the need for surgery compared to placebo in individuals with recurrent nasal polyposis on topical corticosteroids.

Gevaert et al. conducted a double-blind study conducted on thirty patients who had severe nasal polyposis (grade 3 or 4, or recurring after surgery) and were not responding to corticosteroid therapy. The patients were randomly assigned to receive either a placebo (n510) or two single intravenous injections of 750 mg of mepolizumab (n520) spaced 28 days apart [32]. Monthly assessments of the change from baseline in NPscore were conducted until week 8, 1 month following the last dose. At week eight, computed tomographic scans were also carried out. At week 8 relative to baseline, 12 out of 20 patients on mepolizumab had a substantially better NP score and computed tomographic scan score than 1 out of 10 patients on placebo. In conclusion, in 12 out of 20 individuals, mepolizumab produced a statistically significant decrease in NP size for at least 1 month following dosage. A possible new treatment strategy for those with severe eosinophilic nasal polyposis is IL-5 inhibition.

9.1 Conclusion

Because the evidence shown a considerable reduction in patients' need for surgery and an improvement in their symptoms, literature reviews recommend the use of mepolizumab in individuals with CRSwNP that is difficult to treat.

10. Anti-IL4/IL13

Strong type 2 immune mediators, IL-4 and IL-13, have different and overlapping roles. Both IL-13 and IL-4 play a significant role in IgE synthesis, eosinophil activation, mucus secretion, and airway remodeling. They also partially share receptors and signaling pathways. By starting T cell development toward the TH2 subtype, IL-4 is a key differentiating agent that drives a TH2 type response. Moreover, type 2-related chemokines and cytokines as TARC, fotaxin, IL-5, IL-9, and IL-13 are produced in response to IL-4. Additionally, the primary factors that cause B cells to flip their isotype class and generate Ig are IL-4 and IL-13. Dupilumab is a subcutaneous injection-based completely human monoclonal antibody targeting the IL-4 receptor subunit that blocks IL-4 and IL-13 signaling [28].

Bachert et al. conducted a 16-week follow-up randomized, double-blind, placebo-controlled parallel-group trial that involved 60 adults with chronic sinusitis and nasal polyposis who were not responding to intranasal corticosteroids. The study was carried out at 13 sites in the US and Europe between August 2013 and August 2014 [29]. Subcutaneous dupilumab (a 600 mg loading dose followed by 300 mg weekly; n = 30) or placebo (n = 30) plus mometasone furoate nasal spray for 16 weeks. Any changes in the primary end point were recorded, including endoscopic nasal polyp score at 16 weeks (range, 0–8; larger scores indicate worse condition). The 22-item SinoNasal Outcome Test score (range, 0–110; higher scores indicating worse quality of life; minimal clinically important difference = 8.90), the Lund-Mackay computed tomography (CT) score (range, 0–24; higher scores indicate worse status), the sense of smell as measured by the University of Pennsylvania Smell Identification Test (UPSIT) score (range, 0–40; higher scores indicate better status), symptoms, and safety were among the secondary end points. Fifty patients (mean [SD] age, 48.4 years [9.4 years], 34 men [56.7%], and 35 with concomitant asthma) who were randomly assigned were all enrolled in the trial; fifty-one of them finished it. The nasal polyp score exhibited a least squares (LS) mean change of −0.3 (95%CI, −1.0 to 0.4) when administered placebo and − 1.9 (95%CI, −2.5 to −1.2) when administered dupilumab (LS mean difference, −1.6 [95%CI, −2.4 to −0.7]; P < .001). For the Lund-Mackay CT total score, the LS mean difference between the two groups was −8.8 (95%CI, −11.1 to −6.6; P < .001). The 22-item SNOT showed significant improvements with dupilumab (LS mean difference between groups, −18.1 [95%CI, −25.6 to −10.6]; P < .001), as did the UPSIT, which measured sense of smell (LS mean difference, 14.8 [95%CI, 10.9 to 18.7]; P < .001). Nasopharyngitis (33% in the placebo group vs. 47% in the dupilumab group), injection site responses (7 vs. 40%, respectively), and headache (17 vs. 20%) were the most frequent side effects. In conclusion after 16 weeks, the endoscopic nasal polyp load in persons with symptomatic chronic sinusitis and nasal polyposis unresponsive to intranasal corticosteroids was lower when subcutaneous dupilumab was added to mometasone furoate nasal spray as opposed to mometasone alone [29].

Bachert et al. conducted a two international, multicenter, parallel-group, randomized, double-blind, and placebo-controlled trials evaluated the addition of dupilumab

to the standard of therapy for people with severe CRSwNP. SINUS-52 was conducted in 117 centers across 14 nations, while SINUS-24 was conducted in 67 centers across 13 countries. Patients must have been 18 years of age or older, have bilateral CRSwNP, and still be experiencing symptoms even after using intranasal corticosteroids, getting systemic corticosteroids within the last 2 years, or having undergone sinonasal surgery [30]. For a duration of 24 weeks, patients in SINUS-24 were randomized (1:1) to receive subcutaneous dupilumab 300 mg or a placebo every 2 weeks. In SINUS-52, patients were randomized (1:1:1) to receive placebo every 2 weeks for 52 weeks, dupilumab 300 mg every 2 weeks for 24 weeks and then every 4 weeks for the final 28 weeks. Using a permuted block randomization schedule, all patients were assigned at random centrally. Randomization was stratified by nation, prior surgery at screening, and status of respiratory disease aggravated by nonsteroidal anti-inflammatory drugs or asthma at screening. Included were patients with and without co-occurring asthma. In an intention-to-treat population, coprimary outcomes included changes in nasal polyp score (NPS) from baseline to week 24, nasal congestion or obstruction, and sinus Lund-Mackay CT scores (a coprimary endpoint in Japan). A pooled population comprising the dupilumab group in SINUS-52 up to week 24, the dupilumab group in SINUS-24, and the placebo groups in both studies up to week 24 was used to evaluate safety. The results showed a significant and clinically meaningful decrease in MD was observed in the SNOT-22 score (scale 0–110) after 4–6 months (784 individuals; two studies; I2 = 0%). At 4–6 months, the rhinosinusitis disease severity (VAS) demonstrated a substantial and clinically meaningful decline of MD – 2.54 (95% CI −2.84–−2.23); two studies; 784 participants; I2 = 40%). A noteworthy and clinically meaningful decrease of MD – 0.86 (95% CI −0.98–−0.75); 784 individuals; two studies; I2 = 0%) was observed in the nasal congestion/obstruction score at 4–6 months. The UPSIT was utilized to assess smell. A significant and clinically meaningful drop of MD 10.83 (95% CI 9.59–12.08); 784 individuals; two studies; I2 = 0%) was observed in the UPSIT score at 4–6 months. In these investigations, the primary endpoint was the nasal polyp score. In these trials, the average nasal polyp score was approximately 6, which denotes a serious polyp illness. In two investigations with 784 patients, the nasal polyp score at 4–6 months shown a significant decrease of MD −1.79 (95% CI −2.01–−1.56); I2 = 65%. At 4–6 months, the Lund-Mackay score (scale 0-48) revealed a significant decrease in SMD −1.50 (95% CI −1.84–−1.16); there were 784 individuals in two investigations, with an I2 of 71%. Lastly, there was a notable effect on FEV1 and ACQ. Both studies demonstrated a significant improvement over placebo; however, the data could not be merged into a meta-analysis because ACQ5 and ACQ6 were employed. A meta-analysis of the FEV1 data revealed a substantial improvement in FEV1 (l) at 4–6 months of MD 0.21 (95% CI 0.20 – 0.22); there were 488 participants in two investigations, with an I2 of 0%. The most frequent side effects with placebo included headache, epistaxis, injection-site erythema, worsened nasal polyps and asthma, and rhinopharyngitis [30].

In a phase III trial study done by Anju et al. individuals with severe CRSwNP with or without concurrent AR were studied for the safety and effectiveness of dupilumab using this *post hoc* approach. This study used SINUS-24 weeks or SINUS-52 weeks protocol for dupilumab injections [33]. The analysis involved patients who were randomized every 2 weeks for 24 (SINUS-24) or 52 weeks (SINUS-52) to receive subcutaneous dupilumab 300 mg (n = 438) or placebo (n = 286). The first 24 weeks of treatment's pooled data are shown. The patient's self-reported history of allergic rhinitis (AR) status was used to examine changes from baseline in illness outcome measures and biomarker levels. In all, 46.7% (338 out of 724 patients) had AR. Patients

with and without AR had largely comparable baseline characteristics. There was no discernible treatment difference between patients with and without AR at week 24, and dupilumab dramatically improved objective and patient-reported markers of CRSwNP, including loss of smell. It also lowered systemic and nasal biomarker levels compared placebo. Regardless of AR status, there was a substantial decrease in the use of systemic corticosteroids and/or sinonasal surgery with dupilumab compared to placebo ($p < 0.0029$). Dupilumab's safety profile was comparable in those with and without AR. In patients with severe CRSwNP, dupilumab showed statistically significant improvements in both clinical end goals and symptom scores when compared to placebo, regardless of concomitant AR status—a common patient subgroup that is frequently linked to worse CRSwNP outcomes [33].

In a meta-analysis conducted by Qingwu Wu [34], the included nine RCTs involved 1190 patients comparing three distinct biologics (omalizumab, mepolizumab, and dupilumab) with the placebo. Dupilumab demonstrated the highest level of efficacy for surface under the cumulative ranking curve (SUCRA) values of 0.900, 0.916, 1.000, and 0.807, respectively, for nasal polyp score (NPS), SNOT-22 score, University of Pennsylvania Smell Identification Test (UPSIT) score, and nasal congestion score (NCS). When it came to SUCRA values of 0.606, 0.500, and 0.693, omalizumab was the most effective drug in terms of SNOT-22, UPSIT, and NCS. For SUCRA values of 0.563, mepolizumab placed second in terms of NPS effectiveness, while for SUCRA values of 0.746, mepolizumab had the greatest risk of adverse events (AEs). In conclusion Omalizumab is the second-best option for CRSwNP, whereas dupilumab is the best option based on safety (AEs) and effectiveness (NPS). Mepolizumab had the highest risk of adverse events (AEs) while having the second-best effectiveness rating.

10.1 Conclusion

Because the evidence shown a considerable reduction in patients' need for surgery and an improvement in their symptoms, we recommend the use of dupilumab in individuals with CRSwNP that is difficult to treat.

11. Antihistamine

It is unknown how sensitization functions in CRSsNP. One may be tempted to hypothesize that an atopic person is more susceptible to developing CRS if they have allergic irritation in their nose. Nevertheless, there are contradictory studies assessing atopy as a risk factor for CRS. In a DBPCT, Haye et al. [35] randomly assigned 45 CRSwNP patients (16 of whom had allergies) to receive a placebo or 20 mg of cetirizine for a duration of 3 months. Cetirizine, according to the authors, decreased the number of days with a score for nasal sneeze and rhinorrhea that was less than one. At all time periods, the cetirizine-treated group experienced a score of 90–100% compared to the placebo group's 70–80% for rhinorrhea and 80–90% for sneezing. Nevertheless, information about individuals with and without allergies was not provided individually. The cetirizine had no influence on the size of nasal polyps.

11.1 Conclusion

When comparing antihistamines with placebos, the GRADE quality of the evidence was extremely low. Due to the limited number of studies and the absence of the

most significant effectiveness measures, the evidence was downgraded. The effectiveness of regularly administering antihistamines to people with CRS is not established well enough. No meta-analysis is found in litertaure.

12. Anti-leukotrienes

Eosinophils and mast cells produce a family of inflammatory mediators called cysteineyl leukotrienes (CysLT) by breaking down arachidonic acid. CysLT are known to promote bronchoconstriction, mucus formation, edema, and neutrophil and eosinophil chemotaxis, and they may also have a role in the pathogenesis of asthma, rhinitis, and maybe CRSwNP.

Asthma, allergic rhinitis, and CRS with nasal polyposis (CRSwNP) have all been linked to the overproduction of CysLTs and overexpression of the receptor.

In a systemic review conducted by Wentzel et al. [36], studies evaluating the impact of leukotriene antagonists (LTAs) on clinical outcome markers of CRSwNP were included in a systematic review. Trials evaluating LTAs in CRS without nasal polyps or asthma symptoms alone met the exclusion criteria. The aim of this study is to evaluate the effects of LTA therapy on immunological markers, objective clinical outcomes, and nasal symptoms in CRSwNP, both alone and in combination with intranasal corticosteroids (INCSs). Twelve studies met the qualifying requirements: seven case series and five randomized control trials. Compared to placebo, LTAs significantly reduced CRSwNP symptoms; however, a meta-analysis of these randomized studies was not possible. The two studies that were included in the meta-analysis revealed that there was no difference in the treatment modalities, with a standardized mean difference of pooled total symptom scores between the LTA and INCS study arms of 0.02 (95% confidence range, −0.39-0.44). All trials reported improvements in immunological markers, clinical outcomes, and/or symptoms following LTA therapy; larger improvements were noted in a subset of symptoms compared to those seen with INCSs. Atopy, aspirin-exacerbated respiratory disorders, and concurrent asthma did not consistently or substantially alter these findings.

In a randomized controlled trial that evaluated adding montelukast to intransal spry therapy for chronic rhinosinusitis patients. In this study conducted by Suri et al. [37], 40 adult CRSwNP patients were randomly assigned to two groups. The subjects received budesonide nasal spray for 8 weeks, either with or without additional oral montelukast, and oral prednisolone for 14 days. After 8 weeks of therapy, subjects receiving supplemental oral montelukast reported a statistically significant improvement in their overall symptom score, sense of smell, and sneezing, which persisted for 4 weeks after the medication was stopped.

13. Conclusion

The data comparing placebo and montelukast was of extremely poor quality. The limited number of research and patients in the studies resulted in a downgrading of the evidence. The literature does not advise its usage unless a patient is unable to take nasal corticosteroids, based on the data currently available. Furthermore, the data contrasting montelukast with nasal corticosteroids is of low quality. The literature does not advise combining montelukast with nasal corticosteroids based on the available data. No meta-analysis is found.

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References

[1] Lee LN, Bhattacharyya N. Regional and specialty variations in the treatment of chronic rhinosinusitis. The Laryngoscope. 2011;**121**(5):1092-1097

[2] Sabino HAC, Valera FCP, Aragon DC, Fantucci MZ, Titoneli CC, Martinez R, et al. Amoxicillin-clavulanate for patients with acute exacerbation of chronic rhinosinusitis: A prospective, double-blinded, placebo-controlled trial. International Forum of Allergy & Rhinology. 2017;**7**(2):135-142

[3] Van Zele T, Gevaert P, Holtappels G, Beule A, Wormald PJ, Mayr S, et al. Oral steroids and doxycycline: Two different approaches to treat nasal polyps. Journal of Allergy and Clinical Immunology. 2010;**125**(5):1069-1076

[4] Askari M, Khezri M, Zoghi G. Introducing a novel combination therapy with macrolides for the treatment of chronic rhinosinusitis: A randomized controlled trial. Iranian Journal of Medical Sciences. 2022;**47**(6):533

[5] Siu J, Klingler L, Wang Y, Hung CT, Jeong SH, Smith S, et al. Oral antibiotics used in the treatment of chronic rhinosinusitis have limited penetration into the sinonasal mucosa: A randomized trial. Xenobiotica. 2020;**50**(12):1443-1450

[6] Videler WJ, Badia L, Harvey RJ, Gane S, Georgalas C, Van Der Meulen FW, et al. Lack of efficacy of long-term, low-dose azithromycin in chronic rhinosinusitis: A randomized controlled trial. Allergy. 2011;**66**(11):1457-1468

[7] Wallwork B, Coman W, Mackay-Sim A, Greiff L, Cervin A. A double-blind, randomized, placebo-controlled trial of macrolide in the treatment of chronic rhinosinusitis. The Laryngoscope. 2006;**116**(2):189-193

[8] de Oliveira IS, Guimaraes AF, Arantes Pêgas GF, Machado CJ, Cassali GD, Tormin Borges Crosara PF, et al. Azitromycin for chronic eosihophilic rhinosinusitis with nasal polyp: A placebo-controlled trial. Rhinology. 2020;**58**(6):610-617

[9] Kim DH, Shin H, Stybayeva G, Hwang SH. A comparison of doxycycline and conventional treatments of refractory chronic rhinosinusitis with nasal polyps: A systematic review and meta-analysis. European Archives of Oto-Rhino-Laryngology. 2024;**281**:3949-3957

[10] Bonfils P, Escabasse V, Coste A, Gilain L, Louvrier C, Serrano E, et al. Efficacy of tobramycin aerosol in nasal polyposis. European Annals of Otorhinolaryngology, Head and Neck Diseases. 2015;**132**(3):119-123

[11] Day N, Mainardi JL, Malinvaud D, Bonfils P. Bacteriological study of ethmoid specimens from patients with nasal polyposis after ethmoidal surgery. Annales D'oto-laryngologie et de Chirurgie Cervico Faciale: Bulletin de la Societe D'oto-laryngologie des Hopitaux de Paris. 2009;**126**(4):196-202

[12] Lee VS, Pottinger PS, Davis GE. Tolerability and effectiveness of povidone-iodine or mupirocin versus saline sinus irrigations for chronic rhinosinusitis. American Journal of Otolaryngology. 2020;**41**(5):102604

[13] Leopold DA, Elkayam D, Messina JC, Kosik-Gonzalez C, Djupesland PG, Mahmoud RA. NAVIGATE II: Randomized, double-blind trial of

the exhalation delivery system with fluticasone for nasal polyposis. Journal of Allergy and Clinical Immunology. 2019;**143**(1):126-134

[14] Kobayashi Y, Yasuba H, Asako M, Yamamoto T, Takano H, Tomoda K, et al. HFA-BDP metered-dose inhaler exhaled through the nose improves eosinophilic chronic rhinosinusitis with bronchial asthma: A blinded, placebo-controlled study. Frontiers in Immunology. 2018;**9**:2192

[15] Tait S, Kallogjeri D, Suko J, Kukuljan S, Schneider J, Piccirillo JF. Effect of budesonide added to large-volume, low-pressure saline sinus irrigation for chronic rhinosinusitis: A randomized clinical trial. JAMA Otolaryngology–Head & Neck Surgery. 2018;**144**(7):605-612

[16] Bognanni A, Chu DK, Rank MA, Bernstein J, Ellis AK, Golden D, et al. Topical corticosteroids for chronic rhinosinusitis with nasal polyposis: GRADE systematic review and network meta-analysis. Journal of Allergy and Clinical Immunology. 2022;**150**(6):1447-1459

[17] Ecevit MC, Erdag TK, Dogan E, Sutay S. Effect of steroids for nasal polyposis surgery: A placebo-controlled, randomized, double-blind study. The Laryngoscope. 2015;**125**(9):2041-2045

[18] Giotakis AI, Karow EM, Scheithauer MO, Weber R, Riechelmann H. Saline irrigations following sinus surgery-a controlled, single blinded, randomized trial. Rhinology. 2016;**54**(4):302-310

[19] Zhang Y, Wang C, Huang Y, Lou H, Zhang L. Efficacy of short-term systemic corticosteroid therapy in chronic rhinosinusitis with nasal polyps: A meta-analysis of randomized controlled trials and systematic review. American Journal of Rhinology & Allergy. 2019;**33**(5):567-576

[20] Gevaert P, Calus L, Van Zele T, Blomme K, De Ruyck N, Bauters W, et al. Omalizumab is effective in allergic and nonallergic patients with nasal polyps and asthma. Journal of Allergy and Clinical Immunology. 2013;**131**(1):110-116

[21] Pinto JM, Mehta N, DeTineo M, Wang J, Baroody FM, Naclerio RM. A randomized, double-blind, placebo-controlled trial of anti-IgE for chronic rhinosinusitis. Rhinology. 2010;**48**(3):318

[22] Di Bona D, Fiorino I, Taurino M, Frisenda F, Minenna E, Pasculli C, et al. Long-term "real-life" safety of omalizumab in patients with severe uncontrolled asthma: A nine-year study. Respiratory Medicine. 2017;**130**:55-60

[23] Liu L, Pan M, Li Y, Tan G, Yang Y. Eficácia da irrigação nasal com solução salina hipertônica na rinossinusite crônica: revisão sistemática e metanálise. Brazilian Journal of Otorhinolaryngology. 2020;**86**:639-646

[24] Denburg JA, Sehmi R, Upham J. Regulation of IL-5 receptor on eosinophil progenitors in allergic inflammation: Role of retinoic acid. International Archives of Allergy and Immunology. 2001;**124**(1-3):246-248

[25] Johnson PS, Ohlsson B, von Buchwald C, Jannert M, Ahlner-Elmqvist M. A multi-centre study on quality of life and absenteeism in patients with CRS referred for endoscopic surgery. Rhinology. 2011;**49**(4):420-428

[26] Bachert C, Sousa AR, Lund VJ, Scadding GK, Gevaert P, Nasser S, et al.

Reduced need for surgery in severe nasal polyposis with mepolizumab: Randomized trial. Journal of Allergy and Clinical Immunology. 2017;**140**(4):1024-1031

[27] Wu Q, Yuan L, Qiu H, Wang X, Huang X, Zheng R, et al. Efficacy and safety of omalizumab in chronic rhinosinusitis with nasal polyps: A systematic review and meta-analysis of randomised controlled trials. BMJ Open. 2021;**11**(9):e047344

[28] Bagnasco D, Ferrando M, Varricchi G, Passalacqua G, Canonica GW. A critical evaluation of anti-IL-13 and anti-IL-4 strategies in severe asthma. International Archives of Allergy and Immunology. 2016;**170**(2):122-131

[29] Bachert C, Mannent L, Naclerio RM, Mullol J, Ferguson BJ, Gevaert P, et al. Effect of subcutaneous dupilumab on nasal polyp burden in patients with chronic sinusitis and nasal polyposis: A randomized clinical trial. JAMA. 2016;**315**(5):469-479

[30] Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): Results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. The Lancet. 2019;**394**(10209):1638-1650

[31] Peters AT, Wagenmann M, Bernstein JA, Khan AH, Nash S, Jacob-Nara JA, et al. Dupilumab efficacy in patients with chronic rhinosinusitis with nasal polyps with and without allergic rhinitis. In: Allergy and Asthma Proceedings. Vol. 44. issue no. 4. Ocean Side Publications, Inc.; 2023. pp. 265-274

[32] Gevaert P, Van Bruaene N, Cattaert T, Van Steen K, Van Zele T, Acke F, et al. Mepolizumab, a humanized anti–IL-5 mAb, as a treatment option for severe nasal polyposis. Journal of Allergy and Clinical Immunology. 2011;**128**(5):989-995

[33] Akinlade B, Guttman-Yassky E, de Bruin-Weller M, Simpson EL, Blauvelt A, Cork MJ, et al. Conjunctivitis in dupilumab clinical trials. British Journal of Dermatology. 2019;**181**(3):459-473

[34] Wu Q, Zhang Y, Kong W, Wang X, Yuan L, Zheng R, et al. Which is the best biologic for nasal polyps: Dupilumab, omalizumab, or mepolizumab? A network meta-analysis. International Archives of Allergy and Immunology. 2022;**183**(3):279-288

[35] Haye R, Aanesen JP, Burtin B, Donnelly F, Duby C. The effect of cetirizine on symptoms and signs of nasal polyposis. The Journal of Laryngology & Otology. 1998;**112**(11):1042-1046

[36] Wentzel JL, Soler ZM, DeYoung K, Nguyen SA, Lohia S, Schlosser RJ. Leukotriene antagonists in nasal polyposis: A meta-analysis and systematic review. American Journal of Rhinology & Allergy. 2013;**27**(6):482-489

[37] Suri A, Gupta R, Gupta N, Kotwal S. Montelukast as an adjunct to treatment of chronic rhinosinusitis with polyposis: A prospective randomized controlled trial. JK Science. 2015;**17**(2):92

Chapter 4

Psychological Impact of Rhinology Disorders

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Abstract

Rhinology disorders, including sinusitis, rhinitis, allergic diseases, and structural problems, often go unnoticed and undertreated. Yet, these seemingly localized issues can have far-reaching effects. Over time, problems in the rhino-sinus and upper airway systems can impact the nervous system, social interactions, and psychological well-being. Patients may experience anxiety, depression, and difficulties with learning, memory, and social behavior. These hidden complications are crucial for healthcare professionals to recognize, as addressing them can significantly improve patients' quality of life. This chapter will delve deeper into the intricate relationship between rhinology disorders and psychological impacts, exploring the possible underlying mechanisms. It will offer insights into effective management and treatment strategies, aiming to empower healthcare professionals to provide holistic care that encompasses the physical, psychological, and social aspects of their patients' lives.

Keywords: rhinitis, rhinosinusitis, olfactory bulb, depression, anxiety, cognition, behavior, mood, psychiatry, psychology

1. Introduction

Rhinology disorders, while predominantly recognized for their physical manifestations, conceal a profound psychological impact that is often overlooked in clinical practice. This chapter seeks to illuminate the intricate connections between rhinology disorders and mental health, offering healthcare professionals a comprehensive understanding of the emotional burdens these conditions impose on patients. By exploring the psychological ramifications of chronic rhinosinusitis, nasal polyps, allergic rhinitis, and other related disorders, we aim to reveal the extensive influence these ailments have on quality of life and mental well-being. Through this exploration, we will provide valuable insights and strategies to enhance patient care, emphasizing the importance of addressing both the physical and psychological aspects of rhinology disorders.

Understanding the psychological impact of rhinology diseases is crucial for several reasons, as these conditions often extend beyond physical symptoms to profoundly affect mental health and overall quality of life. Here are key reasons why this understanding is essential:

Comprehensive patient care: rhinology diseases often lead to persistent discomfort, pain, and functional impairments. These physical symptoms can contribute to significant psychological distress, including anxiety, depression, and sleep disturbances. Acknowledging the psychological dimensions of these conditions allows healthcare providers to offer more holistic and effective patient care, addressing both physical and mental health needs.

Improved quality of life: patients with rhinology disorders frequently experience a diminished quality of life due to ongoing symptoms such as nasal congestion, headaches, and reduced sense of smell. These symptoms can interfere with daily activities, social interactions, and work productivity. Understanding the psychological impact helps in developing targeted interventions that can alleviate these symptoms and improve patients' overall well-being.

Enhanced treatment outcomes: psychological factors can influence the course and treatment outcomes of rhinology diseases. For instance, stress and mental health conditions can exacerbate physical symptoms and hinder recovery. By integrating psychological assessment and support into the treatment plan, healthcare providers can enhance adherence to medical regimens, promote healthier coping strategies, and ultimately achieve better clinical outcomes.

Identification of comorbidities: patients with rhinology disorders often have comorbid psychological conditions that may go unrecognized and untreated. Understanding the psychological impact helps in early identification and management of these comorbidities, ensuring that patients receive comprehensive care that addresses all aspects of their health.

Patient-centered care: a patient-centered approach to healthcare emphasizes the importance of understanding the full spectrum of a patient's experience, including their psychological and emotional well-being. By recognizing and addressing the psychological impact of rhinology diseases, healthcare providers can build stronger therapeutic relationships, improve patient satisfaction, and empower patients to take an active role in their care.

Public health implications: rhinology disorders are prevalent and can lead to significant healthcare utilization and economic burden. By understanding the psychological impact, public health strategies can be developed to support mental health initiatives, improve access to comprehensive care, and reduce the overall burden of these diseases on the healthcare system.

Research and education: highlighting the psychological impact of rhinology diseases encourages further research into the biopsychosocial aspects of these conditions. It also underscores the need for interdisciplinary education, ensuring that healthcare professionals are equipped with the knowledge and skills to address both the physical and psychological needs of their patients.

2. Common rhinology disorders and their association with psychologic problems

2.1 Chronic rhinosinusitis

Chronic rhinosinusitis (CRS) significantly impacts patients' mental health, with a strong correlation between CRS and psychological disorders such as depression and anxiety. Depression in patients with CRS is often underdiagnosed, yet it profoundly affects treatment outcomes and healthcare utilization. Depression scores using the

Beck Depression Inventory (BDI) are higher in patients with CRS, even when controlling for other comorbid conditions such as asthma, allergies, and aspirin sensitivity. Notably, depression appears more prevalent in patients with CRS without nasal polyps (CRSsNP) compared to those with nasal polyps (CRSwNP). Nearly one-third of CRS patients screened positive for depression, indicating the need for routine mental health evaluations in this population [1, 2].

Patients suffering from both chronic sinusitis and nasal polyps are significantly more likely to experience depression and anxiety. The relationship between CRS and psychological disorders is bidirectional; while CRS exacerbates mental health issues, these psychological conditions can also worsen the symptoms and management of CRS. For example, patients with CRSwNP are often associated with more severe clinical disease, possibly because they are more likely to seek treatment early due to frequent associations with asthma and allergic rhinitis. This continuous medical attention may help mitigate some psychological impacts, although it does not eliminate them [3, 4].

Longitudinal studies reinforce the chronic nature of the psychological burden associated with CRS. In a large cohort study of over 48,000 participants, the incidence of depression and anxiety was significantly higher in the group with CRS compared to a control group over an 11-year follow-up period. Interestingly, the adjusted hazard ratio for developing depression and anxiety was higher in patients with CRSsNP than those with CRSwNP. This distinction highlights that while CRSwNP might lead to more severe physical symptoms and require frequent medical intervention, CRSsNP can have a more profound impact on mental health, possibly due to the chronic, lingering nature of the disease that may not prompt immediate clinical attention [4].

The relationship between CRS and psychological disorders is complex and multifaceted. For instance, while anxiety scores in CRS patients with asthma improved with pharmacological treatment, depression scores did not show the same improvement, suggesting that anxiety might be closely related to the severity of airway disease, whereas depression could be more independent of the physical symptoms of CRS. This finding underscores the necessity for separate mental health care pathways for managing depression in CRS patients. Furthermore, despite the high prevalence of mental health issues among CRS patients, the rates of depression did not differ significantly between those who underwent surgical treatment and those who did not, indicating that surgical interventions alone may not be sufficient to address the psychological impacts of CRS [3].

In conclusion, the interplay between chronic rhinosinusitis and psychological disorders like depression and anxiety necessitates an integrated approach to treatment that addresses both physical and mental health aspects. Routine screening for depression and anxiety in CRS patients should become a standard practice, and mental health interventions should be tailored to the unique needs of CRS patients. This holistic approach can potentially improve overall treatment outcomes and enhance the quality of life for those suffering from this chronic condition.

2.2 Nonallergic and allergic rhinitis

Rhinitis, encompassing both allergic rhinitis (AR) and nonallergic rhinitis (NAR), is significantly associated with psychological disorders, particularly depression and anxiety. Individuals with rhinitis are more prone to developing depression, with the risk being notably higher in patients with NAR compared to those with AR. The

severity of rhinitis symptoms, rather than their persistence or seasonality, is the most critical factor influencing mental health outcomes. Severe symptoms are linked to a worse quality of life, poor sleep, and elevated levels of anxiety and depression. The continuous discomfort and impairment caused by rhinitis symptoms can lead to frustration and feelings of helplessness, further exacerbating psychological distress [5–7].

The psychological impact of rhinitis is further compounded by the presence of comorbid conditions. Patients with rhinitis are more likely to suffer from asthma, chronic bronchitis, and emphysema, contributing to their overall poorer health status. This burden of comorbidities correlates with a higher prevalence of significant depression, particularly among women. The physical strain and discomfort from these associated conditions can intensify mental health challenges, creating a cycle of worsening physical and psychological symptoms. Both AR and NAR are associated with increased frequencies of anxiety and depression, with NAR presenting a stronger association. The unpredictability and chronic nature of these conditions can lead to constant anxiety about managing symptoms and their impact on daily life [6, 8].

In addition to depression and anxiety, rhinitis has been linked to other serious mental health conditions. Adolescents with AR, for instance, have a significantly higher incidence of developing bipolar disorder later in life [9]. Furthermore, young patients with AR may experience difficulty in learning and attention, which can impact academic performance and social development [10]. These cognitive and attention deficits highlight the broader impact of rhinitis beyond immediate physical discomfort, affecting long-term educational and developmental outcomes. This highlights the potential long-term psychological effects of rhinitis, suggesting that early and comprehensive management is crucial in mitigating these impacts [7, 11].

Moreover, the impact of rhinitis on sleep is a critical factor linking it to psychological problems. Poor sleep quality and insomnia are common in individuals with severe rhinitis symptoms, leading to fatigue, irritability, and difficulty concentrating. Chronic sleep disturbances are well-known contributors to anxiety and depression, creating a feedback loop where psychological distress can further disrupt sleep. Addressing sleep issues through both pharmacological and behavioral interventions can significantly improve the overall mental health and quality of life for rhinitis patients. Effective management of sleep disturbances can break this cycle, providing a foundation for better psychological health [10, 12, 13].

These complex and varied associations underscore the necessity for healthcare professionals to adopt a holistic approach in managing rhinitis, considering both the physical symptoms and the profound psychological impacts. By understanding these connections, healthcare providers can develop more effective treatment strategies that address the full spectrum of patient needs, ensuring a higher quality of life and better mental health outcomes for those affected by rhinitis. Integrating mental health support into the care plan for rhinitis patients can facilitate early identification and treatment of psychological issues, promoting a more comprehensive approach to health and well-being.

2.3 Olfactory bulb dysfunction

Olfactory dysfunction, which includes anosmia (complete loss of smell), hyposmia (reduced smell), and hyperosmia (heightened smell), is prevalent in various psychological disorders such as anxiety, depression, schizophrenia, and bipolar disorder. These dysfunctions often manifest as impairments in odor detection, discrimination, and identification. The connection between olfactory deficits and mental health

conditions is crucial as it impacts the diagnosis, treatment, and overall well-being of patients [14, 15].

In anxiety disorders, such as generalized anxiety disorder (GAD) and panic disorder, olfactory dysfunction is common. Patients with moderate to severe anxiety exhibit significant deficits in odor discrimination and identification, which correlate inversely with anxiety severity. This suggests that the poorer the olfactory function, the more severe the anxiety symptoms. Moreover, in panic disorder, a lower odor threshold is often found, indicating that these patients are more sensitive to odors, which correlates with the severity of their symptoms [14, 16–18].

Depression also significantly impacts olfactory function. Patients with depression commonly exhibit impairments in odor threshold, discrimination, and identification, with the olfactory threshold being the most notably affected. Olfactory dysfunction is a potential biomarker for depression, with successful treatment often reversing these deficits. Interestingly, olfactory training has been shown to improve depressive symptoms, although the results are somewhat controversial. These findings underscore the importance of considering olfactory assessments in the management of depression [19–24].

Schizophrenia is another condition where olfactory dysfunction is prevalent. Patients with schizophrenia, especially those in the early stages of psychosis or at high risk, often show impaired odor identification and discrimination. While some individuals with schizophrenia may experience olfactory hallucinations, these are not directly linked to the general olfactory deficits observed, suggesting different underlying neural mechanisms. The olfactory impairments in schizophrenia are associated with negative symptoms and reduced social and cognitive functioning, highlighting the need for comprehensive olfactory evaluations in these patients [25].

Bipolar disorder also shows a notable link with olfactory dysfunction. Patients, even during euthymic phases, often display impaired odor thresholds and reduced odor identification capabilities. However, olfactory discrimination does not seem to be significantly affected. The severity of clinical symptoms in bipolar disorder negatively correlates with odor sensitivity but not odor identification, suggesting a nuanced relationship between olfactory function and mood episodes. This relationship highlights the importance of olfactory assessments in understanding and managing bipolar disorder [20, 26].

The recent COVID-19 pandemic has brought additional focus to the link between olfactory dysfunction and psychological distress. COVID-19 often causes nasal inflammation leading to significant olfactory impairments, which can result in long-lasting neuropsychiatric sequelae. COVID-19-related anosmia can profoundly impact perceived quality of life and psychological well-being. This highlights the importance of olfactory function not just as a sensory ability but as a critical component of overall mental health. Additionally, other viruses, such as influenza and the common cold (caused by rhinoviruses and coronaviruses), have been shown to affect the olfactory bulb, leading to temporary or sometimes prolonged olfactory dysfunction. These viral infections can also trigger inflammatory responses in the nasal passages and olfactory pathways, contributing to sensory deficits and subsequent psychological impacts. These findings reinforce the need for integrated care approaches that address both olfactory and mental health in patients affected by olfactory dysfunction [27–29].

2.4 Structural nose problem

Structural nose problems, such as a deviated nasal septum, enlarged turbinates, and nasal polyps, can lead to significant nasal obstruction and congestion. These

anatomical abnormalities can cause chronic nasal obstruction, which not only impairs physical health but also has profound psychological effects. The persistent nature of nasal obstruction often leads to frustration and can severely impact the quality of life. This chronic frustration can, in turn, contribute to the development of anxiety and depression [30].

One of the primary ways in which nasal obstruction impacts mental health is through its effect on sleep quality. Adequate sleep is essential for maintaining mood and overall mental health. Nasal obstruction can cause sleep disturbances such as sleep apnea or chronic snoring, which result in poor sleep quality [31]. Sleep deprivation has been closely linked to mood disorders, including anxiety and depression. Thus, individuals with chronic nasal obstruction are at a higher risk of developing these psychological conditions due to the compounded effects of disrupted sleep and the frustration caused by persistent breathing difficulties [32, 33].

Patients with unilateral or bilateral complete nasal obstruction exhibit higher psychiatric symptom scores across various personality traits. Although the scores for psychiatric symptoms were elevated in these patients, significant differences were noted particularly in dependent and antisocial personality traits compared to healthy controls [34]. This suggests that structural nose problems not only affect physical health but also influence personality characteristics and psychological well-being. The presence of higher scores for depression and anxiety, even if not significantly different from controls, highlights the mental health burden carried by patients with nasal obstruction [30, 34].

Nasal surgery, such as septoplasty or septorhinoplasty, has been shown to alleviate nasal symptoms and improve nasal obstruction. Interestingly, these surgical interventions also have positive effects on psychiatric symptoms. Patients with structural nasal problems and accompanying psychiatric symptoms can experience significant improvements in their mental health following corrective nasal surgery [35]. However, studies have suggested that isolated nasal surgery does not have a significant impact on apnea-hypopnea index in patients with obstructive sleep apnea [36]. This underscores the importance of a holistic approach in treating nasal obstruction, where both physical and psychological aspects are considered. Patients with personalities of dependent and antisocial personality disorders, in particular, may benefit from such surgical interventions, suggesting a close interplay between nasal structure and personality traits [34, 37].

Given the significant impact of structural nose problems on mental health, it is crucial for healthcare providers to adopt a multidisciplinary approach in managing these conditions. Evaluating patients from both an otorhinolaryngological and psychological perspective can ensure comprehensive care.

2.5 Granulomatosis with polyangiitis

Wegener's granulomatosis, now more commonly referred to as granulomatosis with polyangiitis (GPA), is a type of vasculitis that involves the inflammation of small and medium-sized blood vessels, often affecting the upper respiratory tract. Patients with GPA usually experience persistent nasal congestion and obstruction which are common due to inflammation and swelling of the nasal passages. While the physical manifestations of GPA are well-documented, the psychological impacts are equally significant but less frequently addressed. Research has revealed a high prevalence of psychiatric disorders among GPA patients, with paranoia and depression being particularly common. Additionally, there is a notable correlation between these

psychiatric disorders and the neuroticism personality trait, suggesting that personality factors may influence the mental health outcomes of GPA patients [38].

Furthermore, psychosis has been reported as an initial manifestation in some cases of GPA, illustrating the severe psychological impact this disease can have. Some cases highlight the acute psychiatric symptoms that can arise in GPA [38, 39]. These cases underscore the potential for GPA to manifest with severe psychiatric symptoms, necessitating appropriate psychiatric intervention. Such cases, although rare, emphasize the importance of healthcare providers being vigilant about the psychiatric dimensions of GPA to ensure comprehensive treatment that addresses both the physical and mental health needs of the patient.

Depression, anxiety, sleep disturbances, and fatigue are common yet inadequately addressed comorbidities in GPA. These psychiatric conditions significantly impair the quality of life of GPA patients. Factors such as age, body mass index (BMI), and disease damage have been identified as predictors of depression in these patients. Targeting these potentially modifiable factors could help improve the psychological well-being of GPA patients [40].

The impact of GPA on daily life extends beyond the individual's physical health. There are substantial medical and functional morbidity among GPA patients. Many patients require long-term immunosuppressive treatment and experience significant reductions or constraints in their daily activities. These limitations negatively affect patients' normal daily living, employment, and income, as well as their family and close relationships. The substantial burden on quality of life highlights the need for a holistic approach in managing GPA, incorporating both medical treatment and psychosocial support [40, 41].

While depression is highly prevalent among patients with primary systemic vasculitis and associated with poorer outcomes, there is a need for further research specifically focusing on medium and large vessel vasculitis to better understand and address the psychological dimensions of these conditions. Overall, the psychological burden of GPA is profound, necessitating comprehensive care strategies that address both the physical and mental health aspects to improve patient outcomes and quality of life.

3. Mechanisms linking rhinology disorders and mental health

3.1 Inflammation and immune system mechanisms

The molecular mechanisms linking rhinological diseases to psychological disorders are intricately connected through pathways of inflammation and immune responses. Inflammatory responses in rhinological conditions have profound systemic effects, particularly influencing the central nervous system (CNS). CRS is predominantly associated with type 2 inflammation, where activated T helper (Th2) cells produce cytokines such as IL-4, IL-5, and IL-13. These cytokines facilitate the recruitment of eosinophils and the production of IgE antibodies, perpetuating a cycle of chronic inflammation and tissue remodeling [14, 42].

Elevated levels of IgE, frequently observed in AR, can cross the blood-brain barrier (BBB) and activate microglia, the brain's resident immune cells. This activation polarizes microglia to the M1 phenotype, which is associated with the production of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. These cytokines not only exacerbate neuroinflammation but also disrupt neuronal function, leading

to symptoms of depression and anxiety. Additionally, IgE can activate astrocytes, further amplifying neuroinflammatory processes and potentially leading to neurodegeneration, thereby contributing to cognitive dysfunctions and psychological disturbances [43–45].

A significant pathway involved in this process is the activation of Fc epsilon RI alpha (FcεRIα) by IgE. FcεRIα is a high-affinity IgE receptor that, when activated by IgE, can upregulate its expression on immune cells, thereby enhancing the inflammatory response. This receptor is crucial in mediating allergic reactions and is found on various immune cells, including mast cells and basophils. Upon activation, FcεRIα increases BBB permeability and facilitates the infiltration of inflammatory cells into the CNS. The resulting neuroinflammation can lead to psychological disorders such as depression and anxiety. FcεRIα's role in increasing inflammatory cytokines in the CNS underscores its significance in linking peripheral allergic responses with central neuroinflammatory processes [46–48].

The role of innate immunity, particularly through the Toll-like receptor 4 (TLR4) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathways, is also critical in this context. TLR4 is a pattern recognition receptor that detects pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs), leading to the activation of the NF-κB pathway. This activation triggers the production of various pro-inflammatory cytokines and chemokines, which are key mediators of the immune response. In rhinological conditions, the persistent activation of TLR4 and NF-κB can lead to chronic inflammation not only in the nasal passages but also in systemic circulation, impacting the CNS and contributing to psychological disorders such as behavioral and cognitive changes [49–51].

Chronic nasal obstruction, as seen in conditions like deviated nasal septum and enlarged turbinates, can lead to significant sleep disturbances, which are closely linked to mood disorders. Poor sleep quality and fragmented sleep, common in obstructive sleep apnea, result in intermittent hypoxia and oxidative stress, which can cause neuronal injury and cognitive impairments. The inflammatory mediators released during these episodes of intermittent hypoxia can further disrupt the BBB, allowing inflammatory cells and cytokines to infiltrate the CNS, thereby promoting neuroinflammation and psychological distress. The continuous cycle of poor sleep and heightened inflammation exacerbates symptoms of depression and anxiety, highlighting the interconnectedness of sleep, respiratory health, and mental well-being.

Olfactory dysfunction, which is common in conditions like CRS and AR, also has significant psychological implications. The loss of smell (anosmia) or reduced olfactory sensitivity (hyposmia) can lead to a diminished quality of life, contributing to depression and anxiety. Olfactory sensory neurons, when damaged by inflammation or infection (e.g., SARS-CoV-2), release pro-inflammatory cytokines such as IL-6 and TNF-α. These cytokines can travel to the brain and enhance neuroinflammation, affecting brain regions involved in mood regulation, such as the hippocampus and prefrontal cortex. This inflammatory cascade not only impacts mood but also impairs cognitive functions, leading to learning and memory dysfunctions [14, 52, 53].

Viral infections of the respiratory tract, such as influenza and COVID-19, further illustrate the link between rhinological diseases and psychological disorders. These infections trigger systemic inflammatory responses that extend to the CNS. For instance, the pro-inflammatory cytokines released during and after viral infections can lead to persistent neuroinflammation, contributing to long-term psychological effects such as depression and cognitive impairments. Influenza has been associated

with an increased risk of depression, severe enough to require antidepressant treatment. Similarly, anosmia in COVID-19 patients has been linked to depression, which can persist for months after the resolution of acute symptoms. This highlights the role of viral-induced inflammation in the pathophysiology of psychological disorders [52–54].

In conclusion, the intricate relationship between rhinological diseases and psychological disorders is mediated through complex molecular mechanisms involving chronic inflammation, immune responses, and neuroinflammation. The activation of FcεRIα by IgE plays a crucial role in enhancing BBB permeability and promoting neuroinflammation, which links peripheral allergic responses to central psychological effects. Understanding these pathways provides insight into how conditions like CRS, AR, and olfactory dysfunction can lead to significant psychological distress and cognitive impairments. Additionally, the role of TLR4 and NF-κB in mediating innate immune responses highlights the broader implications of chronic inflammation in the pathophysiology of both rhinological and psychological conditions. This knowledge emphasizes the need for comprehensive management approaches that address both the respiratory and psychological aspects of these conditions, ultimately improving patient outcomes and quality of life.

3.2 Neurobiological mechanisms

The intricate relationship between rhinological diseases with psychological issues can be explained through neural mechanisms and signaling pathways. Rhinological diseases often lead to chronic inflammation, which not only affects the respiratory system but also has far-reaching effects on the CNS. The olfactory system, which begins with the olfactory neurons (ONs) in the olfactory epithelium (OE), plays a pivotal role in this connection. These neurons transmit odor information to the olfactory bulbs (OB), which then project to secondary olfactory structures such as the anterior olfactory nucleus (AON), piriform cortex, and olfactory tubercle, eventually reaching tertiary structures like the orbitofrontal cortex (OFC), insular cortex, and dorsal hippocampus. These pathways highlight how disruptions in the olfactory system can affect broader neural circuits involved in mood regulation and cognitive functions [55–57].

The amygdala and the orbitofrontal cortex (OFC) are key components of the neurocircuitry implicated in anxiety disorders. The primary olfactory cortex, which includes the cortical amygdala nuclei, transmits odor information to other parts of the amygdala [58, 59]. Dysfunction in the amygdala, a region crucial for emotional processing, may be a significant factor linking olfactory dysfunction and anxiety [16, 57, 59]. Odor discrimination, a central sensory process associated with the primary olfactory cortex, is correlated with anxiety symptom severity [60]. This suggests that central processing of olfactory information, rather than peripheral sensory thresholds, is more relevant to the development of anxiety symptoms in patients with olfactory dysfunction [56].

Inflammation in the anterior cingulate cortex (ACC) is another critical factor in the development of neuropsychiatric symptoms in conditions such as AR. Neuroinflammation in the ACC has been linked to anxiety and depression-like behaviors in AR. The anatomical proximity between the nasal cavity and the CNS facilitates the spread of inflammation and neuropeptides released by type C nociceptive nerves in the nasal cavity, which increase plasma extravasation and glandular secretion. Dysfunction of these nerves can lead to the release of proinflammatory cytokines, contributing to both AR and the development of psychological disorders [61].

CRS and other sinonasal diseases often result from viral or bacterial infections, which trigger an inflammatory response. Research has shown that sinus inflammation can alter brain activity, particularly in neural networks that regulate cognition, introspection, and responses to external stimuli. Functional MRI in CRS patients have revealed increased amplitude of low-frequency fluctuations (ALFF) in the left orbital superior frontal cortex and reduced connectivity in the right precuneus. These alterations in brain activity correlate with inflammation severity and psychological symptoms, as indicated by the positive correlation between ALFF values in the orbital superior frontal cortex and scores on the hospital anxiety and depression scale (HADS) [2].

The role of different types of neurons, particularly glutamatergic, GABAergic, and dopaminergic neurons, is critical in understanding how rhinological diseases impact brain function and contribute to psychological problems. Inflammation and neuroimmune responses can alter the balance of excitatory and inhibitory signaling in the brain [62]. Glutamatergic neurons, which are primarily excitatory, can be affected by increased levels of pro-inflammatory cytokines, leading to heightened neuronal excitability and potential excitotoxicity. This imbalance can result in cognitive impairments and mood disorders. Conversely, GABAergic neurons, which are inhibitory, may be downregulated or dysfunctional in inflammatory conditions, contributing to reduced inhibition and increased anxiety and depression [63, 64].

Dopaminergic neurons, which are involved in reward processing and motivation, can also be significantly impacted by inflammatory responses. Chronic inflammation can alter dopamine signaling pathways, leading to anhedonia, reduced motivation, and other depressive symptoms [62]. Dopaminergic signaling in regions such as the prefrontal cortex (PFC) and the ventral tegmental area (VTA) can be disrupted by inflammation [65]. These disruptions may further contribute to the psychological symptoms experienced by patients with rhinological diseases.

In summary, the neural mechanisms linking rhinological diseases to psychological problems involve complex interactions between inflammation, immune responses, and neural signaling pathways. The olfactory system's connection to key brain regions involved in mood regulation, such as the amygdala and OFC, plays a central role. Chronic inflammation, mediated by pathways such as TLR4/NF-κB and FcεRIα, leads to neuroinflammation and disruption of neural circuits, resulting in psychological disorders. Additionally, the balance of excitatory and inhibitory signaling through glutamatergic, GABAergic, and dopaminergic neurons is crucial in maintaining normal cognitive and emotional function. Disruptions in these neuronal pathways due to inflammation and immune responses underscore the importance of addressing both the respiratory and psychological aspects of rhinological diseases to improve patient outcomes and quality of life.

3.3 Social mechanisms

Social factors play a significant role in the interplay between rhinological diseases and psychological conditions. Social determinants of health, including socioeconomic status, access to healthcare, social support, and environmental conditions, can exacerbate both physical and mental health issues, creating a vicious cycle that is difficult to break.

Firstly, socioeconomic status profoundly impacts the prevalence and management of rhinological diseases. Individuals from lower socioeconomic backgrounds often face barriers to accessing quality healthcare, including diagnostic services and effective treatments for conditions like rhinitis and sinusitis. This lack of access can lead

to the progression of these conditions into chronic states, which are associated with a higher risk of developing mental health problems such as depression and anxiety. The chronic discomfort and impaired functioning caused by untreated rhinological diseases can significantly diminish quality of life, leading to psychological distress.

Secondly, social support systems are crucial in managing both physical and mental health conditions. Individuals with strong social networks tend to have better health outcomes because they receive emotional support, practical help, and encouragement to seek medical care. Conversely, those who are socially isolated or have weak support networks are at greater risk of both rhinological diseases and psychological issues. The stress of dealing with health problems without adequate support can exacerbate symptoms of anxiety and depression, making it harder to manage chronic conditions like sleep apnea or structural nose problems.

Environmental conditions also play a vital role in this dynamic. Poor air quality, common in lower-income and densely populated urban areas, can aggravate conditions like rhinitis and sinusitis. Exposure to pollutants and allergens can lead to chronic inflammation of the nasal passages and respiratory system, which not only worsens physical symptoms but also contributes to cognitive impairments and mood disorders. Furthermore, individuals living in such environments often have limited access to clean, quiet, and safe spaces for rest, exacerbating sleep disorders like sleep apnea and increasing the risk of associated psychological problems.

Lastly, the stigma associated with certain rhinological conditions, particularly those that affect physical appearance or breathing, can lead to social anxiety and withdrawal. Conditions such as severe rhinitis, nasal polyps, or structural abnormalities can affect a person's self-esteem and social interactions. The fear of negative judgment or social embarrassment can discourage individuals from seeking help or participating in social activities, leading to increased feelings of isolation and depression. This social withdrawal further reinforces the negative impact on mental health, creating a feedback loop that is challenging to address.

In conclusion, the interplay between rhinological diseases and psychological problems is significantly influenced by social factors. Socioeconomic status, access to healthcare, social support, environmental conditions, and social stigma all contribute to the complexity of managing these intertwined health issues. Addressing these social determinants is crucial for developing comprehensive treatment strategies that not only focus on the medical aspects of rhinological diseases but also consider the broader social context to improve mental health outcomes and overall quality of life.

4. Diagnostic approaches

4.1 Assessing psychological symptoms in rhinology patients

Assessing psychological symptoms in rhinology patients involves a thorough understanding of both the physical and mental health aspects of the patient's condition. Rhinology patients often experience chronic discomfort, breathing difficulties, and sensory impairments such as loss of smell, which can significantly impact their psychological well-being. The assessment process should start with a comprehensive evaluation of the patient's medical history, including any pre-existing mental health conditions and current medications. Clinicians need to be vigilant for signs of depression, anxiety, cognitive dysfunction, and other psychological issues, as these can be both a consequence of and a contributor to chronic rhinological conditions [66–68].

4.2 Screening tools and questionnaires

Utilizing standardized screening tools and questionnaires is a crucial step in identifying psychiatric problems in rhinology patients. The Beck Depression Inventory (BDI) is one of the most widely used self-report measures for assessing the severity of depression. It consists of 21 multiple-choice questions that explore various aspects of depressive symptoms, such as mood, pessimism, sense of failure, self-dissatisfaction, and physical symptoms like fatigue and changes in sleep patterns. The BDI helps clinicians gauge the intensity of depression and monitor changes over time, providing valuable insights into the patient's mental health [69, 70]. The Generalized Anxiety Disorder 7 (GAD-7) scale is a brief, seven-item questionnaire specifically designed to screen for generalized anxiety disorder. Patients rate the frequency of anxiety-related symptoms over the past 2 weeks, including feelings of nervousness, inability to stop worrying, and physical symptoms such as restlessness and muscle tension. The GAD-7 is easy to administer and interpret, making it an effective tool for identifying anxiety disorders in rhinology patients [71]. The Patient Health Questionnaire-9 (PHQ-9) is a multipurpose instrument for screening, diagnosing, monitoring, and measuring the severity of depression. It consists of nine questions that reflect the diagnostic criteria for major depressive disorder in the DSM-5. Patients indicate how often they have been bothered by each symptom over the past 2 weeks. The PHQ-9 is highly effective in primary care settings and can be easily incorporated into routine rhinology assessments to identify patients in need of further mental health evaluation [72].

The Hospital Anxiety and Depression Scale (HADS) is another useful instrument for screening both anxiety and depression in rhinology patients. It consists of 14 items, seven for anxiety and seven for depression, and is designed to avoid reliance on somatic symptoms that might be confounded with physical illness. The HADS is particularly valuable in settings where patients may have overlapping physical and psychological symptoms [70].

The Sinonasal Outcome Test (SNOT-22) is specifically designed to assess the impact of sinonasal conditions on patients' quality of life. It includes questions about physical symptoms, emotional well-being, and functional limitations caused by rhinological issues. While not a direct measure of psychiatric symptoms, the SNOT-22 provides insight into how sinonasal problems affect mental health and daily functioning, allowing clinicians to tailor their interventions accordingly [72, 73].

The Brief Symptom Inventory (BSI) is a shorter version of the Symptom Checklist-90-Revised (SCL-90-R) and is used to evaluate psychological distress and psychiatric disorders. It includes 53 items and provides scores on nine primary symptom dimensions and three global indices of distress. The BSI can be useful for a broad assessment of psychological symptoms in rhinology patients, capturing a range of potential mental health issues [74].

For patients with suspected cognitive dysfunction, the Montreal Cognitive Assessment (MoCA) is a valuable tool. The MoCA assesses various cognitive domains, including attention, concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. This comprehensive screening tool can help identify cognitive impairments that may be contributing to or exacerbated by chronic rhinological conditions [68].

These tools allow clinicians to systematically evaluate the psychological state of the patient and provide a baseline for further investigation. Implementing these screenings in routine rhinology care can aid in early detection of mental health issues, facilitating timely intervention.

4.3 Clinical interviews

Clinical interviews remain a cornerstone of psychiatric assessment in rhinology patients. These interviews should be structured yet flexible to allow for a comprehensive understanding of the patient's psychological and physical health. During the interview, clinicians should explore the patient's mood, anxiety levels, sleep patterns, and cognitive functioning. It is also important to discuss the impact of rhinological symptoms on daily life and mental health. Open-ended questions and active listening can help patients feel comfortable sharing their experiences, which can reveal insights into their mental health status. Clinicians should be trained to recognize subtle signs of psychiatric distress and to differentiate between symptoms caused by rhinological issues and those stemming from psychological conditions [68, 75].

4.4 Integrating psychological assessment into routine care

Integrating psychological assessment into routine rhinology care is essential for holistic patient management. This integration can be achieved by developing multidisciplinary teams that include ENT specialists, psychologists, and psychiatrists. Regular training for rhinology clinicians on the importance of mental health and how to use screening tools effectively can enhance this process. Routine mental health screenings should be part of the standard care protocol for patients with chronic rhinological conditions. Creating a seamless referral pathway to mental health professionals for patients who need further evaluation and treatment is also crucial. By addressing both the physical and psychological aspects of rhinology patients' health, clinicians can improve overall treatment outcomes and patient well-being.

In conclusion, the diagnostic approach to psychiatric problems in rhinology patients involves a multi-faceted strategy that includes thorough assessment of psychological symptoms, utilization of standardized screening tools and questionnaires, comprehensive clinical interviews, and the integration of psychological assessments into routine care. By adopting these practices, clinicians can ensure a more holistic approach to patient care, addressing both the physical and mental health needs of rhinology patients.

5. Therapeutic strategies and interventions for psychiatric problems in rhinology patients

Addressing the psychiatric problems associated with rhinology diseases requires a multidisciplinary approach. Effective management integrates pharmacotherapy, surgical interventions, and psychological therapies to improve both physical and mental health outcomes. Here, we explore various therapeutic strategies and interventions tailored to rhinology patients experiencing psychological distress.

5.1 Pharmacotherapy

Pharmacotherapy plays a vital role in managing psychiatric symptoms in rhinology patients. Antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), are commonly prescribed to alleviate symptoms of depression and anxiety [76]. These medications can help stabilize mood, reduce anxiety, and improve overall quality of life and it should

prescribe under psychiatric. However, it is essential to prescribe these medications under psychiatric guidance, taking into account potential drug interactions. For instance, chlordiazepoxide, alprazolam zolpidem, amitriptyline, chlorpromazine, thioridazine, reserpine, and citalopram can induce rhinitis in some patients [77]. Notably, there is a lack of sufficient studies evaluating the pharmacotherapy effect on psychological symptoms in rhinology patients, highlighting the need for further research to improve this field and inform evidence-based treatment strategies.

Additionally, nasal corticosteroids and antihistamines can be beneficial in reducing the physical symptoms of rhinology diseases like AR, indirectly improving psychological well-being by alleviating discomfort and sleep issues. However, it is important to note that complete relief of rhinosinusitis symptoms may not fully alleviate the psychological aspects of these diseases. Patients with rhinitis can experience anxiety, depression, or cognitive problems even after successful treatment of physical symptoms or regardless of allergen seasonality. Therefore, ongoing therapy may be needed to address psychological symptoms even after physical symptoms have been managed [11, 78].

It is crucial to tailor pharmacotherapy to each patient's specific needs, taking into account any potential interactions between medications used for rhinological conditions and those prescribed for psychiatric symptoms. Consulting with a psychiatry specialist is important for selecting the appropriate treatment for these patients' unique conditions. This collaborative approach ensures that both the physical and mental health aspects of rhinology diseases are effectively managed.

5.2 Surgical interventions

Rhinoplasty significantly influences the psychological health of patients, as highlighted by various studies. Post-surgery, patients often report notable improvements in their social interactions and relationships. These enhancements are frequently linked to better self-perception and body image, leading to reduced body dissatisfaction and increased satisfaction with their nasal appearance. Such positive effects contribute to improved social functioning and are sustained over follow-up periods ranging from months to years [79].

The psychological benefits of rhinoplasty extend beyond physical changes, impacting several mental health areas. Research shows significant reductions in anxiety, depression, emotional distress, and body dysmorphia among rhinoplasty patients, as a study demonstrated a marked decrease in anxiety and depression levels at the 12-month follow-up, as measured by the Beck Depression Inventory [80]. Similarly, other study reported reductions in anxiety, social phobia, depression, and body dysmorphia [79]. These findings underscore the potential of rhinoplasty to alleviate psycho-social distress and enhance overall mental well-being.

Furthermore, rhinoplasty has been shown to improve patients' quality of life. Studies utilizing the Rhinoplasty Outcomes Evaluation (ROE) questionnaire, Body Image Inventory, and EuroQol 5D questionnaire have documented significant enhancements in quality of life post-surgery. These improvements are often attributed to better self-perception, enhanced body image, increased self-esteem, and greater social participation and confidence. However, some research indicates that while psychological improvements are significant, other quality of life aspects may remain unchanged. It is essential for surgeons to identify psychological risk factors during preoperative consultations and carefully select patients to prevent postoperative psychological complications. Utilizing screening tools like the Quality of

Life Scale Short Form (SF-36) questionnaire and general health questionnaire-28 (GHQ-28) can help identify at-risk patients, leading to better surgical outcomes [79, 81–83].

In patients with rhinosinusitis, surgical intervention may be useful in the early stages to prevent the development of psychological disorders. However, in the chronic and late phases of the disease, surgical procedures are generally less helpful, as neuroinflammation has a long-lasting disturbing effect on the central nervous system [4]. In cases where structural abnormalities in the nasal cavity contribute to both physical and psychological distress, surgical interventions can offer significant relief. Procedures such as septoplasty, turbinate reduction, and sinus surgery aim to correct anatomical issues that cause chronic nasal obstruction and sinusitis. By improving nasal airflow and reducing sinus infections, these surgeries can alleviate symptoms that contribute to poor sleep quality, fatigue, and subsequent psychological problems [35, 37].

Post-surgical improvements in breathing and reduction in chronic pain or discomfort can lead to significant enhancements in mental health, as patients experience fewer physical symptoms that exacerbate their psychological distress. It is important for surgeons to collaborate closely with mental health professionals to monitor and support the patient's psychological recovery post-surgery.

5.3 Psychological interventions

Psychological interventions are essential components of a comprehensive treatment plan for rhinology patients with psychiatric problems. These interventions address the mental health issues directly, helping patients develop coping strategies and resilience against the psychological impact of their physical conditions.

Cognitive-Behavioral Therapy (CBT) is a widely used and evidence-based psychological treatment for depression, anxiety, and other mental health issues. CBT helps patients identify and challenge negative thought patterns and behaviors, replacing them with more positive and constructive ones. For rhinology patients, CBT can be particularly effective in managing health-related anxiety, improving mood, and enhancing coping mechanisms for dealing with chronic symptoms and their impact on daily life [84].

5.4 Support groups and counseling

Support groups and counseling provide essential emotional and social support for rhinology patients experiencing psychological distress. Support groups offer a platform for patients to share their experiences, gain insights, and receive encouragement from others facing similar challenges. This peer support can alleviate feelings of isolation and promote a sense of community and understanding.

Individual or group counseling with a licensed therapist can provide a safe space for patients to explore their emotions, develop coping strategies, and address any underlying mental health issues. Counseling sessions can focus on specific areas of concern, such as coping with chronic illness, managing stress, and improving interpersonal relationships.

Integrating these therapeutic strategies and interventions into the care of rhinology patients requires a collaborative approach among healthcare providers. By addressing both the physical and psychological aspects of rhinology diseases, patients can achieve better health outcomes and an improved quality of life.

6. Summary

Addressing psychological issues in patients with rhinological disorders is crucial for improving their overall quality of life. Integrating psychological assessment and support into both medical and surgical management plans can lead to better patient outcomes, enhanced satisfaction, and reduced complications. This comprehensive approach acknowledges the significant interplay between physical symptoms and mental health, ultimately fostering holistic patient care.

Incorporating psychological assessments into the preoperative and postoperative phases of rhinological care ensures that patients' mental health needs are identified and addressed. Preoperative psychological evaluations can help identify patients at risk for anxiety, depression, and body dysmorphic disorder, which are common in individuals seeking rhinoplasty or other nasal surgeries. By recognizing these issues early, healthcare providers can offer appropriate interventions such as counseling, therapy, or medication, thus preparing patients mentally and emotionally for surgery. This proactive approach can mitigate postoperative dissatisfaction and the desire for unnecessary revision surgeries, thereby improving patient satisfaction and outcomes.

Integrating psychological support into the treatment plan for medical management of rhinological disorders, such as chronic rhinosinusitis or allergic rhinitis, can significantly enhance quality of life. Patients with chronic nasal conditions often experience a diminished quality of life due to persistent symptoms like nasal obstruction, facial pain, and impaired sense of smell, which can lead to anxiety and depression. Providing psychological support alongside medical treatments can help patients cope better with their symptoms, adhere more effectively to treatment regimens, and experience an overall improvement in their mental and physical well-being. This dual approach ensures that both the physical and psychological aspects of their condition are addressed, leading to a more comprehensive and effective treatment outcome.

Lastly, incorporating psychological care into the surgical management plan of rhinology patients can reduce perioperative stress and enhance recovery. Educating patients about the surgical process, setting realistic expectations, and providing postoperative psychological support can alleviate anxiety and promote a smoother recovery. Postoperatively, continued psychological support can help patients adapt to changes in their appearance and function, fostering a positive adjustment and long-term satisfaction with the surgical results.

In conclusion, addressing psychological issues in patients with rhinological disorders through integrated medical and surgical management plans can significantly improve their quality of life. This comprehensive approach not only enhances patient satisfaction and outcomes but also underscores the importance of treating the whole patient, not just their physical symptoms. By recognizing and addressing the psychological dimensions of rhinology disorders, healthcare providers can offer more effective, holistic care that leads to better overall health and well-being for their patients.

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References

[1] Schlosser RJ, Storck K, Cortese BM, Uhde TW, Rudmik L, Soler ZM. Depression in chronic rhinosinusitis: A controlled cohort study. American Journal of Rhinology & Allergy. 2016;**30**(2):128-133

[2] Lin S, Nie M, Wang B, Duan S, Huang Q, Wu N, et al. Intrinsic brain abnormalities in chronic rhinosinusitis associated with mood and cognitive function. Frontiers in Neuroscience. 2023;**17**:1131114

[3] Vogt F, Sahota J, Bidder T, Livingston R, Bellas H, Gane SB, et al. Chronic rhinosinusitis with and without nasal polyps and asthma: Omalizumab improves residual anxiety but not depression. Clinical and Translational Allergy. 2021;**11**(1):e12002

[4] Kim JY, Ko I, Kim MS, Yu MS, Cho BJ, Kim DK. Association of chronic rhinosinusitis with depression and anxiety in a nationwide insurance population. JAMA Otolaryngology Head & Neck Surgery. 2019;**145**(4):313-319

[5] Mou YK, Wang HR, Zhang WB, Zhang Y, Ren C, Song XC. Allergic rhinitis and depression: Profile and proposal. Frontiers in Psychiatry. 2021;**12**:820497

[6] Roxbury CR, Qiu M, Shargorodsky J, Woodard TD, Sindwani R, Lin SY. Association between rhinitis and depression in United States adults. The Journal of Allergy and Clinical Immunology in Practice. 2019;**7**(6):2013-2020

[7] Begemann MJH, Linszen MMJ, de Boer JN, Hovenga WD, Gangadin SS, Schutte MJL, et al. Atopy increases risk of psychotic experiences: A large population-based study. Frontiers in Psychiatry. 2019;**10**:453

[8] Bedolla-Barajas M, Morales-Romero J, Pulido-Guillén NA, Robles-Figueroa M, Plascencia-Domínguez BR. Rhinitis as an associated factor for anxiety and depression amongst adults. Brazilian Journal of Otorhinolaryngology. 2017;**83**(4):432-438

[9] Chen M-H, Lan W-H, Hsu J-W, Huang K-L, Chen Y-S, Li C-T, et al. Risk of bipolar disorder among adolescents with allergic rhinitis: A nationwide longitudinal study. Journal of Psychosomatic Research. 2015;**79**(6):533-536

[10] Simons FE. Learning impairment and allergic rhinitis. Allergy and Asthma Proceedings. 1996;**17**(4):185-189

[11] Blaiss MS, Hammerby E, Robinson S, Kennedy-Martin T, Buchs S. The burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents: A literature review. Annals of Allergy, Asthma & Immunology. 2018;**121**(1):43-52.e3

[12] Chirakalwasan N, Ruxrungtham K. The linkage of allergic rhinitis and obstructive sleep apnea. Asian Pacific Journal of Allergy and Immunology. 2014;**32**(4):276-286

[13] Liu J, Zhang X, Zhao Y, Wang Y. The association between allergic rhinitis and sleep: A systematic review and meta-analysis of observational studies. PLoS One. 2020;**15**(2):e0228533

[14] Marin C, Alobid I, Fuentes M, López-Chacón M, Mullol J. Olfactory dysfunction in mental illness. Current Allergy and Asthma Reports. 2023;**23**(3):153-164

[15] Lombion-Pouthier S, Vandel P, Nezelof S, Haffen E, Millot JL. Odor perception in patients with mood disorders. Journal of Affective Disorders. 2006;**90**(2-3):187-191

[16] Chen X, Guo W, Yu L, Luo D, Xie L, Xu J. Association between anxious symptom severity and olfactory impairment in young adults with generalized anxiety disorder: A case-control study. Neuropsychiatric Disease and Treatment. 2021;**17**:2877-2883

[17] Burón E, Bulbena A, Bulbena-Cabré A. Olfactory functioning in panic disorder. Journal of Affective Disorders. 2015;**175**:292-298

[18] Clepce M, Reich K, Gossler A, Kornhuber J, Thuerauf N. Olfactory abnormalities in anxiety disorders. Neuroscience Letters. 2012;**511**(1):43-46

[19] Negoias S, Croy I, Gerber J, Puschmann S, Petrowski K, Joraschky P, et al. Reduced olfactory bulb volume and olfactory sensitivity in patients with acute major depression. Neuroscience. 2010;**169**(1):415-421

[20] Kazour F, Richa S, Abi Char C, Surget A, Elhage W, Atanasova B. Olfactory markers for depression: Differences between bipolar and unipolar patients. PLoS One. 2020;**15**(8):e0237565

[21] Naudin M, El-Hage W, Gomes M, Gaillard P, Belzung C, Atanasova B. State and trait olfactory markers of major depression. PLoS One. 2012;**7**(10):e46938

[22] Zucco GM, Bollini F. Odour recognition memory and odour identification in patients with mild and severe major depressive disorders. Psychiatry Research. 2011;**190**(2-3):217-220

[23] Pabel LD, Hummel T, Weidner K, Croy I. The impact of severity, course and duration of depression on olfactory function. Journal of Affective Disorders. 2018;**238**:194-203

[24] Atanasova B, El-Hage W, Chabanet C, Gaillard P, Belzung C, Camus V. Olfactory anhedonia and negative olfactory alliesthesia in depressed patients. Psychiatry Research. 2010;**176**(2-3):190-196

[25] Chen B, Klarmann R, Israel M, Ning Y, Colle R, Hummel T. Difference of olfactory deficit in patients with acute episode of schizophrenia and major depressive episode. Schizophrenia Research. 2019;**212**:99-106

[26] Swiecicki L, Zatorski P, Bzinkowska D, Sienkiewicz-Jarosz H, Szyndler J, Scinska A. Gustatory and olfactory function in patients with unipolar and bipolar depression. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2009;**33**(5):827-834

[27] Hasegawa Y, Ma M, Sawa A, Lane AP, Kamiya A. Olfactory impairment in psychiatric disorders: Does nasal inflammation impact disease psychophysiology? Translational Psychiatry. 2022;**12**(1):314

[28] Bochicchio V, Mezzalira S, Maldonato NM, Cantone E, Scandurra C. Olfactory-related quality of life impacts psychological distress in people with COVID-19: The affective implications of olfactory dysfunctions. Journal of Affective Disorders. 2023;**323**:741-747

[29] Othman BA, Maulud SQ, Jalal PJ, Abdulkareem SM, Ahmed JQ, Dhawan M, et al. Olfactory dysfunction as a post-infectious symptom of SARS-CoV-2 infection. Annals of Medicine and Surgery (London). 2022;**75**:103352

[30] Fidan T, Fidan V, Ak M, Sütbeyaz Y. Neuropsychiatric symptoms, quality

of sleep and quality of life in patients diagnosed with nasal septal deviation. Kulak Burun Boğaz Ihtisas Dergisi. 2011;**21**(6):312-317

[31] Magliulo G, Iannella G, Ciofalo A, Polimeni A, De Vincentiis M, Pasquariello B, et al. Nasal pathologies in patients with obstructive sleep apnoea. Acta Otorhinolaryngologica Italica. 2019;**39**(4):250-256

[32] Rezaeitalab F, Moharrari F, Saberi S, Asadpour H, Rezaeetalab F. The correlation of anxiety and depression with obstructive sleep apnea syndrome. Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences. 2014;**19**(3):205-210

[33] Su VY, Chen YT, Lin WC, Wu LA, Chang SC, Perng DW, et al. Sleep Apnea and risk of panic disorder. Annals of Family Medicine. 2015;**13**(4):325-330

[34] Yıldırım YS, Deveci E, Ozucer B, Kurt Y. Nasal obstruction in adults: How it affects psychological status? The Journal of Laryngology & Otology. 2024;**138**(2):184-187

[35] Katamanin O, Saini S, Jafferany M. Psychological implications and quality of life after cosmetic rhinoplasty: A systematic review. Discover Psychology. 2024;**4**(1):16

[36] Schoustra E, van Maanen P, den Haan C, Ravesloot MJL, de Vries N. The role of isolated nasal surgery in obstructive sleep Apnea therapy-A systematic review. Brain Sciences. 26 Oct 2022;**12**(11):1446

[37] Marcus P. Psychological aspects of cosmetic rhinoplasty. British Journal of Plastic Surgery. 1984;**37**(3):313-318

[38] Mousavi N, Molaei A, Alesaeidi S, Eftekhari Seas N, Effatpanah M. Prevalence of psychiatric disorders among patients with granulomatosis with polyangiitis (Wegener's) and the predictive role of personality traits. Clinical Practice and Epidemiology in Mental Health. 2024;**20**:e17450179276345

[39] Peeters L, Igodt P. Acute psychiatric symptomatology in Wegener's granulomatosis. Tijdschrift voor Psychiatrie. 2006;**48**(4):325-329

[40] Shrivastava A, Jain S, Damaraju V, Naidu G, Dhir V, Rathi M, et al. Severity and determinants of psychosocial comorbidities in granulomatosis with polyangiitis and their impact on quality of life. Rheumatology International. 2023;**43**(8):1467-1477

[41] Koutantji M, Pearce S, Harrold E. Psychological aspects of vasculitis. Rheumatology (Oxford, England). 2000;**39**(11):1173-1179

[42] Marin C, Alobid I, López-Chacón M, VanStrahlen CR, Mullol J. Type 2 and non-type 2 inflammation in the upper airways: Cellular and molecular alterations in olfactory neuroepithelium cell populations. Current Allergy and Asthma Reports. 2024;**24**(4):211-219

[43] Seals MR, Moran MM, Leavenworth JD, Leavenworth JW. Contribution of dysregulated B-cells and IgE antibody responses to multiple sclerosis. Frontiers in Immunology. 2022;**13**:900117

[44] Rosenwasser LJ. Mechanisms of IgE inflammation. Current Allergy and Asthma Reports. 2011;**11**(2):178-183

[45] Ratzlaff RE, Cavanaugh VJ, Miller GW, Oakes SG. Evidence of a neurogenic component during IgE-mediated inflammation in mouse skin. Journal of Neuroimmunology. 1992;**41**(1):89-96

[46] Cui H, Liu F, Fang Y, Wang T, Yuan B, Ma C. Neuronal FcεRIα directly mediates ocular itch via IgE-immune complex in a mouse model of allergic conjunctivitis. Journal of Neuroinflammation. 2022;**19**(1):55

[47] Liu F, Xu L, Chen N, Zhou M, Li C, Yang Q, et al. Neuronal Fc-epsilon receptor I contributes to antigen-evoked pruritus in a murine model of ocular allergy. Brain, Behavior, and Immunity. 2017;**61**:165-175

[48] Crosson T, Wang JC, Doyle B, Merrison H, Balood M, Parrin A, et al. FcεR1-expressing nociceptors trigger allergic airway inflammation. The Journal of Allergy and Clinical Immunology. 2021;**147**(6):2330-2342

[49] Ebrahim Soltani Z, Badripour A, Haddadi NS, Elahi M, Kazemi K, Afshari K, et al. Allergic rhinitis in BALB/c mice is associated with behavioral and hippocampus changes and neuroinflammation via the TLR4/NF-κB signaling pathway. International Immunopharmacology. 2022;**108**:108725

[50] Elahi M, Ebrahim Soltani Z, Afrooghe A, Ahmadi E, Dehpour AR. Sex dimorphism in pain threshold and neuroinflammatory response: The protective effect of female sexual hormones on behavior and seizures in an allergic rhinitis model. Journal of Neuroimmune Pharmacology. 2024;**19**(1):16

[51] Yeh CF, Huang WH, Lan MY, Hung W. Lipopolysaccharide-initiated rhinosinusitis causes neuroinflammation and olfactory dysfunction in mice. American Journal of Rhinology & Allergy. 2023;**37**(3):298-306

[52] Klein R, Soung A, Sissoko C, Nordvig A, Canoll P, Mariani M, et al. COVID-19 induces neuroinflammation and loss of hippocampal neurogenesis. Research Square. 29 Oct 2021:rs.3.rs-1031824 [Preprint]

[53] Vanderheiden A, Klein RS. Neuroinflammation and COVID-19. Current Opinion in Neurobiology. 2022;**76**:102608

[54] Bornand D, Toovey S, Jick SS, Meier CR. The risk of new onset depression in association with influenza–A population-based observational study. Brain, Behavior, and Immunity. 2016;**53**:131-137

[55] Su CY, Menuz K, Carlson JR. Olfactory perception: Receptors, cells, and circuits. Cell. 2009;**139**(1):45-59

[56] Imamura F, Ito A, LaFever BJ. Subpopulations of projection neurons in the olfactory bulb. Frontiers in Neural Circuits. 2020;**14**:561822

[57] Krusemark EA, Novak LR, Gitelman DR, Li W. When the sense of smell meets emotion: Anxiety-state-dependent olfactory processing and neural circuitry adaptation. The Journal of Neuroscience. 2013;**33**(39):15324-15332

[58] Ressler KJ. Amygdala activity, fear, and anxiety: Modulation by stress. Biological Psychiatry. 2010;**67**(12):1117-1119

[59] Milad MR, Rauch SL. The role of the orbitofrontal cortex in anxiety disorders. Annals of the New York Academy of Sciences. 2007;**1121**:546-561

[60] Nguyen AD, Shenton ME, Levitt JJ. Olfactory dysfunction in schizophrenia: A review of neuroanatomy and psychophysiological measurements. Harvard Review of Psychiatry. 2010;**18**(5):279-292

[61] Gao Z, Lv H, Wang Y, Xie Y, Guan M, Xu Y. TET2 deficiency promotes anxiety and depression-like behaviors by activating NLRP3/IL-1β pathway in microglia of allergic rhinitis mice. Molecular Medicine. 2023;**29**(1):160

[62] Rodrigues J, Rocha MI, Teixeira F, Resende B, Cardoso A, Sá SI, et al. Structural, functional and behavioral impact of allergic rhinitis on olfactory pathway and prefrontal cortex. Physiology & Behavior. 2023;**265**:114171

[63] Tian J, Kaufman DL. The GABA and GABA-receptor system in inflammation, anti-tumor immune responses, and COVID-19. Biomedicines. 18 Jan 2023;**11**(2):254

[64] Luscher B, Shen Q, Sahir N. The GABAergic deficit hypothesis of major depressive disorder. Molecular Psychiatry. 2011;**16**(4):383-406

[65] Bali V, Simmons SC, Manning CE, Doyle MA, Rodriguez M, Stark AR, et al. Characterization of proinflammatory markers in the ventral tegmental area across mouse models of chronic stress. Neuroscience. 2021;**461**:11-22

[66] Strazdins E, Nie YF, Ramli R, Palesy T, Christensen JM, Marcells GN, et al. Association of mental health status with perception of nasal function. Journal of the American Medical Association Facial Plastic Surgery. 2017;**19**(5):369-377

[67] Rodrigues J, Franco-Pego F, Sousa-Pinto B, Bousquet J, Raemdonck K, Vaz R. Anxiety and depression risk in patients with allergic rhinitis: A systematic review and meta-analysis. Rhinology. 2021;**59**(4):360-373

[68] Chang F, Hong J, Yuan F, Wu D. Association between cognition and olfaction-specific parameters in patients with chronic rhinosinusitis. European Archives of Oto-Rhino-Laryngology. 2023;**280**(7):3249-3258

[69] Upton J. Beck depression inventory (BDI). In: Gellman MD, Turner JR, editors. Encyclopedia of Behavioral Medicine. New York, NY: Springer New York; 2013. pp. 178-179

[70] Rodrigues J, Pinto JV, Alexandre PL, Sousa-Pinto B, Pereira AM, Raemdonck K, et al. Allergic rhinitis seasonality, severity, and disease control influence anxiety and depression. The Laryngoscope. 2023;**133**(6):1321-1327

[71] Xu K, Linton S, Sunavsky A, Garvey S, Botting H, Steacy LM, et al. Anxiety in adults with allergic rhinitis during the coronavirus disease 2019 pandemic: A Canadian perspective. Annals of Allergy, Asthma & Immunology. 2022;**129**(5):627-634

[72] Vandelaar LJ, Jiang ZY, Saini A, Yao WC, Luong AU, Citardi MJ. PHQ-9 and SNOT-22: Elucidating the prevalence of depression in chronic rhinosinusitis. Otolaryngology and Head and Neck Surgery. 2020;**162**(1):142-147

[73] Farhood Z, Schlosser RJ, Pearse ME, Storck KA, Nguyen SA, Soler ZM. Twenty-two-item sino-nasal outcome test in a control population: A cross-sectional study and systematic review. International Forum of Allergy & Rhinology. 2016;**6**(3):271-277

[74] Quintana GR, Ponce FP, Escudero-Pastén JI, Santibáñez-Palma JF, Nagy L, Koós M, et al. Cross-cultural validation and measurement invariance of anxiety and depression symptoms: A study of the brief symptom inventory (BSI) in 42 countries. Journal of Affective Disorders. 2024;**350**:991-1006

[75] Mou YK, Wang HR, Zhang WB, Zhang Y, Ren C, Song XC. Allergic rhinitis and depression: Profile and proposal. Frontiers in Psychiatry. 4 Jan 2022;**12**:820497

[76] Gorman JM, Kent JM. SSRIs and SNRIs: Broad spectrum of efficacy beyond major depression. The Journal of Clinical Psychiatry. 1999;**60**(Suppl. 4):33-38; discussion 9

[77] Alromaih S, Alsagaf L, Aloraini N, Alrasheed A, Alroqi A, Aloulah M, et al. Drug-induced rhinitis: Narrative review. Ear, Nose & Throat Journal. 15 Nov 2022:1455613221141214

[78] Muñoz-Cano R, Ribó P, Araujo G, Giralt E, Sanchez-Lopez J, Valero A. Severity of allergic rhinitis impacts sleep and anxiety: Results from a large Spanish cohort. Clinical and Translational Allergy. 2018;**8**:23

[79] Margraf J, Meyer AH, Lavallee KL. Well-being from the knife? Psychological effects of aesthetic surgery. Clinical Psychological Science. 2013;**1**(3):239-252

[80] Moss TP, Harris DL. Psychological change after aesthetic plastic surgery: A prospective controlled outcome study. Psychology, Health & Medicine. 2009;**14**(5):567-572

[81] Kucur C, Kuduban O, Ozturk A, Gozeler MS, Ozbay I, Deveci E, et al. Psychological evaluation of patients seeking rhinoplasty. The Eurasian Journal of Medicine. 2016;**48**(2):102-106

[82] Piromchai P, Suetrong S, Arunpongpaisal S. Psychological status in patients seeking rhinoplasty. Clinical Medicine Insights. Ear, Nose and Throat. 2011;**4**:31-35

[83] Mahmoudi S, Zadeh MR. Development and validation of the Rhinoplasty outcomes evaluation (ROE) questionnaire: An analytical study. World Journal of Plastic Surgery. 2022;**11**(2):68-74

[84] White CA. Cognitive behavioral principles in managing chronic disease. The Western Journal of Medicine. 2001;**175**(5):338-342

Chapter 5

Frontal Sinus Malignancy

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Abstract

Frontal sinus malignancy, though relatively rare compared to malignancies in other anatomical regions, presents unique challenges in diagnosis, treatment and management. These tumours can arise *de novo* within the frontal sinus or extend from adjacent structures, and their proximity to vital anatomical landmarks, such as the orbit, cranial fossa and critical vascular structures, complicates surgical intervention. This chapter delves into the anatomical intricacies of the frontal sinus, the various classifications of frontal sinus cells and tumours, and the diagnostic modalities, including contemporary molecular and genetic markers that are crucial for effective treatment planning. It explores the historical evolution of surgical techniques, highlighting the shift from invasive procedures to advanced endoscopic methods that offer enhanced visualisation and precision. This chapter also describes different forms of adjuvant treatment, such as external beam radiotherapy, proton and carbon ion therapy, chemotherapy and targeted/immune therapy.

Keywords: primary frontal sinus carcinoma, sinonasal undifferentiated carcinoma, frontal sinus carcinoma T staging, IDH2 mutation, Riedel-Schenke's procedure, endoscopic craniofacial resection, intensity-modulated proton therapy, carbon ion therapy, tislelizumab

1. Introduction

Frontal sinus malignancy, though relatively rare compared to malignancies in other anatomical regions, presents unique challenges in diagnosis, treatment and management. These tumours can arise *de novo* within the frontal sinus or extend from adjacent structures, and their proximity to vital anatomical landmarks, such as the orbit, cranial fossa and critical vascular structures, complicates surgical intervention.

The frontal sinus is distinguished by its developmental timeline, not being present at birth and maturing through childhood into early adolescence. Its complex anatomy, including variations in pneumatization and drainage pathways, underscores the necessity for precise imaging and detailed anatomical knowledge before any surgical approach.

Historically, the management of frontal sinus disease, including malignancies, has evolved significantly. From the early radical approaches involving extensive resections and external access to the modern minimally invasive endoscopic techniques,

each phase has contributed to the current understanding and strategies employed in treating frontal sinus tumours.

This chapter delves into the anatomical intricacies of the frontal sinus, the various classifications of frontal sinus cells and tumours, and the diagnostic modalities crucial for effective treatment planning. It also explores the historical evolution of surgical techniques, highlighting the shift from invasive procedures to advanced endoscopic methods that offer enhanced visualisation and precision.

By examining the anatomical, pathological and surgical aspects of frontal sinus tumours, this chapter aims to provide a comprehensive overview for clinicians, aiding in the accurate diagnosis and effective management of these challenging cases.

2. Anatomy

Anatomical variations in the sinuses are common and can obstruct ventilation and drainage, leading to medication-resistant osteomeatal complex disease. Preoperative CT (computed tomography) scans of the paranasal sinuses are essential for identifying these variations and their proximity to vital structures like the orbit, skull base and important blood vessels, helping prevent surgical injuries.

The frontal sinus is the only sinus not present at birth, starting its development around age 2. It reaches the orbital roof between ages 5 and 7 and attains adult size by age 12. Each frontal sinus, positioned in the frontal bone separated by a bony septum, develops independently, often resulting in asymmetrical pneumatization, with one sinus typically crossing the midline and overlapping the other.

The frontal sinus walls are known as the outer and inner tables. The outer table is robust, while the inner table is a thin bony plate separating the sinus from the cranial fossa. Venous channels, called the foramina of Breschet, are found in the inner table and can allow sinus infections to spread to the brain. These foramina also serve as sites where mucosa can invaginate into the bone, potentially leading to mucocoele if not entirely removed during surgery.

The drainage of the frontal sinus is managed through the ostium located at the posteromedial part of the sinus floor, featuring an hourglass shape. This ostium lies within the frontal beak, a projection of the maxilla. The ostium's size and patency depend on the thickness of this beak. A large agger nasi cell results in a smaller beak and a wider ostium, while a small agger nasi cell leads to a more prominent beak and a narrower ostium. Additionally, a large agger nasi cell can obstruct the drainage pathway at the frontal recess [1].

Frontal sinuses can be underdeveloped (hypoplastic) in about 4% of people or absent (aplasia) in about 5%. They may also contain air cells extending from the ethmoidal sinus, known as frontoethmoidal cells, classified as follows [2]:

Type 1 frontal cell: A single cell above the agger nasi but below the frontal ostium.

Type 2 frontal cells: Two or more cells above the agger nasi but below the frontal ostium.

Type 3 frontal cell: A single cell extending from above the agger nasi into the frontal sinus but not exceeding 50% of its vertical height.

Type 4 frontal cell: A single cell extending into the frontal sinus, exceeding 50% of its vertical height, or an isolated cell within the frontal sinus.

Another variation is the frontal bullar cell, which extends from the suprabullar region into the frontal sinus along the posterior wall of the frontal recess. Unlike the suprabullar cell, it extends into the frontal sinus. Its anterior wall relates to the frontal

Cell type	Cell name	Definition
Anterior cells (push the drainage pathway of the frontal sinus medial, posteriorly or posteromedially)	Agger nasi cell	Cell that either sits anterior to the origin of the middle turbinate or sits directly above the most anterior insertion of the middle turbinate into the lateral nasal wall.
	Supra agger cell	Anterior-lateral ethmoidal cell, located above the agger nasi cell (not pneumatizing into the frontal sinus).
	Supra agger frontal cell (SAFC)	Anterior-lateral ethmoidal cell that extends into the frontal sinus. A small SAFC will only extend into the floor of the frontal sinus, whereas a large SAFC may extend significantly into the frontal sinus and may even reach the roof of the frontal sinus.
Posterior cells (push the drainage pathway anteriorly)	Supra-bulla cell	Cell above the bulla ethmoidalis that does not enter the frontal sinus.
	Supra-bulla frontal cell	Cell that originates in the supra-bulla region and pneumatizes along the skull base into the posterior region of the frontal sinus. The skull base forms the posterior wall of the cell.
	Supraorbital ethmoid cell	An anterior ethmoid cell that pneumatizes around, anterior to or posterior to the anterior ethmoidal artery over the roof of the orbit. It often forms part of the posterior wall of an extensively pneumatized frontal sinus and may only be separated from the frontal sinus by a bony septation.

Table 1.
The International Frontal Sinus Anatomy Classification (IFAC) [3].

sinus, while the posterior wall is adjacent to the anterior cranial fossa, requiring caution during surgery to avoid damaging the anterior skull base. The frontal intersinus septal cell, a pneumatized intersinus septum, may communicate with one or both frontal sinuses or exist as an isolated air cell, potentially obstructing the frontal sinus ostium.

Recent new classification of frontoethmoidal air cells is known as the International Frontal Sinus Anatomy Classification (IFAC), which was published in 2016. It has also classified the extent of endoscopic frontal sinus surgery (**Table 1**) [3].

Lymphatics of frontal sinus drain through lymphatic channel that drains skin and nasal cavity. Therefore, spread to periparotid, perifacial and submandibular lymph nodes is common. In the absence of skin involvement, locoregional spread to lymphatics is rare (10–15%). Distant metastasis is approximately 10% at the time of presentation [4].

3. Aetiology

Predisposing factors for development of primary frontal sinus carcinoma are unclear. However, in most of the instances contiguous spread of ethmoid, nasal or maxillary carcinoma is the cause of frontal sinus involvement. Moreover, lining mucosa of paranasal sinus is continuing throughout all sinuses. Therefore, it is assumed that carcinogenic agents responsible for development of ethmoid, nasal or maxillary sinus carcinoma are also a causative factor for development of frontal sinus carcinoma [5–8]. Distant metastasis of primary from kidney, lung, breast or prostate can involve frontal or frontoethmoidal sinus but it is very rare [9].

4. Age & sex

Due to rarity of primary frontal sinus malignancies, it is difficult to estimate age and sex predilection. However, these malignancies occur in late adulthood or elderly. Males are affected 1.7 times more than females [10].

5. Symptoms & signs

Most common presentations are forehead or medial upper eyelid swelling and pain, which are seen in the majority of patients. Diplopia and proptosis are seen in one quarter to half of the patients. Physical examination should include thorough head and neck examination, with special attention to periparotid and cervical nodes (**Figure 1**). Neurological examination including cranial nerve examination should also be done.

6. Pathology

Primary frontal sinus malignancy is extremely rare [11, 12]. In most of the instances, frontal sinus is involved by contiguous spread from nasal cavity or ethmoidal malignancy. WHO's (World Health Organisation) latest pathology classification for sinonasal tumours was published in 2022 [13]. Sinonasal pathologies (benign and malignant), which can affect any of the paranasal sinuses and skull base, are divided into hamartomatous, respiratory epithelial carcinoma, mesenchymal and other tumours. Respiratory epithelial carcinoma is the most common type as far as malignant tumours are concerned and others are rare. Osteoma is a common benign tumour that frequently affects frontal sinus; however, WHO presently classifies this under osteogenic tumours (**Table 2**).

Due to very low incidence of sinonasal malignancies, it is difficult to comment upon the most common site of origin for sinonasal malignant pathologies, except for

Figure 1.
Patient presented with swelling of forehead medial to right brow and medial canthus which is causing diplopia.

Diagnostic group	Category	Diagnostic entity section
Hamartomas		• Respiratory epithelial adenomatoid hamartoma
		• Seromucinous hamartoma
		• Nasal chondromesenchymal hamartoma
Respiratory epithelial lesions	Sinonasal papillomas	• Sinonasal papilloma, inverted type
		• Sinonasal papilloma, oncocytic type
		• Sinonasal papilloma, exophytic type
	Carcinomas	• Keratinizing squamous cell carcinoma
		• Non-keratinizing squamous cell carcinoma
		• NUT carcinoma
		• SWI/SNF complex-deficient sinonasal carcinoma
		• Sinonasal lymphoepithelial carcinoma
		• Sinonasal undifferentiated carcinoma
		• Teratocarcinosarcoma
		• HPV-related multiphenotypic sinonasal carcinoma
	Adenocarcinoma	• Intestinal-type adenocarcinoma of the sinonasal tract
		• Non-intestinal-type sinonasal adenocarcinoma
Mesenchymal tumours of sinonasal tract		• Sinonasal tract angiofibroma
		• Sinonasal glomangiopericytoma
		• Biphenotypic sinonasal sarcoma
		• Chordoma
Other tumours		• Sinonasal ameloblastoma
		• Adamantinomatous craniopharyngioma
		• Meningioma of sinonasal tract
		• Olfactory neuroblastoma

Abbreviations: NUT- nuclear protein in testes, SWI/SNF- SWItch/sucrose non-fermentable, HPV- human papilloma virus.

Table 2.
5th edition of the World Health Organisation (WHO) classification of tumours of the nasal cavity, paranasal sinuses, and skull base [13].

respiratory epithelial carcinoma that is most commonly originated from maxillary sinus or nasal cavity. Hence, primary involvement of frontal sinus by WHO-classified pathologies is extremely rare [10, 12, 14–16].

Bhojwani et al. conducted an analysis of all the frontal sinus malignancy cases reported between 1973 and 2012. They found that most common histologies involving frontal sinus were squamous cell carcinomas (SCCs) followed by mature B-cell NHL (non-Hodgkin's lymphoma), epithelial carcinomas NOS (not otherwise specified) and adenocarcinomas [10]. Another systematic review showed squamous cell carcinoma as the most common pathology, followed by mucosal melanoma and poorly differentiated carcinoma (neuroendocrine carcinoma or sinonasal undifferentiated carcinoma) [16].

7. Staging of frontal sinus carcinoma

The involvement of frontal sinus in primary carcinoma of maxillary, ethmoid or nasal cavity is classified as T4a according to AJCC (American Joint Committee on Cancer) 8th edition. Frontal sinus carcinoma has not been classified separately in AJCC TNM (tumour, node and metastasis) staging system. There are other classification systems that exist, such as the University of Florida classification system for sinonasal malignancies and classification for frontal inverted papillomas [15, 17].

University of Florida staging system for nasal cavity, frontal sinus and sphenoid sinus.

Stage 1- Tumours limited to the site of origin.

Stage 2- Extension to adjacent sites (orbit, paranasal sinuses, skin, nasopharynx, pterygomaxillary fossa).

Stage 3- Base of skull or pterygoid plates' erosion and/or intracranial extension.

Here, we are proposing a T classification for primary frontal sinus carcinoma. This might prove useful in clinical staging of these tumours. However, this needs validation with further studies.

Frontal sinus carcinoma T staging (our proposal)

T staging.

T1 – Limited to frontal sinus mucosa and/or inferior mucosal extension till frontal os with no bony involvement [Extenstion of tumor beyond frontal ostium will involve ethmoid sinus mucosa].

T2 - Involvement of frontal sinus mucosa with bony erosion of at least one (ant table, post table, orbital roof, interfrontal septum) or mucosal spread to anterior ethmoid air cells.

T3- Involvement of dura mater, periorbita, skin and subcutaneous tissue, nasal septum or nasal bone, posterior ethmoid air cells, lateral nasal wall, maxillary sinus, hard palate.

T4 Involvement of subdural space or brain, orbit, sphenoid sinus, nasopharynx, pterygoid plates and muscles, Internal Carotid Artery (ICA).

8. Pathological diagnosis

Histopathological diagnosis of sinonasal carcinoma is difficult, owing to rarity, overlapping features with other malignancies and a wide variety of pathological entities which affect the sinonasal region [13]. Preoperative pathology and postoperative histopathology often have discrepancies [18]. Immunohistochemistry is often required to narrow down the diagnosis (**Figure 2**).

9. Molecular diagnosis and genetic mutations

In recent years, there has been significant development in research as far as molecular diagnosis of sinonasal tumours is concerned. In the last decade, numerous studies have come up describing the role of genetic mutations in sinonasal carcinoma. With increasing molecular testing, new subtypes of tumours have been identified. These subtypes have been identified based on genetic alterations, such as specific gene mutations, chromosomal translocations, specific protein expression and infection by oncogenic virus (**Table 3**) [19–30].

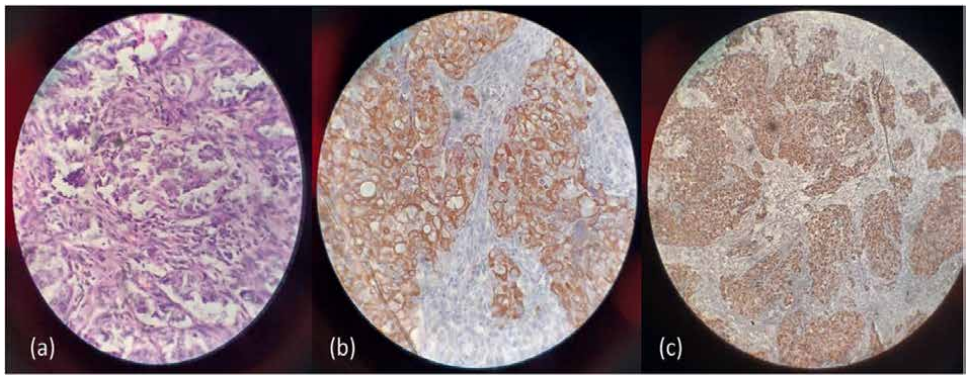

Figure 2.
(a) sheets of undifferentiated pleomorphic malignant epithelial cells on H&E 100X (b) CK7 positivity (c) CKAE1/CKAE3 positivity consistent with diagnosis of sinonasal undifferentiated carcinoma.

Sinonasal CA subtype	Biomarker	Type
Olfactory neuroblastoma	Methylation classifier	Diagnostic
Sinonasal melanoma	NRAS and KIT	Therapeutic
SNUC	IDH2 mutation	Diagnostic
NUT midline carcinoma	Translocation of gene encoding NUTM1	Diagnostic
Neuroendocrine carcinoma	Insulinoma-associated protein 1	Diagnostic
Sinonasal adenocarcinoma	KRAS	Therapeutic
Sinonasal SCC	EGFR, TrkB, TIL	Therapeutic and prognostic

Abbreviations: SNUC-sinonasal undifferentiated carcinoma, NUT- nuclear protein in testes, SCC- squamous cell carcinoma, NRAS- neuroblastoma ras viral oncogene homologue, KIT-tyrosine protein kinase, IDH-isocitrate dehydrogenase, KRAS- Kirsten rat sarcoma viral oncogene homologue, EGFR- epidermal growth factor receptor, TrkB-tropomyosin receptor kinase B, TIL-tumour-infiltrating lymphocytes, NUTM1- NUT Midline Carcinoma Family Member 1.

Table 3.
Recent biomarkers and therapeutic targets [19].

Taverna et al. have extensively studied the role of molecular markers in the causation of all types of sinonasal carcinoma and hinted upon the possibility of molecular classification for sinonasal carcinoma in the near future. Squamous cell carcinoma is the most common type followed by adenocarcinoma. Undifferentiated and poorly differentiated types of carcinoma are rare. A subset of squamous cell carcinoma associated with epidermal growth factor receptor (EGFR) alterations and rare variants with chromosomal translocations (DEK::AFF2; ETV6::NTRK and others) have been identified. The group of adenocarcinoma is very heterogeneous at molecular level; however, researchers identified potentially targetable genetic alterations with some success [22, 31]. EGFR exon 20 insertion mutation has also been studied in relation to inverted papilloma-associated squamous cell carcinoma [32]. TP53 mutation is seen in 80% of sinonasal squamous cell carcinoma and associated with poor survival [33].

Sinonasal undifferentiated carcinoma (SNUC) and poorly differentiated carcinoma are showing aggressive behaviour with poor prognosis. There have been attempts to understand tumour biology at molecular level. SNUC harbours

isocitrate dehydrogenase 2 R172 gene mutation (IDH2R172) in >80% of cases. IDH2 mutated SNUC and large cell neuroendocrine carcinoma represent a phenotypic spectrum of the same entity, which is different from SMARCB1 (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily b, member 1)-deficient sinonasal and small cell neuroendocrine carcinoma. IDH2 mutated carcinomas are associated with better disease-free survival and lower propensity for distant pulmonary metastasis [25, 34]. However, IDH2 mutant sinonasal carcinomas are more likely to metastasize to liver and other rare organs. SMARCA4{SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily a, member 4 (human)} deficiency was mostly associated with teratocarcinosarcoma [35].

10. Imaging

Historically, plain radiograph; the occipitofrontal (Caldwell view) for frontal sinus imaging was used. With the advent of new radiodiagnostic modalities, such as computed tomography scan (CT scan), etc., plain radiograph is no longer used.

10.1 Computed tomography (CT)

Computed tomography scan (CT scan) is a very useful technique for assessment of primary in frontal sinus malignancy patient. The CT scan should be acquired with slice thickness as less as possible (usually 0.75 to 0.6 mm with 128 slice machine).

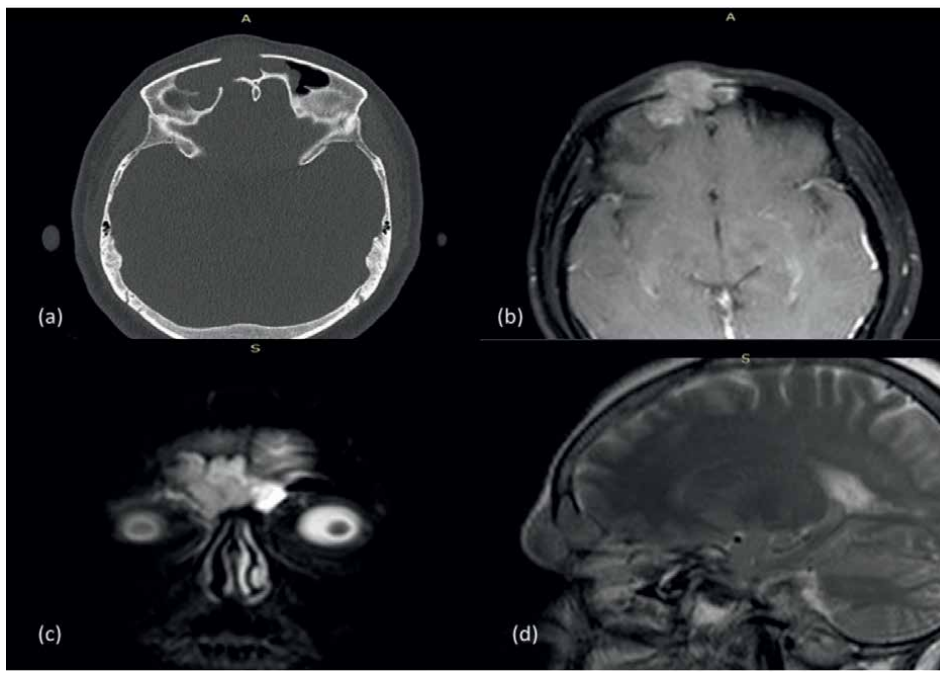

Figure 3.
(a) axial CECT bone window showing erosion of anterior and posterior table of frontal sinus (b) axial CEMRI T1 W showing enhancing tumor (c) coronal T2W MRI (d) saggital T2W MRI.

This can demonstrate involvement of the bone very well. Multiplanar reconstructed CT scan improves understanding in three dimensions [36]. It is important to consider synoptic reporting of CT scan and more important for an endoscopic surgeon to know anatomic variations of frontal sinus anatomy. Cone beam CT can also be used to study the anatomy of frontal sinus (**Figure 3a**) [37].

10.2 Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) and CT scan are complementary to each other in the assessment of frontal sinus malignancy cases where disease is extensive [38]. MRI demonstrates the involvement of soft tissues, such as dura or brain parenchyma more accurately. DW (diffusion-weighted) MRI can also be used to differentiate malignancy from benign lesions or inflammation (**Figure 3b–d**).

10.3 Positron emission tomography (PET)

Positron emission tomography (PET) CT is being increasingly used and few centres are using this modality routinely as baseline imaging and for preoperative assessment of distant metastasis in patients of sinonasal carcinoma [39]. ^{18}FDG (fluorodeoxyglucose) is the most commonly used tracer. The role of ^{68}Ga DOTA-TATE (dodecanetetraacetic acid-TATE or Tyr3-octreotate) has also been studied for neuroendocrine carcinoma of sinonasal carcinoma [40]. SUV (standardised uptake value) of ^{18}FDG may prove useful in treatment planning when the preoperative cytological or histological diagnosis is inconclusive [41].

11. Surgical approaches to frontal sinus

Various approaches have been described for frontal sinus surgery in the last two centuries. A brief description of all these approaches has been given in this section; however, some of them are no longer popular or not feasible in the management of frontal sinus carcinoma. Considerations in determining the surgical approach should include frontal sinus anatomy and its variations, tumour location and disease extension.

11.1 Frontal wall removal and obliteration of sinuses

11.1.1 First wave of open approaches

1800s - Schaeffer laid the groundwork for managing frontal sinusitis, sparking a wave of exploration in surgical techniques.

1884 – Ogston-Luc technique:

Anterior table trephination, nasofrontal duct dilatation, drainage tube insertion and frontal sinus mucosa treatment.

1895-Khunts technique:

Anterior table removal, manipulation of superior nasofrontal duct mucosa, nasofrontal duct stent placement and sinus obliteration using skin on the posterior table.

1898-Riedel-Schenke in 1898 proposed complete frontal sinus obliteration, which involved excising the anterior table and floor, stripping frontal sinus mucosa and utilising skin for sinus obliteration on the posterior table. Despite its

radical approach, poor cosmesis led to its eventual abandonment; however, this procedure still holds importance in the surgical armamentarium of a Head & Neck Oncosurgeon (**Figure 4a–h**) [42].

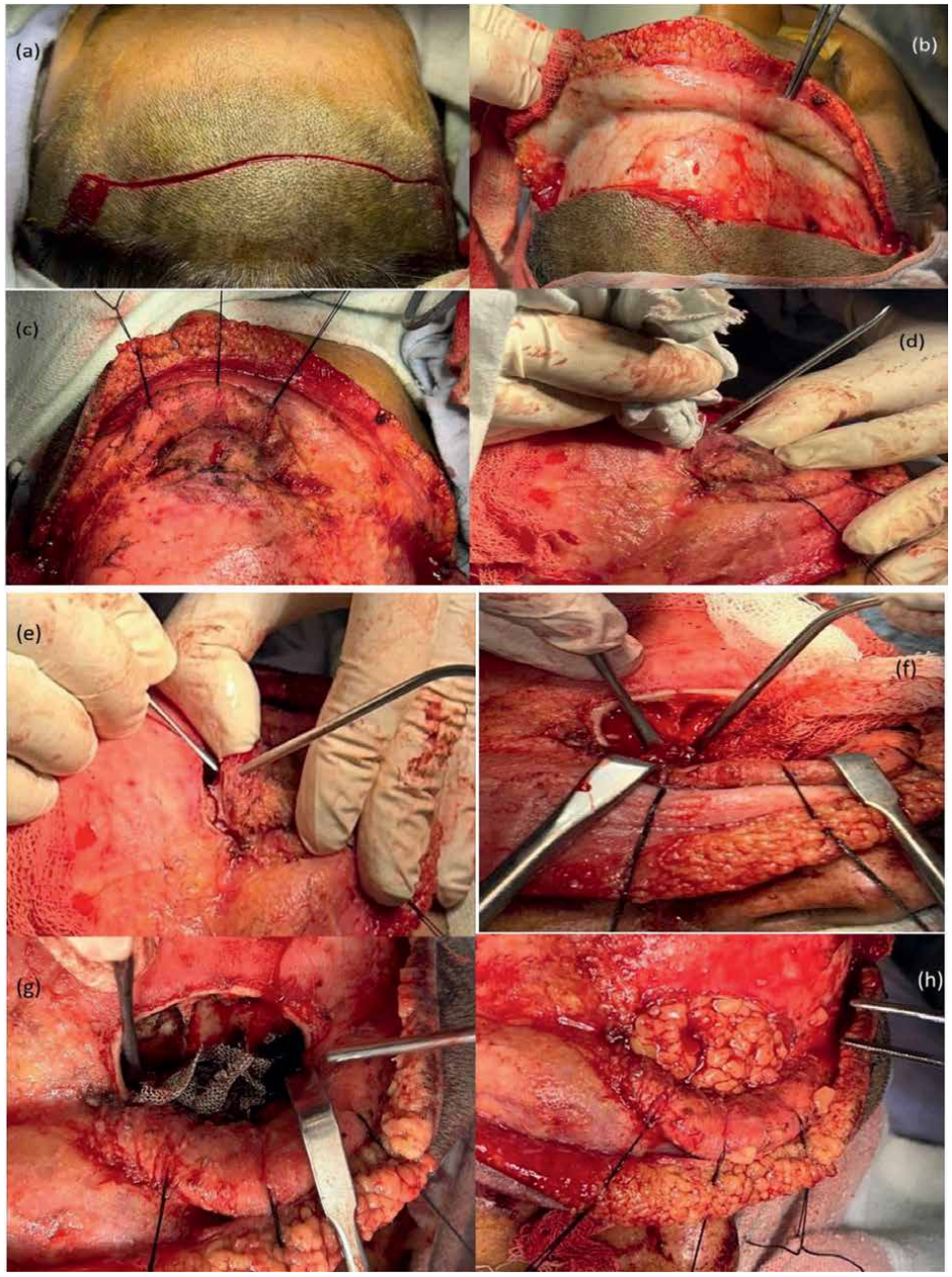

Figure 4.
Riedel's-schenke's procedure in a case of isolated frontal sinus sinonasal undifferentiated carcinoma through bicoronal approach (a)skin incision (b) subgaleal flap elevation (c) tumour delineation (d) drilling of bone with safety margin (e) removal of anterior bony table of frontal sinus with tumor (f) tumor removal from posterior wall (g) complete tumor removal done (h) fat obliteration.

11.1.2 Limitations of the procedures listed included

1. Poor cosmesis

2. Recurrent frontoethmoid outflow stenosis

11.2 Endonasal approaches

1915-Lothrop procedure.
Combined intranasal and extranasal techniques with widening of nasofrontal duct. Involved removing parts of the bilateral anterior ethmoids, the frontal sinus's anterior floor, as well as sections of the superior nasal septum and internasal septum.

11.2.1 Limitations of the procedure listed included

1. Technically demanding

2. Nasofrontal duct narrowing over time

3. Limited visibility

11.3 External approach

11.3.1 Second wave of external approaches

1921-Lynch &Howarth.
External ethmoidectomy technique. It involved a medial periorbital incision, with removal of ethmoidal air cells, excising the lamina papyracea, removal of the frontal sinus, curetting frontal sinus mucosa and placing a drainage tube for 5 days, followed by postoperative dilatation.
1958-Goodale and Montgomery.
Resurgence of osteoplastic flap technique [43].

11.3.2 Limitations of the procedure listed included

1. Restenosis

2. Cerebrospinal fluid (CSF) leaks

3. Frontal paraesthesia

4. Headaches

11.4 Endoscopic techniques

1970-Messerklinger, Kennedy & Stammberger.
Era of endoscopic sinus surgeries.
1990-Schaefer and Close.
Focused on advancing endoscopic approaches for frontal sinus disease.
1991-Draf.

Combined use of microscope and endoscope for frontoethmoidectomy.
Draf procedure is classified as follows-

1. **Draf I:** Simple drainage via anterior ethmoidectomy and opening of the naso-frontal duct

2. **Draf II:** Extended drainage through unilateral resection of the floor of the frontal sinus from the lamina papyracea to the nasal septum

   - **Draf IIa**: Unilateral approach removing a portion of the frontal sinus floor from the lamina papyracea to the middle turbinate.

   - **Draf IIb**: Unilateral approach removing a part of the frontal sinus floor from the lamina papyracea to the nasal septum.

   - **Draf IIc**: Proposed as an extension to IIb wherein frontal sinus is opened across the midline but not extended to the opposite frontal recess [44].

3. **Draf III**: Bilateral frontal sinus floor resection from the lamina papyracea of one orbit to the other and removal of the internisus septum [2].

11.4.1 Limitations of the procedure listed included

1. Limited two-dimensional (2D) visualisation

2. Steep learning curve

3. Difficult access especially in pneumatized frontal sinus

4. Increased risk of complications

5. Incomplete disease removal in case of disease lateralization

6. Postoperative complications (headaches, CSF leaks, infections)

11.5 Current practice

Endoscopic interventions have become predominant, with open procedures reserved for cases with distorted intranasal landmarks, failed multiple endoscopic surgeries, frontal sinusitis with intracranial or intraorbital complications and disease extending to the lateral boundaries. Combined approaches of external and endoscopic surgery may be employed in selected cases [45]. These developments reflect a progressive shift towards minimally invasive techniques and a greater reliance on endoscopic interventions in contemporary skull base and frontal sinus surgery [46].

This current practice of minimal invasive technique (endoscopic) may not be feasible alone in the management of malignant frontal sinus or skull base pathology.

Minimal involvement of frontal sinus in nasal or other paranasal sinus malignancy can be dealt with using endoscopic approach; however, involvement of frontal sinus with primary frontal sinus malignancy often requires external or combined

approach. Riedel's procedure and osteoplastic flap technique can be employed to remove primary frontal sinus tumour *in toto*. The choice of procedure will be based on the involvement of anterior or posterior wall of the frontal sinus. Riedel's procedure can be used for tumour involving anterior wall or posterior wall or both while osteoplastic flap technique is feasible when anterior wall is not involved [42, 43]. Similarly, cranialization of the frontal sinus can be done when anterior wall is not involved [47].

11.6 Craniofacial resection

Required for skull base malignant lesions. Disease extension to frontal sinus involvement in skull base malignancy can be addressed by this approach. Conventional craniofacial resection is an open approach surgery that is not without facial scars and disfigurement eventually. Contemporary craniofacial resection includes purely endoscopic or endoscopy-assisted resection. Endoscopy has clear advantage of magnification and illumination. However, patient selection is of utmost importance [48, 49]. Subfrontal approach is an alternative when the disease necessitates the removal of superior orbit, glabella, nasal root and nasal bones.

12. Adjuvant treatment

Adjuvant treatment in the management of sinonasal tumours is often required and forms an important component of multimodal treatment plan. Given the complex three-dimensional (3D) anatomy of nose and paranasal sinuses, it is often impossible to get clear margins all around whatsoever definition of free margin taken into consideration. In most of the instances, one face of the tumour will always be close to or adherent to skull base structures, which makes the removal of tumour difficult with adequate free margin. Hence, all cases of malignant sinonasal tumours should be discussed in multidisciplinary tumour board preoperatively and postoperatively so as to make appropriate treatment plan tailored according to individual case need.

Below-described modalities are not necessarily to be used postoperatively. Cases where operative risks outweigh benefits, these modalities may be used upfront. Preoperative radiotherapy has a well-documented role in olfactory neuroblastoma and soft tissue sarcoma. Similarly, preoperative chemotherapy can be used for sinonasal undifferentiated carcinoma, neuroendocrine carcinoma, olfactory neuroblastoma and craniofacial sarcoma [50].

Various adjuvant treatment modalities have been described. These treatment modalities can be divided into conventional and newer.

Conventional

1. EBRT (External beam radiotherapy)- Radiation is delivered from a machine that aims at radiations at the diseased part. Most radiation therapy machines use photon beams. However, other source of radiation, such as protons and electrons, can also be used.

2. IMBT (Intensity-modulated brachytherapy)- Brachytherapy is a type of internal radiation therapy. This uses an applicator that delivers radiation dose. Intensity can be modulated using static or dynamic shielding.

3. Chemotherapy- It is a drug treatment that uses chemotherapeutic agents to kill tumour cells.

Newer

1. Hadron therapy (Particle therapy)- Hadron therapy is a type of radiation therapy that uses charged particles, such as proton, carbon ion, etc.., instead of X-rays (photons).

2. Targeted therapy/Immunotherapy (Monoclonal antibodies)- Targeted therapies are small molecule drugs or monoclonal antibodies. Small molecules can enter cells and attack the desired target. Monoclonal antibodies can directly stop or destroy cancer cells or they can mark cancer cells, so that they will be better seen and destroyed by the immune system.

12.1 EBRT

Postoperative radiotherapy has a well-established role in the management of sinonasal malignancies. External beam photon radiotherapy can be delivered as 2D, 3D, Intensity-modulated or volumetric arc radiotherapy. With the advent of intensity-modulated radiation therapy, it is now possible to deliver photon radiations to the tumour tissues precisely. This prevents normal tissue damage which is often a vital organ in a case of sinonasal malignancy, such as orbit, optic nerve, skull base or brain. Radiotherapy can be delivered alone or concomitantly with chemotherapy.

The role of radiotherapy has been studied for primary frontal sinus malignancies [51]. Surgery combined with postoperative radiotherapy might result in satisfactory efficacy. Slevin et al. carried out a retrospective multicentre study of outcomes for locally advanced squamous cell carcinoma that was treated with adjuvant or definitive IMRT. They found poor survival outcome and high locoregional treatment failure [52].

12.2 IMBT

Perioperative fractionated IMBT is useful for advanced or recurrent paranasal sinus SCC that is involving a skull base [53]. However, its role in frontal sinus carcinoma *per se* is not studied.

12.3 Chemotherapy

Chemotherapy plays a vital role in the management of sinonasal carcinoma. The use of multimodal approach (chemoradiotherapy or surgery plus chemoradiotherapy) has shown improved survival than surgery plus radiotherapy or radiotherapy alone [54]. Though we do not have robust data on chemotherapy for primary frontal sinus carcinoma, this seems true for frontal sinus as well and the results of studies on sinonasal carcinoma can be extrapolated. Undoubtedly, surgical resection is the preferred approach for treatment of sinonasal carcinoma like other primaries in the head and neck; however, proximity of paranasal sinuses to critical structures makes R0 resection difficult. In advanced sinonasal carcinoma, upfront surgery can lead to significant morbidity and loss of organ function. In such instances, induction or neoadjuvant chemotherapy can be very useful [55–57]. There have been few studies showing survival benefit with organ preservation in advanced sinonasal squamous

cell carcinoma, which is the most common histopathology affecting paranasal sinuses [58]. Most commonly used chemotherapeutic regimens are TP (taxanes and platinum) or TP with 5 FU (fluorouracil) or ifosfamide [59]. Patients with complete response (CR) or partial response (PR) will be benefitted the most. Patients with stable disease or progressive diseases should be treated with surgery [60, 61].

12.4 Proton therapy

Proton therapy works on the principle of 'Bragg peak'. Protons preferentially deposit energy at the end of their path through the tissues. The desired depth to target malignant tissue can be achieved through computer programming. Lewis et al. selected 10 patients of sinonasal carcinoma who were treated with IMPT (intensity-modulated proton therapy). Dosimetrist generated VMAT (volumetric-modulated arc therapy) plans of all the patients for comparison. They concluded that VMAT had more homogeneous coverage of target volume and spares OAR (organ at risk) better than IMPT which were close to target volume; however, relative risk of secondary malignancy with VMAT compared to IMPT is 3.35. IMPT better spares nonadjacent OAR [62, 63]. Treatment of frontal sinus carcinoma with postoperative proton therapy has been reported [64]. Further studies are required with large number of patients to establish the role of proton therapy in the management of primary frontal sinus carcinoma.

12.5 Carbon ion therapy

The last decade has seen significant advancement in particle radiation treatment, including carbon ion radiation therapy. A recent meta-analysis done by Zhang and colleagues has shown significant benefit of using carbon ion radiation therapy in sinonasal malignancies [65]. The results of 2282 patients of sinonasal malignancies with different histologies from 44 observational studies were analysed. Patients were divided into three groups- 911 in carbon ion radiation therapy group, 599 in proton radiation therapy group and 772 in intensity-modulated photon radiation therapy group. Out of 11 frontal sinus malignancy patients, 9 patients received carbon ion therapy. Considering all subsites together, the overall survival was higher after carbon ion radiation therapy (75.1%) than proton radiation therapy (66.2%) and intensity-modulated photon radiotherapy (63.8%). Similarly, the local control rate was found to be significantly higher after carbon ion radiation therapy. Higher linear energy transfer (LET) and greater relative biological effectiveness (RBE) of carbon ion radiotherapy than proton and photon radiotherapy make carbon ion radiation therapy more useful for relatively radioresistant sinonasal histologies, such as adenoid cystic carcinoma, mucosal melanoma and sarcoma.

12.6 Targeted therapy/immunotherapy

In the era of targeted therapy, efforts are being made to identify specific molecular markers or genetic alterations or immune cells that can be targeted with novel biological agents [66]. This can pave the way for clinicians to provide a longer recurrence-free period and better survival to patients of sinonasal carcinoma. Discovery of different mutations such as IDH2 in sinonasal carcinoma may provide an opportunity for use of targeted therapy. Tislelizumab is a monoclonal antibody and found to be useful in a case of SMARCB1/INI-1-deficient sinonasal carcinoma [65].

Immunotherapy could have a potential role in the management of sinonasal undifferentiated carcinoma and NUT carcinoma, owing to the association of these tumours with immune system-related functional pathways [67–69]. Anti-PD-1 (programmed death ligand-1)-targeted antibodies, such as nivolumab and pembrolizumab, have been found to be useful in sinonasal squamous cell carcinoma, intestinal-type adenocarcinoma and sinonasal undifferentiated carcinoma [70–72]. No study is available on the treatment of isolated frontal sinus malignancy with targeted agents.

13. Conclusion

Frontal sinus is a very uncommon site to be affected by malignant neoplasm of both primary origin and distant secondary. Therefore, there are no robust data available regarding management and survival of frontal sinus malignancies. The management of frontal sinus malignancy poses a specific challenge for Head & Neck Oncosurgeon due to variable and complex anatomy, wide variety of pathologies affecting the frontal sinus and intimate relation with the skull base. Frontal sinus malignancy treatments require a multidisciplinary approach. The advent of endoscopic surgical techniques, newer radiation delivery technologies, particle treatment and targeted therapy has improved survival.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] Wormald PJ. The agger nasi cell: The key to understanding the anatomy of the frontal recess. Otolaryngology and Head and Neck Surgery. 2003;**129**(5):497-507. DOI: 10.1016/S0194-59980301581-X

[2] Bent JP, Cuilty-Siller C, Kuhn FA. The frontal cell as a cause of frontal sinus obstruction. American Journal of Rhinology. 1994;**8**(04):185-191

[3] Wormald PJ, Hoseman W, Callejas C, Weber RK, Kennedy DW, Citardi MJ, et al. The international frontal sinus anatomy classification (IFAC) and classification of the extent of endoscopic frontal sinus surgery (EFSS). International Forum of Allergy & Rhinology. 2016;**6**(7):677-696. DOI: 10.1002/alr.21738. Epub 2016 Mar 14

[4] Osguthorpe JD, Richardson M. Frontal sinus malignancies. Otolaryngologic Clinics of North America. 2001;**34**(1):269-281. DOI: 10.1016/s0030-6665(05)70311-x

[5] Roush GC. Epidemiology of cancer of the nose and paranasal sinuses. Current concepts. Head and Neck Surgery. 1979;**2**:3-11

[6] Holmstrom M, Lund V. Malignant melanoma of the nasal cavity following occupational exposure to formaldehyde. British Journal of Industrial Medicine. 1991;**48**:9-11

[7] Lund VJ, Howard DJ, Battershill J. Olfactory neuroblastoma and occupation. In: Columbus F, editor. Focus on Neuroblastoma Research. Hauppauge, NY: Nova Science Publishers; 2007

[8] Cantor JO, Adelglass J, Cerreta JM, Kancherla PL, Samara M. Collision tumor of the frontal sinus: Evidence of prior intrasinus instillation of thorotrast. The Laryngoscope. 1981;**91**(5):798-803. DOI: 10.1288/00005537-198105000-00013

[9] Jiménez Oliver V, Lazarich Valdés A, Dávila Morillo A, Ruiz del Portal JM, Conde Jiménez M, Fernández Ruiz E, et al. Metástasis fronto-etmoidal de adenocarcinoma prostático. Presentación de un caso clínico y revisión de la literatura [Frontal ethmoid metastases of prostatic carcinoma. Report of one case and review of the literature]. Acta Otorrinolaringológica Española. 2001;**52**(2):151-154. Spanish. DOI: 10.1016/s0001-6519(01)78191-5

[10] Bhojwani A, Unsal A, Dubal PM, Echanique KA, Baredes S, Liu JK, et al. Frontal sinus malignancies: A population-based analysis of incidence and survival. Otolaryngology and Head and Neck Surgery. 2016;**154**(4):735-741. DOI: 10.1177/0194599815621878. Epub 2015 Dec 23

[11] Brownson RJ, Ogura JH. Primary carcinoma of the frontal sinus. The Laryngoscope. 1971;**81**(1):71-89. DOI: 10.1288/00005537-197101000-00007

[12] Jain R, Saharan D, Sukheeja D, Parashar G, Gill N, Meena V. Isolated frontal sinus undifferentiated carcinoma: First case report in the literature. Indian Journal of Otolaryngology and Head & Neck Surgery. 2024;**76**(1):1106-1109. DOI: 10.1007/s12070-023-04142-0. Epub 2023 Aug 26

[13] Thompson LDR, Bishop JA. Update from the 5th edition of the World Health Organization classification of head and neck tumors: Nasal cavity, paranasal sinuses and skull base. Head and Neck Pathology. 2022;**16**(1):1-18. DOI: 10.1007/s12105-021-01406-5. Epub 2022 Mar 21

[14] Athre R, Ducic Y. Frontal sinus hamartomas. American Journal of Otolaryngology. 2005;**26**(6):419-421. DOI: 10.1016/j.amjoto.2005.05.007

[15] Sham CL, van Hasselt CA, Chow SMW, Lee DLY, Cho RHW, Woo JKS, et al. Frontal inverted papillomas: A 25-year study. The Laryngoscope. 2020;**130**(7):1622-1628. DOI: 10.1002/lary.28245. Epub 2019 Aug 16

[16] Sileo G, Valentini M, Gravante G, Monti G, Arosio AD, Bignami M, et al. Sinonasal malignancies involving the frontal sinus: A mono-institutional experience of 84 cases and systematic literature review. Journal of Clinical Medicine. 2023;**12**(9):3186. DOI: 10.3390/jcm12093186

[17] Katz TS, Mendenhall WM, Morris CG, Amdur RJ, Hinerman RW, Villaret DB. Malignant tumors of the nasal cavity and paranasal sinuses. Head & Neck. 2002;**24**(9):821-829. DOI: 10.1002/hed.10143

[18] Ganti A, Tajudeen BA, Plitt MA, Rossi I, Gattuso P, Batra PS. Discordance in preoperative and postoperative histopathology of sinonasal tumors. American Journal of Rhinology & Allergy. 2018;**32**(2):101-105. DOI: 10.1177/1945892418762845

[19] Lechner M, Liu J, Lund VJ. Novel biomarkers in sinonasal cancers: From bench to bedside. Current Oncology Reports. 2020;**22**(10):106. DOI: 10.1007/s11912-020-00947-2

[20] Capper D, Engel NW, Stichel D, et al. DNA methylation-based reclassification of olfactory neuroblastoma. Acta Neuropathologica. 2018;**136**:255-271

[21] Chraybi M, Alsamad IA, Copie-Bergman C, Baia M, André J, Dumaz N, et al. Oncogene abnormalities in a series of primary melanomas of the sinonasal tract: NRAS mutations and cyclin D1 amplification are more frequent than KIT or BRAF mutations. Human Pathology. 2013;**44**:1902-1911

[22] Turri-Zanoni M, Medicina D, Lombardi D, Ungari M, Balzarini P, Rossini C, et al. Sinonasal mucosal melanoma: Molecular profile and therapeutic implications from a series of 32 cases. Head & Neck. 2013;**35**:1066-1077

[23] Wroblewska JP, Mull J, Wu CL, FujimotoM OT, Marszalek A, et al. SF3B1, NRAS, KIT, and BRAF mutation; CD117 and cMYC expression; and tumoral pigmentation in sinonasal melanomas: An analysis with newly found molecular alterations and some population-based molecular differences. The American Journal of Surgical Pathology. 2019;**43**:168-177

[24] Jo VY, Chau NG, Hornick JL, Krane JF, Sholl LM. Recurrent IDH2 R172X mutations in sinonasal undifferentiated carcinoma. Modern Pathology. 2017;**30**:650-659

[25] Dogan S, Chute DJ, Xu B, Ptashkin RN, Chandramohan R, Casanova-Murphy J, et al. Frequent IDH2 R172 mutations in undifferentiated and poorly-differentiated sinonasal carcinomas. The Journal of Pathology. 2017;**242**:400-408

[26] Takahashi Y, Gleber-Netto FO, Bell D, et al. Identification of markers predictive for response to induction chemotherapy in patients with sinonasal undifferentiated carcinoma. Oral Oncology. 2019;**97**:56-61

[27] Rooper LM, Bishop JA, Westra WH. INSM1 is a sensitive and specific marker of neuroendocrine differentiation in head and neck tumors. The American

Journal of Surgical Pathology. 2018;**42**:665-671

[28] Udager AM, Rolland DCM, McHugh JB, et al. High-frequency targetable EGFR mutations in sinonasal squamous cell carcinomas arising from inverted sinonasal papilloma. Cancer Research. 2015;**75**:2600-2606

[29] Li L, Zhu L. Expression and clinical significance of TrkB in sinonasal squamous cell carcinoma: A pilot study. International Journal of Oral and Maxillofacial Surgery. 2017;**46**:144-150

[30] Quan H, Yan L, Wang S, Wang S. Clinical relevance and significance of programmed death-ligand 1 expression, tumor-infiltrating lymphocytes, and p16 status in sinonasal squamous cell carcinoma. Cancer Management and Research. 2019;**11**:4335-4345

[31] Taverna C, Agaimy A, Franchi A. Towards a molecular classification of sinonasal carcinomas: Clinical implications and opportunities. Cancers (Basel). 2022;**14**(6):1463. DOI: 10.3390/cancers14061463

[32] Pacini L, Cabal VN, Hermsen MA, Huang PH. EGFR exon 20 insertion mutations in sinonasal squamous cell carcinoma. Cancers (Basel). 2022;**14**(2):394. DOI: 10.3390/cancers14020394

[33] Doescher J, Piontek G, Wirth M, Bettstetter M, Schlegel J, Haller B, et al. Epstein-Barr virus infection is strictly associated with the metastatic spread of sinonasal squamous-cell carcinomas. Oral Oncology. 2015;**51**(10):929-934. DOI: 10.1016/j.oraloncology.2015.07.008. Epub 2015 Aug 10

[34] Bell D, Hanna EY, Agaimy A, Weissferdt A. Reappraisal of sinonasal undifferentiated carcinoma: SMARCB1 (INI1)-deficient sinonasal carcinoma: A single-institution experience. Virchows Archiv. 2015;**467**(6):649-656. DOI: 10.1007/s00428-015-1853-1. Epub 2015 Sep 25

[35] Vuong HG, Le T, Le TTB, Le HT, El-Rassi ET, McKinney KA, et al. Clinicopathological features and prognostic outcomes of molecularly defined entities in the new edition of the WHO classification of sinonasal carcinoma. Frontiers in Oncology. 2023;**13**:1117865. DOI: 10.3389/fonc.2023.1117865

[36] Kew J, Rees GL, Close D, Sdralis T, Sebben RA, Wormald PJ. Multiplanar reconstructed computed tomography images improves depiction and understanding of the anatomy of the frontal sinus and recess. American Journal of Rhinology. 2002;**16**(2):119-123

[37] Štoković N, Trkulja V, Čuković-Bagić I, Lauc T, Grgurević L. Anatomical variations of the frontal sinus and its relationship with the orbital cavity. Clinical Anatomy. 2018;**31**(4):576-582. DOI: 10.1002/ca.22999. Epub 2017 Oct 30

[38] Ferrari M, Bossi P, Mattavelli D, Ardighieri L, Nicolai P. Management of sinonasal adenocarcinomas with anterior skull base extension. Journal of Neuro-Oncology. 2020;**150**(3):405-417. DOI: 10.1007/s11060-019-03385-8. Epub 2020 Jan 3

[39] Dondi F, Pasinetti N, Guerini A, Piazza C, Mattavelli D, Bossi P, et al. Prognostic role of baseline ^{18}F-FDG pet/CT in squamous cell carcinoma of the paranasal sinuses. Head & Neck. 2022;**44**(11):2395-2406. DOI: 10.1002/hed.27145. Epub 2022 Jul 12

[40] Liu KY, Goldrich DY, Ninan SJ, Filimonov A, Lam H, Govindaraj S, et al. The value of ^{68}Gallium-DOTATATE

PET/CT in sinonasal neuroendocrine tumor management: A case series. Head & Neck. 2021;**43**(6):E30-E40. DOI: 10.1002/hed.26695. Epub 2021 Mar 31

[41] Elkhatib AH, Soldatova L, Carrau RL, Hachem RA, Ditzel L, Campbell R, et al. Role of ^{18}F-FDG PET/CT differentiating olfactory neuroblastoma from sinonasal undifferentiated carcinoma. The Laryngoscope. 2017;**127**(2):321-324. DOI: 10.1002/lary.26194. Epub 2016 Aug 2

[42] Raghavan U, Jones NS. The place of Riedel's procedure in contemporary sinus surgery. The Journal of Laryngology and Otology. 2004;**118**(9):700-705. DOI: 10.1258/0022215042244831

[43] Weber R, Draf W, Keerl R, Kahle G, Schinzel S, Thomann S, et al. Osteoplastic frontal sinus surgery with fat obliteration: Technique and long-term results using magnetic resonance imaging in 82 operations. The Laryngoscope. 2000;**110**(6):1037-1044. DOI: 10.1097/00005537-200006000-00028

[44] Al Komser MK, Goldberg AN. Unilateral transnasal endoscopic approach to frontal sinuses: Draf IIc. Allergy Rhinology (Providence). 2013;**4**(2):e82-e87. DOI: 10.2500/ar.2013.4.0058

[45] Ketcham AS, Wilkins RH, Van Buren JM. A combined intracranial facial approach to the paranasal sinuses. American Journal of Surgery. 1963;**106**:698-703

[46] Lund VJ, Stammberger H, Nicolai P, Castelnuovo P, Beal T, Beham A, et al. European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base. Rhinology. Supplement. 2010;**22**:1-143

[47] Horowitz G, Amit M, Ben-Ari O, Gil Z, Abergel A, Margalit N, et al. Cranialization of the frontal sinus for secondary mucocele prevention following open surgery for benign frontal lesions. PLoS One. 2013;**8**(12):e83820. DOI: 10.1371/journal.pone.0083820

[48] Hanna E, DeMonte F, Ibrahim S, Roberts D, Levine N, Kupferman M. Endoscopic resection of sinonasal cancers with and without craniotomy: Oncologic results. Archives of Otolaryngology – Head & Neck Surgery. 2009;**135**(12):1219-1224. DOI: 10.1001/archoto.2009.173

[49] Kim BJ, Kim DW, Kim SW, Han DH, Kim DY, Rhee CS, et al. Endoscopic versus traditional craniofacial resection for patients with sinonasal tumors involving the anterior skull base. Clinical and Experimental Otorhinolaryngology. 2008;**1**(3):148-153. DOI: 10.3342/ceo.2008.1.3.148. Epub 2008 Sep 30

[50] König M, Osnes T, Bruland Ø, Sundby Hall K, Bratland Å, Meling TR. The role of adjuvant treatment in craniofacial malignancy: A critical review. Frontiers in Oncology. 2020;**7**(10):1402. DOI: 10.3389/fonc.2020.01402

[51] Wang ZK, Yi JL, Zhang Y, Wu RY, Zhang JH, Wang JB, et al. Clinical characteristics and long-term outcomes following surgery combined with adjuvant radiotherapy for patients with frontal sinus malignancies. Journal of Neurological Surgery Part B: Skull Base. 2022;**84**(6):609-615. DOI: 10.1055/a-1924-9319

[52] Slevin F, Pan S, Mistry H, Denholm M, Shor D, Oong Z, et al. A multicentre UK study of outcomes for locally advanced sinonasal squamous cell carcinoma treated with adjuvant or definitive intensity-modulated

radiotherapy. Clinical Oncology (Royal College of Radiologists). 2021;**33**(10):e450-e461. DOI: 10.1016/j.clon.2021.05.012. Epub 2021 Jun 17

[53] Strege RJ, Kovács G, Maune S, Holland D, Niehoff P, Eichmann T, et al. Feasibility of combined operation and perioperative intensity-modulated brachytherapy of advanced/recurrent malignancies involving the skull base. Strahlentherapie und Onkologie. 2005;**181**(2):97-107. DOI: 10.1007/s00066-005-1274-1

[54] Kuo P, Manes RP, Schwam ZG, Judson BL. Survival outcomes for combined modality therapy for sinonasal undifferentiated carcinoma. Otolaryngology and Head and Neck Surgery. 2017;**156**(1):132-136. DOI: 10.1177/0194599816670146. Epub 2016 Oct 5

[55] Lilly G, Geltzeiler M. Induction chemotherapy for orbit preservation in sinonasal squamous cell carcinoma. Journal of Neurological Surgery Reports. 2021;**82**(3):e36-e37. DOI: 10.1055/s-0041-1736160

[56] Licitra L, Resteghini C, Bossi P. The evolving role of systemic therapy in the primary treatment of sinonasal cancer. Advances in Oto-Rhino-Laryngology. 2020;**84**:78-86. DOI: 10.1159/000457927. Epub 2020 Jul 30

[57] Melder KL, Geltzeiler M. Induction chemotherapy for locoregionally advanced sinonasal squamous cell carcinoma and sinonasal undifferentiated carcinoma: A comprehensive review. Cancers (Basel). 2023;**15**(15):3798. DOI: 10.3390/cancers15153798

[58] Abdelmeguid AS, Teeramatwanich W, Roberts DB, Amit M, Ferraroto R, Glisson BS, et al. Neoadjuvant chemotherapy for locoregionally advanced squamous cell carcinoma of the paranasal sinuses. Cancer. 2021;**127**(11):1788-1795. DOI: 10.1002/cncr.33452. Epub 2021 Feb 10

[59] Bossi P, Saba NF, Vermorken JB, Strojan P, Pala L, de Bree R, et al. The role of systemic therapy in the management of sinonasal cancer: A critical review. Cancer Treatment Reviews. 2015;**41**(10):836-843. DOI: 10.1016/j.ctrv.2015.07.004. Epub 2015 Jul 31

[60] Papazian MR, Gordon AJ, Chow M, Patel A, Pacione D, Lieberman S, et al. Sinonasal undifferentiated carcinoma with failed response to induction chemotherapy. Journal of Neurological Surgery Repors. 2022;**83**(3):e83-e86. DOI: 10.1055/a-1871-3586

[61] Amit M, Abdelmeguid AS, Watcherporn T, Takahashi H, Tam S, Bell D, et al. Induction chemotherapy response as a guide for treatment optimization in sinonasal undifferentiated carcinoma. Journal of Clinical Oncology. 2019;**37**(6):504-512. DOI: 10.1200/JCO.18.00353. Epub 2019 Jan 7

[62] Lewis L, Kreinbrink P, Richardson M, Westerfield M, Doberstein M, Zhang Y, et al. Intensity modulated proton therapy better spares non-adjacent organs and reduces the risk of secondary malignant neoplasms in the treatment of sinonasal cancers. Medical Dosimetry. 2022;**47**(2):117-122. DOI: 10.1016/j.meddos.2021.11.002. Epub 2021 Dec 21

[63] Russo AL, Adams JA, Weyman EA, Busse PM, Goldberg SI, Varvares M, et al. Long-term outcomes after proton beam therapy for sinonasal squamous cell carcinoma. International Journal of Radiation Oncology, Biology, Physics.

2016;**95**(1):368-376. DOI: 10.1016/j.ijrobp.2016.02.042. Epub 2016 Feb 18

[64] Tirelli G, Capriotti V, Sartori G, Tofanelli M, Marcuzzo AV. Primary adenoid cystic carcinoma of the frontal sinus: Case description of a previously unreported entity and literature review. Ear, Nose, & Throat Journal. 2019;**98**(4):E8-E12. DOI: 10.1177/0145561319837881. Epub 2019 Mar 28

[65] Zhang W, Hu W, Hu J, Gao J, Yang J, Kong L, et al. Carbon ion radiation therapy for sinonasal malignancies: Promising results from 2282 cases from the real world. Cancer Science. 2020;**111**(12):4465-4479. DOI: 10.1111/cas.14650. Epub 2020 Oct 16

[66] Lehtinen N, Suhonen J, Rice K, Välimäki E, Toriseva M, Routila J, et al. Assessment of targeted therapy opportunities in sinonasal cancers using patient-derived functional tumor models. Translational Oncology. 2024;**44**:101935. DOI: 10.1016/j.tranon.2024.101935. Epub 2024 Mar 23

[67] De Cecco L, Serafini MS, Facco C, Granata R, Orlandi E, Fallai C, et al. A functional gene expression analysis in epithelial sinonasal cancer: Biology and clinical relevance behind three histological subtypes. Oral Oncology. 2019;**90**:94-101. DOI: 10.1016/j.oraloncology.2019.02.003. Epub 2019 Feb 11

[68] Stelow EB, Bellizzi AM, Taneja K, Mills SE, Legallo RD, Kutok JL, et al. NUT rearrangement in undifferentiated carcinomas of the upper aerodigestive tract. The American Journal of Surgical Pathology. 2008;**32**:828-834

[69] Evans AG, French CA, Cameron MJ, Fletcher CD, Jackman DM, Lathan CS, et al. Pathologic characteristics of NUT midline carcinoma arising in the mediastinum. The American Journal of Surgical Pathology. 2012;**36**:1222-1227

[70] Xu CC, Dziegielewski PT, McGaw WT, et al. Sinonasal undifferentiated carcinoma (SNUC): The Alberta experience and literature review. Journal of Otolaryngology - Head & Neck Surgery. 2013;**42**:2

[71] García-Marín R, Reda S, Riobello C, et al. CD8+ tumour infiltrating lymphocytes and tumour microenvironment immune types as biomarkers for immunotherapy in sinonasal intestinal-type adenocarcinoma. Vaccine. 2020;**8**:202

[72] Denaro N, Merlano M, Numico G, Garrone O, Bossi P. Complete response to immunotherapy in sinonasal undifferentiated carcinoma. Tumori. 2021 Dec;**107**(6):NP101-NP104. DOI: 10.1177/03008916211026971. Epub 2021 Jul 6

Section 3

Surgical Rhinology

Chapter 6

Extended Sinus Surgery: Indications, Anatomy, and Step-by-Step Techniques

Ghassan Alokby

Abstract

This chapter provides a comprehensive overview of advancements and methodologies in extended sinus surgeries. It elucidates surgical techniques, key anatomical landmarks, indications, and postoperative care necessary for effectively managing refractory chronic rhinosinusitis and other complex sinonasal conditions. A detailed examination of various approaches, such as Endoscopic Maxillary Mega-Antrostomy (EMMA), Modified Medial Maxillectomy, Denker's approach, and Draf IIb and III procedures, is discussed, highlighting the anatomical considerations, surgical steps, and postoperative protocols to optimize patient outcomes and minimize complications. Extended sinus surgeries offer enhanced access to difficult-to-reach areas, allow better management of extensive disease processes, and provide improved pathways for drainage and disease resolution, utilizing advanced endoscopic techniques that preserve critical structures and promote faster recovery compared to traditional methods. The evolution of endoscopic sinus surgery has significantly transformed the management of sinus diseases, making extended sinus surgeries crucial for patients who have failed conventional treatments and presenting a viable option for addressing severe and complex pathologies. By understanding the detailed surgical techniques and postoperative care outlined in this chapter, surgeons can achieve better outcomes and improve the quality of life for their patients.

Keywords: extended sinus surgery, chronic rhinosinusitis, endoscopic sinus surgery, maxillary sinus, frontal sinus, sphenoid sinus, postoperative care

1. Introduction

The management of chronic sinus disease has evolved significantly over the last decade. With the advent of endoscopic sinus surgery (ESS) and continuous advancements in understanding sinonasal anatomy, technology, and surgical techniques, the field of rhinology and skull base surgery has undergone transformative changes. Modern nasal endoscopes, with various angles, high-definition cameras, and navigation systems, have paved the way for these advancements, enabling more precise and effective interventions. These technological improvements have allowed surgeons

to perform intricate procedures with better visualization and control, significantly reducing the risks associated with traditional open surgeries [1, 2].

Sinus surgery today is not only aimed at managing chronic sinus disease but also at addressing recalcitrant sinus disease and providing corridors to access various areas of the skull base. To fulfill these objectives, the limited approaches used in standard sinus surgery have been expanded, allowing for more comprehensive management of complex sinus conditions and improving surgical outcomes. Extended sinus surgeries have become a crucial aspect of modern rhinology, offering solutions for conditions that were previously deemed inoperable or required invasive open surgical techniques [3].

Extended sinus surgeries are indicated for several reasons, including the need to create gravity-dependent drainage pathways, as seen in cystic fibrosis patients. It is also indicated to ensure safe entry into extensively diseased sinuses where the natural ostium is obstructed by remodeling, often requiring access through the contralateral side. These procedures are crucial for patients who have failed appropriate medical therapy and traditional endoscopic sinus surgery. By expanding the surgical approach, surgeons can address more extensive disease processes, reduce the risk of recurrence, and improve overall patient outcomes [4].

In this chapter, we will delve into the various extended approaches in sinus surgery, focusing on their indications, key anatomical landmarks, and surgical techniques. By understanding these advanced procedures, we aim to provide a comprehensive guide for the effective management of refractory chronic rhinosinusitis and other complex sinonasal conditions. This knowledge will equip surgeons with the necessary skills to handle challenging cases and enhance the quality of care provided to patients.

2. Extended maxillary sinus procedures

A number of different procedures have been described to access the maxillary sinus, varying in their indications and conservativeness. Generally, extended sinus surgeries are indicated for the need for gravity-dependent drainage, as in cases of ciliary dyskinesia or thick secretions in cystic fibrosis. Other indications include the management of benign or malignant tumors, inverted papilloma, odontogenic sinusitis, mucocele, or fungus ball. These procedures are also used in cases of recalcitrant sinus disease or extensive osteogenesis [4].

3. Key anatomical landmarks

Identifying and understanding the key anatomical landmarks is crucial for the success of extended maxillary sinus procedures. These landmarks provide reference points that guide the surgeon during the procedure, ensuring precision and minimizing the risk of complications.

- *Inferior meatus wall:* Forms the lower boundary of the nasal cavity, crucial for procedures like inferior meatal antrostomy.

- *Medial floor of the orbit:* Serves as the superior boundary during maxillary sinus procedures. Careful identification and preservation of this structure are necessary to prevent injury to the orbital contents, which can result in serious complications such as vision loss or diplopia.

- *Nasolacrimal duct:* Located lateral to the lacrimal bone and the frontal process of the maxillary bone, it must be identified during maxillary sinus procedures to prevent postoperative complications like nasolacrimal duct injury, which can lead to chronic tearing and recurrent dacryocystitis.

- *Pyriform aperture:* The bony opening of the nasal cavity, serving as a landmark for accessing the anterior maxillary wall during procedures like Denker's approach. Understanding the anatomy of the pyriform aperture helps in the precise removal of bone to access the anterior and lateral walls of the maxillary sinus.

- *Hasner's valve:* Located at the distal end of the nasolacrimal duct, it must be preserved during inferior meatal antrostomy. Preserving this valve is crucial to maintain the normal function of the nasolacrimal duct and prevent postoperative obstruction.

4. Extended approaches to the maxillary sinus

4.1 Endoscopic maxillary mega-antrostomy (EMMA)

Endoscopic Maxillary Mega-Antrostomy (EMMA) is appropriate for patients with chronic recalcitrant maxillary sinusitis that has not responded to standard therapies and for those who benefit from gravity-dependent drainage. In our experience, a 30-degree nasal endoscope is used for this procedure, as it allows the surgeon to have better visualization of the operating field. The process begins with a partial inferior turbinectomy, where the anterior one-third of the inferior turbinate is preserved. This initial step is essential for maintaining some of the turbinate's physiological functions while allowing better access to the maxillary sinus.

The core of the procedure involves significantly widening the maxillary antrostomy down to the nasal cavity floor. This expansion facilitates gravity-assisted drainage, which is particularly beneficial for patients with impaired ciliary function or thick secretions, such as those with cystic fibrosis. The removal of a large portion of the medial wall of the maxillary sinus improves ventilation and drainage, reducing the likelihood of recurrent infections and inflammation.

Postoperatively, the large antrostomy enables effective irrigation and topical medication delivery directly into the sinus cavity, ensuring better disease management and reducing the likelihood of recurrence. Long-term outcomes have shown significant improvements in symptom resolution, highlighting the procedure's efficacy. Patients often report improved quality of life due to reduced symptoms and fewer sinus infections [5].

4.2 Extended maxillary sinusotomy with preservation of the inferior turbinate

This procedure differs from EMMA by preserving the inferior turbinate. Patients undergoing this procedure typically have failed a previous standard maxillary antrostomy. The procedure begins by revising the middle meatus antrostomy, ensuring a patent and wide middle meatus antrostomy with the removal of any residual uncinate process, and incorporating the natural ostium.

The inferior turbinate is temporarily outfractured and possibly reduced while preserving the medial mucosa, facilitating clear inspection of the lateral wall of the inferior meatus. An inferior meatus antrostomy is then performed, removing the

lateral wall of the inferior meatus down to the floor of the nose. It is crucial to identify and preserve Hasner's valve (**Figure 1**), as this procedure does not involve removing the nasolacrimal duct. The middle meatus antrostomy and inferior meatus antrostomy are then combined into one common antrostomy, with the inferior turbinate preserved and attached anteriorly and posteriorly like a hammock. This approach maintains the physiological functions of the inferior turbinate while providing extensive access for sinus drainage and disease management (**Figure 2**).

4.3 Endoscopic medial maxillectomy

Endoscopic Modified Medial Maxillectomy is primarily indicated for managing benign sinonasal neoplasms and extensive maxillary sinus disease. The procedure starts with the complete removal of the inferior turbinate, which is essential to provide maximum access to the maxillary sinus. This step is crucial, as it allows for a more extensive view and access to the sinus cavity, enabling thorough removal of diseased tissue.

The surgical approach involves expanding the maxillary antrostomy to its anatomical limits, extending inferiorly to the nasal cavity floor, superiorly to the medial orbital floor, posteriorly to the posterior wall of the maxillary sinus, and anteriorly

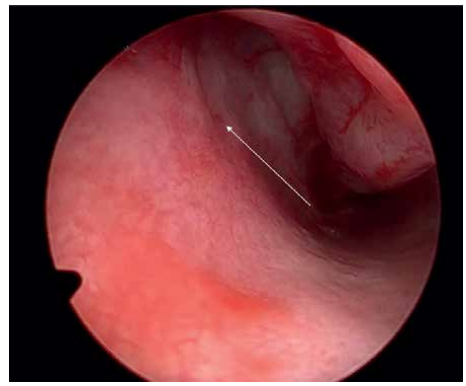

Figure 1.
The right inferior meatus ins visualized using a 30-degree endoscope and Hesner's valve is seen.

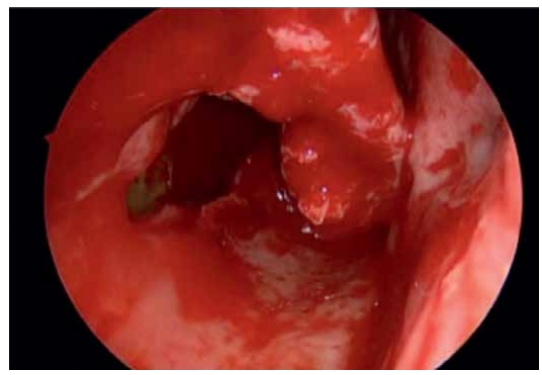

Figure 2.
Extended maxillary antrosotmy. This figure shows the inferior meatus antrostomy that is communicating with the middle meatus antrostomy while preserving the inferior turbinate.

to the anterior wall of the maxillary sinus. Complementary procedures include a complete ethmoidectomy and sphenoid sinusotomy. This comprehensive approach ensures that all diseased tissues are addressed, reducing the risk of recurrence [6].

This approach allows access to the medial wall of the orbit, which can be removed depending on its involvement with the disease, and the nasolacrimal duct, which is resected anteriorly and superiorly as needed. It is essential to complete the surgery by performing a dacryocystorhinostomy or at least vertical marsupialization of the nasolacrimal duct remnants to prevent nasolacrimal duct obstruction. A 70-degree nasal endoscope is often necessary for inspecting the anterior and lateral wall of the maxillary sinus, providing a detailed view of the surgical field.

At the end of the procedure, the comprehensive opening allows for thorough exploration and treatment of the sinus, including hard-to-reach areas such as the lateral recesses and the floor of the maxillary sinus. In cases of chronic recurrent sinusitis, the goal maybe to auto-obliterate the sinus by eradicating the maxillary sinus mucosa, thereby triggering the natural obliteration process and preventing future disease recurrence. This approach provides long-term relief for patients suffering from chronic and recalcitrant sinusitis [7].

4.4 Endoscopic Denker approach

Despite advances in endoscopic endonasal approaches, the anterolateral and anteroinferior aspects of the maxillary sinus and the infratemporal fossa remain challenging to reach through a purely transnasal approach. The Endoscopic Denker approach addresses these limitations by removing parts of the anterior wall of the maxillary sinus, providing more lateral access. This method combines the open procedures described by Denker and Sturmann/Canfield, performed entirely under endoscopic visualization. It offers the same port of entry into the maxillary sinus as the Caldwell-Luc procedure with similar indications [8].

The procedure begins with an incision in the mucosa at the junction of the nasal floor and lateral nasal wall, extending through the periosteum. A second mucosal incision is made superiorly along the lateral nasal wall, carried anteroinferiorly in front of the anterior head of the inferior turbinate, overlying the edge of the pyriform aperture. Following this, a subperiosteal dissection is performed to expose the anterior aspect of the maxilla, the infraorbital foramen, and its neurovascular bundle. A high-speed drill creates a bony window into the anterior wall of the maxillary sinus, staying inferior to the infraorbital nerve. Burrs connect the window to the inferior bony cut of the medial maxillectomy, allowing access to the anteroinferior corner of the maxillary sinus.

Once the tumor or diseased tissue is dissected free from the surrounding structures, the remaining bony and mucosal cuts are completed with burrs, osteotomes, and endoscopic scissors. Specifically, a superior cut is made at the level of the roof of the maxillary sinus, an inferior cut at the junction of the nasal floor and medial maxillary wall, and a posterior cut along the posterior wall of the maxillary sinus. At the end of the procedure, the nasolacrimal duct is identified, preserved, and sharply cut at an oblique angle to prevent stenosis (**Figure 3**), (Video 1, https://youtu.be/GXyKCt5UfGg).

5. Extended frontal sinus procedures

The primary surgical management of frontal sinus disease that has failed maximum medical treatment involves a frontal sinusotomy to reestablish the drainage

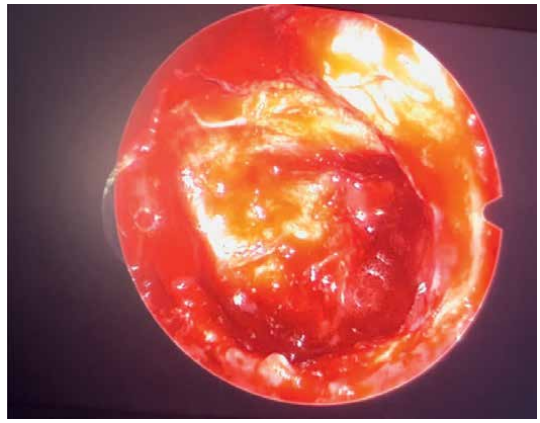

Figure 3.
70-degree nasal endoscope showing all the walls of the left maxillary sinus following and endoscopic Denker's procedure.

pathway. This approach can be extended to involve dilating the sinus by limited removal of the floor, as in the Draf IIa procedure, extending the opening from the middle turbinate to the lamina papyracea. When this procedure is inadequate, further management is required. Multiple extended frontal sinus procedures have been described, effectively replacing previously popular open procedures such as frontal sinus obliteration [9].

Extended frontal sinus surgery is indicated for various conditions, including recalcitrant sinus disease that failed primary sinus surgery, access to the lateral frontal sinus, severe stenosis due to osteoneogenesis, and remodeling in the frontal sinus recess that makes it unsafe to enter through the ipsilateral side. It is also indicated in cases of failed frontal sinus obliteration and cranialization, where failure often results from leaving mucosa behind, leading to the formation of a mucocele. Open approaches for these procedures are technically challenging, as the mucosa tends to adhere to the dura. In the case of benign and some malignant tumors, extended sinus surgery can offer the surgeon access to completely remove the tumor. For

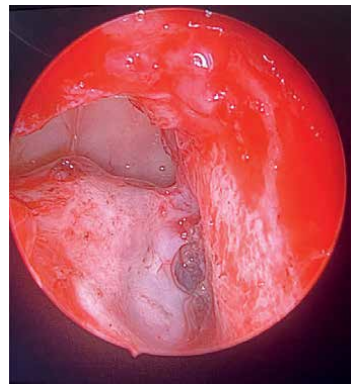

Figure 4.
A modified Lothrop procedure was used for access and repair of a left frontal sinus posterior table meningocele.

meningoencephaloceles, the extended approach allows for removal and repair while keeping the drainage of the frontal sinus patent (**Figure 4**) [10].

6. Key anatomical landmarks

Identifying the key anatomical landmarks is crucial for the success of extended frontal sinus procedures. These landmarks guide the surgeon during the procedure, ensuring precision and minimizing the risk of complications.

- *Anterior one-fourth of the middle turbinate vertical lamella:* Essential for orienting the surgeon during the initial stages of the procedure, its removal is necessary for completing the extended procedure and for the complete drilling of the floor of the frontal sinus.

- *Anterior olfactory cleft and olfactory fibrils:* Located medial to the middle turbinate vertical lamella, these structures are critical for avoiding skull base injury during Draf IIb or III procedures as they define the posterior limit of the resection.

- *Frontal sinus infundibulum posterior wall:* A critical reference point for performing extended frontal sinusotomies, helping maintain orientation and avoid inadvertent damage to the anterior skull base and cribriform plate.

- *Anterosuperior perpendicular plate and septectomy:* Facilitates exposure and allows the introduction of instrumentation from both sides of the nasal cavity, crucial for creating a common frontal sinus drainage pathway.

- *Frontal intersinus septum:* Necessary for combining the left and right frontal sinuses into a single, large cavity, a crucial step in Draf III (Modified Lothrop) procedures.

- *Nasal process of the frontal bone:* Drilling in this area helps enlarge the lateral dimensions of the frontal sinus opening, providing greater access to the supraorbital recesses.

- *Nasion:* The dense bone at the nasion is removed to enlarge the common frontal ostium, ensuring complete transillumination and visualization of the frontal sinus.

7. Extended approaches to the frontal sinus

7.1 Draf IIb procedure

This approach involves removing the frontal sinus floor from the nasal septum medially to the lamina papyracea laterally, creating a unilateral maximal opening of the frontal sinus outflow tract. This is particularly useful in cases of severe stenosis and for accessing the lateral frontal sinus (**Figure 5**) [11].

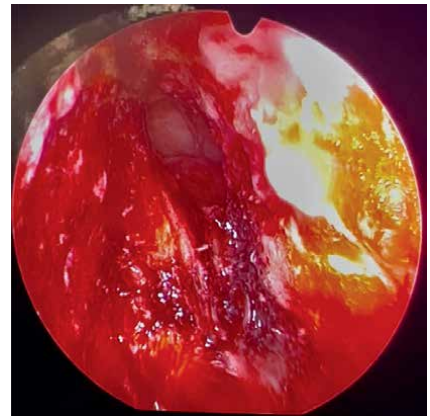

Figure 5.
The left frontal sinus following a Draf 2b procedure looked at using a 70- degree nasal endoscope.

7.2 Draf III (modified Lothrop) procedure

The Draf III procedure, or Modified Lothrop Procedure, is an endoscopic modification of the original procedure described by Lothrop in 1914. It involves the bilateral removal of the frontal sinus floor from one lamina papyracea to the other, including a superior septectomy and intersinus septectomy, creating a large common frontal sinus drainage pathway. This procedure is ideal for severe bilateral frontal sinus disease, failed prior frontal sinus surgeries, or extensive osteoneogenesis [12]. This procedure can also provide access for the repair of a posterior table cerebrospinal fluid (CSF) leak (**Figure 4**).

There are several modifications of the Draf III procedure tailored to specific anatomical and pathological challenges: [7].

- *Modified hemi-Lothrop procedure:* Adds a superior septectomy to a Draf IIb to increase access to the far lateral frontal sinus recess or a supraorbital ethmoid cell from the contralateral side (video 2, https://youtu.be/pHw8hR-vC00).

- *Modified mini-Lothrop procedure:* Combines resection of the contralateral frontal sinus floor with a frontal intersinus septectomy, preserving the ipsilateral frontal sinus floor. This is suitable for cases where the ipsilateral frontal sinus cannot be safely accessed from the same side due to extensive scarring, previous medial orbital wall decompression, significant intraorbital contents obstructing the ipsilateral frontal sinus outflow tract, complex anatomy, severe stenosis, or pronounced osteoneogenesis.

- *Modified subtotal-Lothrop procedure:* Unilaterally removes the frontal sinus floor with a superior septectomy and intersinus septectomy, preserving as much normal sinonasal architecture as possible.

- *Modified central-Lothrop procedure:* Bilaterally resects the medial frontal sinus floor with a superior septectomy and intersinus septectomy, providing access and visualization to both frontal sinuses. This procedure is effective for addressing frontal sinus disease near the midline, particularly suitable for cases involving isolated disease or mucoceles in a frontal intersinus cell, central neoplastic processes, or skull base defects. The frontal sinus recesses and middle turbinates are left undisturbed.

8. Procedure details

8.1 Draf IIb procedure

The anterior one-fourth of the middle turbinate vertical lamella is removed, starting at its anterior insertion and heading superiorly in the direction of the posterior wall of the frontal sinus infundibulum or the superior aspect of the nasoseptal angle. This step is crucial for orienting the surgeon away from the skull base and anterior cribriform plate. The bony medial margin of the frontal infundibular opening is the superior point of insertion of this portion of the middle turbinate vertical lamella, which is removed with curettes or powered instruments to identify the junction of the perpendicular plate with the frontal intersinus septum. The mucosa on the posterior wall of the frontal infundibular area is preserved whenever feasible. However, significant fibrosis or osteoneogenesis in the area often makes this preservation impossible, and in that case, a Draf III procedure should be done.

8.2 Draf III (modified Lothrop) procedure

For a midline approach to access the frontal sinus, the anterior olfactory filaments should first be identified, located medial to the vertical lamella of the middle turbinate and posterior to the coronal plane of the posterior wall of the frontal infundibulum. Only the anterior quarter of the middle turbinate vertical lamella forms the medial margin of the frontal infundibulum. The rest is situated lateral to the cribriform plate, connecting with the lateral lamella of the cribriform plate and the medial fovea ethmoidalis.

Intraoperative navigation is beneficial for determining the correct trajectory during a transnasal midline frontal sinus approach and is typically used in all Draf III procedures. Elevating a posteriorly based flap starting in the wider septal angle area anterior to the cribriform plate, at the coronal plane just in front of the anterior attachment of the middle turbinate, helps identify the narrow V-shaped groove of the anterior cribriform plate and the first olfactory filaments, as well as the posterior wall of the frontal infundibulum. This step ensures that the posterior limit of the dissection is under direct vision, preventing inadvertent skull base injury and cerebrospinal fluid leaks. A 70-degree endoscope can be used for superior visualization.

The anterosuperior septectomy is performed anterior to the level of the anterior cribriform plate using cutting forceps or powered instrumentation, aligning with the coronal plane of the posterior wall of the frontal sinus infundibulum as viewed through a transethmoid or transseptal frontal sinusotomy. Posterior to this plane, there is a heightened risk of inadvertent intracranial penetration or damage to the cribriform plate or olfactory nerve fibers. The coronal plane of the posterior wall of the frontal sinus should always be kept in view to prevent accidental injury to the skull base and subsequent cerebrospinal fluid leaks. The size of the septal window should be adequate to enhance exposure and allow instrument insertion from both sides of the nose. Once the septal window is created, even straight instruments can access the common frontal cavity from either side of the nose. If this is not possible, the septal window should be lowered until bilateral access to the common frontal sinus is feasible.

The dense bone at the nasofrontal beak area, corresponding to the nasion, is removed using angled cutting burs, progressively enlarging the common frontal ostium and enhancing access to the superior and anterior aspects of the frontal sinus. Additionally, lateral enlargement toward the orbit is performed to increase the lateral

dimensions of the opening, providing greater access to the supraorbital recesses of the frontal sinus from the contralateral side. The limits of the procedure are the dermis at the level of the nasion anteriorly and the supracanthal dermis on either side. Drilling the supracanthal bone of the orbit is usually done under endoscopic visualization, with the drill introduced through the contralateral nostril. Intermittent palpation of the nasion dermis and supracanthal dermis helps determine the anterior and lateral limits of drilling. Generally, limited exposure of the nasion or supracanthal dermis does not result in adverse cosmetic effects. The additional enlargement of the common frontal sinus ostium reduces the chances of failure due to restenosis, and maximizing the width of the opening should be attempted.

It is not uncommon to encounter one or more frontal intersinus cells that need to be removed to effectively enlarge the common frontal ostium and ensure adequate outflow. The final common extended frontal sinusotomy opening is a horseshoe-shaped opening measuring approximately 8–10 mm anteroposteriorly at the nasofrontal bone and 20–26 mm laterally from the orbital wall to the orbital wall. The posterior, lateral, and anterior walls of the common frontal ostium are composed of the posterior wall of the frontal sinus, the supracanthal lateral nasal dermis, and the anterior wall of the frontal sinus at the nasion, respectively. The final ostium should allow complete transillumination and visualization of the entire frontal sinus (**Figures 6** and 7) [4, 13].

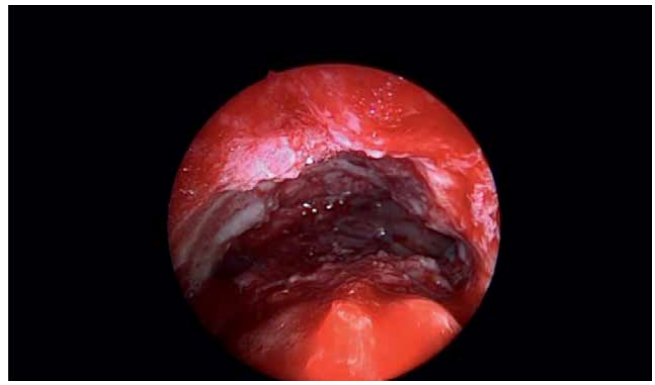

Figure 6.
Endoscopic view after a completed modified Lothrop procedure. The boundaries were reached to the limits to the medial canthi laterally and to the nasion anteriorly.

Figure 7.
Transillumination of both sides of the frontal sinus following a modified Lothrop procedure.

9. Extended sphenoid sinus procedures

Extended sphenoid sinusotomy is likely the most frequently performed extended sinus procedure as it is pivotal in transsphenoidal approaches to pituitary gland tumors, providing essential access to the skull base. This procedure creates a common sphenoid sinus cavity by removing the intersinus septum along with performing a posterior septectomy. Like other extended sinus procedures, extended sphenoid sinusotomy is crucial for managing recalcitrant sinus disease that has failed both appropriate medical therapy and primary sinus procedures. It is also indicated in cases of severe osteoneogenesis, which can obstruct entry to the ipsilateral sphenoid sinus through the natural ostium, as well as for the drainage of mucoceles and the resection of tumors [14].

The objective of performing this procedure, other than the common indication of gaining access to the skull base, is to minimize the chances of restenosis in chronic sinus disease, ensuring better long-term outcomes. Additionally, this procedure enhances access for postoperative examinations, debridement, and the administration of topical medications. Conceptually, it is similar to a frontal sinus Draf III (Lothrop) procedure, as it provides maximal access to the sphenoid sinus, facilitating improved sinus drainage and allowing for effective postoperative management and in-office debridement. By establishing a larger, more accessible cavity, it allows for thorough monitoring and treatment of any residual or recurring disease. This is particularly important for patients with complex sinus conditions, where meticulous postoperative care and the ability to apply topical medications are essential to prevent further recurrence and ensure sustained relief from symptoms.

10. Key anatomical landmarks

Identifying the key anatomical landmarks is crucial for the success of extended sphenoid sinus procedures. These landmarks provide reference points that guide the surgeon during the procedure, ensuring precision and minimizing the risk of complications.

- *Superior turbinate:* Acts as a key landmark for locating the sphenoid ostium. Identifying the superior turbinate and following it posteriorly often leads to the sphenoid ostium.

- *Sphenoid ostium:* The natural opening of the sphenoid sinus into the nasal cavity, essential for initial access.

- *Sphenoid rostrum:* The anterior bony wall of the sphenoid sinus, often removed or drilled to enlarge the sphenoidotomy and gain better access to the sinus cavity.

- *Optic nerve canal:* The bony canal through which the optic nerve runs, located in the lateral wall of the sphenoid sinus.

- *Internal Carotid Artery (ICA):* Runs laterally and inferiorly to the sphenoid sinus. Identifying and preserving this artery is critical to avoid catastrophic hemorrhage or stroke.

- *Vidian canal:* The bony canal containing the vidian nerve, located at the base of the sphenoid sinus. It serves as an important landmark for the ICA in complex skull base procedures.

- *Floor of the sella:* Important for transsphenoidal approaches to the pituitary gland.

- *Middle third of the clivus:* Inferior to the floor of the sella and providing a reference point for posterior sphenoid sinusotomy and access corridor in skull base surgeries.

11. Procedure details

The patient is placed in a supine position with the head slightly elevated, and the nose is decongested. A 30-degree or 0-degree endoscope is inserted into the nasal cavity. The natural sphenoid ostium is located, typically found superior to the choana and medial to the superior turbinate. The ostium is then enlarged using a microdebrider or Kerrison rongeurs to facilitate better access. The sinus that is opened first is typically the one easier to access and leads to a more pneumatized sphenoid sinus.

The sphenoid rostrum is removed completely using a high-speed drill or rongeurs to create a wider sphenoidotomy. This step involves careful drilling to avoid damage to surrounding structures, including the optic nerve and ICA. Subsequently, a posterior septectomy is performed by removing the posterior portion of the nasal septum, creating a common cavity between the left and right sphenoid sinuses, and enhancing surgical access and drainage.

Following the septectomy, the intersinus septum between the left and right sphenoid sinuses is removed, creating a single, large sphenoid cavity. The common sphenoid sinus opening is enlarged superiorly to the level of the planum sphenoidale and inferiorly to the floor of the sphenoid sinus, and laterally until the sphenoid cavity is contiguous with the medial orbital wall. This facilitates access and improves postoperative management, reducing the risk of restenosis. Identifying the optic nerve canal and ICA is crucial. The intersinus septum is removed using true-cutting instruments or a diamond burr. It is important to avoid pulling the intersinus septum using non-true-cutting instruments, as it may be attached to the parasellar or paraclival ICA, and pulling on it may result in catastrophic bleeding.

If pathologies such as mucoceles, tumors, or severe osteoneogenesis is present, the diseased tissue is carefully resected using various surgical instruments. The goal is to remove diseased tissue while preserving healthy mucosa. If the procedure is done as part of access to the skull base and a septal flap is needed, the flap should be raised before the procedure and tucked in the nasopharynx for later use in skull base repair.

12. The ethmoid sinus and the management of the middle turbinate

Anterior or total ethmoidectomy is the standard surgical procedure for managing ethmoid sinus disease that has not responded to medical treatment. This procedure emphasizes the concept of mucosal preservation. However, more aggressive approaches have been described for cases where standard ethmoidectomy fails. Jankowski et al. presented results of a more radical approach known as nasalization, or radical ethmoidectomy. This procedure involves removing all the bony lamellae

and mucosa within the ethmoid sinus and includes performing a large maxillary antrostomy, sphenoidotomy, frontal sinusotomy, and middle turbinectomy.

In their study, Jankowski and colleagues compared nasalization to conventional ethmoidectomy. Patients who underwent nasalization showed better outcomes in terms of nasal symptoms compared to those who had conventional ethmoidectomy. Notably, olfactory improvement remained stable for three years in the nasalization group, whereas it worsened after 2 years in the ethmoidectomy group [15]. In a 2006 follow-up study, Jankowski and colleagues further found that nasalization was superior in terms of overall symptoms, as assessed by a questionnaire, endoscopic appearance of the mucosa, appearance on CT scan, and recurrence rate. This evidence supports the use of nasalization in more severe cases of ethmoid sinus disease that do not respond to standard surgical treatments [16].

13. Postoperative care

Postoperative care is a critical component of managing patients undergoing extended sinus surgeries. Proper care and monitoring following surgery can significantly impact the overall success and long-term outcomes of the procedure. Initially, patients may be prescribed antibiotics based on the cultures taken at the time of surgery. Saline irrigations mixed with topical corticosteroids, depending on the pathology, will help promote healing and reduce crusting [17].

Regular follow-up visits are crucial for assessing the surgical site and identifying any early signs of complications. During these visits, endoscopic examinations are performed to monitor the healing process, remove any crusts or debris, and ensure that the surgical cavities remain patent. Debridement may be necessary to remove any granulation tissue or crusts and to release any synechiae that could obstruct the sinus openings [18, 19].

Patients are advised to avoid activities that may increase nasal pressure, such as nose blowing or heavy lifting, to prevent disruption of the surgical site. They are also instructed to avoid exposure to irritants like smoke or dust, which can exacerbate inflammation and impede healing.

Long-term follow-up is necessary for patients with chronic conditions to monitor for any disease recurrence and to manage it as indicated.

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References

[1] Snyderman CH et al. Technologic innovations in Neuroendoscopic surgery. Otolaryngologic Clinics of North America. 2009;**42**(5):883-890, x. DOI: 10.1016/j.otc.2009.08.019

[2] Alokby G et al. Endoscopic reconstruction of Skull Base defects using Tutoplast. Allergy & Rhinology (Providence, R.I.). 2021;**12**:21526567211009200. DOI: 10.1177/21526567211009200

[3] Eloy JA, Marchiano E, Vázquez A. Extended endoscopic and open sinus surgery for refractory chronic Rhinosinusitis. Otolaryngologic Clinics of North America. 2017;**50**(1):165-182. DOI: 10.1016/j.otc.2016.08.013. PMID: 27888912

[4] Casiano RR, Herzallah IR, Eloy JA, editors. Endoscopic Sinonasal Dissection Guide: Including Orbit and Skull Base. Second ed. New York: Thieme; 2018

[5] Costa ML et al. Long-term outcomes of endoscopic maxillary mega-Antrostomy for refractory chronic maxillary sinusitis. International Forum of Allergy & Rhinology. 2015;**5**(1):60-65. DOI: 10.1002/alr.21407

[6] Konstantinidis I, Constantinidis J. Medial Maxillectomy in recalcitrant sinusitis: When, why and how? Current Opinion in Otolaryngology & Head and Neck Surgery. 2014;**22**(1):68-74. DOI: 10.1097/MOO.0000000000000009

[7] Eloy JA, Marchiano E, Vázquez A. Extended Endoscopic and Open Sinus Surgery for Refractory Chronic Rhinosinusitis. Otolaryngol Medical Clinics of North America. Feb 2017;**50**(1):165-182. DOI: 10.1016/j.otc.2016.08.013. PMID: 27888912

[8] McCormick JP et al. Modified endoscopic Denker's approach for Management of Anterior Maxillary Sinus Tumors: Multicenter series of 58 cases. American Journal of Rhinology & Allergy. 2022;**36**(6):763-772. DOI: 10.1177/19458924221110652

[9] Turner JH, Vaezeafshar R, Hwang PH. Indications and outcomes for Draf IIB frontal sinus surgery. American Journal of Rhinology & Allergy. 2016;**30**(1):70-73. DOI: 10.2500/ajra.2016.30.4268

[10] Casiano RR, Livingston JA. Endoscopic Lothrop procedure: The University of Miami experience. American Journal of Rhinology. 1998;**12**(5):335-339. DOI: 10.2500/105065898780182444

[11] Draf W. Endonasal micro-endoscopic frontal sinus surgery: The Fulda concept. Operative Techniques in Otolaryngology-Head and Neck Surgery. 1991;**2**(4):234-240. DOI: 10.1016/S1043-1810(10)80087-9

[12] Gross CW, Gross WE, Becker DG. Modified Transnasal endoscopic Lothrop procedure: Frontal Drillout. Operative Techniques in Otolaryngology-Head and Neck Surgery. 1995;**6**(3):193-200. DOI: 10.1016/S1043-1810(06)80012-6

[13] Wormald P-J, Valentine R. Endoscopic Sinus Surgery: Anatomy, Three-Dimensional Reconstruction, and Surgical Technique. 3rd ed. New York Stuttgart: Thieme; 2013

[14] Simmen D, Jones N. Manual of Endoscopic Sinus Surgery and its Extended Applications. Stuttgart: Thieme; 2005

[15] Jankowski R, Pigret D, Decroocq F. Comparison of functional results after

Ethmoidectomy and nasalization for diffuse and severe nasal polyposis. Acta Oto-Laryngologica. 1997;**117**(4):601-608. DOI: 10.3109/00016489709113445

[16] Jankowski R et al. Comparison of radical (nasalisation) and functional Ethmoidectomy in patients with severe Sinonasal polyposis. A retrospective study. Revue De Laryngologie - Otologie - Rhinologie. 2006;**127**(3):131-140

[17] Rudmik L et al. Early postoperative care following endoscopic sinus surgery: An evidence-based review with recommendations. International Forum of Allergy & Rhinology. 2011;**1**(6):417-430. DOI: 10.1002/alr.20072

[18] Bugten V, Nordgård S, Steinsvåg S. The effects of debridement after endoscopic sinus surgery. The Laryngoscope. 2006;**116**(11):2037-2043. DOI: 10.1097/01.mlg.0000241362.06072.83

[19] Nilssen ELK et al. A randomized control trial of post-operative care following endoscopic sinus surgery: Debridement versus No debridement. The Journal of Laryngology and Otology. 2002;**116**(2):108-111. DOI: 10.1258/0022215021910041

Chapter 7

Dacryocystitis and Its Management

Sindhuja Bhanwala

Abstract

The lacrimal apparatus drains into the inferior meatus of the nose via the nasolacrimal duct. Blockage of this drainage pathway leads to a consistent and continuous epiphora which tends to become sticky and thick over time. Thus, it can lead to recurrent episodes of acute infections which present with a swelling in the medial canthal region (acute dacryocystitis). Dacryocystorhinostomy (DCR) is recognized as the most suitable treatment for patients with obstruction of the lacrimal system at the level of the sac or the nasolacrimal duct. This operation aims to create a bypass between the lacrimal sac and the nasal cavity. Traditionally, this was achieved by performing an external DCR using an external skin incision. But over the past two decades, we have seen advances in rigid endoscopic equipment, which have led to the development of a safer and less-invasive technique, namely, endoscopic DCR for treating symptomatic lacrimal apparatus disorders. This chapter provides a comprehensive overview of the lacrimal system, dacryocystitis etiology and management. It delves into the indications for surgical intervention and compares traditional external DCR with the less-invasive endoscopic DCR technique. By detailing postoperative care, this chapter aims to offer a streamlined approach to understanding and treating symptomatic lacrimal apparatus disorders.

Keywords: lacrimal apparatus diseases, dacryocystorhinostomy, endoscopic, epiphora, dacryocystitis

1. Introduction

Dacryocystitis, an inflammation of the nasolacrimal sac, often stems from an obstruction within the nasolacrimal duct (NLDO), resulting in tear stagnation and the hallmark symptom of epiphora. Additionally, it may manifest as a tender swelling near the eye's inferomedial canthus, periorbital cellulitis, erythema and purulent discharge. Timely diagnosis and effective management are pivotal in averting potential complications. Treatment typically encompasses antibiotics, wound care and addressing the underlying obstruction, often requiring surgical intervention such as dacryorhinocystostomy in chronic cases [1].

Collaborative efforts amongst ophthalmologists, otorhinolaryngologists, nurses, physicians and pharmacists are indispensable for comprehensive patient care and favorable outcomes.

2. Anatomy of the lacrimal system and its drainage pathway

The lacrimal sac, nestled within the lacrimal fossa, drains into the nasolacrimal duct. Lacrimal puncta, situated at the medial ends of the upper and lower eyelids, connect to the lacrimal sac via the upper and lower canaliculi. These canaliculi converge to form the common canaliculus, which opens high on the lateral wall of the lacrimal sac. It extends about 9 mm above the axilla of the middle turbinate. The thick anterior limb of the medial canthal tendon wraps along the anterior upper half of the lacrimal sac to insert onto the anterior lacrimal crest, and then the posterior limb passes behind the sac to insert onto the posterior lacrimal crest. The nasolacrimal duct travels within a bony canal formed by the maxillary and lacrimal bones, terminating at the inferior meatus of the nose.

Tear production by the lacrimal gland, along with accessory glands of Wolfring and Krause, nourishes and lubricates the eye. Tears flow through the puncta, ampullae, canaliculi and, finally, the lacrimal sac, before descending through the nasolacrimal duct and reaching the nasal cavity (**Figure 1**) [2, 3].

3. Classification and etiology

Dacryocystitis, resulting from obstruction in the lacrimal drainage pathway, manifests as either acute or chronic, congenital, or acquired.

Acute dacryocystitis, an infectious state, can be caused by various Gram-positive and Gram-negative bacteria including *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Serratia marcescens* and *Pseudomonas aeruginosa* [1].

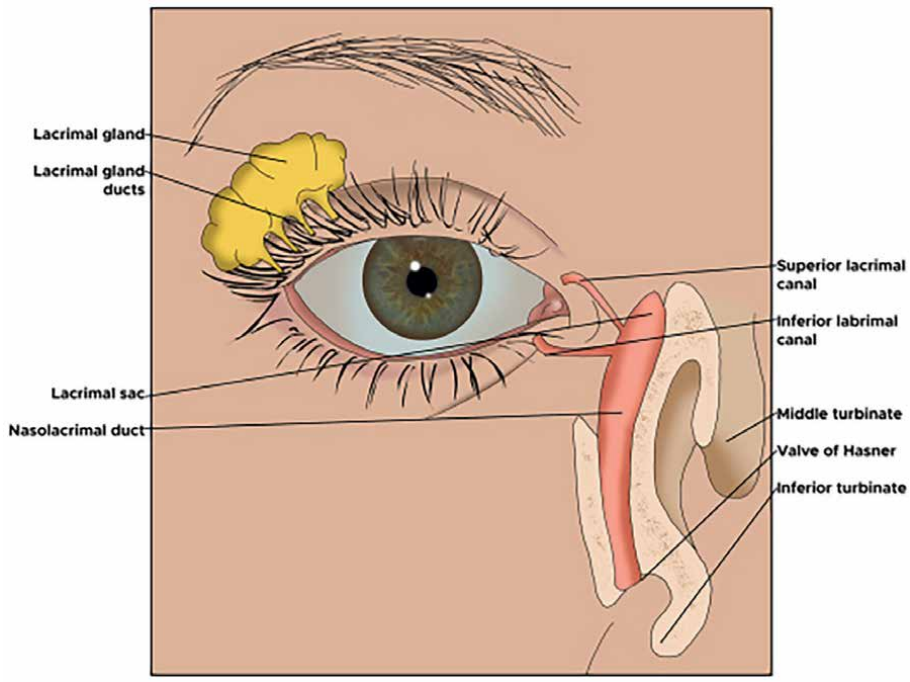

Figure 1.
Anatomy of the lacrimal apparatus and its drainage pathway.

Chronic dacryocystitis ensues from persistent obstruction, attributed to recurrent infections, dacryoliths, or systemic diseases like sarcoidosis and systemic lupus erythematosus.

Congenital dacryocystitis may stem from infection, failure of membrane rupture at the valve of Hasner, or persistent epithelial plugs [4].

Acquired dacryocystitis may be primary, characterized by chronic inflammation and fibrosis of the NLDO, or secondary, resulting from trauma, dacryolithiasis, tumors, or certain medications such as timolol, flourouracil and docetaxel.

4. Epidemiology

Dacryocystitis exhibits a bimodal distribution, with most cases occurring shortly after birth (congenital) or beyond 40 years of age. Predominantly affecting white individuals, over 75% of cases occur in females [1].

5. Pathophysiology

Obstruction within the nasolacrimal drainage system sets the stage for dacryocystitis, leading to the accumulation of tears in the lacrimal sac. Subsequent bacterial colonization incites infection, characterized by erythema, swelling and tenderness over the lacrimal sac. Untreated, it can progress to complications such as orbital abscess, cellulitis, necrotizing fasciitis and even meningitis [5].

6. Risk factors

Various factors contribute to the development of dacryocystitis, including gender (females have narrower ducts), older age (due to narrowed punctual openings and slower tear drainage), dacryoliths, nasal septal deviation, rhinitis, turbinate hypertrophy, idiopathic or iatrogenic trauma to the nasolacrimal system, systemic disorders and certain medications.

7. Clinical features

Acute dacryocystitis presents with sudden pain, erythema, fever and edema around the medial canthus and orbit. Symptoms progress over hours to days, often accompanied by purulent discharge. Chronic dacryocystitis typically manifests as epiphora, sometimes accompanied by conjunctival chemosis and changes in visual acuity due to altered tear film production (**Figure 2**).

8. Complications

Without intervention, dacryocystitis can extend to adjacent orbital tissues, leading to preseptal cellulitis, orbital cellulitis, orbital abscess, optic nerve compression and eventual vision loss.

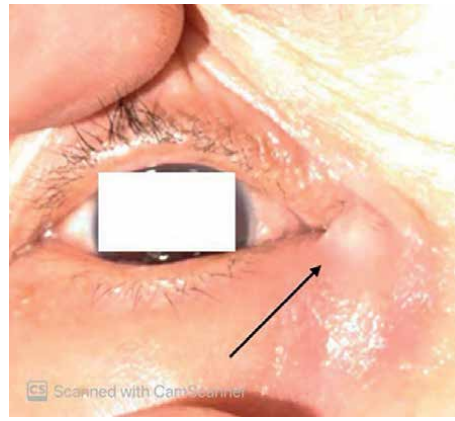

Figure 2.
Acute dacryocystitis with swelling and erythema at the inferomedial aspect of the eye.

9. Evaluation and investigations

Diagnosis of dacryocystitis relies primarily on clinical assessment and patient history. Imaging and blood work are reserved for acutely ill patients. Diagnostic procedures include tear duct massage for microbiological evaluation, serologic testing for systemic diseases suspicion and various tests like syringing, diagnostic probing and nasal endoscopy for surgical planning. In recurrent cases, additional tests such as the Jones test, fluorescein dye disappearance test, dacryocystography and imaging modalities like CT/MRI may be employed. Secretory tests like Schirmer's test may also be performed occasionally to rule out dry eye syndromes.

The following diagnostic tests are performed routinely if a surgical intervention is being planned:

- Syringing: used to check for the presence of any pre-sacral obstruction. Sterile saline solution is injected into the punctum, and if after 15–30 seconds, there was no regurgitation and if the patient appreciates a salty taste with awakening of the swallowing reflex, then the lacrimal passage is considered to be fully patent. If some saline regurgitated from either puncta and some saline passed into the nose, then the lacrimal passage is partially obstructed. A functional blockage is said to be present if there is no regurgitation of saline but a swelling developed in the lacrimal sac region (**Figure 3**) [6].

- Diagnostic probing: a lacrimal probe is passed through the punctum towards the canaliculus. If the common canaliculus is patent, the probe touches the medial wall of the sac and its underlying bone, giving a hard and bony feel (Hard stop). Hard stops are usually amenable to surgical correction. If there is a blocked common canaliculus, we encounter a soft, spongy feel.

- Diagnostic nasal endoscopy: is used to assess the nasal septum for deviation, middle meatus for any sinus disorders, osteomeatal complex and turbinates. It helps to exclude any rhinological pathology as the underlying etiology for dacryocystitis as well as helps in surgical planning.

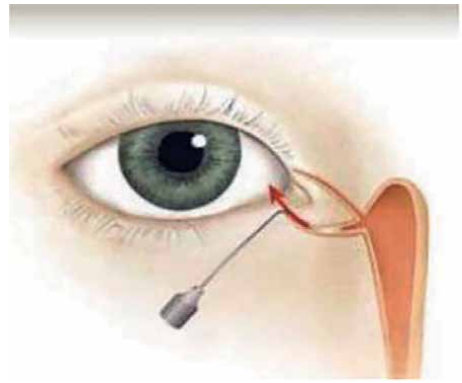

Figure 3.
Lacrimal syringing which shows regurgitation and an incomplete canalicular block.

Additionally, in recurrent cases, the following additional tests may be required to rule out any other causes for excessive tearing:

- Jones Test: *Primary Jones Test*—2% fluorescence dye is instilled in the conjunctival sac, and a cotton tip applicator moistened with 4% lignocaine is inserted into the inferior meatus. If the applicator is stained with the dye, then the nasolacrimal passage is patent. *Secondary Jones Test*—it is only performed if the primary test is suggestive of an obstructed nasolacrimal passage. After 5 minutes, the conjunctival sac is flushed with normal saline to remove any residual dye, and then clear normal saline is injected into the sac. If the dye appeared in the nose after injecting, then it is suggestive of a partial blockage of the passage. If no dye was recovered from the nose, then it is suggestive of a canaliculus block. If no fluid is recovered from the nose, then it is suggestive of a complete blockage of the nasolacrimal passage.

- Fluorescein dye disappearance test: a drop of 2% fluorescence dye is instilled into the conjunctival cul de sac. After 5 minutes, if all the dye had disappeared, then there is no obstruction. However, if there is presence of residual dye, it indicates an obstruction.

- Dacryocystography: it is a relatively simple, inexpensive and straightforward procedure in which a radiographic contrast material (either water based or oil based) is injected into the lower lid canalicular system using a lacrimal cannula. Serial postero-anterior and lateral X-ray films of the orbit are obtained immediately after the injection and also after 30 minutes. A delay in emptying time, or failure of the dye to appear in the nasal cavity or nasopharynx, is indicative of an obstruction (**Figure 4**).

- CT/MRI: is usually reserved of traumatic cases or if there is extensive infection with a suspicion of orbital cellulitis. It helps in surgical planning especially if an endonasal and endoscopic intervention is being planned. These are very useful in evaluating infants with congenital dacryocystitis as they delineate the potential aetiologies of a medial canthal mass such as congenital encephaloceles or vascular malformations [7].

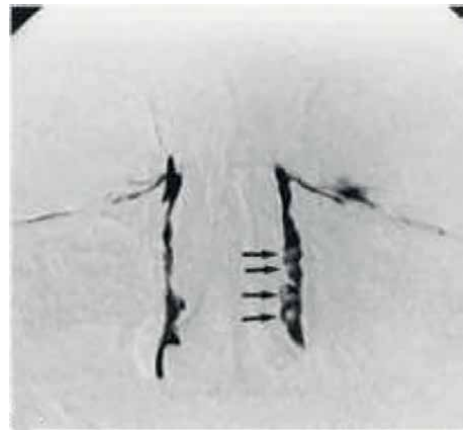

Figure 4.
Dacryocystogram showing left lacrimal dacryolithiasis.

- Secretory tests: are occasionally performed to rule out dry eye syndromes. Schrimer's test, Bengal rose staining test and lysozyme lysis tests are some examples of secretory tests which are occasionally performed.

10. Management

Dacryocystitis necessitates a combined approach of medical and surgical interventions. While acute cases typically respond well to conservative management, surgical intervention becomes more favorable for chronic cases.

Congenital dacryocystitis often resolves spontaneously within the first year of life in about 80–100% cases, with a significant percentage achieving resolution within the initial 6 months [8]. For symptomatic cases not showing spontaneous resolution, lacrimal sac massage with high-pressure irrigation can be attempted. Probing, once considered the primary intervention, is now reserved for children over 1 year of age, after failed spontaneous resolution, with a success rate of approximately 70%. However, it carries risks of creating false passages and epithelial injury leading to fibrosis and scarring, thus reserved for children older than 1 year [9]. If primary probing fails, alternative surgical interventions such as silicone tube intubation, dacryocystorhinostomy, balloon catheter dilation and inferior turbinate fracture may be explored. Topical antibiotics are usually reserved for any acute flare ups.

Acute dacryocystitis is managed with oral antibiotics covering both Gram-positive and Gram-negative organisms (preferably with antistaphylococcal activity), warm compresses and Crigler massage. Lacrimal probing is discouraged during acute episodes. Unresponsive cases are managed with incision and drainage with direct antibiotic application to the lacrimal sac, to provide immediate pain relief and rapid infection control [10, 11].

Chronic dacryocystitis typically necessitates surgical management, with probing often performed initially in outpatient settings. However, most cases eventually require surgical intervention to prevent disease progression. Techniques such as balloon dilation, silicone tube intubation and nasolacrimal stenting may be attempted. However, the primary management remains dacryocystorhinostomy (DCR), either through external or endoscopic endonasal approaches.

11. Dacryocystorhinostomy (DCR)

DCR creates an anastomosis between the lacrimal sac and nasal mucosa, bypassing the obstructed drainage pathway. External DCR, described by Adeo Toti in 1904, historically served as the standard surgical approach until the late twentieth century. But was associated with external scarring and a failure rate of 3–15% [12]. In pursuit of a less invasive, more physiological and more effective technique, endoscopic endonasal DCR (EE-DCR) emerged. Initially described by Rice in 1988 [13] and first performed on live patients by McDonough and Meiring in 1989 [14], EE-DCR offers a more physiological approach with potentially higher success rates compared to traditional external DCR.

- Indications: persistent congenital dacryocystitis not responding to conservative measures, congenital lacrimal duct obstruction associated with mucocele, dacryocystitis, acquired nasolacrimal duct obstruction

- Contraindications: acute dacryocystitis, malignant lacrimal sac mass, dry eye syndromes, bleeding dycrasias

- Surgical prerequisites: confirmation of diagnosis and clinical features, blood investigations like a complete hemogram, serological evaluation for HIV, HBV and HCV, coagulation profile, additional anesthetic investigations such as blood pressure measurement and random blood sugars based on the patient's age and comorbidities.

- Equipment and instruments: toothed forceps, needle holder, punctual dilator, Bowman's probe, Freer's periosteal elevator, blades (number 15, crescent knife), Kerrison punch, sutures (6-0 vicryl and 6-0 silk) and lacrimal (Crawford) stents.

- Anesthesia: can be performed under local or general anesthesia, but usually local anesthesia is preferred. Local infiltration to block the infratrochlear nerve in conjunction with topical anesthesia of the nasal mucosa is the preferred technique.

- Steps:

  A. A curvilinear incision, measuring about 1 cm in length, is given along the anterior lacrimal crest, 3–4 mm short of the medial canthus (**Figure 5**).

  B. Blunt subcutaneous dissection is done to expose the periosteum overlying the lacrimal fossa. Care is taken to avoid injury to the medial canthal tendon (**Figure 6**).

  C. Bone punches are made at the junction of the lamina payracea and the lacrimal bone to create a bony ostium which is then sequentially enlarged (**Figure 7**).

  D. Sac flaps are then created anteriorly and posteriorly using a Bowma's probe.

  E. H-shaped incision is then made across the sac funds till the nasolacrimal duct. The flaps are then raised, and the posterior one is cut.

F. Nasal mucosal flaps are then fashioned using an 11 blade along the bony ostium (**Figure 8**).

G. The nasal mucosal and the sac flaps are then anastomosed edge to edge.

H. Once the anastomosis is secure, the orbicularis is sutured back with 6-0 vicryl followed by skin with 6-0 silk (**Figure 9**).

I. Additionally, if there are adhesions within the lacrimal sac, 0.04% Mitomycin C can be applied intraoperatively. Intubation can be done simultaneously especially in case of inadequate flaps [15–17].

J. Nasal packing is optional, but may be required at times to achieve hemostasis.

- Postoperative care: postoperatively, the patient is prescribed analgesics, topical and oral antibiotics. Nasal decongestants and saline nasal drops are prescribed as well for wound care. The sutures are removed after 1 week, and the patient is regularly followed up in the clinic at 6 weeks, 12 weeks and 6 months.

- Complications:

A. Early (1–4 weeks): wound dehiscence, infection, tube displacement, nasal crusting and intranasal synechiae.

B. Intermediate (1–3 months): granulomas, tube displacement (**Figure 10**), synechiae, punctual cheese wiring, facial scar and nonfunctional DCR

C. Late (>3 months): rhinostomy fibrosis, webbed facial scar, medial canthal distortion and failed DCR

11.1 Endoscopic endonasal DCR

- Indications: epiphora caused by anatomic or functional obstruction of the lacrimal sac or the nasolacrimal duct, chronic relapsing dacryocystitis with purulent discharge, active infection of the lacrimal sac with infection of the overlying skin, acute dacryocystitis, nasolacrimal duct injury, dacryolithiasis, dacryocele and benign lacrimal sac mass

- Contraindications: dry eye syndromes, chronic epiphora due to presaccal obstruction, lagophthalmos with facial nerve palsy, ectropion of the lower lid, malignancy of the lacrimal system, extensive synechiae between the nasal septum and lateral nasal wall, sinonasal malignancy, Wegener's granulomatosis, significant collapse of the nasal dorsal due to trauma, bleeding dycrasias

- Surgical prerequistes: confirmation of diagnosis and clinical features, syringing and diagnostic probing, diagnostic nasal endoscopy, blood investigations like a complete hemogram, serological evaluation for HIV, HBV and HCV, coagulation profile, additional anesthetic investigations such as blood pressure measurement and random blood sugars based on the patient's age and comorbidities.

- Equipment and instruments: endoscopic camera system, video monitor, suction apparatus, antifog solution, light source and cable, 0° and 30° rigid nasal

endoscopes, Blakesley forceps, endoscopic scissors, through cut forceps, Freer's elevator, ball probe, sickle knife, suction cannulas, Kerrison rongeur and burr tips (optional).

- Anesthesia: general anesthesia is the preferred modality for performing an endoscopic end-nasal DCR as it facilitates correction of any simultaneous nasal pathology which contributes to NLDO. However, in cases of severe and uncontrolled comorbidities, it can be performed under local anesthesia as well.

- Steps:

A. Nasal cavity is packed with cottonwoods soaked in 4% lignocaine with 1 in 10,000 adrenaline for about 5–10 minutes to decongest the nasal mucosa. If required, a septoplasty is then done to improve surgical exposure.

B. Lateral wall of the nose is infiltrated with 2% lignocaine with adrenaline, just anterior to the uncinate process.

C. A C-shaped mucosal flap measuring about 1.5 × 1 cm is then fashioned using a 15 number surgical knife. The first incision starts 1 cm above the axilla of the middle turbinate and runs forward by 1 cm, the blade is then turned vertically, a 1.5 cm incision is made downwards, the blade is then turned posteriorly and a 1 cm horizontal incision is made to create a posteriorly bases mucosal flap (**Figure 11**).

D. The mucosal flap is then elevated and is then reflected or excised, to expose the underlying lacrimal bone and the frontal process of the maxilla.

E. The thin lacrimal bone is elevated with a Freer elevator and removed with a forceps.

F. Kerrison rongeur is then used to take off the frontal process of the maxilla (some surgeons prefer to drill it out with microdrills and burr attachments, especially if the bone is very thick)

G. This exposes the medial wall of the lacrimal sac in its entirety.

H. The medial wall of the sac is incised with a sickle knife and excised with a Blakesly forceps or a through cut forceps.

I. Patency confirmed with saline irrigation via the inferior canaliculus.

J. The mucosal flap is then repositioned to cover any exposed bone. Care should be taken to prevent the flap from covering the sac incision.

K. Silicone stents can then be inserted, particularly in revision cases, from the upper and lower canaliculus. Once both the ends are visible inside the nasal cavity, they are held together using a Watzke sleeve or are gently tied together. The excess length of the tube is then excised intranasally.

L. 0.04% Mitomycin C can then be applied to prevent granuloma formation.

M. Nasal packs can be inserted to ensure hemostasis.

- Postoperative care: the patient is usually prescribed oral antibiotics, analgesics and saline nasal drops for 1 week in conjunction with topic antibiotic eye drops. Lacrimal syringing is performed twice daily on first and second postoperative days, and then the patients are discharged. They are followed up in the outpatient clinic at 1 week, 3 weeks and 3 months after the surgery. Nasal endoscopy is usually performed in the follow-up visits to ensure lacrimal passage latency and to remove any excessive crusting. In such cases, it is worthwhile to give saline nasal rinses and douches as well.

- Complications:

A. Early (1–4 weeks): hemorrhage and bleeding into the orbit (in 5–10% cases), ecchymosis of the lower lid, emphysema of the lower lid or cheek, injury to lamina papyracea exposing the orbital fat, medial rectus injury leading to diplopia

B. Intermediate (1–3 months): granulations, granulomas, synechiaea, stent migration, cheese wiring (excessively tight stent cuts through the canaliculus and the skin between them at the medial canthus) (**Figure 12**)

C. Late (>3 months): synechiaea, granuloma formation, stent migration and cheese wiring, lacrimal sump syndrome (block of the common canaliculus intranasally due to mucus accumulation and accompanying sac inflammation, usually responds to external sac massage which helps to clear the accumulated mucus)

11.2 Ex-DCR vs. EE-DCR

EE-DCR has got several advantages over an Ex-DCR. It is a more physiological procedure as it avoids injury to the orbicularis oculi muscle, thereby preserving its pumping function. It avoids an external facial scar and any concomitant nasal pathologies

Figure 5.
Curvilinear incision used for ExDCR.

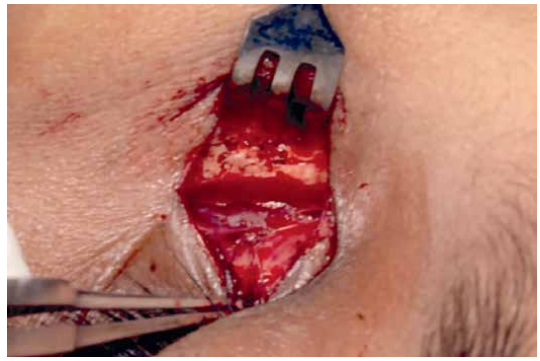

Figure 6.
Dissection of the lacrimal sac to expose the bony lacrimal fossa.

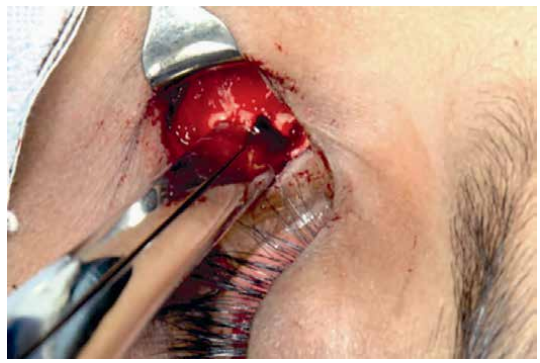

Figure 7.
Creation of bony ostium using a Kerrison punch.

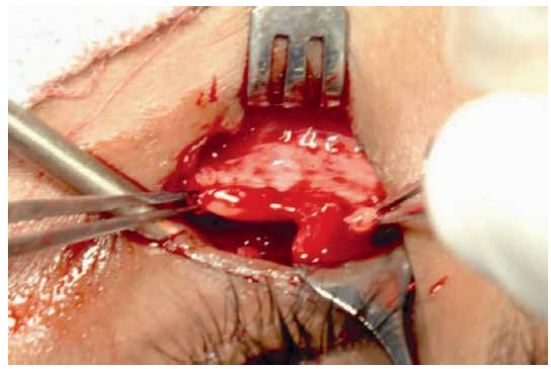

Figure 8.
Raising the nasal mucosal flap after making an incision in the sac.

can be corrected in a single procedure. However, it does require specialized training for performing procedures with endoscopic assistance, and moreover, the endoscopic equipment is expensive as well.

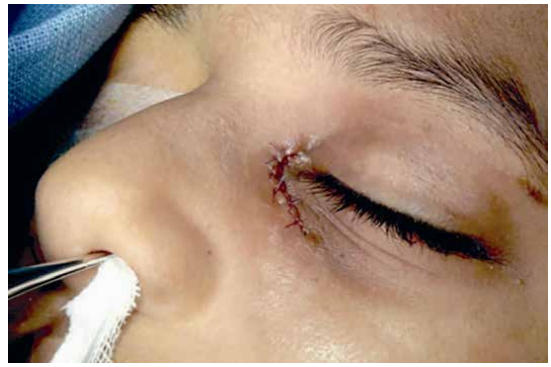

Figure 9.
Wound closure with sutures showing an external facial scar.

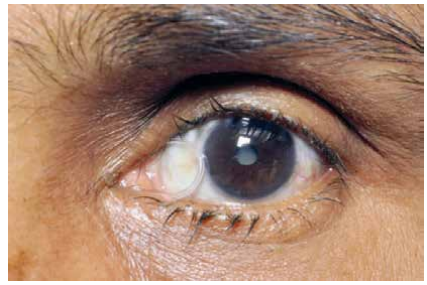

Figure 10.
Postoperative complication showing tube displacement.

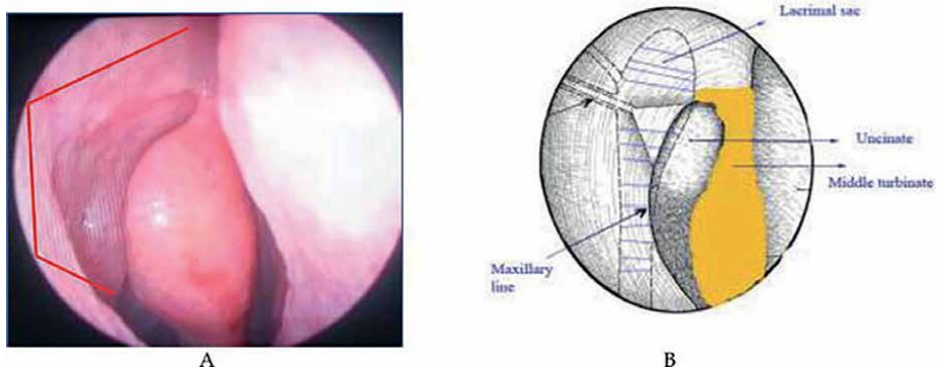

Figure 11.
Endoscopic view of the left lateral nasal wall showing the maxillary line and uncinate process (A) and a diagrammatic illustration demonstrating relationship of lacrimal sac to uncinate process and middle turbinate (B).

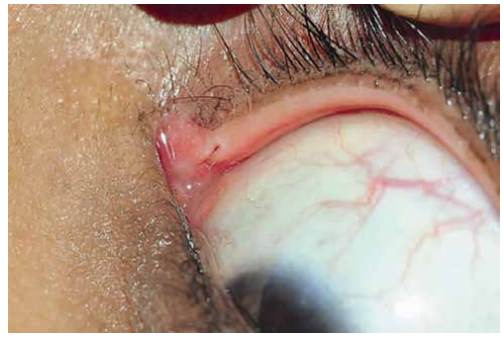

Figure 12.
Postoperative complication showing cheese wiring.

Aspect	EX-DCR	EE-DCR
Approach	External	Endoscopic, endonasal
Physiological consideration	Less physiological as orbicularis oculi gets severed	More physiological as orbicularis oculi and its pumping mechanism are preserved
Scar	External facial scar present	Avoids a facial scar
Correction of nasal pathologies	Cannot be corrected	Can be corrected in a single procedure
Anesthesia	Local anesthesia is preferred	General anesthesia is preferred
Training requirement	No additional training	Requires specialized training for using endoscopes
Equipment	Inexpensive	Relatively expensive
Active infection	Cannot be done in cases of active infection	Active infection is not a contraindication

Table 1.
Comparison between external and endoscopic DCR.

The major differences between the two procedures are summarized below in a tabular manner (**Table 1**).

12. Balloon catheter dilation of NLD/balloon dacryoplasty

It is a minimally invasive procedure to establish lacrimal system patency in patients with congenital NLDO [18]. It is typically performed in children above 12 months of age.

- Indications: failed probing, restenosis after failed silicone intubation
- Anesthesia: performed under general anesthesia
- Steps:

  A. Superior and inferior puncta are dilated using a punctual dilator

B. The balloon catheter is lubricated and inserted into the upper lacrimal system till the 15 mm mark. It is slowly advanced towards the nose and can be grasped via the nostril once it is in place.

C. The balloon is then inflated to 8 atmospheres for 90 seconds, then deflated, and then reinflated to 8 atmospheres for 60 seconds.

D. It is then gently retracted 5 mm where the same steps are repeated.

E. It is then removed by twisting in an anticlockwise manner.

- Postoperative care: topical antibiotic eye drops are prescribed for a week after the procedure. Usually analgesics are not required.

13. Recent advances

A new, novel lacrimal ostium stent (LOS) is currently being evaluated for use in patients with a small lacrimal sac, who are undergoing EE-DCR. Most cases of EE-DCR with a failed result, are attributed to the closure of the nasal ostium. In such cases, LOS comes in handy as it prevents the closure of the nasal ostium and thus, can enhance the success rate of the procedure.

The LOS is a tripartite structure composed of silicone. It has a smooth surface and has a central hollow tube which facilitates lacrimal drainage. It has also got an elliptical repositioning plate and four buckles which facilitate a strong fixation [19].

14. Conclusion

Dacryocystitis stands as a primary culprit behind epiphora and periorbital swelling, stemming from either nasolacrimal duct obstruction or lacrimal passage blockage, culminating in infection. It presents as either congenital or acquired, with the latter further categorized into primary or secondary forms. A comprehensive assessment involving physical examination and diagnostic tests is imperative for accurate diagnosis, emphasizing collaborative efforts between ophthalmologists and otorhinolaryngologists for optimal patient care. While acute cases typically receive conservative management, surgical intervention emerges as the cornerstone for chronic cases. Although external DCR (Ex-DCR) historically served as the gold standard surgical intervention, the tide is shifting towards Endoscopic Endonasal DCR (EE-DCR) owing to its myriad advantages.

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Conflict of interest

None.

Notes

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References

[1] Chen L, Fu T, Gu H, Jie Y, Sun Z, Jiang D, et al. Trends in dacryocystitis in China. Medicine. 2018;**97**(26):e11318

[2] Singh S, Ali MJ. Congenital dacryocystocele: A major review. Ophthalmic Plastic & Reconstructive Surgery. 2019;**35**(4):309-317

[3] Sáenz González AF, Busquet I, Duran N, Arámbulo O, Badal Alter JM. Chronic dacryocystitis caused by sarcoidosis. Archivos De La Sociedad Espanola De Oftalmologia. 2019;**94**(4):188-191. Available from: https://www.pubmed.ncbi.nlm.nih.gov/30558969/

[4] Takahashi Y, Kakizaki H, Chan WO, Selva D. Management of congenital nasolacrimal duct obstruction. Acta Ophthalmologica. 2009;**88**(5):506-513

[5] Engelsberg K, Sadlon M. First-onset dacryocystitis: Characterization, treatment, and prognosis. Ophthalmology and therapy. 2022;**11**(5):1735-1741

[6] DrPA S. Chronic dacryocystitis—It's evaluation and management by various investigative and diagnostic test. IOSR Journal of Pharmacy (IOSRPHR). 2013;**03**(10):28-33

[7] Philadelphia LK, Beirut, Lebanon, and William R. Katowitz, MD. Managing Dacryoceles and Dacryocystitis. Newark, New Jersey: Jobson Medical Information LLC; [Internet]. 2018. Available from: https://www.reviewofophthalmology.com/article/managing-dacryoceles-and-dacryocystitis

[8] Vagge A, Ferro Desideri L, Nucci P, Serafino M, Giannaccare G, Lembo A, et al. Congenital nasolacrimal duct obstruction (CNLDO): A review. Diseases. 2018;**6**(4):2-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6313586/

[9] JDH Y, CJ ME, Ogston SA. Congenital nasolacrimal duct obstruction in the second year of life: A multicentre trial of management. Eye. 1996;**10**(4):485-491. Available from: https://www.nature.com/articles/eye1996107

[10] Prat D, Magoon K, Revere KE, Katowitz JA, Katowitz WR. Management of pediatric acute dacryocystitis. Ophthalmic Plastic and Reconstructive Surgery. 2021;**37**(5):482-487. Available from: https://www.pubmed.ncbi.nlm.nih.gov/33782322/

[11] Cahill KV, Burns JA. Management of acute dacryocystitis in adults. Ophthalmic Plastic & Reconstructive Surgery. 1993;**9**(1):38-42

[12] Metson R. The endoscopic approach for revision dacryocystorhinostomy. The Laryngoscope. 1990;**100**(12):1344-1347. Available from: https://www.pubmed.ncbi.nlm.nih.gov/2243532/

[13] Rice DH. Endoscopic intranasal dacryocystorhinostomy—A cadaver study. American Journal of Rhinology. 1988;**2**(3):127-128

[14] McDonogh M, Meiring JH. Endoscopic transnasal dacryocystorhinostomy. The Journal of Laryngology & Otology. 1989;**103**(6):585-587

[15] Dresner SC, Klussman KG, Meyer DR, Linberg JV. Outpatient dacryocystorhinostomy. Ophthalmic Surgery. 1991;**22**(4):222-224. Available from: https://www.pubmed.ncbi.nlm.nih.gov/1772483/

[16] Emmerich KH, Busse H, Meyer-Rüsenberg HW. Dacryocystorhinostomia externa. Technique, indications and results. Der Ophthalmologe: Zeitschrift Der Deutschen Ophthalmologischen Gesellschaft. 1994;**91**(3):395-398. Available from: https://www.pubmed.ncbi.nlm.nih.gov/8086760/

[17] Çokkeser Y, Evereklioglu C, Comparative EH, Dacryocystorhinostomy EVE. Results in 115 patients (130 eyes). Otolaryngology-Head and Neck Surgery. 2000;**123**(4):488-491

[18] Robbins Tien D, Young D. Balloon dilation of the nasolacrimal duct. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2005;**9**(5):465-467

[19] Yu B, Zhou GM, Shi JL, Wu ED, Wu WC. Management of chronic dacryocystitis cases after failed external dacryocystorhinostomy using endoscopic technique with a novel lacrimal ostium stent. International Journal of Ophthalmology. 2022;**15**(3):413-419

Chapter 8

Advancements in the Application of Medical Laser in Rhinology

Lingling Zhou and Yu Huang

Abstract

With the development of laser technology and the advancement of otolaryngology, medical laser is playing increasingly important roles in the treatment of otolaryngology diseases, especially in early-stage laryngeal cancer by trans-oral endoscopic surgery, which significantly improved patients' survival and quality of life. Medical laser in the treatment of nasal diseases started, respectively, late, which is still under exploration. To advocate the application of medical laser in rhinology and provide inspiration for exploring new ideas of medical laser in this field, current application of medical laser in the treatment of nasal diseases is discussed, combined with our experience in clinical practice. Medical laser can be applied in various rhinologic practices. Laser surgery technology is playing increasing roles in rhinology, and it is of great potential that medical laser will bring new expansion to the field of minimally invasive nasal surgery.

Keywords: medical laser, rhinology, dacryocystorhinostomy, turbinate reduction, nostril atresia, rosacea

1. Introduction

Medical laser refers to utilization of advanced laser technology in a broad area to meet challenges in clinical diagnosis and therapy and to address healthcare issues that impact broad populations [1]. With the development of laser technology as well as the advancement of otolaryngology surgery conceptions and skills, new applications of medical laser have been explored to help diagnosis and therapy for otolaryngology diseases. Medical laser is playing increasingly important roles in the treatment of otolaryngology diseases, for instance, especially in the treatment of early and middle-stage laryngeal cancer by trans-oral endoscopic minimally invasive surgery, which has modified surgical approaches and significantly improved patients' survival and quality of life. Medical laser in the treatment of nasal diseases started, respectively, late, which is still in the stage of exploration. In this chapter, we will discuss the application of medical laser in the treatment of nasal diseases, combined with our experience of diagnosis and treatment in clinical practice, in order to advocate the applications of medical laser in rhinology and promote inspiration for exploring new applications of medical laser in this field.

2. Laser characteristics for medical application

Laser is abbreviated terminology of light amplification by stimulated emission of radiation. In 1960, physicist Theodore Maiman invented the world's first laser device, a ruby laser [2].

Laser has high monochromaticity, high directivity, high brightness, and good coherence. In medical procedures, these characteristics are utilized to convert laser energy into thermal effect on the focused area, so that the instantaneous temperature can reach up to 200 ~ 1000°C, leading to coagulation, incision, and vaporization of the target tissue.

Coagulation: The thermal effect of laser causes the temperature rising of target tissue, and when it exceeds 56°C, the tissue protein becomes denatured and coagulated, which can destroy the lesion, or achieve hemostasis by closing the blood vessels.

Incision: Laser energy and thermal effect are enhanced compared to coagulation mode, to achieve incising effect by rapidly burning up of target tissue, leaving necrotic areas on both sides of the incision.

Vaporization: The laser energy and thermal effect are further enhanced, and the local high temperature makes the tissue instantaneously transform into smoke and vapor, so as to eliminate the lesion.

3. Classification of commonly used medical lasers

Classification of medical lasers is typically according to the main materials they are composed of. Commonly used medical lasers include solid-state laser, gas laser, excimer laser, dye laser, semiconductor laser, and so on, and each of them have diverse characteristics, respectively.

3.1 Solid-state laser

The main material is glass or crystal material, adding ionic elements such as ruby, sapphire, neodymium-doped yttrium aluminum garnet (Nd:YAG), erbium-doped garnet (Er:YAG), neodymium-doped glass (Nd:Glass), KTP laser, holmium laser, thulium laser, and so on. The solid-state laser has the merits of high optical power, excellent beam quality, and wide tuning range [3].

3.2 Gas laser

The main material to release gas laser is the gas inside the medium such as helium-neon (He-Ne), argon ion, CO_2, copper vapor laser, and so on. Gas lasers were the first continuous wave (CW) lasers [4].

3.3 Excimer laser

The reactive gas is mixed with the inert gas as the medium to generate the laser such as chlorine/fluorine - argon/krypton/xenon laser. Excimer lasers have the characteristics of short wavelength and high power, belonging to the pulse laser.

3.4 Dye laser

Organic dyes are used as laser media in solution or suspensionsuch as PDL laser, high power, and good optics, but low efficiency, need to replace the dye. They generally allow for a wider range of wavelengths compared to solid-state or gas lasers [4].

3.5 Semiconductor laser

Generally refers to diode laser, which has low price, high efficiency, low environmental requirements, and long service life. The p–n junction of a semiconductor diode forms the active medium [4].

Among them, solid-state laser and gas laser are considered to have higher output power and energy efficiency. The commonly used lasers in otolaryngology include neodymium-doped yttrium aluminum garnet (Nd:YAG), KTP laser, holmium laser, helium-neon (He-Ne), CO_2, PDL laser, and so on.

4. History of medical laser application in otolaryngology

The technology of laser was first introduced by Theodore Maiman in Hughes Aircraft Laboratories (HRL) in 1960 [5]. The 33-year-old physicist created a kind of light that had not been observed previously from any natural origin, by stimulating specific cubic ruby material to emit red pulsating light with high brightness and high strength. Thereafter, a variety of materials have been gradually found presenting similar characteristics.

Ophthalmologist Charles J Campbell from Columbia Presbyterian Medical Center, who noticed the potential value of laser for clinical application, performed a retinal laser surgery in 1961, which was the first laser surgery in human body [6], resecting retinal neoplasm using a ruby laser.

In 1963, Kumar Patel invented CO_2 laser, which was considered a most appropriate solution designed for clinical use in otolaryngology [7].

In 1967, Polanyi and Bredemeier invented an optical transmission system suitable for otolaryngological endoscopic procedures [8]. The equipment was composed of quite similar components like lasers we use today.

In 1972, Strong and Jako performed the first laser surgery of laryngeal cancer resection [9]. Continuous CO_2 laser was coupled to surgical microscope, to resect lesions on vocal cord in a highly controllable mean.

Medical laser has played a significant role in changing surgical methods, improving patients' quality of life and prognosis in the treatment of early and middle-stage laryngeal cancer through oral endoscopic minimally invasive surgery. Applications in the ear include laser tympanostomy, stapedotomy, etc. Medical laser in remedy for nasal diseases started late, which is still in the stage of exploration.

Application of medical laser in rhinology started in late 1970s [10], as H Lenz from Germany utilized argon-ion laser in carbonization of the respiratory mucosa of the lower turbinates in vasomotor rhinitis [11]. Argon, KTP, and diode lasers were used in managing epistaxis resulting from hereditary hemorrhagic telangiectasia [12]. A variety of rhinology scenarios have been explored to attempt applicability of medical laser till now, which will be introduced in this chapter.

5. Laser commonly used in otolaryngology

Based on the classification of lasers referred above, there are various lasers for medical use in different medical fields. Among them, lasers commonly used currently in otolaryngology are listed below.

5.1 CO_2 laser

Of 10,600 nm wavelength, it is easily absorbed by water components in soft tissue, with rapid gasification and cutting effect on tissue. CO_2 laser causes mild damage to peripheral tissue. The classic optical guide arm mode is mostly used, and the optical fiber mode has appeared in recent years, as supplementary component to access particular surgical field that could not be reached by optical guide arm mode. CO_2 laser is the most commonly used laser in otorhinolaryngology.

5.2 Nd:YAG laser

Of 1064 nm wavelength, it is mainly absorbed by cellular proteins, so as to take thermal effect on deep tissue. On the other hand, this type of laser is of higher possibility in inducing postoperative scar and blisters.

5.3 Ho:YAG laser

Of 2014 nm wavelength, it is easily absorbed by water in the tissue, producing micro-bubbles to separate and cut hard tissue, like bones or calculi. The cutting effect on tissue is relatively superficial.

5.4 KTP laser (potassium titanium oxide phosphate laser, green laser)

Of 532 nm wavelength, it can be selectively absorbed by hemoglobin in the tissue, exhibiting good hemostatic effect. It produces less vapor in surgical field, providing a better view for surgeons.

5.5 PDL laser (pulsed dye laser)

Of 585/595 nm wavelength, it is mainly absorbed by hemoglobin and melanin in tissue, which can effectively treat a variety of vascular diseases.

5.6 He-Ne laser (red laser)

Of 632.8 nm wavelength, it is the most commonly used gas laser in medical field, which can be non-specifically absorbed by hemoglobin and proteins in tissue.

6. The application of medical laser in nasal diseases

Medical laser can be applied in various rhinologic clinical practices, ranging from inflammatory situations as allergic or nonallergic rhinitis, sinusitis, structural disease as turbinate hypertrophy, nostril atresia, nasal adhesion, nasal-orbital disease as dacryocystitis and abscess, epistaxis, and selected situation of neoplasms. Specific applications

mainly include dacryocystorhinostomy, resection of external nasal masses and pigmented nevus, resection of benign and malignant tumors of nasal cavity and sinuses, hemostasis of nasal hemorrhage, and laser resection of nasal mucosal hemangioma, partial turbinectomy, sinusotomy and resection of nasal polyps, choanal plasty for posterior nostril atresia, nasal adhesion separation, and treatment of rosacea.

6.1 Dacryocystorhinostomy

Dacryocystorhinostomy is indicated in dacryocystitis and abscess caused by chronic lacrimal duct obstruction resulting from various reasons. Laser is utilized to incise the dacryocyst projection area on the lateral wall of the nasal cavity, including the bony structures of lacrimal bone and agger nasi, to achieve the effect of fusion of the dacryocyst cavity and the nasal cavity, as treatment of lacrimal cyst obstructive inflammation (See **Figure 1**). High power laser such as Ho-YAG laser is proposed [13, 14].

In clinical practice, the authors' experience is that after ablating the frontal process of maxilla and the lacrimal bone covering the dacryocyst area, a perpendicular incision could be made along the posterior margin of the cyst to incise into it, in order to avoid damaging the common lacrimal duct. The fusion of the dacryocyst cavity and the nasal cavity should be sufficient, so as to access full drainage.

6.2 Resection of external nasal masses and pigmented nevus

Regarding the size and depth of external nose, lesions like epithelial masses and pigmented nevus can be completely removed by cutting or vaporizing with the laser's photothermal effect. Commonly used lasers are CO_2 laser, and Nd:YAG laser [15, 16]. In case some lesion should have potentiality of malignancy, cutting with laser and keeping certain safe margins is abiding by the principle of en-bloc resection for tumors.

Furthermore, local treatment with CO_2 laser and pulsed dye laser is reported being a new and effective method for skin flap necrosis after basal cell carcinoma resection [17].

6.3 Resection of benign and malignant tumors of nasal cavity and sinuses

Laser has a unique role in the resection of benign and malignant tumors in the nasal cavity and sinuses, such as the resection and photocoagulation of the original

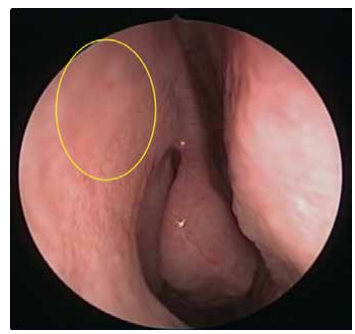

Figure 1.
Laser for dacryocystorhinostomy. Yellow circle: Dacryocyst projection area.

site of inverted papilloma (See **Figure 2**), the resection of malignant tumors regarding the safe margin, and the coagulation treatment of the tumor bed. Suggested types are KTP laser, PDL laser, etc. [14]. Some tumors are associated with possibility of bone invasion, while bone drilling should be performed along with laser resection and coagulation, to confirm acquisition of safe margins.

6.4 Hemostasis of nasal hemorrhage and laser resection of nasal mucosal hemangioma

For nasal bleeding of small vessel rupture, or mucosal hemangioma, the bleeding site and the surrounding area can be coagulated by laser in a non-contact way, and the small hemangioma was coagulated and blocked (See **Figure 3**). Suggested types are KTP laser, PDL laser, etc. [14]. The non-contact coagulation on the mucosa can minimize irritation to nasal normal condition, so as to help the patients recover with minimized nasal discomfort including nasal blockage, rhinorrhea, or subsequent risk of adhesion.

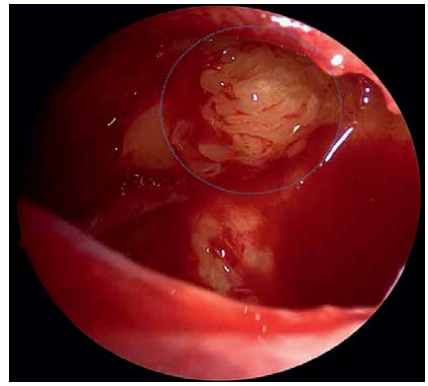

Figure 2.
Resection of stage 1 inverted papilloma. Blue dotted circle: Laser applied region.

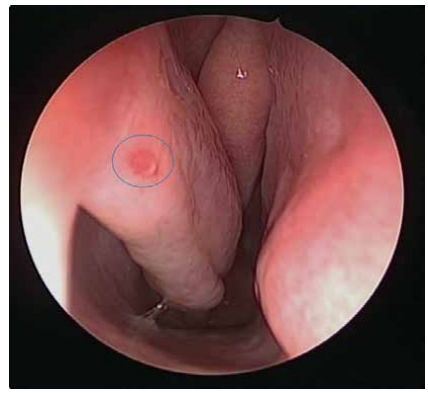

Figure 3.
Hemostasis of nasal hemorrhage by laser. Blue circle: Laser applied region.

6.5 Partial turbinectomy

For some patients suffering from nasal blockage by turbinate hypertrophy due to allergic rhinitis, vasomotor rhinitis, hypertrophic rhinitis, etc., nasal spray and oral medication effect are sometimes not satisfying. By laser surgery, partial removal of the turbinate tissue, coagulation, and postoperative scarring of the tissue can achieve the effect of reducing the volume of the turbinate, improving nasal ventilation and drainage, as well as reducing nasal secretions, which is rapid, effective, and with few complications. On the other hand, posterior nasal nerve ablation by laser can relieve nasal irritation symptoms of AR and VMR (See **Figure 4**) [14, 18]. CO_2 laser, KTP laser, and He-Ne laser can be used.

Raj Tajamul Hussain et al. conducted a prospective observational study of 53 symptomatic inferior turbinate hypertrophy patients who had poor effect by medication and found that CO_2-laser turbinoplasty improved nasal symptom scores, including nasal congestion symptom rating scale (NOSE) and visual analog scale (VAS) scores [19].

6.6 Sinusotomy and resection of nasal polyps

For patients with chronic rhinosinusitis and nasal polyps, laser can be used in functional nasal endoscopic sinus surgery, so as to reduce the sinus scarring, ensure

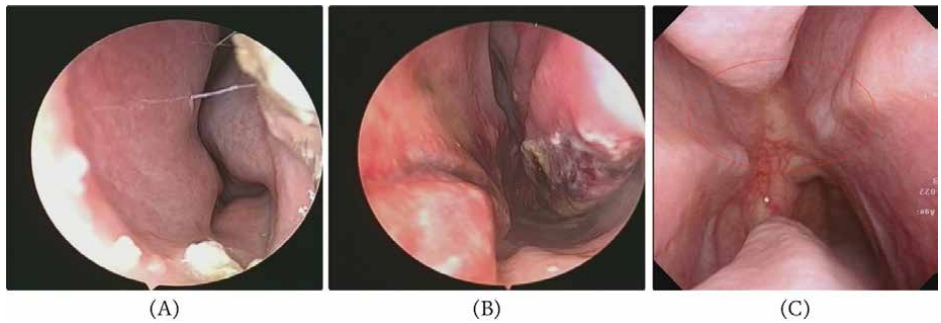

Figure 4.
Turbinate hypertrophy due to allergic rhinitis, vasomotor rhinitis, hypertrophic rhinitis, etc. A. Turbinate hypertrophy before laser. B. Nasal cavity view 1.5 weeks after laser surgery. C. Laser applied region for posterior nasal nerve ablation (Red oval).

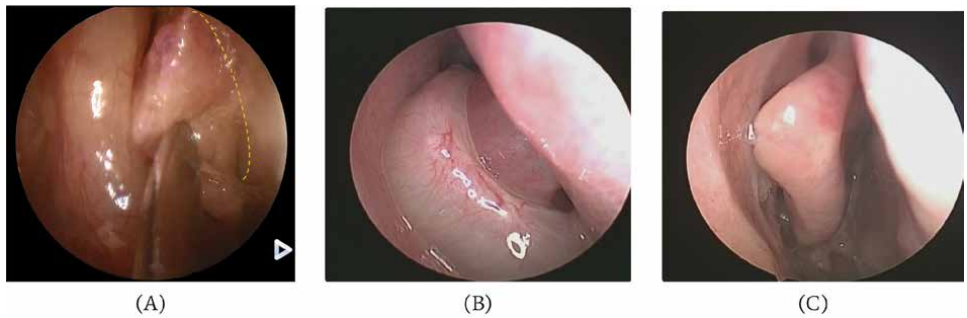

Figure 5.
A. Resection of polyps by laser. Yellow dotted line: Laser applied region. B. Polyp before laser surgery. C. Nasal cavity view 2 months after polyps laser surgery.

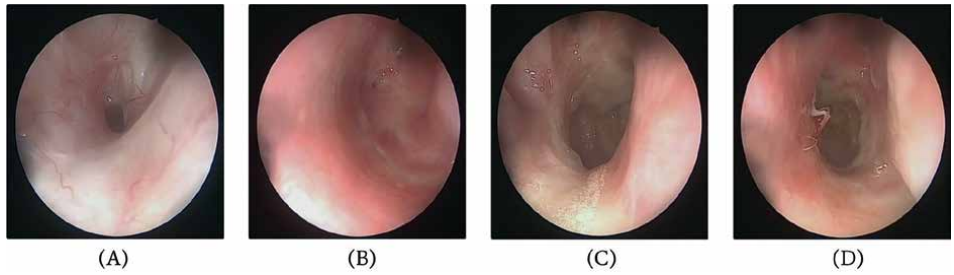

Figure 6.
Endoscope view of a patient with bilateral posterior nostril atresia treated by laser choanal plasty. A. Right side, before surgery. B. Left side, before surgery. C. Right side, 1 month after surgery. D. Left side, 1 month after surgery.

long-term drainage, and carry out vaporization of nasal polyps. Laser ablation of the base of nasal polyposis can promote tissue scarring and reduce recurrence (See **Figure 5**) [14]. Fiber laser such as KTP laser and Ho:YAG laser can be used. As development of more effective instruments like powered microdebrider and plasma ablation, laser is relatively less suitable for sinusotomy and resection of nasal polyps, while it could still be an alternative in particular scenarios.

6.7 Choanal plasty for posterior nostril atresia

Posterior nostril atresia can be caused by congenital malformation/trauma/post-radiotherapy scar adhesion. The atretic tissue is different according to etiology, mainly of membrane/bone/mixed composition. According to the specific atretic tissue, appropriate type of laser is selected for excision, with less trauma and less scar contracture, and can be formed in one stage [20]. Suggested types are CO_2 laser, KTP laser, Ho:YAG laser, etc., depending on the atretic tissue. As shown in the figure, the author treated a patient with bilateral posterior nostril atresia after radiotherapy for nasopharyngeal carcinoma and achieved good results after CO_2 laser treatment, who has fluent nasal airflow and is under further follow-up (See **Figure 6**).

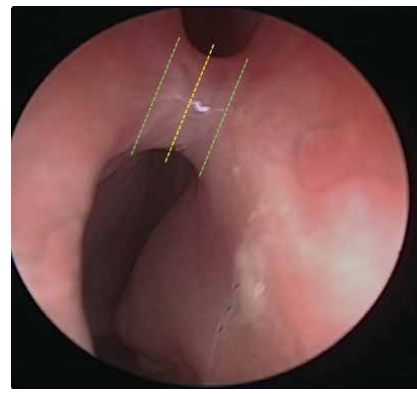

Figure 7.
Nasal adhesion to be separated by laser surgery. Yellow dotted line: Laser incision. Green dotted line: Laser ablation on proliferated scar tissue.

6.8 Nasal adhesion separation

Nasal adhesion is a usual complication after endoscopic surgery, nasal trauma, or inflammation. Fiber laser can be used to separate nasal adhesions, and local combination with mitomycin can enhance the efficacy and prevent re-adhesions [21]. CO_2 laser and KTP laser can be selected.

In clinical practice of the authors' institute, a 'incise-coagulate' method is utilized. The adhesion tissue is incised in the middle, then both ends are coagulated in endoscopic vision, to ensure sufficient coagulation of scar tissue, as well as avoid extensive injury to normal mucosa and vessels (See **Figure** 7).

6.9 Treatment of rosacea

Rosacea is a common chronic progressive skin inflammation characterized by persistent flushing, skin erythema, subcutaneous telangiectasia, papules, pustules, and nodoid changes in nasal appearance [22]. The laser of 500–600 nm wavelength can be selectively absorbed by the target tissue of rosacea lesion, to eliminate erythema and capillary dilatation, and the combination with hydroxymethazoline/hydroxychloroquine can enhance the efficacy [23]. Options include PDL laser, KTP laser, etc. Local skin pain, purpura, and pigmentation may occur after treatment. PDL laser significantly reduces nasal erythema and swelling.

There are some cautions after rosacea laser surgery. After laser surgery, patients may experience purple skin discoloration and discomfort as the area heals. Ice packs and steroids can reduce postoperative pain and swelling. Keeping the treatment area covered with vaseline ointment may support healing. Pain can usually be controlled with over-the-counter medications. It is recommended to use sunscreen outdoors during the healing period [24].

7. The development of new laser technology

With the development of new laser technology, we expect to apply some new technologies to the field of nasal surgery in the future. Femtosecond laser technology and lattice laser technology are introduced here. Furthermore, new materials are continuously being found capable for laser mediums, which have various new characteristics, presenting potentials for expanding the utilization of medical lasers.

7.1 Femtosecond laser technology

Femtosecond laser (FSL) works in ultrafast pulses with short duration of each pulse (10^{-15} second level), operates in the range of tens of to hundreds of femtoseconds, which can be focused in a very small space volume with a very high instantaneous power, generating little effect on the surrounding tissue. As high instantaneous power, focused precisely on the target lesion, a large number of microbubbles are generated through photolysis to separate tissues. FSL can easily achieve a spatial resolution of less than 100 nm to assure accuracy in operation [25]. The current application of FSL is mainly in the field of ophthalmic precise surgeries. It may be developed and applied in the field of rhinology surgery as necessity for specific scenarios requiring higher precision.

7.2 Lattice laser technology

Lattice laser was introduced by Dr. Rox Anderson of Harvard University in 2004. A lattice microtherapy area (MTZ) is arranged by the fusion of superpulse laser technology and computer graphics technology, as tissue vaporization caused by laser to produce many three-dimensional tiny thermal damage strips of uniform size and uniform arrangement surrounded by otherwise normal tissue, to stimulate the initiation of target tissue repair and reconstruction. The treatment depth, density, and treatment range can be preset, with high precision and small collateral damage [26–28]. It is mainly used in the treatment of skin hemangioma, pigmented nevus, vitiligo, scar, and so on. It may be developed and applied in the field of rhinology plastic surgery or therapy for other superficial lesions in epithelium or mucosa.

7.3 New laser types for candidate application in rhinology

There are continuously new laser types emerging along with the advancement of technology. Here, the author takes thulium fiber laser and autofocusing Bessel beams for example to introduce.

7.3.1 Thulium fiber laser

A novel thulium fiber laser (TFL) has been reported successfully moved forward from the preclinical trials into clinical practice and now is being widely used in clinics around the world. The wavelength of TFL is closer to the water absorption peak. It decreases carbonization and retropulsion ,which makes TFL an advantage in urologic surgery [29]. Thulium fiber laser has been subsequently compared with holmium laser in urologic clinical practice, to find TFL performing effective quick dusting and producing smaller fragments, as well as working at a lower power, leading to higher stone-free rate and lower risk of complications [30, 31]. TFL is currently mainly utilized in urology, while some situations similar to lithotripsy occurring in rhinology, such as dacryocystorhinostomy or other possible scenarios, should have the potential for application of TFL.

7.3.2 Autofocusing Bessel beams

A new family of abruptly autofocusing waves named autofocusing Bessel beams (ABBs) was introduced by Ding Z et al. in 2023, which only strongly influence the area near the focus. Such beams have a unique property: their maximum intensity changes slowly during propagation and suddenly increases by orders of magnitude near the focus [32]. This new kind of laser is of definite potential in medical field, playing profound roles in precise surgery meeting the need of medical frontiers, which may affect rhinology in unimaginable means.

8. Advantages of medical laser in rhinology

According to the authors' clinical experience, medical laser has some obvious advantages when applied in rhinology, mainly as listed below.

8.1 Non-contact resection or ablation

Nasal mucosa composed the lining surface of nasal cavity and sinuses, where extra touch applied by contacting devices such as microdebrider or coblation always causes extensive irritation to nasal mucosa, affecting comparatively more depth and/or area of the surgical region, inducing more scab formation followed by prolonged recovery and scar formation. Laser applied in rhinology works in a non-contact way to accomplish resection or ablation, reducing the extra risk attributed by contacting.

8.2 Instant closure of the wound

Laser energy absorbed by tissue cells or hemoglobin instantly degenerates the protein of the focused region, closing the wound and blood vessels in an efficient way, to reduce hemorrhage and tissue injury. Blood vessels less than 1 mm in diameter can be closed by laser.

8.3 Precise targeting

Laser beams applied in rhinology are usually less than 1 mm in diameter, restricting the target area of thermal effect. Comparing with microdebrider (about 4 mm in diameter) and coblation (about 4–5 mm in diameter for resecting, about 1 mm in diameter for submucosal coblation but invisible beneath the mucosa), laser has advantage in precise targeting and manipulation.

9. Potential risks and hazards of medical laser in rhinology

The most dangerous risk of medical laser in otolaryngology is airway fire [33, 34], which is a disastrous complication that should be carefully prevented, especially in trans-oral laryngeal surgeries. Laser in rhinology, as introduced above, also has potential risks of airway fire complication in some particular scenarios, resulting from the consistency of airway, which should be kept in mind.

Particulate matter exposures from medical lasers have been noticed, which was furthermore reported being able to cause dose-dependent respiratory inflammatory response in laboratory animals, and may contain viable bacteria and viruses, including human papilloma virus. A two-zone model was applied by Ramon Lopez, etc., in 2015 to estimate medical laser-generated particulate matter (LGPM) exposures in laser operations. Comparing to near-field from the simulated treatment room, far-field was detected to find significantly lower concentrations of LGPM. Larger room volume and higher air exchange rate were associated with lower LGPM concentrations in the near-field [35].

Another potential hazard is unexpected laser radiation to eyes of either operators or patients, which may cause eye injuries. Laser eyewear protection against laser radiation was suggested by Mike Regan on the 40th Annual Conference of the British Medical Laser Association in 2023 [36]. Appropriate eyewear protection for both operators and patients, which may be of different shapes or visibilities from each other, can avoid laser radiation injuries to their eyes.

10. Prospects

Laser surgery technology is playing increasing roles in rhinology, and it is of great potential that medical laser will bring new expansion to the field of minimally invasive nasal surgery. According to the different characteristics of different existing lasers, the application of these medical lasers in rhinology needs to be further explored and expanded in clinical practice (new application of existing technology), combining their characteristics and surgical need of rhinology to emerge new junctions. On the other hand, according to the needs of nasal surgery, new applicable laser hand-pieces will be developed, such as different integrated instrument functions (navigation, positioning, aspiration, etc.), to deliver laser beams in adequate forms and angles, or other specific desired ways. Laser surgery technology has been widely used in minimally invasive oral surgery, and it is of great potential that medical laser will bring new expansion, new surgical methods, and new surgical concepts, to the field of rhinology.

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Conflict of interest

There is no conflict of interest for this chapter.

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References

[1] Sroka R, Stepp H, Hennig G, et al. Medical laser application: Translation into the clinics. Journal of Biomedical Optics. 2015;**20**(6):061110. DOI: 10.1117/1.JBO.20.6.061110

[2] Hecht J. A short history of laser development. Applied Optics. 2010;**49**(25):F99-F122. DOI: 10.1364/AO.49.000F99

[3] Qiao S, He Y, Sun H, et al. Ultra-highly sensitive dual gases detection based on photoacoustic spectroscopy by exploiting a long-wave, high-power, wide-tunable, single-longitudinal-mode solid-state laser. Light: Science & Applications. 2024;**13**(1):100. DOI: 10.1038/s41377-024-01459-5

[4] Mirza FN, Khatri KA. The use of lasers in the treatment of skin cancer: A review. Journal of Cosmetic and Laser Therapy. 2017;**19**(8):451-458. DOI: 10.1080/14764172.2017.1349321

[5] Maiman TH. Stimulated optical radiation in ruby. [J]. Nature. 1960;**187**:493-494

[6] Koester C, Campbell CJ. The first clinical application of the laser. In: Fankhauser F, Kwasniewska S, editors. Lasers in Ophthalmology: Basic, Diagnostic, and Surgical Aspects: A Review. The Hague: Kugler Publications; 2003. pp. 115-117

[7] Yan Y, Olszewski AE, Hoffman MR, et al. Use of lasers in laryngeal surgery. Journal of Voice. 2010;**24**(1):102-109. DOI: 10.1016/j.jvoice.2008.09.006

[8] Polanyi TG, Bredemeier HC, Davis TJ. A CO_2 laser for surgical research. Medical & Biological Engineering. 1970;**8**(6):541-548. DOI: 10.1007/BF02478228

[9] Strong MS, Jako GJ. Laser surgery in the larynx. Early clinical experience with continuous CO_2 laser. The Annals of Otology, Rhinology, and Laryngology. 1972;**81**(6):791-798. DOI: 10.1177/000348947208100606

[10] Karkos PD, Koskinas IS, Triaridis S, et al. Lasers in omicrontolaryngology: A laser odyssey from carbon dioxide to true blue. Ear, Nose, & Throat Journal. 2021;**100**(1_suppl):1S-3S. DOI: 10.1177/0145561320951681

[11] Lenz H, Preussler H. Histologic changes in the epithelium of the respiratory mucosa of the lower turbinates following argon laser strip carbonization in vasomotor rhinitis. Laryngologie, Rhinologie, Otologie. 1986;**65**(8):438-444

[12] Abiri A, Goshtasbi K, Maducdoc M, et al. Laser-assisted control of epistaxis in hereditary hemorrhagic telangiectasia: A systematic review. Lasers in Surgery and Medicine. 2020;**52**(4):293-300. DOI: 10.1002/lsm.23147

[13] Goel R, Nagpal S, Kamal S, et al. Study of microbial growth on silicone tubes after transcanalicular laser-assisted dacryocystorhinostomy and correlation with patency. Nepalese Journal of Ophthalmology. 2016;**8**(16):119-127. DOI: 10.3126/nepjoph.v8i2.16992

[14] Levine HL. Endonasal laser surgery: An update. Otolaryngologic Clinics of North America. 2006;**39**(3):493-501, viii. DOI: 10.1016/j.otc.2006.01.015

[15] Forbat E, Al-Niaimi F. Fractional radiofrequency treatment in acne scars: Systematic review of current evidence. Journal of Cosmetic and Laser Therapy. 2016;**18**(8):442-447. DOI: 10.1080/14764172.2016.1225964

[16] Delaney SW, Zhang P. Systematic review of low-level laser therapy for adult androgenic alopecia. Journal of Cosmetic and Laser Therapy. 2018;**20**(4):229-236. DOI: 10.1080/14764172.2017.1400170

[17] Nistico SP, Bennardo L, Sannino M, et al. Combined CO(2) and dye laser technique in the treatment of outcomes due to flap necrosis after surgery for basal cell carcinoma on the nose. Lasers in Surgery and Medicine. 2022;**54**(4):523-529. DOI: 10.1002/lsm.23502

[18] Krespi YP, Wilson KA, Kizhner V. Laser ablation of posterior nasal nerves for rhinitis. American Journal of Otolaryngology. 2020;**41**(3):102396. DOI: 10.1016/j.amjoto.2020.102396

[19] Hussain RT, Ahmad R. Role of CO(2) laser in the management of symptomatic hypertrophy of inferior nasal turbinates. Indian Journal of Otolaryngology and Head & Neck Surgery. 2022;**74**(Suppl. 2):826-834. DOI: 10.1007/s12070-020-01876-z

[20] Kubba H, Bennett A, Bailey CM. An update on choanal atresia surgery at Great Ormond Street Hospital for Children: Preliminary results with mitomycin C and the KTP laser. International Journal of Pediatric Otorhinolaryngology. 2004;**68**(7):939-945. DOI: 10.1016/j.ijporl.2004.02.010

[21] Hesham A, Fathi A, Attia M, et al. Laser and topical mitomycin C for management of nasal synechia after FESS: A preliminary report. European Archives of Oto-Rhino-Laryngology. 2011;**268**(9):1289-1292. DOI: 10.1007/s00405-011-1587-x

[22] Husein-ElAhmed H, Steinhoff M. Laser and light-based therapies in the management of rosacea: An updated systematic review. Lasers in Medical Science. 2021;**36**(6):1151-1160. DOI: 10.1007/s10103-020-03200-1

[23] Shaker G, Shaker A. A unique case of facial hypervascularity responding to pulsed-dye laser. Cureus. 2022;**14**(9):e28726. DOI: 10.7759/cureus.28726

[24] DeHart AN, Richter GT. Laser treatment of vascular anomalies. Dermatologic Clinics. 2022;**40**(4):481-487. DOI: 10.1016/j.det.2022.06.002

[25] Yan Q, Han B, Ma ZC. Femtosecond laser-assisted ophthalmic surgery: From laser fundamentals to clinical applications. Micromachines (Basel). 2022;**13**(10):1653. DOI: 10.3390/mi13101653

[26] Srisong H, Daduang S, Lopata AL. Current advances in ant venom proteins causing hypersensitivity reactions in the Asia-Pacific region. Molecular Immunology. 2016;**69**:24-32. DOI: 10.1016/j.molimm.2015.11.003

[27] Khan A, Al-Kathiri WH, Balkhi B, et al. The burden of bites and stings management: Experience of an academic hospital in the Kingdom of Saudi Arabia. Saudi Pharmaceutical Journal. 2020;**28**(8):1049-1054. DOI: 10.1016/j.jsps.2020.07.004

[28] Jin W, Li Z, Jin Z, et al. A novel technique for treating atrophic facial scars in Asians using ultra-pulse CO(2) laser. Journal of Cosmetic Dermatology. 2020;**19**(5):1099-1104. DOI: 10.1111/jocd.13335

[29] Taratkin M, Azilgareeva C, Cacciamani GE, et al. Thulium fiber laser in urology: Physics made simple. Current Opinion in Urology. 2022;**32**(2):166-172. DOI: 10.1097/MOU.0000000000000967

[30] Traxer O, Pearle M. Thulium fiber laser versus holmium:yttrium aluminum garnet for lithotripsy: Which

is the winner? European Urology. 2024;**85**(6):541-542. DOI: 10.1016/j.eururo.2024.02.023

[31] Uleri A, Farre A, Izquierdo P, et al. Thulium fiber laser versus holmium:yttrium aluminum garnet for lithotripsy: A systematic review and meta-analysis. European Urology. 2024;**85**(6):529-540. DOI: 10.1016/j.eururo.2024.01.011

[32] Ding Z, Yu Y, Li X, et al. Focusing property of autofocusing Bessel beams. Optics Express. 2023;**31**(20):33228-33240. DOI: 10.1364/OE.500383

[33] Leemann B, Heidegger T, Grossenbacher R, et al. A severe complication after laser-induced damage to a transtracheal catheter during endoscopic laryngeal microsurgery. Anesthesia and Analgesia. 2004;**98**(6):1807-1808. DOI: 10.1213/01.ANE.0000117144.16826.61

[34] Hermsen HW, Snijdelaar DG, Marres HA. Airway fire, a serious complication during laryngeal laser surgery. Nederlands Tijdschrift voor Geneeskunde. 2002;**146**(9):427-431

[35] Lopez R, Lacey SE, Jones RM. Application of a two-zone model to estimate medical laser-generated particulate matter exposures. Journal of Occupational and Environmental Hygiene. 2015;**12**(5):309-313. DOI: 10.1080/15459624.2014.989361

[36] Mike R. Update on laser eyewear standards. Selected abstracts from the 40th Annual Conference of the British Medical Laser Association: BMLA 2023 Annual Conference. Lasers in Medical Science. 2023;**38**(1):197. DOI: 10.1007/s10103-023-03842-x

Chapter 9

Implants and the Maxillary Sinus: Modern Oral Implantology Changed Paradigms

Stefan Ihde and Fadia Awadalkreem

Abstract

The maxillary sinus is the largest paranasal sinus located within the maxilla's body. The health of the maxillary sinus is of significant importance for the body's functions and health. Sinus pneumatization is a physiological process in which the volume of the sinus increases over time, exposing the roots of the teeth and leading to direct engagement of the roots with the sinus. Similarly, implants may protrude inside the maxillary sinus in cases with compromised ridge support, posing a challenge in implant treatment with respect to sinus health and implant survival rate. This chapter aims to elucidate the main aspect of the maxillary sinus's health and to analyse the various aspects of implant protrusion inside the maxillary sinuses.

Keywords: dental implant, implant protrusion, maxillary sinus, osseofixated implant, sinus health

1. Introduction

The paranasal sinuses are paired air-filled spaces, lined with mucosa, situated in the maxillofacial region and communicating with the nasal cavity [1]. The paranasal sinuses form an integral part of the respiratory tract in addition to the nose, tracheobronchial tree and lung.

Four pairs of paranasal sinuses have been elucidated, including the maxillary, ethmoid, frontal and sphenoid sinuses. Among them, the maxillary sinus is the largest, with a pyramidal shape with a variable size [2–11], not only between the different individuals [higher volume in male] [3, 11], but also between the two sides of the same individual, and an average volume of around 15–30 cubic centimetres (cc) per side 4–10 [3, 11]. It was first described by Leonardo da Vinci in 1489, and later in 1651, an English anatomist named Nathaniel Highmore documented it as *the antrum of highmore*.

2. Development of the maxillary sinus

The maxillary sinus is the first paranasal sinus to develop. At the 10th week of foetal life, it appeared as a mucosal invagination associated with the deeper cranial

tip ethmoidal infundibulum; later, at the 11th week, it formed an oval-shaped space, indicating the primitive (early) maxillary sinus [3, 12]. A rapid maxillary sinus growth occurred during the 4th to 5th and 6th to 7th months to be measured at birth (10 mm × 3 mm × 4 mm). Additional episodes of slow and rapid growth continue after birth until it reaches its full size after the eruption of all the permanent teeth [13].

3. Anatomy of the maxillary sinus

The maxillary sinus is situated within the body of the maxillary bone with six wall boundaries: the superior, inferior, anterior, posterior, medial and lateral walls. The superior, anterior, lateral and medial walls are broad, while the posterior and inferior walls are narrow [1, 14–16].

By forming the orbital floor, the superior wall separates the maxillary sinus from the orbital content. The front wall has a noticeable infero-lateral focal convexity, a canine eminence and a slightly anteriorly concave surface. The narrow and thin posterior bony border correlates with the maxillary artery, maxillary vein and the maxillary division of the trigeminal nerve. On the buccal side, the lateral wall descends and meets the lower part of the alveolar ridge. It faces posterior-laterally towards the infratemporal fossa. The lateral wall of the nasal cavity forms the medial wall of the sinus, while the inferior wall of the sinus continues with the maxillary alveolar process and contains the roots of the maxillary dentition (**Figures 1, 2**) [1, 14–16].

A thin layer of compact bone typically separates the molar roots from the floor of the antrum. However, the roots of the first and second molars may form conical projections (recess) while projecting into the antral floor. In some cases, the first, second, pre-molar and third molar roots, rarely canine roots, may protrude into the sinus (**Figure 3**) [3, 17, 18].

The maxillary sinus had four recesses: the infraorbital recess superiorly, the zygomatic recess laterally, the alveolar recess inferiorly and finally, the palatine recess. The sinus opening is located superiorly, where the ostium communicates with the nasal cavity [19].

The inside of the maxillary sinus is lined with a pseudostratified columnar ciliated epithelium with many goblet cells and the *Schneiderian membrane* that provide

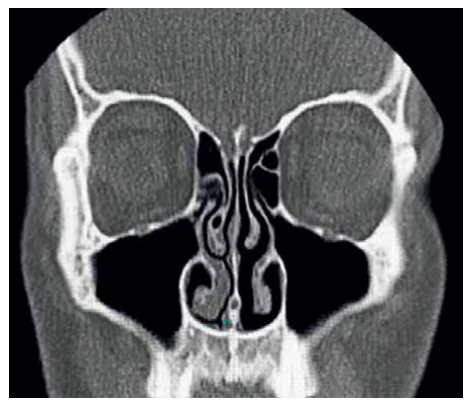

Figure 1.
A. cone beam CT showing a normal maxillary sinus.

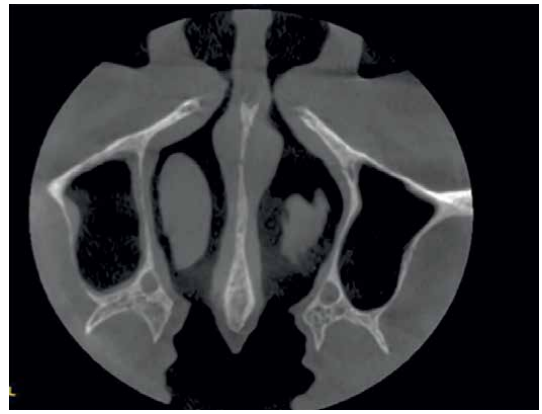

Figure 2.
A cone beam CT, axial view, illustrating a normal maxillary sinus.

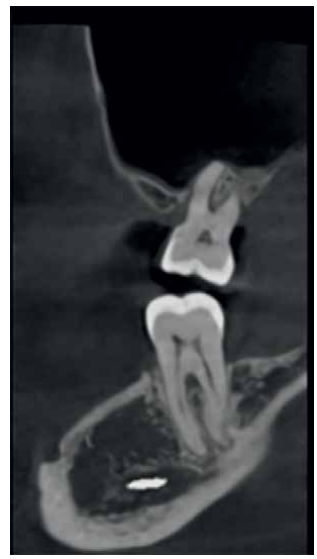

Figure 3.
A cone beam CT, sagittal view, showing the protrusion of the maxillary molar's root inside the sinus.

the necessary blood supply and serve thereby as a periosteum [1, 20–22]. Since the forces acting on the inside of the maxillary sinus are nil and almost no blood supply is required for the underlying bone, its secretorial function into the lumen of the maxillary sinus consumes most of the available blood.

4. Blood supply for the maxillary sinus

The maxillary artery, through the posterior superior alveolar artery, the infraorbital artery and the posterior lateral nasal artery, provides the core blood supply for the maxillary sinus [22–24].

5. Innervation of the maxillary sinus

The infraorbital, anterior, middle and posterior superior alveolar branches of the maxillary nerve provide the sinus with nerve sensation [22–25].

6. Detox-function of the maxillary sinus

The nasal mucosa provides the respiratory tract's primary defence mechanism against inhaled pollutants, allergens and pathogens. The maxillary sinus is protected against the intrusion of infective agents by the constant outflow of liquid. Each maxillary sinus produces more than 1.5 l liquid per day, and this liquid also rinses the nose. The mucociliary clearance mechanism provides the necessary layer of mucous and the direction of the clearance. The mucous will then glue all particles and pathogens inhaled by the nose to the mucus for natural excretion [26, 27].

Consequently, there is a direct correlation between the health of the paranasal sinuses and the nose and the efficacy of mucociliary clearance. Any condition that disturbs the normal mucociliary clearance function can result in rhinosinusitis [26, 27].

Just as the mucosa of the pharynx, the Schneiderian Membrane allows the ejection of exosomes that are transported through the lymphatic system, as a result, this mucosa in the pharynx and the maxillary sinus performs a very important function for body detoxification. The content of the exosomes will be forwarded by ciliae out of the maxillary sinus and into the nose [26, 27]. From there, this outflow of the maxillary sinus, including the toxins, is swallowed (or cleaned) and then excreted [26, 27]. If a massive toxic attack on the human body occurs, a large number of exosomes will require their own elimination, which may lead to symptoms of the flu.[1] The British medical researcher Herbert Sheldon clarified already in 1944 as follows: "There was never any medicine against the flu, the flu is the medicine". This sentence clarifies that therapy against detoxification must be done and that all medical efforts to reduce this natural process of detoxification are resulting in even more problems.

7. Sinus "pneumatization" and "contraction"

The bones surrounding the maxillary sinus have a large potential to undergo morphological changes. This is due to the fact that they undergo frequent waves of remodelling in response to tooth extractions and changes in the masticatory pattern. Both the inner and outer cortical of the maxillary sinus are not stable and are prone to atrophy due to ageing mechanisms as well as disuse atrophy.

Sinus "pneumatization" is a physiological process in which the volume of the paranasal sinuses increases over time through the progressive expansion of the sinus volume, a process that begins after birth and continues until the 2nd–3rd decades of life [28–31]. Pneumatization proceeds in an inferomedial direction into the hard

[1] This specific function of the soft tissues of the pharynx and maxillary sinus was (mis-)used during the recent "pandemic" to quantify toxins in the individual through a "PCR"test and to (wrongly) label them as effects of viruses.

palate, laterally into the zygomatic bone and posteriorly into the ethmoids [32]. The most pneumatized area, according to the literature, is the anteromedial wall of the maxillary sinus [33, 34].

Disuse atrophy as well as "Sinus pneumatization" can be extensive, exposing the roots of the respected teeth and leading to direct engagement of the roots of the posterior teeth within the sinus. Moreover, this disuse atrophy can affect both bone quality and quantity [35]. Furthermore, the loss of posterior maxillary teeth aggravates the situation [31, 36–42]. According to Elsayed et al. [28], sinus pneumatization significantly reduces the average bone height and density in the edentulous locations. A consequence that may lead to complications during extraction and present a challenge during implant placement [42, 43]. Additionally, cortically anchored implants may lose contact with the 2nd cortical as a result of sinus expansion or contraction.

Although tooth loss in the posterior maxilla leads to a collapse of the corticals that surround the roots, in our experience, immediate functional loading protocols using method of osseofication can overcome this collapse by generating new functions in these cortical themselves. Hence, emphasising the use of immediate functional loading over the sinus lifting and bone augmenting procedure (**Figures 4a** and **b** and **5a** and **b**).

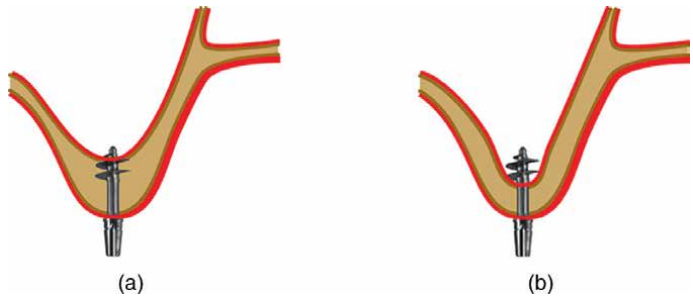

Figure 4.
a: baseline situation. b: due to bone loss and sinus "pneumatization" of the maxillary sinus, the load transmitting threads of the implants have lost contact with the 2nd cortical. The implant does not contribute to load transmission and more and a corrective intervention may be indicated.

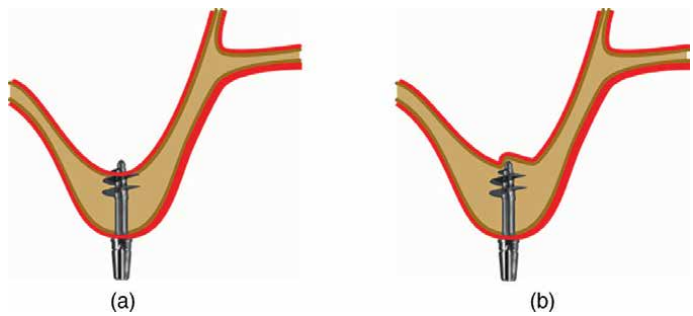

Figure 5.
a: baseline situation. b: Due to bone growth inside the maxillary sinus, the load-transmitting threads of the implants have lost contact with the 2nd cortical. The implant does not contribute to load transmission and more and a corrective intervention may be indicated.

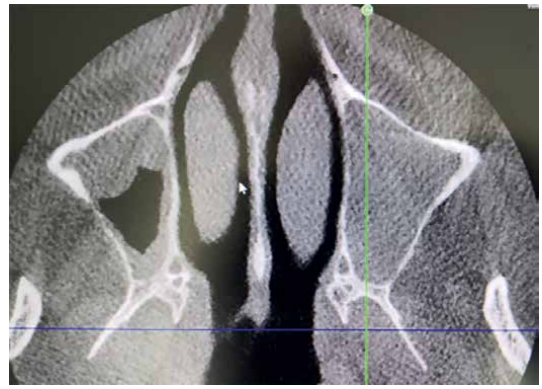

Figure 6.
A cone beam cross-section of the maxillary sinus with the anterior cortical wall of the maxillary sinus on the left side of the picture shows thickening due to the persistence of chronic granulation in that area (inside the maxillary sinus) that created changes in the cortical border of the maxillary sinus, including increased bone mass and mineralisation. While the opposite maxillary sinus (right side of the picture) shows signs of an acute infection.

8. Thickening of the bone structures around the sinus cavity

The literature demonstrates that mesenchymal stem cells derived from the sinus membrane possess the capacity to create bone and thicken the Schneiderian membrane using various techniques such as cadaver inspections, CT scans and CBCT imaging [43–46].

The normal thickness of the Schneiderian membrane is 1 mm [46, 47]–2 mm [44, 46], with many reported factors associated with a symptomatic increase in membrane thickness. Monje et al. [48] and Munakata et al. [49] categorised these factors into patient-related factors (age and smoking habits), teeth-related factors (like periodontitis, bone loss and lesions near the gums) and maxillary sinus variations (including sinus septa and nasal septum deviation).

Recently, Alghofaily et al. [50] highlighted the association between the increased thickness of the sinus membrane with male's gender, the periapical lesions, inadequate endodontic treatment and sinusitis.

Cone beam CT can be successfully used to distinguish between chronic and acute infections of the maxillary sinus, as chronic infections lead to a thicker and more mineralised cortical (**Figure 6**).

9. Diseases in the maxillary sinus

A wide spectrum of diseases can involve the maxillary sinus, originating either from or within the lining of the sinus; the other paranasal sinuses; the nasal space; dental and oral tissues; the adjacent bone; and hence extending to the sinus [51]. These diseases can be either inflammatory (the result of a bacterial infection, an allergy, or a result of detox function), neoplastic (benign or malignant, or metastases), odontogenic (infections, cysts, foreign body), mucocele and granulomatous vasculitis (**Figure 7**).

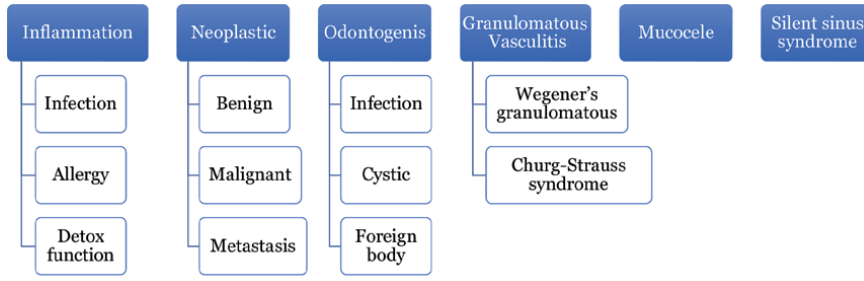

Figure 7.
Diseases of the maxillary sinus.

10. The odontogenic maxillary sinusitis (OMS)

Acute or chronic maxillary sinusitis is defined as symptomatic inflammation of the maxillary sinus due to bacterial, allergic or fungal rhinitis [52, 53]. Nowadays, we have to add symptoms of overly strong detox function of the maxillary sinus.

Odontogenic maxillary sinusitis (OMS) is a type of sinusitis caused by infections that originate from dental or dentoalveolar structures, affecting the floor of the maxillary sinus and the sinus membrane. It is slightly more common in females, with the commonest age group being 40–60 years [44, 54].

11. Historical background of the odontogenic maxillary sinusitis (OMS) and incidence

The concept of the odontogenic maxillary sinus (OMS) was first proposed by William H. Bauer in 1943 [54].

Brook [55] and Mehra and Jeong [56] documented that odontogenic infections account for approximately 10–12% of maxillary sinusitis cases, with the high prevalence of dental caries serving as a causative factor [53]. Later, Maillet et al. [43] reported an increase in incidence to 51.8% while Wuokko-Landén et al. [57] mentioned 15% and Patel and Ferguson [58] reported 40%.

The main causes of sinusitis can be either odontogenic infection and/or dentoalveolar surgery, which is associated with perforation of the Schneiderian membrane and oroantral fistula formation [52, 59–62]. Some authors reported some iatrogenic causes, such as impacted teeth after dental care, implants, dental amalgams and the oro-antral fistula [54, 62–66].

Lechien et al. [61] investigated the different causes of odontogenic sinusitis among 674 patients from January 1980 to January 2013. They reported 65.7% for iatrogenic aetiology and 25.1% for apical periodontal pathologies, which were distributed as follows: apical periodontitis—16%, apical granulomas—5%, odontogenic cysts—2.5 and 8.3% for marginal periodontitis. Molteni et al. [63] identified oroantral communication as the causative factor in 45.8% of patients. Troeltzsch et al. [60] reported that extractions with subsequent OAF or healing disturbances were the main cause of sinusitis (64%). Almost a similar percentage (57%) was reported by Zirk et al. [64], while Puglisi et al. [65] consider oroantral communication as a consequence of tooth extraction, sinus lift, third molar removal, improper implant placement, cyst excision

and dislodged tooth fragments. Moreover, Troeltzsch et al. [60] reported 5.2% and 2.3% for dental implants and periimplantitis, while Lechien et al. [61] documented a lower rate (0.3%).

Furthermore, Craig et al. [67] reported a higher percentage of endodontic sources than an iatrogenic one. More recently, Yassin-Kassab et al. [68] documented the same observation (51.7% compared to 48.3%).

The percentage of older people has increased significantly in recent years as the world population grows. In 2019, 703 million people aged 65 years or older were documented, a number that may reach up to 1.5 billion [69, 70] by 2050. The growing percentage of elderly people and patients suffering from tooth loss is increasing the demand for dental rehabilitation [69, 70]. Today, dental implants [69–71] have become the gold standard treatment for dental rehabilitation in edentulous patients with an increasing percentage of use and a high reported success rate. Frequent and recurring problems with "sinus lifts" [69] have instilled justified fears in the field of conventional implantology, and this method, in our opinion, is becoming more and more left.

Several studies have proved that well-installed and healed implants are never the cause of maxillary sinusitis per se [72–84], independent of their penetration depth into the maxillary [72–75].

12. Implants and the maxillary sinuses

Cases with compromised ridge support present a challenge for implant rehabilitation due to the compromised bone quality and quantity, which adversely affect implant primary stability and diminish implant survival rate. Moreover, sinus pneumatizion may complicate the situation [75–77].

The literature describes numerous treatment alternatives, including sinus left and bone grafting procedures [75–77, 84–86], the use of short implants [69–71, 82, 84], the all-on-4, and even all-on-3 techniques [85, 87, 88], implants in remote bony areas such as zygomatic and tubero-pterygoid regions [72–74, 85, 89, 90] and basal implants [72–74, 91–93].

Several authors recommended using a bi-cortical or tri-cortical design to improve implant stability [73, 74, 88–96]. In this scenario, sinus membrane perforation and subsequent implant protrusion within the maxillary sinus could occur. Al-Salman and Almas [96] documented that perforation of the Schneiderian membrane (range 7–35%), while Stacchi et al. [97] reported that sinus membrane perforation and haemorrhage are the most common intraoperative complications associated with sinus floor elevation, with overall occurrences of 15.7 and 0.4%, respectively.

12.1 Implant protrusion inside the maxillary sinus and the maxillary sinus's health

In 2007, Jung et al. [75] studied the consequences of implant penetration in the maxillary sinus in mongrel dogs for 6 months and reported that none of the investigated sinus cavities displayed any features of inflammation.

Moreover, Tabrizi et al. [77] in 2012 retrospectively investigated the effects of the implant's tip penetration inside the maxillary sinuses. They documented no problem associated with implants protruding inside the sinuses; all the investigated implants

remained successfully integrated, with no radiographic evidence of bone loss or other complications. They highlighted that in cases where no membrane penetrated, bone formation was noticed in the maxillary sinus floor.

Zhong et al. [78] investigated the effect of different depth implant penetrations (group A: 0 mm; group B: 1 mm; group C: 2 mm; group D: 3 mm) on maxillary sinus health in a dog mode. None of the maxillary sinuses showed any signs of sinus inflammation. At penetrating depths of 1–2 mm, newly formed membrane and partially formed bone completely covered the implants, while at depths of 3 mm or more, neither membrane nor bone were present. All the implants showed an obvious increase in bone-to-implant contact (BIC). The same observation was reported by Abi Najm et al. [79], Ghnaem and Gad [80], Elhamruni et al. [81], Shihab [82] and Ragucci et al. [72]. While Awadalkreem et al. [73] and Ahmad et al. [74] stated that implant penetration per se has no adverse effect either on maxillary sinus health or on the survival rate, moreover, Lazarov [76] reported only one maxillary sinus adverse reaction that does not necessitate the use of antibiotic among 131 maxillary sinuses penetrated with 217 implants, with none of the implants failing.

Sala et al. [35] conducted a recent systematic review and meta-analysis, which concluded that the prevalence of postoperative infection, including sinusitis, is low and has a reported correlation with the dimensions of the perforation and the anatomical predisposition.

On the other hand, some investigators reported the occurrence of sinusitis, including Nooh [84] (in one patient out of 63 patients), and Lazarov [76] (in one sinus out of 131, after Corticobasal® implants were used) Lazarov identified however retrospectively surgical error (too short implant chosen) and subsequent prosthetic mistake (to deep cementation zone inside the palatal mucosa in combination with effects of the open bone wound) as the origins of the problem.

12.1.1 The "bony seal"

Ihde postulated, based on observation of polished osseofixated implants, that it is not the implant's body inside the maxillary sinus that causes the infection, but the fact that the implant's endosseous surface is partially not in direct contact with the bone, which leads to a loss of the seal between the bacterial-loaded oral cavity and the potentially sterile maxillary sinus (**Figure 8a–f**).

12.2 Bone augmentation and sinusitis

Sinus grafting is a common procedure used to increase the vertical and horizontal amount of bone in the maxillary sinus, with a high reported implant success rate (after successful grafting). Several complications have been documented: membrane perforation, infections, bleeding, implant migration and dissemination or loss of the graft material [98–111].

Barone et al. [102] found that membrane perforation (60%), infection (21%), bleeding (9%) and implant migration were the most common problems that could happen in connection with a maxillary sinus graft.

Lu et al. [45] recently reported that the most common problems with sinus grafts were perforation of the Schneiderian membrane, bleeding, infection, persistent sinusitis and loss of the graft material.

Iușan et al. [69] documented membrane perforation and the formation of an oro-antral fistula; the occurrence of acute and chronic rhinosinusitis; facial congestion;

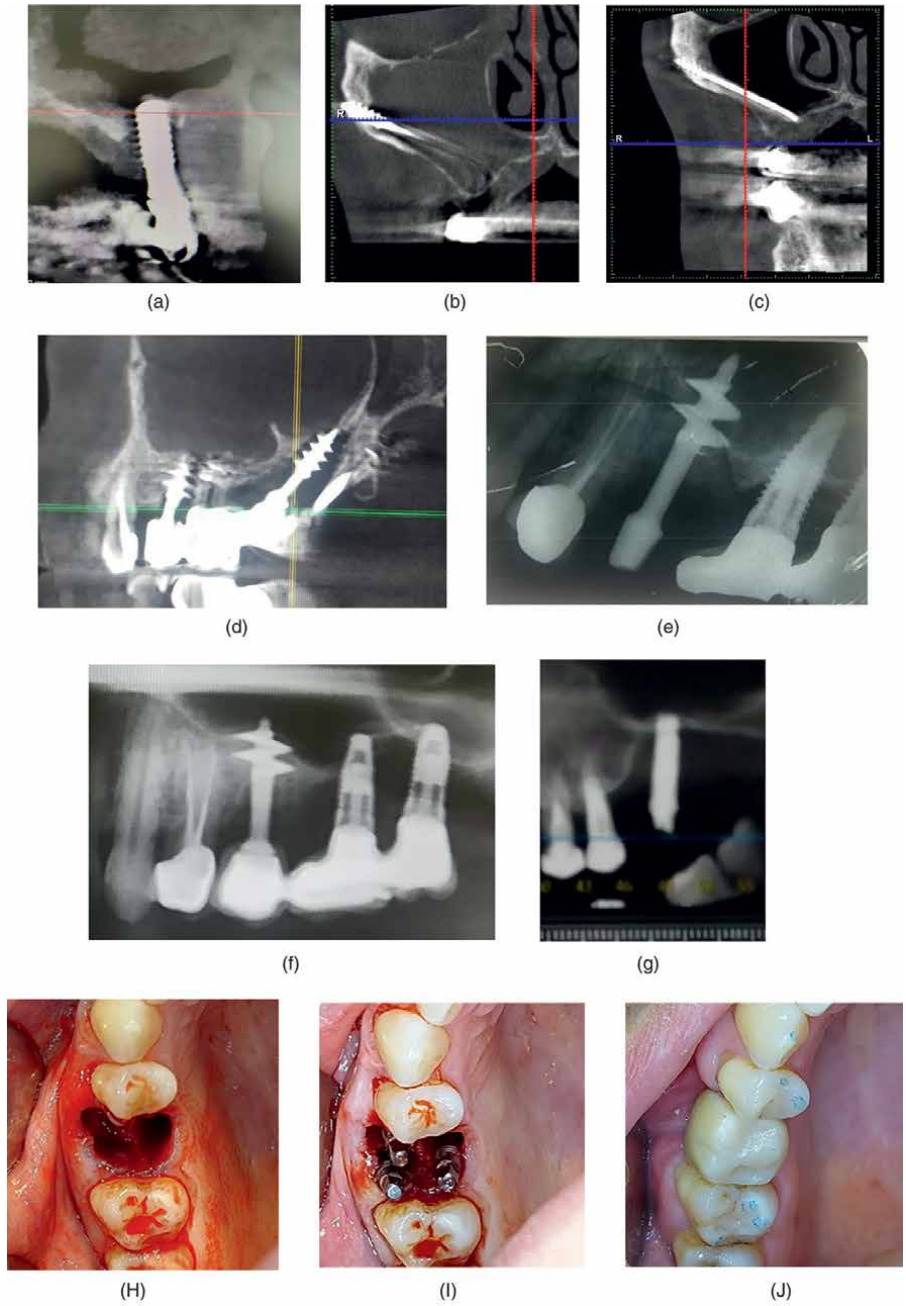

Figure 8.
a: Shows that the infection and detachment of a 2-stage endosseous surface from the bone happens from the nose down, and from the oral cavity up. b and c: A zygomatic implant penetrates the maxillary sinus, leading to subsequent maxillary sinusitis. The origin of the problem, in our opinion, was the missing seal between the oral cavity and the maxillary sinus. The management approach to the situation was as follows: the implant was left within the sinus; however, it was detached from the cementing abutment and the bridge by removing the abutment. After 6 weeks, no signs of infection were visible on the control scan, while the bridge was still in full function. d: shows the detachment of the peri-implant bone from the oblique ossefixated implant in area 26; the osteolytic zone has reached the maxillary sinus, causing maxillary sinusitis. The bony seal was replaced by connective tissue. This tissue has no sealing function. e and f: when the bone seal is ensured, the protrusion of osseofixated implants may even lead to a considerable increase in the size of the basal membrane of the maxillary

sinus (image after 19 months of follow-up). 8F. Note the increase in mineralised bone in area 25, while peri-implantitis progresses in areas 26 and 27. g. Peri-implantitis had resorbed all of the alveolar bone. Nevertheless, the basal and cortical bones of the floor of the maxillary sinus keep the implant stable. This portion of the cortical (around the implant's apex) even shows an increase in bone volume due to increased (cantilever) forces. h: After the extraction of an upper 1st molar, three root extraction sockets were available, allowing the placement of three osseofixated implants. i: Osseofixated implants (BCS® implant designs) of adequate diameters and length were placed into each of the three extraction sockets. j: After the temporary crown had been in place for 9 months, tooth 16 was replaced by a full zirconium crown. The high polish surface of both the implant's shafts and the zirconium crown ensures excellent periodontal health. Using a thin interdental brush, the patients can clean and maintain their oral hygiene.

the incidence of nasal obstruction, the possibility of implant displacement into the maxillary sinus; and sinus graft failure as the main complications associated with sinus grafting procedures. Moreover, they reported a positive correlation between peri-implant infection and sinus pathology.

In the same line, literature [83, 104–112] highlighted that membrane perforation, dislodgement of the graft material into the sinus, disrupting the normal sinus physiology, overfilling of the maxillary sinus with graft material, as well as graft infection, can be the main predisposing factors for sinusitis. This reported sinusitis may require antibiotic treatment or an evenly distributed surgical draining procedure [82].

In augmented sinuses, the cause of the infection cannot be diagnosed, because even if the implant is the cause, the augmented area will be affected by the infection **Figure 8g**.

In the sinus site where bone augmentation "sinus-lift" has been performed, the basal cortical of the maxillary sinus is, however, missing due to resorption. Therefore, the infection from peri-implantitis could potentially spread to the maxillary sinus, leading to the development of pan-sinusitis. An explanation that is in line with Iușan et al. [69].

A reported relation between implant surface tomography and an increased risk of peri-implantitis, including orthograde and retrograde peri-implantitis has been emphasised by many investigators [112, 113]. Hence, this infection affects both the first and the second cortical bones, resulting in implant mobility and consequence implant loss. A complication that presents a challenge for using this implant in severely resorbed posterior maxillary bone, especially with the increased demands of the patient for immediate loading.

Hence, there is an increase in demand for a treatment modality with a high success rate and fewer complications. Today the use of use of osseofixated implants in compromised ridge support areas, including the posterior maxilla, has been emphasised with high success and survival rates, numerous biological and mechanical advantages, limited complications and significant improvements in patient satisfaction and quality of life owing to their smooth surface, thin penetrating tip, small diameter, devoid of bone grafting, and most importantly, no risk of peri-implantitis [73, 76, 91–93]. From our experience, and as shown in **Figure 8**(**e** and **f**), the cortical floor of the maxillary sinus tends to increase in thickness after being mechanically loaded by cortically anchored implants (osseofixated implants). This increase in both volume and mineralization is not astonishing: as the bone is loaded through the roots of the premolars and molars. However, following tooth extraction, the caudal cortical of the maxillary sinus receives close to zero functional stimuli and hence atrophies. As we do not know if the additional bone is going to be generated inside the maxillary sinus or inside the maxillary bone, the rationale of osseofixated implants is to place approximately half of the implant thread into the maxillary sinus and half of it into the maxillary bone.

Similarly, when osseofixated implants are placed into fresh extraction sockets of upper molars and premolars, the lamina cribrosa of these teeth remains under constant functional stimulus and it does not atrophy away (**Figure 8h–j**).

12.3 Implant protrusion inside the maxillary sinus and the peri-implant bone contact

Khairnar and Gaur [114] reported an increase in bone apposition and excellent implant stability in bi-cortical implants anchored in rabbits. Moreover, Kim et al. [115] reported a significant increase in peri-implant bone level when the initial bone height was less than 5 mm, but no increase in peri-implant level when it was 5 mm or more. Furthermore, after 12 months of follow-up, Tabrizi et al. [77] found no radiographic signs of bone loss in any of the penetrated implants.

In the same line, Awadalkreem et al. [73] reported the absence of any osteolytic reaction around the penetrated implants with increased bone-implant contact after 18 months of follow-up. The growth of bone was assumed to be a result of increased local function.

12.4 Implant protrusion inside the maxillary sinus and implant survival rate

Implant penetration inside the maxillary sinus has no significant effect on the implant survival rates. This observation has been emphasised by Awadalkreem et al. [73] who reported a 100% survival rate after 18 months of follow-up, and Kim et al. [116] who documented a high survival rate. Ragucci et al. [72] documented a 95.6% survival rate after a 52.7-month follow-up of implants. Furthermore, Ghnaem et al. [80] reported a survival rate of 100% after 6 years of follow-up, while Nooh [83] mentioned a survival rate of 98.4%.

12.5 Implant protrusion inside the maxillary sinus and the incidence of epistaxis

Despite the fact that implant penetration inside the nasal and maxillary sinuses does not adversely affect the health of the nasal and maxillary sinuses, some investigators [72, 83], reported the incidence as an immediate postoperative complication. Nooh [83] reported mild epistaxis as an immediate postoperative occurrence in 7 of the 63 patients in their study. Kim et al. [115] noted similar observations, reported by 3 of the 39 patients immediately postoperatively. Furthermore, according to Ragucci et al. [72], epistaxis is the most common complication associated with implant pentation inside the maxillary sinus. Tabrizi et al. [77] reported the incidence of transit epistasis in one patient.

12.6 Implant protrusion inside the maxillary sinus and the thickening in the Schneiderian membrane

As described previously, several factors can be interlinked with the thickening of the Schneiderian membrane [48, 49, 52, 72, 75]. Researchers found a significant relationship between the thickness of the membrane and the patient's gender, hypertension and smoking habits [48, 49, 52, 72, 75]. In the same line, Tabrizi et al. [77] reported a nonsignificant thickening of the sinus membrane radiologically in two patients with no clinical signs of sinusitis. Both patients who showed membrane thickness in the present study were men and smokers.

Ragucci et al. [72] found that the radiological complications associated with implant penetration inside the maxillary sinus were 14.8%, with no significant difference between the different implant penetration levels.

12.7 Implant protrusion inside the maxillary sinuses and its effect on patient satisfaction and quality of life

Now a day, implant-supported prostheses represent one of the most common treatment alternatives to treat edentulism, with significant improvements in patient's aesthetic and oral functions, including mastication and phonation, patient satisfaction and quality of life [116–118].

Implant protrusion inside the maxillary sinuses does not affect patient satisfaction and quality of life, as reported by Awadalkreem et al. [73] and Ahmad et al. [74]. All the investigated patients showed a substantial improvement following implant treatment, despite the fact that implants protruded inside the sinuses.

A recent consensus from 2022 [119], which included 31 experts (23 in implantology, 6 otolaryngologists and 2 radiologists), looked into what happens when implants stick out into the maxillary sinuses and nasal fossae. They featured significant statements emphasising that: implants protruding into the sinus do not always imply implant protrusion through the sinus mucosa is not necessarily related to sinus pathology; implants should be monitored clinically during the maintenance programme; but the implants should not be removed; and ENT consultation is not mandatory. Even when implants are associated with symptoms (foul smell, loss of smell, posterior nasal drainage, anterior nasal drainage, nasal obstruction and facial pressure) and radiographic signs of sinus or sinonasal pathology, the patient should be referred to an ENT specialist or surgical provider for evaluation; implants should not be removed, and pharmacological treatment should be attempted first.

13. Conclusion

Implant therapy is a successful treatment option for patients with complete and partial edentulous conditions. Implants can protrude inside the maxillary sinus without clinical or radiographic evidence of sinusitis, having a negative effect on implant survival as well as a positive effect on patient satisfaction. During the patient's follow-up schedule, we can regularly monitor protruded implants, both clinically and radiographically.

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Conflict of interest

There are no conflicts of interest to declare.

Ethical approval

Institutional approval was not required.

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References

[1] Whyte A, Boeddinghaus R. The maxillary sinus: Physiology, development and imaging anatomy. Dento Maxillo Facial Radiology. 2019;**48**(8):20190205. DOI: 10.1259/dmfr.20190205

[2] Aktuna Belgin C, Colak M, Adiguzel O, Akkus Z, Orhan K. Three-dimensional evaluation of maxillary sinus volume in different age and sex groups using CBCT. European Archives of Oto-Rhino-Laryngology. 2019;**276**(5):1493-1499. DOI: 10.1007/s00405-019-05383-y

[3] Somayaji K, Muliya VS, Kg M, et al. A literature review of the maxillary sinus with special emphasis on its anatomy and odontogenic diseases associated with it. Egypt The Journal of Otolaryngology. 2023;**39**:173. DOI: 10.1186/s43163-023-00536-7

[4] Testori T. Maxillary sinus surgery: Anatomy and advanced diagnostic imaging. Journal of Prosthodontics-Implant Esthetic and Reconstructive Dentistry. 2011;**2**:6-14

[5] Sargi ZB, Casiano RR. Surgical anatomy of the paranasal sinuses. In: Kountakis SE, Onerci TM, editors. Rhinologic and Sleep Apnea Surgical Techniques. New York: Springer; 2007. pp. 17-26

[6] Van den Bergh JP, ten Bruggenkate CM, Disch FJ, Tuinzing DB. Anatomical aspects of sinus floor elevations. Clinical Oral Implants Research. 2000;**11**(3):256-265. DOI: 10.1034/j.1600-0501.2000.011003256.x

[7] Gosau M, Rink D, Driemel O, Draenert FG. Maxillary sinus anatomy: A cadaveric study with clinical implications. The Anatomical Record (Hoboken). 2009;**292**(3):352-354. DOI: 10.1002/ar.20859

[8] Guo ZZ, Liu Y, Qin L, Song YL, Xie C, Li DH. Longitudinal response of membrane thickness and ostium patency following sinus floor elevation: A prospective cohort study. Clinical Oral Implants Research. 2016;**27**(6):724-729. DOI: 10.1111/clr.12655

[9] Rancitelli D, Borgonovo AE, Cicciù M, Re D, Rizza F, Frigo AC, et al. Maxillary sinus septa and anatomic correlation with the Schneiderian membrane. The Journal of Craniofacial Surgery. 2015;**26**(4):1394-1398. DOI: 10.1097/SCS.0000000000001725

[10] Kalyvas D, Kapsalas A, Paikou S, Tsiklakis K. Thickness of the Schneiderian membrane and its correlation with anatomical structures and demographic parameters using CBCT tomography: A retrospective study. International Journal of Implant Dentistry. 2018;**4**(1):32. DOI: 10.1186/s40729-018-0143-5

[11] Wallace JA. Transantral endodontic surgery. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 1996;**82**(1):80-83. DOI: 10.1016/s1079-2104(96)80381-7

[12] Nuñez-Castruita A, López-Serna N, Guzmán-López S. Prenatal development of the maxillary sinus: A perspective for paranasal sinus surgery. Otolaryngology and Head and Neck Surgery. 2012;**146**(6):997-1003. DOI: 10.1177/0194599811435883

[13] Bailey BJ. Head and Neck Surgery Otolaryngology. 2nd ed. Philadelphia: Lip-Pincott Raven Publishers; 1998. pp. 418-446

[14] Lovasova K, Kachlik D, Rozpravkova M, Matusevska M, Ferkova J, Kluchova D. Three-dimensional CAD/CAM imaging of the maxillary sinus in ageing process. Annals of Anatomy. 2018;**218**:69-82. DOI: 10.1016/j.aanat.2018.01.008

[15] Boeddinghaus R, Whyte A. Trends in maxillofacial imaging. Clinical Radiology. 2018;**73**:4-18

[16] Tian XM, Qian L, Xin XZ, Wei B, Gong Y. An analysis of the proximity of maxillary posterior teeth to the maxillary sinus using cone-beam computed tomography. Journal of Endodontia. 2016;**42**(3):371-377. DOI: 10.1016/j.joen.2015.10.017

[17] Schuh E, Schmiedl R, Vogel G. Anatomische Grenzen der enossalen zahnärztlichen implantologie [Anatomic limits of endosseous dental implantation]. Zeitschrift für Stomatologie (1984). 1984;**81**(2):81-90. German

[18] Wyler B, Mallon WK. Sinusitis update. Emergency Medicine Clinics of North America. 2019;**37**(1):41-54. DOI: 10.1016/j.emc.2018.09.007

[19] Ford RL, Barsam A, Velusami P, Ellis H. Drainage of the maxillary sinus: A comparative anatomy study in humans and goats. Journal of Otolaryngology—Head and Neck Surgery. 2011;**40**(1):70-74

[20] Lin Y-H, Yang Y-C, Wen S-C, Wang H-L. The influence of sinus membrane thickness upon membrane perforation during lateral window sinus augmentation. Clinical Oral implants Research. 2015;**00**:1-6. DOI: 10.1111/clr.12646

[21] Iwanaga J, Wilson C, Lachkar S, Tomaszewski KA, Walocha JA, Tubbs RS. Clinical anatomy of the maxillary sinus: Application to sinus floor augmentation. Anatomy and Cell Biology. 2019;**52**(1):17-24. DOI: 10.5115/acb.2019.52.1.17

[22] Standring S. Gray's Anatomy: The Anatomical Basis of Clinical Practice. 41st ed. London: Elsevier Health Sciences; 2015

[23] Kqiku L, Biblekaj R, Weiglein AH, Kqiku X, Städtler P. Arterial blood architecture of the maxillary sinus in dentate specimens. Croatian Medical Journal. 2013;**54**(2):180-184. DOI: 10.3325/cmj.2013.54.180

[24] Flanagan D. Arterial supply of maxillary sinus and potential for bleeding complication during lateral approach sinus elevation. Implant Dentistry. 2005;**14**(4):336-338. DOI: 10.1097/01.id.0000188437.66363.7c

[25] Duncavage J. The Maxillary Sinus: Medical and Surgical Management. New York: Thieme Medical Publishers; 2011

[26] Cohen NA. Sinonasal mucociliary clearance in health and disease. The Annals of Otology, Rhinology and Laryngology. Supplement. 2006;**196**:20-26. DOI: 10.1177/00034894061150s904

[27] Bustamante-Marin XM, Ostrowski LE. Cilia and Mucociliary Clearance. Cold Spring Harbor Perspectives in Biology. 3 Apr 2017;**9**(4):a028241. DOI: 10.1101/cshperspect.a028241

[28] Elsayed SA, Alassaf MS, Elboraey MO, Mohamado LL, Huwaykim DA, Albouq AK, et al. The impact of maxillary sinus pneumatization on the quality of the alveolar bone in dentated and edentulous patients: A cone-beam computed tomography radiographic analysis.

Cureus. 2023;**15**(9):e46005. DOI: 10.7759/cureus.46005

[29] Jun BC, Song SW, Park CS, Lee DH, Cho KJ, Cho JH. The analysis of maxillary sinus aeration according to aging process; volume assessment by 3-dimensional reconstruction by high-resolutional CT scanning. Otolaryngology and Head and Neck Surgery. 2005;**132**(3):429-434. DOI: 10.1016/j.otohns.2004.11.012

[30] Nimigean V, Nimigean VR, Măru N, Sălăvăstru DI, Bădiță D, Tuculină MJ. The maxillary sinus floor in the oral implantology. Romanian Journal of Morphology and Embryology. 2008;**49**(4):485-489

[31] Alqahtani S, Alsheraimi A, Alshareef A, Alsaban R, Alqahtani A, Almgran M, et al. Maxillary sinus pneumatization following extractions in Riyadh, Saudi Arabia: A cross-sectional study. Cureus. 2020;**12**(1):e6611. DOI: 10.7759/cureus.6611

[32] Lang J. Clinical Anatomy of the Nose, Nasal Cavity and Paranasal Sinuses. New York, US: Georg Thieme Verlag; 1989

[33] Mauri M, de Oliveira CO, Franche G. Pneumosinus dilatans of the maxillary sinus. Case report. The Annals of Otology, Rhinology, and Laryngology. 2000;**109**(3):278-280. DOI: 10.1177/000348940010900308

[34] Tovi F, Gatot A, Fliss DM. Air cyst of the maxillary sinus (pneumosinus dilatans, pneumocoele). The Journal of Laryngology and Otology. 1991;**105**(8):673-675. DOI: 10.1017/s0022215100116998

[35] Sala YM, Lu H, Chrcanovic BR. Clinical outcomes of maxillary sinus floor perforation by dental implants and sinus membrane perforation during sinus augmentation: A systematic review and meta-analysis. Journal of Clinical Medicine. 2024;**13**(5):1253. DOI: 10.3390/jcm13051253

[36] Lim HC, Kim S, Kim DH, Herr Y, Chung JH, Shin SI. Factors affecting maxillary sinus pneumatization following posterior maxillary tooth extraction. Journal of Periodontal and Implant Science. 2021;**51**(4):285-295. DOI: 10.5051/jpis.2007220361

[37] Yücesoy T, Göktaş TA. Evaluation of sinus pneumatization and dental implant placement in atrophic maxillary premolar and molar regions. The International Journal of Oral & Maxillofacial Implants. 2022;**37**(2):407-415. DOI: 10.11607/jomi.9215

[38] Levi I, Halperin-Sternfeld M, Horwitz J, Zigdon-Giladi H, Machtei EE. Dimensional changes of the maxillary sinus following tooth extraction in the posterior maxilla with and without socket preservation. Clinical Implant Dentistry and Related Research. 2017;**19**(5):952-958. DOI: 10.1111/cid.12521

[39] Sarilita E, Lita YA, Nugraha HG, Murniati N, Yusuf HY. Volumetric growth analysis of maxillary sinus using computed tomography scan segmentation: A pilot study of Indonesian population. The Anatology and Cell Biology. 2021;**54**(4):431-435. DOI: 10.5115/acb.21.051

[40] Li Y, Deng S, Mei L, Li J, Qi M, Su S, et al. Accuracy of alveolar bone height and thickness measurements in cone beam computed tomography: A systematic review and meta-analysis. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology. 2019;**128**(6):667-679. DOI: 10.1016/j.oooo.2019.05.010

[41] Cavalcanti MC, Guirado TE, Sapata VM, Costa C, Pannuti CM, Jung RE, et al. Maxillary sinus floor pneumatization and alveolar ridge resorption after tooth loss: A cross-sectional study. Brazilian Oral Research. 2018;**32**:e64. DOI: 10.1590/1807-3107BOR-2018.vol32.0064

[42] Lawson W, Patel ZM, Lin FY. The development and pathologic processes that influence maxillary sinus pneumatization. The Anatomical Record (Hoboken). 2008;**291**(11):1554-1563. DOI: 10.1002/ar.20774

[43] Maillet M, Bowles WR, McClanahan SL, John MT, Ahmad M. Cone-beam computed tomography evaluation of maxillary sinusitis. Journal of Endodontia. 2011;**37**(6):753-757. DOI: 10.1016/j.joen.2011.02.032

[44] Shanbhag S, Karnik P, Shirke P, Shanbhag V. Association between periapical lesions and maxillary sinus mucosal thickening: A retrospective cone-beam computed tomographic study. Journal of Endodontia. 2013;**39**(7):853-857. DOI: 10.1016/j.joen.2013.04.010

[45] Lu Y, Liu Z, Zhang L, Zhou X, Zheng Q, Duan X, et al. Associations between maxillary sinus mucosal thickening and apical periodontitis using cone-beam computed tomography scanning: A retrospective study. Journal of Endodontia. 2012;**38**(8):1069-1074. DOI: 10.1016/j.joen.2012.04.027

[46] Nascimento EH, Pontual ML, Pontual AA, Freitas DQ, Perez DE, Ramos-Perez FM. Association between odontogenic conditions and maxillary sinus disease: A study using cone-beam computed tomography. Journal of Endodontia. 2016;**42**(10):1509-1515. DOI: 10.1016/j.joen.2016.07.003

[47] Abrahams JJ, Glassberg RM. Dental disease: A frequently unrecognized cause of maxillary sinus abnormalities? AJR. American Journal of Roentgenology. 1996;**166**(5):1219-1223. DOI: 10.2214/ajr.166.5.8615273

[48] Monje A, Diaz KT, Aranda L, Insua A, Garcia-Nogales A, Wang HL. Schneiderian membrane thickness and clinical implications for sinus augmentation: A systematic review and meta-regression analyses. Journal of Periodontology. 2016;**87**(8):888-899. DOI: 10.1902/jop.2016.160041

[49] Munakata M, Yamaguchi K, Sato D, Yajima N, Tachikawa N. Factors influencing the sinus membrane thickness in edentulous regions: A cone-beam computed tomography study. The International Journal of Implant Dentistry. 2021;**7**(1):16. DOI: 10.1186/s40729-021-00298-y

[50] Alghofaily M, Alsufyani N, Althumairy RI, AlSuhaibani A, Alfawzan F, AlSadhan L. Odontogenic factors associated with maxillary sinus Schneiderian membrane thickness and their relationship to chronic Sinonasal symptoms: An ambispective cohort study. Diagnostics (Basel). 2023;**13**(16):2710. DOI: 10.3390/diagnostics13162710

[51] Bell GW, Joshi BB, Macleod RI. Maxillary sinus disease: Diagnosis and treatment. British Dental Journal. 2011;**210**(3):113-118. DOI: 10.1038/sj.bdj.2011.47

[52] Ferguson M. Rhinosinusitis in oral medicine and dentistry. Australian Dental Journal. 2014;**59**(3):289-295. DOI: 10.1111/adj.12193. Epub 2014 Jul 30

[53] Psillas G, Papaioannou D, Petsali S, Dimas GG, Constantinidis J. Odontogenic maxillary sinusitis: A comprehensive review. Journal of Dental

Science. 2021;**16**(1):474-481. DOI: 10.1016/j.jds.2020.08.001

[54] Bauer WH. Maxillary sinusitis of dental origin. American Journal of Orthodontics and Oral Surgery. 1943;**29**(3):B133-B151

[55] Brook I. Sinusitis of odontogenic origin. Otolaryngology and Head and Neck Surgery. 2006;**135**(3):349-355. DOI: 10.1016/j.otohns.2005.10.059

[56] Mehra P, Jeong D. Maxillary sinusitis of odontogenic origin. Current Allergy and Asthma Reports. 2009;**9**(3):238-243. DOI: 10.1007/s11882-009-0035-0

[57] Wuokko-Landén A, Blomgren K, Välimaa H. Acute rhinosinusitis—Are we forgetting the possibility of a dental origin? A retrospective study of 385 patients. Acta Oto-Laryngologica. 2019;**139**(9):783-787. DOI: 10.1080/00016489.2019.1634837

[58] Patel NA, Ferguson BJ. Odontogenic sinusitis: An ancient but under-appreciated cause of maxillary sinusitis. Current Opinion in Otolaryngology and Head and Neck Surgery. 2012;**20**(1):24-28. DOI: 10.1097/MOO.0b013e32834e62ed

[59] Gaudin RA, Hoehle LP, Smeets R, Heiland M, Caradonna DS, Gray ST, et al. Impact of odontogenic chronic rhinosinusitis on general health-related quality of life. European Archives of Oto-Rhino-Laryngology. 2018;**275**(6):1477-1482. DOI: 10.1007/s00405-018-4977-5

[60] Troeltzsch M, Pache C, Troeltzsch M, Kaeppler G, Ehrenfeld M, Otto S, et al. Etiology and clinical characteristics of symptomatic unilateral maxillary sinusitis: A review of 174 cases. Journal of Cranio-Maxillo-Facial Surgery. 2015;**43**(8):1522-1529. DOI: 10.1016/j.jcms.2015.07.021

[61] Lechien JR, Filleul O, Costa de Araujo P, Hsieh JW, Chantrain G, Saussez S. Chronic maxillary rhinosinusitis of dental origin: A systematic review of 674 patient cases. International Journal of Otolaryngology. 2014;**2014**:465173. DOI: 10.1155/2014/465173

[62] Akhlaghi F, Esmaeelinejad M, Safai P. Etiologies and treatments of odontogenic maxillary sinusitis: A systematic review. Iranian Red Crescent Medical Journal. 2015;**17**(12):e25536. DOI: 10.5812/ircmj.25536

[63] Molteni M, Bulfamante AM, Pipolo C, Lozza P, Allevi F, Pisani A, et al. Odontogenic sinusitis and sinonasal complications of dental treatments: A retrospective case series of 480 patients with critical assessment of the current classification. Acta Otorhinolaryngologica Italica. 2020;**40**(4):282-289. DOI: 10.14639/0392-100X-N0457

[64] Zirk M, Dreiseidler T, Pohl M, Rothamel D, Buller J, Peters F, et al. Odontogenic sinusitis maxillaris: A retrospective study of 121 cases with surgical intervention. Journal of Cranio-Maxillo-Facial Surgery. 2017;**45**(4):520-525. DOI: 10.1016/j.jcms.2017.01.023

[65] Puglisi S, Privitera S, Maiolino L, Serra A, Garotta M, Blandino G, et al. Bacteriological findings and antimicrobial resistance in odontogenic and non-odontogenic chronic maxillary sinusitis. Journal of Medical Microbiology. 2011;**60**(Pt 9):1353-1359. DOI: 10.1099/jmm.0.031476-0

[66] George M, Noor A, Thorpe AR, Sritharan N, Riffat F. Odontogenic sinusitis: A literature review. Oral Surgery. 2024;**17**(2):170-178. DOI: 10.1111/ors.12861

[67] Craig JR, Poetker DM, Aksoy U, Allevi F, Biglioli F, Cha BY,

et al. Diagnosing odontogenic sinusitis: An international multidisciplinary consensus statement. International Forum of Allergy and Rhinology. 2021;**11**(8):1235-1248. DOI: 10.1002/alr.22777

[68] Yassin-Kassab A, Peterson EL, Craig JR. Total times to treatment completion and clinical outcomes in odontogenic sinusitis. American Journal of Otolaryngology. 2023;**44**(4):103921. DOI: 10.1016/j.amjoto.2023.103921

[69] Iușan SAL, Costache C, Lucaciu OP, Petrescu BN, Mirică IC, Toc DA, et al. Correlations between dental implant infectious pathologies and maxillary sinusitis: A review article. Journal of Clinical Medicine. 2023;**12**(15):5059. DOI: 10.3390/jcm12155059

[70] Kim WJ, Cho YD, Ku Y, Ryoo HM. The worldwide patent landscape of dental implant technology. Biomaterials Research. 2022;**26**(1):59. DOI: 10.1186/s40824-022-00307-0

[71] Carinci F, Lauritano D, Bignozzi CA, Pazzi D, Candotto V, Santos de Oliveira P, et al. A new strategy against peri-implantitis: Antibacterial internal coating. International Journal of Molecular Sciences. 2019;**20**(16):3897. DOI: 10.3390/ijms20163897

[72] Ragucci GM, Elnayef B, Suárez-López Del Amo F, et al. Influence of exposing dental implants into the sinus cavity on survival and complications rate: A systematic review. The International Journal of Implant Dentistry. 2019;**5**(1):6. DOI: 10.1186/s40729-019-0157-7

[73] Awadalkreem F, Ahmad AG, Ihde S, et al. Effects of corticobasal implant protrusion inside the nasal and maxillary sinus. Annals of Maxillofacial Surgery. 2020;**10**(1):114-121. DOI: 10.4103/ams.ams_42_20

[74] Ahmad AG, Awadalkreem F, Osman M, Palka L. Does the protrusion of corticobasal implants in the maxillary sinuses affect sinus health? A retrospective study. The Journal of Contemporary Dental Practice. 2023;**24**(6):357-363. DOI: 10.5005/jp-journals-10024-3521

[75] Jung JH, Choi BH, Jeong SM, Li J, Lee SH, Lee HJ. A retrospective study of the effects on sinus complications of exposing dental implants to the maxillary sinus cavity. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2007;**103**(5):623-635. DOI: 10.1016/j.tripleo.2006.09.024

[76] Lazarov A. A prospective cohort study of maxillary sinus complications in relation to treatments with strategic implants® penetrating into the sinus. Annals of Maxillofacial Surgery. 2020;**10**(2):365-369. DOI: 10.4103/ams.ams_85_20

[77] Tabrizi R, Amid R, Taha Özkan B, Khorshidi H, Langner NJ. Effects of exposing dental implant to the maxillary sinus cavity. The Journal of Craniofacial Surgery. 2012;**23**(3):767-769. DOI: 10.1097/SCS.0b013e31824dbd19

[78] Zhong W, Chen B, Liang X, Ma G. Experimental study on penetration of dental implants into the maxillary sinus in different depths. Journal of Applied Oral Science. 2013;**21**(6):560-566. DOI: 10.1590/1679-775720130078

[79] Abi Najm S, Malis D, El Hage M, Rahban S, Carrel JP, Bernard JP. Potential adverse events of endosseous dental implants penetrating the maxillary sinus: Long-term clinical evaluation. The Laryngoscope. 2013;**123**(12):2958-2961. DOI: 10.1002

[80] Ghnaem A, Gad HM. The influence of exposing dental implants

to the maxillary sinus cavity on sinus complications and implant survival rate: 6 years prospective follow-up. Egyptian Dental Journal. 2014;**60**(3):2-9

[81] Elhamruni LM, Marzook HA, Ahmed WM, Abdul-Rahman M. Experimental study on penetration of dental implants into the maxillary sinus at different depths. Oral and Maxillofacial Surgery. 2016;**20**(3):281-287. DOI: 10.1007/s10006-016-0568-z

[82] Shihab OI. Intentional penetration of dental implants into the maxillary sinus: A retrospective study. Zanco Journal of Medical Sciences. 2017;**21**(1):1536-1539. DOI: 10.15218/zjms.2017.001

[83] Nooh N. Effect of Schneiderian membrane perforation on posterior maxillary implant survival. The International Journal of Oral Health. 2013;**5**(3):28-34

[84] Ali SA, Karthigeyan S, Deivanai M, et al. Implant rehabilitation for atrophic maxilla: A review. The Journal of Indian Prosthodontic Society. 2014;**14**(3):196-207. DOI: 10.1007/s13191-014-0360-4

[85] Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. The International Journal of Oral and Maxillofacial Implants. 2009;**24**(Suppl):237-259

[86] Starch-Jensen T, Nielsen HB. Prosthetic rehabilitation of the partially edentulous atrophic posterior mandible with short implants (≤8 mm) compared with the sandwich osteotomy and delayed placement of standard length implants (>8 mm): A systematic review. Journal of Oral and Maxillofacial Research. 2018;**9**(2):e2. DOI: 10.5037/jomr.2018.9202

[87] Soto-Penaloza D, Zaragozí-Alonso R, Penarrocha-Diago M, et al. The all-on-four treatment concept: Systematic review. Journal of Clinical and Experimental Dentistry. 2017;**9**(3):e474-e488. DOI: 10.4317/jced.53613

[88] Bocklage R. Advanced alveolar crest atrophy: An alternative treatment technique for maxilla and mandible. Implant Dentistry. 2001;**10**(1):30-35. DOI: 10.1097/00008505-200101000-00009

[89] Goiato MC, Pellizzer EP, Moreno A, et al. Implants in the zygomatic bone for maxillary prosthetic rehabilitation: A systematic review. International Journal of Oral and Maxillofacial Surgery. 2014;**43**(6):748-757. DOI: 10.1016/j.ijom.2014.01.004

[90] Sharma A, Rahul GR. Zygomatic implants/fixture: A systematic review. The Journal of Oral Implantology. 2013;**39**(2):215-224. DOI: 10.1563/AAID-JOI-D-11-00055

[91] Ihde S, Kopp S, Maier T. Comparison of implant survival with implants placed in acceptable and compromised bone: A literature review. Journal of Oral and Maxillofacial Research. 2009;**8**(1):1-7. DOI: 10.1007/s12663-009-0001-3

[92] Ihde S, Ihde A. Immediate Loading Guideline to Successful Implantology. 2nd ed. Munich, Germany: International Implant Foundation Publishing; 2010. pp. 2-12

[93] Awadalkreem F, Khalifa N, Satti A, Suliman AM. Rehabilitation of patients with compromised ridge support using immediately loaded corticobasal implant-supported prostheses: A prospective observational study. The Journal of Contemporary Dental Practice. 2022;**23**(10):971-978. DOI: 10.5005/jp-journals-10024-3416

[94] Morgano AT. Functional load in oblique bicortical implants: Parasinusal implants and palatine implants. The Journal of Oral Implantology. 2013;**39**(4):467-474. DOI: 10.1563/AAID-JOI-D-09-00121.1

[95] Scortecci G. Basal Implantology. New York: Springer International Publishing; 2019. DOI: 10.1007/978-3-319-44873-2

[96] Al-Salman WT, Almas K. Maxillary sinus and success of dental implants: An update. General Dentistry. 2015;**63**(4):47-54

[97] Stacchi C, Andolsek F, Berton F, et al. Intraoperative complications during sinus floor elevation with lateral approach: A systematic review. The International Journal of Oral and Maxillofacial Implants. 2017;**32**(3):e107-e118. DOI: 10.11607/jomi.4884

[98] Chan HL, Wang HL. Sinus pathology and anatomy in relation to complications in lateral window sinus augmentation. Implant Dentistry. 2011;**20**(6):406-412. DOI: 10.1097/ID.0b013e3182341f79

[99] Shiffler K, Lee D, Aghaloo T, Moy PK, Pi-Anfruns J. Sinus membrane perforations and the incidence of complications: A retrospective study from a residency program. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology. 2015;**120**(1):10-14. DOI: 10.1016/j.oooo.2015.02.477

[100] Kim J, Jang H. A review of complications of maxillary sinus augmentation and available treatment methods. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2019;**45**(4):220-224. DOI: 10.5125/jkaoms.2019.45.4.220

[101] Barone A, Santini S, Sbordone L, Crespi R, Covani U. A clinical study of the outcomes and complications associated with maxillary sinus augmentation. The International Journal of Oral & Maxillofacial Implants. 2006;**21**(1):81-85

[102] Nolan PJ, Freeman K, Kraut RA. Correlation between Schneiderian membrane perforation and sinus lift graft outcome: A retrospective evaluation of 359 augmented sinus. Journal of Oral and Maxillofacial Surgery. 2014;**72**(1):47-52. DOI: 10.1016/j.joms.2013.07.020

[103] Manor Y, Mardinger O, Bietlitum I, Nashef A, Nissan J, Chaushu G. Late signs and symptoms of maxillary sinusitis after sinus augmentation. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2010;**110**(1):e1-e4. DOI: 10.1016/j.tripleo.2010.02.038

[104] Timmenga NM, Raghoebar GM, van Weissenbruch R, Vissink A. Maxillary sinus floor elevation surgery. A clinical, radiographic and endoscopic evaluation. Clinical Oral Implants Research. 2003;**14**:322-328

[105] Hainarosie R, Pietrosanu C, Cherecheanu A, Stoian AP, Stefanescu C, Pituru S. Risk factors for dental implant failure and medicolegal implications. Romanian Journal of Legal Medicine. 2019;**27**:52-56

[106] Park WB, Kim YJ, Herr Y, Lim HC. Functional endoscopic sinus surgery for paranasal sinusitis originating from a peri-implantitis-triggered infection in the augmented maxilla: A case report. The Journal of Oral Implantology. 2020;**46**(4):423-429. DOI: 10.1563/aaid-joi-D-19-00381

[107] Scarano A, Cholakis AK, Piattelli A. Histologic evaluation of sinus grafting materials after peri-implantitis-induced failure: A case series. The International Journal of Oral and Maxillofacial Implants. 2017;**32**(2):e69-e75. DOI: 10.11607/jomi.5303

[108] Hong SO, Shim GJ, Kwon YD. Novel approach to the maxillary sinusitis after sinus graft. Maxillofacial Plastic and Reconstructive Surgery. 2017;**39**(1):18. DOI: 10.1186/s40902-017-0115-3

[109] Park WB, Han JY, Oh SL. Maxillary sinusitis associated with peri-implantitis at sinus floor augmented sites: Case series. Implant Dentistry. 2019;**28**(5):484-489. DOI: 10.1097/ID.0000000000000922

[110] Rodriguez AE, Nowzari H. The long-term risks and complications of bovine-derived xenografts: A case series. Journal of Indian Society of Periodontology. 2019;**23**(5):487-492. DOI: 10.4103/jisp.jisp_656_18

[111] Park MJ, Park HI, Ahn KM, Kim JH, Chung YS, Jang YJ, et al. Features of odontogenic sinusitis associated with dental implants. The Laryngoscope. 2023;**133**(2):237-243. DOI: 10.1002/lary.30069

[112] Caccianiga G, Rey G, Caccianiga P, Leonida A, Baldoni M, Baldoni A, et al. Rough dental implant surfaces and peri-implantitis: Role of phase-contrast microscopy, laser protocols, and modified home oral hygiene in maintenance. A 10-year retrospective study. Applied Sciences. 2021;**11**:4985. DOI: 10.3390/app11114985

[113] Sinjab K, Sawant S, Ou A, Fenno JC, Wang HL, Kumar P. Impact of surface characteristics on the peri-implant microbiome in health and disease. Journal of Periodontology. 2024;**95**(3):244-255. DOI: 10.1002/JPER.23-0205

[114] Khairnar M, Gaur V. Evidence of bone formation in the nasal floor around polished surface bi-cortical screw implants after indirect nasal lift in an atrophied maxilla: Cone beam computed tomography-based case report. Journal of Indian Society of Periodontology. 2015;**19**(2):236-238. DOI: 10.4103/0972-124X.149941

[115] Kim HY, Yang JY, Chung BY, Kim JC, Yeo IS. Peri-implant bone length changes and survival rates of implants penetrating the sinus membrane at the posterior maxilla in patients with limited vertical bone height. Journal of Periodontal and Implant Science. 2013;**43**(2):58-63. DOI: 10.5051/jpis.2013.43.2.58

[116] Altayyar S, Al-Zordk W, Algabri R, Rajah E, Al-Baadani A, Alqutaibi AY, et al. Prospective evaluation of implants-supported, tooth-implant supported, and teeth-supported 3-unit posterior monolithic zirconia fixed restorations: Bite force and patient satisfaction. Cllinical and Experimental Dental Research. 2023;**9**(5):810-819. DOI: 10.1002/cre2.780

[117] Beuer F, Sachs C, Groesser J, Gueth JF, Stimmelmayr M. Tooth-implant-supported posterior fixed dental prostheses with zirconia frameworks: 3-year clinical result. Clinical Oral Investigations. 2016;**20**(5):1079-1086. DOI: 10.1007/s00784-015-1594-1

[118] Lemos CAA, Verri FR, de Luna Gomes JM, Santiago Junior JF, Miyashita E, Mendonca G, et al. Survival and prosthetic complications of monolithic ceramic implant-supported

single crowns and fixed partial dentures: A systematic review with meta-analysis. The Journal of Prosthetic Dentistry. 2022, 2022:S0022-3913(22)00736-3. DOI: 10.1016/j.prosdent.2022.11.013. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0022391322007363

[119] Testori T, Clauser T, Saibene AM, Artzi Z, Avila-Ortiz G, et al. Radiographic protrusion of dental implants in the maxillary sinus and nasal fossae: A multidisciplinary consensus utilising the modified Delphi method. International Journal of Oral Implantology (Berlin). 2022;**15**(3):265-275. Erratum in: International Journal of Oral Implantology (Berlin). 2022;15(4):371-373

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The current conceptual knowledge of rhinology has evolved over the last decades. The approach to many sinonasal disorders has changed based on our new understanding of their pathogeneses. Rhinological diseases are common and cover a wide spectrum of disorders that usually share similar clinical presentations; thus, a fundamental scientific comprehension is required to properly choose the correct medical or surgical management. This book discusses an updated review of contemporary disorders in the sinonasal region.

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