

Review

Surgical management of rhinosinusitis for the allergist-immunologist



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Key Messages

- Chronic rhinosinusitis (CRS) is a chronic inflammatory condition with 2 categories: CRS with nasal polyps and CRS without nasal polyps.
- Although medical management is key for disease control in patients with CRS, several factors, including phenotype, endotype, patient compliance and preference, and anatomy, can affect outcomes of treatment. For a certain subset of patients, adjunct functional endoscopic sinus surgery (FESS) is critical for improving topical medication delivery and reducing disease burden.
- FESS serves to enlarge the natural openings of diseased sinuses, thus restoring ventilation and drainage and improving delivery of topical medications.
- Expanded surgical approaches have been shown to significantly improve sinonasal outcome scores by maximizing postoperative topical medical delivery and improving long-term sinus patency.
- Biologics show great promise in the treatment of CRS with nasal polyps, both alone and combined with FESS. However, more high-quality studies and trials are needed.

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ABSTRACT

Chronic rhinosinusitis (CRS) is a common chronic inflammatory disease characterized by inflammation of the sinus, with or without nasal passage inflammation, occurring for more than 12 weeks at a time. CRS has historically been classified in 2 categories: CRS without nasal polyps or CRS with nasal polyps (25%-30% of cases). The mainstay of treatment for CRS with or without nasal polyps is medical management, and options may include a combination of saline irrigation, nasal steroids, allergy medications, antibiotics, oral steroids, and treatment with targeted monoclonal antibodies. Unfortunately, up to 60% of patients report symptoms refractory to maximal medical therapy. As such, a combined approach of surgery and medical therapy may be offered. Endoscopic sinus surgery for CRS is approached in a stepwise fashion, ranging from the simplest technique, such as polyp removal, to more expanded approaches that open the paranasal sinuses and allow gravity-dependent drainage. This review article provides a review and in-depth explanation of various surgical approaches for CRS, including the indications, techniques, and respective outcomes for each one.

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Introduction

Chronic rhinosinusitis (CRS) is a common chronic inflammatory disease with an estimated prevalence of 4.5% to 12% in North America and Europe.¹ CRS is characterized by inflammation of the sinus, with

or without nasal passage inflammation, occurring for more than 12 weeks at a time. Symptoms may include nasal congestion, loss of smell, facial pain, and rhinorrhea. CRS has historically been classified in 2 categories: CRS without nasal polyps or CRS with nasal polyps (CRSwNP ~25%-30% of cases).² Although the mechanism is still not entirely understood, CRSwNP is predominately associated with type 2 inflammation.^{3,4} Various comorbidities also exist in high prevalence with CRS, including cystic fibrosis (CF) and most notably, asthma, with an approximately 50% prevalence in the patient population

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with CRS.⁵ CRS has been shown to significantly impair health-related quality of life (QOL)^{6–8} and accounts for an economic burden of more than \$12.5 billion annually in North America.⁹ The mainstay of treatment for patients who meet the criteria for CRS with or without nasal polyps is medical management. Options may include a combination of saline irrigation, nasal steroids, allergy testing and treatment, if applicable, and antibiotics or oral steroids for acute flare ups. In addition, inhaled steroids and/or treatment with targeted monoclonal antibodies may be warranted for those with concomitant asthma.

The composition and duration of optimal medical duration for CRS remain variable, and high-level evidence is lacking. The international consensus statement on rhinosinusitis summarized 55 medical therapies and their level of evidence.¹⁰ Generally, the strongest evidence and recommendation exist for intranasal saline irrigations and topical steroids as the mainstay of medical treatment for CRS with or without nasal polyps, which coincides with standard clinical practice.¹⁰ The consensus statement also provides recommendation for short-term oral corticosteroid courses for CRS without nasal polyps in addition to long-term oral macrolide antibiotics for CRSwNP. Maximal medical therapy (MMT) is considered appropriate for patients with CRS who do not respond to nasal steroids and irrigation.^{1,10} Unfortunately, definitions of intensity and duration of MMT have been inconsistent. Dautremont et al¹¹ conducted a systematic review in which they found that most authors included an 8-week course of topical intranasal corticosteroids and a 3-week course of oral antibiotics as the MMT offered to patients.

Unfortunately, up to 60% of patients with CRS report continued symptoms refractory to MMT, though this number is thought to be an underestimation.¹² In cases in which standard medical management has not achieved a meaningful difference in symptoms burden for the patient, a combined approach of surgery and medical therapy may be offered. Patel et al¹³ conducted a systematic review to better characterize outcomes for surgical therapy vs continued medical therapy for medically refractory CRS. The results indicated that when considering disease-specific QOL scores, health utility value QOL scores, nasal endoscopic scores, olfaction, and economic impact, surgery yielded better results than did continued medical therapy in patients who failed appropriate medical therapy. In addition, patients who decided to undergo sinus surgery seemed to base their decision on the severity of baseline disease-specific QOL. Specifically, patients who decided to continue with medical therapy tended to have less severe baseline disease-specific QOL.

This article will serve to provide a review and explanation of the indications and methods for different surgical approaches and their respective outcomes.

Surgical Approaches

The nasal cavity is a cylindrical airway passage divided in the midline by the nasal septum. On each side, it is flanked by 4 air-filled paranasal sinuses lined with respiratory epithelium. The 4 paired sinuses—the maxillary, ethmoid, sphenoid, and frontal—and all

sinuses drain into the nasal cavity through various outflow tracts (Fig 1). The maxillary sinuses are located within the maxillary bones, under the eyes. The ethmoid sinuses comprise several air cells within the ethmoid bone, between the nose and eyes. The sphenoid sinuses are located most posteriorly within the sphenoid bone. The frontal sinuses are located superior to the eyes, within the frontal bone.¹⁴ The lateral nasal wall has 3 bony outgrowths called turbinates. The superior, middle, and inferior turbinates are covered by mucosa and play an important role in filtration, humidification, and regulation of the flow of air passing through the nasal cavity. The turbinates also serve as important landmarks during sinus surgery. Throughout the years, surgical approaches have varied, ranging from simple polyp removal to complete opening of the nasal cavity and sinuses. No matter the technique, the goal of sinus surgery is to attempt long-term control of disease and thus improve patient symptoms and QOL. To maintain healthy functional status, the paranasal sinuses rely on intact innate and adaptive immunity, intact mucociliary clearance, and patent sinonasal drainage pathway. For those patients with CRS unresponsive to appropriate medical therapy, a graduated surgical approach has been recommended. The objectives of functional endoscopic endonasal sinus surgery include the following:

1. Restoring ventilation or drainage pathways (to allow effective delivery of topical rinses and medications)
2. Removing disease (ie, polyps, osteitic bone, accumulation of mucus or fungal debris)
3. Preserving sinus and nasal mucosa (to aid in mucociliary clearance)
4. Preserving anatomic landmarks to reduce risk of intraoperative injury.

CRS is a condition that has been shown to negatively affect QOL. As such, patient-reported outcome measures serve to help evaluate symptom burden. The 22-item Sinonasal Outcome Test (SNOT-22) is a patient-reported outcome measure that captures symptom severity, social and emotional impact, and productivity and sleep consequences of CRS.^{15,16} Scoring is conducted through a 6-point Likert scale, with 0 representing no problem to 5 representing a problem as bad as it can be. The scores are summed to form a total score of 0 to 110. The SNOT-22 score has become a useful tool to measure outcomes for both medical and surgical management of CRS and will be referred to throughout the remainder of this article. It is important to note that although the SNOT-22 score is useful, it does not entirely dictate decisions for management.

The following section reviews surgical approaches for CRS refractory to MMT in a stepwise fashion, from techniques considered least to most invasive.

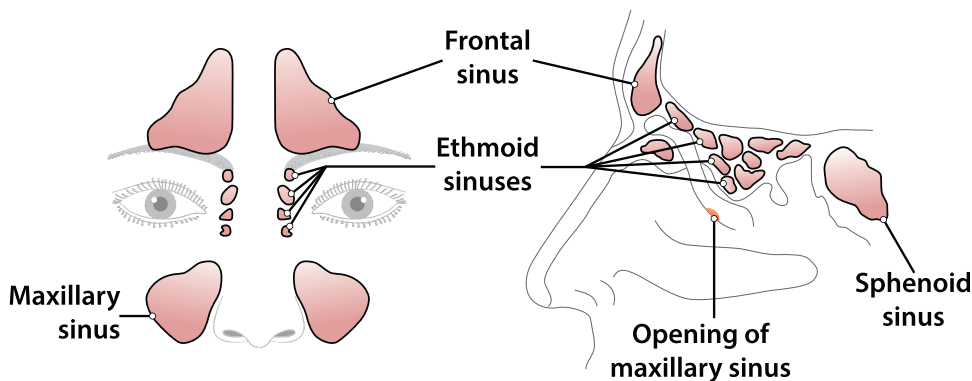


Figure 1. Coronal (A) and sagittal (B) illustration of the paranasal sinuses and nasal cavity.

Balloon Dilation of the Sinuses

Balloon dilation of the paranasal sinuses was approved by the Food and Drug Administration in 2005 as an alternative treatment for patients with CRS. The system uses high-pressure, low-volume balloons to dilate the natural ostia or openings of the occluded sinus, thus aiding in restoration of sinus ventilation and drainage pathways under endoscopic guidance. Multiple authors have shown that balloon dilation is a safe and effective treatment for patients with CRS.^{17–19} Bikhazi et al¹⁹ carried out a prospective randomized multicenter controlled trial to compare outcomes for balloon dilation with those of functional endoscopic sinus surgery (FESS) in the treatment of uncomplicated CRS. Specifically, the authors looked at patients with maxillary sinus disease with or without anterior ethmoid disease who failed medical therapy and met the criteria for medically necessary FESS.¹⁹ At both 6 months and 18 months follow-up, they found that standalone balloon dilation was as effective as FESS. Specifically, both study arms showed similar, statistically significant improvement in SNOT-20 (a variation of the SNOT-22 score), with overall SNOT-20 scores being twice the clinically meaningful threshold.^{19,20} The decision for balloon dilation for CRS should be made in an individual considering challenging or unconventional anatomy, such as osteoneogenesis, significant polyp disease burden, and bony dehiscence.

Polypectomy and Functional Endoscopic Sinus Surgery

Approximately 25% to 30% of patients with CRS develop polyps, which can significantly obstruct the nasal passageway and subsequently sinus drainage tracts. The simplest surgical intervention available to these patients is termed a polypectomy. This is a procedure to remove polyps in the nasal airway (without opening the paranasal sinuses) and relieve the associated nasal airway obstruction. This approach is commonly performed in the operating room or in the office for selected cases. Polypectomy has been shown to significantly reduce the SNOT-22 scores for patients; however, postoperative recurrence rates reach up to 60% at long-term follow-up in the literature.^{21–23} High recurrence rates are especially prevalent in patients with severe inflammation or comorbidities (such as asthma).^{24,25} Consequently, a more comprehensive surgical approach, FESS, which involves removing any obstruction (such as polyps) and opening up all diseased sinuses, has gained favor for CRSwNP refractory to medical management and/or polypectomy. The general approach for FESS involves enlarging the natural ostium of all diseased sinuses. This helps restore ventilation/drainage pathways of the sinuses and allows improved topical delivery, which more limited approaches such as a polypectomy cannot achieve.²⁶ This is thought to be because the natural ostia are predisposed to scarring or obstruction by even a small degree of polyp burden, especially if the sinus is not widely opened. This stems from the concept that the risk of scarring is theoretically greatest when opposing mucosal cut edges are in proximity.²⁷ The shift to a more comprehensive initial approach is also largely on the basis of the evolving understanding that the mucociliary clearance of the sinuses is often impaired in CRS and restoring ventilation/outflow drainage can help re-establish function. Multiple authors have shown significantly improved SNOT-22 scores with a comprehensive FESS compared with more limited or targeted surgery and that the difference in scores was preserved after controlling for asthma, aspirin exacerbated respiratory disease, and nasal polyposis using linear regression modeling.²³

Nasalization

Nasalization is a more comprehensive surgical approach that first gained traction in the 1990s, particularly for patients with CRSwNP refractory to medical management. The approach comprises completely opening the ethmoid air cells, resecting the middle turbinate and thus opening the middle meatus (into which the anterior

ethmoid cells and maxillary and frontal sinuses all drain), dissecting the frontal cells, and finally, resection of the ethmoidal mucosa (sparing the olfactory cleft).^{28,29} The ultimate goal is to reduce polyp formation from the ethmoid sinuses and largely open the nasal cavity so that it can be reached by topical medications.³⁰ Various studies have shown that nasalization is associated with lower recurrence rates and better symptom and asthma control, in addition to olfactory improvement.^{28,29,31} Like any surgery, nasalization carries risk of complication, namely, mucocele formation.^{32,33} This has led to modified versions over time in an attempt to reduce complication rates.³⁴

Expanded Approaches

Traditionally, endoscopic sinus surgery targeted removal of obstructions and widening of narrow anatomy that were thought to cause post-obstructive sinus inflammation. However, as our understanding of CRS has evolved, it has emerged that this is a multifactorial disease in which some subsets of patients with recalcitrant disease may benefit from a more extensive surgical approach. Specifically, expanded surgical approaches have been shown to improve distribution of topical therapies, such as steroid irrigations,²³ which is particularly valuable to patients with steroid-responsive sinonasal disease and CRSwNP.

Draf Procedures

One post-FESS characteristic that has been increasingly studied is maintenance of patency of the sinus outflow tract because this helps ensure long-term successful delivery of topical medications and ciliary clearance. Patency outcomes have especially been studied regarding the frontal sinuses because historically, this is often the most common site of polyp recurrence and reobstruction.³⁵

Similar to disease processes in the other paranasal sinuses, the frontal sinuses are surgically approached in a stepwise fashion. Traditionally, the simplest option is used first, whereas more comprehensive approaches are reserved for patients with complex pathology, higher risk endotypes such as aspirin-exacerbated respiratory disease (AERD), or in cases of revision surgery. In the 1990s, Prof Wolfgang Draf described a series of procedures aimed at opening the frontal ostium through an intranasal approach and allowing the sinus to drain.³⁶ Draf I involves opening the anterior ethmoid air cells, thus opening the frontal recess. Draf II, in addition, involves unilateral resection of the floor of the frontal sinus. Specifically, Draf IIa widens the frontal sinus outflow tract from the lamina papyracea to the middle turbinate; Draf IIb extends to the nasal septum medially. Draf type III, also named the modified Lothrop procedure, is an approach that allows the formation of a wide common frontal outflow tract for both frontal sinuses by removing both frontal sinus floors, the intersinus septum, superior nasal septum, and frontal beak (Fig 2). Draf III is traditionally reserved for patients in whom sinus inflammation is persistent or recurrent despite initial surgery and medical management and more comprehensive technique is warranted. This approach has increasingly become a popular option for refractory CRS owing to the long-term postoperative patency.³⁷ The success of this surgery is emphasized in patients with AERD, a notoriously recalcitrant disease process. In fact, many studies advocate for more extensive surgery such as Draf III in patients with AERD.^{35,38} More data have emerged in recent years showing that patients with AERD who undergo a comprehensive sinus surgery (bilateral maxillary antrostomies, bilateral total ethmoidectomies, bilateral sphenoidotomies, and bilateral frontal sinusotomies (ie, Draf IIa, IIb, or III)) experience improved QOL compared with conservative surgery.²⁶ These QOL gains are further preserved with postsurgical aspirin desensitization and long-term aspirin maintenance.^{39–41}

Frontal sinus surgery has greatly evolved in the past century. A more aggressive initial approach may reduce the risk of polyp recurrence and/or disease process by allowing long-term patency and

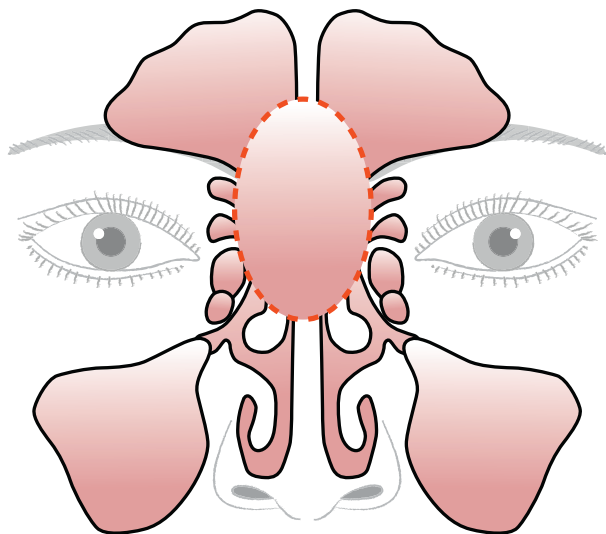


Figure 2. Coronal illustration of the Draf III (modified Lothrop) procedure, showing formation of a common enlarged frontonasal drainage pathway through removal of the frontal sinus floor bilaterally, intersinus septum, superior nasal septum, and frontal beak.

delivery of topical medications that reduce inflammatory burden and provide better symptom control.

Reboot Approach

Patients with CRSwNP because of type-2 eosinophilic inflammation (which represents 80% of patients with nasal polyps) often have higher recurrence rates.^{42,43} The reboot technique, which was introduced in 2019, is meant to reduce polyp recurrence in cases in which type-2 eosinophilic inflammation is thought to contribute to CRSwNP. The reboot technique, as described by Alsharif et al,⁴⁴ aims to accomplish total clearance of all affected mucosa from all sinuses, leaving the periosteum intact. This contrasts with classical FESS, in which mucosa sparing is prioritized. In a retrospective, case control study, Alsharif et al⁴⁴ compared patients who underwent standard FESS with those who underwent either a partial reboot technique (clearance of all sinonasal polyps and mucosa) or a full reboot technique, which also includes a Draf III procedure. All patients underwent standard postoperative care, including nasal hygiene and 6 weeks of oral antibiotics and topical steroids. The authors found that the patients who underwent the reboot

approach had significantly reduced relapse rates compared with those who underwent a classical FESS approach. The FESS group also had shorter time to relapse after surgery. Moreover, the full reboot group showed superior results in terms of number and timing of recurrence to those of the partial reboot and nonreboot groups.⁴⁴ The authors hypothesize that complete removal of the sinus mucosa also allows clearance of dysregulated microbiome and thus positively affects the natural course of this difficult-to-control disease.

Maxillary Mega Antrostomy

Similar to the frontal sinuses, the maxillary sinuses are at risk of recurrent/persistent disease. Risk factors for recalcitrant disease include innate or acquired impairments of mucociliary clearance (eg, primary ciliary dyskinesia, CF); odontogenic sinusitis; biofilm-mediated disease; immunologic impairment; and previous surgery.^{45–47} In such cases, the endoscopic mega maxillary antrostomy (EMMA) is an option. The EMMA is a mucosal-sparing procedure that allows an enlarged opening of the maxillary sinus extending from the natural ostium down to the nasal cavity floor. This facilitates improved sinus irrigation and topical drug delivery, allows gravity-dependent drainage of the sinus, and improves access for in-office debridement (Fig 3). A large study by Costa et al⁴⁸ found that EMMA resulted in significant improvement in symptom scores and endoscopic scores over a mean follow-up period of 2.2 years. In addition, the results were significant in the 25% of patients with CF. This is especially important given that revision surgery rates have been reported to be higher in the patient population with CRS and with CF than in those with CRS alone.⁴⁹

Sphenoid Nasalization

The sphenoid sinus is located behind the posterior ethmoids and superior turbinate.⁵⁰ The natural opening lies high in the anterior face of the sphenoid, which can lead to mucus pooling, bacterial colonization, and diminished irrigation delivery.²³ The challenging location of the sphenoid opening combined with inflammation or polypoid edema can significantly limit penetration of topical medical treatment to the sphenoid.^{23,51}

In most cases, enlarging the natural opening of the sinus can provide sufficient drainage of any retained secretions or debris and subsequently allow the sinus to re-establish mucociliary clearance.⁵² However, an estimated 30% to 50% of patients who undergo

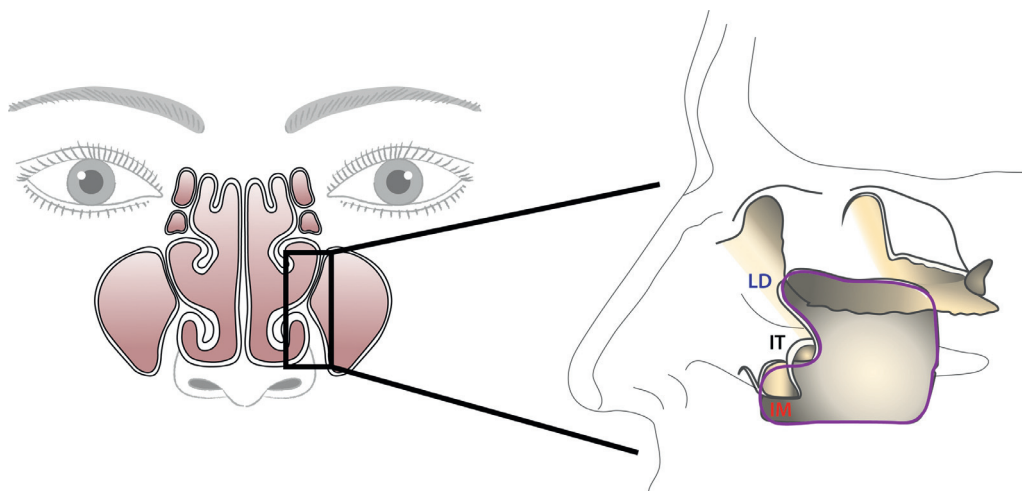


Figure 3. The endoscopic mega maxillary antrostomy. A subtotal IM resection is performed, and an opening is created into the maxillary sinus through the IM (the space between the inferior turbinate and floor of nasal cavity). The natural maxillary opening has been widened by taking down the anterior and posterior walls and connecting this opening to the nasal cavity floor. The resulting opening that allows gravity-dependent drainage is highlighted by the purple box in the sagittal view (B). This is also highlighted by the black box in the coronal view (A). Note the proximity of the lacrimal duct (connecting to the lacrimal sac), which great care is taken to avoid damaging, depicted on the sagittal view (B). IM, inferior meatus; IT, inferior turbinate; LD, lacrimal duct.

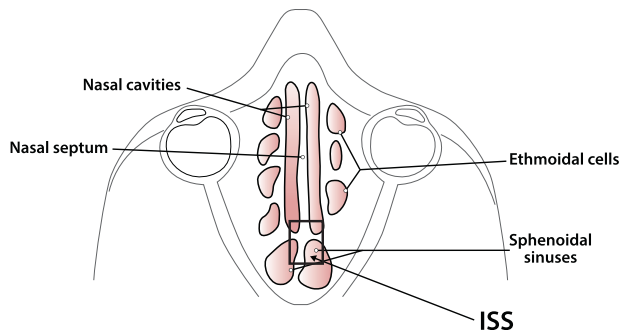


Figure 4. Sphenoid nasalization. The illustration depicts an axial view of the technique. The sphenoid sinuses are opened; the posterior 1-to-2 cm of the septum is removed, and the ISS between the 2 sinuses is also taken down. This is depicted by the black box in the image. This results in a common sphenoid sinus. ISS, intersinus septum.

revision sinus surgery require sphenoid revision to manage ongoing inflammation and resulting symptoms.^{53,54} Sphenoid nasalization is a technique used to widely open the sphenoid sinus, specifically by removing the anterior face and floor (Fig 4). This allows gravity-dependent drainage directly into the nasal cavity and enhanced postoperative topical medication delivery through irrigation.⁵⁵ For CRS, this expanded approach to the sphenoid sinus has been shown to provide long-term sinus patency and improved topical delivery of medications and therefore reduction of inflammatory symptoms.^{55,56}

Outcomes

Surgical

The outcomes of nasal polyp and CRS symptom recurrence are widespread in the literature. This is due to several factors, including, but not limited to, the inherent variation in disease subtype and severity, diagnostic criteria, follow-up time, medical management, and extent of surgical approach/description. In addition, nondifferentiation of patient grouping, for example, patients with and without asthma or different endotypes such as AERD and allergic fungal rhinosinusitis, has contributed to discrepancies in the literature.

To better characterize the risk factors that can contribute to polyp recurrence, Loftus et al⁵⁷ conducted a large meta-analysis. The article included 45 reviewed studies and a total of 34,220 subjects and found the overall revision rate for patients with CRSwNP to be approximately 18%. However, patients with allergic fungal rhinosinusitis, AERD, and asthma had significantly higher revision rates, ranging from 23% to 28%. Interestingly, publications before 2008 were also found to have significantly higher recurrence and revision rates. Authors theorize that the decreasing revision rates over time are due to an increase in more comprehensive surgeries that facilitate topical steroid rinse delivery and to the introduction of expanded procedures earlier on in patients with more aggressive disease. It is becoming increasingly recognized that widely opened sinuses improve access for topical therapies to reach the sinus mucosa.^{23,56,58} This is particularly important in patients with recalcitrant disease, in whom many studies have indicated the positive effects of nasal steroid irrigations on QOL measurements and SNOT-22 scores.^{59,60}

Biologics

Monoclonal antibodies targeting the type 2 inflammatory pathway have been developed with promising results in patients with CRSwNP. Although there are emerging and limited data regarding both the outcomes and cost-effectiveness of these medications, data have slowly been accruing that evaluate the role of biologics both with and without adjunct surgical intervention. Dharmarajan et al⁶¹ conducted a retrospective matched study evaluating outcomes after

FESS vs Dupilumab—an immunoglobulin G4 human monoclonal antibody that targets the interleukin 4 receptor alpha subunit. The study found that both FESS and Dupilumab patient groups showed significant improvement in SNOT-22 scores.⁶¹ However, patients treated with FESS had a greater reduction in nasal polyp burden, whereas patients treated with Dupilumab reported improved perception of smell and decreased extranasal rhinologic symptoms such as cough, postnasal drip, and thick nasal drainage. A subset of patients with AERD was analyzed and showed improvement in SNOT-22 scores and nasal polyp burden with either FESS or Dupilumab.

Scangas et al⁶² evaluated outcomes and cost-effectiveness of Dupilumab vs FESS for CRSwNP. Their results were similar in that Dupilumab did show some clinical benefit over FESS alone, but the authors determined that it would take years of therapy to see a meaningful clinical difference between these treatments. Indeed, the authors found that FESS produced 1.526 QOL years for \$20,626, whereas Dupilumab produced 1.779 QOL years for a total cost of \$194,764. This translated to a 9-fold increase in cost of treatment of Dupilumab compared with that of FESS. Their findings were similar to other studies evaluating the cost-effectiveness of biological therapy for CRSwNP.^{62,63}

Although biologics such as Dupilumab show great promise in the patient population with CRSwNP, FESS remains the most cost-effective treatment option.⁶² More studies will be needed to help provide guidance on which patients would best benefit from targeted biological therapy.

Conclusion

As our understanding of CRS continues to evolve, several factors have been identified that can aid in successful management of the disease. These include, but are not limited to, understanding of endotype and phenotype, patient compliance and preference, and anatomic considerations that must be addressed for ideal medical and surgical management. All these factors play significant roles in deciding on which medical management to use, in addition to the surgical approach when indicated.

In this review, we outline several surgical approaches, including the benefits and possible complications, namely, recurrence and need for revision. Significant evidence exists to support less invasive approaches, such as balloon dilation, for patients with CRS refractory to medical management and with otherwise uncomplicated anatomy. Meanwhile, expanded approaches such as the modified Lothrop procedures, reboot technique, maxillary mega antrostomy, and sphenoid nasalization are used, particularly in patients with CRSwNP refractory to conservative management, to allow maximal postoperative topical medical delivery through intranasal steroid irrigations and to improve long-term patency. Lastly, biologics show great promise in the treatment of CRSwNP; however, more high-quality studies and trials are needed to better evaluate appropriate application of these therapies and the long-term effects and outcomes of these monoclonal antibodies, both alone and in combination with appropriately comprehensive sinus surgery.

Disclosures

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