

Allergic Rhinitis and Chronic Rhinosinusitis

Their Impact on Lower Airways

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KEYWORDS

• Unified airway • Inflammation • Sinusitis • Asthma • Nasal polyps

KEY POINTS

- Several inflammatory mechanisms exist that connect the upper and lower airways through infectious, allergic, and nonallergic pathways.
- Patients with the most severe disease will benefit from thorough consideration, workup, and management of coexisting upper and lower airway disease.
- Long-lasting benefits may be achieved for lower airway disease with aggressive management of the upper airways.
- Surgical treatment of the nose and sinuses is known to improve nasal airflow, sleep quality, sense of smell, and sinonasal symptoms. There are also anatomic benefits that facilitate topical drug distribution, and the potential for decreased systemic inflammation related to the underlying disease.

INTRODUCTION

The notion that coincident inflammation commonly affects both the upper and lower airways via similar mechanisms has been well established. This idea has been reinforced over recent years with both basic and clinical research findings as well as with clinical observation.

Chronic airway inflammation commonly presents clinically as allergic rhinitis (AR) and chronic rhinosinusitis (CRS) in the upper airway, and as asthma in the lower airway. These conditions often coexist in the same patient, and are seen by a variety of general and specialty practitioners including family physicians, pediatricians, interntists, pulmonologists, allergists, and otolaryngologists, as well as mid-level providers

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such as nurses and physician assistants. The incidence and prevalence of these disorders are high, and for allergy and asthma appear to be increasing over time. In addition, it is common for patients complaining of upper airway symptoms to have their lower airway overlooked, and vice versa.

Because of these factors, it is important for clinicians to be aware of the relationship between these disorders and how they can affect one another, to ensure optimal diagnosis and treatment. In patients with asthma, it is important to also evaluate the upper airway for symptoms and signs of AR and/or CRS. Diagnosing and treating these upper airway disorders can have a direct impact on lower airway inflammation and are important for optimizing patient outcomes. The impact on the lower airway of these upper airway conditions and their treatment are discussed here in detail.

UNIFIED AIRWAY THEORY

The unified airway theory has several suppositions.¹ First, pathophysiologic mechanisms ought to be similar despite the distance between the upper and lower airways. Anatomically the upper and lower airways are lined entirely with the same respiratory type of ciliated, pseudostratified columnar epithelium, which includes the mucosa of the middle ear, nose, sinuses, larynx, trachea, and down to the distal bronchioles. The unified airway theory considers these distinct anatomic units as a single functional unit. Continuing along this line of reason, when a pathophysiologic process, such as inflammation, affects one anatomic unit, the same process can be stimulated in another anatomic unit. This phenomenon can occur because of a local or systemic stimulus, and presents clinically when a patient with AR and asthma presents with worsening wheezing and chest tightness after an allergy exacerbation with increased nasal obstruction. The second postulate of the unified airway theory is that as the severity of airway disease fluctuates, both the upper and lower airways are affected to similar degrees. This notion implies that when effective treatment is initiated for upper airway symptoms, lower airway symptoms are expected to improve, and vice versa. Basic science and translational clinical research have largely supported these theories.¹ Understanding the pathophysiologic mechanisms affecting the respiratory system is essential for better understanding of how to optimally treat these patients. It is beyond the scope of this article to thoroughly review the concepts of the unified airway theory, but the general concept is presented as an underlying framework for the remainder of the article.

RHINITIS AND LOWER AIRWAYS

The understanding of the relationship between rhinitis and asthma has evolved over the years to reveal some important associations. Many studies have shown that patients with rhinitis often have coexisting asthma, and that treatment of rhinitis can improve the control of asthma. In this section, the epidemiology, pathophysiology, and clinical relevance are explored in detail.

Epidemiology

AR occurs with a prevalence of somewhere between 15% and 40%,² making it one of the most prevalent conditions among the general population. Asthma is estimated to affect about 7% of the general population.² As many as 38% of patients with AR have been shown to have concurrent asthma.³ Overall, the epidemiologic data suggest that these conditions occur together more frequently than expected for either condition alone. In addition, several studies have shown that patients diagnosed with rhinitis have a significantly increased risk of developing asthma over time.⁴⁻⁶

In patients diagnosed with asthma, concurrent rhinitis is likewise a very common finding, occurring somewhere between 50% and 85% of the time. This finding is important, as patients with asthma and rhinitis appear to have more severe asthma in comparison with patients with asthma alone. Studies have shown increased cost of medical care and increased need for hospitalization in such patients with concomitant rhinitis and asthma.⁷⁻¹⁰ These findings highlight the importance of evaluating the upper airway in patients with asthma.

Pathophysiology

As already mentioned, the histology of the upper airway from the nose to the bronchioles is identical. It follows logically that inflammation would affect these anatomically distinct areas in a similar fashion, at least at a cellular level. It has indeed been shown that the inflammatory cascade of lymphocytes, eosinophils, cytokines, and other inflammatory mediators share a similar profile, whether they occur in the upper or lower airway.¹¹⁻¹³ In addition, inflammation in the upper and lower airways is often caused by the same airborne irritants, such as pollutants or allergens, suggesting similar pathophysiologic mechanisms. Indeed, it has been demonstrated that patients with rhinitis have increased bronchial reactivity, even without a diagnosis of asthma.^{14,15} Additional studies have looked at inflammatory markers in the upper and lower airways.¹⁶⁻¹⁸ When allergic patients are stimulated with nasal provocation, changes include eosinophilia in the bronchial mucosa, elevated cytokine levels, and decreased peak expiratory flow when compared with nonallergic controls. Conversely, bronchial provocation of allergic patients causes an increase in cytokines, such as interleukin (IL)-5, eotaxin, and eosinophils, in nasal mucosa. These studies demonstrate that rhinitis and asthma are linked in their pathophysiology and can be thought of as different manifestations of a similar reactive airway disease.

Treatment

If inflammation of the upper airway can stimulate the same process in the lower airway, and vice versa, it seems possible that treatment of such inflammation could work the same way. However, the results of studies investigating this concept are mixed. Nevertheless, several studies have shown that treatment of patients with asthma with intranasal steroid spray for rhinitis resulted in fewer visits to the emergency department, fewer lost work days, and improved sleep quality.¹⁹⁻²² There is also convincing evidence that treatment of rhinitis in children with immunotherapy reduces bronchial reactivity and the risk of subsequently developing asthma.²³

Summary

Patients with rhinitis are at increased risk of developing asthma, and most patients with asthma have rhinitis. The pathophysiology of these conditions is closely related, and may in fact be different manifestations of the same disease process. Health care providers must be aware of this relationship, and must evaluate for both of these conditions when evaluating a patient for upper or lower airway complaints, as early recognition and appropriate treatment can improve quality of life, save costs, and prevent future morbidity.

CHRONIC RHINOSINUSITIS AND LOWER AIRWAYS

CRS can potentially contribute to lower airway disease through infectious mechanisms, such as in chronic bronchitis, bronchiectasis, or mucociliary dysfunction. In addition, inflammatory or neurogenic pathways may link CRS to lower airway disease

in asthma, aspirin-exacerbated respiratory disease (AERD), and chronic cough. In certain cases, therapy for CRS can be expected to yield measurable benefits for the lower airways.

Epidemiology

CRS is responsible for nearly 20 million physician office visits per year.²⁴ This condition is increasing in prevalence and incidence with time, and its detrimental effects on quality of life and daily functioning are well accepted. Quality-of-life impairments in CRS patients are comparable in severity with those in disease states such as congestive heart failure, chronic obstructive pulmonary disease, and chronic low back pain.²⁵ Approximately \$200 million per year are being spent on prescription medication, and \$2 billion per year on nonprescription medication, to treat symptoms of sinusitis. There are also indirect accumulated costs, including time away from work/school and the associated loss of productivity. In the United States overall, CRS results in almost \$4 billion of direct health care costs per year, and almost \$6 billion of direct and indirect costs per year.^{26,27}

Pathophysiology

CRS is no longer considered purely an infectious disease, but can be thought of as a multifactorial disease process of continued inflammation whereby infection may play a role in the initiation or sustenance of inflammation (**Tables 1** and **2**).²⁸

Diagnosis of CRS

Over the past 20 years there has been a steady increase in clinical interest and research on rhinosinusitis. More recently, the quality of this research has steadily improved to include higher levels of evidence and more sophisticated methods of study. Beginning in 1996, there has been an evolving effort by the American Academy of Otolaryngology—Head and Neck Surgery, the American Rhinologic Society, the American Academy of Otolaryngic Allergy, and other collaborating, multidisciplinary organizations to define the diagnostic criteria for sinusitis. The modern definition was put forth in 2004 by a multidisciplinary task force, describing CRS in adults as “a group of disorders characterized by inflammation of the mucosa of the nose and paranasal sinuses of at least 12 weeks’ duration.”²⁶ The diagnosis is made by eliciting a combination of symptoms from the patient, as well as some form of confirmatory physical findings, as it is well known that diagnosis of CRS based on symptoms alone has a high false-positive rate (**Table 3**).

In addition to characteristic symptoms, objective evidence of disease is required to establish the diagnosis. Potential findings on nasal endoscopy may include discolored drainage, nasal polyps, and mucosal edema or erythema in the middle meatus. Alternatively, if no abnormalities are found on examination, noncontrast computed tomography (CT) can be used to confirm the diagnosis if bony and/or mucosal changes are demonstrated. This method of diagnosis by using a combination of subjective and objective findings has increased in accuracy since its introduction, and is the current recommended method.^{28,29}

A few lessons on initial CRS diagnosis that can be gleaned from recent work are worthy of mention. Ideally an accurate history and physical examination would reliably predict the presence of CRS without the need for CT scan; however, AR and headache disorders can mimic many of the symptoms used for diagnosis. Amine and colleagues³⁰ have demonstrated that the more symptoms present, the more reliable the diagnosis, suggesting that in patients with many symptoms, objective confirmation with endoscopy or CT scan may not be absolutely required. Conversely, in patients

Table 1
Diagnostic subgroups of distinct types of rhinosinusitis and implicated inflammatory mediators

Classification	Subtypes	Inflammatory Categorization	Selected Inflammatory Mediators
Acute rhinosinusitis	Viral	T _H 1, neutrophilic	IL-1 β , -6, -8
	Nonviral		TNF- α
CRS without NP	Anatomic obstruction	T _H 1, neutrophilic	IL-1 β , -6, -8
	Bacterial Inflammatory without eosinophilia		IFN- γ , TNF- α , TGF- β , GM-CSF, ICAM-1, MPO, MMR, TLR, MUC 5AC/B/8
CRS with NP	AFS	T _H 2, eosinophilic	IL-5, -13
	AFS-like (without fungus)		IgE, TGF- β , MMP 7/9, MUC 1/4/8, VCAM-1, VEGF, GM-CSF,
	Eosinophilic CRS		eotaxin, RANTES, periostin, osteopontin, leukotrienes
	Gram-negative sinusitis with NP Aspirin-exacerbated respiratory disease		

Abbreviations: AFS, allergic fungal sinusitis; CRS, chronic rhinosinusitis; GM-CSF, granulocyte macrophage colony-stimulating factor; ICAM, intercellular adhesion molecule; IFN, interferon; IgE, immunoglobulin E; IL, interleukin; MMP, matrix metalloproteinase; MMR, macrophage mannose receptor; MPO, myeloperoxidase; MUC, mucin; NP, nasal polyps; RANTES, regulated and normal T-cell expressed and secreted; TGF, transforming growth factor; TLR, toll-like receptor; TNF, tumor necrosis factor; VCAM, vascular cell adhesion molecule; VEGF, vascular endothelial growth factor.

Adapted from Timperley D, Schlosser RJ, Harvey RJ. Chronic rhinosinusitis: an education and treatment model. *Otolaryngol Head Neck Surg* 2010;143 (5 Suppl 3):S3–8.

Table 2 Etiologic factors in CRS		
Environmental Factors	Local Host Factors	Systemic Host Factors
Smoking	Anatomic abnormality	Atopy
Pollution	Persistent local inflammation	Mucosal hyperreactivity
Allergens	Biofilms	Immune deficiency
Nonspecific particulate matter	Osteitis	Ciliary dysfunction
Microbes	Obstructing lesion	Cystic fibrosis
	Mucus character, innate immune function	Stress

Adapted from Kennedy DW, Ramakrishnan VR. Functional endoscopic sinus surgery: concepts, surgical indications, and techniques. In: Kennedy DW, Hwang PH, editors. Rhinology: diseases of the nose, sinuses and skull base. Thieme; 2012;306.

who have relatively few CRS symptoms and negative endoscopy, or in those whose primary complaint is headache, point-of-care CT scan frequently rules out CRS and eliminates the need for unnecessary empiric medical therapies, which are destined for failure and have associated costs and side effects.^{31,32}

CRS Subtypes

As a multifactorial, chronic, inflammatory condition, significant heterogeneity may exist within this diagnostic group. In general, CRS can be divided into disease without nasal polyps (CRSsNP) and with nasal polyps (CRSwNP) (see [Table 1](#)). Each of these groups can be subdivided into more specific groups depending on comorbid factors, such as the presence of allergy and/or asthma (or eosinophilic inflammatory features), presence of inflammatory reaction to fungal antigens, or presence of aspirin intolerance (AERD). These subtypes of CRS continue to evolve as our understanding of the pathophysiology expands, and they are important because they have the potential to direct specific treatment, provide prognostic information, and improve research study design. Using a clinical phenotype to classify CRS patients is clearly oversimplified and not optimal. The move toward defining the disease and categorizing patients based on molecular profile has begun and provides great hope for the development of improved treatment paradigms in the future.

Understanding these subtypes of CRS is also important when trying to understand the relationship between CRS and the lower airways. Of the various subtypes, it is CRSwNP (also known as chronic hyperplastic sinusitis with nasal polyps, or eosinophilic CRS) that is most closely related to lower airway disease. In CRSwNP there is

Table 3 Diagnostic criteria for CRS		
Major Symptoms	Minor Symptoms	Objective Evidence
Nasal congestion	Halitosis	Nasal endoscopy
Nasal obstruction	Fatigue	CT scan
Facial pain/pressure/fullness	Dental pain	
Purulent discharge	Cough	
Hyposmia/anosmia	Ear pressure	

The diagnosis is probable with two or more major symptoms, or one major and two or more minor symptoms.

often, but not always, tissue eosinophilia and frequently peripheral eosinophilia. Nearly half of these patients also have inhalant allergies, about half have asthma, and up to one-third may exhibit aspirin intolerance.^{26,28} Similar to the relationship between rhinitis and asthma, asthma and CRS coexist at a higher frequency than one would expect based on the prevalence of each condition alone (about 20% of patients with CRS have asthma, compared with 5–8% of the general population). In addition, patients with severe asthma are much more likely to have concomitant CRS.

AERD (Samter's triad) is a chronic inflammatory condition that consists of CRSwNP, asthma, and aspirin insensitivity, and serves as a dramatic model of how the upper and lower airways are related. These patients typically present in adulthood with progressive sinonasal symptoms and rapidly develop aspirin insensitivity and asthma that is severe in about 50% of cases. Histopathology of both the upper and lower airways in this disease shows mast cell activation, marked eosinophilia, epithelial disruption, and pro-inflammatory cytokine production.^{33–36} Treatment of this condition is targeted at both upper and lower airway inflammation. Basic medical treatment includes standard asthma care, oral and intranasal steroids, antihistamines, and nasal saline irrigations. Aspirin desensitization and antileukotriene therapy has also been shown to provide additional clinical benefit in this scenario. Endoscopic sinus surgery is frequently required as an adjunct to control the CRS and nasal polyposis, which frequently recur despite aggressive treatment.

Histopathologic studies show striking similarities in the cellular processes between CRS and asthma, including eosinophilic infiltration, lymphocytic infiltration, major basic protein deposition, basement membrane thickening, goblet cell hyperplasia, mucus hypersecretion, subepithelial edema, epithelial damage, and submucosal gland formation. There are a variety of cytokines and inflammatory mediators common to both disease processes, including IL-4, IL-5, IL-13, eotaxin, intercellular adhesion molecule 1, and vascular cell adhesion molecule 1. This similarity is even more apparent when comparing nonallergic CRSwNP with nonallergic, or intrinsic, asthma.^{33,35} Clinical studies have shown that among patients with asthma and CRS, the severity of the asthma tended to correlate with the severity of CRS based on CT-scan scores, lung function testing, eosinophil counts, and exhaled nitric oxide.^{37,38}

Coinfection of Upper and Lower Airways

Patients frequently relate the history during an acute exacerbation that symptoms began with a sinus infection and quickly progressed to bronchitis. Such reporting has led to the supposition that the sinus infection and postnasal drip physically passes through the glottis and trachea into the lower airways. Although this direct infection mechanism is possible in the absence of cough reflex, it is unlikely that the infection truly drips from the sinuses into the lungs. However, nuclear medicine studies have shown trace amounts of silent aspiration of nasopharyngeal secretions that occurs in nearly half of normal and diseased patients.^{39,40} Alternatively, lower airway symptoms may arise in a delayed fashion as a result of circulating systemic inflammatory mediators or from a common susceptibility to bacterial epithelial attachment and disease progression, given the histologic similarity of the upper and lower airway.

Bacterial and fungal cultures from the upper and lower airways have been most frequently studied in the cystic fibrosis population. Some studies have shown similar bacteria and even similar strains, whereas others have not found a correlation between the two sites.^{41–44} In CRS populations without concomitant pulmonary disease, there is no correlation between sinus and pulmonary fungal culture.⁴⁵ It is likely that direct infection of the lower airways is not a true result of bacteria "dripping"

from the sinuses, but that lower airway symptoms may result from coinfection or may be a reactive phenomenon to systemic or reflex neurogenic inflammation.

TREATMENT OF CRS

Further evidence for the linkage between CRS and asthma lies in the data showing the effect of treatment of CRS on asthma. Many studies have shown that medical and surgical treatment of CRS in patients with asthma results in improved asthma control in the form of improved symptom scores, improved pulmonary function tests, decreased use of asthma medications, and prolonged benefits lasting months to years^{46–49} (also noted in the pediatric population).^{50,51} However, the majority of these studies were not randomized or controlled.

Medical Management of CRS

Medical therapies are central to the management of CRS with and without nasal polyps. Although data are lacking for much of the pharmaceutical interventions, medical treatment of CRS often includes antibiotics, oral and intranasal steroids, nasal saline irrigations, and adjunctive treatments such as antihistamines and decongestants (Table 4). Newer targeted therapies, such as anti-IgE and anti-IL5 antibody therapy, is under study.

There is good evidence to support the use of topical corticosteroids in CRSwNP, particularly in the setting of eosinophilia. Regular use of intranasal steroids is known to decrease mucosal eosinophilia, reduce polyp size, and improve sinonasal symptoms.^{52–54} The most commonly used medications for CRSsNP include oral steroids and oral antibiotics. However, recent evidence-based reviews have shown that there is poor evidence for these therapies as “shotgun” therapies for CRS, and treatments are better selected based on patient-specific disease characteristics.^{55,56} Antileukotriene therapy is frequently used in patients with CRSwNP and lower airway disease, although well-designed studies are lacking. Improvements in smell, rhinorrhea, and nasal congestion were seen in patients with AERD receiving 16 weeks of zileuton when compared with controls.⁵⁷ Another study examined both zafirlukast (26 patients) and zileuton (10 patients) in the management of nasal polyposis,⁵⁸ reporting 72% subjective improvement and 50% objective improvement or stabilization of disease. Ragab and colleagues⁵⁹ looked at the use of montelukast as an add-on therapy to topical and inhaled corticosteroids in patients with asthma and nasal polyps, with and without AERD. These investigators found subjective and objective improvement

Table 4 Common medical therapies for CRS, and associated level of evidence		
Therapy	CRS Without NP	CRS with NP
Mucolytic	C	D
Saline rinse	C	D
Antibiotics	C	C
Topical steroid	A	A
Oral steroid	D	C
Decongestant	D	D
Immunotherapy	D	D
Proton-pump inhibitor	C	C

Data from Fokkens W, Lund V, Bachert C, et al. EAACI position paper on rhinosinusitis and nasal polyps executive summary. Allergy 2005;60:583–601.

in asthma and nasal polyps independent of AERD status. There appears to be a subgroup of patients with nasal polyps and asthma in whom leukotriene receptor antagonists are effective. Overall, antileukotriene medications seem to play a variable role in the management of select patients with nasal polyposis. For AERD patients, aspirin desensitization improves both short-term and long-term outcomes with regard to the sinuses and lower airway.^{60–63} Many mechanisms for its actions are hypothesized and are currently under study.

Surgical Management of CRS and Nasal Polyps

In patients with continued symptoms despite appropriate use of medical therapies, consideration should be given to surgical intervention. Endoscopic sinus surgery (ESS) may consist of simple polypectomy or progressively more thorough techniques such as functional endoscopic sinus surgery (FESS) or, rarely, nasalization (**Table 5**). The FESS technique stresses mucosal preservation and complete dissection of the involved sinuses, including removal of bony partitions and inflammatory foci, as well as identification and possible enlargement of sinus ostia.⁶⁴ FESS is the most widely used approach for general CRS and CRSwNP, and most current studies are performed using this technique. Although rare, potential complications must be considered and include epistaxis, orbital injury, and skull-base penetration.⁶⁵ Surgical goals include the removal of diseased tissue from the ethmoid cells, improving sinus ventilation, preserving or improving mucociliary clearance, and improving postoperative topical drug distribution within the sinuses.^{66–68}

Several surgical indications exist, and as has been learned, there are a wide variety of patients who fall under the diagnosis of CRS. In general, even when considering the range of patient subgroups, overall success rates for ESS have been reported to range from 85% to 97%.^{66,69,70} It has been suggested in the past that the presence of nasal polyps is predictive of worse surgical outcome and poor response to therapy. However, recent prospective data have demonstrated the benefits of ESS in patients with and without nasal polyps.^{59,71} Poetker and colleagues⁷² reported on the subjective and objective outcomes of 43 polyp and 76 nonpolyp patients undergoing ESS. In this study all patients, regardless of polyp status, had significant improvement in both subjective and objective parameters. Of note, patients with polyps showed a greater degree of improvement than patients without polyps, despite worse preoperative and postoperative CT and endoscopy scores.

Table 5
Endoscopic sinus surgery techniques

Polypectomy	Removal of nasal polyps, no surgical dissection of sinus tissues
Functional endoscopic sinus surgery	Mucosal preservation, removal of diseased sinus tissue and bone, consider enlargement of sinus ostia
Nasalization (radical spheenoethmoidectomy)	Middle turbinectomy, total ethmoidectomy with mucosal stripping
Minimally invasive surgical technique	Enlarging transition spaces without manipulation of ostia, minimal tissue removal
Balloon sinus surgery	Balloon catheter dilates transition spaces and ostia, no tissue removal

Before sinus surgery, patients with asthma should be asked about symptoms such as cough, wheezing, shortness of breath, and chest tightness. Their medication regimen should be reviewed. Frequent use of a rescue inhaler or oral steroid dose packs may indicate that the asthma is not well controlled and warrants further discussion among the treatment team, including the asthma/pulmonary specialist, otolaryngologist, and anesthesiologist, before proceeding with surgery. Obviously it is ideal to have asthma optimally controlled before surgery to minimize the risk of an anesthetic pulmonary complication. Preoperative treatment with oral steroids is often used to mitigate some of these risks by decreasing airway hyperreactivity. Postoperatively these patients also require extra consideration, as the upper airway has just been manipulated with surgery and could potentially exacerbate lower airway inflammation. It is helpful to minimize nasal packing as much as possible to maximize nasal respiration and the associated humidification. Postoperative oral steroids are also helpful in controlling both upper and lower airway inflammation. Finally, consideration should be given to overnight observation in an inpatient setting if there is concern for lower airway obstruction perioperatively.

SPECIFIC OUTCOMES MEASUREMENTS FOR SURGERY IN CRS

Symptoms

Only recently have several validated, rhinology-specific, patient-based quality-of-life measurements come into common use. Coincidentally, improvements in surgical technique have been credited with enhanced outcomes. Many older studies are now considered outdated, as they used irregular and/or poorly supported methodologies for measurements of disease severity and outcomes after intervention, as well as less refined surgical techniques.⁷³ Many of these studies used inconsistent and subjective outcomes, such as time to recurrence of disease or time to revision surgery.

CRS patients refractory to medical therapies seek improvements in several symptoms, namely nasal congestion, fatigue, headache, decreased sense of smell, and nasal drainage. In a prospective study of medical management for CRS, gains were demonstrated in all domains except headache.⁷⁴ In a separate study, visual analog symptom scores improved after surgery in all symptoms except headache, and had lasting improvements to the study end point of 18 months.⁷⁵ A multi-institutional prospective study was performed comparing the results of continued medical therapy versus surgery in CRS patients who failed initial medical management.⁷⁶ In this landmark study, a total of 115 patients were followed to the 12-month end point (50 patients in the medical management arm and 65 patients in the surgery arm). During the study period, 17 patients elected to cross over from the medical cohort to the surgical cohort, owing to continued symptom severity. All 3 cohorts showed symptom improvement at 12 months, but interestingly greater improvements were noted in the surgery and cross-over groups. This study not only found significantly better symptom control but also documented less medication usage and fewer missed work/school days in the group who underwent surgery.

Sense of smell has not been extensively studied in all patient groups. In a prospective study of CRS patients undergoing FESS, the Smell Identification Test was performed preoperatively, and at 6 and 12 months postoperatively.⁷⁷ The investigators found that patients with severe olfactory dysfunction had significant improvements with surgery, whereas those with milder dysfunction did not. Patients with nasal polyps, asthma, and/or aspirin sensitivity were more likely to be anosmic preoperatively. Of note, anosmic patients with nasal polyps had significant improvements in smell after surgery, whereas anosmic nonpolyp patients did not. In a recent study

using the Sniffin' Sticks smell test on polyp patients who underwent FESS, the presence of AERD was found to significantly limit olfactory restoration in comparison with aspirin-tolerant patients.⁷⁸ At this point, it is difficult to predict the restoration of sense of smell with sinus surgery, but this is certainly an area of interest and ongoing research.

Objective Outcomes

It is important to examine objective measurements of disease in addition to subjective quality-of-life measurements, as the two may not always correlate. Objective measurements of disease include CT staging systems and nasal endoscopy scoring systems. When comparing CRSwNP and CRSsNP populations, polyp patients, not surprisingly, have worse disease preoperatively on both CT and nasal endoscopy scoring.⁷² Both populations made significant improvements in CT and endoscopy after surgery; polyp patients improved more in the endoscopic score, but still remained worse than those without polyps owing to their worse starting point. When specifically comparing AERD polyp patients to aspirin-tolerant polyp patients, AERD patients generally had significantly worse preoperative CT and nasal endoscopy scores.⁷⁹ However, after ESS there was no difference between the two groups in their degree of improvement on nasal endoscopy at a mean follow-up of 18 months, suggesting that significant benefits can be obtained in AERD patients with surgery.

Effects on Asthma

Several studies have demonstrated the benefits of ESS on lower airway disease in patients with CRS and asthma.^{80–82} The mechanism of this improvement is incompletely defined, but may be related to decreased systemic proinflammatory mediators, such as leukotriene E4.⁸³ Several retrospective analyses of polyp patients undergoing ESS have compared aspirin-sensitive with aspirin-tolerant patients, and have found ESS to improve sinus and asthma symptoms, improve nasal endoscopy scores, improve FEV1, and decrease the use of inhaled corticosteroids in both groups.^{71,84,85} This issue has been of particular interest in patients with AERD, especially in terms of the durability of benefit. Long-term asthma outcomes were assessed by surveying 65 patients with AERD who underwent ESS, with a mean 10-year follow-up.⁸⁶ Out of 34 respondents, 29 (94%) patients with asthma preoperatively noticed a subjective asthma improvement at least 1 year postoperatively. Improvements were also noted in the use of oral and inhaled steroids, frequency of asthma attacks, frequency of physician visits for asthma-related concerns, and hospitalizations for asthma exacerbations.

SUMMARY

A clear link exists between the upper and lower airways, based on anatomy, pathophysiology, epidemiology, and disease severity. Medical therapies directed at the management of AR and CRS can be effective for both upper and lower airway symptoms. In addition, overall quality of life can be improved by concomitant management of both sites of disease. There is now strong evidence to support the value of surgery in CRS patients for sinonasal symptoms, but there are also several lower-level studies suggesting that ESS may benefit lower airway disease in a subset of patients. This finding does not imply that medical therapies should not be entertained, but rather that surgery can be considered an adjunct to medical therapies in refractory patients and that well-designed larger-scale studies should be performed in this patient population.

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