HHS Public Access

Author manuscript

Allergy. Author manuscript; available in PMC 2018 March 01.

Published in final edited form as:

Allergy. 2017 March ; 72(3): 483–491. doi:10.1111/all.13048.

Asthma quality of life and control after sinus surgery in patients with chronic rhinosinusitis

Rodney J. Schlosser, MD[1], **Timothy L. Smith, MD, MPH**[2], **Jess Mace, MPH**[2], and **Zachary M. Soler, MD, MSc**[1]

[1]Department of Otolaryngology – Head and Neck Surgery, Medical University of South Carolina, Charleston, SC

[2]Department of Otolaryngology – Head and Neck Surgery, Oregon Health Sciences University, Portland, Oregon

Abstract

Background—Patients with chronic rhinosinusitis (CRS) often have comorbid asthma. Prior studies have not examined the impact of CRS or endoscopic sinus surgery (ESS) upon asthma quality-of-life (QOL) and asthma control using validated outcome metrics.

Methods—Patients with CRS, both with and without polyps, and comorbid asthma completed the Mini-Asthma QOL Questionnaire (miniAQLQ) and Asthma Control Test (ACT) at baseline and 6 months postoperatively as part of a multi-institutional, prospective study.

Results—Baseline metrics were available on 86 patients. Patients undergoing ESS reported improved miniAQLQ (0.5 [SD±1.1], 95%CI: 0.2–0.7; p=0.002) and ACT scores (1.3 [±4.1], 95%CI: 0.2–2.4; p=0.025). Uncontrolled baseline asthma (ACT<20) was present in 51% of patients undergoing ESS. In uncontrolled patients, ESS resulted in a minimal clinically important difference 57% of the time for miniAQLQ scores (≥0.5 points) and 50% of the time for ACT scores (≥3.0 points). After adjustment with linear regression, baseline miniAQLQ scores were worse in patients with comorbid allergy (p=0.045) and chronic obstructive pulmonary disease (COPD; p=0.015). Adjusted baseline ACT scores were worse in patients with COPD (p=0.004). Covariates associated with changes in miniAQLQ scores after ESS were preoperative corticosteroid dependency (p=0.011) and change in total SNOT-22 score (p=0.010). Covariate associated with significantly less improvement in ACT scores was obstructive sleep apnea (p=0.016).

Conclusions—Patients with CRS often present with uncontrolled asthma, and ESS improves both miniAQLQ and ACT. Approximately half of patients with uncontrolled asthma improve after ESS, yet there are few CRS-specific factors associated with asthma QOL or control or ESS outcomes.

Contact author: Rodney J. Schlosser, MD 135 Rutledge Ave, MSC550, Charleston, SC 29425. Fax 843-792-0546, schlossr@musc.edu.

Statement of contribution: All authors contributed to study design and concept, statistical analysis and writing/review of manuscript.

Keywords

asthma; chronic rhinosinusitis; endoscopic sinus surgery; quality of life

INTRODUCTION

The co-existence of asthma in patients with chronic rhinosinusitis (CRS) is well known (1). The current treatment paradigm for CRS is to treat patients with maximal medical therapy, but unfortunately, in some patients this fails to control CRS symptoms. Thus a common clinical question which arises is whether CRS-specific treatment, particularly sinus surgery, will also result in improved outcomes for comorbid asthma. Two recent meta-analyses have been performed examining asthma outcomes after endoscopic sinus surgery (ESS). While they demonstrate improvement in asthma symptoms, they emphasize that the current literature suffers from small numbers, retrospective study design, significant heterogeneity in patient populations and non-validated, asthma-specific outcome metrics(2, 3).

While it has been commonly reported that asthma is more prevalent in patients with nasal polyps and atopy(4), factors which are associated with the *severity* of asthma-specific quality of life (QOL) and asthma control in patients with CRS are largely unknown. Additionally, it is unknown if there are preoperative factors that can aid clinicians in identifying patients most likely to experience improvement in asthma QOL or asthma control after ESS.

The primary aim of our study was to prospectively study patients with CRS and co-morbid asthma to examine validated, asthma-specific outcomes after ESS. Our secondary aims were to determine preoperative factors predictive of the severity of baseline asthma QOL and control, as well as factors predictive of asthma-specific outcomes after ESS.

MATERIALS and METHODS

Patient Population and Study Inclusion Criteria

Adult patients (>18 years of age) were recruited into a prospective, multi-center, observational cohort study to evaluate treatment outcomes for CRS. The Institutional Review Board (IRB) at each enrollment center governed study protocols and annual safety monitoring. Previous outcome findings from this cohort have been reported(5, 6). Enrollment centers consisted of sinus surgical centers located within academic hospitals in North America including: Oregon Health & Science University (OHSU; Portland, OR), Stanford University (Palo Alto, CA), the Medical University of South Carolina (Charleston, SC), and the University of Calgary (Calgary, Alberta, Canada). Patients were asked to provide a comprehensive assessment of medical comorbidity and social history during baseline interview and enrollment meetings. Study participants with CRS were included if diagnosed with current comorbid asthma as indicated by either physician diagnosis and active therapeutic treatment or prior lung function study.

All participants were diagnosed with medically recalcitrant CRS as defined by the American Academy of Otolaryngology-Head and Neck Surgery (7, 8) and European Position Paper

2012 (9). All patients reported continuing “cardinal symptoms” associated with CRS. Study participants completed initial trials of medical therapy including: at least one course of either topical corticosteroids (≥21-days) or a 5-day course of oral corticosteroids, and at least one course (≥14-days) of culture-directed or broad spectrum antibiotics per the standard of care. Participants voluntarily selected endoscopic sinus surgery (ESS) as treatment for improved mitigation of symptoms. Postoperative therapeutics included daily nasal saline irrigations and appropriate continued medical therapy, as needed, for targeted symptom resolution and optimal postoperative healing.

Exclusion criteria

Participants were excluded from the final analysis if they failed to complete study-related evaluations correctly, without errors or omissions, and were considered lost to follow-up if they did not complete follow-up evaluations at least 6 months after initial baseline evaluations. Additional exclusions included study participants with any variant of comorbid ciliary dyskinesia or cystic fibrosis.

Evaluations of Asthma Severity

Considered the main outcomes of interest, two complementary, patient-based outcome tools were utilized to identify the severity of comorbid asthma in this patient population: the Mini Asthma Quality of Life Questionnaire (miniAQLQ) and the Asthma Control Test (ACT). The miniAQLQ is a validated 15 item self-administered survey used to describe both the symptom severity and limitation as a result of asthma during the preceding 2-week period, using summarized Likert response scales (range: 1–7) (10). The miniAQLQ consists of four domains including: symptoms (5 items), activity (4 items), emotional function (3 items), and environmental stimuli (3 items). Higher total scores on the miniAQLQ and its domains are reflective of better quality of life and less asthma-related impairment. Score change of at least 0.50 points has been previously defined as minimal clinically important difference (MCID).

The second asthma-specific outcome was the ACT, a validated, self-administered survey tool used to assess a patients’ perception of disease control over the preceding 4-week period using Likert scale responses (range: 0–5) (11). The ACT consists of 5 items regarding the frequency of asthma related symptoms, the need for rescue medications, and perceived control of disease. Higher total scores (range: 0–25) indicate better levels of asthma control, however scores less than 20 reflect uncontrolled asthma at the time of completion. Score change of at least 3 points has been previously defined as MCID.

CRS-specific Quality of Life Evaluation

Disease-specific quality of life was evaluated using the 22 item SinoNasal Outcome Test (SNOT-22), a validated instrument developed to quantify symptom severity associated with sinonasal conditions (©2006, Washington University, St. Louis, MO)(12). Item scores are categorized using patient selected Likert scale responses (item score range: 0–5) where higher scores indicate worse symptom severity.

Clinical Measures of CRS

Per the standard of care, high resolution computed tomography (CT) without contrast was used to assess sinonasal disease severity using 1mm. contiguous images in the axial plane. Bilateral image staging was completed by each enrolling physician in accordance with the Lund-Mackay scoring system (range: 0–24) which estimates opacification severity in the maxillary, ethmoidal, sphenoidal, ostiomeatal complex, and frontal sinus regions (13).

Sinonasal regions were also evaluated using rigid, fiber-optic endoscopes (Karl Storz, Tuttlingen, Germany). Bilateral endoscopic examinations were staged by each enrolling physician using the Lund-Kennedy scoring system (range: 0–20) which estimates pathologic characteristics within the paranasal sinuses including the severity of nasal polyposis, discharge, edema, scarring, and crusting (13). Higher total scores on both staging systems represent worse overall disease severity.

Data Management and Statistical Analyses

Protected health information was removed and study data was safeguarded using unique study identification number assignment for each participant. Study data was securely transferred to OHSU from each performance site for manual entry into a HIPAA compliant, relational database (Access, Microsoft Corp, Redmond, WA). All statistical analyses were completed using commercially available software (SPSS version 22.0, IBM Corporation, Armonk, NY). Study data was evaluated descriptively (means, standard deviations, ranges, and prevalence) while assumptions of distribution normality were verified for all ordinal and continuous measures. Postoperative asthma-specific outcome scores were operationalized using last available response and postoperative change scores were calculated by subtracting preoperative scores from last postoperative scores.

Matched pairing t-test statistics and Wilcoxon signed rank test to evaluate within-subjects improvement over time across asthma-specific and CRS-specific QOL scores. Independent t-testing or Mann Whitney U testing was used to compare improvement between discrete subgroups and two-tailed Spearman’s rank correlation coefficients (Rs) were used to evaluate the magnitude of associations between continuous independent variables and postoperative changes in asthma-specific outcome measures.

Basic, stepwise, linear regression was used to identify significant cofactors associated with preoperative patient-reported asthma severity, as measured by the miniAQLQ and ACT total scores. Following univariate screening of potential cofactors ($p<0.250$), final models were constructed using manual forward selection ($p<0.100$) and backwards elimination ($p<0.050$). Coefficient of multiple determination (R^2) to evaluate goodness of model fit and the proportion of total variation in the dependent variable explained by model cofactors. Multi-collinearity between significant cofactors was evaluated with variance inflation factors (VIFs) and final model diagnostics were performed to confirm assumptions of error normality and independence using residual and normal probability (“quantile-quantile” plots). Regression effect estimates (β), standard errors, 95% confidence intervals, and estimates of type-I error (p-values) are reported, where appropriate, for all results.

RESULTS

Baseline Study Population

A total of 86 study participants with CRS and comorbid asthma met inclusion criteria, completed baseline asthma severity evaluations, and were prospectively enrolled between October 2012 and June 2015. Overall demographics, prevalence of treatment modality, comorbid disease characteristics, evaluations of asthma severity, and CRS-specific disease severity measures are described for all study participants in Table 1. The mean miniAQLQ was 4.6 ± 1.4 and the mean ACT was 18.4 ± 5.3, with 51% reporting uncontrolled asthma (ACT<20).

Postoperative Changes in Asthma and CRS Outcomes

Postoperative asthma outcomes using the miniAQLQ were available on 61 of 86 (71%) patients undergoing ESS for an average of 13.7 [± 5.1] months (range: 4–25 months). There were no significant differences in baseline miniAQLQ (4.6 ± 1.3 vs. 4.5 ± 1.5; p=0.795) or ACT scores (18.5 ± 4.9 vs. 18.0 ± 6.0; p=0.711) between subjects who followed up and those lost to follow up. Average within-subjects post-surgical improvements were reported in miniAQLQ scores (mean change: 0.5 ± 1.1, p=0.002) and ACT scores (mean change: 1.3 ± 4.1, p=0.025, Table 2). When examining the prevalence of patients reporting at least one MCID for the miniAQLQ and ACT total scores, a total of 27/61 (44%) of study participants reported postoperative improvement of at least 0.5 units on the miniAQLQ, while 16/52 (31%) reported improvement of at least 3.0 units on ACT total scores.

Patients with preoperative uncontrolled asthma as defined by preoperative ACT total scores (< 20), had even greater improvements in both miniAQLQ scores (mean change: 0.7 ± 1.3, p=0.004) and ACT scores (mean change: 2.9 ± 4.4, p=0.002, Table 2). The prevalence of uncontrolled comorbid asthma, as evaluated by the ACT, decreased from 51% to 32% after ESS (p=0.004). When examining CRS patients with preoperative uncontrolled asthma, a total of 57% of patients reported an MCID on miniAQLQ total scores while 50% reported an MCID on ACT total scores.

CRS-specific outcomes also significantly improved, with a mean change in SNOT-22 total score of 33.8 ± 22.8 (p<0.001).

Predictors of Baseline Asthma Severity

Given that both asthma-specific outcomes improved after ESS, we further sought to determine factors which would aid clinicians in predicting both baseline asthma severity, as well as asthma-specific improvement after ESS. Average baseline miniAQLQ and ACT total scores were evaluated across patient cofactors to assess the associations between those cofactors and the asthma-related outcome measures of interest. Without multivariate adjustment, independent subgroups with comorbid allergy and COPD reported significantly worse miniAQLQ total scores compared to subjects without those comorbidities. Also, subgroups of participants with comorbid COPD reported significantly worse asthma control as measured by average ACT total scores at baseline, compared to subjects without.

Significant, but weak correlations were also found between total scores of the SNOT-22 and CT score and both the miniAQLQ and ACT survey responses (Rs≤ −0.246; p≤0.031).

After manual control and adjustment for enrollment site variation, simple linear regression was able to identify statistically significant clinical factors associated with both worse miniAQLQ (Table 3) and ACT (Table 4) total scores at baseline. COPD was associated with both asthma PROMs and allergy was associated with miniAQLQ. No other CRS-specific factors, including SNOT-22 or CT score, were associated with asthma PROMs. No evidence of multi-collinearity was found between any final model cofactors (VIFs < 2.0) and while residual and normal probability plotting suggested normal error distribution for both final models.

Predictors of postoperative improvement in comorbid asthma severity

Baseline cofactors, as well as measures of disease-specific QOL and asthma severity were compared between participants with and without post-surgical follow-up. Study participants who voluntarily provided study follow-up were found to be significantly older, on average, compared to participants who did not return for study follow-up (49.4[±15.9] vs. 41.6[±13.4] years; p=0.035). Study participants were similar in regards to all other study cofactors, disease-specific QOL scores, and measures of baseline asthma severity on average (all p≥0.082).

Average postoperative differences in miniAQLQ (n=61) and ACT total scores (n=52) were evaluated across other patient cofactors to assess differences between independent cofactors and the primary outcomes of interest and to identify potential significant predictors of asthma-related QOL improvement following sinus surgery (Tables 5–6). Multivariate adjustment was not performed due to the limited numbers of patients and the large numbers of cofactors, however without multivariate adjustment, subgroups of study participants with corticosteroid dependent conditions reported significant post-treatment worsening on miniAQLQ total scores compared to subjects not using regular corticosteroid therapies. Improvement in miniAQLQ scores was associated with improvement in total SNOT-22 scores after ESS. Also without multivariate adjustments, subgroups of participants with obstructive sleep apnea reported significant postoperative worsening in asthma control as measured by ACT total scores compared to subjects without. Not unexpectedly, patients with uncontrolled asthma at baseline received the greatest benefit in both miniAQLQ scores, as well as ACT scores, after ESS.

DISCUSSION

Our study demonstrated that patients with pre-existing asthma and CRS experience improved asthma-specific QOL and asthma control after ESS. This supports the findings of recent meta-analyses that ESS improves asthma symptoms(2, 3), but we have now demonstrated this in a prospective fashion with validated asthma-specific outcome metrics. When comparing our outcomes to prior reports, it is important to note the apparent differences in severity of asthma in various publications. Our baseline cohort had fairly severe asthma, with 19% steroid dependency (n=10 for asthma, n=5 for CRS and n=1 for vocal cord dysfunction) and was not limited by polyp status or aspirin sensitivity. Fifty-one

percent of our patients had uncontrolled asthma with ACT scores < 20 and 19% had aspirin exacerbated respiratory disease. As shown in Table 2, this uncontrolled group demonstrated greater improvements after ESS in every domain of the miniAQLQ, as well as the ACT, when compared to the overall group. This is not unexpected, as patients with well controlled asthma have less room for reportable improvement than those with uncontrolled asthma (i.e. a ceiling effect). Additionally, it is possible that our findings are a demonstration of regression to the mean, as asthma is a dynamic disease and a significant number of patients with uncontrolled asthma at baseline may have improved independent of surgery. Future studies with observational and/or medically treated arms for comparison will be useful.

Chen et al (14), previously examined ACT outcomes after ESS. They demonstrated improvement in ACT categorization of asthma control, but failed to show improvement in mean postoperative ACT scores. In their study cohort, only 11% of patients had poorly controlled asthma preoperatively, compared to 51% of our patients. Additionally, their mean preoperative ACT score was 22.1 out of a maximum possible score of 25, compared to 18.4 in our study, further demonstrating poorer preoperative asthma control in our patient cohort. Given the relatively well controlled baseline asthma in the Chen study, it is not surprising that there was little room for additional improvement after ESS. While absolute changes in QOL and control metrics are important, likelihood of achieving an MCID is also important for preoperative counseling. Approximately half of our patients with uncontrolled baseline asthma achieved an MCID in both mini AQLQ and ACT.

Other studies have examined asthma symptoms after ESS using non-validated metrics. Ehnhage studied CRS with nasal polyp (CRSwNP) patients who were not steroid dependent and found improvements in asthma symptoms and pulmonary function tests (PFTs)(15, 16). Batra examined one of the most severe cohorts limited to steroid dependent asthmatics with CRSwNP and reported improved PFTs and steroid dependency(17). While these studies did not report validated asthma QOL or control instruments, in general they support our findings.

Having found that asthma outcomes improve after ESS, one of our secondary goals was to seek preoperative factors that could aid clinicians in identifying the severity of baseline asthma QOL and control. COPD was associated with both baseline mini AQLQ and ACT scores and allergies were associated with mini AQLQ scores. This is not surprising given the likely impact of these additional co-morbidities upon patient reported outcome measures assessing QOL and control of a pulmonary condition. Initial bivariate analysis suggested sinus CT score and baseline SNOT-22 may be associated but these variables become non-significant in the regression modeling. Thus, despite previous reports regarding the increased *prevalence* of asthma patients with nasal polyps or atopy(1), we were only able to identify an association between atopy and asthma *severity* as assessed by mini AQLQ scores. Polyp status did not correlate with any metrics of asthma severity. One prior study by Lin et al. (18) did look at asthma severity, but rather than using mini AQLQ or ACT, they classified asthma severity into 2 groups (intermittent/mild vs moderate/severe) using National Institutes of Health clinical guidelines based upon frequency and severity of symptoms. They studied patients presenting with CRS and nearly 75% did not have any asthma. Of the 47 patients with asthma, 38% were clinically classified with moderate/severe asthma. They

found that as asthma severity increased, the prevalence of allergies, polyps and CT score increased. The strength of their study was clinical classification by asthma specialists, but it is not known if this clinical classification correlates with the validated miniAQLQ or ACT in this patient population. Additionally, it is unknown if these associations would still be present if they had limited their study to patients with pre-existing asthma as we did or if their findings were driven by the large numbers of non-asthmatic patients in the study.

In addition to looking for factors associated with baseline asthma severity, we examined preoperative factors that could potentially aid clinicians in predicting asthma-specific outcomes after ESS. As shown in Tables 5 and 6, the only variables that were associated with improved asthma outcomes after ESS were lack of corticosteroid dependency, postoperative change in total SNOT-22 (miniAQLQ) and lack of obstructive sleep apnea (ACT). The impact of steroid dependence and OSA is not surprising given the severity of those associated co-morbidities. The correlation between improvements in SNOT-22 and miniAQLQ could be interpreted in a couple of ways. It could be that improvements in upper airway symptoms truly drive improvements in the lower airway. Alternatively, both instruments contain overlapping systemic domains, including sleep and psychological aspects, thus improvements in systemic domains after ESS would be reflected in improved miniAQLQ scores as well as total SNOT-22 scores. Further study into which subdomains are driving these associations remains an area for further research. Due to limited numbers, we were unable to perform regression models for postoperative outcomes. While there were no novel factors predictive of asthma outcomes after ESS, this indicates similar benefit across all groups, including those with atopy, AERD and polyposis.

One weakness of our study is lack of medication usage specifically for asthma. Prior meta-analyses of asthma outcomes after ESS found that hospitalizations and medication usage decreased(2, 3). In many cases, it may be difficult to separate the indications for medication usage, such as systemic steroids, as patients are often placed on these medications for both sinus and asthma symptoms. One advantage in our use of the ACT was that it contains a question specifically inquiring about use of rescue inhalers, thus demonstrating some benefit in asthma-specific medications. However it is possible that patients on oral steroids used fewer rescue inhalers, artificially improving their ACT and miniAQLQ scores. These medications are also prescribed by a variety of healthcare providers, including primary care physicians, otolaryngologists and asthma/allergy specialists, making precise indications for their use difficult to ascertain. Additionally, our study lacked PFTs. Prior meta-analyses report that PFTs typically do not change after ESS(2, 3). Combining our resulting using validated asthma QOL and control instruments, with other outcomes, including PFTs, hospitalizations and asthma-specific medication usage remains an interesting area for future research. Our study also relied upon prior physician diagnosis of asthma, rather than confirming this diagnosis with PFTs and bronchodilator response, thus some patients may have been misdiagnosed. Finally, the results of our study should be limited to similar populations – patients presenting with symptomatic CRS that has failed appropriate medical therapy and have co-morbid asthma. Asthma-specific outcomes in other populations, such as CRS patients who are asymptomatic or who have not undergone medical therapy for CRS, are unknown.

Our findings that ESS improves asthma-specific outcomes parallel that of many studies of ESS for CRS-specific outcomes(6, 19, 20). It is consistently reported that ESS improves CRS-specific QOL, yet these PROMs correlate weakly, if at all, with objective CRS-specific clinical metrics, including CT, endoscopy, polyp status or atopy, and physicians are still left with few prognostic factors to aid in guiding treatment decisions. Our study now confirms that surgical treatment of symptomatic CRS does improve asthma-specific outcomes, yet factors which predict severity of QOL and provide prognostic information regarding treatment outcomes remain unknown. Studies using cluster analysis for novel classification and prognostication have been performed, both in CRS and asthma(6, 21). It appears that some clinical factors provide prognostic information in these diseases. Future studies combining refined clinical categorization of both upper and lower airway disease with enhanced endotyping will likely improve our ability to provide individualized medicine for patients with co-morbid respiratory tract disease.

Recent studies have reported that early ESS for symptomatic CRS may decrease the development of asthma(22–24). Our study population was limited to patients with pre-existing asthma, so unfortunately we are unable to determine the relationship between the timing of ESS, duration of pre-existing asthma, its severity or the impact upon ESS outcomes, but this remains an interesting area for further studies.

CONCLUSION

Patients presenting with CRS refractory to medical therapy and co-existent asthma who undergo ESS experience improvement in asthma QOL and control. This benefit is most evident in patients with uncontrolled preoperative asthma. Further correlation to pulmonary function tests, medication usage and healthcare utilization are needed.

Acknowledgments

Dr. T. L. Smith, Dr. Z. M. Soler, and J. C. Mace are supported by a grant from the National Institutes of Health (NIH; R01 DC005805). The NIH had no role in the preparation, review, or approval of this article or decision to submit it for publication. Dr. Z. M. Soler and J. C. Mace received grant support from the NIH/NIDCD. Dr. R. J. Schlosser is consultant for Olympus, Medtronic, and Arrinex; and received grant support from Intersect ENT and Entellus. Dr. Z. M. Soler is consultant for Olympus; and received grant support from Intersect ENT and Entellus. The authors have no other funding, financial relationships, or conflicts of interest to disclose.

References

1. Bachert C, Claeys SE, Tomassen P, van Zele T, Zhang N. Rhinosinusitis and asthma: a link for asthma severity. Current allergy and asthma reports. 2010; 10(3):194–201. Epub 2010/04/29. DOI: 10.1007/s11882-010-0096-0 [PubMed: 20424997]
2. Vashishta R, Soler ZM, Nguyen SA, Schlosser RJ. A systematic review and meta-analysis of asthma outcomes following endoscopic sinus surgery for chronic rhinosinusitis. International forum of allergy & rhinology. 2013; 3(10):788–94. Epub 2013/07/03. DOI: 10.1002/alr.21182 [PubMed: 23818462]
3. Rix I, Hakansson K, Larsen CG, Frendo M, von Buchwald C. Management of chronic rhinosinusitis with nasal polyps and coexisting asthma: A systematic review. Am J Rhinol Allergy. 2015; 29(3): 193–201. Epub 2015/05/16. DOI: 10.2500/ajra.2015.29.4178 [PubMed: 25975250]
4. Jarvis D, Newson R, Lotvall J, Hastan D, Tomassen P, Keil T, et al. Asthma in adults and its association with chronic rhinosinusitis: the GA2LEN survey in Europe. Allergy. 2012; 67(1):91–8. Epub 2011/11/05. DOI: 10.1111/j.1398-9995.2011.02709.x [PubMed: 22050239]

5. Schlosser RJ, Storck K, Smith TL, Mace JC, Rudmik L, Shahangian A, et al. Impact of postoperative endoscopy upon clinical outcomes after endoscopic sinus surgery. International forum of allergy & rhinology. 2016; 6(2):115–23. Epub 2015/10/16. DOI: 10.1002/alr.21651 [PubMed: 26458330]
6. Soler ZM, Hyer JM, Rudmik L, Ramakrishnan V, Smith TL, Schlosser RJ. Cluster analysis and prediction of treatment outcomes for chronic rhinosinusitis. The Journal of allergy and clinical immunology. 2016; Epub 2016/01/26. doi: 10.1016/j.jaci.2015.11.019
7. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015; 152(2 Suppl):S1–S39. Epub 2015/04/04. DOI: 10.1177/0194599815572097
8. Rosenfeld RM, Andes D, Bhattacharyya N, Cheung D, Eisenberg S, Ganiats TG, et al. Clinical practice guideline: adult sinusitis. Otolaryngol Head Neck Surg. 2007; 137(3 Suppl):S1–31. Epub 2007/09/28. DOI: 10.1016/j.otohns.2007.06.726 [PubMed: 17761281]
9. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. Rhinology Supplement. 2012; (23):3. preceding table of contents, 1–298. Epub 2012/07/07. [PubMed: 22764607]
10. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. Eur Respir J. 1999; 14(1):32–8. Epub 1999/09/18. [PubMed: 10489826]
11. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. The Journal of allergy and clinical immunology. 2004; 113(1):59–65. Epub 2004/01/10. DOI: 10.1016/j.jaci.2003.09.008 [PubMed: 14713908]
12. DeConde AS, Bodner TE, Mace JC, Smith TL. Response shift in quality of life after endoscopic sinus surgery for chronic rhinosinusitis. JAMA otolaryngology-- head & neck surgery. 2014; 140(8):712–9. Epub 2014/07/31. DOI: 10.1001/jamaoto.2014.1045 [PubMed: 25074504]
13. Orlandi RR, Kingdom TT, Hwang PH, Smith TL, Alt JA, Baroody FM, et al. International Consensus Statement on Allergy and Rhinology: Rhinosinusitis. International forum of allergy & rhinology. 2016; 6(Suppl 1):S22–209. Epub 2016/02/20. DOI: 10.1002/alr.21695 [PubMed: 26889651]
14. Chen FH, Zuo KJ, Guo YB, Li ZP, Xu G, Xu R, et al. Long-term results of endoscopic sinus surgery-oriented treatment for chronic rhinosinusitis with asthma. Laryngoscope. 2014; 124(1): 24–8. Epub 2013/05/21. DOI: 10.1002/lary.24196 [PubMed: 23686815]
15. Ehnhage A, Olsson P, Kolbeck KG, Skedinger M, Stjarne P. One year after endoscopic sinus surgery in polyposis: asthma, olfaction, and quality-of-life outcomes. Otolaryngol Head Neck Surg. 2012; 146(5):834–41. Epub 2012/01/31. DOI: 10.1177/0194599811435638 [PubMed: 22287580]
16. Ehnhage A, Olsson P, Kolbeck KG, Skedinger M, Dahlen B, Alenius M, et al. Functional endoscopic sinus surgery improved asthma symptoms as well as PEFR and olfaction in patients with nasal polyposis. Allergy. 2009; 64(5):762–9. Epub 2009/02/05. DOI: 10.1111/j.1398-9995.2008.01870.x [PubMed: 19191775]
17. Batra PS, Kern RC, Tripathi A, Conley DB, Ditto AM, Haines GK 3rd, et al. Outcome analysis of endoscopic sinus surgery in patients with nasal polyps and asthma. Laryngoscope. 2003; 113(10): 1703–6. Epub 2003/10/02. [PubMed: 14520093]
18. Lin DC, Chandra RK, Tan BK, Zirkle W, Conley DB, Grammer LC, et al. Association between severity of asthma and degree of chronic rhinosinusitis. Am J Rhinol Allergy. 2011; 25(4):205–8. Epub 2011/08/09. DOI: 10.2500/ajra.2011.25.3613 [PubMed: 21819754]
19. Smith TL, Kern R, Palmer JN, Schlosser R, Chandra RK, Chiu AG, et al. Medical therapy vs surgery for chronic rhinosinusitis: a prospective, multi-institutional study with 1-year follow-up. International forum of allergy & rhinology. 2013; 3(1):4–9. Epub 2012/06/28. DOI: 10.1002/alr.21065 [PubMed: 22736422]
20. Smith TL, Batra PS, Seiden AM, Hannley M. Evidence supporting endoscopic sinus surgery in the management of adult chronic rhinosinusitis: a systematic review. Am J Rhinol. 2005; 19(6):537–43. Epub 2006/01/13. [PubMed: 16402637]

21. Schatz M, Hsu JW, Zeiger RS, Chen W, Dorenbaum A, Chipps BE, et al. Phenotypes determined by cluster analysis in severe or difficult-to-treat asthma. The Journal of allergy and clinical immunology. 2014; 133(6):1549–56. Epub 2013/12/10. DOI: 10.1016/j.jaci.2013.10.006 [PubMed: 24315502]

22. Benninger MS, Sindwani R, Holy CE, Hopkins C. Impact of medically recalcitrant chronic rhinosinusitis on incidence of asthma. International forum of allergy & rhinology. 2016; 6(2):124–9. Epub 2015/12/02. DOI: 10.1002/alr.21652 [PubMed: 26624856]

23. Hopkins C, Rimmer J, Lund VJ. Does time to endoscopic sinus surgery impact outcomes in Chronic Rhinosinusitis? Prospective findings from the National Comparative Audit of Surgery for Nasal Polyposis and Chronic Rhinosinusitis. Rhinology. 2015; 53(1):10–7. Epub 2015/03/11. DOI: 10.4193/Rhin13-217 [PubMed: 25756072]

24. Hopkins C, Andrews P, Holy CE. Does time to endoscopic sinus surgery impact outcomes in chronic rhinosinusitis? Retrospective analysis using the UK clinical practice research data. Rhinology. 2015; 53(1):18–24. Epub 2015/03/11. DOI: 10.4193/Rhin14.077 [PubMed: 25756073]

Table 1

Baseline descriptive cofactors for patients undergoing ESS with comorbid asthma (n=86)

Cofactors:	**Mean ± SD**	**Range [LL, UL]**	**N (%)**
Age (years) at enrollment	47.1 ± 15.6	[18, 78]	
White/Caucasian			71 (83%)
African American			10 (12%)
Hispanic/Latino			6 (7%)
Males			28 (33%)
Nasal polyposis			42 (49%)
Deviated septum			25 (29%)
Turbinate hypertrophy			7 (8%)
Allergies (skin prick/RAST confirmed)			61 (71%)
AERD			16 (19%)
COPD			7 (8%)
Depression (self-reported)			9 (11%)
Obstructive sleep apnea			15 (17%)
Current tobacco use/smoking			2 (2%)
Current alcohol use			19 (22%)
Previous sinus surgery			50 (58%)
Diabetes mellitus (Type I/II)			9 (11%)
Corticosteroid dependency (eg. asthma, CRS)			16 (19%)
GERD			20 (23%)
CRS-specific factors:			
Computed tomography score	13.2 ± 6.1	[0, 24]	
Endoscopy score	6.2 ± 3.8	[0, 14]	
SNOT-22 total score (n=86)	61.6 ± 20.3	[13, 102]	
Rhinologic symptoms	18.8 ± 6.4	[2, 30]	
Extra-nasal rhinologic symptoms	10.0 ± 2.9	[3, 15]	
Ear / facial symptoms	10.2 ± 5.6	[0, 22]	
Psychological dysfunction	18.7 ± 7.8	[0, 35]	
Sleep dysfunction	16.3 ± 6.4	[0, 25]	
Asthma-specific factors:			
miniAQLQ total score (n=86)	4.6 ± 1.4	[1, 7]	
Symptom score	4.3 ± 1.4	[1, 7]	
Activity score	5.1 ± 1.5	[1, 7]	
Emotional function score	4.8 ± 1.7	[1, 7]	
Environmental stimuli score	4.0 ± 1.6	[1, 7]	
ACT total score (n=77)	18.4 ± 5.3	[5, 25]	
Uncontrolled asthma (ACT < 20)			39 (51%)

CRS, chronic rhinosinusitis; SD, standard deviation; N, sample size; LL, lower limit; UL, upper limit; RAST, radioallergosorbent testing; BSIT, Brief Smell Identification Test; AERD, aspirin exacerbated respiratory disease; COPD, chronic obstructive pulmonary disease; miniAQLQ, the Mini Asthma Quality of Life Questionnaire; ACT, the Asthma Control Test survey. SNOT-22, 22-item SinoNasal Outcome Test. BSIT, Brief Smell Identification Test; GERD, gastroesophageal reflux disease.

Table 2

Within-subjects improvement in patient reported outcome measures following endoscopic sinus surgery.

	Baseline Mean ± SD	Last Follow-up Mean ± SD	Within- subject Δ Mean ± SD	95% CI for Δ [LB, UB]	p-value
All subjects:					
miniAQLQ total score (n=61)	4.6 ± 1.3	5.0 ± 1.5	0.5 ± 1.1	[0.2, 0.7]	**0.002**
Symptom score	4.2 ± 1.4	4.9 ± 1.6	0.7 ± 1.2	[0.3, 1.0]	**<0.001**
Activity score	5.3 ± 1.4	5.6 ± 1.6	0.3 ± 1.4	[0.02, 0.7]	0.056
Emotional function score	4.7 ± 1.6	5.2 ± 1.7	0.4 ± 1.2	[0.1, 0.8]	**0.004**
Environmental stimuli score	4.1 ± 1.6	4.4 ± 1.6	0.3 ± 1.6	[−0.1, 0.7]	0.186
ACT total score (n=52)	18.5 ± 4.9	19.8 ± 5.0	1.3 ± 4.1	[0.2, 2.4]	**0.025**
Subjects with preoperative uncontrolled asthma: (n=28)					
miniAQLQ total score	3.9 ± 1.0	4.7 ± 1.6	0.7 ± 1.3	[0.3, 1.2]	**0.004**
Symptom score	3.6 ± 1.1	4.5 ± 1.7	0.9 ± 1.3	[0.4, 1.4]	**0.001**
Activity score	4.7 ± 1.3	5.4 ± 1.7	0.7 ± 1.6	[0.1, 1.3]	**0.023**
Emotional function score	4.1 ± 1.5	4.7 ± 1.9	0.6 ± 1.3	[0.1, 1.1]	**0.026**
Environmental stimuli score	3.4 ± 1.5	4.1 ± 1.6	0.7 ± 1.7	[0.04, 1.3]	**0.036**
ACT total score	15.0 ± 3.9	17.9 ± 5.8	2.9 ± 4.4	[1.2, 4.6]	**0.002**
All subjects CRS-specific quality of life scores: (n=61)					
SNOT-22 total score	60.1 ± 19.6	26.3 ± 19.8	−33.8 ± 22.8	[−39.5, −28.1]	**<0.001**
Rhinologic symptoms	18.5 ± 6.4	8.3 ± 6.0	−10.2 ± 7.5	[−12.0, −8.3]	**<0.001**
Extra-nasal rhinologic symptoms	9.7 ± 2.9	4.9 ± 3.5	−4.8 ± 3.8	[−5.8, −3.9]	**<0.001**
Ear / facial symptoms	10.0 ± 5.6	4.2 ± 4.5	−5.8 ± 5.4	[−7.1, −4.4]	**<0.001**
Psychological dysfunction	18.2 ± 7.5	7.3 ± 7.6	−10.9 ± 8.9	[−13.1, −8.7]	**<0.001**
Sleep dysfunction	15.8 ± 6.0	7.3 ± 6.7	−8.5 ± 7.0	[−10.3, −6.8]	**<0.001**

SD, standard deviation; Δ, delta (change); LB, lower bound; UB, upper bound; CI, confidence interval; SNOT-22, 22-item SinoNasal Outcome Test; miniAQLQ, the Mini Asthma Quality of Life Questionnaire; ACT, the Asthma Control Test; Within-subject improvement in all outcome measures was evaluated using either matched pairs t-testing or Wilcoxon signed-rank testing, depending on distribution normality.

Table 3

Final simple linear regression modeling for independent, predictive factors associated with baseline miniAQLQ total scores

Final miniAQLQ total score model:	**β**	**SE**	**95% CI for β [LB, UB]**	**t-test**	**p-value**	**R^2**
Constant term	5.54	0.52	[4.50, 6.57]	10.65	<0.001	----
Enrollment site	−0.19	0.19	[−0.56, 0.19]	−1.00	0.321	----
Allergies (skin prick/RAST confirmed)	−0.62	0.31	[−1.23, −0.01]	−2.04	**0.045**	----
COPD	−1.27	0.51	[−2.29, −0.25]	−2.48	**0.015**	0.137

miniAQLQ, the Mini Asthma Quality of Life Questionnaire; B, beta effect estimates; SE, standard error; CI, confidence interval; LB, lower bound; UB, upper bound; R2, coefficient of multiple determination (explained model variance); RAST, radioallergosorbent; COPD, chronic obstructive pulmonary disease;

Table 4

Final simple linear regression modeling for independent, predictive factors associated with baseline ACT total scores

Final ACT total score model:	**β**	**SE**	**95% CI for β [LB, UB]**	**t-test**	**p-value**	**R^2**
Constant term	20.74	1.82	[17.12, 24.36]	11.42	<0.001	----
Enrollment site	−0.84	0.76	[−2.34, 0.67]	−1.11	0.272	----
COPD	−6.96	2.32	[−11.58, −2.35]	−3.00	**0.004**	0.130

ACT, the Asthma Control Test; B, beta effect estimates; SE, standard error; CI, confidence interval; LB, lower bound; UB, upper bound; R2, coefficient of multiple determination (explained model variance); COPD, chronic obstructive pulmonary disease.

Table 5

Comparison of postoperative changes in miniAQLQ total scores across descriptive cofactors for patients with CRS and comorbid asthma (n=61)

Cofactors:	**Present Mean ± SD**	**Absent Mean ± SD**	**p-value**
White/Caucasian	0.4 ± 1.1	0.6 ± 0.9	0.691
Hispanic/Latino	0.2 ± 1.4	0.5 ± 1.1	0.481
Males	0.2 ± 1.0	0.6 ± 1.1	0.267
Nasal polyposis	0.5 ± 1.2	0.5 ± 1.0	0.914
Deviated septum	0.6 ± 0.7	0.4 ± 1.2	0.203
Turbinate hypertrophy	0.6 ± 0.4	0.4 ± 1.1	0.375
Allergies (skin prick/RAST confirmed)	0.5 ± 1.2	0.5 ± 0.9	0.794
AERD	0.2 ± 1.1	0.5 ± 1.1	0.509
COPD	−0.1 ± 0.9	0.5 ± 1.1	0.176
Depression (self-reported)	0.7 ± 1.8	0.4 ± 1.0	0.868
Obstructive sleep apnea	−0.04 ± 0.7	0.6 ± 1.1	0.063
Current tobacco use/smoking	----	0.5 ± 1.1	----
Current alcohol use	0.9 ± 1.1	0.4 ± 1.1	0.063
Previous sinus surgery	0.7 ± 1.1	0.1 ± 0.9	0.109
Diabetes mellitus (Type I/II)	0.6 ± 1.0	0.4 ± 1.1	0.765
Corticosteroid dependency	−0.3 ± 0.9	0.6 ± 1.1	**0.011**
GERD	0.4 ± 1.3	0.5 ± 1.0	0.973
Uncontrolled asthma at baseline (ACT < 20)	0.7 ± 1.3	0.2 ± 0.8	**0.024**
Continuous measures:	**Correlation Coefficient (Rs)**		**p-value**
Age (years) at enrollment	−0.031		0.815
Computed tomography score (preoperative)	−0.083		0.525
Endoscopy score (preoperative)	−0.165		0.203
SNOT-22 total score (preoperative)	0.003		0.981
SNOT-22 postoperative change total score	−0.327		**0.010**

CRS, chronic rhinosinusitis; SD, standard deviation; RAST, radioallergosorbent testing; BSIT, Brief Smell Identification Test; AERD, aspirin exacerbated respiratory disease; COPD, chronic obstructive pulmonary disease; miniAQLQ, the Mini Asthma Quality of Life Questionnaire; GERD, gastroesophageal reflux disease. SNOT-22, 22-item SinoNasal Outcome Test; ACT, the Asthma Control Test. Cofactors do not represent mutually exclusive subgroups. Rs, Spearman's rank correlation coefficient (two-tailed). Negative scores reflect postoperative worsening on average. Between-subject differences were evaluated using either independent t-testing or Mann Whitney-U testing, depending on distribution normality.

Table 6

Comparison of postoperative changes in ACT total scores across descriptive cofactors for patients with CRS and comorbid asthma (n=52)

Cofactors:	**Present Mean ± SD**	**Absent Mean ± SD**	**p-value**
White/Caucasian	1.2 ± 4.2	2.1 ± 2.9	0.303
Hispanic/Latino	0.0 ± 1.8	1.4 ± 4.2	0.518
Males	0.3 ± 2.5	1.7 ± 4.5	0.302
Nasal polyposis	1.4 ± 4.2	1.2 ± 4.0	0.718
Deviated septum	1.7 ± 3.7	1.2 ± 4.2	0.370
Turbinate hypertrophy	2.4 ± 3.4	1.2 ± 4.2	0.449
Allergies (skin prick/RAST confirmed)	1.2 ± 4.4	1.8 ± 3.0	0.539
AERD	0.1 ± 2.3	1.6 ± 4.4	0.283
COPD	−0.3 ± 0.5	1.4 ± 4.2	0.496
Depression (self-reported)	3.0 ± 5.7	1.2 ± 3.9	0.607
Obstructive sleep apnea	−1.0 ± 1.0	1.8 ± 4.3	**0.016**
Current tobacco use/smoking	----	1.3 ± 4.1	----
Current alcohol use	1.5 ± 4.3	1.3 ± 4.1	0.756
Previous sinus surgery	1.9 ± 4.2	0.3 ± 3.7	0.152
Diabetes mellitus (Type I/II)	2.0 ± 2.8	1.2 ± 4.2	0.492
Corticosteroid dependency	0.1 ± 2.8	1.5 ± 4.2	0.389
GERD	2.5 ± 4.1	0.8 ± 4.0	0.199
Uncontrolled asthma at baseline (ACT < 20)	2.9 ± 4.4	−0.5 ± 2.8	**0.007**
Continuous measures:	**Correlation Coefficient (Rs)**		**p-value**
Age (years) at enrollment	−0.059		0.677
Computed tomography score (preoperative)	−0.104		0.462
Endoscopy score (preoperative)	−0.112		0.429
SNOT-22 total score (preoperative)	0.004		0.978
SNOT-22 postoperative change total score	−0.075		0.596

CRS, chronic rhinosinusitis; SD, standard deviation; RAST, radioallergosorbent testing; BSIT, Brief Smell Identification Test; AERD, aspirin exacerbated respiratory disease; COPD, chronic obstructive pulmonary disease; miniAQLQ, the Mini Asthma Quality of Life Questionnaire; GERD, gastroesophageal reflux disease. SNOT-22, 22-item SinoNasal Outcome Test; ACT, the Asthma Control Test. Cofactors do not represent mutually exclusive subgroups. Rs, Spearman's rank correlation coefficient (two-tailed). Negative scores reflect postoperative worsening on average. Between-subject differences were evaluated using either independent t-testing or Mann Whitney-U testing, depending on distribution normality.