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## Impact of Mucosal Eosinophilia and Nasal Polyposis on Quality of Life Outcomes after Sinus Surgery

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### Abstract

**Objective**—Assess whether the presence of mucosal eosinophilia correlates with surgical outcomes in patients with chronic rhinosinusitis.

**Study Design**—Prospective cohort

**Setting**—Tertiary medical center

**Subjects and Methods**—Adult patients with chronic rhinosinusitis were prospectively enrolled and demographic data and medical comorbidities recorded. Preoperative quality-of-life (QOL) was measured by the Chronic Sinusitis Survey (CSS), Rhinosinusitis Disability Index (RSDI), and Short Form-36 General Health Survey (SF-36). Sinus mucosal specimens were collected at the time of surgery and the degree of eosinophilia quantified. Postoperative QOL was measured and differences in QOL improvement were compared between those with and without eosinophilia.

**Results**—A total of 102 patients had both histopathologic and QOL outcome data available for review. Follow-up averaged 16.5 months. Patients with eosinophilia showed significantly less improvement in the RSDI total (17.9 vs 25.0;  $p=0.044$ ), RSDI functional (5.7 vs 8.8;  $p=0.018$ ), CSS medication (3.6 vs 17.3;  $p=0.013$ ), SF-36 general health (0.6 vs 9.6;  $p=0.008$ ), SF-36 physical role (16.1 vs 34.7;  $p=0.036$ ), and SF-36 vitality (11.9 vs 21.2;  $p=0.034$ ) scales than those without eosinophilia. The greatest improvement in QOL was seen in patients without eosinophilia or polyps and the least improvement seen in those with eosinophilia but without polyps.

**Conclusion**—The presence of mucosal eosinophilia at the time of surgery consistently predicted less improvement in both disease-specific and general QOL compared to those without eosinophilia. The impact of eosinophilia on outcomes was greatest for patients without nasal polyposis, a group which demonstrated the least improvement in QOL measures.

### Keywords

Chronic rhinosinusitis; quality of life; eosinophils; eosinophilia; pathology; sinusitis

## INTRODUCTION

Numerous authors and consensus groups have argued the merits of various classification schemes for chronic rhinosinusitis (CRS). Some have proposed including the presence or absence of eosinophilic inflammation as a defining feature.<sup>1</sup> We recently published histologic findings from a cohort of patients with CRS undergoing endoscopic sinus surgery (ESS).<sup>2</sup> Our data show that mucosal eosinophilia correlates with baseline objective disease severity as defined by computed tomography (CT), endoscopy, and olfactory testing. Although numerous other histologic markers of inflammation were present, none showed similar correlations.

Despite predicting worse objective disease severity, the presence of mucosal eosinophilia did not correlate with baseline disease-specific or general quality-of-life (QOL). The question remains whether the knowledge of eosinophilic status provides useful long-term prognostic information. The primary goal of the current study is to assess whether the presence of mucosal eosinophilia correlates with long-term surgical outcomes in patients with chronic rhinosinusitis.

## METHODS

### Study Population

Adult ( $\geq 18$  yrs) participants were prospectively recruited from a tertiary care center over a 3-year period with approval of the Oregon Health and Science University Institutional Review Board. All patients had a diagnosis of CRS based on the Rhinosinusitis Task Force criteria endorsed by the American Academy of Otolaryngology Head and Neck Surgery.<sup>3</sup> Patients were enrolled at the time they had failed medical management and had elected to undergo ESS. Medical management included at least a prolonged course of broad-spectrum or culture-directed antibiotics for 4 weeks and a trial of topical nasal corticosteroid spray. All patients were on medical co-interventions at the time of surgery for ongoing medical management of their disease and to prepare their sinonasal mucosa for surgery. These co-interventions included an oral prednisone taper beginning seven days prior to surgery (30mg/day for 4 days, then 20mg/day for 3 days) and oral antibiotics. Patients were also instructed to continue topical nasal steroid application and allergy therapy.

Preoperative demographic and medical history was obtained from both the patient and the medical record including age, gender, history of prior sinus surgery, nasal polyposis, asthma, allergic rhinitis (confirmed by either skin prick testing or modified radioallergic sorbent testing), and acetylsalicylic acid (ASA) intolerance. CT scans in the coronal plane were obtained by the physician principal investigator (PI) preoperatively and evaluated using the Lund-Mackay CT scoring system (0–24 point scale).<sup>4</sup> Rigid sinonasal endoscopy was performed preoperatively and quantified using the endoscopic scoring system outlined by Lund and Kennedy (0–20 point scale).<sup>5</sup> The Smell Identification Test (SIT; Sensonics, Inc.; Haddon Heights, NJ) was administered as an objective measure of olfactory function (0–40 point scale).

### QOL Evaluation

Consenting patients were asked to complete two disease-specific QOL instruments, the Rhinosinusitis Disability Index (RSDI) and the Chronic Sinusitis Survey (CSS), and one general QOL instrument, the 36-Item Short Form Health Survey (SF-36), both prior to and after surgery.<sup>6,7,8</sup> The RSDI measures rhinologic health by way of 30 questions separated by physical, functional, and emotional subscales (0–120 point scale). The CSS is an 8-week duration monitor of sinusitis-specific outcomes comprised of six questions in each of symptom and medication subscales (0–100 point scale). The SF-36 is a multi-purpose general health survey which measures eight domains of health: physical functioning, role limitations due to

physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health (0–100 point scale). Higher scores on the RSDI represent overall higher impact and worse disease severity, while higher scores on the CSS and SF-36 domains represent lower impact and lesser disease severity. A research coordinator administered all survey instruments pre- and postoperatively during the normal delivery of care for each patient. Data collected at the last postoperative clinic visit during the study period was considered for outcome analyses. The principal investigator was blinded to all QOL responses for the study duration.

### Histologic Evaluation

Sinus mucosal tissue was collected from the ethmoid cavity at the time of surgery. These specimens represented the mucosa removed as necessary to complete a standard endoscopic ethmoidectomy. Standard pathological laboratory techniques were used to prepare all samples. Tissue specimens were promptly immersed in 10% neutral buffered formalin (NBF) and fixed for a minimum of 4 hours. The specimens were grossly examined and submitted into a plastic mesh cassette in-toto and again immersed in NBF for an additional 3–12 hours. Following a three minute cold water rinse, the tissue cassette was immersed in an acid decalcification solution (Decal Stat; Tallman, NY) for 8 hours and again rinsed with cold water for three minutes. Tissue cassettes then underwent a 12 hour cycle in an automated processor (Sakura VIP; Sakura Finetek USA, Torrance, CA) prior to paraffin embedding (Sakura Tissue-Tec; Sakura Finetek USA, Torrance, CA). Histological sections of 4 $\mu$  were prepared on a microtome and the slide was placed in an automated stainer and glass coverslipper. The hematoxylin and eosin (H&E)-stained slides were then banked for review.

Microscopic review was performed by a single board-certified surgical pathologist using a binocular microscope (Leica DM2000; Leica Microsystems Inc., Bannockburn, IL) with a graduated reticle mounted within one of the eyepiece objectives (10 $\times$ 10mm, 1.0mm divisions). At 400x power the reticle field is 250 $\mu$   $\times$  250 $\mu$ , yielding an area of approximately 0.13 square millimeters (mm<sup>2</sup>). Histologic review was performed to assess the number of mucosal eosinophils present. Eosinophils were quantified in the foci of densest cellular infiltrate to ensure that patients were consistently classified based on the area of greatest inflammation. Eosinophil count was recorded in each reticle field at 400x power and reported as absolute number per high power field. The pathologic review was done in a blinded fashion in regards to all clinical data.

### Statistical Analysis

All histologic data and QOL responses were compiled and recorded on standardized clinical research forms. Statistical analyses were completed using SPSS v16.0 statistical software (SPSS, Inc., Chicago, IL.). Change in QOL scores was calculated for all patients from preoperative to postoperative time points. Differences in QOL improvement were then compared between those with and without mucosal eosinophilia using independent t-tests for parametric and Mann-Whitney U tests for nonparametric data.

### Optimal Eosinophilia Cutpoint

Because specific criteria for what constitutes clinically relevant mucosal eosinophilia remain undefined, a combination of methods was utilized to identify the optimal cut-point for dichotomizing subjects into those with and those without eosinophilia. These methods included the graphical examination of nonparametric distribution for evidence of an eosinophilia threshold effect and the minimum p-value approach. Focusing on the RSDI total, six cut-points were compared including: >1 eosinophil/HPF, >5 eosinophils/HPF, >10 eosinophils/HPF, >50 eosinophils/HPF, >100 eosinophils/HPF, and >250 eosinophils/HPF. The optimal cut-point was then defined as the candidate cut-point with the largest absolute difference in disease-

specific QOL change scores (postoperative minus preoperative) and smallest corresponding p-value. Patients with an eosinophil count above the cut-point were considered to have mucosal eosinophilia for the purposes of this study.

### CRS Subtype Comparison

Finally, patients were classified into four subtypes of CRS based on the clinical presence of nasal polyps and histologic presence of mucosal eosinophilia as defined by the optimal cut-point determination: Eosinophilic CRS with Nasal Polyposis (ECSRswNP), Non-Eosinophilic CRS with Nasal Polyposis (CRSwNP), Eosinophilic CRS without Nasal Polyposis (ECSRsnNP), and Non-Eosinophilic CRS without Nasal Polyposis (CRSsnNP). Differences in QOL outcomes between these subtypes were compared using Kruskal-Wallis and Mann-Whitney U tests where appropriate. A p-value of  $\leq 0.05$  was considered statistically significant for all analyses. Means and standard deviations ( $\pm$ ) are reported.

## RESULTS

### Baseline Findings

A total of 147 patients were enrolled into the study at baseline. Of this group, 102 had both histopathologic and QOL outcome data available for analyses. For the 45 patients not included in the final analyses (lost to follow up), a baseline comparison of disease-severity (CT, endoscopy, olfaction, and QOL scores) revealed no differences when compared to the final cohort. The demographic and comorbidity characteristics of the cohort are shown in Table 1, along with CT, endoscopy, and SIT scores. The average age was 46.7 (range: 23–79), with 51% males and 49% females. Overall follow-up averaged 16.5 months (range: 4–37 months). Overall, 79.4% of patients had  $>1$  eosinophil/HPF, 51.0% had  $>5$  eosinophils/HPF, 47.1% had  $>10$  eosinophils/HPF, 28.4% had  $>50$  eosinophils/HPF, 22.5% had  $>100$  eosinophils/HPF, and 11.8% had  $>250$  eosinophils/HPF (Figure 1).

### Eosinophilia Cut-Point

The change in RSDI total scores after surgery (postoperative minus preoperative) for patients above and below each eosinophilia cut-point are shown in Table 2. Also shown is the absolute difference in RSDI change score between those above and below the specific cut-point. The greatest difference in outcome was seen when using a cut-point of  $\geq 10$  eosinophils/HPF. Patients with  $\geq 10$  eosinophils/HPF averaged 7.1 points less improvement on the RSDI total scale than those with  $<10$  eosinophils/HPF. This difference also had the greatest statistical significance at  $p < 0.04$ . Therefore, a value of  $\geq 10$  eosinophils/HPF was defined as the optimal cut-point and referred to as “mucosal eosinophilia” for the remainder of the analyses.

### Quality of Life Outcomes

A comparison of disease-specific and general health QOL scores between those with and without eosinophilia are shown in Tables 3 and 4. As in our prior study, no baseline differences were seen for any QOL instrument between patients with and without eosinophilia on the RSDI, CSS, or SF-36. Statistically significant postoperative improvement (postoperative minus preoperative) was seen across most QOL indices for patients whether or not they had eosinophilia. However, when comparing the level of improvement, there was a global tendency for those with eosinophilia to show less improvement in QOL than those without eosinophilia. Patients with eosinophilia showed significantly less improvement in the RSDI total (17.9 vs 25.0;  $p=0.044$ ), RSDI functional (5.7 vs 8.8;  $p=0.018$ ), CSS medication (3.6 vs 17.3;  $p=0.013$ ), SF-36 general health (0.6 vs 9.6;  $p=0.008$ ), SF-36 physical role (16.1 vs 34.7;  $p=0.036$ ), and SF-36 vitality (11.9 vs 21.2;  $p=0.034$ ) scales than those without eosinophilia. In addition, patients with eosinophilia also showed a similar trend ( $p < 0.10$ ) towards worse improvement

in the CSS total, RSDI emotional, SF-36 physical functioning, SF-36 social functioning, and SF-36 mental health scales, although these did not reach our defined significance level.

### CRS Subtype Outcomes

Patients were classified into four subtypes based on the presence or absence of nasal polyposis and mucosal eosinophilia. Most patients were classified as CRSsNP (n=38), followed by ECRSwNP (n=34), CRSwNP (n=16), and ECRSsNP (n=14). The QOL outcomes for each subtype are shown in Figures 2–4. When comparing outcomes for the subtypes, the greatest improvement in QOL was seen in the CRSsNP (non-eosinophilic) subtype and the least improvement seen in the ECRSsNP subtype. The difference in improvement between CRSsNP and ECRSsNP was significant for the RSDI total (26.4 vs 13.9;  $p=0.024$ ), RSDI functional (9.3 vs 4.6;  $p=0.020$ ), CSS total (29.7 vs 12.5;  $p=0.017$ ), CSS medication (21.7 vs 1.8;  $p=0.013$ ), and SF 36 general health (12.7 vs 4.4;  $p=0.003$ ).

## DISCUSSION

Prior studies investigating surgical outcomes for CRS have shown significant improvements in mean symptom scores and QOL.<sup>9,10</sup> However, these studies also reveal that significant variability exists as to the degree of improvement in individual patients. Past studies have highlighted various demographic factors, clinical factors, and comorbidities which explain some differences in disease severity and outcomes after ESS.<sup>11,12</sup> This study defines a histopathologic finding (mucosal eosinophilia) which, if present, predicts less long-term QOL improvement after ESS.

Numerous authors have argued the merits of a clinical classification scheme which includes the presence or absence of nasal polyposis and mucosal eosinophilia as defining features.<sup>1</sup> To be clinically useful, the knowledge of mucosal eosinophilic status would either provide certain prognostic information about disease severity/outcome or allow for specific tailored treatments. This study supports classifying patients based on the presence or absence of mucosal eosinophilia as it shows that the knowledge of mucosal eosinophilic status provides important prognostic information about long-term outcomes. Perhaps what is most interesting is that the greatest impact of eosinophilia on outcomes was seen in those patients without nasal polyposis. In CRS patients without nasal polyps, the presence of eosinophilia ( $\geq 10$  eosinophils/HPF) predicted the least improvement in QOL as compared to those without eosinophilia who experienced the greatest improvement. Interestingly, based on clinical presentation alone, these patients might be otherwise indistinguishable.

The presence or absence of mucosal eosinophilia did not seem to affect QOL improvement for patients with polyposis in this study cohort. Patients with polyps have long been thought of as a separate and distinct subgroup of CRS. Prior studies have shown the physical presence of polyps filling the nasal cavity leads to worse objective findings on CT and endoscopy compared to the average CRS patient. Additionally, patients with polyps typically complain of nasal obstruction as the dominant symptom with a lower incidence of symptoms such as facial pain/pressure or nasal discharge. The physical removal of polyps as done during ESS would be expected to dramatically improve nasal obstruction and thus improve the dominant symptom contributing to QOL decline. This would be true regardless of whether or not mucosal eosinophilia is present. The tendency for polyps to recur is well established, but may take many years to manifest in symptomatic decline. The follow-up for this study (16.5 month average) may not have been long enough to detect a difference in polyp recurrence rates based on eosinophilia, if one in fact exists. Further research is necessary with longer-term outcomes in order to fully address this issue.



When analyzing outcomes research, one must make a distinction between statistically significant findings and those which are also clinically relevant to the individual patient or physician. Generally speaking, QOL changes become clinically meaningful when they approximate  $\frac{1}{2}$  of the standard deviation of the baseline QOL value. This seemingly arbitrary definition of clinical relevance has been validated across many disease-specific and general QOL instruments.<sup>13</sup> In this study, clinically significant differences were seen in the CRS subtype comparisons for each QOL instrument studied. For example, patients without polyps or eosinophilia (CRSsNP) improved by 26.4 points on the RSDI total versus only 13.9 for those without polyps but with eosinophilia (ECRSsNP), a difference of 12.5 points ( $\frac{1}{2}$ SD=9.0 points; 0–120 scale). The difference between these two subtypes was 17.2 points on the CSS total scale ( $\frac{1}{2}$ SD=10.0 points; 0–100 scale) and 35.8 points on the CSS medication scale ( $\frac{1}{2}$ SD=13.3 points; 0–100 scale). Regarding the SF-36, the minimal clinically important difference has been established at 10–12.5 points for diseases such as asthma, COPD, and coronary artery disease.<sup>14</sup> ECRSsNP patients had 17.5 points less improvement on the SF-36 general health scale than patients classified as CRSsNP, a level well above the threshold of clinical relevance.

If mucosal eosinophilia is going to be used for classification purposes, criteria must be outlined as to what exactly defines the condition. In our earlier work we used a cut-point of  $>5$  eosinophils/HPF to define clinically relevant mucosal eosinophilia.<sup>2</sup> This was based in part on a prior study which suggested that  $>5$  eosinophils/HPF was associated with *in vivo* evidence of eosinophil activation.<sup>15</sup> In the current study, we explored numerous cut-points in order to better understand the impact of eosinophilia on outcomes. The greatest impact on QOL outcomes was seen when the mucosal infiltrate reached  $>10$  eosinophils/HPF. Interestingly, there did appear to be a threshold effect at, or near, 10 eosinophils/HPF. Above this level, increasing density of eosinophils did not result in progressively more effect on QOL. Future research is needed in order to fully establish the optimal cut-point that identifies clinically relevant mucosal eosinophilia.

The results of this study have both research and clinical implications. Clinical outcomes research on CRS often seeks to investigate the pertinent factors which predict treatment response. Prior studies have shown that patient factors identifiable at presentation can impact treatment outcomes, such as gender and medical comorbidities.<sup>11,12</sup> This study shows that microscopic pathologic factors also provide predictive information. Future outcomes studies will need to evaluate differences on the molecular and genetic levels in order to fully explore the root causes of patient variability. From a clinical standpoint, the data from this study highlight the importance of detailed surgical pathology reports, especially with respect to mucosal eosinophilia. The technique used in this study to quantify eosinophilia should translate well to the clinical realm as it utilizes standard H&E stains and has been shown to be highly reproducible.<sup>16</sup>

The strengths of this study include sample size, length of follow-up, the prospective nature of data collection, and the rigorous methodology used to quantify eosinophilia. Additionally, both disease-specific and general QOL were assessed using previously validated instruments. There are, however, caveats to consider in the interpretation of these findings. Mean Lund-Mackay CT scores on this cohort were 13.0 suggesting moderate to severe inflammatory mucosal disease. Therefore, patients in this study were on medical co-interventions which included topical nasal steroids and preoperative oral steroids to reduce inflammatory mucosal disease and prepare the sinonasal mucosa for surgery. This preoperative regimen has the potential to impact mucosal inflammation, including the degree of mucosal eosinophilia. Studies evaluating patients with CRS who are not exposed to medical co-interventions at the time of mucosal biopsy would assist in determining medication effect on mucosal eosinophilia. Finally, the cohort was enrolled and studied at a tertiary rhinology center and may not be generalizable

to the entire population undergoing sinus surgery. Larger multicenter and community based studies will be necessary to validate the results.

## CONCLUSION

Many feel that patients with eosinophilic CRS represent a unique subgroup which is especially refractory to medical and surgical intervention.<sup>17</sup> However, few studies have sought to prospectively evaluate the clinical relevance of mucosal eosinophilia with regard to treatment outcomes. This study evaluated the relationship between mucosal eosinophilia at baseline and QOL outcomes after sinus surgery. The presence of mucosal eosinophilia (>10 eosinophils/HPF) at the time of ESS consistently predicted less improvement in both disease-specific and general QOL compared to those without eosinophilia. The impact of eosinophilia on outcomes was greatest for CRS patients without nasal polyposis, a group which demonstrated the least improvement in QOL measures.

## Acknowledgments

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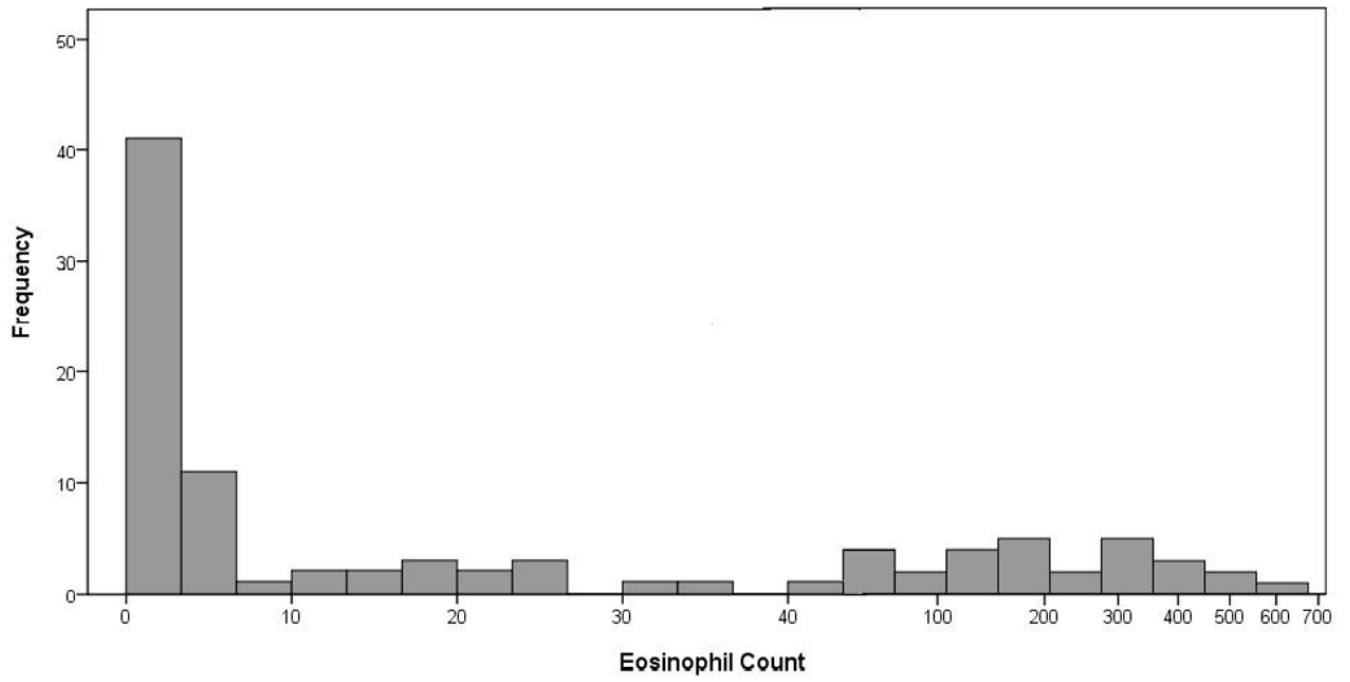
Supported by grant funding from the NIH/NIDCD #R01 DC005805 (PI/PD: Smith, TL) Public clinical trial registration (<http://www.clinicaltrials.gov>) ID: NCT00799097

## References

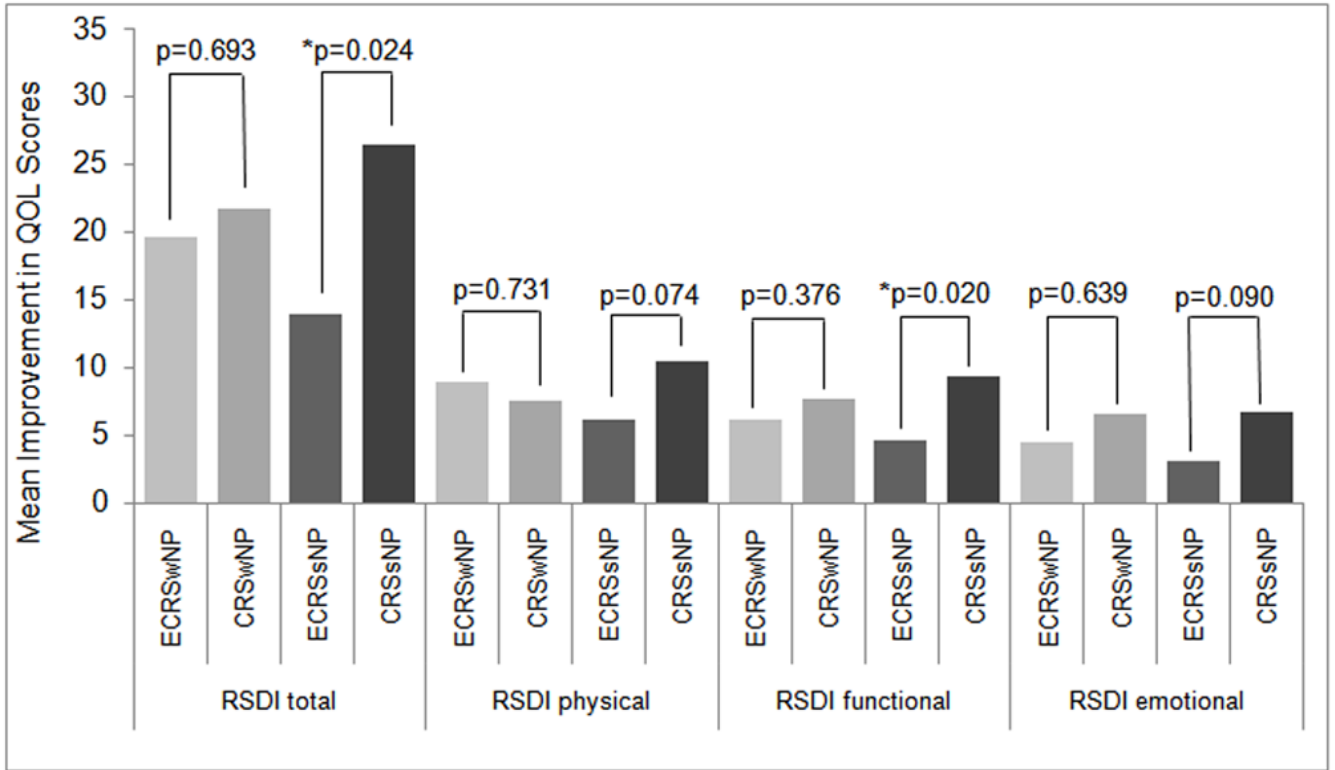
1. Meltzer EO, Hamilos DL, Hadley JA, et al. Rhinosinusitis: Establishing definitions for clinical research and patient care. *Otolaryngol Head Neck Surg* 2004;131(suppl):S1–S62. [PubMed: 15577816]
2. Soler ZM, Sauer D, Mace J, Smith TL. Relationship between Clinical Measures and Histopathologic Findings in Chronic Rhinosinusitis. *Otolaryngol Head Neck Surg*. 2009 Accepted for publication June 16<sup>th</sup>, 2009.
3. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline. *Otolaryngol Head Neck Surg* 2007;137(Suppl):S1–S31. [PubMed: 17761281]
4. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology* 1993;31:183–184. [PubMed: 8140385]
5. Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg* 1997;117:S35–40. [PubMed: 9334786]
6. Benninger MS, Senior BA. The development of the rhinosinusitis disability index. *Arch Otolaryngol Head Neck Surg* 1997;123:1175–1179. [PubMed: 9366696]
7. Gliklich RE, Metson R. Techniques for outcomes research in chronic rhinosinusitis. *Laryngoscope* 1995;105:387–390. [PubMed: 7715384]
8. Ware JE, Kosinski M, Gandek BG, et al. The factor structure of the SF-36R health survey in 10 countries: Results from the International Quality of Life Assessment (IQOLA) project. *J Clin Epidemiol* 1998;51(11):1159–1165. [PubMed: 9817133]
9. Smith TL, Mendolia-Loffredo S, Loehrl TA, et al. Predictive factors and outcomes in endoscopic sinus surgery for chronic rhinosinusitis. *Laryngoscope* 2005;115(11):2199–205. [PubMed: 16369166]
10. Bhattacharyya N. Symptom outcomes after endoscopic sinus surgery for chronic rhinosinusitis. *Arch Otolaryngol Head Neck Surg* 2004;130:329–333. [PubMed: 15023842]
11. Mendolia-Loffredo S, Laud PW, Sparapani R, Loehrl TA, Smith TL. Sex differences in outcomes of sinus surgery. *Laryngoscope* 2006;116(7):1199–1203. [PubMed: 16826060]
12. Robinson JL, Griest S, James KE, Smith TL. Impact of aspirin intolerance on outcomes of sinus surgery. *Laryngoscope* 2007;117(5):825–830. [PubMed: 17473677]
13. Norman GR, Sloan JA, Wyrwick KW. Interpretation of changes in health related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;41:582–592. [PubMed: 12719681]

14. Wyrwick KW, Tierney WM, Babu AN, et al. A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease, asthma, or heart disease. *Health Serv Res* 2005;40(2):577–592. [PubMed: 15762908]
15. Kountakis SE, Arrango P, Dewayne Bradley, et al. Molecular and cellular staging for the severity of chronic rhinosinusitis. *Laryngoscope* 2004;114(10):1895–1905. [PubMed: 15510011]
16. Bhattacharyya N, Vyas DK, Fechner FP, et al. Tissue eosinophilia in chronic sinusitis: Quantification techniques. *Arch Otolaryngol Head Neck Surg* 2001;127:1102–1105. [PubMed: 11556861]
17. Ferguson BJ. Categorization of eosinophilic chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg* 2004;12:237–42. [PubMed: 15167036]

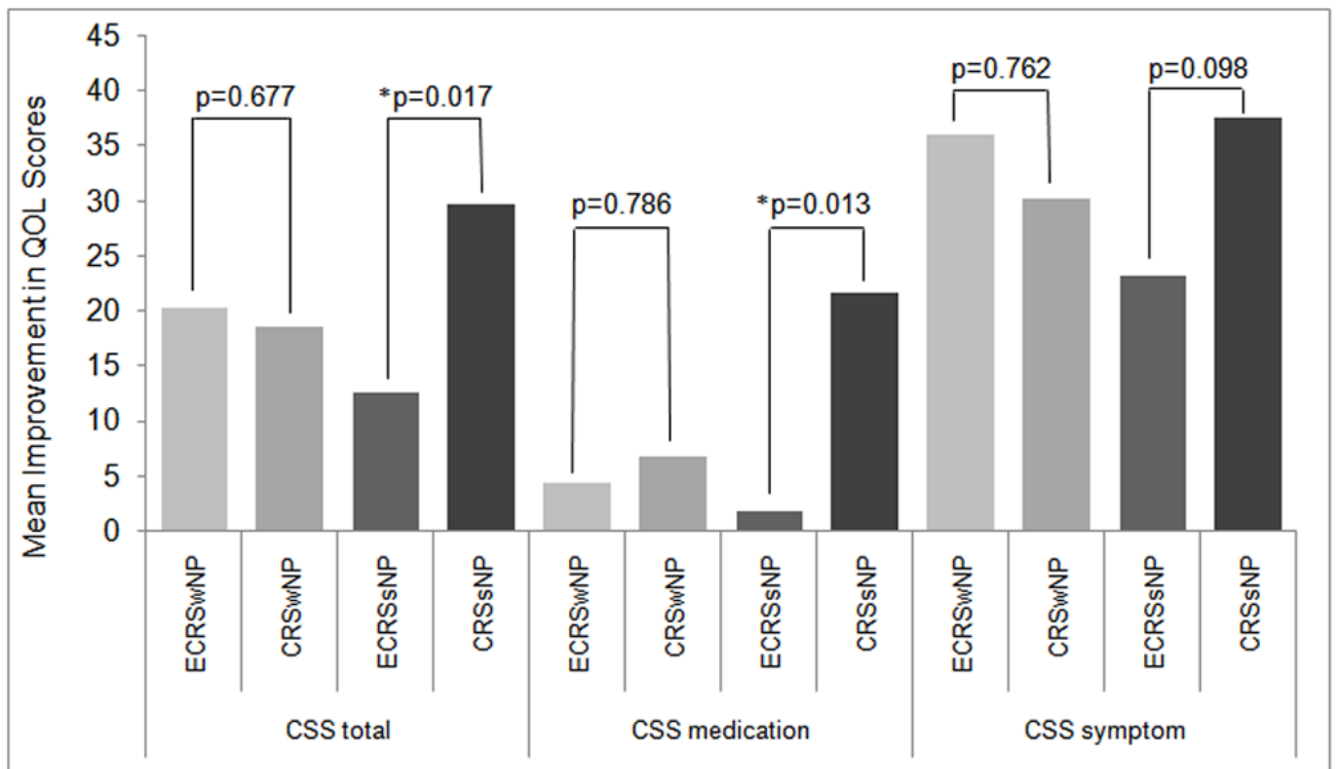




**Figure 1.** Frequency distribution and range of absolute eosinophil counts for study subjects (n=102).

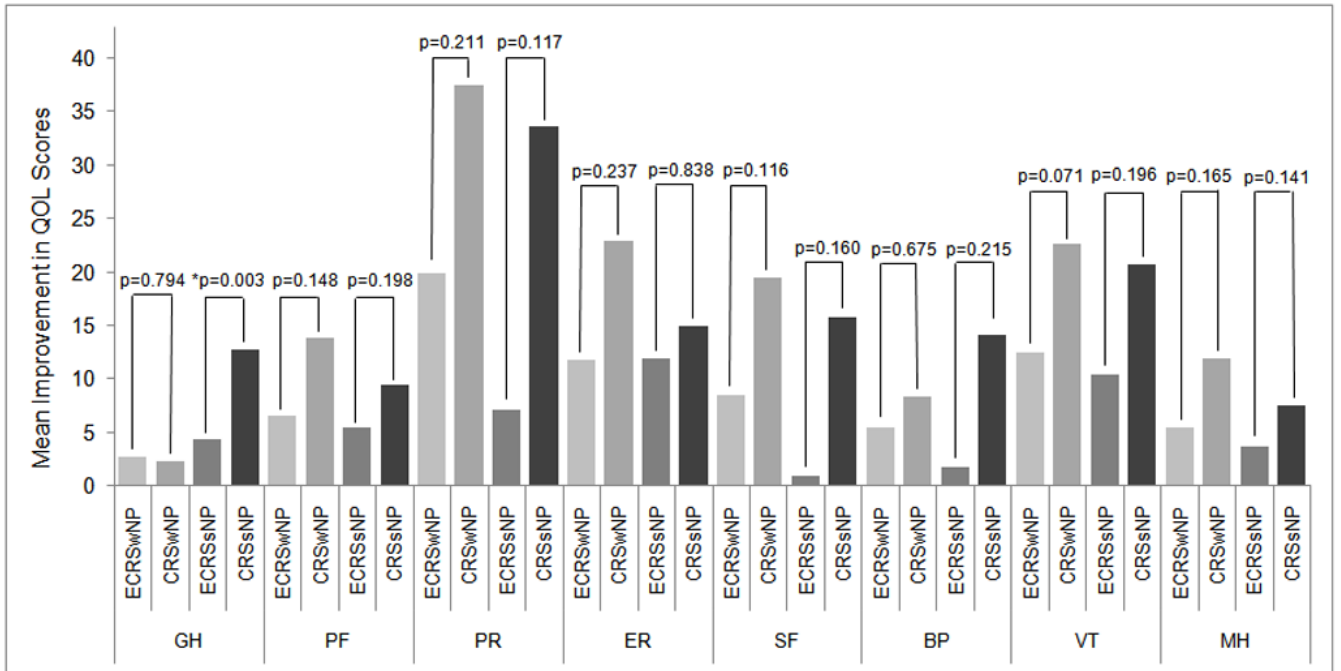


**Figure 2.** Differences in postoperative disease-specific QOL improvement on the RSDI instrument between CRS subtypes. Total and subscale scores are reported. QOL = quality-of-life. RSDI = Rhinosinusitis Disability Index. ECRSwNP = Eosinophilic CRS with nasal polyposis. CRSwNP = Non-eosinophilic CRS with nasal polyposis. ECRSsNP = Eosinophilic CRS without nasal polyposis. CRSsNP = Non-eosinophilic CRS without nasal polyposis. \*indicates a statistically significant subtype difference  $\leq 0.05$ .



**Figure 3.**

Differences in postoperative disease-specific QOL improvement on the CSS instrument between CRS subtypes. Total and subscale scores are reported. QOL = quality-of-life. CSS = Chronic Sinusitis Survey. ECRSwNP = Eosinophilic CRS with nasal polyposis. CRSwNP = Non-eosinophilic CRS with nasal polyposis. ECRSSNP = Eosinophilic CRS without nasal polyposis. CRSSNP = Non-eosinophilic CRS without nasal polyposis. \*indicates a statistically significant subtype difference  $\leq 0.05$ .



**Figure 4.** Differences in postoperative general QOL improvement on the SF-36 instrument between CRS subtypes. Separate subscale scores are reported. QOL = quality-of-life. SF-36 = Medical Outcomes Short Form-36. ECRSwNP = Eosinophilic CRS with nasal polyposis. CRSwNP = Non-eosinophilic CRS with nasal polyposis. ECRSsNP = Eosinophilic CRS without nasal polyposis. CRSsNP = Non-eosinophilic CRS without nasal polyposis. GH = General health subscale. PF = Physical functioning subscale. PR = Physical role subscale. ER = Emotional role subscale. SF = Social functioning subscale. BP = Bodily pain subscale. VT = Vitality subscale. MH = Mental health subscale. \*indicates a statistically significant subtype difference  $\leq 0.05$ .

**Table 1**

Preoperative cohort demographics, comorbidities, and measures of disease severity (n=102)

	[range]	mean $\pm$ SD	n (%)
<b>Demographics:</b>			
Follow-up (mo.)	[4–37]	16.5 $\pm$ 6.0	
Age	[23–79]	46.7 $\pm$ 13.3	
<b>Gender</b>			
Male			52 (51.0)
Female			50 (49.0)
<b>Comorbidities:</b>			
Prior sinus surgery			53 (52.0)
Nasal polyposis			50 (49.0)
Asthma			41 (40.2)
ASA Intolerance			11 (10.8)
Allergic rhinitis			30 (29.4)
Current smoker			7 (6.9)
<b>Disease severity:</b>			
CT scores	[2–24]	13.0 $\pm$ 6.5	
Endoscopy scores	[0–20]	7.8 $\pm$ 4.8	
Olfactory (SIT) scores	[0–40]	27.0 $\pm$ 10.7	

**Table 2**

Optimal eosinophilic cut point determination using the Rhinosinusitis Disability Index

Cut-points: eosinophilia/HPF	Improvement in RSDI scores (below cutpoint)	Improvement in RSDI scores (above cutpoint)	Difference (mean $\pm$ SE)	p-value
$\leq 1$ eos/HPF	22.9 $\pm$ 18.0	21.4 $\pm$ 18.9	1.5 $\pm$ 4.1	0.487
$\leq 5$ eos/HPF	24.6 $\pm$ 18.9	18.8 $\pm$ 17.9	5.8 $\pm$ 3.7	0.100
$\leq 10$ eos/HPF	25.0 $\pm$ 19.0	17.9 $\pm$ 17.6	7.1 $\pm$ 3.6	<b>0.044</b>
$\leq 50$ eos/HPF	23.7 $\pm$ 18.3	17.0 $\pm$ 18.8	6.7 $\pm$ 4.1	0.101
$\leq 100$ eos/HPF	22.2 $\pm$ 18.7	20.1 $\pm$ 18.5	2.0 $\pm$ 4.3	0.684
$\leq 250$ eos/HPF	22.2 $\pm$ 18.6	18.4 $\pm$ 19.1	3.7 $\pm$ 5.5	0.508

Optimal eosinophilic cut-point was determined by comparing differences in average RSDI improvement between those above and below the cut-point. Means and standard deviations are reported for improvement after surgery. The mean difference in improvement is reported with standard errors. RSDI = Rhinosinusitis Disability Index. HPF= high power field (400x). eos = eosinophilia.  $p \leq 0.05$  is statistically significant.



**Table 3**

Mean preoperative, postoperative, and change in disease-specific outcome measures for patients with and without eosinophilia (n=102)

	Preoperative			Postoperative			Absolute Change		
	≤10 eos/HPF	> 10 eos/HPF	p-value	≤10 eos/HPF	> 10 eos/HPF	p-value	≤10 eos/HPF	> 10 eos/HPF	p-value
RSDI physical	19.2 ± 6.9	20.8 ± 7.2	0.377	9.7 ± 7.3	12.7 ± 7.6	0.062	9.5 ± 7.9	8.1 ± 7.5	0.229
RSDI functional	15.5 ± 6.3	15.1 ± 6.7	0.543	6.7 ± 6.5	9.4 ± 6.9	<b>0.044</b>	8.8 ± 6.8	5.7 ± 6.5	<b>0.018</b>
RSDI emotional	13.5 ± 8.3	13.1 ± 7.4	0.778	6.8 ± 7.4	9.0 ± 6.8	0.057	6.7 ± 8.2	4.1 ± 6.3	0.092
<b>RSDI TOTAL</b>	48.2 ± 18.0	48.9 ± 18.4	0.960	23.2 ± 19.6	31.0 ± 19.2	<b>0.042</b>	25.0 ± 18.9	17.9 ± 17.6	<b>0.044</b>
CSS medication	48.2 ± 26.9	46.4 ± 26.6	0.613	65.4 ± 23.3	50.0 ± 22.5	<b>0.002</b>	17.3 ± 31.6	3.6 ± 24.9	<b>0.013</b>
CSS symptom	27.9 ± 26.6	20.5 ± 25.4	0.113	63.5 ± 27.3	52.8 ± 32.8	0.088	35.4 ± 31.0	32.3 ± 29.5	0.388
<b>CSS TOTAL</b>	38.0 ± 21.2	33.4 ± 18.3	0.248	64.9 ± 20.3	51.4 ± 22.1	<b>0.003</b>	26.3 ± 26.1	17.9 ± 21.5	0.086

Means and standard deviations are reported for each subgroup. Eos = eosinophilia. HPF = high powered field (400x). RSDI = Rhinosinusitis Disability Index. CSS = Chronic Sinusitis Survey, p ≤ 0.05 is statistically significant.

Table 4

Mean preoperative, postoperative, and change in general health related QOL domains for patients with and without eosinophilia (n=102)

	Preoperative			Postoperative			Absolute change		
	≤10 eos/HPF	> 10 eos/HPF	p-value	≤10 eos/HPF	> 10 eos/HPF	p-value	≤10 eos/HPF	> 10 eos/HPF	p-value
SF-36 GH	52.5 ± 24.1	53.1 ± 24.6	0.827	62.1 ± 22.6	53.8 ± 24.9	0.101	9.6 ± 19.3	0.6 ± 15.6	<b>0.008</b>
SF-36 PF	74.8 ± 22.7	76.4 ± 27.2	0.324	85.6 ± 20.5	82.6 ± 23.7	0.357	10.7 ± 16.7	6.3 ± 12.8	0.052
SF-36 PR	32.4 ± 39.0	45.8 ± 39.7	0.062	67.1 ± 42.6	61.9 ± 44.1	0.344	34.7 ± 45.7	16.1 ± 38.8	<b>0.036</b>
SF-36 ER	62.3 ± 40.5	70.8 ± 39.9	0.260	79.6 ± 36.3	82.6 ± 30.7	0.943	17.3 ± 34.7	11.8 ± 40.9	0.464
SF-36 SF	60.4 ± 24.1	66.7 ± 26.8	0.108	77.3 ± 25.7	72.9 ± 26.1	0.313	16.9 ± 28.8	6.3 ± 25.4	0.063
SF-36 BP	51.5 ± 20.4	57.8 ± 24.1	0.057	63.9 ± 24.7	62.1 ± 24.4	0.856	12.4 ± 27.3	4.4 ± 21.5	0.132
SF-36 VT	33.5 ± 22.3	34.4 ± 23.5	0.877	54.3 ± 24.3	46.3 ± 23.3	0.101	21.2 ± 23.9	11.9 ± 19.7	<b>0.034</b>
SF-36 MH	65.2 ± 20.1	67.8 ± 20.0	0.431	73.6 ± 18.0	72.7 ± 15.7	0.376	8.8 ± 17.1	4.9 ± 14.3	0.062

Means and standard deviations are reported for each subgroup. Eos = eosinophilia. HPF = high powered field (400x). SF-36 = Medical Outcomes Short Form-36. GH = General health subscale. PF = Physical functioning subscale. PR = Physical role subscale. ER = Emotional role subscale. SF = Social functioning subscale. BP = Bodily pain subscale. VT = Vitality subscale. MH = Mental health subscale. p ≤ 0.05 is statistically significant.