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Relationship between Clinical Measures and Histopathologic Findings in Chronic Rhinosinusitis

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Abstract

Objective—Describe detailed histopathologic findings from a cohort of patients with chronic rhinosinusitis and evaluate whether histologic measures correlate with baseline clinical factors.

Study Design—Cross-sectional study with planned data collection

Setting—Tertiary medical center

Subjects and Methods—Adult patients with chronic rhinosinusitis were prospectively enrolled and demographic data and medical comorbidities recorded. Disease severity was measured by computed tomography (CT), endoscopy, Smell Identification Test (SIT), the Chronic Sinusitis Survey, Rhinosinusitis Disability Index, and SF-36 General Health Survey. Mucosal specimens were assessed for the presence of mucosal inflammation, including cellular (eosinophils, neutrophils, lymphocytes, mast cells, plasma cells, macrophages), epithelial (squamous metaplasia, basement membrane thickening, goblet cells), and stromal markers (subepithelial edema, fibrosis). Histopathologic findings were correlated to baseline clinical factors.

Results—A total of 147 subjects were enrolled with histologic samples available for review. Presence of inflammatory markers was diverse with lymphocytes present in 100% of subjects, eosinophils in 49.7%, and neutrophils found in 0.7%. Total eosinophil counts correlated with the presence of nasal polyposis ($r = -0.367$; $p < 0.001$), asthma ($r = 0.264$; $p = 0.001$), and aspirin intolerance ($r = 0.279$; $p = 0.001$). Mucosal eosinophilia correlated with worse disease severity on CT ($r = 0.414$; $p < 0.001$), endoscopy ($r = 0.376$; $p < 0.001$), and SIT ($r = -0.253$; $p = 0.002$) with the highest correlations seen in subgroups without nasal polyps. Histopathologic findings did not significantly correlate with any quality-of-life measure.

Conclusion—Mucosal eosinophilia correlates with objective disease severity as defined by CT, endoscopy, and SIT scores. Although other histologic markers of inflammation are present, none show similar correlations. The presence of mucosal eosinophils does not correlate with quality-of-life scores.

Keywords

Chronic rhinosinusitis; sinusitis; histology; pathology; quality of life

Introduction

Consensus guidelines have defined chronic rhinosinusitis (CRS) on clinical grounds based on the presence of characteristic symptoms combined with objective evidence of mucosal inflammation¹. This definition of CRS, although useful for diagnosis, describes a generic condition, wherein multiple underlying etiologies, pathophysiologies, and phenotypes exist². The categorization of CRS into subtypes may have important implications for treatment and expected long-term outcomes. Prior studies investigating surgical outcomes for CRS patients have shown significant improvements in symptom scores and quality-of-life (QOL) across all patients with CRS^{3,4}. Subgroup analysis has shown that various demographic factors, clinical factors, and comorbidities can affect baseline disease severity and outcomes^{5,6}. Recently the importance of eosinophilic inflammation has been recognized, and it is felt that patients with eosinophilic CRS represent a unique subgroup which is especially refractory to medical and surgical intervention⁷. Few studies, however, have sought to systematically evaluate the clinical relevance of histologic inflammatory markers. The purpose of this study is to describe detailed, reproducible histopathologic findings from a cohort of patients with CRS undergoing endoscopic sinus surgery (ESS) and evaluate whether these measures correlate with baseline clinical factors. The presence of specific histologic findings will then be used to classify patients into subgroups which can later be used for outcome studies.

Methods

Study Population

Adult (≥ 18 yrs) participants were prospectively recruited from a tertiary care center over a 3-year period with approval of the Institutional Review Board at Oregon Health and Science University. All patients had a diagnosis of CRS based on the Rhinosinusitis Task Force criteria endorsed by the American Academy of Otolaryngology Head and Neck Surgery⁸. Patients were enrolled at the time they had failed extended 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. Pre-operative 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.

QOL Evaluation and Objective Testing

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 (36-Item Short Form Health Survey (SF-36)) prior to surgery.^{9,10,11} A research coordinator administered all survey instruments. 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.

Computed tomography (CT) scans in the coronal plane were obtained by the physician principal investigator (PI) pre-operatively and evaluated using the Lund-Mackay CT scoring system¹². Rigid sinonasal endoscopy was performed pre-operatively and quantified using the endoscopic scoring system outlined by Lund and Kennedy¹³. The Smell Identification Test (SIT; Sensonics, Inc.; Haddon Heights, NJ) was administered as an objective measure of olfactory function¹⁴. Higher scores on CT and endoscopy represent worse disease severity, while higher SIT scores represent superior olfaction. The PI was blinded to all QOL responses and SIT scores during the study duration.

Histologic Evaluation

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 followed with 20mg/day for 3 days) and oral antibiotics. Patients were also instructed to continue topical nasal steroid application and allergy therapy.

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 fixed, decalcified, and paraffin embedded. Hematoxylin and eosin staining was done and the slides were banked for review.

Microscopic review was performed by a single board-certified surgical pathologist using a binocular microscope (Leica DM2000; Bannockburn, IL) with a graduated reticle mounted within one of the eyepiece objectives (10×10mm, 1.0mm divisions). The pathologic review was done in a blinded fashion in regards to all clinical and QOL data. A detailed histological review and quantification was performed at 400x power utilizing the graduated reticle. At 400x power the reticle field is 250μ × 250μ, yielding an area of approximately 0.13 square millimeters (mm²).

Histologic review was performed to assess the presence of mucosal inflammation including cellular, epithelial, and stromal markers (Table 1). Cellular marker evaluation included absolute counts of eosinophils, neutrophils, lymphocytes, mast cells, plasma cells, and macrophages. Cellular markers were quantified in the foci of densest cellular infiltrate in each reticle field at 400x power and reported as absolute number per high power field (HPF). The epithelial markers evaluated included presence of squamous metaplasia, basement membrane (BM) thickening, and goblet cells. Goblet cells were quantified at 400x as a percentage of epithelial cells within 200-250μm long mucosal fragments. Maximal BM thickening was measured in the curettage fragment(s) with the most optimal transverse mucosal histological orientation and recorded as <5μm, 5-10μm, 10-15μm, and 15+ μm. The epithelial lining was scanned to determine the degree of squamous metaplasia and recorded as a categorical variable (0=not present, 1=focal/mild, 2=patchy/moderate and 3=extensive/marked). Subepithelial edema and fibrosis were also assessed in a categorical fashion (0=not present, 1=focal/mild, 2=patchy/moderate and 3=extensive/marked).

CRS Subtypes

Patients were classified into four subgroups of CRS based on the clinical presence of polyps and histologic presence of mucosal eosinophilia. Mucosal eosinophilia was defined as having an absolute count of >5 eosinophils/HPF. Subgroups were compared for differences in the prevalence of demographic factors and comorbid conditions, as well as objective and QOL measures.

Statistical Analysis

All statistical analyses were completed using SPSS v16.0 statistical software (SPSS, Inc., Chicago, IL.). Pearson's, Spearman's Rank, and Phi correlation coefficients (r) were utilized to correlate the presence of histologic findings with baseline demographic information and comorbidities where appropriate. A correlation coefficient value $0.250 \leq r < 0.400$ was defined as a weak correlation, $0.400 \leq r < 0.600$ a moderate correlation, and $r \geq 0.600$ a strong correlation. Histopathologic findings were also correlated with patient-based measures of disease severity (RSDI, CSS, and SF-36 instruments), as well as baseline objective measures of disease severity (CT score, endoscopy score, and SIT score). Pearson and Mantel-Haenszel

chi-square tests were used to explore differences in histology markers and comorbid prevalences for subjects with and without nasal polyposis in both the total cohort and CRS subtypes where appropriate. Independent t-tests, Mann Whitney U, and Kruskal-Wallis tests were used to examine differences in histology, demographics, comorbidity, objective testing, and QOL for the total cohort as well as CRS subtypes. Differences within each subgroup were analyzed to assess whether the presence and/or level of histological markers significantly contributes to each disease classification. A p-value of ≤ 0.05 was considered statistically significant for all analyses. Means and standard deviations ($\pm$) are reported.

Results

Overall Findings

All enrolled subjects (n=147) had histopathologic samples collected for analysis. The average age 46.4 ± 13.8 years with a majority of male patients (n=78; 53.1%). Over half of all subjects has a history of prior sinus surgery (n=78; 53.1%), while 44.9% were found to have nasal polyposis (n=66), 38.1% reported asthma (n=56), 10.2% with ASA intolerance (n=15), and 27.2% with allergic rhinitis (n=40). Baseline CT, endoscopy, QOL and SIT scores are shown in Table II. As expected, CT and endoscopy scores strongly correlated ($r=0.734$; $p \leq 0.001$), and SIT scores moderately correlated with both CT and endoscopy ($r = -0.485$; $p \leq 0.001$ and $r = -0.462$; $p < 0.001$).

Overall histopathologic findings are shown in Table III. After quantifying cellular markers of inflammation, only one patient was found with neutrophils. Conversely, all patients had appreciable numbers of lymphocytes present (range: 4-1500/HPF). Mucosal eosinophils were present in 78.9% of all mucosal samples with 49.7% of patients having >5 eosinophils/HPF. Mast cells, plasma cells, and macrophages were present in 10.2% (range: 1-7), 99.3% (range: 1-230), and 4.1% (range: 1-11) of subjects, respectively. Regarding epithelial markers, the mean percentage of goblet cells was 19.9%, BM thickening was $>5\mu\text{m}$ in 49.7% of all specimens and squamous metaplasia was present in 53.1% of all patients. The majority of all specimens were found to have focal/mild subepithelial edema (41.5%) and mucosal fibrosis (40.8%).

Overall Histologic Correlations

Demographic/Clinical—No significant correlations were found between the absolute count of neutrophils, lymphocytes, mast cells, plasma cells, and macrophages and any demographic or clinical features including gender, history of prior sinus surgery, nasal polyposis, asthma, ASA intolerance, or allergic rhinitis. Total eosinophil count did positively correlate with the presence of nasal polyposis ($r=0.367$; $p<0.001$), asthma ($r= 0.264$; $p=0.001$), and ASA intolerance ($r=0.279$; $p=0.001$), but not allergic rhinitis ($r=0.003$; $p=0.966$) or history of prior sinus surgery ($r=-0.019$; $p=0.819$). A statistically significant but weak correlation between eosinophils and male gender was found ($r=0.170$; $p=0.039$).

Basement membrane thickening correlated weakly with asthma ($r=0.252$; $p=0.025$). Squamous metaplasia and goblet cell percentage did not correlate with any clinical features. Subepithelial edema correlated weakly with asthma ($r=0.348$; $p=0.005$), moderately with ASA intolerance ($r=0.570$; $p=0.006$), and strongly with nasal polyposis ($r=0.634$; $p<0.001$).

Objective Testing—Histologic inflammatory markers were correlated with CT, endoscopy, and SIT scores. Higher eosinophil counts correlated with worse CT ($r=0.414$; $p<0.001$), endoscopy ($r=0.376$; $p<0.001$), and SIT scores ($r=-0.253$; $p=0.002$). The presence of subepithelial edema correlated with worse CT ($r=0.366$; $p<0.001$) and endoscopy scores

($r=0.313$; $p<0.001$). No other cellular, epithelial, or stromal markers significantly correlated with objective testing.

QOL Findings—No histologic inflammatory markers correlated significantly with total scores or subscale scores from the RSDI, CSS, or SF-36 instruments.

Subgroup Analysis

Polyp Patients—Polyps were present in 66 of 147 patients (44.9%). Eosinophils (>5 /HPF) were present in 44 (66.7%) polyp patients with a mean count of 192.7 ± 211.8 . Within this group, eosinophil counts did not correlate with CT, endoscopy, SIT, or QOL scores. Subgroups comprised of patients with polyps and each of asthma, ASA intolerance, and allergies were evaluated both inclusively and exclusively. Within these subgroups, eosinophil levels did not predict significantly worse scores on any objective or QOL measures.

Non-polyp Patients—Polyps were absent in 81 of 147 patients (55.1%). Eosinophils (>5 /HPF) were present in 29 (35.8%) patients without polyps with a mean count of 60.3 ± 66.5 . Within this group, eosinophil counts correlated positively with CT ($r=0.324$; $p=0.003$) and endoscopy scores ($r=0.278$; $p=0.012$). Subgroups comprised of patients without polyps but with asthma and/or allergic rhinitis were evaluated. In the subgroup comprised of all subjects with asthma, stronger correlations were found with CT score ($r=0.490$; $p<0.001$) and endoscopy score ($r=0.434$; $p<0.001$). The correlation between eosinophil count and CT score was also present in patients with asthma exclusive of allergies ($r=0.579$; $p=0.038$), all patients with allergic rhinitis ($r=0.528$; $p=0.008$), and patients with allergic rhinitis exclusive of asthma ($r=0.504$; $p=0.033$). However, eosinophil counts were no longer associated with CT score or endoscopy in patients without asthma or allergic rhinitis in this subgroup. For patients without polyps, no correlations were found between eosinophil counts and SIT scores or the RSDI, CSS, or SF-36 instruments.

CRS Subtypes

Patients were classified into four subtypes of CRS based on the clinical presence of polyps and histologic presence of mucosal eosinophilia. The majority of patients (35.4%) were classified as Non-Eosinophilic CRS without Nasal Polyposis (CRSsNP), followed by Eosinophilic CRS with Nasal Polyposis (ECRSwNP; 29.9%), Eosinophilic CRS without Nasal Polyposis (ECRSsNP; 19.9%), and Non-Eosinophilic CRS with Nasal Polyposis (CRSwNP; 15%). The demographic breakdown and associated medical comorbidities for each subtype are shown in Table IV.

CRS Subtype Comparisons

The four subtypes of CRS were compared in regards to objective and patient-based measures of disease severity including CT score, endoscopy score, SIT score, and QOL scores (Figures I and II; Table V). CT and endoscopy scores were worse in the two subtypes with nasal polyposis ($p<0.001$) compared to the subtypes without nasal polyposis. However, CT and endoscopy scores did not differ between ECRSwNP and CRSwNP subtypes. For the two subtypes without nasal polyposis, mucosal eosinophilia did predict worse CT and endoscopy scores with the highest scores found in the ECRSsNP subtype as compared to CRSsNP subtype. Olfaction scores were influenced by mucosal eosinophilia with lower scores being found in the ECRSwNP subtype as compared to the CRSwNP subtype (19.3 ± 11.3 vs. 25.1 ± 9.8 ; $p<0.001$). Olfaction scores were not influenced by eosinophils in the non-polyposis subtypes. In regards to QOL, ECRSwNP patients had worse total CSS score than CRSwNP patients (31.3 ± 17.6 vs. 42.0 ± 20.8 ; $p=0.029$). ECRSsNP patients had worse scores on the Physical Functioning subscale of the SF-36 (70.3 ± 24.60 vs 81.9 ± 16.2 ; $p=0.041$) than CRSsNP

patients. No other significant differences were found between CRS subgroups for the total RSDI or any general QOL subscales.

Discussion

This study evaluated 11 distinct cellular, epithelial, and stromal inflammatory markers in 147 subjects presenting with CRS and electing endoscopic sinus surgery. In general, the mucosal inflammation seen in CRS can be described as a predominantly lymphocytic infiltrate with roughly 50% of cases having significant eosinophilia present. Depending on the case, other findings of chronic inflammation will often be present including macrophages, mast cells, plasma cells, goblet cell hyperplasia, BM thickening, subepithelial edema, and mucosal fibrosis. Despite a variety of inflammatory markers being present, only eosinophilia correlated with specific baseline clinical factors in a consistent fashion. It thus appears that of all the inflammatory markers evaluated only eosinophils are useful as a defining histologic feature.

Numerous authors and consensus groups have argued the merits of various classification schemes for CRS, both from a clinical and research perspective¹⁵. Most focus first on the presence or absence of polyps as the defining feature. Some then seek to include the presence or absence of eosinophilic inflammation as the next stratification in the schema, as done in this study. The question remains whether this type of classification is useful in the clinical setting. To be clinically useful, the knowledge of eosinophilic status would either provide certain prognostic information about disease severity or allow specific tailored treatments. Our data offer some support in favor of using eosinophils for clinical classification. Eosinophils were predictive of worse scores on objective testing across all patients, with certain subgroups such as non-polyp patients with asthma or allergic rhinitis showing quite robust correlations. However, objective tests have consistently correlated poorly with disease-specific QOL scores in patients with CRS. In this study eosinophils did not independently correlate with any QOL finding. Studies by Kountakis and Boudain have similarly failed to show a correlation between symptoms and eosinophil counts^{16,17}. We are currently collecting long-term QOL data to assess whether the presence of eosinophils or any other mucosal inflammatory markers affects QOL outcomes after ESS. This information will be instrumental in understanding whether information on mucosal inflammation provides prognostic information.

At present, the majority of anti-inflammatory medications such as topical nasal steroids are relatively nonspecific in their targets. Therefore, understanding the inflammatory milieu is not critical to prescribe such treatment. However, future medications will only become more targeted in their mechanism of action. Medications such as the monoclonal antibody mepolizumab specifically target eosinophilic inflammation by blocking the IL-5-driven recruitment of eosinophils from the bloodstream. Identifying which patients have mucosal eosinophilia would thus be a critical step before prescribing such a targeted treatment.

If mucosal eosinophilia is going to be used for classification purposes, criteria must be adopted as to what exactly defines the condition. Is the presence of one eosinophil in a sample enough to call it eosinophilia? In this study, mucosal eosinophilia was defined as >5 eosinophils/HPF in the region of densest cellular infiltrate. A similar definition was utilized by Kountakis et al¹⁶, wherein immunostaining was performed for EG2 as a marker of activated eosinophils. Staining was only positive in mucosal specimens in which >5 eosinophils/HPF were present. EG2 immunostaining has been shown to be a clinically useful indicator of airway inflammation in asthmatics¹⁸. Interestingly, the distribution of eosinophil counts in our cohort had a natural breakpoint which supports the use of >5 eosinophils/HPF as a defining criterion (Figure III). Further research is necessary to determine whether this definition is truly ideal.

There are caveats to consider in the interpretation of these findings. Patients in this study were on medical co-interventions which included preoperative oral steroids and antibiotics to reduce inflammatory mucosal disease and prepare the sinonasal mucosa for surgery. This preoperative regimen has the potential to impact mucosal inflammation. This may explain in part why so few patients had neutrophils present within the inflammatory infiltrate. However, these preoperative medications represent our standard practice and thus were not felt modifiable for strict research purposes. 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 inflammation. 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.

The strengths of this study include its size, the prospective nature of data collection, and the rigorous histologic methodology. The methodology for quantifying cellular inflammatory infiltrate was based on work described by Bhattacharyya and Metson who were able to show a strong intra-rater ($r > 0.91$, $p < 0.001$) and inter-rater ($r > 0.82$; $p < 0.001$) reliability for these quantification techniques.¹⁹ Future clinical and scientific studies using mucosal eosinophilia as a defining feature should strongly consider adhering to similar standardized techniques.

Conclusion

This study sought to describe detailed, reproducible histologic findings from a cohort of patients with CRS undergoing ESS in order to evaluate whether these measures correlate with baseline clinical factors. Our data show that eosinophils correlate with objective disease severity as defined by CT, endoscopy, and SIT scores even after controlling for comorbidities such as asthma, ASA intolerance, and polyposis. Although numerous other histologic markers of inflammation were present, none showed similar correlations. Despite predicting worse objective disease severity, the presence of mucosal eosinophils did not correlate with baseline disease-specific or general QOL scores. The presence or absence of polyps combined with information on mucosal eosinophilia can be used to define four subtypes of CRS which differ in regards to CT, endoscopy, SIT, and certain QOL scores.

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Figure I.

Comparison of mean olfactory (SIT) scores between CRS subtypes with and without nasal polyposis and measurable eosinophilia. 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. Bars represent ± 1.0 standard deviation from the mean. * indicates a non-significant subtype difference $p=0.649$.

Figure II.

Comparison of mean CT and endoscopy scores between CRS subtypes with and without nasal polyposis and measurable eosinophilia. 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. Bars represent ± 1.0 standard deviation from the mean. * indicates a significant subtype difference $p=0.037$. ** indicates a significant subtype difference $p=0.006$.

Figure III.

Frequency distribution and range of absolute eosinophil counts for subjects with chronic rhinosinusitis (n=147).

Table I

Overview of histologic, inflammatory markers and definitions of numerical data collection

INFLAMMATORY MARKERS	Variable Type	Measurement
Cellular Markers		
Eosinophils	Continuous	Absolute number/HPF
Mast cells	Continuous	Absolute number/ HPF
Lymphocytes	Continuous	Absolute number/ HPF
Plasma cells	Continuous	Absolute number/ HPF
Macrophages	Continuous	Absolute number/ HPF
Neutrophils	Continuous	Absolute number/ HPF
Epithelial Markers		
Goblet cells	Continuous	Percentage (%)
Basement membrane thickening	Categorical	<5µm; 5-10 µm; 10-15 µm; 15+µm
Squamous metaplasia	Dichotomous	Grade 0,1,2,3
Stromal Markers		
Subepithelial edema	Categorical	Grade 0,1,2,3
Mucosal fibrosis	Categorical	Grade 0,1,2,3

HPF = high power field (0.13 mm² @ 400x magnification).

µm = micrometers.

Table II

Mean preoperative objective clinical measures, disease-specific and general quality of life measures (n=147)

Measures:	[range]	Mean $\pm$ SD
Clinical measures:		
Preoperative CT scores	[1 - 24]	12.6 $\pm$ 6.5
Preoperative endoscopy scores	[0 - 20]	7.4 $\pm$ 4.6
Preoperative olfaction (SIT)	[0 - 39]	26.9 $\pm$ 10.8
Disease-specific QOL:		
RSDI total	[8 - 39]	48.5 $\pm$ 18.2
RSDI physical	[2 - 36]	20.0 $\pm$ 7.1
RSDI functional	[0 - 31]	15.3 $\pm$ 6.6
RSDI emotional	[0 - 39]	13.3 $\pm$ 7.5
CSS total	[0 - 100]	38.5 $\pm$ 20.9
CSS symptom	[0 - 100]	26.8 $\pm$ 26.7
CSS medication	[0 - 100]	50.6 $\pm$ 28.1
General health QOL:		
SF-36 General health	[5 - 100]	53.3 $\pm$ 24.5
SF-36 Physical functioning	[5 - 100]	75.6 $\pm$ 23.7
SF-36 Physical role	[0 - 100]	37.4 $\pm$ 39.5
SF-36 Emotional role	[0 - 100]	62.6 $\pm$ 42.2
SF-36 Social functioning	[0 - 100]	64.0 $\pm$ 25.8
SF-36 Bodily pain	[0 - 100]	53.8 $\pm$ 22.2
SF-36 Vitality	[0 - 100]	35.5 $\pm$ 23.4
SF-36 Mental health	[0 - 100]	66.1 $\pm$ 20.3

SD = standard deviation. CT = computed tomography. SIT = Smell Identification Test. QOL = quality of life. RSDI = Rhinosinusitis Disability Index.
 CSS = Chronic Sinusitis Survey. SF-36 = Medical Short Form-36.

Table III
Histopathologic inflammatory markers in subjects with CRS

Inflammatory markers	[range]	Mean $\pm$ SD	n(%)
Cellular markers:			
Eosinophils	[0 - 1025]	70.3 $\pm$ 4.9	116 (78.9)
0-5/HPF			74 (50.3)
Mast cells	[0 - 7]	0.3 $\pm$ 1.0	15 (10.2)
Lymphocytes	[4 - 1500]	298.4 $\pm$ 370.3	147 (100.0)
Plasma cells	[0 - 230]	32.9 $\pm$ 49.4	146 (99.3)
Macrophages	[0 - 11]	0.2 $\pm$ 1.0	6 (4.1)
Neutrophils	[0 - 104]	0.7 $\pm$ 8.6	1 (0.7)
Epithelial markers:			
Goblet cells (%)		19.9 $\pm$ 22.5	
0-25%			113 (76.9)
26-50%			17 (11.6)
51-75%			10 (6.8)
76-100%			7 (4.8)
BM thickening			
< 5 μ m			74 (50.3)
5-10 μ m			54 (36.7)
10-15 μ m			18 (12.2)
>15 μ m			1 (0.7)
Squamous metaplasia			
Not present			69 (46.9)
Focal / mild			40 (27.2)
Patchy / moderate			30 (20.4)
Extensive / marked			8 (5.4)
Stromal markers:			
Subepithelial edema			
Not present			33 (22.4)
Focal / mild			61 (41.5)
Patchy / moderate			38 (25.9)
Extensive / marked			15 (10.2)
Mucosal fibrosis			
Not present			48 (32.7)
Focal / mild			60 (40.8)
Patchy / moderate			32 (21.8)
Extensive / marked			7 (4.8)

SD = standard deviation. HPF = high power field (400x). BM = basement membrane, μ m = micrometers.

Table IV

Subject characteristics and frequency of comorbid conditions by CRS subtype.

	ECRSwNP	CRSwNP	ECRSsNP	CRSsNP
Characteristics:	(n=44; 29.9%)	(n=22; 15.0%)	(n=29; 19.9%)	(n=52; 35.4%)
Age (mean yrs $\pm$ SD)	46.3 $\pm$ 13.7	48.2 $\pm$ 17.3	45.9 $\pm$ 12.4	46.1 $\pm$ 13.4
Gender: n(%)				
Male	32 (72.7)	12 (54.5)	15 (51.7)	19 (36.5)
Female	12 (27.3)	10 (45.5)	14 (48.3)	33 (63.5)
Prior sinus surgery	23 (52.3)	18 (81.8)	12 (41.4)	25 (48.1)
Asthma	29 (65.9)	8 (36.4)	12 (41.4)	7 (13.5)
ASA intolerance	12 (27.3)	3 (13.6)	0 (0.0)	0 (0.0)
Allergy	12 (27.3)	4 (18.2)	7 (24.1)	17 (32.7)

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. SD = standard deviation. ASA = acetylsalicylic acid.

Table V

Comparison of mean QOL measures between CRS subtypes with and without nasal polyps and measurable eosinophilia.

Measures:	ECRSwNP (n=44)	CRSwNP (n=22)	p-value	ECRSsNP (n=29)	CRSsNP (n=52)	p-value
Disease-specific QOL:						
RSDI total	50.7 ± 20.2	51.7 ± 17.4	0.833	48.3 ± 15.8	45.6 ± 17.9	0.752
CSS total	31.3 ± 17.6	42.0 ± 20.8	0.029	43.0 ± 20.7	40.6 ± 22.8	0.671
General health QOL:						
SF-36 General health	56.4 ± 27.3	49.4 ± 24.6	0.273	50.3 ± 21.8	54.1 ± 23.6	0.474
SF-36 Physical functioning	74.8 ± 28.2	69.5 ± 25.4	0.348	70.3 ± 24.6	81.9 ± 16.2	0.041
SF-36 Physical role	47.7 ± 40.3	28.4 ± 40.3	0.065	33.6 ± 37.4	34.6 ± 39.0	0.971
SF-36 Emotional role	66.7 ± 43.1	53.0 ± 44.4	0.241	59.8 ± 44.0	64.7 ± 39.8	0.692
SF-36 Social functioning	64.8 ± 29.1	59.7 ± 26.1	0.375	65.9 ± 24.1	64.2 ± 24.1	0.710
SF-36 Bodily pain	57.7 ± 24.9	51.7 ± 17.1	0.150	54.0 ± 21.3	51.3 ± 22.2	0.523
SF-36 Vitality	38.5 ± 24.7	30.0 ± 18.6	0.240	30.5 ± 23.3	38.1 ± 22.8	0.176
SF-36 Mental health	66.3 ± 20.4	57.6 ± 22.2	0.117	68.1 ± 22.5	68.3 ± 17.8	0.722

ECRSwNP = Eosinophilic CRS with nasal polyps. CRSwNP = Non-eosinophilic CRS with nasal polyps. ECRSsNP = Eosinophilic CRS without nasal polyps. CRSsNP = Non-eosinophilic CRS without nasal polyps. QOL = quality of life. RSDI = Rhinosinusitis Disability Index. CSS = Chronic Sinusitis Survey. SF-36 = Medical Short Form-36, p < 0.05 is statistically significant.