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Olfactory cleft and sinus opacification differentially impact olfaction in chronic rhinosinusitis

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Abstract

Objectives—Prior studies have indicated that olfactory cleft (OC) opacification correlates with olfaction in patients with chronic rhinosinusitis (CRS). However, in patients without polyps, the results have been unclear. The purpose of this study was to further explore the relationship between OC opacification, sinus opacification, and olfactory function in patients with CRS.

Methods—148 patients with CRS were prospectively enrolled across 5 institutions. Olfactory function was evaluated using the “Sniffin’ Sticks” tests and the 17-item Questionnaire of Olfactory Disorders (QOD-NS). Computed tomography (CT) scans for each patient were acquired and Lund-Mackay scores recorded. Opacification of the OC was determined using OsiriX MD and correlated with olfaction scores.

Results—A total of 148 CRS patients, 73 CRS without nasal polyps (CRSsNP) and 75 CRS with nasal polyps (CRSwNP), and 30 control subjects were enrolled. Overall OC opacification averaged 63.7% in CRS patients and 47.1% in control subjects ($p<0.001$). In the overall cohort, OC opacification significantly correlated with Threshold/Discrimination/Identification (TDI) ($r=-0.520$; $p<0.001$) and QOD-NS scores ($r=0.374$; $p<0.001$). CRSwNP patients demonstrated a significant correlation between OC opacification and TDI scores ($r=-0.464$; $p<0.001$), but not the CRSsNP group ($r=-0.143$; $p=0.229$). Lund-Mackay score correlated with TDI in both the CRSsNP ($r=-0.300$; $p=0.010$) and CRSwNP ($r=-0.271$; $p=0.019$) groups.

Conclusion—CT opacification is associated with olfactory dysfunction differentially based on nasal polyp status. Smell loss in CRSwNP correlated with both OC opacification and Lund-Mackay score, whereas CRSsNP correlated only with Lund-Mackay score, indicating different relationships between olfactory function and local inflammatory processes in these disorders.

Keywords

Computed tomography; chronic rhinosinusitis; sinusitis; olfactory disorders

INTRODUCTION

Chronic rhinosinusitis (CRS) is one of the most common causes of impaired olfaction in the United States (US), with a population prevalence estimated as high as 10–15%, a rate similar across all racial and ethnic subgroups.^{1,2} Olfactory loss is considered a defining feature of CRS and can be found in 40–80% of patients.³ Olfactory dysfunction is thought to result from the mucosal inflammation characteristic of CRS.^{4,5} Mucosal inflammation could affect olfaction directly via inflammatory-mediated damage to the olfactory epithelium, by physically impeding delivery of odorant-containing air to the olfactory cleft (OC), or a combination of both mechanisms.^{6,7} Understanding how inflammation at various anatomic sites impacts olfaction across a population of patients with CRS may offer insights regarding mechanisms of disease, outcome prediction, and even potential treatment options.

Assessing the degree of OC inflammation using computed tomography (CT) scan is an attractive option, considering that most patients with persistent disease will undergo imaging prior to consideration of treatments such as sinus surgery. A number of prior studies have found that OC opacification visible on CT appears to correlate with objective olfaction as determined by psychophysical testing.^{8–12} Most of these studies have been relatively small in size, single institution, lacked age-matched controls, and primarily utilized supra-threshold identification testing. In our prior investigations, we have consistently seen significant correlation between OC opacification and olfaction in patients with polyps, whereas, the results have been contradictory in patients without polyps, with one study showing a significant correlation and another failing to see an association.^{11,12} Given these contradictory findings, the relationship between local inflammation and olfactory function remains unclear. The purpose of the current study was to more fully explore the relationship between OC and sinus opacification and olfactory function in patients with CRS, utilizing a larger, multi-institutional cohort study design, a control population, and more comprehensive olfactory testing that includes threshold testing, supra-threshold measures, and olfactory-specific quality of life (QOL).

METHODS

Study Population

Adults aged 18 years or older meeting diagnostic criteria for CRS established by the Clinical Practice Guideline of the American Academy of Otolaryngology-Head and Neck Surgery¹ were recruited from rhinology clinics at Medical University of South Carolina (Charleston, SC), Oregon Health and Sciences University (Portland, OR), University of Utah (Salt Lake

City, UT), University of Virginia (Charlottesville, VA), and University of Colorado (Aurora, CO) as part of a prospective, olfactory outcomes study (Clinical Trial #NCT02720653; National Institutes of Health, Federal grant identifier: R01 DC005805).¹³ All included patients must have received a high resolution CT scan of the sinuses as part of their clinical care. Exclusion criteria included endoscopic sinus surgery in the previous 6 months. In addition, 30 control subjects were selected consecutively from a list of patients who underwent sinus CT for non-rhinologic indications and matched by age and sex. In order to qualify as a non-CRS control, there must have been no visible inflammation in any sinus on CT scan (ie Lund-Mackay score of 0). The study was approved by the institutional review board at each site and all subjects were provided with written, informed consent.

Demographic information and history of comorbidities, such as asthma, aspirin exacerbated respiratory disease (AERD), and depression was collected using standardized questionnaires for all participants, based on patient report of a prior physician's diagnosis. Allergic rhinitis was established for those who carried a physician's diagnosis and had confirmation with previous positive objective testing. Patients were categorized as "CRS with nasal polyposis" (CRS_{NP}) and "CRS without polyposis" (CRS_{NP}) based upon nasal endoscopy. At the time of enrollment, each physician graded the CT scan of each patient using the Lund-Mackay scoring method, blinded to all data regarding olfaction. Total Lund-Mackay scores were calculated (0–24), as were scores for each set of sinuses (0–4), with higher scores representing greater opacification. Sinus-specific QOL was assessed using the Sino-nasal Outcomes Test (SNOT-22). The SNOT-22 contains 22 questions scored from 0–5 and provides a total score that ranges from 0–110, with higher scores indicating a more severe impact on sinus-specific QOL.

Olfactory Evaluation

Objective olfaction was quantified using the Sniffin' sticks (Burgardt, Wedel, Germany).¹⁴ The test is comprised of odor threshold, odor discrimination and odor identification. Odor threshold for n-butanol was assessed using a single-staircase procedure with three alternative choices. Only one of the three pens contained an odor, and subjects had to correctly detect the odor-containing pen. The odor discrimination test involved triplets of pens, two with the same scent and one with a different scent. Subjects were required to identify which pen contained the "different" scent. Odor identification consisted of 16 common odors that were presented individually with multiple choice options. The three component scores have a maximum of 16 and are summed to give a composite TDI score of 1–48 with higher scores representing superior olfaction.^{14,15} Olfactory-specific QOL was assessed using the 17-item Questionnaire of Olfactory Disorders (QOD-NS). Each item is scored 0–3 for a total score of 0–51. Higher scores indicate decreased QOL.¹⁶

Radiologic Evaluation

Cross-sectional analysis of CT scans was performed using OsiriX MD imaging software (Pixmeo, Bernex, Switzerland).¹⁷ Digital Imaging and Communication in Medicine (DICOM) images were uploaded and 2D segmentation was performed manually in OsiriX using the bone window in the coronal plane. The olfactory cleft was considered to start at the anterior most olfactory filament (the anterior plane of middle turbinate) and end just anterior

to the face of the sphenoid sinus. The lateral boundary of the olfactory cleft was the attachment of the middle and/or superior turbinates. The roof of the olfactory cleft was the cribriform plate and the floor was an imaginary line drawn 1 cm inferior to the cribriform. Anterior, middle and posterior 2D cross sectional areas (CSA) were demarcated in the coronal plane using the axial and sagittal planes for reference of anatomic landmarks. The anterior CSA was represented by anterior-most section of olfactory cleft, the middle CSA was drawn at the posterior globe, and the posterior CSA was taken just anterior to the sphenoid sinus. The quantitative opacification was determined using a pixel-based analysis on OsiriX. Utilizing 10 scans chosen at random, the mucosa of the inferior turbinate was used as a surrogate for soft tissue structures based on Hounsfield units (HU), and it had a mean value of 84 HU with SD of 91.5. We thus defined soft tissue as any pixel from -183 to $+267$ HU (the mean $\pm$ 2SD). Bone was defined as $>2SD$ (>267 HU) above soft tissue and air was defined as $<2SD$ (-1024 to -183 HU) below soft tissue. All pixels in HU range of bone were excluded. Pixels representing soft tissue were then divided by all remaining pixels (soft tissue + air) to determine the percentage opacification for each section (Supplemental Figure 1). The average opacification of the OC was then determined by averaging across the three sections. Each scan was reviewed by one of two trained research personnel (C.L. and E.M.) who were blinded to olfactory function. Scans were randomly divided between the two reviewers. An intraclass correlation coefficient of 0.828 (95% CI: 0.656–0.918) was established based on grading of 10 scans prior to randomly dividing the remaining scans.

Statistical Analysis

Statistical analysis was performed using SPSS 24.0 (IBM Corporation, Armonk, NY). Descriptive statistics were performed for demographics, comorbidities, QOL, objective olfaction, and CT opacification measures. Correlations were assessed using either two-sided Pearson's or Spearman correlation coefficients (r) based on linearity/non-linearity of associations on scatter plots. Differences between continuous variables and those with and without various baseline characteristics were evaluated using Welch's t-test. Chi squared tests or Fisher's exact tests when any cells had an expected value less than 5 were used to determine differences between categorical variables. A conventional 0.050 type-I error probability (p -value) determined statistically significant associations.

RESULTS

Study population

The overall study cohort contained 148 CRS patients with a mean age of 50 years and a gender distribution of 51.4% female and 48.6% male. The control population had a similar age and gender distribution to the CRS cohort ($p=0.769$ and $p=0.640$, respectively). Table 1 shows the demographic characteristics and medical comorbidities of the CRS cohort. A total of 73 (49.3%) patients had CRSsNP and 75 (50.7%) were classified as CRSwNP, with 43.2% having comorbid asthma. The mean ($\pm$ standard deviation (SD)) total Sniffin' Sticks TDI test score for the cohort was $22.8(\pm 9.4)$, mean SNOT-22 score was $49.3(\pm 20.6)$, and mean Lund-Mackay score was $13.6(\pm 5.1)$. The mean olfactory cleft opacification was 63.7% ($\pm 26.7\%$) in the CRS population and 47.1% ($\pm 10.6\%$) in the control population ($p<0.001$). The difference between cases and controls was driven by opacification in the CRSwNP

group; whereas no difference in OC opacification was seen between CRSsNP and controls (Table 2). The OC opacification of the anterior, middle and posterior sections is shown in Table 2 for each group (Supplemental Figure 2). In the CRS population, OC opacification was significantly higher in patients with CRSwNP (77.6% vs. 49.5%; $p<0.001$), those who had asthma (71.2% vs. 58.1%; $p=0.003$), and in those with AERD (90.0% vs. 60.6%; $p<0.001$; Table 3).

Overall CRS cohort OC opacification and olfaction

In the CRS cohort, the average opacification of the OC was significantly correlated with objective olfaction as measured by the total TDI score ($r=-0.520$; $p<0.001$) (Figure 1), as well as individual threshold, discrimination and identification scores (Table 4). These results indicate that as opacification of the olfactory cleft increases, olfactory function declines. This significant correlation was observed in anterior, middle, and posterior sections across total TDI scores, as well as individual threshold, discrimination and identification scores. A significant correlation was also observed between average OC opacification and QOD-NS score ($r=0.374$; $p<0.001$), indicating that as OC opacification increases, olfactory-specific QOL worsens.

CRS by polyp status OC opacification and olfaction

The overall CRS cohort was then analyzed separately by polyp status (Table 5). Patients with CRSwNP demonstrated significant correlations between OC opacification and total TDI scores ($r=-0.464$; $p<0.001$). Significant correlations were also seen between total opacification and threshold, discrimination, identification, and QOD-NS scores. However, in patients with CRSsNP, no correlation was seen between OC opacification and total TDI score ($r=-0.143$; $p=0.229$) (Figure 2). Findings for anterior, middle, and posterior cross-sections generally mirrored the overall average findings for both CRSwNP and CRSsNP subgroups.

Lund-Mackay CT score and olfaction

Across the overall CRS cohort, total Lund-Mackay score correlated with all olfactory measures, including TDI ($r=-0.497$; $p<0.001$), threshold ($r=-0.379$; $p<0.001$), discrimination ($r=-0.450$; $p<0.001$), identification ($r=-0.458$; $p<0.001$) and QOD-NS ($r=0.369$; $p<0.001$). When stratified by polyp status, overall Lund Mackay correlations were significant for TDI in both the CRSsNP ($r=-0.300$; $p=0.010$) and CRSwNP ($r=-0.271$; $p=0.019$) groups, with the former being stronger compared with the correlation observed for OC opacification and the latter being weaker (Table 6, Supplemental Figure 3). The Lund-Mackay score was then broken down into component scores. When the individual components of the Lund Mackay score were stratified by polyp status, the results of the subgroups generally paralleled each other with the exception of the maxillary and sphenoid sinuses. In CRSsNP, the maxillary sinus opacification showed a stronger correlation with TDI than CRSwNP ($r=-0.369$; $p<0.001$ vs. $r=-0.037$; $p=0.755$). In the sphenoid sinus, the opposite was observed, with the CRSsNP showing a weaker correlation with TDI than the CRSwNP group ($r=-0.162$; $p=0.171$ vs. $r=-0.295$; $p=0.010$; Table 6).

DISCUSSION

Results from this study confirm that in patients with CRS there is a significant correlation between the degree of OC opacification visible on CT scan and a patient's olfactory function as assessed by psychophysical testing and olfactory-specific QOL. However, this relationship is largely driven by the correlation seen in the CRSwNP subgroup. We were unable to show any significant correlation between OC opacification and objective olfaction in the CRSsNP subgroup. These findings contradict results from our smaller, pilot study that did find significant moderate correlation in the CRSsNP subgroup.¹¹ Instead, our current findings more closely mimic results from an earlier study that utilized identification testing and patients enrolled from a single institution.¹² In both the earlier study and the current study, the correlation between Lund-Mackay scores and olfaction was stronger in the CRSsNP group than the correlation between OC opacification and olfaction.¹²

This study is not necessarily designed to answer the question regarding why OC opacification correlates with olfactory function in CRSwNP but not CRSsNP subgroups. However, one might speculate that differing mechanisms of disease may be present. CRSwNP is typically considered a diffuse inflammatory disease characterized by increased type 2-mediated cytokine expression.¹⁸ The degree to which this mucosal inflammation is present in the olfactory cleft dictates to a large extent the degree of olfactory dysfunction experienced by the patient. In some ways, CRSsNP is a more heterogeneous disease and may have a mixed inflammatory profile.¹⁹ Furthermore, CRSsNP can at times be reflective of underlying ostial blockage and may be more patchy or localized in nature.²⁰ For most patients with CRSsNP, it appears that direct mucosal inflammation in the OC (as determined by CT) is not an important predictor of olfactory function, suggesting some other mechanism to explain olfactory loss in these patients²¹. In fact, we did not see a notable difference between the amount of OC opacification in CRSsNP and control subjects of similar age and gender.

The non-CRS control population was included in order to serve as a reference for baseline OC opacification in a non-CRS population matched by age and gender. There are several caveats worth keeping in mind with regard to this non-CRS control population. First, these individuals are confirmed to not have CRS as evidence by complete absence of inflammation visible on CT scan in any sinus. Additionally, it is important to point out that the baseline average OC opacification in this group was 47.1% using our methods. On the surface, one might expect this percentage to be much closer to zero. However, soft tissue normally lines boundaries of the OC (ie medial turbinate and septum) and this soft tissue is visible on CT scan even in controls. Therefore, one should expect a non-zero degree of opacification, which reflects the presence of this mucosal lining and inter-individual differences in the bony width of the olfactory cleft. Comparing the CRS group to the controls thus allows these "baseline" differences to be appreciated. The fact that the CRSsNP group was not appreciably different than the control group with regard to OC opacification is a novel finding which was not entirely expected.

Considering both the OC opacification and Lund-Mackay sinus opacification data concurrently offers some interesting insights. For patients with CRSwNP, the degree of

opacification of the OC is a stronger predictor of olfactory function than overall sinus opacification. This suggests that treatments which directly impact inflammation within the olfactory cleft may be more efficacious for management of smell loss. Treatment strategies would include topical anti-inflammatory medications instilled directly into the olfactory cleft or systemic medications that would perfuse to olfactory mucosa, such as oral corticosteroids or systemic biologics. For CRSsNP, direct instillation of corticosteroids into the olfactory cleft may not have the same impact. A greater understanding of the underlying mechanisms that drive olfactory loss in CRSsNP would be necessary to understand whether any specific systemic medication would be efficacious. Lastly, it is worth pointing out that CRSwNP and CRSsNP are not always exclusive, discrete categories. On a molecular inflammatory level, some patients with CRSsNP may closely resemble CRSwNP patients and this could explain some discrepancy across prior studies, if for example, one cohort contained a higher proportion of CRSsNP patients with a type-2 inflammatory profile.¹⁹ Future studies that characterize patients on a biomolecular level would likely give even greater insights.

This study evaluated opacification averaged across the entire olfactory cleft, as well as anterior, middle, and posterior sections. The reasoning behind this method was to determine whether differences existed across regions. One could hypothesize that anterior opacification might correlate more strongly with anterograde testing as done in this study. However, we did not find compelling evidence that any specific anatomic site was more important for olfactory function. This was true for TDI and QOD-NS, the latter of which presumably represents real-world olfactory-specific QOL impacts. At present, determining CT opacification is a manual process that is time intensive and requires specialized software and training. Considering data from the present study and past investigations, it would be reasonable to only utilize the anterior cross-section as a proxy for the entire olfactory cleft in future studies, particularly those not interested in taste, flavor, or retrograde olfaction.^{11,12}

Strengths of this study include a relatively large sample size, prospective design, inclusion of multiple centers spread across North America, and utilization of more comprehensive measures of olfactory function, including TDI and sinus-specific QOL. However, there are a number of caveats worth mentioning. The strength of correlation between OC opacification and TDI is moderate, suggesting that other factors impact olfaction in patients with CRS. This should not be surprising considering that CT is assessing just a small portion of the olfactory pathway and that non-CRS related factors may impact TDI score, such as age and cognitive function. The correlation between TDI and QOD-NS is even weaker, suggesting again that other factors often influence how a patient quantifies QOL impacts. The study was carried out at tertiary rhinology clinics and thus includes a higher proportion of patients with severe disease than might be seen across the entire population, as evidenced by the high number with prior sinus surgery. No biomolecular data is available for these patients, so hypotheses based on underlying inflammatory profile remains speculative at present. Olfactory data was also not available for controls, so correlation between TDI and OC opacification could not be done in this subgroup. Lastly the study data presented is cross-sectional and represents an association at a single point in time. Therefore, one cannot definitely conclude that the OC opacification seen on CT is the cause of olfactory loss. Data which tracks OC opacification and olfactory function longitudinally after treatment would

provide additional insight into the relationship between these measures in each of these subgroups.

CONCLUSION

Olfactory dysfunction in CRS likely occurs via multiple mechanisms. In CRSwNP patients, opacification of the olfactory cleft is more strongly associated with olfaction than adjacent sinus opacification. This is in contrast to CRSsNP patients where olfactory dysfunction appears to be more strongly associated with sinus, rather than olfactory cleft opacification. The exact relationship between CT opacification, inflammatory conditions in the local microenvironment, and clinical response to various medical and surgical therapies merit further study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1:

Correlations Between Average Olfactory Cleft Opacification and TDI score.

Total TDI score vs. total olfactory cleft opacification. TDI= composite of threshold (T), discrimination (D) and identification(I).

Figure 2:

Correlations Between Average Olfactory Cleft Opacification and TDI score by Nasal Polyp Status.

Total TDI score vs. total olfactory cleft opacification by Nasal Polyp Status. TDI= composite of threshold (T), discrimination (D) and identification (I); CRSwNP=chronic rhinosinusitis with nasal polyposis; CRSsNP=chronic rhinosinusitis without nasal polyposis.

Table 1:

Baseline Characteristics of the study cohort.

	All CRS (n=148)	CRSsNP (n=73)	CRSwNP (n=75)	p value
Demographics				
Age (mean[SD], y)	50 [16.1]	48 [17.3]	52[14.8]	0.209
Sex, no. (%)				0.619
Men	72(48.6%)	34(46.6%)	38(50.7%)	
Women	76(51.4%)	39(53.4%)	37(49.3%)	
Race, no. (%)				0.025
White	136(91.9%)	71(97.3%)	65(86.7%)	
African American	9(6.1%)	1(1.4%)	8(10.7%)	
American Indian/Alaskan native	1 (0.7%)	0(0%)	1(1.3%)	
Asian	1(0.7%)	0(0%)	1(1.3%)	
Other	1(0.7%)	1(1.4%)	0(0%)	
Ethnicity, no. (%)				0.717
Hispanic/Latino	7(4.7%)	4(5.5%)	3(4.0%)	
Non-Hispanic/Latino	141(95.3%)	69(94.5%)	72(96.0%)	
Comorbidities				
Asthma, no. (%)	64(43.2%)	21(28.8%)	43(57.3%)	<0.001
AERD, no. (%)	16(10.8%)	02(0%)	16(21.3%)	<0.001
Allergies by testing, no. (%)	73(49.3%)	26(25.6%)	47(62.7%)	0.001
COPD, no. (%)	7(4.7%)	5(6.8%)	2(2.7%)	0.272
Depression, no. (%)	49(33.1%)	24(32.9%)	25(33.3%)	0.953
Fibromyalgia, no. (%)	3(2%)	3(4.1%)	0(0%)	0.117
Autoimmune Disease, no. (%)	18(12.2%)	11(15.1%)	7(9.3%)	0.286
Diabetes, no. (%)	16(10.9%)	9(12.5%)	7(9.3%)	0.538
Smoking status, Packs per day, mean[SD]	0.1[0.3]	0.1[0.3]	0.1[0.3]	0.688
Alcohol use, drinks/wk, no., mean[SD]	2.4[4.7]	2.4[5.1]	2.4[4.3]	0.372
Olfaction and CRS metrics				
TDI (mean[SD])	22.8[9.4]	27.9[6.9]	17.7[8.8]	<0.001
SNOT-22 (mean[SD])	49.3[20.6]	45[20.8]	53.4[19.6]	0.012
Lund Mackay (mean[SD])	13.6[5.1]	10.7[4.3]	16.3[4.3]	<0.001

CRS = Chronic rhinosinusitis; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP=chronic rhinosinusitis with nasal polyposis; SD=standard deviation; AERD: Aspirin-exacerbated respiratory disease; COPD=chronic obstructive pulmonary disease; SNOT-22=22-item Sino-Nasal Outcome Test; TDI= composite of threshold(T), discrimination(D) and identification(I); CT=computed tomography; y=years

Table 2:

Olfactory cleft opacification (%).

	Anterior Opacification	Middle Opacification	Posterior Opacification	Average Opacification
All CRS, mean [SD]	57.3[31.3]	63.4[29.2]	70.8[27.6]	63.7[26.7]
CRSsNP, mean[SD]	41.2[24.2]	49.9[25.4]	57.4[26.1]	49.5[22.3]
CRSwNP, mean[SD]	72.9[29.4]	76.5[26.8]	83.8[22.4]	77.6[23.3]
Controls, mean[SD] (n=30)	40.4[12.2]	46.0[12.9]	54.8[16.5]	47.1[10.6]
p (between CRSsNP and CRSwNP)	<0.001	<0.001	<0.001	<0.001
p (between all CRS and Controls)	<0.001	<0.001	<0.001	<0.001
p (between CRSsNP and Controls)	0.839	0.308	0.541	0.459
p (between CRSwNP and Controls)	<0.001	<0.001	<0.001	<0.001

CRS = Chronic rhinosinusitis; SD = standard deviation; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis

Table 3:

Clinical characteristics of the CRS cohort and olfactory cleft opacification.

	Yes, mean%[SD]	No, mean %[SD]	p value
Male	63.4%[25.5]	64.0%[28.0]	0.894
Nasal Polyposis	77.6%[23.3]	49.5%[22.3]	<0.001
Asthma	71.2%[26.5]	58.1%[25.7]	0.003
AERD	90.0%[15.3]	60.6%[26.1]	<0.001
Allergic Rhinitis	67.0%[27.6]	60.9[25.8]	0.173
Depression	61.9%[26.6]	64.7%[26.9]	0.545
Diabetes Mellitus	71.3%[27.2]	63.0%[26.6]	0.264
Smoking History	59.0%[33.5]	64.0[26.5]	0.735
Oral Steroid Dependency	61.8%[23.2]	63.9[27.1]	0.764
Previous Sinus Surgery	66.3%[28.9]	61.5[24.7]	0.281

SD=standard deviation; AERD: Aspirin-exacerbated respiratory disease

Table 4:

Relationship between olfactory cleft opacification and olfactory measures.

	Anterior Opacification		Middle Opacification		Posterior Opacification		Average Opacification	
	r	p	r	p	r	p	r	p
Threshold	-0.321	<0.001	-0.330	<0.001	-0.361	<0.001	-0.368	<0.001
Discrimination	-0.484	<0.001	-0.411	<0.001	-0.416	<0.001	-0.478	<0.001
Identification	-0.505	<0.001	-0.438	<0.001	-0.407	<0.001	-0.493	<0.001
TDI-total	-0.513	<0.001	-0.458	<0.001	-0.455	<0.001	-0.520	<0.001
QOD-NS	0.396	<0.001	0.332	<0.001	0.291	<0.001	0.374	<0.001

TDI total=composite of threshold(T), discrimination(D) and identification(I); QOD-NS=short modified version of the Questionnaire of Olfactory Disorders.; r=correlation coefficient (either Pearson or Spearman).

Table 5:

Relationship between olfactory cleft opacification and olfactory measures by nasal polyp status.

	Polyp Status		Threshold	Discrimination	Identification	TDI total	QOD-NS
Anterior Opacification	CRSsNP	r	-0.138	-0.088	-0.141	-0.160	0.282
		p	0.243	0.457	0.232	0.176	0.016
	CRSwNP	r	-0.233	-0.422	-0.452	-0.430	0.277
		p	0.044	<0.001	<0.001	<0.001	0.016
Middle Opacification	CRSsNP	r	-0.140	0.004	-0.044	-0.079	0.211
		p	0.238	0.971	0.710	0.506	0.073
	CRSwNP	r	-0.291	-0.401	-0.432	-0.430	0.218
		p	0.011	<0.001	<0.001	<0.001	0.061
Posterior Opacification	CRSsNP	r	-0.166	-0.035	-0.120	-0.140	0.088
		p	0.160	0.768	0.313	0.236	0.458
	CRSwNP	r	-0.342	-0.381	-0.319	-0.383	0.233
		p	0.003	0.001	0.005	0.001	0.044
Average Opacification	CRSsNP	r	-0.168	-0.044	-0.115	-0.143	0.217
		p	0.155	0.711	0.334	0.229	0.066
	CRSwNP	r	-0.317	-0.448	-0.454	-0.464	0.273
		p	0.006	<0.001	<0.001	<0.001	0.018

CRS = Chronic rhinosinusitis; SD = standard deviation CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; QOD-NS=short modified version of the Questionnaire of Olfactory Disorders. r=correlation coefficient (either Pearson or Spearman). TDI= composite of threshold(T), discrimination(D) and identification(I)

Table 6:

Relationship between Lund-Mackay score and olfactory measures.

	Polyp Status		Threshold	Discrimination	Identification	TDI total	QOD-NS
LM Score Total	CRSSNP	r	-0.320	-0.099	-0.296	-0.300	0.179
		p	0.006	0.405	0.011	0.010	0.131
	CRSwNP	r	-0.227	-0.342	-0.235	-0.271	0.285
		p	0.050	0.003	0.042	0.019	0.013
Maxillary	CRSSNP	r	-0.347	-0.247	-0.314	-0.369	0.347
		p	0.003	0.035	0.007	0.001	0.003
	CRSwNP	r	-0.061	-0.026	-0.071	-0.037	0.087
		p	0.602	0.826	0.547	0.755	0.456
Anterior Ethmoid	CRSSNP	r	-0.318	-0.066	-0.225	-0.274	0.173
		p	0.006	0.578	0.055	0.019	0.143
	CRSwNP	r	-0.158	-0.207	-0.195	-0.195	0.140
		p	0.175	0.074	0.093	0.094	0.233
Posterior Ethmoid	CRSSNP	r	-0.251	-0.156	-0.284	-0.239	0.324
		p	0.032	0.188	0.015	0.041	0.005
	CRSwNP	r	-0.181	-0.265	-0.172	-0.214	0.373
		p	0.121	0.021	0.139	0.066	0.001
Frontal	CRSSNP	r	-0.184	-0.234	-0.300	-0.267	0.156
		p	0.120	0.047	0.010	0.022	0.188
	CRSwNP	r	-0.154	-0.358	-0.291	-0.302	0.107
		p	0.186	0.002	0.011	0.008	0.363
Sphenoid	CRSSNP	r	-0.118	-0.106	-0.161	-0.162	0.149
		p	0.322	0.372	0.173	0.171	0.209
	CRSwNP	r	-0.283	-0.319	-0.232	-0.295	0.097
		p	0.014	0.005	0.045	0.010	0.406

LM=Lund-Mackay score; TDI= composite of threshold(T), discrimination(D) and identification(I); QOD-NS=short modified version of the Questionnaire of Olfactory Disorders. r=correlation coefficient (either Pearson or Spearman).