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Superior turbinate eosinophilia predicts olfactory decline in patients with chronic rhinosinusitis

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ABSTRACT

Background: Predicting postoperative olfactory decline in patients with chronic rhinosinusitis (CRS) remains a considerable challenge.

Objective: To evaluate patterns of postoperative olfactory function in patients with CRS and explore potential predictors of postoperative olfactory decline.

Methods: A total of 76 patients with CRS electing endoscopic sinus surgery (ESS) were enrolled in this prospective study. Olfaction was assessed with Sniffin' Sticks preoperatively and 3 months postoperatively. Preoperative peripheral venous blood and superior turbinate at surgery were collected for eosinophil quantification. Olfactory cleft was evaluated by computed tomography and endoscopy. Postoperative olfactory decline was defined by a decrease in threshold-discrimination-identification (TDI) score more than 0 point. Multivariable logistic regression analysis was conducted to identify potential predictors associated with postoperative olfactory decline in TDI score.

Results: A total of 30.26% of patients with CRS (23/76) presented with olfactory decline 3 months post-ESS. Patients with CRS with olfactory decline showed significantly higher preoperative tissue eosinophils ($P < .001$), blood eosinophil count ($P = .002$), blood eosinophil percentage ($P = .009$), and preoperative TDI scores ($P = .017$) than patients with CRS without olfactory decline. After adjusting for patient demographics and comorbidities, the preoperative tissue eosinophilia was significantly associated with patients with CRS with postoperative olfactory decline (odds ratio = 1.103; $P = .038$). An absolute count of 23.5 eosinophils per high-power field in superior turbinate was the best predictor of olfactory decline with the highest area under the receiver operating characteristic curve of 0.901.

Conclusion: Superior turbinate eosinophilia is highly associated with olfactory decline in patients with CRS 3 months after ESS.

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Introduction

Chronic rhinosinusitis (CRS)—associated olfactory dysfunction is the most frequent cause of smell loss, accounting for 14–30% of all cases.^{1–3} Furthermore, olfactory dysfunction has been reported to affect up to 83% of patients with CRS irrespective of subtype.⁴ It is highly associated with poor quality of life, increased medication use, and reduced economic productivity.^{5–7} Endoscopic sinus surgery (ESS) is a common therapeutic option to treat medically refractory olfactory dysfunction in patients with CRS.^{1,8,9} Indeed, the literature supports that ESS is associated with a high success rate in improving olfaction in patients with CRS, especially those

with chronic rhinosinusitis with nasal polyps.^{10,11} Despite these successes, predicting individual patient response remains a challenge because of the heterogeneous nature of CRS.¹²

Recent studies suggest that some patients with CRS may experience early olfactory improvement followed by a subsequent olfactory decline during follow-up.^{13,14} A series of factors in patients with CRS, such as eosinophilia, osteitis, and high level of type 2 helper T-cell (T_H2) cytokines, have been identified to be associated with olfactory deterioration 3 to 12 months after medical treatment or ESS.¹⁵ A study by Oka et al found that olfactory disorders in eosinophilic CRS showed transient improvement that deteriorated as time passed postoperatively.¹⁶ Notably, the level of eosinophils within the olfactory cleft significantly and positively correlated with the degree of olfactory dysfunction in patients with CRS both pre- and postoperatively.^{17–19} Endoscopic sinus surgery could dramatically decrease the level of eosinophils in patients with CRS which might partly contribute to the olfactory improvement.²⁰ Given the refractory nature of the type 2 immune response (eg, eosinophilic inflammation),^{21,22} an eosinophilic phenotype of CRS appears to be associated with this mid to late olfactory decline after ESS.^{16,23}

Based on the confluence of these findings, we hypothesized that the eosinophilic phenotype may be associated with postoperative olfactory decline and that analysis of superior turbinate eosinophilia preoperatively may aid in selecting which patients are at risk for this decrement in function. This study aimed to to analyze a variety of preoperative variables in patients undergoing ESS, including superior turbinate eosinophil levels, and determine whether any could be used to predict postoperative olfactory decline.

Methods

Patients

This study was approved by the institutional review board. Patients were recruited from January 1, 2016, through December 31, 2018. Biopsy specimens of the superior turbinate were obtained from patients with CRS undergoing ESS.^{17,24} Inclusion criteria included patients diagnosed as having CRS according to the International Consensus Statement on Allergy and Rhinology:

Rhinosinusitis.²⁵ Exclusion criteria included patients with cystic fibrosis, ciliary dysfunction, autoimmune disease, immunodeficiency, or a history of exposure to antibiotics or any topical/systemic steroids for minimum 4 weeks. Demographic characteristics were further collected, and the presence of environmental allergy was diagnosed by positive skin test results or history. Written informed consent was obtained from all the patients. The flow diagram of the study design was given in Figure 1.

Qualification of Tissue and Blood Eosinophils

The olfactory mucosa specimens were collected from the anterior part of the superior turbinate using a through-cut forceps during the surgery from patients with CRS. Tissue biopsy specimens were immediately formalin fixed and then paraffin embedded for routine hematoxylin and eosin staining to quantify tissue eosinophilia. The number of eosinophils per high-power field (HPF) was calculated according to our previous study.²⁶ Briefly, 5 fields were randomly selected per slide and scored by 2 independent observers. An eosinophilic phenotype of CRS was defined when the frequency of tissue eosinophils exceeded 10% of the total infiltrating cells per HPF.²⁶ A total of 5 mL of peripheral venous blood was collected from each participant before surgery for complete blood cell count by an automated analyzer (Beckman Coulter, Miami, Florida). The blood eosinophil count and percentage were recorded.

Olfactory Function Test and Definitions of Olfactory Outcome after ESS

Sniffin' Sticks (Burghardt, Wedel, Germany) were utilized to evaluate olfactory threshold (OT), olfactory discrimination (OD), olfactory identification (OI), and the overall composite scores (TDI; composite score of threshold, discrimination, and identification).²⁷ Sniffin' Sticks have been evaluated in healthy Chinese adults and various patients with olfactory dysfunction in our previous studies.^{28–30} Sniffin' Sticks is suitable for application in the Chinese population to differentiate normosmia from hyposmia and anosmia.³¹ Standard administration was performed according to the manufacturer's instructions. For the testing, odors were presented in felt-tip pens when the cap was removed. The felt tip was positioned approximately 2 cm in front of the participant's nostrils

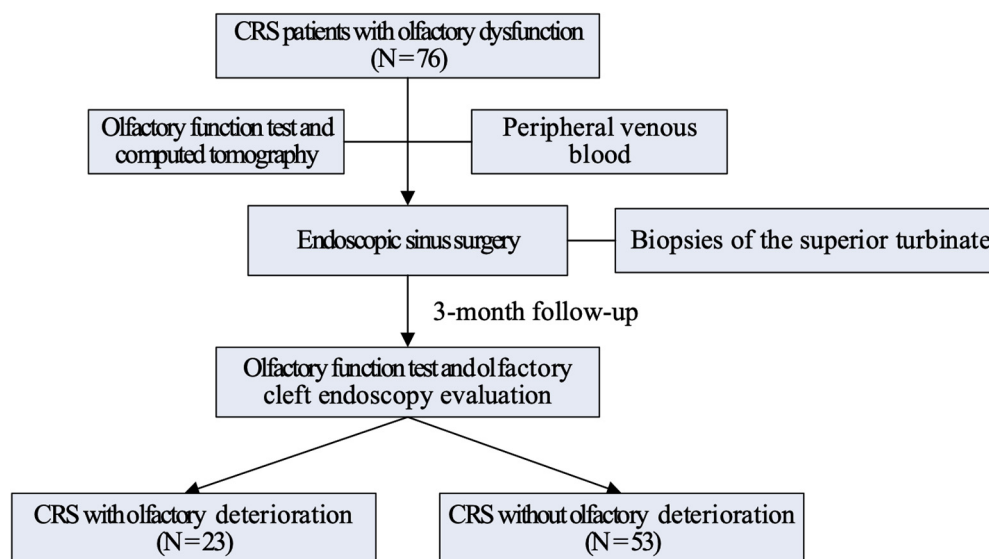


Figure 1. Flow diagram of the study design. CRS, chronic rhinosinusitis.

Table 1
Comparison of Baseline Characteristics

Characteristic	CRS with olfactory decline (N = 23)	CRS without olfactory decline (N = 53)	P value
Age (year), mean $\pm$ SD, year	46.09 $\pm$ 12.16	51.06 $\pm$ 14.80	.183
Men, n (%)	14 (60.87)	34 (64.15)	.785
Disease duration (year), mean $\pm$ SD, year	3.00 (1.00–10.00)	2.00 (1.00–4.00)	.079
Environmental allergy, n (%)	9 (39.13)	30 (56.60)	.161
Comorbid asthma, n (%)	3 (13.04)	5 (9.43)	.638
CRSwNP, n (%)	9 (39.13)	21 (39.62)	.968
AERD, n (%)	2 (8.70)	0 (0)	.163
Smoker, n (%)	2 (8.70)	12 (22.64)	.150
Previous sinus surgery, n (%)	3 (13.04)	11 (20.75)	.426
Preoperative olfactory cleft CT score, median (IQR)	2.00 (1.00–5.00)	3.00 (1.00–6.00)	.536
Presence of OC lesions before surgery	16 (69.57)	29 (54.72)	.226
Preoperative TDI score, median (IQR)	24.50 (19.00–29.00)	18.00 (9.00–25.50)	.017
Postoperative TDI score, median (IQR)	24.00 (18.00–27.25)	20.00 (15.00–27.75)	.699

Abbreviations: AERD, aspirin-exacerbated respiratory disease; CRS, chronic rhinosinusitis; CRSwNP, chronic rhinosinusitis with nasal polyps; CT, computed tomography; IQR, interquartile range; OC, olfactory cleft; SD, standard deviation; TDI, threshold-discrimination-identification.

NOTE. Smoker included current smokers; OC lesions included mucosal edema, polyps, and adhesion; previous sinus surgery included endoscopic sinus surgery for chronic rhinosinusitis.

for approximately 3 seconds. Briefly, the OT test was performed using different dilutions of n-butanol in a single-staircase, triple-forced choice procedure. The OD test used triplets of pens presented in random order with 2 containing the same odorant and the third with a different odorant. The OI test utilized 16 odorants presented at suprathreshold intensity using multiple-choice procedure. All subjects were blindfolded to avoid visual identification of odorant-containing pens. The 3 test scores were reported independently. Discrimination and identification were scored from 0 to 16, and the threshold was scored from 1 to 16. The overall results were combined and reported as TDI score which ranged from 1 to 48, with higher scores indicating superior olfactory performance. A TDI score ≥ 31 , 16–30, and ≤ 15 indicated normosmia, hyposmia, and anosmia, respectively.²⁹

Postoperative olfactory change 3 months after ESS compared with the baseline was calculated. The postoperative olfactory outcomes of CRS were defined as follows: CRS with olfactory decline including only a decreased olfactory score and clinical deterioration (a decreased TDI score >0 point); patients with clinical deterioration of olfaction indicated that the decrease of the olfactory score had a clinical significance and the patients felt the change in symptoms. Chronic rhinosinusitis without olfactory decline including only an increased olfactory score and olfactory improvement (an increased TDI score of ≥ 0 point).³² The definition of olfactory outcome was shown in eTable 1.

Evaluation of Olfactory Cleft by Computed Tomography and Endoscopy

Computed tomography (CT) scans were obtained in every participant before surgery, and olfactory cleft opacification was graded according to the following criteria.³³ The borders of the olfactory cleft in CT were defined as follows: anterior (anterior attachment of the middle turbinate); posterior (anterior wall of the sphenoid sinus); medial (nasal septum); and lateral borders (middle and superior turbinate). The superior border was the skull base,

and the inferior border was the inferior portion of the middle turbinate. The olfactory cleft was divided into anterior and posterior divided by the anterior end of the superior turbinate. The anterior and posterior olfactory cleft opacifications were graded separately on a scale of 0–4 by the ratio of the opacified area to the whole area of the olfactory cleft, with 0 (no opacification), 1 ($\leq 25\%$), 2 (25–50%), 3 (50–75%), and 4 ($>75\%$) (eTable 2).³³ The olfactory cleft opacification score, which was calculated as the sum of the anterior olfactory cleft score and the posterior olfactory cleft score, ranged from 1 to 8. During surgery and 3 months after surgery, the olfactory cleft was endoscopically evaluated to confirm whether lesions were present, including mucosal edema, polyps, and adhesion.

Surgical Intervention and Postoperative Care

Bilateral ESS, including complete ethmoidectomy, sphenoidectomy, and opening of the maxillary sinus and frontal sinus, was performed under general anesthesia. For the treatment of the olfactory clefts, the superior meatus was opened to remove diseased mucosa, including polyps and edematous mucosa. Septoplasty and conchotomy of the middle turbinate were also performed. The surgical procedure to all the patients was performed by the same surgeon. Patients were treated with oral antibiotics (a dose of clarithromycin, 250 mg, twice a day) for 2 weeks after surgery. Topical nasal steroids (budesonide nasal spray, once a day) and saline irrigation (a dose of 250 mL, twice a day) were utilized for 3 months after surgery. Patients with an exacerbation of CRS during the follow-up received a 7-day course of cefuroxime (250 mg, twice a day). On the day of the postoperative assessment, no adjunctive treatments were used.

Statistical Analysis

For the patient demographic data, the two-sample *t* test was applied for continuous variables that followed a normal distribution. A nonparametric Mann-Whitney *U* test was applied for continuous

Table 2
Olfactory Outcome in Patients With CRS after ESS

Characteristic	CRS (N = 76)		CRS without olfactory decline (N = 53, 69.74%)	
	CRS with olfactory decline (N = 23, 30.26%)		Only an increased olfactory score	Clinical improvement
Olfactory outcome after ESS	Clinical deterioration	Only a decreased olfactory score	Only an increased olfactory score	Clinical improvement
Number of patients, n (%)	10 (13.16)	13 (17.11)	40 (52.63)	13 (17.11)

Abbreviations: CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery.

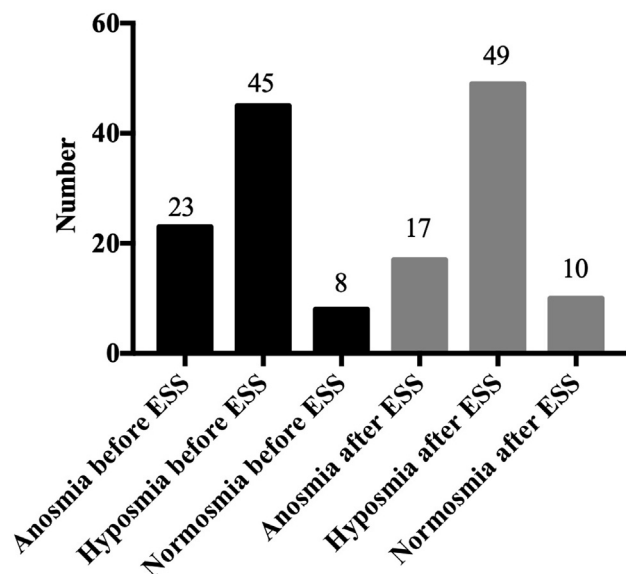


Figure 2. Patterns of olfactory dysfunction before and after ESS. ESS, endoscopic sinus surgery.

variables that did not follow a normal distribution. The one-sample Kolmogorov-Smirnov test was used to test whether a continuous variable was normally distributed. Categorical variables were compared using the χ^2 test. To identify variables associated with olfactory decline after adjusting for demographic factors and comorbidities, a multivariable logistic regression model was estimated by a forward stepwise procedure, using $P < .05$ and $P > .10$ from the Wald's test as entering and removing criteria, respectively. A receiver operating characteristic (ROC) curve, which is widely applied to assess the predictive value of clinical parameters, was generated to find the best cutoff point for each potential predictor of patients with CRS with olfactory decline after ESS. The best cutoff point was identified when the value of $(1 - \text{sensitivity})^2 + (1 - \text{specificity})^2$ was the smallest on the ROC curve. A P value of less than .05 was considered statistically significant. Tests were performed using SPSS statistical software version 17.0 (IBM, Armonk, New York).

Results

Patient Demographics

A total of 76 patients diagnosed as having CRS (30 with nasal polyps and 46 without nasal polyps) were enrolled in the study. Based on the olfactory outcome compared with the baseline during the 3-month follow-up, patients with CRS were classified into the following 2 groups: CRS with olfactory decline ($N = 23$, 30.26%) and CRS without olfactory decline ($N = 53$, 69.74%) (Table 1). The percentage of patients with different postoperative olfactory outcome was also presented in Table 2. The preoperative TDI scores were significantly higher in patients with olfactory decline as compared with those without ($P < .017$) (Table 1). No significant differences were found in the postoperative TDI score among groups ($P = .669$). No significant differences were observed among patients with or without olfactory decline with respect to age, sex, disease duration, environmental allergy, comorbid asthma, nasal polyps, preoperative olfactory cleft CT score, presence of olfactory cleft lesions, aspirin-exacerbated respiratory disease, smoking status, or previous sinus surgery (Table 1).

Patterns of Olfaction Among Patients With CRS before and after ESS

The patterns of olfaction in patients with CRS before and after ESS were indicated in Figure 2. The number of anosmia, hyposmia,

and normosmia in patients with CRS preoperatively was 23 (30.26%), 45 (59.21%), and 8 (10.53%), respectively. The number of anosmia, hyposmia, and normosmia in patients with CRS postoperatively was 17 (22.37%), 49 (64.47%), and 10 (13.26%), respectively. Among patients with CRS with olfactory decline, there were 10 patients with clinical deterioration and 13 patients with only a decreased olfactory score. Among patients with CRS without olfactory decline, there were 40 patients with only an increased olfactory score and 13 patients with clinical improvement. We further analyzed which subgroups did patients with CRS with olfactory decline originated from. After the 3-month follow-up, 23 patients with CRS with olfactory decline progressed from 3 patients with anosmia (13.04%), 18 patients with hyposmia (78.26%), and 2 patients with normosmia (8.70%).

Relationship Between Olfactory Function and Clinical Parameters Between the 2 Groups

Preoperative tissue eosinophils were also significantly higher in patients with olfactory decline as compared with those without decline (Table 3 and Fig 3) ($P < .001$). Similarly, both the preoperative blood eosinophil count and percentage were significantly higher in patients with olfactory decline compared with those without decline ($P = .002$ and $P = .009$, respectively) (Table 3). The eosinophilic phenotype of CRS was significantly higher in patients with CRS with olfactory decline than in those without olfactory decline ($P < .001$).

Multivariable Logistic Regression Analysis for Patients With CRS With Postoperative Olfactory Decline

After adjusting for age, sex, disease duration, environmental allergy, comorbid asthma, nasal polyps, smoking status, previous sinus surgery, preoperative TDI scores, and preoperative blood eosinophil count and percentage, the preoperative tissue eosinophilia was significantly associated with postoperative olfactory decline in patients with CRS (odds ratio [OR] = 1.103; 95% confidence interval [CI] = 1.084–2.152; $P = .038$).

Utility of Predictors for Patients With CRS With Postoperative Olfactory Decline

The ROC curve analysis of predictors for patients with CRS with olfactory decline was summarized (Table 4 and Fig 4). The

Table 3

Comparisons of Clinical Parameters Between CRS With or Without Olfactory Decline after ESS

Characteristic	CRS with olfactory decline (N = 23)	CRS without olfactory decline (N = 53)	P value
Preoperative tissue eosinophils, median (IQR)	56.00 (26.00–69.00)	12.00 (5.00–22.50)	<.001
Preoperative blood eosinophil count, median (IQR)	0.33 (0.14–0.59)	0.17 (0.09–0.29)	.002
Preoperative blood eosinophil percentage, median (IQR)	5.50 (1.90–8.40)	2.80 (1.70–4.20)	.009
Eosinophil phenotype of CRS, n (%)	19 (56.52)	17 (33.96)	<.001

Abbreviations: CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery; IQR, interquartile range.

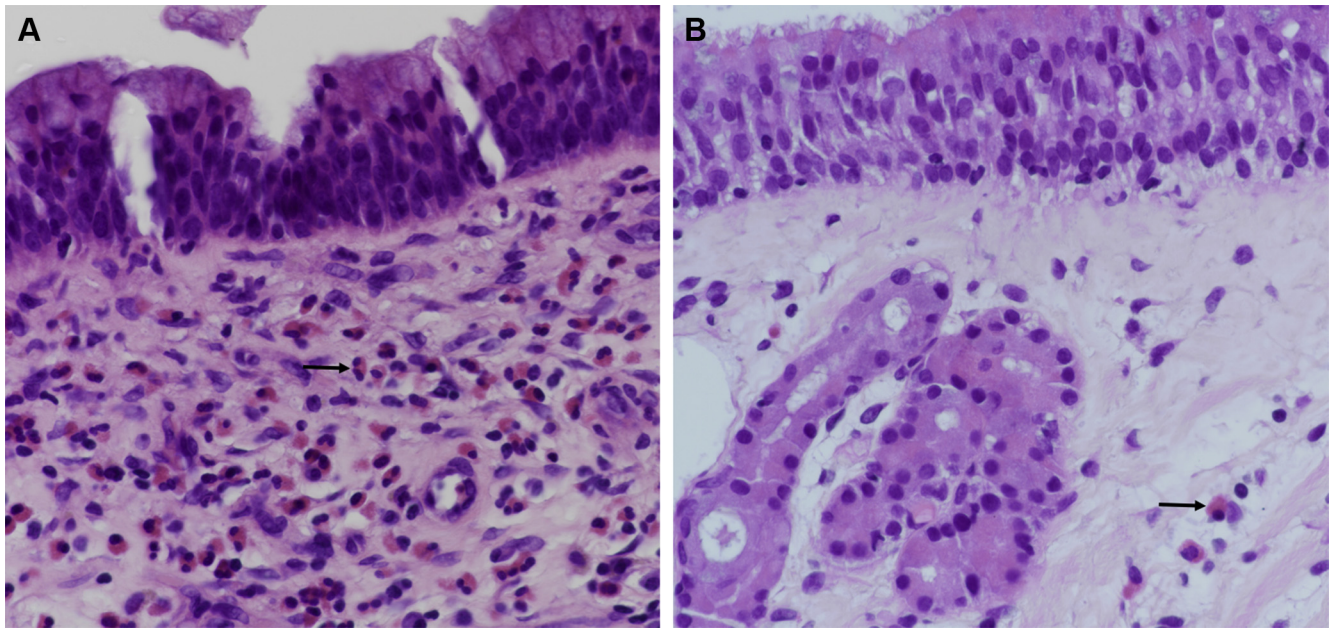


Figure 3. Representative histopathologic sections of superior turbinate biopsy specimens in patients with CRS with olfactory decline (A) and patients with CRS without olfactory decline (B) (hematoxylin-eosin, original magnification $\times 200$). (A) Superior turbinate infiltrated by a large number of eosinophils (indicated by arrows). (B) Superior turbinate infiltrated by a few eosinophils (indicated by arrows). CRS, chronic rhinosinusitis.

preoperative tissue eosinophil count had a higher accuracy as a predictor for patients with CRS with olfactory decline (AUC = 0.901) than did other variables, such as preoperative blood eosinophil count (AUC = 0.723), preoperative blood eosinophil percentage (AUC = 0.692), and preoperative TDI score (AUC = 0.675). The evaluation indexes for the cutoff point of each predictor were given in Table 4. A higher Youden index (sensitivity + specificity – 1) indicated a higher diagnostic predictive ability. As listed in Table 4, the preoperative tissue eosinophil count with a cutoff point greater than 23.50 indicated a higher predictive accuracy (specificity of 79.6%, sensitivity of 91.3%, and Youden index of 0.709), whereas a preoperative blood eosinophil percentage with a cutoff point greater than 3.65 indicated the lowest predictive accuracy (specificity of 67.3%, sensitivity of 60.9%, and Youden index of 0.282).

Discussion

In this study, we found that 30.26% of patients with CRS demonstrated olfactory decline 3 months after ESS and that patients with CRS with olfactory decline showed distinct clinical profiles when compared with patients with CRS without olfactory decline. Only one study by Kim et al reported the prevalence of postoperative olfactory deterioration in CRS, and approximately 23% of the patients with CRS experienced deteriorated olfactory function measured by butanol threshold test 6 months after

surgery.¹⁴ Difference in terms of methods of olfactory evaluation, definitions of olfactory outcome, and follow-up periods might account for the inconsistent results.

Furthermore, 78.26% of patients with CRS with olfactory decline progressed from patients with hyposmia and the rest (21.74%) progressed from patients with anosmia and normosmia, indicating patients with CRS with hyposmia tend to present with olfactory decline after treatment. We firstly reported the patterns of olfactory outcome in patients with CRS 3 months after ESS. It can be inferred that the olfactory function among patients with severe olfactory loss (eg, anosmia) or healthy subjects (eg, normosmic) had less possibility to fluctuate after treatment, which is mainly because of the severe damage or well preservation of the olfactory epithelium. Our findings were partly consistent with those of the previous studies indicating more profound preoperative olfactory dysfunction (eg, anosmic) has a higher likelihood of postoperative olfactory improvement, not olfactory decline.^{10–12}

Previous studies have thoroughly explored the postoperative olfactory outcome for CRS, and most of the studies focused on which subgroups of CRS gained more benefit from surgery in terms of olfaction.^{3,10} The olfaction in patients with CRS with noneosinophilic phenotypes, nasal polyps, preoperative olfactory dysfunction, no history of previous sinus surgery, good responsiveness to glucocorticosteroids, or high anterior olfactory cleft opacification score tended to improve to a greater degree after ESS.^{10,11,33,34} In this study, we found that patients with CRS with

Table 4
Predictors for Patients With CRS With Olfactory Decline after ESS

Predictor	AUC (95% CI)	P value	Cutoff value	Specificity, %	Sensitivity, %	Youden index
Preoperative tissue eosinophil count	0.901 (0.853–0.941)	.000	23.50	79.6	91.3	0.709
Preoperative blood eosinophil count	0.723 (0.635–0.813)	.002	0.23	67.3	69.6	0.369
Preoperative blood eosinophil percentage	0.692 (0.582–0.735)	.009	3.65	67.3	60.9	0.282
Preoperative TDI score	0.675 (0.583–0.746)	.017	20.75	61.2	73.9	0.351

Abbreviations: CI, confidence interval; CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery; TDI, threshold-discrimination-identification.

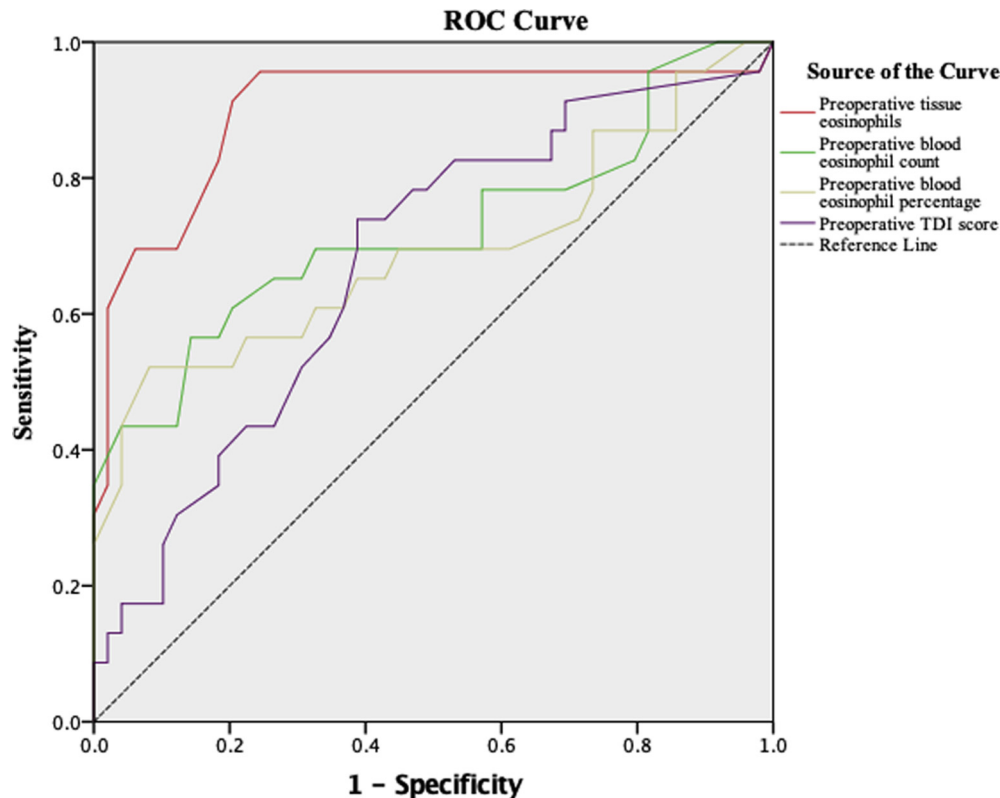


Figure 4. ROC curve for predictors of patients with CRS with postoperative olfactory decline. The preoperative tissue eosinophil count had a higher accuracy as a predictor for patients with CRS with olfaction decline (AUC = 0.901) than did other variables. CRS, chronic rhinosinusitis; ROC, receiver operating characteristic; TDI, threshold-discrimination-identification.

postoperative olfactory decline were characterized by preoperative eosinophilia both locally and systematically. Although ESS or medical treatment could significantly reduce inflammatory burden including the level of eosinophils followed by increased smell ability,^{15,35} the eosinophilic phenotype of CRS was frequently associated with posttreatment recurrence of chronic inflammation which might account for the olfactory fluctuation.²¹⁻²³ A recent study by Kashiwagi et al found that patients with eosinophilic CRS presented with significantly more eosinophils, fewer olfactory marker protein-positive cells, and greater epithelial erosion in the superior turbinate than those with noneosinophilic CRS 3 months after ESS, indicating eosinophilic inflammation might cause olfactory mucosal injury/dysfunction.²³ After adjusting for patient demographics and comorbidities, the preoperative tissue eosinophilia was associated with postoperative olfactory decline, which further supports the crucial and independent role of eosinophilic inflammation in determining the olfactory outcome after ESS. For the first time, we have found that the eosinophilic phenotype of patients with CRS is highly associated with early olfactory decline 3 months after ESS, and future treatment should aim for the continuous elimination of eosinophilic inflammation to fascinate the stable and lasting olfactory improvement in patients with CRS after treatment.

This study found that an AUC of 0.901 for superior turbinate eosinophil counts per HPF had a higher accuracy for all markers investigated. The optimal cutoff point of >23.5 per HPF indicated a specificity of 79.6% and a sensitivity and of 91.3% for postoperative olfactory decline. In addition, the Youden index of the cutoff point was the highest one (0.709). However, few studies have addressed the prediction of postoperative olfactory decline based on the biopsy of superior turbinate eosinophils. A study by Soler and colleagues found that ethmoid histologic findings did

not predict the postoperative olfactory outcome in patients with CRS.³⁶ The fact that olfactory mucosa did not distribute in the ethmoid might explain why ethmoid histologic findings did not associate with postoperative olfactory outcome. For the first time, we proposed a prediction model for postoperative olfactory outcome based on the histologic findings of superior turbinate, and this would aid in selecting which patients are at risk for olfactory decline and promote the biomarker-guided treatment strategies.

The most frequent cause of olfactory dysfunction in the general ear, nose, and throat clinic is the CRS-associated olfactory disorder.^{37,38} For patients with CRS inquiring about the postoperative olfactory status, this study provided some valuable preoperative assessment of olfaction. More importantly, this study established a pathologic criterion for postoperative olfactory decline in patients with CRS. Other noninvasive and efficient methods based on this pathologic criterion, such as nasal fluid cytology within olfactory cleft, should be further explored.

There were several limitations to our study. First, the sample size was relatively small and the results should be further validated in a larger multicenter study. Second, our definition of olfactory decline was based on the numerical difference of olfactory scores before and after ESS. It is not clear if this quantitative definition of olfactory decline translated into significant subjective symptoms as perceived by the patients. Third, long-term olfactory outcomes in patients with CRS after ESS were not evaluated, and thus, it is possible that some proportion of patients with CRS went on to progress from olfactory improvement to olfactory decline or vice versa. Finally, computational fluid dynamics and anatomic variation, such as deviated nasal septum and concha bulla, should also be evaluated because of the crucial role of conductive olfactory losses.

Our study showed that patients with CRS experiencing post-operative olfactory decline are characterized by high preoperative eosinophilic burden within the olfactory cleft. Preoperative tissue eosinophil counts per HPF higher than 23.5 strongly predicted the occurrence of olfactory decline 3 months after ESS. For patients with CRS with superior turbinate eosinophilia, continuous suppression of eosinophilic inflammation within olfactory cleft with medication may be the key to obtain the sustained olfactory improvement after the sinus surgery.

Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.anai.2020.04.027>.

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Supplementary Data

eTable 1

Definitions of Postoperative Olfactory Outcome in Patients With CRS

Characteristic	CRS with olfactory decline (a decreased TDI score >0 point)		CRS without olfactory decline (an increased TDI score of ≥ 0 point)	
Changes of olfactory score	≤ -5.5	-5.5 to 0	$0 \leq$ approximately 5.5	≥ 5.5
Definition	Clinical deterioration	Only a decreased olfactory score	Only an increased olfactory score	Clinical improvement

Abbreviations: CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery; TDI, threshold-discrimination-identification.

NOTE. Midfield from the study (Whitcroft KL, Cuevas M, Andrews P, Hummel T. Monitoring olfactory function in chronic rhinosinusitis and the effect of disease duration on outcome. *Int Forum Allergy Rhinol*. 2018; 8(7):769-776).**eTable 2**

Preoperative Olfactory Cleft Computed Tomography

	Ratio of the opacified area to the whole area of the olfactory cleft				
	0 (no opacification)	1 ($\leq 25\%$)	2 (25-50%)	3 (50-75%)	4 ($> 75\%$)
Anterior olfactory cleft score					
Posterior olfactory cleft score					
Total olfactory cleft score					

NOTE. The anterior end of the superior turbinate splits the olfactory cleft into 2 parts, the anterior olfactory cleft and the posterior olfactory cleft.