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Longitudinal Improvement and Stability of Olfactory Function in the Evaluation of Surgical Management for Chronic Rhinosinusitis

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Abstract

BACKGROUND—Abnormal olfaction is common with chronic rhinosinusitis (CRS) and associates with various measures of sinonasal inflammation. The Brief Smell Identification Test (BSIT) has demonstrated improvements in abnormal olfactory detection following endoscopic sinus surgery (ESS), but olfaction remains understudied using this instrument. Discerning longitudinal, postoperative durability in olfaction is critical for patient counseling.

METHODS—Adult participants with medically recalcitrant CRS were prospectively enrolled into a multi-institutional cohort study and observed for 18-months following ESS. Olfaction was operationalized using BSIT scores collected at baseline, 6-months, 12-months, and 18-months postoperatively and compared using repeated measures ANOVA.

RESULTS—122 participants met inclusion criteria and were recruited between March, 2011 and February, 2014. Improvement in mean BSIT scores at 6-month follow-up were reported for all participants ($p=0.014$) with greatest improvement in subjects with nasal polypsis ($p=0.001$). No differences in mean BSIT scores were found between 6-month and 18-months overall, however subjects with comorbid asthma ($F_{(2)}=5.29$; $p=0.010$) and nasal polypsis ($F_{(2)}=3.99$; $p=0.033$) reported significant mean worsening. Prevalence of abnormal olfaction decreased from 28% preoperatively to 17% at 6-months ($p=0.015$), for all subjects, without significant change 12-months (19%; $p=0.791$) or 18-months (21%; $p=0.581$) postoperatively.

CONCLUSIONS—Postoperative improvement in olfaction was reported 6-months after ESS using BSIT scores, with greatest improvements in patients undergoing polypectomy. Overall improvement persisted between 6-month and 18-month following ESS for most patient subgroups, however, dysosmia worsened after initial improvement in patients with asthma and nasal polyps,

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highlighting the need for further identification of prognostic factors associated with abnormal olfaction in CRS.

Keywords

Sinusitis; endoscopy; chronic disease; smell; longitudinal studies

INTRODUCTION

Olfactory dysfunction is a criterion for diagnosis of chronic rhinosinusitis (CRS)¹, with a prevalence of 30-60% across patient populations.²⁻⁴ The extent of olfactory impairment correlates with objective endoscopic and radiographic measures of sinonasal inflammation and is represented in several health related quality-of-life (QOL) measures.⁴⁻⁸ Therefore, improvement in olfactory dysfunction is an important outcome metric for the treatment for sinonasal disease.^{9,10} Despite the high prevalence of olfactory dysfunction among patients with CRS, the impact of endoscopic sinus surgery (ESS) on olfactory function and detection remains understudied.

Assessment of olfactory outcomes in CRS can be limited by time consuming testing evaluations which are difficult to integrate into a busy clinical practice.^{11,12} Patient self-report is conventionally utilized in the assessment of olfactory dysfunction in these settings, but a recent study suggested that self-reported olfactory loss significantly underestimates objective findings.¹³ The Brief Smell Identification Test (BSIT) is a minimally time invasive instrument which has been utilized to measure olfactory dysfunction and detection in CRS, with recent refinement of instrument sensitivity and accuracy.^{4,14}

Understanding the durability of initial changes in olfactory function following surgery is critical for patient counseling and future clinical trial design. However, longitudinal olfactory outcomes remain poorly defined following ESS. The aim of this study was to determine the longitudinal stability of olfactory outcomes following ESS for CRS using the BSIT instrument. Secondary aims were to identify cofactors associated with different olfactory outcomes following ESS.

MATERIALS and METHODS

Study Population and Inclusion Criteria

Study participants were diagnosed with medically refractory CRS as defined by both the American Academy of Otolaryngology-Head and Neck Surgery and the European Position Paper on Rhinosinusitis and Nasal Polyps 2012 (EPOS 2012).^{1,15} Previous findings from this investigation have been extensively reported.^{9,14,16-18} Adult study patients (>18 years of age) were recruited as part of a prospective, multi-center, observational cohort study developed to evaluate treatment outcomes of endoscopic sinus surgery (ESS) using a non-randomized methodology. The Institutional Review Board (IRB) at each enrollment site governed all study protocols and safety monitoring. Enrollment sites were comprised of sinus centers located within academic hospital systems in the United States (U.S.) including: Oregon Health & Science University (OHSU; Portland, OR; IRB#7198), Stanford

University (Palo Alto, CA; IRB#4947), and the Medical University of South Carolina (Charleston, SC; IRB#12409).

Study participants voluntarily selected ESS as a subsequent treatment option for mitigation of symptoms related to CRS after initial trials of medical therapy including, but not limited to, at least one course of either topical corticosteroids (>21-days) or a 5-day course of oral corticosteroid therapy, and at least one course (>14-days) of culture-directed or broad spectrum antibiotic therapy. Following standard informed consent, study participants were screened for demographic information, as well as social and medical history, including a physician established diagnosis of allergies (confirmed by skin prick/RAST), aspirin intolerance, asthma, depression and diabetes mellitus. Participants were followed through the postoperative standard of care, including saline irrigations and topical nasal corticosteroids for 18-months and were asked to complete postoperative BSIT tests either during physician-directed appointments or via follow-up mailings, utilizing the U.S. Postal Service and self-addressed return envelopes, at standardized 6-month intervals.

Exclusion Criteria

Data were excluded from final analyses if study participants failed to complete preoperative study evaluations as well as postoperative olfactory evaluations at 6-months, 12-months, and 18-months. Additionally, participants with either ciliary dyskinesia and/or corticosteroid dependent conditions were excluded from final analyses due to variations in global health, differential treatment considerations surrounding standard of care, and potential confounding of olfactory status.¹⁹

Surgical Intervention

Surgical approach was directed by the discretion of each on-site enrolling clinician and guided by both radiographic and endoscopic indications of disease severity on an individual basis. Primary or revision endoscopic sinus surgery procedures consisted of either unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, or frontal sinusotomy (Draf I, IIa/b, or III) procedures, with septoplasty and inferior turbinate reductions as adjunctive procedures as needed. All surgical cases were followed with postoperative therapeutic regimens including 8oz. daily nasal saline irrigation and non-standardized medical therapy as needed.¹⁵

Imaging Measurements of Disease Severity

Measures of disease severity, collected as part of the standard of care, were used simultaneously as investigational cofactors. Preoperative, high resolution computed tomography (CT) without contrast was utilized to assess sinonasal disease severity using 1mm. contiguously sliced images. Bilateral image staging was completed by the enrolling physician at each site in accordance with the Lund-Mackay scoring system (range: 0–24).²⁰

Sinonasal regions were evaluated using rigid endoscopy before and after ESS. Bilateral endoscopic examinations were staged by each enrolling physician using the Lund-Kennedy scoring system (range: 0–20).²¹ Higher total scores on both staging systems reflect worse overall objective disease severity.

Olfactory Identification Testing

Olfactory detection was measured during preoperative study evaluations and all postoperative evaluations, including 6-months, 12-months, and 18-months, using BSIT (Sensonics, Inc., Haddon Heights, NJ). The BSIT is a validated 12-item, cross-cultural, non-invasive test of olfactory detection utilizing 4 microencapsulated odorant strips containing one correct response and 3 distractor odorant strips. The BSIT is designed for “scratch-and-sniff” identification using standard #2 pencil strikes for odorant activation. Higher BSIT total scores (range: 0-12) indicate a better sense of smell. Total BSIT scores ≥ 9 can be clinically interpreted as “normal” for healthy males and females of all ages using gender adjusted, adult, normative data. Lower BSIT scores (< 8) can be clinically interpreted as either some degree of severity of olfactory dysfunction or patient malingering.^{14,22}

Data Collection and Statistical Analyses

Protected health information was removed and study data was safeguarded using unique study identification number assignments. Study data was securely transferred to OHSU from each enrollment site for manual entry into a password protected, relational database (Access, Microsoft Corp, Redmond, WA). Statistical analyses were completed using commercially available software (SPSS v.22, IBM Corp., Armonk, NY). All study data was evaluated descriptively and data normality or skewness was verified for all ordinal or continuous measures. Statistical comparison utilized complete case analysis.

Initial improvement in 6-month postoperative BSIT scores was evaluated using matched paired samples t-test statistics. Repeated measures analysis of variance (ANOVA) with Greenhouse-Geisser corrections, when necessary, was used to evaluate within-subject mean BSIT scores (dependent variable), between 6-month and 18-month follow-up, using level III modeling. Covariate subgroups were assessed as between-subject factors. When F-testing identified overall significant within-subject associations, Bonferroni correction testing was used to evaluate matched pairwise comparisons between discrete time points. The prevalence of olfactory dysfunction between independent subgroups, as well as study time points, was compared using Pearson’s Chi-square (χ^2) or McNemar’s χ^2 testing, respectively. All statistical analysis determined significance using a conventional 0.050 error probability.

RESULTS

Final Study Cohort

A total of 138 study participants with CRS, enrolled between March, 2011 and February, 2014, met all inclusion criteria and completed all preoperative and postoperative study evaluations. A total of 4 participants were excluded due to comorbid ciliary dyskinesia while 12 participants were excluded to comorbid steroid dependent conditions [asthma (n=8); sinusitis (n=2); other (n=2)] allowing for 122 participants for final analyses. Preoperative characteristics of the final study cohort are described in Table 1 while the frequency of interventional surgical procedures is described in Table 2.

Initial Postoperative Improvement in Average Olfactory Scores

Unadjusted mean BSIT scores were found to significantly improve 6-months following endoscopic sinus surgery for the total cohort (n=122; Table 3). Within-subjects average BSIT scores across several independent patient characteristics also significantly improved following ESS. Patients with CRSwNP were found to experience the greatest average improvements in BSIT scores during the initial postoperative period.

Longitudinal Stability in Postoperative Olfactory Scores

Unadjusted BSIT scores were found to remain longitudinally stable with no significant difference between 6-month, 12-month, and 18-month follow-up evaluations for the total cohort (n=122; Table 4). Within-subjects BSIT scores were reported to significantly worsen on average, between 6-month and 18-month follow-up, for subgroups with asthma and nasal polyposis. Similar but non-significant postoperative trends in average BSIT scores were reported in study participants with comorbid allergy, aspirin intolerance, and history of previous sinus surgery, likely due to limited sample size in those subgroups.

Total Cohort - Normal and Abnormal Baseline Olfactory Status

Comparisons in average longitudinal BSIT scores were evaluated for participants with both baseline normal olfactory function (n=88; 72%) and abnormal olfactory function (n=34; 28%; Figure 1). For participants with normal baseline olfactory function, no significant difference in mean BSIT scores was found 6-month following ESS ($t=1.76$; $p=0.082$) while average BSIT scores between 6-month and 18-month follow-up were statistically similar ($F_{(2)}=2.56$; $p=0.087$). For participants with abnormal baseline olfactory function, highly significant overall improvement in mean BSIT scores was reported 6-months after ESS ($t=-5.34$; $p<0.001$) without significant change between 6- and 18-month follow-up ($F_{(2)}=0.47$; $p=0.612$).

Nasal Polyposis – Improvements from Normal and Abnormal Baseline Olfactory Function

Comparisons in average longitudinal BSIT scores were further evaluated for participants both with nasal polyposis (n=38; CRSwNP) and without nasal polyposis (n=84; CRSNP) across baseline olfactory status (Figure 2). For CRSwNP participants with normal baseline olfactory function (n=20), no significant difference in mean BSIT scores was found 6-months after ESS ($t=-1.00$; $p=0.330$) while average BSIT scores between 6-month and 18-month follow-up did statistically worsen ~1.0 unit over time ($F_{(2)}=4.28$; $p=0.024$). For CRSwNP participants with abnormal baseline olfactory function (n=18), highly significant improvement in mean BSIT scores was found 6-months after ESS ($t=-4.21$; $p=0.001$) while average BSIT scores between 6-month and 18-month follow-up remained statistically similar ($F_{(2)}=1.08$; $p=0.333$).

For CRSsNP participants with normal baseline olfactory function (n=68), a modest significant reduction in mean BSIT scores was found 6-months after ESS ($t=2.11$; $p=0.038$) while average BSIT scores between 6-month and 18-month follow-up did not statistically change over time ($F_{(2)}=1.47$; $p=0.236$). For CRSsNP participants with abnormal baseline olfactory function (n=16), highly significant improvement in mean BSIT scores was found

6-months after ESS ($t = -3.65$; $p = 0.002$) while average BSIT scores between 6-month and 18-month follow-up remained statistically similar ($F_{(2)} = 0.04$; $p = 0.906$).

Comorbid Asthma - Improvements from Normal and Abnormal Baseline Olfactory Function

Comparisons in average longitudinal BSIT scores were evaluated for participants both with comorbid asthma ($n = 38$) and without comorbid asthma ($n = 84$) across baseline olfactory status (Figure 3). For asthmatic participants with normal baseline olfactory function ($n = 25$), no significant difference in mean BSIT scores was found 6-months after ESS ($t = -1.06$; $p = 0.298$) while average BSIT scores between 6-month and 18-month follow-up did statistically worsen ~ 1.1 units over time ($F_{(2)} = 4.96$; $p = 0.012$). For participants with both comorbid asthma and abnormal baseline olfactory function ($n = 13$), highly significant improvement in mean BSIT scores was found 6-months after ESS ($t = -3.68$; $p = 0.003$) while average BSIT scores between 6-month and 18-month follow-up remained statistically similar ($F_{(2)} = 1.46$; $p = 0.255$).

For participants without comorbid asthma, with normal preoperative olfactory function ($n = 63$), a modest significant reduction in mean BSIT scores was found 6-months after ESS ($t = 2.36$; $p = 0.021$) while average BSIT scores between 6-month and 18-month follow-up did not statistically change over time ($F_{(2)} = 0.87$; $p = 0.407$). For participants without asthma but with abnormal baseline olfactory function ($n = 21$), highly significant improvement in mean BSIT scores was found 6-months after ESS ($t = -3.84$; $p = 0.001$) while average BSIT scores between 6-month and 18-month follow-up remained statistically similar ($F_{(2)} = 0.16$; $p = 0.809$).

Prevalence of Olfactory Dysfunction

The prevalence of any severity of dysfunction in olfactory detection (BSIT ≥ 8) was evaluated across each study time point for both the total cohort and participants with and without nasal polyposis (CRSwNP and CRSsNP, respectively; Table 5). The prevalence of abnormal olfactory function significantly decreased from 28% at baseline to 17% at 6-month follow-up ($p = 0.015$), and remained statistically similar ($p = 0.581$) between 6-months, 12-months, and 18-months for the total cohort following ESS.

Participants with CRSwNP demonstrated a significantly higher prevalence of olfactory dysfunction at baseline compared to CRSsNP (47% vs. 19%; $p < 0.001$). The prevalence of olfactory dysfunction for CRSwNP significantly decreased from 47% at baseline to 24% ($p = 0.012$), and remained statistically similar ($p = 0.625$) between 6-months, 12-months, and 18-months following ESS. The prevalence of olfactory dysfunction for CRSsNP decreased from 19% at baseline to 14% but not to a significant degree ($p = 0.424$). No further differences in the prevalence of olfactory function between 6-months, 12-months, and 18-months ($p = 0.549$) were found for this patient subgroup.

DISCUSSION

This investigation identified dysfunction in olfactory detection in 28% of patients treated for CRS, with a statistically significant decrease in the prevalence of olfactory dysfunction 6-months following ESS (17%; $p = 0.015$). Postoperative improvements in mean BSIT scores

were found to be longitudinally stable through 18-months for the total cohort, however with significant worsening of mean BSIT scores among patients with comorbid asthma ($p=0.010$) and nasal polyposis ($p=0.033$) between 6-month and 18-month follow-up. Similar patterns of worsening BSIT scores following initial postoperative improvement at 6-month follow-up was also reported by patients with comorbid allergies, aspirin intolerance, and previous ESS ($p=0.186$).

When comparing outcomes among study participants with and without baseline olfactory dysfunction, only participants with baseline olfactory dysfunction noted significant improvement in mean BSIT scores 6-months following ESS, with longitudinal stability through 18-months of follow-up. Among patients with nasal polyposis, the prevalence of dysfunction in olfactory detection significantly decreased from 47% to 24% at 6-months, and remained statistically similar at 12-months (29%) and 18-months (29%) following sinus surgery.

These olfactory outcomes are consistent with previous study among patients with CRS.²³ In a separate multi-center cohort study, Litvack et al.¹⁰ noted that only baseline anosmic patients, as determined by the 40-item Smell Identification Test (SIT), demonstrated significant improvement in olfactory dysfunction 6-months and 12-months following ESS. However, after controlling for nasal polyp status, only anosmic patients with CRSwNP showed significant improvement in SIT scores 12-months postoperatively.

This association between nasal polyposis and improved olfactory function following ESS is further supported by Pade et al.²⁴, Hsu et al.²⁵, and Minovi et al.²⁶ using Sniffin' Sticks, SIT testing, and other non-validated measures of olfaction testing, respectively. DeConde et al.⁹ utilized the BSIT instrument to evaluate changes in olfactory detection following medical or surgical treatment, demonstrating significant improvements in BSIT scores among patients with baseline dysfunction in olfactory detection. Reported outcomes were independent of polyp status or treatment decision, and measured at last available follow-up without further evidence of longitudinal stability in that cohort.

Evaluation of the longitudinal stability of olfactory improvements following ESS remains understudied. Katotomichelakis et al.²⁷ evaluated olfactory outcomes among patients with CRSwNP at three time-points following ESS, noting a stepwise improvement in tested indices up to 6-months follow-up. While Litvack et al.¹⁰ evaluated olfactory outcomes at 6-months and 12-months following ESS, investigation of postoperative stability in mean olfactory scores between postoperative time-points was not reported.

One inherent challenge in measuring overall olfactory function in CRS outcomes research is that a single standardized test has not been universally accepted as 'gold standard' for olfactory evaluation. In this study, the BSIT was chosen due to simplicity and the ability to administer to study participants while maintaining the pace of a busy clinical practice. This study builds on previous work using the BSIT to evaluate olfactory detection and represents the first evaluation of longitudinal postoperative stability using this particular instrument. While the BSIT is a validated test for olfactory detection, it has somewhat limited diagnostic discrimination and is unable to diagnostically identify odorant thresholds or severities of

abnormal detection compared to the full 40-item SIT test. Doty reports that “the norms provided for [for the BSIT] allow the administrator to establish the relative degree of loss of function in percentile rank form.”²² These percentile rankings do represent an ability to interpret olfactory severity using BSIT scores, albeit to a limited degree compared to the full 40-item SIT test. Moreover, additional work from our group has previously reported a very strong linear correlation between BSIT and SIT scores ($R_p=0.893$; $p<0.001$) which would suggest an inherent ability to detect severity of olfactory dysfunction in the BSIT to a relative degree similar to the SIT.¹⁴ Future investigations using the BSIT could benefit from validation study to determine, at a minimum, what post-treatment score change might constitute a minimal clinically important difference.

The diagnostic accuracy of the BSIT instrument for this cohort has been described as 71% (95% CI: 65%-78%) when compared to the 40-item SIT,¹⁴ representing a potential source of misclassification bias and underreporting of patients with olfactory dysfunction. This potential bias may have contributed to reported outcomes, whereas the majority of covariate groups were found to have mean BSIT scores representing normal olfactory detection (BSIT 9.0) at all study time points.

There are a number of caveats to consider when interpreting these findings. First, a minimal clinically important difference has not been defined for the BSIT instrument in patients undergoing ESS. Thus, while we noted statistically significant improvements in both average BSIT scores and the prevalence of olfactory dysfunction following ESS, we are unable to comment on whether or not this is of clinical significance to patients electing surgical intervention for symptoms of CRS. Secondly, as a primary inclusion criteria for the investigation, only study participants who completed BSIT testing at all study time points were included for final analysis. While the omission of patients with incomplete follow-up may introduce a potential source of missing data bias, the number of patients not responding to all follow-up evaluations was minimal and we cannot accurately infer as to why some of our study participants did not respond to BSIT follow-up mailings. While there are statistical modeling techniques available to assist with missing data (eg generalized linear modeling, imputation techniques, etc) we felt these analytical approaches too strongly rely on assumptions of unobserved variables. Lastly, BSIT scores should not be extrapolated before 6-month follow-up or past the last follow-up time point; consequently, the longitudinal durability of mean olfactory improvement after ESS should not be presumed beyond 18 months.

A potential limitation of this study is a lack of statistical control for postoperative steroid use (oral or intranasal topical), which may introduce a source of unmeasured confounding on olfactory status. While these findings may represent patient outcomes in a “real world” clinical practice milieu, previous findings have found no significant association between postoperative corticosteroids and olfactory outcomes.¹⁰ Lastly, it is important to note that study patients were treated within academic, tertiary care facilities and findings may not consequently reflect postoperative outcomes for other patient populations undergoing sinus surgery.

CONCLUSIONS

Improvement in average BSIT scores following ESS was reported among CRS patients with baseline dysosmia, with a significant reduction of initial average improvements among patients with comorbid asthma and nasal polyposis. Despite a significant reduction in the overall prevalence of olfactory dysfunction following ESS, dysosmia persisted in 17-21% of patients. Further understanding of prognostic factors related to olfactory dysfunction in CRS is needed in order to optimize treatment outcomes following endoscopic sinus surgery.

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Figure 1.

Longitudinal trends in mean BSIT scores between study participants with and without normal olfactory function before endoscopic sinus surgery. The black dotted line represents the score threshold for normal olfactory function (BSIT = 9.0). BSIT, Brief Smell Identification Test;

Figure 2.

Longitudinal trends in BSIT olfactory scores for subjects with and without nasal polyposis across baseline olfactory status following endoscopic sinus surgery. BSIT, Brief Smell Identification Test; CRSsNP, chronic rhinosinusitis without nasal polyposis; CRSwNP, chronic rhinosinusitis with nasal polyposis.

Figure 3.
Longitudinal trends in BSIT olfactory scores for subjects with and without comorbid asthma across baseline olfactory status following endoscopic sinus surgery. BSIT, Brief Smell Identification Test.

Table 1

Demographics and patient characteristics in final cohort electing endoscopic sinus surgery (n=122)

Preoperative Characteristics:	(Mean $\pm$ SD)	N (%)
Age at enrollment (years)	54.1 $\pm$ 13.7	
White/Caucasian		108 (89%)
Hispanic/Latino		4 (3%)
Males		56 (46%)
Asthma		38 (31%)
Nasal polyposis (CRSwNP)		38 (31%)
Deviated septum		49 (40%)
Allergies (skin prick/RAST)		49 (40%)
Aspirin intolerance		9 (7%)
Depression		18 (15%)
Current tobacco use		1 (1%)
Previous sinus surgery		62 (51%)
Diabetes mellitus (Type I/II)		4 (3%)
Computed tomography score	12.1 $\pm$ 5.6	
Endoscopy score	5.7 $\pm$ 3.6	

SD, standard deviation; N, sample size; RAST, radioallergosorbent testing;

Table 2

Frequency of surgical procedures in final cohort (n=122)

Surgical procedures:	Left side N (%)	Right side N (%)
Maxillary antrostomy	111 (91%)	112 (92%)
Partial ethmoidectomy	14 (12%)	15 (12%)
Total ethmoidectomy	95 (78%)	97 (80%)
Sphenoidotomy	82 (67%)	86 (71%)
Middle turbinate resection	18 (15%)	21 (17%)
Inferior turbinate reduction	24 (20%)	24 (20%)
Frontal sinusotomy <i>Draf</i> I	12 (10%)	11 (9%)
Frontal sinusotomy <i>Draf</i> IIa	57 (47%)	56 (46%)
Frontal sinusotomy <i>Draf</i> IIb	9 (7%)	11 (9%)
Frontal sinusotomy <i>Draf</i> III *	3 (3%)	
Septoplasty	42 (34%)	
Image guidance	81 (66%)	

* bilateral by definition; N, sample size;

Table 3

Comparison between baseline and 6-month postoperative unadjusted mean BSIT scores for both the total cohort (n=122) and covariate subgroups.

Characteristics:	Baseline (Mean $\pm$ SD)	6-month follow-up (Mean $\pm$ SD)	t-test statistic	p-value
Total cohort	9.1 $\pm$ 3.0	9.7 $\pm$ 2.4	-2.49	0.014
Males	8.5 $\pm$ 3.4	9.1 $\pm$ 3.0	-1.41	0.164
Females	9.7 $\pm$ 2.4	10.2 $\pm$ 1.6	-2.38	0.020
Asthma	8.2 $\pm$ 3.3	9.4 $\pm$ 2.8	-3.15	0.003
Nasal polyposis (CRSwNP)	7.5 $\pm$ 3.7	9.3 $\pm$ 3.0	-3.64	0.001
Allergies (skin prick/RAST)	9.0 $\pm$ 2.9	9.7 $\pm$ 2.7	-1.77	0.083
Aspirin intolerance	6.6 $\pm$ 3.8	8.2 $\pm$ 3.7	-1.93	0.090
Depression	9.6 $\pm$ 2.8	9.1 $\pm$ 3.2	0.65	0.526
Current tobacco use	----	----	----	----
Previous sinus surgery	8.8 $\pm$ 3.2	9.5 $\pm$ 2.8	-1.85	0.069
Primary sinus surgery	9.5 $\pm$ 2.7	10.0 $\pm$ 1.9	-1.67	0.101

SD, standard deviation; df, degrees of freedom; RAST, radioallergosorbent testing confirmed;

Table 4

Unadjusted mean BSIT total scores across all follow-up study time points for the total cohort (n=122) and covariate subgroups.

Characteristics:	6-month follow-up (Mean $\pm$ SD)	12-month follow-up (Mean $\pm$ SD)	18-month follow-up (Mean $\pm$ SD)	F-test (df)	p-value
Total cohort	9.7 $\pm$ 2.4	9.7 $\pm$ 2.5	9.3 $\pm$ 2.5	2.78 ₍₂₎	0.069
Males	9.1 $\pm$ 3.0	9.2 $\pm$ 3.1	8.8 $\pm$ 3.0	2.91 ₍₂₎	0.383
Females	10.2 $\pm$ 1.6	10.1 $\pm$ 1.6	9.8 $\pm$ 1.9	2.32 ₍₂₎	0.109
Asthma	9.4 $\pm$ 2.8	9.2 $\pm$ 2.7	8.5 $\pm$ 2.7	5.29 ₍₂₎	0.010
Nasal polyposis (CRSwNP)	9.3 $\pm$ 3.0	8.8 $\pm$ 3.4	8.4 $\pm$ 3.4	3.99 ₍₂₎	0.033
Allergies (skin prick/RAST)	9.7 $\pm$ 2.7	9.5 $\pm$ 2.6	9.1 $\pm$ 2.4	1.68 ₍₂₎	0.197
Aspirin intolerance	8.2 $\pm$ 3.7	8.1 $\pm$ 3.2	7.3 $\pm$ 3.0	2.58 ₍₂₎	0.119
Depression	9.1 $\pm$ 3.2	9.5 $\pm$ 2.5	9.8 $\pm$ 2.4	0.97 ₍₂₎	0.365
Current tobacco use	----	----	----	----	----
Previous sinus surgery	9.5 $\pm$ 2.8	9.2 $\pm$ 2.9	9.0 $\pm$ 2.8	1.74 ₍₂₎	0.186
Primary sinus surgery	10.0 $\pm$ 1.9	10.2 $\pm$ 1.8	9.7 $\pm$ 2.1	2.86 ₍₂₎	0.069

SD, standard deviation; df, degrees of freedom; RAST, radioallergosorbent testing confirmed; reported p-values are reflective of Level III within-group effects over time.

Table 5

Percentage of patients with olfactory dysfunction at 6, 12 and 18-month follow-up for subjects with and without nasal polyposis

	CRSwNP	CRSsNP	Total Cohort
Study Time Points:	N(%)	N(%)	N(%)
Baseline	18 (47%)	16 (19%)	34 (28%)
6-Month Follow-up	9 (24%)	12 (14%)	21 (17%)
12-Month Follow-up	11 (29%)	12 (14%)	23 (19%)
18-Month Follow-up	11 (29%)	15 (18%)	26 (21%)

CRSwNP, chronic rhinosinusitis with nasal polyposis; CRSsNP, chronic rhinosinusitis without nasal polyposis