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Olfactory-specific quality of life outcomes after endoscopic sinus surgery

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Abstract

Introduction—Olfactory loss is a cardinal symptom of chronic rhinosinusitis (CRS) and affects 40–80% of patients. However, common sinus-specific quality-of-life (QOL) instruments include only single questions related to olfaction. Few studies have explored olfactory outcomes after surgery utilizing validated, olfaction-specific QOL questionnaires.

Methods—Patients with CRS were enrolled from 3 centers across North America into a prospective cohort study. Patients completed the short modified version of the Questionnaire of Olfactory Disorders (QOD-NS) and the 40-item Smell Identification Test (SIT-40) before and at least 6 months after endoscopic sinus surgery (ESS). Multivariate linear regression was used to determine whether specific demographic, comorbidity, or disease severity measures were independently associated with QOD scores at baseline or predicted change after surgery.

Results—A total of 121 patients, equally split between genders, were enrolled with an average age of 47.9 years (range: 18–80). Baseline total QOD-NS scores were significantly associated with SIT-40 scores, with a moderate strength of correlation ($R_s=0.400$; $p<0.001$). The average QOD-NS score improved after ESS (35.7 ± 13.0 vs. 39.7 ± 12.2 ; $p=0.006$). Allergy, polyps, and steroid dependent conditions were found to be independently associated with worse preoperative QOD-NS scores, while septal deviation was associated with better QOD-NS scores. Baseline computed tomography (CT) scores were the only variable which significantly predicted change in QOD-NS after surgery.

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Conclusion—Olfaction-specific QOL is worse in patients with polyps and comorbid allergy. Significant improvements in olfaction-specific QOL are seen after ESS, with the greatest gains seen in those with worse CT scores at baseline.

Keywords

sinusitis; olfaction; quality of life; clinical outcomes; patient reported outcome measures

INTRODUCTION

Olfactory loss is one of four cardinal symptoms of chronic rhinosinusitis (CRS) and can affect up to 80% of patients¹. In CRS a number of potential factors have been proposed to relate to *objective* olfactory function, including nasal polyps, gender and age. When examining objective olfactory outcomes using validated instruments, such as Smell Identification Test 40 (SIT40) or Sniffin' Sticks, endoscopic sinus surgery (ESS) improves objective olfaction in 23 – 68% of patients with baseline olfactory dysfunction^{2–4}. Few studies, however, have examined patient-reported, olfaction-specific quality of life (QOL) in CRS or outcomes after ESS.

Numerous studies have demonstrated that ESS improves subjective CRS outcomes, including overall sinus-specific QOL by approximately 50%⁵. The cardinal symptoms of nasal discharge, facial pain/pressure and blockage/congestion of the nose also improved by 50% or greater², but subjective olfactory loss had the least improvement of the cardinal symptoms, improving by only 37%². Additionally, common sinus-specific QOL instruments, such as the Sinonasal Outcome Test-22 (SNOT-22), may be limited in their ability to measure true differences in olfactory loss, as only one question relates to olfaction. Thus the true impact of olfactory loss upon QOL and subjective olfactory outcomes after surgery utilizing validated, olfaction-specific QOL questionnaires remains to be determined.

The goals of this study were: 1) to examine baseline olfactory-specific QOL, as measured by Questionnaire of Olfactory Disorders (QOD-NS)⁶, in a cohort of patients with CRS who had failed medical therapy and were preparing to undergo ESS; 2) to examine changes in QOD-NS after ESS; and 3) to determine clinical factors that correlate with both baseline and post ESS changes in QOD-NS.

METHODS

Study Population

Adult (≥ 18 years) patients with CRS were recruited from rhinology clinics at Medical University of South Carolina (MUSC, Charleston, SC), Oregon Health and Sciences University (OHSU, Portland, OR), and University of Utah (Salt Lake City, UT), as part of an on-going prospective cohort study. This study was approved in advance by the Institutional Review Boards at each institution and all subjects provided written, informed consent in English. Each patient fulfilled diagnostic criteria for CRS according to Clinical Practice Guideline of the American Academy of Otolaryngology-Head and Neck Surgery. Each study participant self-selected endoscopic sinus surgery (ESS) for treatment of recalcitrant

symptoms associated with CRS. Using standardized questionnaires, preoperative characteristics related to demographics and medical comorbidities was collected for each patient, including the presence of septal deviation, nasal polyposis, asthma, aspirin exacerbated respiratory disease (AERD), allergic rhinitis, depression, diabetes mellitus, tobacco use, oral steroid dependency, and a history of previous sinus surgery. High resolution computed tomography (CT) scans were obtained on each patient during the course of routine clinical care and prior to sinus surgery in all instances. CT scans were evaluated by the enrolling physician and the degree of sinus opacification was scored using the Lund-Mackay staging system, with the reviewer blinded to other study data. Nasal endoscopy was performed on each patient and those with visible polyps were classified as CRS with nasal polyposis (CRSwNP) and those without visible polyps as CRS without polyps (CRSsNP). Nasal endoscopy exams were scored semi-quantitatively using the Lund-Kennedy staging system.

Olfactory outcome metrics

Objective olfactory function was quantified using the 40-item Smell Identification Test (SIT-40, Sensonics Inc., Haddon Heights, NJ). The SIT-40 is a validated, forced choice, “scratch and sniff” test utilizing microencapsulated odorant strips (score: 0–40). Our primary outcome of interest was olfactory-specific QOL that was assessed using the previously validated, short modified version of the Questionnaire of Olfactory Disorders (QOD-NS)⁶. This instrument consists of 17 negative statements that are graded on a scale from 0 to 3 for a total score ranging from 0 to 51 with higher scores reflecting better QOL. Each patient completed two surveys of sinus-specific QOL: the Rhinosinusitis Disability Index (RSDI) and the Sinonasal Outcome Test-22 (SNOT-22). Olfactory specific questions from these questionnaires were assessed independently, including question 21 of the SNOT-22, “how bad is your sense of smell/taste” and question 7 from the physical subdomain of the RSDI “food does not taste good because of my change in smell”. All olfactory metrics were collected preoperatively and again after ESS (minimum 6 months).

Statistical analysis

Statistical analyses were performed using a commercially available software application (SPSS v.22, IBM Corporation, Armonk, NY). Descriptive statistics are reported using means [standard deviation], frequency, and range where appropriate and graphical analysis evaluated linear trends between continuous study variables. Mann Whitney U tests were used to compare mean QOD-NS among various demographic, co-morbid and disease classifications. Omnibus comparisons of mean QOL measures between olfactory subgroups (anosmia, hyposmia, and normosmia) were conducted using analysis of variance (ANOVA) with subsequent adjustments for multiple comparisons. Spearman’s rank correlation coefficients (Rs) were used to evaluate non-parametric correlations between study variables. Multivariate linear regression was used to determine whether specific demographic, comorbidity, or disease severity measures were independently associated with QOD-NS scores at baseline or predicted change after surgery.

RESULTS

Study Cohort

The overall cohort included 121 patients with CRS, equally split between genders, with 51 (42%) having CRSwNP. Other demographic factors, medical comorbidities, and measures of disease severity are summarized in Table 1. Overall baseline SIT40 scores were 26.4 [10.3], with 28 patients categorized with anosmia (23%) and 59 with hyposmia (49%) based on SIT score classifications. Significant differences were seen in QOD-NS scores among patients with normosmia, hyposmia, and anosmia (Table 2). After adjusting for multiple comparisons, each QOD-NS baseline mean score is significantly different ($p<0.001$) between each of the three SIT-40 categories (anosmic vs hyposmic, $p<0.001$; anosmic vs normosmic, $p<0.001$; hyposmic vs normosmic, $p<0.001$). The average SNOT-22 Q#21 baseline score is significantly different between anosmic and hyposmic categories ($p<0.001$) as well as between anosmic and normosmic categories ($p<0.001$), but not different between hyposmic and normosmic categories ($p=0.291$). Similarly, the average RSDI physical subdomain Q#7 baseline score is significantly different between anosmic and hyposmic categories ($p<0.001$) as well as anosmic and normosmic categories ($p<0.001$), but not significantly different between hyposmic and normosmic categories ($p=0.578$).

Factors associated with baseline QOD-NS

The impact of various demographic, comorbidities and disease severity measures upon baseline QOD-NS was examined (Table 3). Baseline QOD-NS was worse in patients with asthma, allergy, AERD, obstructive sleep apnea, nasal polyps and steroid dependency. Baseline QOD-NS was significantly associated with all CRS specific measures: total SNOT-22, RSDI, CT and endoscopy. Baseline QOD-NS was also associated with olfactory metrics including SIT-40 scores, with a moderate strength of correlation ($R_s=0.400$; $p<0.001$) and an even stronger correlation between baseline QOD-NS and other subjective olfactory-specific questions from existing QOL instruments (Table 3).

Regression analysis was performed on the multiple baseline demographic and comorbidity factors to determine independent predictors of baseline QOD-NS. Allergy, polyps and steroid dependency remained significantly associated with poorer (lower) baseline QOD-NS scores, while septal deviation was associated with better (higher) QOD-NS scores (Table 4).

Postoperative changes in QOD-NS

A total of 61 patients of the 121 baseline cohort (51%) reached at least 6 month follow up at the end of the study. There were no differences in baseline QOD-NS and SIT-40 scores between patients that completed 6 month follow up and those that did not ($p=0.656$ and 0.371 , respectively). The average QOD-NS score improved after ESS (35.7 ± 13.0 vs. 39.7 ± 12.2 ; $p=0.006$). When examining demographic, comorbid and CRS severity measures, baseline computed tomography (CT) scores were the only variable which significantly predicted change in QOD-NS after surgery (Table 5). Changes in QOD-NS scores after surgery did not correlate with SIT40 change scores, however it did correlate with other subjective olfactory questions from the SNOT-22 and RSDI.

We then examined the likelihood of a patient achieving the minimal clinically important difference (MCID) in QOD-NS after ESS. As previously described, we used ½ the standard deviation of the QOD-NS at baseline or for this study, an improvement of at least 6.5 points. Twenty-two patients had baseline pre-operative QOD-NS scores of 45 or greater. They had relatively good olfactory-specific QOL at baseline and were unable to improve by 7 points. Among the remaining 39 patients with relatively poor olfactory-specific QOL, 21 patients (53.8%) improved QOD-NS by at least one MCID, 4 patients (10%) had worsening QOD-NS by at least one MCID and the remainder were unchanged.

DISCUSSION

Olfactory dysfunction affects up to 80% of patients with CRS¹, yet remains an enigma to most rhinologists. The relationship between objective measures of olfaction and the impact of olfactory loss upon QOL is not well studied. It is difficult to directly extrapolate objective deficits to a patient's perception of smell and how it impacts their day to day function and QOL. Olfaction is critical to overall social functioning and pleasurable activities such as eating, and simple objective measures may not accurately reflect the true impact of olfactory loss. This may also explain why olfactory loss is commonly associated with other comorbidities such as depression⁶. The development of olfactory-specific QOL instruments, such as the QOD-NS, is critical to improve our understanding of this complex relationship. Another important factor regarding the utility of the QOD-NS is its ability to discriminate among patients with anosmia, hyposmia and normosmia as determined by SIT-40 (Table 2). Simple questions regarding olfaction from common CRS-specific instruments are able to identify anosmics, but cannot differentiate between normosmics and hyposmics.

When examining baseline demographic factors and comorbidities that could potentially impact olfaction, our study found that olfaction-specific QOL is worse in patients with steroid dependency, polyps and comorbid allergy. Prior studies have shown that *objective* olfaction is worse in patients with eosinophilia⁷, nasal polyps, older age, asthma and smoking⁸. While we did not find age, asthma or smoking status to correlate with QOD-NS, there may be subtle differences between correlations among subjective and objective olfaction as mentioned above. Additionally, some of our variables, such as smoking status, were recorded as yes or no. While this study did not demonstrate statistical significance (p=0.098), further studies investigating quantification of smoke exposure may be worthwhile⁹.

With regard to CRS and olfactory specific metrics, we found that the QOD-NS correlates strongly with other olfactory-specific subjective and objective measures. QOD-NS also correlates with CRS disease severity measures of CT, endoscopy and sinus-specific QOL, but not as strongly. Others report that objective olfaction correlates to CRS specific metrics of endoscopy and CT, but not RSDI, CSS or SF36^{10,11}. These traditional CRS-specific QOL instruments have potentially underweighted the importance of olfaction. Most questionnaires have a single question regarding olfaction. Litvack et al¹⁰ highlighted the lack of olfactory specific QOL instruments available at that time, which may explain the lack of correlation between objective olfaction and CRS-specific QOL instruments.

In determining the success of ESS in treating CRS-related olfactory dysfunction, most previous studies have examined improvement in objective olfaction. Success rates vary depending upon the methodology used and the population studied, but range from 23%³ to 68%⁴. Baseline predictive factors vary among studies, but improved objective olfactory outcomes have been associated with severity of baseline olfactory loss, age less than 55 years, duration of olfactory loss less than 10 years, eosinophilia, polyps, and no prior ESS^{12–16}.

There have been limited reports on the impact of ESS upon subjective olfactory outcomes. We found significant improvements in olfaction-specific QOL after ESS, with the greatest gains seen in those with worse CT scores at baseline. Other baseline factors were not predictive and this may be useful in counseling patients regarding olfactory recovery. Just over half (53%) of our patients with impaired olfactory-specific QOL at baseline achieved a clinically significant improvement in QOD-NS. Improvement in QOD-NS did correlate with subjective changes in SNOT-22 and RSDI olfaction questions, but not objective olfaction as measured by SIT-40. Similar success rates (68%) in subjective olfaction were reported in patients with CRSwNP after ESS⁴. Katotomichelakis reported improvement in QOD-NS after ESS that did correlate with objective improvements in Threshold/Discrimination/Identification (TDI)¹³. In their series, they actually achieved a mean QOD-NS after ESS that was essentially perfect (50.08 out of possible 51). They had 45% normosmics at baseline, compared to 28% in our study which may be one important difference. One of the only negative studies in olfactory outcomes¹⁷ found that while olfactory symptom scores improved after ESS, SIT-40 and other objective olfaction metrics did not. There are a number of possible explanations for the conflicting reports between olfactory-specific QOL and objective testing after ESS. Heterogeneous patient populations and varying degrees of baseline olfactory dysfunction are obvious confounding factors. Furthermore, while improvements in objective testing are typically seen after ESS, it is possible that changes are simply identifying the difference that is perceptible to a patient and not necessarily whether or not that difference impacts their overall QOL. Additionally, studies examining SIT-40 measure olfactory identification. Other studies that use Sniffin' Sticks examine olfactory discrimination and threshold in addition to identification and it may be that olfactory QOL is linked more closely to these other areas that are not measured by the SIT-40. This remains an interesting area for further study.

CONCLUSION

Olfaction remains one of the most puzzling cardinal symptoms for rhinologists and improves the least with our current treatment strategies. Olfactory-specific QOL instruments, such as the QOD-NS, correlate more strongly with other objective and patient-reported olfactory measures and provide a more comprehensive picture of how olfactory dysfunction affects our patients with CRS and their treatment outcomes.

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Table 1

Baseline demographic, comorbidity, CRS and olfactory metrics of all patients (n=121)

Demographics:	Mean [SD]	[RANGE]	N (%)
Age (years)	47.9 [17.2]	[18 – 80]	
Males			61 (50%)
White/caucasian			109 (90%)
African American			10 (8%)
Asian			1 (1%)
Hispanic/Latino			1 (1%)
Comorbid conditions:			
Asthma			52 (43%)
Allergy (testing confirmed)			80 (66%)
AERD			14 (12%)
Diabetes mellitus (Type I or II)			10 (8%)
Depression			23 (19%)
Obstructive sleep apnea			15 (12%)
Ciliary dyskinesia			3 (3%)
GERD			37 (31%)
Current tobacco use			8 (7%)
Disease characteristics:			
Nasal polyposis			51 (42%)
Prior sinus surgery			69 (57%)
Septal deviation			30 (25%)
Turbinate hypertrophy			17 (14%)
Corticosteroid dependency			17 (14%)
Disease severity:			
SNOT-22 total score	56.8 [20.3]	[6 – 102]	
RSDI total score	51.1 [24.1]	[2 – 111]	
Computed tomography score	12.9 [6.3]	[1 – 24]	
Endoscopy score	5.9 [3.2]	[0 – 20]	
Olfactory function measures:			
QOD-NS score	35.2 [13.3]	[0 – 51]	
SIT-40 score	26.4 [10.3]	[0 – 38]	
SNOT-22 Q#21	3.0 [1.8]	[0 – 5]	
RSDI physical subdomain Q#7	2.0 [1.4]	[0 – 4]	

SD, standard deviation; AERD, aspirin exacerbated respiratory disease; GERD, gastroesophageal reflux disease; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; QOD, Questionnaire for Olfactory Disorders; NS, negative statements; SIT-40, Smell Identification Test-40; Q, question item

Table 2

Average baseline olfactory-specific scores classified by SIT-40

Olfactory-specific metric mean [SD]	Anosmic (n=28)	Hyposmic (n=59)	Normosmic (n=34)	p-value
SIT-40	9.6 [4.3]	29.0 [4.1]	35.7 [1.2]	<0.001
QOD-NS	25.0 [10.1]	36.7 [13.8]	41.1 [9.9]	<0.001
SNOT-22 Q#21	4.6 [0.8]	2.8 [1.8]	2.2 [1.6]	<0.001
RSDI physical subdomain Q#7	3.3 [1.0]	1.8 [1.3]	1.4 [1.2]	<0.001

SD, standard deviation; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; QOD, Questionnaire for Olfactory Disorders; NS, negative statements; SIT-40, Smell Identification Test-40; Q, question item. p-values reflect omnibus ANOVA results.

Table 3

Comparison of baseline QOD-NS measures across demographics, comorbidity, and disease characteristics (n=121)

	Present	Absent	
Demographics:	Mean [SD]	Mean [SD]	p-value
Males	35.9 [13.2]	34.6 [13.5]	0.730
White/caucasian	35.6 [13.1]	32.2 [15.4]	0.383
Hispanic/Latino	48.0 [---]	35.1 [13.3]	0.479
Comorbid conditions:			
Asthma	31.9 [13.9]	37.8 [12.4]	0.014
Allergy (testing confirmed)	32.5 [13.1]	40.7 [12.2]	0.001
AERD	25.4 [14.8]	36.5 [12.6]	0.006
Diabetes mellitus (Type I or II)	39.0 [7.9]	34.9 [13.7]	0.540
Depression	34.7 [13.4]	35.4 [13.4]	0.856
Obstructive sleep apnea	27.8 [14.0]	36.3 [13.0]	0.029
Ciliary dyskinesia	40.7 [16.2]	35.1 [13.3]	0.381
GERD	35.7 [13.7]	35.0 [13.2]	0.698
Current tobacco use	28.4 [10.5]	35.7 [13.4]	0.098
Disease characteristics:			
Nasal polyposis	28.6 [13.2]	40.1 [11.3]	<0.001
Prior sinus surgery	34.2 [13.0]	36.6 [13.7]	0.276
Septal deviation	41.6 [10.4]	33.1 [13.6]	0.001
Turbinate hypertrophy	36.6 [14.0]	35.0 [13.3]	0.530
Corticosteroid dependency	25.8 [15.4]	36.8 [12.4]	0.004
Age and CRS disease severity measures:	Rs (p-value)		
Age	0.055 (0.549)		
SNOT-22 total score	−0.502 (<0.001)		
RSDI total score	−0.546 (<0.001)		
Computed tomography score	−0.414 (<0.001)		
Endoscopy score	−0.316 (0.001)		
Olfactory specific measures:			
SIT-40 score	0.400 (<0.001)		
SNOT-22 Q#21	−0.631 (<0.001)		
RSDI physical subdomain Q#7	−0.673 (<0.001)		

SD, standard deviation; AERD, aspirin exacerbated respiratory disease; GERD, gastroesophageal reflux disease; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; QOD, Questionnaire for Olfactory Disorders; NS, negative statements; SIT-40, Smell Identification Test-40; Q, question item

Table 4

Regression analysis of baseline factors to predict baseline QOD-NS

Factor	Unstandardized coefficients		Standardized coefficients	t	P value
	B	Standard error	Beta		
CRSwNP	-9.276	2.115	-.345	-4.386	<0.001
Allergy by testing	-5.227	2.267	-.186	-2.306	0.023
Steroid dependence	-9.547	2.947	-.250	-3.239	0.002
Septal deviation	4.895	2.469	.159	1.983	0.050

CRSwNP, Chronic rhinosinusitis with nasal polyps; QOD, Questionnaire for Olfactory Disorders; NS, negative statements

Table 5

Comparison of postoperative change in mean QOD-NS measures across demographics, comorbidity, and disease characteristics (n=61)

	Present	Absent	
Demographics:	Mean [SD]	Mean [SD]	p-value
Males	4.8 [10.4]	3.1 [10.9]	0.761
White/caucasian	4.0 [10.8]	3.0 [8.9]	0.645
Hispanic/Latino	3.0 [---]	3.9 [10.7]	0.984
Comorbid conditions:			
Asthma	6.4 [10.2]	2.1 [10.7]	0.196
Allergy (testing confirmed)	5.2 [9.9]	1.2 [11.6]	0.059
AERD	7.7 [10.1]	3.4 [10.7]	0.379
Diabetes mellitus (Type I or II)	1.3 [9.6]	4.2 [10.8]	0.259
Depression	2.1 [10.7]	4.3 [10.6]	0.785
Obstructive sleep apnea	2.2 [6.8]	4.1 [11.0]	0.530
Ciliary dyskinesia	----	3.9 [10.6]	----
GERD	2.1 [9.4]	5.0 [11.2]	0.451
Disease characteristics:			
Nasal polyposis	7.8 [10.0]	2.1 [10.5]	0.066
Prior sinus surgery	2.1 [10.6]	7.1 [10.1]	0.121
Septal deviation	2.1 [11.2]	4.4 [10.5]	0.283
Turbinate hypertrophy	3.3 [10.0]	4.0 [10.8]	0.654
Corticosteroid dependency	2.6 [8.6]	4.1 [10.9]	0.521
Age and baseline CRS severity measures:	Rs (p-value)		
Age	0.076 (0.561)		
SNOT-22 total score	0.004 (0.973)		
RSDI total score	0.047 (0.722)		
Computed tomography score	0.353 (0.005)		
Endoscopy score	0.116 (0.373)		
Olfactory specific measures:			
SIT-40 change score	0.180 (.185)		
SNOT-22 Q#21 change	-0.488 (<0.001)		
RSDI physical subdomain Q#7 change	-0.436 (<0.001)		

SD, standard deviation; AERD, aspirin exacerbated respiratory disease; GERD, gastroesophageal reflux disease; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; QOD, Questionnaire for Olfactory Disorders; NS, negative statements; SIT-40, Smell Identification Test-40; Q, question item