Published in final edited form as:

Int Forum Allergy Rhinol. 2018 July ; 8(7): 777–782. doi:10.1002/alr.22112.

Factor Analysis of the Questionnaire of Olfactory Disorders in Patients with Chronic Rhinosinusitis

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Abstract

Introduction—Olfactory-specific quality of life (QOL) can be measured using the Questionnaire of Olfactory Disorders Negative Statements (QOD-NS) which examines various aspects of olfactory dysfunction. It is unknown if certain factors of the QOD-NS differentially impact QOL.

Methods—Patients with chronic rhinosinusitis (CRS) completed the QOD-NS, 22-item Sinonasal Outcomes Test (SNOT-22), Medical Outcomes Study Short Form 6-D (SF-6D) health utility measure, and Patient Health Questionnaire-2 (PHQ-2) depression screen. Exploratory factor analysis of the QOD-NS was performed. Associations between QOD-NS factors and other QOL metrics were analyzed before and after endoscopic sinus surgery (ESS).

Results—Outcomes were examined on 132 patients. The QOD-NS contains four distinct factors. There was no difference in associations between the different factors and baseline clinical characteristics. ESS had greatest effect size (d) on factors 2 and 4 (d = 0.29 and 0.27, p<0.05). Post-surgical changes in the SF-6D and SNOT-22 had the strongest correlation with factor 2 scores (r=0.29 and 0.34, p<0.05), and changes in the PHQ-2 had the strongest correlation to factor 3 (r=0.24, p<0.05). Abnormal QOD-NS scores at baseline were associated with effect size increases of 50 to 100% (p<0.05).

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Potential Conflicts of Interest: There are no disclosures for Jose L. Mattos or Timothy L. Smith.

Accepted for oral presentation to the American Rhinologic Society during the American Academy of Otolaryngology-Head and Neck Surgery Annual Meeting & OTO Experience in Chicago, IL, September, 2017. Abstract #2054

Conclusions—The QOD-NS measures four distinct factors. Eating-related questions had the greatest improvement after ESS. Health utility and CRS-specific QOL improvement most strongly associated with factor 2, while PHQ-2 changes are most highly associated with factor 3, suggesting a differential impact of the factors of the QOD-NS on varying aspects of QOL.

Keywords

sinusitis; quality of life; eating; taste; olfaction; QOD

Introduction

Olfactory dysfunction (OD) is a known sequela of chronic rhinosinusitis (CRS).^{1,2} OD affects between 40% and 80% of patients with CRS depending on the method of measurement and population studied, while significantly decreasing olfactory-specific quality of life (QOL).³

Olfactory-specific QOL can be measured using the Questionnaire of Olfactory Disorders Negative Statements (QOD-NS), which is a previously validated instrument analyzing multiple aspects of how changes in olfaction impact an individual's daily life.⁴ While overall QOL assessments are important, there are multiple ways in which OD could potentially impact QOL. Changes in smell could limit the enjoyment of food, render patients unable to identify potentially harmful odors, impair social interactions, and possibly impact mental health. Understanding each of these different components of olfactory-specific QOL could prove useful for both clinical and research endeavors. Careful examination of the QOD-NS reveals that several of the items appear to have common themes, which may allow the instrument to be subcategorized into specific domains.

Exploratory factory analysis is a statistical technique that attempts to expose whether responses to certain questions in self-reported instruments group together.⁵ Consequently, different “factors” or themed question groups can be identified which add granularity to the overall instrument score. Further understanding the underlying themes that the QOD-NS is measuring would enhance our ability to interpret the results of the QOD-NS. The current study has the following objectives: 1) determine whether QOD-NS survey items can be grouped into distinct, thematic factors that could be used for future study; 2) understand the relationship between baseline clinical characteristics and the different QOD-NS factors; 3) analyze whether surgical therapy differentially impacts the QOD-NS factors; and 4) understand how changes in alternative, disease-specific and overall QOL scores correlate with changes in QOD-NS factors.

Methods

Enrollment and Study Population

Adult study participants (>18 years of age) were prospectively enrolled between August, 2012 and June, 2015 into a non-randomized, multi-center, North American cohort evaluating various treatment outcomes for CRS. Study participants were diagnosed with CRS as defined by both the American Academy of Otolaryngology-Head and Neck Surgery.⁶ Study

participants had completed pre-operative, initial medical therapy including, but not limited to: 240ml. of daily saline irrigation, at least one course of either topical corticosteroids (>21 days) or trial of oral corticosteroid therapy (>5 days), and at least one trial (>14 days) of broad spectrum or culture-directed antibiotics. Enrollment procedures occurred after study participants underwent surgical counseling and voluntarily elected endoscopic sinus surgery (ESS). The Institutional Review Board (IRB) at each enrollment site governed investigational protocols and informed consent. Enrollment locations included sinus clinics within tertiary referral, academic hospital systems in the United States including: Oregon Health & Science University (OHSU; Portland, OR; IRB#7198), Stanford University (Palo Alto, CA; IRB#4947), the Medical University of South Carolina (Charleston, SC; IRB#12409), and the University of Calgary (Calgary, Alberta, Canada; IRB#E-24208). Data was obtained at baseline, and at follow-up time intervals. The follow up data presented in this manuscript is for the last available follow-up interval, ranging between 6 and 18 months.

Chronic rhinosinusitis disease severity

Sinusitis-specific disease severity was assessed based on endoscopy, computed tomography (CT) imaging, and patient-reported outcome measures at baseline and at follow-up. Sinonasal endoscopy was performed on each patient and scored according the Lund-Kennedy algorithm (range 0-20; higher scores indicate greater disease) by their treating physician, who was blinded to other study data.⁷ Patients were further categorized as those without polyps (CRSsNP) and those with visible polyps (CRSwNP). CT images, performed during the course of clinical care, were graded by the physician according to the Lund-Mackay scoring system (range 0-24; higher scores indicate greater disease).⁸

Patient Reported Outcome Measures

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 Negative Statements (QOD-NS) at baseline and at follow-up.⁴ This instrument consists of 17 statements that are graded on a scale from 0 to 3, for a total score ranging from 0 to 51. We coded the QOD-NS so that higher scores reflect better olfactory-specific QOL. Sinus-specific QOL was assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22)⁹. The SNOT-22 contains 22 questions (total score range, 0–110), with higher scores representing more severe QOL impact. Additionally, subjects completed the Medical Outcomes Short Form-6D (SF-6D). The SF-6D is a subset of questions from the 36-item Medical Outcomes Study Short-Form (SF-36) which are transformed into health utility values using a previously described algorithm developed by Brazier et al. and used with permission from the Department of Health Economics and Decision Science at the University of Sheffield, Sheffield, UK.¹⁰ Finally, participants also completed the Patient Health Questionnaire-2 (PHQ-2) which is a brief, validated screening tool for depressive disorders.¹¹

Statistical Analysis

Patient demographic and clinical characteristics are presented as mean $\pm$ standard deviation for continuous variables and frequency (%) for categorical variables for this cross-sectional evaluation. To identify subgroups of questions with common themes within the QOD-NS, a factor analysis of the baseline data was completed. The optimal number of factors was

identified when the change in eigenvalues was less than 0.20 and the approximate variance explained was at least 0.70. To aid in the interpretation of factors, a varimax rotation was utilized. Once the number of factors were identified, the rotated factor loadings were evaluated to group individual questions into a proposed factor (see Supplemental Table 1). To facilitate between factor comparisons, QOD-NS factor scores were calculated as averages amongst the individual questions that were deemed to be the comprising questions.

To assess the associations between baseline and change in clinical characteristics with QOD-NS factors, a Spearman's rho was calculated for each comparison. In order to compare baseline QOD-NS factor scores and clinical characteristics, descriptive statistics were presented and compared using Wilcoxon rank-sum test. Changes in QOD-NS factors were assessed from pre- and post-surgery linear regression models and effect sizes (d) were calculated within the framework of the model ($\frac{\Delta}{SE \times \sqrt{df+1}}$).

Further, similar models were constructed controlling for high vs. low QOD-NS scores at baseline (at or above 38.5 total baseline QOD-NS) and statistical assessments were reevaluated, stratifying on high vs. low QOD-NS status. A QOD-NS score cut-off of 38.5 has been previously reported that stratifies QOD-NS scores in patient with normal vs. abnormal olfaction on objective psychophysical testing (hyposmia and anosmia).¹² This cut-off score of 38.5 was calculated using a QOD-NS scoring method where high scores reflected better QOL and low scores reflected poor QOL. For this study, we reverted our scoring to the original scoring method reported by Hummel et al.¹³, where high scores reflect poor QOL and low scores reflect good QOL. As such, we used the numerical inverse of 38.5 to obtain a cut-off score of 12.5 in order to reflect normal vs. abnormal scores. Finally, changes in covariates were assessed linear regression models controlling for QOD-NS factor scores. Statistical significance was assessed at $\alpha = 0.05$. All analyses were performed using SAS v9.4 © software.

Results

Baseline Characteristics

In this prospective longitudinal cohort, there were 132 unique who completed the QOD before and after ESS. These 132 patients had a total of 164 visits with data. The cohort had an average age of approximately 51 years (± 16.5) and mostly Caucasian (87.9%) and female gender (57.6%). Overall, there was a high burden of sinonasal disease as evidenced by SNOT-22 scores, endoscopy scores, and presence of prior sinus surgery. Table 1 details all of the baseline patient characteristics.

Factor Analysis

Factory analysis revealed four distinct factors within the QOD-NS which are detailed in Table 2. The questions clustered into groups which appeared sufficiently similar in overall theme. There was some overlap between the thematic content of each of the factors, but they were sufficiently distinct and consistent. As expected, the eating-related questions clustered together in factor 2. One eating-related question did cross-over into factor 4.

Baseline Associations

At baseline, there were no detectable associations between the different QOD-NS factors and the clinical characteristics studied (Table 3). For the dichotomous baseline characteristics of allergy status, aspiring sensitivity, history of asthma, and prior sinus surgery, we also did not note any significant differences between these baseline characteristics and the different QOD-NS factors. We did note that many of the CRS severity metrics and the patient reported outcome measures had a significant correlation with all or most of the QOD-NS factors.

Effect of Surgical Therapy on QOD-NS Factors and QOL Measures

Comparison of QOD factors before and after ESS showed the greatest improvement was found in factor 2 ($d=0.29$) and factor 4 ($d=0.27$), with lesser but still statistically significant improvement in factor 3 ($d=0.16$) and factor 1 ($d=0.11$). While at baseline there were no significant difference between the QOD-NS factors, surgical therapy appears to differentially impact their change. Pairwise comparison of all of the factors showed that factor 2 and factor 4 had the greatest change after surgery when compared with factors 1 and 3 ($p<0.05$). Furthermore, ESS had the greatest effect size on changes on the eating-related factor as compared to the other QOD-NS factors (Table 4). After stratifying by high/abnormal vs. low/normal QOD-NS at baseline, effect sizes changed for both statuses. Using a cut-off QOD-NS score of 12.5 we noted that surgical therapy only had a significant effect on QOD-NS factors when baseline scores were abnormal, and that factors 2 and 4 had the greatest change after surgery in this setting. For the high/abnormal QOD-NS score group (>12.5), effect sizes increased for all factors with factor 2 ($d=0.40$) and factor 4 ($d=0.36$) remaining greater than factor 3 ($d=0.30$) and factor 1 ($d=0.20$). For the low/normal QOD-NS score group (<12.5), all effect sizes decreased to no statistical significance. All QOL measures showed a statistically significant change from before and after ESS with SNOT-22 showing the greatest improvement ($d=-0.64$) and SF-6D ($d=0.48$) and PHQ-2 ($d=-0.50$) also showing improvement (Table 4). The associations between changes in the different QOD-NS factors after surgery and changes in our three QOL instruments were analyzed (Table 5).

Discussion

The QOD-NS provides unique insight into the effect that olfactory dysfunction has on QOL. The current study aimed to analyze whether the QOD-NS evaluates multiple factors of olfactory-specific QOL versus a single construct via exploratory factor analysis, and the relationship of clinical characteristics to the different factors. Four distinct factors of the QOD-NS were identified. ESS appears to differentially impact some these factors. The factors that contained eating related questions (factors 2 and 4) were associated with the greatest improvement after surgery compared to the other factors. In our analysis, sinus surgery has the greatest effect on factor 2, which improved twice as much as the factors 1 and 3 with $2.6\times$ effect size of factor 1 and $1.8\times$ the effect size of factor 3. Interestingly, while most of the eating-related questions are found in factor 2, factor 4 also contains an eating-related which might explain why these two factors cluster together throughout our analysis. As expected, surgery conveys a significant improvement of SF-6D, SNOT-22, and PHQ-2 scores, with the greatest effect seen in the SNOT-22.

We have previously reported that ESS leads to improvement in olfactory-specific QOL as measured by total QOD-NS scores.³ The present study adds to the understanding of how ESS positively impacts olfactory QOL. ESS leads to improvements of all of the QOD-NS factors, however, the impact is greatest on the factors containing eating-related questions. This suggests that ESS leads to greater enjoyment of food and drink in CRS patients, which are essential components of personal behavior and social interactions. The present analysis might provide another layer to our understanding of how ESS leads to improvements in health utility as well as overall and disease-specific QOL.^{14,15} In fact, a study of a European cohort has shown that reduced pleasure from eating is the primary complaint from which patients with chemosensory dysfunction, including smell loss, seek medical care.¹⁶

In addition to eating-related questions, the QOD-NS measures other important aspects of olfactory-specific QOL. The different factors, while not perfectly consistent and with some thematic overlap do show some consistency which could suggest specific subject domains found within the QOD-NS. Factor 1 contains a large number of social-related questions which may illustrate how olfactory dysfunction might lead to social isolation, and impairment of interpersonal relationships. Factor 3 gives insight into how olfactory impairment might increase a patient's stress level or cause impairment in mental health. Finally, while factor 4 contains an eating-related question it also helps inform our understanding of the how frequently olfaction changes can affect QOL and how bothersome these changes can be to patients. Taken together, these factors then illustrate that olfactory dysfunction can lead to patients who are socially isolated, stressed and anxious, frequently bothered and worried, and with a lessened ability to enjoy food and drink due to changes in their sense of smell. This granular understanding of the QOD-NS will allow clinicians to better evaluate exactly how olfactory dysfunction impacts their patients' lives, and may lead to better counseling and treatment options. These findings are also consistent with studies of other cohorts which have found a high burden of psychosocial dysfunction in patients with olfactory impairment.¹⁷

From a research perspective, this greater understanding of the QOD-NS may provide a deeper level of information as we continue our attempts to understand the nature of the relationship between olfactory dysfunction and QOL. We know that the QOD-NS and objective psychophysical smell testing correlated at baseline, but only weakly.^{3,12} Perhaps the social and mental health impacts of olfactory dysfunction are not well captured by objective smell testing. Alternatively, all commercially available or commonly performed objective smell tests rely on orthonasal (anterograde) olfaction. If indeed eating-related problems are a major contributor to decreases in olfactory-specific QOL, then perhaps retronasal smell testing might be a more informative tool than orthonasal testing alone.

This study is a prospective longitudinal study. The data collected includes demographics, comorbidities, CRS-specific disease severity measures, and olfactory-specific QOL, it does have several limitations. This is a cohort recruited from tertiary rhinology practices with a high burden of disease and large incidence of prior sinus surgery, and so the results may not be broadly applicable. The nature of the data does not allow insights into mechanisms of disease. Nonetheless, to our knowledge, this is the first attempt at understanding the different domains of the QOD-NS, how ESS might impact these different constructs, and

what the effect of differential changes to QOD-NS factors might be. The discovery of these factors may allow for more in-depth investigations of olfactory-specific QOL in the future.

Conclusion

The QOD-NS measures four distinct factors. All four of the factors improve after ESS, particularly with those patients who had abnormal QOD scores at baseline. Eating-related questions had the greatest improvement after ESS. Each of the factors correlates to a variable degree with health utility, CRS QOL, and depressive symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work was supported by grants from the National Institute on Deafness and Other Communication Disorders (NIDCD), one of the National Institutes of Health, Bethesda, MD (R03 DC013651-01; PI: ZM Soler and R01 DC005805; PIs: TL Smith and ZM Soler).

Zachary M. Soler is supported by grants from Entellus, Intersect, and Optinose, none of which are affiliated with this manuscript. Dr. Soler is a consultant for Olympus, which is not affiliated with this manuscript. Rodney J. Schlosser is supported by grants from OptiNose, Entellus and IntersectENT, none of which are associated with this manuscript. Dr. Schlosser is also a consultant for Olympus, Medtronic and Arrinex, which are not affiliated with this study. Adam S. DeConde is a consultant for Olympus, Stryker Endoscopy and Intersect ENT.

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Table 1
Patient Characteristics at Baseline

Demographic/QOL Measure		Mean (SD) Count (%)
Age		50.9 (16.5)
Sex	Male	56 (42.4)
	Female	76 (57.6)
Race	White	116 (87.9)
	Non-White	16 (12.1)
Ethnicity	Hispanic	7 (5.3)
	Non-Hispanic	125 (94.7)
Asthma		59 (44.7)
AERD		11 (8.3)
Allergy history		87 (65.9)
Smoking history		4 (3.1%)
CRS Measures		
Polyp status	CRSwNP	46 (34.9)
	CRSsNP	86 (65.1)
SNOT-22 Score		54.8 (21.1)
Previous sinus surgery		80 (62.0)
Endoscopy score		5.6 (3.8)
CT score		11.4 (6.4)
QOL Measures		
QOD-NS		13.8 (12.9)
PHQ-2		1.8 (1.6)
SF-6D		0.7 (0.1)

AERD: Aspiring Exacerbated Respiratory Disease

SNOT-22: 22-item sinonasal outcomes test

SF6D: Short Form 6D

CRS: Chronic Rhinosinusitis

CT: computed tomography

PHQ2: Patient Health Questionnaire 2

CRSwNP: Chronic Rhinosinusitis with Nasal Polyps

CRSsNP: Chronic Rhinosinusitis without Nasal Polyps

Table 2
Questionnaire of Olfactory Disorders - Negative Statements Factor Analysis

Factor 1	
Question #	Question text
11	The changes in my sense of smell make me feel isolated.
12	Because of the changes in my sense of smell I avoid groups of people.
14	Because of the difficulties with smelling, I am scared of getting exposed to certain dangers (e.g., gas, rotten food).
15	Because of the changes in my sense of smell I have problems with taking part in activities of daily life.
16	The changes in my sense of smell make me feel angry.
17	Because of the changes in my sense of smell, my relationship with my wife / husband / partner is affected.
Factor 2	
Question #	Question text
1	Because of the changes in my sense of smell, I go to restaurants less often than I used to.
3	Because of the changes in my sense of smell, I don't enjoy drinks or food as much as I used to.
10	Because of the changes in my sense of smell I have weight problems.
13	Because of the changes in my sense of smell I eat less than I used to or more than I used to.
Factor 3	
Question #	Question text
5	Because of the changes in my sense of smell, I feel more anxious than I used to feel.
6	The changes in my sense of smell cause most of my problems.
8	Because of the changes in my sense of smell I visit friends, relatives, or neighbors less often.
9	Because of the changes in my sense of smell, I try harder to relax.
Factor 4	
Question #	Question text
2	I am always aware of the changes in my sense of smell.
4	I am worried that I will never get used to the changes in my sense of smell.
7	The changes in my sense of smell annoy me when I am eating.

Table 3
Correlation Coefficients Between Continuous Baseline Clinical Characteristics, QOL Instruments, and QOD Factors

Variable	BL Factor 1	BL Factor 2	BL Factor 3	BL Factor 4
BL Endoscopy score	0.37 *	0.26 *	0.31 *	0.37 *
BL SIT score	-0.16	-0.20 *	-0.27 *	-0.34 *
BL CT score	0.39 *	0.30 *	0.36 *	0.37 *
Age	-0.10 *	0.01	-0.09	-0.11 *
BL SNOT-22	0.38 *	0.44 *	0.33 *	0.39 *
BL PHQ-2	-0.02	-0.01	-0.01	0.03
BL SF-6D	-0.02	0.04	-0.05	-0.02

All numbers are presented as Spearman's rho and its associated p-value.

*
 = p<0.05

QOL: Quality of Life

BL: Baseline

SIT: Smell Identification Test

CRS: Chronic Rhinosinusitis

CT: computed tomography

SNOT-22: 22-item sinonasal outcomes test

PHQ2: Patient Health Questionnaire 2

SF6D: Short Form 6D

Table 4
Pre- and Post-Surgery QOD Factor and Covariate Scores

Stratified Status				Effect Size
Not stratified	QOD Factor	Mean QOD Factor Score		d
		Before Surgery	After Surgery	
	Factor 1	0.55 (0.74)	0.41 (0.64)	-0.11 *
	Factor 2	0.95 (0.90)	0.58 (0.76)	-0.29 *
	Factor 3	0.65 (0.83)	0.43 (0.71)	-0.16 *
	Factor 4	0.39 (1.00)	1.05 (0.96)	-0.27 *
QOD > 12.5 At baseline	QOD Factor	Mean QOD Factor Score		d
		Before Surgery	After Surgery	
	Factor 1	1.13 (0.76)	0.75 (0.78)	-0.20 *
	Factor 2	1.72 (0.70)	0.97 (0.85)	-0.40 *
	Factor 3	1.32 (0.80)	0.76 (0.89)	-0.30 *
	Factor 4	2.24 (0.65)	1.55 (0.97)	-0.36 *
QOD ≤ 12.5 At baseline	QOD Factor	Mean QOD Factor Score		d
		Before Surgery	After Surgery	
	Factor 1	0.08 (0.19)	0.14 (0.31)	0.04
	Factor 2	0.31 (0.41)	0.27 (0.49)	-0.03
	Factor 3	0.10 (0.23)	0.15 (0.34)	0.03
	Factor 4	0.71 (0.66)	0.64 (0.75)	-0.04
Not stratified	Covariate	Mean Score		d
		Before Surgery	After Surgery	
	SF-6D	0.66 (0.14)	0.76 (0.15)	0.48 * ^a
	SNOT-22	54.77 (21.10)	28.20 (21.28)	-0.64 * ^a
	PHQ-2	1.76 (1.63)	1.07 (1.57)	-0.50 * ^a

Scores presented as mean (standard deviation).

Effect sizes were calculated and statistical significance was assessed within the framework of linear models.

d: effect size

QOD-NS: Questionnaire of Olfactory Disorders-Negative Statements

SNOT-22: 22-item sinonasal outcomes test

PHQ2: Patient Health Questionnaire 2

SF6D: Short Form 6D

* : p < 0.05

^a : Presented are LSMeans (standard error) calculated and assessed in model controlling for change in QOD factors.

Table 5
Correlation Coefficients Between Pre- and Post-Surgical Changes in QOL Instruments, and QOD Factors

Variable	Factor 1	Factor 2	Factor 3	Factor 4
SF-6D	-0.27 *	-0.29 *	-0.19 *	-0.20 *
SNOT-22	0.31 *	0.34 *	0.27 *	0.32 *
PHQ-2	0.22 *	0.22 *	0.24 *	0.20 *

All numbers are presented as Spearman's rho and its associated p-value.

*
 = p<0.05

QOL: Quality of Life

: Change from baseline

SNOT-22: 22-item sinonasal outcomes test

PHQ2: Patient Health Questionnaire 2

SF6D: Short Form 6D