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Association of olfactory dysfunction in chronic rhinosinusitis with economic productivity and medication usage

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Abstract

Background—Chronic rhinosinusitis (CRS) has significant impacts upon productivity, economic metrics and medication usage; however, factors that are associated with these economic outcomes are unknown.

Methods—We evaluated olfactory dysfunction in 221 patients with CRS using the Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS) and the 40 item Smell Identification Test (SIT) and assessed whether an association between these olfactory metrics and healthcare utilization, productivity and medication usage over the preceding 90 days existed.

Results—After adjusting for CRS-associated comorbidities, objective measures of disease, demographics and CRS-specific quality of life (QOL), patients with lower QOD-NS scores (worse patient-reported olfaction) had more missed days of normal productivity and employment, worse productivity levels, more hours of missed employment due to physician visits, more time caring for sinuses, greater distance traveled to medical appointment, more days of oral steroid use and higher odds of being on disability insurance. Clinical olfaction, as measured by SIT, was associated with greater distance traveled to medical appointment and higher odds of being on disability insurance, but did not correlate with other productivity measures.

Conclusions—Impaired olfactory-specific QOL is associated with significantly worse economic and productivity metrics and increased medication usage even after adjusting for CRS-specific comorbidities, objective measures of disease, demographics and severity of CRS-specific QOL. Future studies are warranted to determine if targeting the impaired olfactory-specific QOL noted in patients with CRS results in improved productivity and economic outcomes.

Keywords

chronic rhinosinusitis; olfaction; olfactory test; quality of life

Introduction

While the impact of chronic rhinosinusitis (CRS) upon quality of life (QOL) is well known, studies are just beginning to describe its impact upon healthcare utilization and daily productivity.¹ The overall annual economic burden of CRS in the United States is estimated to be \$22 billion in 2014,² with \$13 billion of this total attributed to reduced work productivity.³ Furthermore, direct CRS-related healthcare costs are estimated to be nearly \$10 billion and include annual medication costs up to \$2,700 per patient.³ A better understanding of which factors drive impaired productivity and increased healthcare utilization in CRS is critical from both a patient and societal perspective.

Factors predictive of economic impact and healthcare utilization in CRS are just beginning to be explored. It has previously been shown that patients in the prime of their earning capacity, between 30 and 49 years of age, and those with worse sinus-specific QOL scores have higher productivity costs. However, traditional CRS-specific factors, such as polyp status, comorbid asthma and endoscopy were not associated with productivity costs.² There are a number of factors that could drive economic outcomes and healthcare utilization in CRS which merit further study, including olfactory dysfunction. A number of studies have documented associations between olfactory dysfunction, psychiatric dysfunction, and even all-cause mortality.^{4,5} With these findings in mind, we hypothesized that olfactory impairment might be associated with declines in personal productivity and increased healthcare utilization in CRS, independent of CRS-specific disease severity. The goal of this study was to explore the impact of olfactory dysfunction, as measured by olfactory-specific QOL and clinical measures of olfaction (Smell Identification Test), in CRS upon economic metrics, including daily productivity, healthcare utilization and medication usage.

Methods

Study Design

Adult (≥ 18 years of age) patients with CRS were evaluated from 4 tertiary rhinology clinics including the Medical University of South Carolina (Charleston, SC, IRB #12409), Oregon Health and Science University (Portland, OR, IRB #7198), Stanford University (Palo Alto, CA, IRB #4947), and the University of Calgary (Calgary, Alberta, Canada, IRB #E-24208) in a cross-sectional fashion. All patients classified as having CRS fulfilled diagnostic criteria for CRS according to the Clinical Practice Guideline of the American Academy of Otolaryngology-Head and Neck Surgery⁶ and the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS2012).⁷ As we have previously published, inclusion criteria dictated that patients had already received initial medical therapy but continued to have persistent symptoms and were considering surgical intervention.^{8,9}

Demographics, Comorbidities, and Disease Severity

Patients completed questionnaires on demographic information. Medical comorbidities required a patient self-report of a doctor diagnosis. Sinus-specific quality of life (QOL) was assessed using the 22-item Sino-Nasal Outcome Test (SNOT22). The SNOT22 contains 22 questions (total score range, 0–110), with higher scores representing more severe QOL impact.¹⁰ Computed tomography (CT) scans of the sinuses were graded according to Lund-Mackay staging system with reviewers blinded to patient-reported clinical data.¹¹ Sinonasal endoscopy was performed and graded according to the Lund-Kennedy system with reviewing physicians blinded to questionnaires.¹²

Economic and medication use variables

As the primary outcomes of interest, patients self-reported the following economic variables they had experienced over the previous 90 days. 1) days of normal productivity (i.e. work, school, volunteering, otherwise) missed as a result of sinusitis, 2) days of employment missed as a result of sinusitis, 3) hours of employment missed as a result of physician visits for sinusitis, 4) average productivity level during work (0% = no work and 100% = full work productivity coded as decimals: e.g. 0.25 = 25%), 5) minutes per day caring for sinuses, 6) hours of child care required as a result of sinusitis (i.e. during a physician visit, or during a sick day), and 7) distance travelled to attend medical appointments for sinusitis. Status of having been on disability insurance for any period of time in the past year as a result of sinus problems and estimates for patient salary, child care costs and travel expenses were requested. Number of days of medication use in the last 90 days was recorded for oral antibiotics and oral steroids, as these were considered “rescue medications” used for disease exacerbations. Maintenance medications, such as nasal steroid sprays, steroid drops/rinses, saline rinse, antihistamines, decongestants and leukotriene antagonists were not assessed, as these are typically used for control of CRS, rather than for exacerbations.

Olfactory Measures

Olfactory function, the primary exposure of interest, was assessed using two metrics. Patient-based olfactory-specific QOL was assessed using the previously validated, short modified version of the Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS). This instrument consists of 17 negative statements that are graded on a scale from 0 to 3 (total score range, 0–51). Higher QOD-NS scores reflected better olfactory-specific QOL.¹³ Clinical olfactory function was evaluated using the 40 item Smell Identification Test (SIT, Sensonics Inc., Haddon Heights, NJ). The SIT is a validated, forced choice, “scratch and sniff” identification test utilizing microencapsulated odorant strips (total scores range, 0–40) with higher scores indicating superior olfaction.¹⁴

Statistical Analysis

Statistical analyses were performed using a commercially available software application (SPSS v. 22; IBM Corporation, Armonk, NY). Descriptive statistics (means, standard deviations, percentages, etc.) were used to characterize CRS patients with respect to all study measures, including demographics, comorbidities, and other potential confounding factors. The primary exposure variables of interest, SIT and QOD-NS were associated with

economic outcome measures of various types: count, continuous, and binary. Negative binomial regression was performed to measure the association between olfaction and dependent count variables (days of missed productivity, days of missed employment, days on oral steroids and days on oral antibiotics). Linear regression was used to assess associations between olfaction and continuous dependent variables (hours of missed employment due to physician visits, average percent productivity, minutes spent in sinus care, hours of child care, and distance traveled to medical appointment). Logistic regression was used on the association between olfaction and the binary dependent variable disability insurance status. QOD-NS and SIT were inversely recoded so interpretations would reflect worsening olfaction. For each significant bivariate relationship between olfaction and economic outcome measures ($p < 0.05$), age, gender, nasal polyp status, depression, asthma, allergy, CT score, endoscopy score, and SNOT22 were also evaluated to determine their presence as confounders or correlates. These variables were each added to the unadjusted model to assess the effect of that particular variable on the beta (β) estimate of the exposure of interest in order to identify confounders. Confounding covariates that changed the β estimate by 10% or more were included in the final model. Correlates were defined by an association with the economic and medication use dependent variables ($p < 0.10$). Confounders were left in the final model regardless of statistical significance; correlates that were not significant ($p < 0.05$) were removed in a backward selection stepwise procedure. P-values in Tables 2 and 3 represent statistical significance after adjustment for the variables left in the model after this process. Multicollinearity between all model cofactors was assessed using variance inflation factors. Pearson's correlation coefficients (R_p) were used to evaluate associations between SIT and QOD-NS scores.

Results

Baseline Demographic Characteristics

A total of 221 patients were enrolled between June 2013 and June 2015. The mean age of the group was 49.3 (SD 15.9) years and just over half of the participants were female (54.3%). Patients had a mean endoscopy score of 5.6 (SD 3.8), mean CT score of 11.7 (SD 6.3), and total SNOT22 score of 53.3 (SD 21.6). A majority had nasal polyps (62.4%) and had undergone previous sinus surgery (58.8%). The mean SIT score was 28.0 (SD 9.2) and the mean QOD-NS was 37.1 (SD 12.9). SIT scores did significantly, but weakly, correlate with QOD-NS ($R_p = 0.294$, $p = 0.002$) scores. Demographics and comorbidities are described in detail in Table 1.

QOD-NS and Economic/Medication Use Outcomes

After adjusting for significant confounders and correlates, QOD-NS associated with eight of ten economic/medication usage variables measured. Lower QOD-NS was associated with more missed days of normal productivity, with a 1 point decrease in QOD-NS score being associated with an average increase of 3.2% in days of missed productivity ($\beta = 0.031$; 95% CI: 1.016, 1.047). Similarly, a 1 point decrease in QOD-NS was associated with an average 0.5% decrease in reported productivity level ($\beta = -0.005$; 95% CI: -0.008 , -0.001). Significant associations were also seen for days of missed employment, hours of missed employment due to physician visits, sinus care time, distance traveled to medical

appointment, odds of being on disability insurance, and oral steroid use (Table 2). QOD-NS was not associated with oral antibiotics used in the past 90 days nor hours of childcare required as a result of sinus related care.

SIT and Economic/Medication Use Outcomes

SIT scores were available for 104 of the 221 patients (47%). After adjusting for confounders, lower SIT (worse olfaction) scores were associated with greater distance traveled to medical appointment ($\beta=3.08$; 95% CI: 0.177–5.97) and with greater odds of being on disability insurance (Prevalence Odds Ratio=1.156; 95% CI: 1.018–1.312). No associations were found between SIT scores and missed days of normal productivity, missed days of employment, missed hours of employment due to physician visits, average productivity level, sinus care time, hours of childcare as a result of sinus problems, oral steroid use or oral antibiotic use (Table 3).

Discussion

CRS is becoming increasingly recognized as a significant economic burden and identifying those factors which impact health care utilization and daily productivity is especially important in the current healthcare environment. In this study, we were able to correlate olfactory-specific QOL, as measured by QOD-NS, to nearly all productivity and medication utilization metrics. These associations remained independent of a number of factors commonly associated with impaired olfaction, including polyp status, asthma and allergies. Most importantly, these associations remained even after adjusting for overall sinus-specific QOL as measured by the SNOT22. In our cohort, there was a significant correlation between patient reported olfactory QOL (QOD-NS) and olfactory function measured via clinical testing (SIT), but this was overall weak ($R_p=0.294$, $p=0.002$). Furthermore, the associations between SIT and economic variables were less robust, only reaching statistical significance for two metrics, distance traveled to medical appointment and disability insurance status.

The finding that olfactory-specific QOL was associated with economic variables to a greater degree than clinical olfaction scores (SIT) is interesting and worth further discussion. On one hand, it is tempting to want to emphasize the importance of clinically based olfactory function above a patient-reported metric such as QOD-NS score, attributing findings from the latter to psychometrics or an unrelated confounding factor. However, the weak correlation between clinical tests and patient experience is common to many chronic diseases, including CRS. For example, most studies examining CT scores for CRS often show relatively poor correlations with sinus-specific QOL, a result which has led to an emphasis on patient-reported outcome metrics over purely objective findings for clinical decision-making.¹⁵ Perhaps it is not surprising that the patient's experience of their olfactory loss is more closely associated with real world impacts on productivity and healthcare utilization than the absolute olfactory impairment itself. Additionally, SIT only measures a patient's ability to correctly identify odors presented at supra-threshold levels, without providing information regarding impairment in olfactory threshold. Despite these concepts, it should be kept in mind that QOD-NS and SIT scores do correlate, albeit weakly, and that most associations between SIT and economic measures in this study were in the expected

direction (eg. worse SIT scores correlate with higher economic impact), although not reaching significance. This lack of association could be due to the need for a more sensitive clinical measure of olfactory dysfunction or variations in the type of CRS being studied. These explanations remain speculative and will require a much larger study to allow definitive conclusions.

It was somewhat surprising that the impact of patient-reported olfactory dysfunction was found to be independent of SNOT22 scores. In most cases, QOL instruments have significant overlap due to inherent within-subjects associations. For example, both the SNOT22 and QOD-NS contain questions regarding psychosocial symptoms and the SNOT22 has a single question related to olfaction; therefore, it would not have been surprising if adjusting for SNOT22 scores eliminated the association between QOD-NS and economic variables. The fact that QOD-NS remained highly significant suggests that olfactory impact in and of itself may contribute to overall economic impacts. Studies that seek to fully understand and predict economic impacts of CRS should thus consider measuring olfactory impairment separate and apart from overall sinus-specific measurements such as the SNOT22 survey.

Clinical olfaction as measured by SIT significantly correlated with only two economic metrics: distance traveled to medical appointment and disability insurance status. As discussed above, this lack of significant correlation with other metrics may indicate the need for alternative clinical olfactory metrics or heterogeneity in the population studied, but these suggestions remain conjecture and will require further study. Regardless, it is apparent that impaired olfaction can be quite troubling to patients, particularly when it persists despite extensive prior treatments such as surgery. It is not uncommon for these patients to seek tertiary referral and travel greater distances for additional opinions before they accept olfactory impairment as permanent.

There are a number of potential mechanisms by which olfactory dysfunction could lead to impaired personal productivity, including increased mood disturbance. Many studies have demonstrated associations between olfactory loss, depression, and social isolation.¹⁶ These associations may be positively reinforcing, as mood disturbance can further impact olfaction. Olfactory loss may also be a marker of overall worse CRS disease severity not otherwise captured via traditional objective (CT or endoscopy) or subjective (sinus-specific QOL) measures. In this scenario, the olfactory impairment is not directly causal with regard to productivity loss or healthcare utilization, but instead is a marker of some other direct, multi-factorial mechanism.

While associations appear to exist between olfaction and economic outcomes in this study, the magnitude of some of these associations is small. However, economic outcomes are affected by numerous variables that are unmeasured in this study and it is not expected that olfaction alone drives the variation in economic outcomes. The cross-sectional nature of this study to some degree limits the conclusions which can be made. Future studies are needed to determine if improvement in olfactory dysfunction following medical or surgical treatment results in improved economic outcomes. Medical or surgical therapy for CRS tends to result in less improvement in olfaction than other cardinal symptoms.¹⁷ While improvement in

QOD-NS scores has been noted in 53% of patients undergoing ESS,¹⁸ improvement in more objective measures of olfaction may only be seen in 38%.¹⁹ This may indicate residual impairment in productivity due to persistent olfactory dysfunction despite improvement in other cardinal symptoms. Future therapies targeting olfactory dysfunction may result in greater improvements in productivity and this may be beneficial in developing societal strategies to address the economic impact of CRS.

Conclusion

Patient-reported olfactory dysfunction in patients with CRS is significantly associated with daily productivity metrics and medication utilization independent of other common CRS-associated comorbidities, objective measures of disease, demographics, and sinus-specific QOL. Additional study is needed to explore the impact of objective olfactory dysfunction and to determine whether treatment of olfactory dysfunction improves patient productivity and healthcare utilization.

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Table 1

Demographics, Comorbidities, CRS Characteristics and Olfactory Metrics (n=221 patients)

Variable		Mean (SD)	Count (%)
Demographics			
Age (years)		49.3 (15.9)	
Sex	Female		120 (54.3%)
	Male		101 (45.7%)
Race	African American		15 (6.8%)
	Asian		9 (4.1%)
	Other		5 (2.3%)
	White		192 (86.9%)
Ethnicity	Hispanic/Latino		11 (5.0%)
	Non-Hispanic/Latino		210 (95.0%)
Education (years)		14.8 (2.4)	
Comorbidities			
Asthma			97 (43.9%)
AERD			14 (6.3%)
Allergy by Testing			140 (63.4%)
COPD			12 (5.4%)
Depression			23 (10.4%)
Fibromyalgia			7 (3.2%)
Immunodeficiency			9 (4.1%)
Ciliary dysfunction			2 (0.9%)
Cystic fibrosis			7 (3.2%)
Autoimmune disease			9 (4.1%)
Diabetes (type 2)			20 (9.1%)
CRS characteristics			
Previous Sinus Surgery			130 (58.8%)
CRSwNP			138 (62.4%)
Endoscopy Score		5.6 (3.8)	
CT Score		11.7 (6.3)	
SNOT22		53.3 (21.6)	
Olfactory metrics			
SIT Score Overall (n=104 patients)		28.0 (9.2)	
Anosmic		11.2 (3.1)	20 (19.2%)
Hyposmic		29.8 (3.7)	54 (51.9%)
Normosmic		35.9 (1.3)	30 (28.8%)
QOD-NS Overall (n=104 patients)		37.1 (12.9)	
Anosmic (by SIT)		29.2 (12.2)	20 (19.2%)
Hyposmic (by SIT)		38.3 (12.7)	54 (51.9%)

Variable	Mean (SD)	Count (%)
Normosmic (by SIT)	39.8 (11.2)	30 (28.8%)

SD: Standard deviation; AERD: Aspirin exacerbated respiratory disease; COPD: Chronic obstructive pulmonary disease; CRS: Chronic rhinosinusitis; NP: Nasal polyps; CT: Computed tomography; SNOT: Sinonasal Outcome Test; SIT: Smell Identification Test; QOD-NS: Questionnaire of Olfactory Disorders

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Table 2

Negative binomial, linear, and logistic regressions assessing associations between QOD-NS and 90 day economic measures/medication use variables

Economic Measures	Unadjusted β	Adjusted β	P-Value	Prevalence Ratio	CI
Days of missed productivity ^a	0.037	0.031	<0.001	1.032	(1.016, 1.047)
Days of missed employment ^a	0.050	0.034	<0.001	1.035	(1.020, 1.049)
Hours of missed employment due to physician visits ^b	1.123	1.275	0.002	-	(0.455, 2.096)
Average percent productivity ^b	-0.005	-0.005	0.014	-	(-0.008, -0.001)
Minutes spent in sinus care ^b	0.561	0.355	0.015	-	(0.069, 0.641)
Hours of child care ^b	-0.007	-0.007	0.813	-	(-0.065, 0.051)
Distance traveled to medical appointment ^b	2.583	3.387	<0.001	-	(1.785, 4.990)
Disability Insurance ^c	0.076	0.083	0.003	1.086	(1.028, 1.147)
Medication usage					
Days on oral steroid ^a	0.020	0.014	0.044	1.014	(1.000, 1.028)
Days on oral antibiotic ^a	0.002	0.002	0.766	1.002	(0.991, 1.013)

QOD-NS: Questionnaire of Olfactory Disorders

Models were adjusted for age, gender, nasal polyp status, depression, asthma, allergy, SNOT22, CT score, and endoscopy score in combinations specific to each economic variable.

^a Interpretation example for negative binomial regression: On average, for a one point decrease in QOD-NS, days of missed productivity increased by 3.2% and we are 95% confident that the true estimate is between 1.6% and 4.7%.

^b Interpretation example for linear regression: On average, for a one point decrease in QOD-NS, hours of missed employment goes up by 1.275 and we are 95% confident that the true estimate is between 0.455 and 2.096 hours.

^c Interpretation for logistic regression (Prevalence Odds Ratio): On average, for a one point decrease in QOD-NS, the odds of being on disability insurance increases by 8.6% and we are 95% confident that the true estimate is between 2.8% and 14.7%.

Negative binomial, linear, and logistic regressions assessing associations between SIT scores and 90 day economic measures/medication use variables

Table 3

Economic Measures	Unadjusted β	Adjusted β	P-Value	Prevalence Ratio	CI
Days of missed productivity	0.012	0.012	0.298	1.012	(0.989, 1.036)
Days of missed employment	0.041	-0.006	0.780	0.994	(0.956, 1.034)
Hours of missed employment due to physician visits	1.232	1.232	0.249	-	(-0.877, 3.341)
Average percent productivity	0.001	0.001	0.779	-	(-0.007, 0.010)
Minutes spent in sinus care	-0.462	-0.462	0.082	-	(-0.985, 0.060)
Hours of childcare	-0.048	-0.048	0.204	-	(-0.123, 0.027)
Distance traveled to medical appointment ^a	2.569	3.075	0.038	-	(0.177, 5.974)
Disability Insurance ^b	0.115	0.145	0.025	1.156	(1.018, 1.312)
Medication Usage					
Days on oral steroid	0.036	0.015	0.279	1.015	(0.988, 1.043)
Days on oral antibiotic	0.008	0.008	0.443	1.009	(0.987, 1.031)

SIT: Snell Identification Test

Models were adjusted for age, gender, nasal polyp status, depression, asthma, allergy, SNOT22, CT score, and endoscopy score in combinations specific to each economic variable.

^a Interpretation for linear regression: On average, for a one point decrease in SIT, distance traveled to medical appointment goes up by 3.075 miles and we are 95% confident that the true estimate is between 0.177 and 5.974 miles.

^b Interpretation for logistic regression (Prevalence Odds Ratio): On average, for a one point decrease in SIT, the odds of being on disability insurance increases by 15.6% and we are 95% confident that the true estimate is between 1.8% and 31.2%.