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Does Comorbid Anxiety Predict Quality of Life Outcomes in Patients with Chronic Rhinosinusitis Following Endoscopic Sinus Surgery?

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Abstract

Background—Approximately 25% of patients with chronic rhinosinusitis (CRS) have comorbid anxiety and both conditions independently decrease quality-of-life (QOL). QOL outcomes for CRS and depression have garnered the majority of research attention but efforts to better understand the impact of anxiety disorders on QOL are increasing. We evaluated the role of comorbid *anxiety* in patients with CRS undergoing endoscopic sinus surgery (ESS).

Methods—Adult patients (n=148) with CRS with and without comorbid anxiety were prospectively enrolled into a treatment outcomes investigation. History of comorbid anxiety was retrospectively identified (n=30;20%) and preoperative and postoperative QOL (RhinoSinusitis Disability Index; RSDI, and 22-item SinoNasal Outcome Test; SNOT-22) scores were compared to patients without comorbid anxiety.

Results—Compared to patients without anxiety, patients with anxiety were found to be younger ($p=0.02$) and have a higher prevalence of female gender ($p=0.05$), diabetes mellitus ($p<0.001$), depression ($p<0.001$), and tobacco use ($p=0.03$). Participants with comorbid anxiety reported significantly worse preoperative psychological dysfunction as measured by SNOT-22 subdomain scores ($p= 0.02$), as well as worse preoperative functional ($p=0.04$) and emotional ($p=0.001$) impairment as evaluated by RSDI subdomain scores. After adjustment for other cofactors, patients with anxiety improved significantly less on SNOT-22 total scores compared to participants without anxiety after ESS ($p=0.02$).

Conclusions—Anxiety occurs with higher prevalence in patients with CRS and the presence of comorbid anxiety is associated with worse preoperative QOL and reduced QOL improvement following ESS. These findings warrant improvement in screening, diagnosis, and treatment for patients with CRS and comorbid anxiety.

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MeSH Key Words

Sinusitis; endoscopy; chronic disease; anxiety; quality of life; mental health; depression; general surgery; psychiatric distress

INTRODUCTION

Chronic rhinosinusitis (CRS) shares considerable overlap in symptomatology with many co-morbid conditions such as sleep apnea, asthma, allergic rhinitis, gastroesophageal reflux disease, migraine, and psychiatric disorders. The impact of these comorbid conditions on quality of life (QOL) outcomes for patients undergoing endoscopic sinus surgery (ESS) has been the focus of several recent studies allowing clinicians improved insight into the interpretation of QOL outcomes in patients electing endoscopic sinus surgery.[1–3]

Previous investigations have established that psychiatric illness is found more frequently in patients with chronic rhinosinusitis, with higher prevalence rates for both depression (20–25%) and anxiety (17–32%).[4–6] Furthermore, patients given a diagnosis of CRS have a significantly higher prevalence of premorbid anxiety.[7] The presence of comorbid anxiety may alter the patient's experience of their chronic disease process and lead to increases in symptom severity reporting.[5]

While the role that depression assumes in outcomes of ESS has been well studied, comorbid anxiety in CRS patients electing sinus surgery has received less attention. As such, we sought to further clarify the impact of comorbid anxiety on QOL measures in patients undergoing endoscopic sinus surgery for chronic sinusitis. Based on previous data published on comorbid depression and CRS[8,9], we hypothesized that patients with comorbid anxiety would report lower pre-operative QOL scores, but experience similar gains in QOL following endoscopic sinus surgery as those patients without comorbid anxiety.

MATERIALS and METHODS

Inclusion criteria and study population

Adult patients (≥18 years) were recruited from the Oregon Sinus Center at the Oregon Health & Science University (OHSU, Portland, OR, USA) as part of a continuing, multi-site, observational, prospective cohort investigation to evaluate various treatment outcomes following endoscopic sinus surgery (ESS). Results from this investigation have been previously published.[1–3, 10, 11] All patients were diagnosed with recurrent exacerbations of recalcitrant rhinosinusitis following criteria currently endorsed by the Rhinosinusitis Task Force [12] and self-selected ESS as the next treatment option. All patients had previously taken medical therapies including at least one course (≥14-days) of broad spectrum or culture directed antibiotics and at least one trial of topical corticosteroids (≥21-days) or a 5-day course of oral corticosteroid therapy.

All enrolled study participants provided informed consent in English and agreed to complete all preoperative study-related evaluations. Participants were asked to provide personal demographic information, as well as complete social and medical histories. Participants

were assured study involvement was completely voluntary and standard of care was in no way altered during the study duration. The Institutional Review Board at OHSU granted study approval and annual review of safety protocols and enrollment progression (*eIRB* #7198). Consenting participants were followed for a total of 18-months postoperatively with observational, follow-up assessments 6-month intervals either during routine, physician-directed clinical appointments or via follow-up mailings using the U.S. Postal Service with self-addressed return envelopes. Concurrent follow-up clinical examinations were also collected at 6-month intervals when feasible.

Retrospective review of comorbid anxiety

Participant data collection for this cohort did not originally include information regarding a diagnosis of comorbid anxiety, generalized anxiety disorder, symptomatic information, or medical treatment for symptoms related to anxiety. Retrospective chart review was completed for all participants for a diagnosis of anxiety, or anxiety related disorders, depression, and to identify those participants being actively treated with a selective serotonin reuptake inhibitor (SSRI), benzodiazepine, or additional class of medication designed to treat symptoms of anxiety. Participants were operationalized as having a comorbid diagnosis of anxiety if the following inclusion criteria were identified: A history of anxiety or related disorders as defined by the International Classification of Diseases, Ninth Revision[13] (ICD-9: 300.0X; generalized anxiety disorder, panic disorder, agoraphobia, social phobia, simple phobia, post-traumatic stress disorder, obsessive-compulsive disorder). Current use or history of use of prescribed medications for treatment of anxiety was recorded from the medical record and included:

- **a.** Benzodiazepines
  - **i** Alprazolam, Clonazepam, Diazepam, Lorazepam, Oxazepam, Chlordiazepoxide
- **b.** Tricyclic anti-depressants
  - **ii** Imipramine, Desipramine, Notriptyline, Amitriptyline, Doxepin, Clomipramine
- **c.** Selective serotonin reuptake inhibitors (SSRIs)
  - **iii** Fluoxetine, Fluvoxamine, Sertraline, Paroxetine, Escitalopram oxalate, Citalopram
- **d.** Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
  - **iv** Venlafaxine, Venlafaxine XR, Duloxetine
- **e.** Psychotropic medications [not belonging to above medication classes]:
  - **v** Buspirone, Buproprion, Carbamazepine
- **f.** Dual modality therapy

Given multiple medical indications (i.e. depression, smoking cessation) for which the above classes of medications are prescribed, participants identified as taking one or more of the above medications were also required to have a concurrent diagnosis of anxiety or anxiety

related disorder. Classes of treatment medication were included during retrospective review in an attempt to comprehensively gather those patients in whom listed ICD-9 diagnosis of anxiety may be part of a supplemental the medical record. Conversely, patients with a diagnosis of anxiety were not excluded if they lacked treatment with any of the above medication classes.

Exclusion criteria

Study participants were excluded from final analysis if they were prescribed any of the above classes of medication without a concurrent diagnosis of anxiety, found to have additional or comorbid psychiatric illness (eg. bipolar disorder, schizophrenia, attention deficit hyperactivity disorder), or if they had not yet entered the initial follow-up period (≤6-months). Patients with recurrent acute rhinosinusitis were also excluded due to different pathophysiology of disease. Any participants who failed to provide any study-related evaluations within the 18-months after ESS were categorized as lost to follow-up.

Clinical measures of disease severity

Standard clinical measures of disease severity, collecting during preoperative evaluations, were used simultaneously for investigational purposes. High resolution computed tomography (CT) with bone and tissue windows was utilized to evaluate sinonasal disease severity using 1.0*mm* contiguous images in both sagittal and coronal planes. Images were also staged by the enrolling physician in accordance with the Lund-Mackay bilateral scoring system (score range: 0–24) which quantifies the severity of image opacification in the maxillary, ethmoidal, sphenoidal, ostiomeatal complex, and frontal sinus regions using a Likert scale.[14]

The paranasal sinuses were also evaluated bilaterally using rigid, 30° fiberoptic endoscopes (SCB Xenon 175, Karl Storz, Tuttlingen, Germany) by the enrolling physician (TLS). Endoscopic exams were staged by the enrolling physician using the bilateral Lund-Kennedy scoring system (score range: 0–20) which quantifies pathologic states within the paranasal sinuses including the severity of polyposis, discharge, edema, scarring, and crusting on a Likert scale.[15] Endoscopic examinations were collected during concurrent 6-month intervals when feasible during standard clinic follow-up visitations. Higher scores on both staging systems reflect worse disease severity.

Preoperative and postoperative olfactory function was evaluated using the Brief Smell Identification Test (BSIT) screening tool concurrently with QOL survey evaluations. The BSIT is a validated 12-item, noninvasive test of olfactory function that uses microencapsulated odorant strips which are activated with a standard #2 pencil in a ‘scratch ‘n sniff’ format.[16] Participants are instructed to identify each odorant using a method of forced choice (score range: 0–12). Higher total scores represent better olfactory status whereas both male and females can be categorized as having “normal” (score >9) or “abnormal” (score <9) olfactory function.

Disease-specific quality of life measures

Participants completed two patient-based QOL surveys during both preoperative evaluation and at all subsequent follow-up time points, as part of a larger total battery of evaluative instruments. The 22-item Sinonasal Outcome Test (SNOT-22) is a validated survey developed to evaluate symptom severity in rhinosinusitis (©2006, Washington University, St. Louis, MO, USA).[17] Exploratory factor analysis of SNOT-22 scores using this cohort identified 5 distinct subdomains which have been previously described.[10] Subdomains include rhinologic symptoms (score range: 0–30), extra-nasal rhinologic symptoms (score range: 0–15), ear and/or facial symptoms (score range: 0–25), psychological dysfunction (score range: 0–35), and sleep dysfunction (score range: 0–25). Higher subdomain and SNOT-22 scores (score range: 0–110) represent worse QOL and symptom severity.

The Rhinosinusitis Disability Index (RSDI) is a 30-item survey instrument comprised of 3 subdomains to assess the impacts of rhinosinusitis on a participants physical (score range: 0–44), functional (score range: 0–36), and emotional (score range: 0–40) status.[18] Higher subdomain and total RSDI scores (score range: 0–120) represent worse QOL and greater impact of rhinosinusitis symptoms on patients' daily function.

Surgical intervention

The extent of endoscopic sinus surgery was contingent upon and directed by intraoperative physician's discretion and reflected disease progression on a case-by-case basis. Endoscopic sinus surgery consisted of either unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, middle turbinate resection or inferior turbinate reduction, septoplasty, or frontal sinusotomy (*Draf* I, IIa, IIb, or III) procedures and involved judicious use of image guidance. Study participants were either primary or revision surgery cases.

Data management and statistical analyses

All study data was de-identified and manually entered into a relational database (Microsoft Access; Microsoft Corp., Redmond, WA, USA). Statistical analyses were completed using SPSS v.22 statistical software (IBM Corp., Armonk, NY, USA). Baseline study population characteristics, clinical measures of disease severity, disease-specific quality of life scores, measures of surgical extent, and designations of comorbid anxiety were evaluated descriptively and data normality was verified for all continuous measures using graphical analysis. Final cohort data was dichotomized between participants with and without an indication of comorbid anxiety. Furthermore, due to known clinical associations between anxiety and depression[19, 20] further analysis compared both pre- and postoperative associations between distinct study subgroups of participants including those without anxiety or depression, anxiety without depression, depression without anxiety, and those with a history of both anxiety and depression. Bivariate group comparisons of baseline characteristics, clinical measures of disease severity, and preoperative QOL scores were evaluated using either two-tailed sample t-testing or Mann Whitney U tests for all continuous measures or chi-square ($\chi 2$) testing for all contingency tables. Subgroups comparisons integrated either Kruskall-Wallis nonparametric testing, with adjustments for multiple comparisons when appropriate for continuous measures, or $\chi 2$ testing to evaluate differences in frequency between subgroups. Matched pairing t-tests and Wilcoxon signed

rank tests were used to evaluate significant differences over time between preoperative and last postoperative scores. Last available SNOT-22 and RSDI scores were used to operationalize each postoperative time point due to previously reported consistency of postoperative scores between 6, 12, and 18-months.[11, 21] To account for variation in baseline status, the percentage (%) of absolute relative change in mean outcome scores was reported for subgroups with and without comorbid anxiety using the following algorithm: [(mean preoperative score – mean postoperative score) / mean preoperative score] × 100.

Stepwise linear regression was used to identify significant independent predictors associated with significant mean postoperative improvement in QOL scores. The primary outcome of interest was operationalized by subtracting preoperative scores from the last available postoperative score for each participant. All preliminary models included a binary measure of comorbid anxiety (Yes/No) as the main exposure variable of interest. An additional 15 variables, representing baseline patient characteristics, were screened for univariate significance at a 0.250 alpha level. Without adjustment for preoperative QOL measures final models were built using manual forward selection ($p<0.10$) and backwards elimination ($p<0.05$) methods. Due to historic associations between anxiety and depression, depression as was considered not only an independent predictive value, but also a potential confounding factor and effect modifier. Any cofactor resulting in an absolute difference of greater than ±10% in the effect estimate for the anxiety variable was considered a significant confounder. Multiplicative interaction between anxiety and depression was also evaluated with both independent factors placed in each model. Multi-collinearity between all variables in final model was evaluated using variance inflation factors (VIFs) while cofactors with VIFs > 10 were prioritized and removed if clinically irrelevant. Unadjusted and adjusted regression coefficients (β), standard errors (SE), 95% confidence intervals, and estimates of type I error (p) were reported for all final models. The percentage of model variance was assessed using coefficients of multiple determination (R^2).

RESULTS

Preoperative characteristics

A total of 185 study participants undergoing ESS were enrolled between March, 2011 and July, 2014. After retrospective chart review, 9 participants were excluded due to comorbid psychiatric illnesses including: attention deficit disorder (ICD-9: 314.00), attention deficit hyperactive disorder (ICD-9: 314.01), bipolar II disorders (ICD-9: 296.89), psychiatric disorder with pain manifestations (ICD-9: 307.80), and psychosis not otherwise specified (ICD-9: 298.90). An additional 27 participants were removed due to exacerbations associated with recurrent acute rhinosinusitis and 1 participant was removed as they had been enrolled and undergone ESS within the 6-months preceding this investigation. A total of 148 participants were included in all final analyses, including 30 (20%) participants with comorbid anxiety. Both patient groups with and without comorbid anxiety were found to have a statistically comparable ($p=0.20$) prevalence of postoperative follow-up (67% vs. 78%, respectively).

Bivariate comparisons of baseline characteristics and clinical measures of disease severity are described in Table 1. Compared to participants without anxiety, patients with anxiety

were found to be significantly younger and have a significantly higher prevalence of female gender, diabetes mellitus, depression, and tobacco use while having a greater lower prevalence of reported alcohol use. The prevalence of medication usage for symptoms of anxiety is described in Table 2.

Subgroup Preoperative Characteristics

Preoperative characteristics for distinct study subgroups including those without anxiety or depression, anxiety without depression, depression without anxiety, and those with a history of both anxiety and depression are listed in Table 3. The subgroup of participants with anxiety and no depression were found to have a significantly higher prevalence of current tobacco use compared to all other subgroups. Additionally, the subgroup of participants with both comorbid anxiety and depression were found to have a significantly lower prevalence of alcohol use compared to other subgroups.

Preoperative quality of life measures/subgroup preoperative quality of life measures

Participants with comorbid anxiety reported significantly worse preoperative psychological dysfunction as measured by mean SNOT-22 subdomain scores, as well as worse preoperative mean functional and emotional impairment scores as evaluated by the subdomains of the RSDI (Table 4). After statistical adjustments for multiple comparisons, subgroup comparisons found that participants with depression without anxiety (n=16) reported significantly worse SNOT-22 total mean preoperative scores compared to participants without anxiety or depression (n=102; 67.3[12.2] vs. 53.1[19.6]; p= 0.03). Differences between those group scores were comprised by worse ear and/or facial symptom mean scores (9.2[2.9] vs. 8.1[3.7]; p=0.03) and psychological dysfunction mean scores (21.4[4.2] vs. 15.9[7.8]; p=0.04). Participants with a history of both anxiety and depression were also found to have significantly worse RSDI emotional subdomain mean scores compared to those without anxiety or depression (19.2[9.5] vs. 11.6[8.9]; p=0.02). Likewise, those with a history of depression without anxiety reported worse average RSDI emotional subdomain scores compared to patients without anxiety or depression (18.3[6.9]; p=0.03).

Postoperative improvements in clinical measures

Both participants with and without comorbid anxiety were found to have significant improvement in mean endoscopy scores but did not reported improved olfaction function mean scores after ESS (Table 5). Participant subgroups were found to have comparable improvement over time. Subgroups comparisons found no statistical differences in mean endoscopy scores or BSIT olfactory function scores between any group with or without comorbid anxiety or depression.

Postoperative quality of life improvements

Mean postoperative scores were found to have significant improvement following ESS for both groups with and without comorbid anxiety, with the exception of the RSDI emotional subdomain (Table 6). The magnitude of improvement was identified as significantly greater for study participants without anxiety for average SNOT-22 total scores, as well as average rhinologic symptom and sleep dysfunction subdomain scores of the SNOT-22.

After adjustments for multiple comparisons, subgroup comparisons found that participants with anxiety without depression improved to a significantly lesser average extent on SNOT-22 rhinologic symptom scores compared to participants without anxiety or depression (−2.1[4.7] vs. −9.5[6.3]; p=0.005). Similar findings between these subgroups was reported on mean improvement on SNOT-22 extra-nasal rhinologic symptom scores (−0.7[3.0] vs. −4.6[3.8]; p=0.02).

Linear regression modeling for postoperative QOL improvement

Study participants with comorbid anxiety were found to be statistically and clinically associated with less average postoperative improvement across several QOL survey scores ($p<0.10$; Table 6) without adjusting for other patient variables or potential confounding factors. Simple linear regression was utilized to control for the effect of covariates on any significant association between anxiety and QOL improvement measures (Table 7). After adjustment, comorbid anxiety was found to be significantly associated with less/worse improvement in reported SNOT-22 scores. For example, after adjustment for all independent covariates, participants with anxiety were significantly associated with an 11-point lesser improvement on SNOT-22 total scores following endoscopic sinus surgery.

Depression was not found to be a significant independent predictor of mean score improvement, but did significantly negatively confound effect estimates for anxiety for the SNOT-22 total scores when included in preliminary models both alone and with a multiplicative interaction term (anxiety * depression). Final regression models were capable of explaining between 13% – 24% of total model variance. No further evidence of meaningful confounding, interactions, or multi-collinearity was found as all VIFs were less than 2.0.

DISCUSSION

Patients with a history of psychiatric illness and CRS can pose challenges to manage. Depressive and anxiety disorders may present with physical complaints with or without objective findings, leading to both patient and provider confusion and frustration.[22,23] Moreover, exploration of emotional issues may be uncomfortable for a provider who has yet to establish a strong physician-patient relationship.[22] Anxiety has been shown to play an important role in the management of patients with CRS, affecting both presenting symptoms and treatment outcomes. Comorbid anxiety is present in between 17–32%[4–6] of patients with CRS and is associated with greater sinus symptom reporting, health-care use, and occupational impairment.[24] Furthermore, patients with psychiatric comorbidity have been shown to report more severe CRS related symptoms following surgical treatment for CRS.[4]

This study expands on previous investigations characterizing QOL outcomes in patients with CRS and comorbid anxiety and further evaluates QOL outcomes following endoscopic sinus surgery. Patients with comorbid anxiety within this cohort tended to be younger than patients without comorbid anxiety, report current tobacco use, and have co-existing diabetes mellitus (Type I or II). Interestingly, anxiety disorders are known to have a complex interrelationship with nicotine use, with genetic, biochemical, psychological, interpersonal, and environmental vulnerability factors.[25] There is also clear evidence that cigarette smoke,

either through active or passive exposure, contributes to CRS.[26, 27] Data from this cohort is consistent with previous research demonstrating increased prevalence of anxiety disorders in patients with diabetes mellitus.[28, 29] Furthermore, recent data has shown clinically significant less improvement of postoperative SNOT-22 scores from baseline to 6-month follow up in patients with diabetes mellitus.[30] Despite the above influences on QOL outcomes in CRS, linear regression modelling did not show any significant confounding influence by age, smoking, or comorbid diabetes mellitus on QOL outcomes for patients with CRS and comorbid anxiety.

Anxiety and depression are the two most common mental health disorders seen in the general medical population.[22] Despite overlapping symptoms between the two conditions, anxiety disorders are characterized by distinct symptoms of avoidant behavior, tension, fear, physiologic arousal, escape behaviors, and elevated responses to disorder-specific or personally relevant stressors.[31] While depression has garnered the majority of research attention and medical interest in screening, diagnosis, and treatment, efforts to understand the impact of anxiety disorders on general health are increasing. Epidemiological research suggests that anxiety disorders are among the most prevalent psychiatric disorders, with a 12-month rate of 18.1% and a lifetime rate of 28.8%.[20] Furthermore, over 30 million Americans have a lifetime history of anxiety[32], and estimated annual costs for anxiety disorders are over 40 billion dollars, including $23 billion in non-psychiatric medical treatment costs, $13.3 billion in psychiatric treatment costs, $4.1 billion in indirect workplace costs, $1.2 billion in mortality costs, and $0.8 billion in prescription pharmaceutical costs.[33]

Anxiety often accompanies chronic disease, though the relationship between the two is complex and multi-factorial. The prevalence of anxiety is more common in chronic diseases such as asthma, chronic obstructive pulmonary disease, stroke, coronary artery disease, and chronic sinusitis.[4,34, 35] Anxiety may manifest as uncertainty regarding the unpredictability of chronic disease, difficulty sleeping at night due to worry about their chronic disease, and uncertainty as to the ability to cure chronic disease.[35] Several pathways have been proposed to better understand the relationship between anxiety and chronic disease. Patients may experience anxiety as a consequence of chronic disease, as an etiological factor for their chronic disease, as cyclical with their chronic disease, or as completely independent of their chronic disease. In the clinical setting, the overlap in symptoms between the two may make it more challenging for patients to recognize anxiety as a separate condition and increase difficulty in establishing a formal diagnosis for the clinician.[35]

The use of QOL measures has allowed for insight into the patient's experience of anxiety and CRS. Patients with anxiety disorders have been shown to have impaired QOL across multiple dimensions including vitality, physical health, mental health, family life, activities of daily living, social and leisure activities, relationships, and activities outside occupation.[36] Robust data exists documenting declines in both disease-specific and general QOL in patients with CRS.[37] Recently, five correlated yet distinguishable sub-domains within the SNOT-22 were described.[10] As might be expected, patients within this cohort with comorbid anxiety were found to have significantly worse baseline measures of QOL within the psychological subdomain of the SNOT-22, but no difference in total SNOT-22

score. This is consistent with previous data that identified a strong association between psychological symptoms in the SNOT-22 and anxiety[6] and suggests that the psychological subdomain of the SNOT-22 may be sensitive to changes based on comorbid anxiety. Furthermore, baseline QOL measures within the RSDI demonstrated worse overall baseline QOL scores with statistically significant differences in both the emotional and functional subdomains. While data from patients with CRS and comorbid anxiety has not been published using the RSDI, our data is consistent with previously published literature utilizing the RSI in which patients with anxiety tended to report higher oropharyngeal and total symptoms.[5] Furthermore, Davis et al. reported that subjects with high degrees of anxiety reported significantly higher/worse pre-operative SNOT-16 scores, and subjects with persistent anxiety at the 12 month follow up reported higher symptom scores/worse as measured by the SNOT-16. Relative improvements in SNOT-16 total scores, for patients with persistent anxiety, were 26% while those without improved by 39%.[4] Likewise, in our study the percentage relative change/postoperative improvement in SNOT-22 total scores in patients with anxiety was 31% while those without anxiety improved by 52%. The differences in relative changes between the two studies are likely multifactorial and include the use of two differing instruments for measuring quality of life, possible differences in patient characteristics, and a lack of validated measure of postoperative anxiety in the current study.

Clinical measures of disease status including Lund-McKay CT score and Lund-Kennedy endoscopy score within this cohort were not significantly different between anxiety groups either pre-operatively or post-operatively. Both patients with and without comorbid anxiety were found to have significant improvements in endoscopy scores over time, though there was no difference between the two groups in the degree of improvement. Similar to these findings, Bhattacharyya previously reported that CT scores were not correlated with symptom reporting in patients with anxiety and depression.[24]

Despite no differences in clinical measures of disease severity, patients with anxiety were found to experience significantly less postoperative improvement in QOL scores following endoscopic sinus surgery. Specifically, participants with anxiety alone improved to nearly 11 points less on total Snot-22 scores, exceeding the minimally clinically significant detectable change based on comparisons to patient reported transition scales.[17] Moreover, linear regression modelling was used to control for comorbid depression with anxiety, with combined anxiety-depression patients exhibiting greater QOL improvements than patients with comorbid anxiety alone, though this difference was not statistically significant. This change likely reflects previously reported data in which patients with depression improved to a similar magnitude following ESS in disease specific QOL (RSDI) scores than patients without depression.[8,9] This data has several important implications for the Otolaryngologist. High prevalence rates of comorbid psychiatric illness exist within the CRS population. While screening for anxiety may be tedious in a busy clinical practice, consideration should be given to the implementation of validated instruments to screen for mental health disorders such as the Hospital Anxiety and Depression Scale, Beck Anxiety Inventory, and the State Trait Anxiety Inventory.[38–40] We find it important to note that patients with comorbid anxiety do in fact exhibit postoperative QOL improvements, though to a lesser degree as

seen in this study. This data may assist with pre-operative and post-operative counseling of the anxious patient in terms of both patient and treating physician expectations.

There are several notable limitations to this study. Although we attempted to ascertain medical treatment regimens for patients with comorbid anxiety, we could not account for individual severity levels of anxiety or successful control of anxiety related symptoms. The diagnosis of anxiety and depression was obtained through chart review rather than prospective use of validated instruments or screening tools, thus introducing the potential for underreporting of anxiety and depression. This allows for potential non-differential misclassification bias by including patients with true anxiety into the non-anxiety group and patients with true depression into the non-depression group. Interestingly this would bias any effect estimates (β) of anxiety towards the null hypothesis and inherently reduce our ability to evaluate the true effect of anxiety on QOL outcomes. Additionally, this study was conducted at a single institution tertiary rhinology center. Conceivably, patients seeking care at a tertiary rhinology center may experience increased levels of anxiety and results may not be generalizable to the CRS patient electing ESS in an alternate setting. While a diagnostic instrument was not used, the prevalence of comorbid anxiety in this cohort was 20%, which is akin to previously reported data.[4,5,24] Furthermore, it is possible that QOL improvement post-operatively could vary by severity of comorbid mental illness, and future prospective studies are needed to clarify this issue. Future studies of patients with comorbid anxiety and CRS should also preferably utilize validated QOL instruments in combination with screening/diagnostic tools to identify those patients with anxiety disorders. Additionally, prospective evaluation of the role of active psychiatric treatment (pharmacologically or with behavioral therapy) in patients with comorbid CRS and anxiety would help to clarify the role of anxiety related symptoms in surgical outcomes.

CONCLUSION

Anxiety occurs with increased prevalence in patients with CRS. The presence of co-morbid anxiety with CRS leads to increased symptom reporting at baseline and poorer QOL outcomes following endoscopic sinus surgery. Insight into the role of mental illness in CRS is progressing; however there is need for improvements in screening, diagnosis and treatment for patients with mental illness and CRS.

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Table 1

Comparison of baseline demographic and clinical measures of disease severity for CRS patients with and without anxiety

	Comorbid anxiety (n=30)		Without comorbid anxiety (n=118)		
Baseline Characteristics:	**Mean [SD]**	**N(%)**	**Mean [SD]**	**N(%)**	**p-value**
Age (years)	46.3 [15.1]		53.6 [14.5]		0.02
Follow-up duration (months)	16.5 [5.3]		16.0 [4.8]		0.66
Male		10 (33%)		63 (53%)	----
Female		20 (67%)		55 (47%)	0.05
Previous sinus surgery		14 (47%)		55 (47%)	0.99
Nasal polyposis		10 (33%)		51 (43%)	0.33
Septal deviation		15 (50%)		55 (47%)	0.74
Turbinate hypertrophy		3 (10%)		28 (24%)	0.13
Diabetes Mellitus (type I or II)		9 (30%)		3 (3%)	<0.001
Asthma		9 (30%)		39 (33%)	0.75
Aspirin intolerance		0 (0%)		10 (9%)	0.21
Allergies (history)		2 (7%)		17 (14%)	0.37
Allergies (mRAST confirmed)		8 (27%)		48 (41%)	0.16
Depression		14 (47%)		16 (14%)	<0.001
Current tobacco use		5 (17%)		6 (5%)	0.03
Alcohol use		8 (27%)		68 (58%)	0.002
Oral steroid dependency		1 (3%)		1 (1%)	0.37
Clinical measures of disease severity:					
Computed tomography (CT) score	13.5 [5.6]		14.1 [6.0]		0.51
Endoscopy score	7.4 [3.7]		7.2 [3.5]		0.82
BSIT olfactory function score	9.0 [3.2]		8.7 [3.3]		0.66

SD, standard deviation; mRAST, modified radioallergosorbent testing; BSIT, Brief Smell Identification Test.

Table 2

Prevalence of patient-reported medication use for subjects with comorbid anxiety

Patient-reported medication use:	**N(%)**
None	1 (3%)
Benzodiazepines	12 (40%)
Tricyclic anti-depressants	1 (3%)
Selective serotonin reuptake inhibitors (SSRIs)	7 (23%)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	1 (3%)
Psychotropic medications	3 (10%)
Dual modality therapy	4 (13%)
Marijuana	1 (3%)

Table 3

Comparison of baseline demographic and clinical measures of disease severity across subgroups with and without comorbid anxiety and depression

	No anxiety / no depression (n=102)		Anxiety w/o depression (n=16)		Depression w/o anxiety (n=16)		Anxiety & depression (n=14)		
Baseline Characteristics:	**Mean [SD]**	**N(%)**	**Mean [SD]**	**N(%)**	**Mean [SD]**	**N(%)**	**Mean [SD]**	**N(%)**	**p-value**
Age (years)	54.2 [14.4]		46.1 [13.5]		49.6 [15.4]		46.5 [17.4]		0.08
Follow-up duration (months)	15.7 [4.9]		17.8 [5.9]		17.6 [4.7]		15.4 [4.7]		0.20
Male		58 (57%)		5 (31%)		5 (31%)		5 (36%)	----
Female		44 (43%)		11 (69%)		11 (69%)		9 (64%)	0.06
Previous sinus surgery		48 (47%)		6 (38%)		7 (44%)		8 (57%)	0.75
Nasal polyposis		47 (46%)		5 (31%)		4 (25%)		5 (36%)	0.31
Septal deviation		44 (43%)		9 (56%)		11 (69%)		6 (43%)	0.23
Turbinate hypertrophy		25 (25%)		2 (13%)		3 (19%)		1 (7%)	0.37
Asthma		32 (31%)		6 (38%)		7 (44%)		3 (21%)	0.58
Aspirin intolerance		8 (8%)		0 (0%)		2 (13%)		0 (0%)	0.36
Allergies (history)		14 (14%)		1 (6%)		3 (19%)		1 (7%)	0.66
Allergies (mRAST confirmed)		43 (42%)		5 (31%)		5 (31%)		3 (21%)	0.39
Depression		0 (0%)		0 (0%)		16 (100%)		14 (100%)	<0.001
Current tobacco use		6 (6%)		4 (25%)		0 (0%)		1 (7%)	0.03
Alcohol use		62 (61%)		6 (38%)		6 (38%)		2 (14%)	0.003
Oral steroid dependency		1 (1%)		0 (0%)		0 (%)		1 (7%)	0.25
Clinical measures of disease severity:									
Computed tomography (CT) score	14.4 [6.0]		14.3 [5.3]		12.4 [6.0]		12.6 [6.1]		0.52
Endoscopy score	7.3 [3.4]		7.6 [3.6]		6.7 [4.5]		7.3 [4.0]		0.76
BSIT Olfactory function score	8.6 [3.3]		9.4 [3.0]		8.9 [3.1]		8.5 [3.4]		0.84

SD, standard deviation; mRAST, modified radioallergosorbent testing; BSIT, Brief Smell Identification Test. p-values represent omnibus test statistics across all four patient subgroups.

Table 4

Comparison of preoperative quality of life scores for CRS patients with and without comorbid anxiety

	CRS with comorbid anxiety (n=30)	CRS without comorbid anxiety (n=118)	
Preoperative quality of life measures:	**Mean [SD]**	**Mean [SD]**	**p-value**
SNOT-22 total score	59.6 [16.8]	55.0 [19.3]	0.30
Rhinologic symptoms	15.9 [5.7]	16.8 [6.6]	0.45
Extra-nasal rhinologic symptoms	7.7 [3.4]	8.2 [3.6]	0.44
Ear and/or facial symptoms	10.6 [5.8]	9.4 [5.2]	0.25
Psychological dysfunction	20.5 [6.8	16.7 [7.6]	0.02
Sleep dysfunction	16.0 [5.7]	15.1 [6.4]	0.61
RSDI total scores	57.2 [24.2]	46.3 [23.8]	0.02
Physical subdomain	20.7 [8.6]	19.0 [8.3]	0.34
Functional subdomain	18.1 [8.3]	14.8 [8.7]	0.04
Emotional subdomain	18.4 [9.3]	12.5 [8.9]	0.001

SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; RSDI, Rhinosinusitis Disability Index.

Table 5

Comparison of mean improvement in clinical measures for CRS patients with and without comorbid anxiety

	CRS with comorbid anxiety (n=20)		CRS without comorbid anxiety (n=85)		
Clinical measure of disease severity:	**Mean [SD]**	**Relative Change**	**Mean [SD]**	**Relative Change**	**p-value**
Endoscopy score	−3.2 [3.8]**	30%	−3.6 [3.8]*	51%	0.72
BSIT olfactory function score	−0.6 [2.8]	7%	0.3 [2.6]	2%	0.31

* indicates significant postoperative improvement over time ($p<0.001$)

** indicates significant postoperative improvement over time ($p<0.050$).

Negative mean scores indicate improvement over time. SD, standard deviation; BSIT, Brief Smell Identification Test.

Table 6

Comparison of mean improvement in quality of life scores for CRS patients with and without comorbid anxiety

	CRS with comorbid anxiety (n=20)		CRS without comorbid anxiety (n=92)		
Quality of life measures:	**Mean [SD]**	**Relative Change**	**Mean [SD]**	**Relative Change**	**p-value**
SNOT-22 total score	−18.1[19.5] **	31%	−29.0[21.0] *	52%	0.03
Rhinologic symptoms	−5.4[6.4] **	34%	−9.0[6.3] *	53%	0.02
Extra-nasal rhinologic symptoms	−2.4[4.0] **	31%	−4.3[3.7] *	52%	0.08
Ear and/or facial symptoms	−4.3[3.9] *	42%	−5.5[5.0] *	56%	0.28
Psychological dysfunction	−5.2[8.4] **	27%	−8.3[8.5] *	49%	0.19
Sleep dysfunction	−4.2[7.1] **	28%	−7.7[7.1] *	49%	0.04
RSDI total scores	−17.3[29.3] **	32%	−26.5[22.4] *	57%	0.12
Physical subdomain	−6.9[9.8] **	34%	−11.7[9.1] *	61%	0.05
Functional subdomain	−6.1[10.2] **	36%	−8.8[8.4] *	59%	0.29
Emotional subdomain	−4.3[12.0]	25%	−5.9[7.6] *	48%	0.59

* indicates significant postoperative improvement over time ($p<0.001$)

** indicates significant postoperative improvement over time ($p<0.050$).

Negative mean scores indicate improvement over time. SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; RSDI, Rhinosinusitis Disability Index.

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Table 7

Unadjusted and adjusted effect estimates for postoperative improvement in outcome measures associated with comorbid anxiety.

Quality of life measures:	**Unadjusted β Mean (SE)**	**Adjusted β Mean (SE)**	**95% CI [LL, UL]**	**p-value**	**R^2**
SNOT-22 total score[1]	11.0 (5.1)	11.1 (4.7)	[1.7, 20.5]	0.02	0.244
Rhinologic symptoms[2]	3.6 (1.6)	3.5 (1.6)	[0.4, 6.6]	0.03	0.220
Extra-nasal rhinologic symptoms[3]	1.9 (0.9)	1.8 (0.9)	[−0.01, 3.6]	0.05	0.125
Ear and/or facial symptoms	----	----	----	----	----
Psychological dysfunction	----	----	----	----	----
Sleep dysfunction[4]	3.5 (1.8)	4.2 (1.7)	[0.9, 7.5]	0.01	0.159
RSDI total scores	----	----	----	----	----
Physical subdomain[5]	4.9 (2.3)	4.2 (2.2)	[−0.2, 8.4]	0.06	0.140
Functional subdomain	----	----	----	----	----
Emotional subdomain	----	----	----	----	----

Positive unadjusted and adjusted effect estimates (β) indicate less/worse improvement associated with comorbid anxiety. CI, confidence interval; LL, lower limit; UL, upper limit; R^2, coefficient of multiple determination; SNOT-22, 22-item Sinonasal Outcome Test; Rhinosinusitis Disability Index. Models were only built for outcomes with clinically significant bivariate mean differences ($p<0.100$) between anxiety subgroups.

[1] Final models controlled for significant independent predictors ($p<0.050$) including: gender (female reference group; $p=0.008$), previous sinus surgery ($p=0.002$), and allergy (mRAST confirmed; $p=0.018$).

[2] Final models controlled for significant independent predictors ($p<0.050$) including: previous sinus surgery ($p=0.003$), nasal polyposis ($p=0.003$), and alcohol use ($p=0.008$).

[3] Final models controlled for significant independent predictors ($p<0.050$) including: previous sinus surgery ($p=0.031$), and allergy (mRAST confirmed; $p=0.011$).

[4] Final models controlled for significant independent predictors ($p<0.050$) including: previous sinus surgery ($p=0.020$), and gender ($p=0.003$).

[5] Final models controlled for significant independent predictors ($p<0.050$) including: previous sinus surgery ($p=0.005$), aspirin intolerance ($p=0.019$), and gender ($p=0.077$).