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Endoscopic Sinus Surgery Improves Cognitive Dysfunction in Patients with Chronic Rhinosinusitis

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Abstract

Background—Patients with chronic rhinosinusitis (CRS) have been found to have cognitive deficit, identified using the Cognitive Failures Questionnaire (CFQ), however the exact etiology of cognitive decline is unknown. This study aimed to determine if improvement in concomitant inflammation and disease burden in CRS, using endoscopic sinus surgery (ESS), improves cognitive deficit and to identify comorbid conditions that effect improvement likelihood.

Methods—Study participants (n=247) with and without nasal polyposis (CRSwNP, CRSsNP) were prospectively enrolled in a multi-institutional, observational, outcomes study. Preoperative and postoperative cognitive dysfunction was evaluated using the CFQ instrument. Quality-of-life (QOL) and disease burden was also evaluated using the Rhinosinusitis Disability Index (RSDI), 22-item SinoNasal Outcome Test (SNOT-22), nasal endoscopy, computed tomography, and the Patient Health Questionnaire (PHQ-2).

Results—Average CFQ total scores significantly improved ($p=0.012$) after ESS for patients with follow-up (n=141). Participants with CRSwNP (n=51) reported significant postoperative improvements in mean CFQ total scores ($p=0.002$) and CFQ distractibility and blunders domain scores ($p=0.006$). No significant postoperative improvement for any average CFQ score was found in CRSsNP ($p=0.086$). The magnitude of postoperative improvement in CFQ total and domain mean scores was statistically similar between CRSsNP and CRSwNP ($p=0.115$). Depressive disorder, identified using PHQ-2 screening, was the only comorbid condition significantly associated with measurable cognitive deficit ($p<0.001$).

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Conclusions—Patients with CRS have measurable cognitive decline and ESS may modestly improve cognitive deficit/CFQ scores. Future investigations are needed to further elucidate the underlying mechanisms responsible for cognitive deficit in patients with CRS and significant associations with depression.

MeSH Key Words

Sinusitis; rhinosinusitis; chronic disease; quality of life; rhinitis; cognition; chronic pain; sleep

INTRODUCTION

Chronic rhinosinusitis (CRS) has dramatic effects on patients overall well-being and quality-of-life (QOL). A growing body of literature suggests that a major component of patients' reduced QOL may be secondary to non-rhinogenic symptoms such as depression,¹ sleep,² and more recently cognitive dysfunction.³ Cognitive dysfunction is best defined as alterations in attention, executive function, learning and memory, language, the perceptual-motor, or social cognition. It has been demonstrated that patients with CRS report significantly more cognitive impairment as measured by the Cognitive Failure Questionnaire (CFQ) than control subjects without a history of sinusitis.³ Furthermore, this decline in cognition significantly correlates with sinus-specific QOL.⁴ Although cognitive impairment appears to associate with CRS, the exact etiology and potential treatments of cognitive impairment remains unknown.

A body of literature exists which suggests an association between cognitive dysfunction and chronic inflammation. Chronic inflammatory conditions such as heart disease, sarcoidosis, inflammatory bowel disease, and sickle cell anemia have all been linked to some measure of cognitive dysfunction.⁵⁻⁹ Similarly, cognitive deficits have been observed in patients with upper airway inflammation from allergic rhinitis during seasonal flares, negatively impacting daily performance.¹⁰ Although patients with sinonasal inflammation associated with CRS have reported significantly worse CFQ scores than control subjects without inflammatory morbidity, it remains unknown whether sinus-specific therapies improve cognitive performance.³ Endoscopic sinus surgery (ESS) may be offered to those patients with refractory CRS and has been found to provide durable improvements in sinus-specific outcome measures.^{11,12} It is unclear if similar improvements in cognitive dysfunction would be observed after ESS.

The objective of this study was to investigate if ESS improves patient-reported cognitive dysfunction in patients with CRS. We also sought to determine if any patient cofactors associated with CRS might significantly influence cognitive improvement. We hypothesized that improvement in sinus disease burden after ESS would improve cognitive dysfunction as measured by the CFQ instrument.

MATERIALS AND METHODS

Patient Population and Inclusion Criteria

Adult subjects (≥ 18 years of age) diagnosed with medically refractory CRS, defined by Adult Sinusitis Guidelines¹³, were prospectively enrolled into an on-going, observational, treatment outcomes cohort. Findings from this cohort have been previously published.^{1–3} Patients were recruited and enrolled between June, 2013 and February, 2015 from Rhinology and Sinus Surgery clinics within: the University of Utah School of Medicine (Salt Lake City, UT.), Oregon Health & Science University (Portland, OR.), the Medical University of South Carolina (Charleston, SC.), Stanford University (Palo Alto, CA.), and the University of Calgary (Calgary, Alberta, Canada). The Institutional Review Boards at each enrollment location approved investigational protocols. Patients were approached for study enrollment and informed consent after completion of their standard clinical evaluation and after treatment recommendations had been provided by each enrolling physician. At minimum, patients completed prior medical treatment including: at least a 14-day course of broad spectrum or culture directed antibiotics and a 3-week course of topical corticosteroids (and/or a 5-day trial of oral corticosteroids). All participants were asked to provide demographic and medical history characteristics as described in Table 1.

Exclusion criteria

Patients diagnosed with comorbid ciliary disorder were excluded to minimize cohort heterogeneity and subsequent variations in treatment strategy. Patients failing to provide informed consent, including those with diagnosed mental handicap, or complete all relevant questionnaires at admission were excluded. Patients who did not complete follow-up evaluations were also excluded from final analysis.

Patient Reported Outcome Measures

Study participants were directed to complete several patient-reported outcome measures (PROMs) during initial enrollment including: the Cognitive Failures Questionnaire (CFQ), the Rhinosinusitis Disability Index (RSDI), the Sinonasal Outcomes Test-22 (SNOT-22), and the Patient Health Questionnaire-2 (PHQ-2). Participants were also asked to complete the same PROMs during scheduled visits up to 18-months postoperatively.

Cognitive Failures Questionnaire—The CFQ is a 25-question self-report instrument.^{14,15} These questions elicit the frequency with which events of cognitive failure occur. The responses range from 0 (“Never”) to 4 (“Very often”). The responses are then summed (range: 0–100); greater values indicate greater severity of cognitive impairment. The CFQ is a well-validated instrument for cognitive assessment and has been used in CRS and other chronic disease processes.^{3,16} Principal component factor analysis has identified 4 subdomains of the CFQ including items pertaining to: memory (range: 0–32), distractibility (range: 0–36), blunders (range: 0–28), and names (range: 0–8).¹⁷

Rhinosinusitis Disability Index—The RSDI is a self-report questionnaire listing 30 statements relating to physical, functional, and emotional sequela of CRS. Responses range from 0 (“Never”) to 4 (“Always”) on a Likert-like scale. Subdomains of the RSDI include:

the physical (11 items; range: 0–44), functional (9 items; range: 0–36) and emotional (10 items; range: 0–40). Summing subdomain scores (range: 0–120) provides an index of overall disability with increased values indicating greater overall CRS-related disability.¹⁸

Sinonasal Outcome Test-22—The 22-Item SinoNasal Outcome Test (SNOT-22) questionnaire measures disease-specific QOL and symptom severity (©2006, Washington University, St. Louis, MO).¹⁹ Responses range from 0 (“No problem”) to 5 (“Problem as bad as it can be”). Previous factor analysis has demonstrated that the SNOT-22 items can be categorized into 5 subdomains including: rhinologic symptoms (range: 0–30), extranasal rhinologic symptoms (range: 0–15), ear/facial symptoms (range: 0–25), psychological dysfunction (range: 0–35), and sleep dysfunction (range: 0–25).²⁰ Individual factors of the SNOT-22 are summarized (range: 0–110) whereas higher values are indicative of worse disease-specific QOL.

Patient Health Questionnaire-2—The 2-item Patient Health Questionnaire (PHQ-2) is an abbreviated, self-administered survey that can be used as a depression screening tool and a measure of depression severity (range: 0–6). Items of the PHQ-2 inquire about symptoms of anhedonia and depressive mood during the preceding 2-week period; scored between 0 (“Not at all”) to 3 (“Nearly every day”). PHQ-2 scores of ≥ 3, as a cut-off for positive major depression screening, have been found to have a sensitivity of 83% and specificity of 92% for major depressive disorders.²¹

Clinical Measures of Disease Severity

Per the standard of care, endoscopy exams were completed with a 0–30° rigid endoscope and staged by each enrolling physician using the Lund-Kennedy (LK) endoscopy scoring system. The degree of polypoid, discharge, scarring, edema, and crusting are evaluated bilaterally and graded on a scale from 0 (“Normal”) to 2 (“Severe”). These scores are summed (range: 0–20) whereas higher scores indicate more severe endoscopic findings.²²

Patients also underwent high-resolution computed tomography (CT) radiographic imaging of the paranasal sinuses. The enrolling physician reviewed each CT image and staged using the Lund-Mackay (LM) scoring system. Opacification of the bilateral maxillary, anterior and posterior ethmoid, sphenoid, and frontal sinuses is graded from 0 (“Normal”) to 2 (“Complete opacification”). The ostiomeatal complex is also graded as 0 (“Patent”) or 2 (“Opacified”). Higher total scores (range: 0–24) indicate greater opacification.²³

Olfactory detection/function was evaluated for study participants using the Smell Identification Test (SIT; Sensonics, Inc., Haddon Heights, NJ.). The SIT is a validated, 40-item “scratch-and-sniff” test with high test-retest reliability ($r > 0.90$).^{24,25} Total SIT scores are categorized into olfactory dysfunction diagnoses based on gender-adjusted normative data with higher scores representing better olfactory function.

Surgical Intervention

Surgical procedures were determined by the disease pattern, radiographic and endoscopic evaluations, and clinical judgment of the enrolling physician. Primary or revision endoscopic

sinus surgery procedures consisted of either unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, or frontal sinusotomy (*Draf* IIa/b, or III) procedures, with septoplasty and inferior turbinate reductions as adjunctive procedures as needed.

Data Management and Statistical Analysis

Study data were collected using standardized clinical research forms and electronic database procedures (Microsoft Access; Microsoft Corp., Redmond, WA). Independent samples t-testing or Mann-Whitney U testing was used to compare independent subgroups for all preoperative and postoperative continuous data, while chi-square (χ^2) testing was used to compare prevalence measures between independent subgroups. Paired sample t-testing or Wilcoxon signed-rank testing was used to evaluate within-pair differences over time, when appropriate for parametric or non-parametric distributions, respectively. Spearman's correlation (R_s) coefficients were employed to screen potential relationships between preoperative, postoperative, and postoperative change measures of QOL, cognition, and comorbid depression. SPSS software (IBM Corp., Armonk, NY, ver. 22.0) was used for all statistical analysis.

Simple stepwise linear regression was used to identify significant independent risk factors associated with two primary outcome measures: 1) preoperative CFQ total scores, and 2) postoperative mean improvement (postoperative scores minus preoperative scores) in CFQ total scores. A total of 17 variables were screened for univariate, independent significance including preoperative demographic and medical history variables and preoperative QOL status. Preliminary models included all independent factors screened for univariate significance ($p < 0.250$). Final models used a manual forward selection ($p < 0.100$) and backwards elimination ($p < 0.050$) process and multi-collinearity was evaluated using variance inflation factors (VIFs). Significant covariates were introduced into final models to assess potential confounding of the effect estimate for enrollment site difference. Any covariate resulting in an absolute difference of $\pm 10\%$ in the effect estimate for the site variable was considered a confounder. Unadjusted and adjusted regression coefficients (β), standard errors [SE], 95% confidence intervals, relative t-test statistics, and estimates of type-I error (p-values) are reported. The percentage of final model variance explained by each model was calculated using coefficients of multiple determination (r^2).

RESULTS

Final Study Cohort and Surgical Procedures

After exclusion of 10 participants with comorbid ciliary disorder, a total of 247 participants undergoing ESS completed all eligibility requirements and were included for final analysis. Patient characteristics, preoperative QOL scores, measures of disease severity, and preoperative cognition scores were compared between 141 participants with follow-up (57%) and 106 participants without follow-up (43%) evaluations (Table 1). Participants who were lost to follow-up were significantly younger, presented with a lower prevalence of prior endoscopic sinus surgery and a higher prevalence of current tobacco use. There was no significant difference in mean preoperative QOL, clinical measures of disease severity,

preoperative cognition severity, or measures of comorbid depression between study subjects with or without follow-up ($p = 0.306$). The prevalence and description of bilateral surgical procedures for participants with follow-up is described in Table 2.

Postoperative Improvement in Cognition and Other PROMs

Study participants with follow-up ($n=141$) were followed for an average of 11.5 [standard deviation ± 4.5] months postoperatively. Improvement in average CFQ and QOL total and component scores was calculated for all subjects with follow-up. Statistically significant mean improvement was reported for CFQ total scores and the distractibility domain of the CFQ instrument (Table 3). Further, significant improvement in mean QOL and depression measures was reported for all scores of the PHQ-2, SNOT-22, and RSDI total scores and domain scores ($p=0.001$). Mean scores of the memory, blunders, or names domains of the CFQ were not found to significantly improve following ESS surgery.

Improvement in average CFQ and QOL scores was calculated for participants with CRSsNP (Table 4) and CRSwNP (Table 5). Statistically significant mean improvement was reported in CRSsNP for SNOT-22 and RSDI instruments ($p<0.001$). Mean scores of the PHQ-2 significantly improved postoperatively as did the prevalence of positive screenings for depression in CRSsNP (32% to 16%; $p=0.001$). However, improvement in CFQ total scores and domain scores did not reach significance for those with CRSsNP ($p = 0.086$). Patients with CRSwNP were found to have statistically significant mean improvement in CFQ total scores and for the distractibility and blunders domain scores of the CFQ instrument (Table 5). As expected, improvements were also seen in SNOT-22 and RSDI scores following surgery. Mean scores of the PHQ-2 did not significantly improve postoperatively nor did the prevalence of positive screenings for major depressive disorder (26% to 22%; $p=0.727$).

A total of 78/141 (55%) study participants reported some magnitude of improvement (1-point) in total CFQ scores following ESS (range: -1 to -88). For participants with CRSsNP, a total of 46/90 (51%) reported some degree of improvement in total CFQ scores (range: -1 to -88) while 32/51 (63%) of participants with CRSwNP reported at least 1-point improvement (range: -1 to -33) in CFQ total scores after surgery.

Postoperative Improvements in Cognition between CRSsNP and CRSwNP

No significant between-subject differences were reported for either preoperative mean CFQ total scores ($p=0.559$) or CFQ domain scores ($p = 0.360$) between participants with and without nasal polyposis. Similarly no significant between-subject differences were reported for either postoperative mean CFQ total scores ($p=0.114$) or CFQ domain scores ($p = 0.106$) between participants with and without nasal polyposis. Comparisons in average absolute improvement in all CFQ scores between CRSsNP and CRSwNP are further described in Figure 1.

Correlation between Measures of QOL, Cognition, and Depression

Correlative relationships between all outcome measures were evaluated for postoperative and postoperative change scores. Bivariate correlation analysis was used to determine if patients who report improved cognition scores have a corresponding association with

disease-specific QOL as measured by the RSDI and SNOT-22 survey scores. We also sought to determine if an association exists between measures of cognition and depression (PHQ-2) used in this investigation. Associations between cognition scores and disease-specific QOL scores were evaluated postoperatively and between postoperative change scores as previously defined. Postoperative CFQ total scores positively correlated with both SNOT-22 total scores ($R_s=0.503$; $p<0.001$), RSDI total scores ($R_s=0.522$; $p<0.001$), and PHQ-2 scores ($R_s=0.388$; $p<0.001$) suggesting poor cognition scores significantly, but moderately, correlate with worse disease or symptom severity before and after surgical intervention for CRS. The magnitude of correlation between CFQ, SNOT-22, and RSDI, change scores was slightly less than that found for postoperative associations. The magnitude of correlation between CFQ and depression was lost in addition to the physical subdomain of the RSDI after ESS.

Multivariate Modeling for Cognitive Function

Following covariate screening, final multivariate linear models were constructed to identify all significant associations between patient characteristics and clinical measures of disease severity to: 1) preoperative CFQ total scores, and 2) postoperative improvement in CFQ total scores. After adjusting for age ($p=0.002$), only a positive screening for comorbid depression with PHQ-2 scores was found to be highly significantly associated with preoperative CFQ scores. Study participants with positive depression screen were found to report worse preoperative CFQ total scores compared to non-depressed counterparts ($\beta=12.2$ [2.3], 95% CI: 7.8 – 16.7; $t=5.42$; $p<0.001$).

Similarly, after removing outlying CFQ change scores (-88 ; $n=1$) only diabetes mellitus was clinically associated with less postoperative improvement in CFQ scores ($\beta=7.0$ [3.7], 95% CI: $-0.2 - 14.2$; $t=1.92$; $p=0.057$). For either model, less than 14% of model variation (r^2) in CFQ scores was explained by the aforementioned covariates indicating poor overall model utility in predicting improvement in CFQ scores. No evidence of covariate multi-collinearity was detected ($VIFs<2.0$).

DISCUSSION

Sinus-specific “cardinal” symptoms are the hallmark of CRS and certainly contribute to the poor QOL reported in this population. Recent investigations suggest that the health impacts of CRS extend beyond the sinuses and can impact more basic functions such as sleep²⁶ and cognition⁴, which can be defined as “extra-rhinologic” manifestations of CRS. Further, it is becoming evident these extra-rhinologic symptoms are associated with reduced disease-specific QOL as seen in the correlations between CFQ and various QOL surveys. Sinus surgery aimed at improving sinonasal inflammation and QOL has been shown to have durable improvements from both a disease-severity and QOL perspective. Remenschneider et al. found that extra-rhinologic symptoms are a contributing factor behind patient-reported health utility scores in CRS.²⁷ Similarly, the presence of extra-rhinologic symptoms may heavily influence a patients’ decision to seek sinus surgery as opposed to ongoing appropriate medical therapy for CRS, despite similar rhinologic-specific symptom severity.^{1,28} Current evidence suggests ESS significantly improves extra-rhinologic

symptom manifestations with corresponding improvement in reported QOL.² The data reported herein also suggests that ESS does provide some magnitude of improvement in measures of cognitive dysfunction, as measured by the CFQ instrument. Likewise, this improvement appears to associate with significant improvement in disease-specific QOL for patients with CRS.

It is worth mentioning that the largest contributor of total cognitive dysfunction scores seen in patients with CRS appears to be due to the presence of absent-mindedness and attention failure, captured by the distractibility domain of the CFQ. Prior work has established the validity in quantifying distractibility with varying perceptual loads (eg. distraction) using the CFQ instrument.²⁹ Patients with CRS have unremitting levels of distraction secondary to disease manifestations captured by both the SNOT-22 and RSDI. This suggests patients with CRS have a difficult time suppressing these task-irrelevant distractions. Following ESS there are significant improvements in “distractions” as both the SNOT-22 and the RSDI total and subdomain scores improve, with associated improvement seen on the CFQ total and distractibility domain. This association needs to be further investigated as distraction can impair many aspects of daily living, work productivity, and may ultimately lead to increased risk of accidents.³⁰

Although this study suggests surgical intervention may lead to some improvement in cognitive status, the mechanism through which these improvements may occur within the framework of CRS treatment remains unknown and is likely highly multi-factorial. There have been many plausible hypotheses concerning the pathophysiology of cognition in both health and disease, with increasing evidence implicating inflammatory cytokines as the link between the immune system and central behavior.^{7–10, 31} Cytokines have the ability to modulate neuronal signaling and behavior by passage across the blood brain barrier, stimulation of afferent transmission, and/or altering the level or activity of another substance that subsequently alters neurotransmission.^{32,33} We posit that the decline in inflammation/ cytokines following ESS may be one factor that is driving the improvements seen in cognition. Interestingly, CRSwNP and CRSsNP are chronic inflammatory diseases with unique inflammatory phenotypes consisting of changes in cytokines, their receptors, and downstream products. The failure to identify a significant improvement in CFQ in patients with CRSsNP may represent a difference in the underlying inflammatory phenotypes between those with CRSwNP and CRSsNP, but at present this remains conjecture and requires further investigation.

Another, potential explanation may be explained via the complex interactions between poor sleep, fatigue, and cognition. This symptomology triad is commonly seen in both infection and inflammation and highly prevalent in patients with CRS.³⁴ Fatigue has been demonstrated by previous research to be correlated with higher frequencies of reported cognitive failures and a significant predictor of higher scores on the CFQ.³⁵ It is known that CRS leads to alterations in sleep quality and daytime fatigue, suggesting plausibility that this leads to problems with cognition. We have previously shown that subjective sleep quality is “poor” in roughly 75% of patients with CRS and that sleep quality accounted for some group differences in cognitive failures.^{2,3} CRS is a chronic inflammatory disease that is associated with changes in cytokines, their receptors, and downstream products.³⁴ In

humans, sleep loss and altered pro-inflammatory cytokine levels are associated but not limited to fatigue,^{36,37} pain,³⁸ depression,³⁹ impaired cognition,⁴⁰ and memory.⁴¹ Future studies that explore the mechanisms underlying cognitive dysfunction in CRS should evaluate its association to sleep, fatigue, and inflammatory signaling in a rigorous fashion.

Another possibility is that depression, a common comorbidity in patients with CRS, contributes to and/or affects cognitive dysfunction. Problems with cognitive processing have been well documented with mood disorders. For instance, higher levels of cognitive failure (eg. greater CFQ scores) are significantly associated with a negative effect, such as depression, and anxiety.^{35,42} Payne et al., argue that this is consistent with the hypothesis that disorders characterized by negative emotional experiences, such as depression and anxiety, tax patients attentional processes and lead to noticeable changes in the experience of failures in routine activities that are reported in CFQ. It has been well documented that depression is reported in higher prevalence in patients with CRS compared to national averages.⁴³ In this cohort the prevalence of depression were found to be 30% as measured using the PHQ-2 screening tool. We demonstrate that study participants with depression were found to report worse CFQ total scores compared to non-depressed counterparts. However, cognitive improvement remained significant after controlling for PHQ-2 scores, suggesting a more complex, multi-factorial association.

Evaluating outcomes in a prospective, multi-institutional manner adds credibility to this investigation. However, several limitations are inherent in outcomes research and should be considered. The study design does not allow for definitive conclusions on causality, and subgroup sample sizes for both CRSsNP and CRSwNP may have limited statistical power. Factors, which significantly differed between study subjects with or without follow-up included younger age, lower prevalence of prior ESS, and a higher current tobacco use, suggesting possible selection bias in patients with follow-up. However, clinical measures of disease severity and preoperative cognition scores did not differ between study subjects with or without follow-up suggesting limited follow-up bias within reported PROMs. Also, differences in the extent of surgery between patients has not been well defined and was not controlled for through regression modeling, which introduces the potential for some level of unmeasured confounding. This study did not include a control arm of patients with CRS not undergoing surgery, so one cannot fully exclude the influence of the natural history of disease progression or continued medical therapy.

Clinical interpretability of mean improvement in CFQ total scores retains inherent challenges due to the fact that a minimal clinically important difference (MCID) has not been previously defined in patients undergoing ESS. The absence of a defined MCID does not allow clinicians to properly counsel patients in regard to cognitive comorbidity and surgical expectation. Additionally, this study was conducted within tertiary rhinology practices across North America. Findings may not necessarily be externally generalizable to all patients having sinus surgery in alternate settings, or to the average follow-up time period beyond ~12 months. We also acknowledge that the clinical relevance of the degree of correlation must be considered when interpreting the results of this study, which is true in general, as statistical significance does not necessarily indicate clinical importance and correlation does not infer causality. This study does suggest that mechanisms of cognitive

function in CRS require further exploration, including the influences of sleep, depression, and inflammatory cytokine expression.

CONCLUSION

Patients with CRS have measurable cognitive dysfunction using a validated CFQ instrument. Following ESS, patients with CRSwNP reported significant improvement in cognitive scores that were not reported by patients without nasal polyposis. This improvement in CFQ scores remained after controlling for various cofactors. Additional studies are necessary to validate these findings, explore potential mechanisms, and determine whether available treatments impact overall cognitive function for both patients with and without nasal polyposis.

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Figure 1.

Comparison of absolute postoperative improvement in average CFQ scores between subjects with and without nasal polyposis. CRSsNP, chronic rhinosinusitis without nasal polyposis; CRSwNP, chronic rhinosinusitis with nasal polyposis; CFQ, Cognitive Failures Questionnaire.

Table 1

Characteristics of final study cohort with and without postoperative follow-up

Characteristics:	Postoperative follow-up (n=141)		Without postoperative follow-up (n=106)		p-value
	Mean [± SD]	N (%)	Mean [± SD]	N (%)	
Age (years)	52.2 [± 16.8]		44.6 [± 14.5]		<0.001
Males		60 (43%)		56 (53%)	0.109
White / caucasian		127 (90%)		95 (90%)	0.908
Prior endoscopic sinus surgery		89 (63%)		53 (50%)	0.039
Nasal polypsis		51 (36%)		48 (45%)	0.148
Asthma		66 (47%)		42 (40%)	0.260
ASA sensitivity		16 (11%)		8 (8%)	0.318
Allergy (positive testing)		100 (71%)		64 (60%)	0.082
Current tobacco use		3 (2%)		11 (10%)	0.010
Alcohol consumption		43 (31%)		32 (31%)	0.939
Corticosteroid dependency		17 (12%)		13 (12%)	0.961
Diabetes mellitus (Type I / II)		11 (8%)		6 (6%)	0.511
PHQ-2 total score	1.8 [± 1.8]	1.8 [± 1.7]	0.797		
Positive depression screen (3)		41 (30%)		28 (26%)	0.595
Preoperative quality of life measures:					
SNOT-22 total score	56.1 [± 21.4]		56.4 [± 20.5]		0.890
RSDI total score	51.0 [± 25.2]		47.7 [± 24.8]		0.306
Clinical measures of disease severity:					
LK endoscopy score	5.7 [± 3.8]		5.7 [± 3.7]		0.988
LM computed tomography score	11.4 [± 6.9]		12.0 [± 6.6]		0.464
Preoperative cognition measures:					
CFQ total score	37.6 [± 17.2]		37.2 [± 16.9]		0.825
Memory score	9.4 [± 5.8]		9.3 [± 5.8]		0.896
Distractibility score	15.6 [± 6.7]		15.3 [± 6.6]		0.765
Blunders score	9.5 [± 5.1]		9.3 [± 4.9]		0.734

Characteristics:	Postoperative follow-up (n=141)		Without postoperative follow-up (n=106)		p-value
	Mean [± SD]	N (%)	Mean [± SD]	N (%)	
Names score	4.4 [± 2.1]		4.4 [± 2.1]		0.846

N, sample size; SD, standard deviation; ASA, acetylsalicylic acid; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; LK, Lund-Kennedy; LM, Lund-Mackay; CFQ, cognitive failures questionnaire; PHQ-2, 2-item Patient Health Questionnaire.

Table 2

Description of unilateral and bilateral surgical procedures (n=141)

Surgical procedures:	Left side N (%)	Right side N (%)
Maxillary antrostomy	128 (91%)	123 (87%)
Partial ethmoidectomy	19 (14%)	14 (10%)
Total ethmoidectomy	104 (74%)	107 (76%)
Sphenoidotomy	96 (68%)	99 (70%)
Middle turbinate resection	22 (16%)	27 (19%)
Inferior turbinate reduction	42 (30%)	44 (31%)
Septoplasty	63 (45%)	
Frontal sinusotomy - <i>Draf</i> IIa	66 (47%)	65 (46%)
Frontal sinusotomy - <i>Draf</i> IIb	11 (8%)	11 (8%)
Frontal sinusotomy - <i>Draf</i> III	2 (1%)	
Image guidance	101 (72%)	

N, sample size

Table 3

Comparisons of mean preoperative and last postoperative CFQ scores for total participants with follow-up (n=141)

	Preoperative		Postoperative		Change Mean [± SD]	95% CI ¹ (UL, LL)	p-value ²
	Mean [± SD]		Mean [± SD]				
CFQ total score	37.6 [± 17.2]		34.9 [± 16.3]		-2.8 [± 13.8]	(-0.5, -5.1)	0.012
Memory domain	9.4 [± 5.8]		8.9 [± 5.5]		-0.4 [± 4.9]	(0.4, -1.2)	0.370
Distractibility domain	15.6 [± 6.7]		14.0 [± 6.4]		-1.6 [± 5.4]	(-0.7, -2.5)	0.001
Blunders domain	9.5 [± 5.1]		8.8 [± 4.6]		-0.8 [± 3.9]	(0.1, -1.4)	0.058
Names domain	4.4 [± 2.1]		4.2 [± 2.0]		-0.2 [± 1.7]	(0.1, -0.5)	0.216

¹ indicates 95% confidence interval for the mean difference;

² p-value indicates significant within-pair differences over time via Wilcoxon signed rank testing;
SD, standard deviation; LL, lower limit; UL, upper limit; CFQ, Cognitive Failures Questionnaire.

Table 4

Comparisons of mean preoperative and last postoperative CFQ, QOL, and depression scores for CRSsNP (n=90)

	Preoperative	Postoperative	Change	95% CI ¹	p-value ²
	Mean [± SD]	Mean [± SD]	Mean [± SD]	(UL, LL)	
PHQ-2 total score	1.9 [± 1.9]	1.2 [± 1.6]	0.6 [± 1.6]	(0.3, 0.9)	0.001
SNOT-22 total score	54.2 [± 21.8]	31.2 [± 22.4]	-20.3 [± 22.2]	(-14.7, -26.4)	<0.001
Rhinologic domain	15.5 [± 6.5]	8.6 [± 6.2]	-6.9 [± 7.7]	(-5.2, -8.3)	<0.001
Extra-nasal domain	8.6 [± 3.9]	5.1 [± 3.6]	-3.5 [± 4.4]	(-2.6, -4.3)	<0.001
Ear / Facial domain	9.4 [± 5.9]	5.3 [± 5.4]	-4.1 [± 5.5]	(-3.0, -5.2)	<0.001
Psychological domain	17.3 [± 8.4]	9.5 [± 8.9]	-7.8 [± 7.8]	(-6.4, -9.6)	<0.001
Sleep Dysfunction domain	14.7 [± 6.5]	8.8 [± 7.2]	-5.9 [± 6.6]	(-4.6, -7.3)	<0.001
RSDI total score	49.0 [± 25.3]	27.0 [± 25.7]	-22.0 [± 21.4]	(-17.5, -26.3)	<0.001
Physical domain	19.7 [± 10.1]	9.9 [± 9.4]	-9.9 [± 9.5]	(-7.9, -11.7)	<0.001
Functional domain	15.6 [± 8.5]	8.4 [± 8.9]	-7.2 [± 7.9]	(-5.4, -8.6)	<0.001
Emotional domain	13.7 [± 9.3]	8.8 [± 8.9]	-4.9 [± 6.7]	(-3.6, -6.3)	<0.001
CFQ total score	38.9 [± 18.8]	36.6 [± 16.6]	-2.3 [± 16.0]	(5.6, -1.1)	0.248
Memory domain	9.9 [± 6.4]	9.4 [± 5.7]	-0.5 [± 5.8]	(1.7, -0.7)	0.537
Distractibility domain	16.0 [± 7.3]	14.7 [± 6.5]	-1.3 [± 6.2]	(2.6, -0.2)	0.086
Blunders domain	9.8 [± 5.5]	9.2 [± 4.8]	-0.6 [± 4.4]	(1.5, -0.4)	0.551
Names domain	4.5 [± 2.2]	4.4 [± 1.9]	-0.1 [± 1.8]	(0.5, -0.2)	0.469

¹ indicates 95% confidence interval for the mean difference;

² p-value indicates significant within-pair differences over time;

QOL, quality of life; SD, standard deviation; LL, lower limit; UL, upper limit; CFQ, Cognitive Failures Questionnaire; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; CRSsNP, chronic rhinosinusitis without nasal polypsis.

Table 5

Comparisons of mean preoperative and last postoperative CFQ, QOL, and depression scores for CRSwNP (n=51)

	Preoperative		Postoperative		Change Mean [± SD]	95% CI ¹ (UL, LL)		p-value ²
	Mean [± SD]		Mean [± SD]					
PHQ-2 total score	1.7 [± 1.6]		1.4 [± 1.9]		-0.4 [± 1.6]	(0.8, -0.1)		0.098
SNOT-22 total score	59.4 [± 20.7]		26.0 [± 17.6]		-34.2 [± 21.6]	(-25.7, -42.8)		<0.001
Rhinologic domain	20.1 [± 6.5]		8.4 [± 6.1]		-11.8 [± 7.3]	(-9.8, -13.9)		<0.001
Extra-nasal domain	9.0 [± 3.7]		4.1 [± 3.3]		-4.8 [± 3.8]	(-3.7, -5.9)		<0.001
Ear / Facial domain	9.8 [± 5.5]		3.6 [± 3.7]		-6.3 [± 5.1]	(-4.8, -7.7)		<0.001
Psychological domain	17.5 [± 8.1]		8.9 [± 8.2]		-8.6 [± 9.0]	(-6.0, -11.2)		<0.001
Sleep Dysfunction domain	14.7 [± 6.6]		7.9 [± 6.6]		-6.8 [± 7.8]	(-4.6, -9.0)		<0.001
RSDI total score	54.5 [± 24.7]		22.8 [± 24.6]		-32.0 [± 22.0]	(-25.8, -38.3)		<0.001
Physical domain	22.5 [± 9.5]		8.7 [± 8.7]		-13.8 [± 8.8]	(-11.3, -16.3)		<0.001
Functional domain	17.2 [± 9.4]		6.4 [± 8.3]		-10.8 [± 8.6]	(-8.4, -13.2)		<0.001
Emotional domain	14.8 [± 8.2]		7.5 [± 9.1]		-7.3 [± 7.5]	(-5.2, -9.4)		<0.001
CFQ total score	35.4 [± 13.8]		31.7 [± 15.4]		-3.7 [± 8.4]	(-1.3, -6.0)		0.002
Memory domain	8.4 [± 4.5]		8.1 [± 5.0]		-0.3 [± 2.8]	(0.4, -1.1)		0.462
Distractibility domain	14.9 [± 5.6]		12.8 [± 6.0]		-2.1 [± 3.6]	(-1.1, -3.1)		<0.001
Blunders domain	9.1 [± 4.2]		8.0 [± 4.3]		-1.1 [± 2.9]	(-0.3, -1.9)		0.006
Names domain	4.2 [± 1.9]		3.9 [± 2.2]		-0.3 [± 1.5]	(0.2, -0.7)		0.255

¹ indicates 95% confidence interval for the mean difference;

² p-value indicates significant within-pair differences over time;

QOL, quality of life; SD, standard deviation; LL, lower limit; UL, upper limit; CFQ, Cognitive Failures Questionnaire; SNOT-22, 22-item SinoNasal Outcome Test; RSDI, Rhinosinusitis Disability Index; CRSwNP, chronic rhinosinusitis with nasal polypsis.