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Improvements in sleep-related symptoms after endoscopic sinus surgery in patients with chronic rhinosinusitis

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Abstract

Background—Sleep impairment is highly prevalent in patients with CRS. While endoscopic sinus surgery (ESS) has been shown to improve overall patient-reported sleep quality, the postoperative impact on individual sleep symptoms remains unclear.

Methods—Patients with medically-recalcitrant CRS who elected to undergo ESS were prospectively enrolled into a multi-institutional, observational cohort study. Sleep-related symptom severity and treatment outcomes were assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22) sleep domain.

Results—A total of 334 participants met criteria and were followed postoperatively for an average of 14.5[SD×4.9] months. Mean SNOT-22 sleep domain scores improved from 13.7[6.8] to 7.7[6.6] ($p<0.001$). Significant mean relative improvements were reported in “difficulty falling asleep” (45%; $p<0.001$), “waking up at night” (40%; $p<0.001$), “lack of a good night”s sleep” (43%; $p<0.001$), “waking up tired” (40%; $p<0.001$), and “fatigue” (42%; $p<0.001$) scores. A total of 66% of study participants reported postoperative improvement in “lack of a good night”s sleep”, “waking up tired”, and “fatigue,” 62% of the cohort reported improvement in “waking up at night,” and 58% reported improvement in “difficulty falling asleep”.

Conclusion—Patients with CRS report significant and sustained improvements following ESS in common sleep-related symptoms as assessed by the SNOT-22 sleep domain. Despite these significant improvements, some degree of persistent postoperative sleep impairment was reported.

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Further study is necessary to determine what factors are associated with continued sleep dysfunction after sinus surgery.

Keywords

Sinusitis; sleep; patient outcome assessment; endoscopy; treatment outcome

INTRODUCTION

The association between chronic rhinosinusitis (CRS) and sleep impairment is well documented. Over 70% of patients with CRS report poor sleep quality and the degree of sleep disturbance has been shown to correlate with decreased overall quality of life (QOL).[1] Recent investigation has demonstrated that sleep impairment in CRS exerts a greater relative influence on the decision to pursue endoscopic sinus surgery (ESS) when compared to rhinologic-specific symptom domains.[2] While ESS has been shown to improve overall patient-reported sleep quality, the postoperative impact on discrete sleep symptoms remains unclear. Furthermore, 26-78% of patients report ongoing sleep dysfunction postoperatively suggesting that perhaps patient-centered interests are not congruent with outcomes of ESS.[3-5] Additional data addressing individual, sleep-related symptoms would thus be of great value in order to accurately counsel patients and set reasonable expectations regarding post-operative improvements in sleep quality.

The objective of this study is to evaluate the effect of ESS on common, patient-reported sleep symptoms in patients with CRS. Understanding which sleep-related symptoms improve as well as the expected magnitude of improvement will be vital to the shared patient-provider decision-making process.

MATERIALS and METHODS

Study Population and Inclusion Criteria

Study participants were recruited and prospectively enrolled into a continuing, multi-institutional, observational, prospective cohort investigation designed to evaluate treatment outcomes following endoscopic sinus surgery. Patients were diagnosed with medically recalcitrant CRS defined by criteria outlined by the American Academy of Otolaryngology.[6] All adult study participants (≥18 years of age) elected endoscopic sinus surgery (ESS) as the subsequent treatment option for alleviation of symptoms related to CRS after previous medical therapy including, but not limited to, at least one course of broad spectrum or culture-directed antibiotics (≥14 days) and at least one course of either topical corticosteroid (≥21 days) or oral corticosteroid (≥5 days) therapy. Preliminary findings from this investigation have been previously reported.[7-9]

The Institutional Review Board (IRB) at each enrollment center governed all investigational protocols and informed patient consent documentation. Enrollment centers were comprised of sinus and skull base surgery clinics within academic, tertiary hospital systems in North America including Oregon Health & Science University (OHSU; Portland, OR, eIRB#7198), Stanford University (Palo Alto, CA, IRB#4947), the Medical University of

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South Carolina (Charleston, SC, IRB#12409), and the University of Calgary (Calgary, Alberta, Canada, IRB#E-24208), while central coordinating services were conducted at OHSU. Study participants were assured that study consent was voluntary and standard of care surrounding ESS was not altered due to study protocols.

During each preoperative enrollment meeting participants were asked to provide detailed demographic information, as well as social and medical history cofactors including, but not limited to: age, gender, race, asthma, nasal polyposis, depression, allergy, acetylsalicylic acid (ASA) sensitivity, current tobacco and alcohol use, ciliary dyskinesia, obstructive sleep apnea (OSA), corticosteroid dependency, and diabetes mellitus. Participants were followed for up to 18 months after ESS and completed survey evaluations postoperatively at regular 6 month intervals, either during physician-directed clinical appointments or via follow-up mailings using postal service and self-addressed return envelops.

Surgical Intervention

The extent of ESS was directed by the discretion of each enrolling physician and reflected disease progression on an individual patient basis. Study participants were either primary or revision surgical cases. Endoscopic sinus surgery consisted of either unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, or frontal sinusotomy procedures (Draf I, IIa, IIb, or III), with septoplasty and inferior turbinate reductions as adjunctive procedures as needed. All surgical cases were followed with postoperative therapeutic regimens including daily nasal saline rinses and subsequent medical therapy if necessary.

Exclusion Criteria

Due to variations in disease etiology and potential variability in treatment study, participants with recurrent acute rhinosinusitis (RARS) were excluded from final analysis. Additionally, participants with a history of obstructive sleep apnea or corticosteroid dependency were excluded due to suspected confounding influences on sleep related QOL responses and outcomes. The presence of obstructive sleep apnea was identified either by patient-reporting, diagnosis codes (International Classification of Diseases, Ninth Revision; ICD-9), and/or sleep study results, when available. Prior study has shown patient-reporting to be accurate in identifying patients with OSA.[10] Corticosteroid dependency was defined as chronic daily oral steroid use of any dose. Participants were excluded if less than 6 months had lapsed since ESS as these individuals would not have completed a post-operative survey evaluation. Participants failing to provide any study related QOL evaluation within 18 months following ESS were considered lost to follow-up.

Clinical Measures of Disease Severity

Clinical measures of disease severity, collected during preoperative clinical assessments, were used simultaneously for investigational purposes. The bilateral paranasal sinuses were evaluated preoperatively using rigid fiberoptic endoscopes (SCB Xenon 175, Karl Storz, Tuttlingen, Germany) and endoscopic exams were staged by the enrolling physician at each site using the bilateral Lund-Kennedy scoring system (score range: 0-20) which quantifies visualized pathologic states within the paranasal sinuses including the severity of polyposis,

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discharge, edema, scarring, and crusting on a Likert scale.[11] High resolution computed tomography (CT) imaging with landmark navigation (Medtronic, Minneapolis, MN) was also utilized to evaluate preoperative sinonasal disease severity using 1.0 mm contiguous images in both sagittal and coronal planes. Images were 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.[12] Postoperative CT images were not collected due to risks associated with elevated radiation exposure and divergence from the standard of care. Higher scores on both the Lund-Kennedy and Lund-Mackay staging systems indicate worse disease severity.

Sleep Related Symptom Outcome Measures

Participants were asked to complete the 22-item SinoNasal Outcome Test (SNOT-22) to evaluate the severity of symptoms related to CRS (©2006, Washington University, St. Louis, MO) preoperatively and during each follow-up evaluation. The SNOT-22 is a validated, treatment outcome measure applicable to chronic sinonasal conditions.[13] Higher total scores on the SNOT-22 suggest worse patient functioning or symptom severity (total score range: 0-110). The 22-items of the SNOT-22 survey can be categorized and summarized into five distinct domains including: rhinologic symptoms, extra-nasal rhinologic symptoms, ear / facial symptoms, psychological dysfunction, and sleep dysfunction as previously described.[2] Individual item scores are measured using patient selected responses on a Likert scale where higher scores indicate worse symptom severity as follows: 0× “No problem”; 1×“Very mild problem”; 2×“Mild or slight problem”; 3×“Moderate problem”; 4×“Severe problem”; 5× “Problem as bad as it can be”. Sleep symptom severity was operationalized using the 5 discrete survey items of the SNOT-22 sleep domain (***Table 1***).

Data Management and Statistical Analyses

Sample size estimations were completed using two-tailed tests for two dependent means. A total of 27 study participants were required to detect a 1.0 difference on SNOT-22 item responses, corresponding to a discernible change in Likert scale responses for each sleep related symptom score over time, a 0.050 alpha level and 80% 1-β error probability, a conservative between group correlation of 0.300, and equal variance assumption of 1.5 units.

Study data was coded using a unique study identification number to ensure confidentiality and transferred to OHSU from each enrollment site. All study data was manually entered into a relational database (Access, Microsoft Corp., Redmond, WA) and statistical analyses were conducted using commercially available software (SPSS v.22, IBM Corp., Armonk, NY). Preoperative cofactors, clinical measures of disease severity, measures of surgical extent, and sleep related symptom outcome scores were evaluated descriptively while data normality was verified for all continuous measures using distributive analysis. Last available SNOT-22 item scores were used to operationalize each postoperative evaluation due to previously reported stability of postoperative scores between 6, 12, and 18 month follow-up in this cohort.[5] Preoperative and postoperative distributions were evaluated for all symptom item scores to identify potential floor or ceiling effects. Improvement over time, between mean preoperative and postoperative symptom scores, were compared with Wilcoxon

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signed-rank testing for matched pairings. Spearman"s rank correlation coefficients (Rs) were used to described non-linear correlation between variables of interest. Significant improvement in the proportion (%) of participants reporting the presence of any symptom was also compared using McNemar chi-square (χ^2) testing for matched pairings. To account for variations in preoperative scores, mean relative improvement (%) was calculated for each symptom score using the formula: [(mean postoperative score – mean preoperative score) / mean preoperative score] x 100. All comparisons were reported with a type I error probability (p-value) determined at the 0.05 level of significance.

RESULTS

Final Cohort Characteristics

A total of 590 study participants completed enrollment procedures and received ESS between March, 2011 and February, 2015. A total of 334 participants were selected for final analyses after exclusions for RARS (n×38), OSA (n×86), corticosteroid dependency (n×31), and removal of remaining subjects without postoperative follow-up survey evaluations (n×101) to date. No significant differences in patient characteristics were found between participants with and without postoperative follow-up except for a slightly lower average age (45.1 [SD×13.5] years; p×0.002) and a higher prevalence of tobacco smoking (12%; p×0.026) in those without any follow-up. Participant characteristics and preoperative clinical measures of disease severity and QOL are described in ***Table 2*** while the frequency of each endoscopic sinus surgery procedure is described in ***Table 3.*** Participants were followed for an average of 14.5 [4.9] months following endoscopic sinus surgery.

Postoperative Improvement is QOL and Sleep Related Symptoms

A total of 317 (95%) of all participants reported at least one sleep related symptom, with any level of severity, before sinus surgery compared to 259 (78%) participants who reported at least one sleep related symptom postoperatively ($p<0.001$). Significant postoperative improvements in mean SNOT-22 scores as well as all sleep-related item scores of the SNOT-22 were reported. Mean preoperative SNOT-22 total scores improved from 53.0 [19.7] to 27.1 [20.2] ($p<0.001$). Mean SNOT-22 sleep dysfunction domain scores improved from 13.7[6.8] to 7.7 [6.6] ($p<0.001$) while significant improvements in mean sleep related symptom scores are described in ***Table 4***. Corresponding mean relative improvement for SNOT-22 total scores was determined to be 46%. Mean relative improvement on the SNOT-22 sleep dysfunction domain scores was found to be 43% with similar relative improvements in "difficulty falling asleep" (45%), "waking up at night" (40%), "lack of a good night"s sleep" (43%), "waking up tired" (40%), and "fatigue" (42%) item scores. Spearman"s correlations between sleep-related symptoms and nasal obstruction scores of the SNOT-22 found that nasal obstruction scores significantly ($p<0.001$), but only weakly, correlated to sleep-related symptoms scores ($Rs \leq 0.356$). Additionally, Spearman"s correlations were performed to determine the relationship between patient reported sleep-related symptoms and clinical measures of disease severity. There was no significant correlation between preoperative CT scores and sleep-related symptoms ($Rs \leq 0.083$, $p \geq 0.130$) while correlations between preoperative endoscopy scores and sleep-related symptoms identified only very weak associations ($Rs \leq 0.141$; $p \geq 0.010$).

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Reported sleep-related symptom scores of the SNOT-22 were further characterized by evaluating the percentage of patients who reported either no postoperative change, improvement (≥1 point), or worsening (≥1 point) of symptom severity (***Table 5***).

The proportion of study participants reporting no "difficulty falling asleep" significantly improved from 22% to 44% ($p<0.001$) after ESS. Significant postoperative improvements were additionally seen in patients reporting no problem with "waking up at night" (13% to 31%; $p<0.001$), "lack of a good night"s sleep" (12% to 31%; $p<0.001$), "waking up tired" (9% to 31%; $p<0.001$), or "fatigue" (10% to 34%; $p<0.001$). For participants with follow-up, corresponding distributions of total cumulative proportions of preoperative and postoperative score responses for each discrete sleep related symptom on the SNOT-22 are displayed in ***Figures 1-5***.

DISCUSSION

This study examines the impact of ESS on common, patient-reported sleep symptoms in patients with CRS. An overwhelming majority of our cohort demonstrated some level of preoperative sleep impairment with 95% reporting the presence of at least one sleep-related symptom. The average reported preoperative score for each individual symptom ranged from 2.3 for "difficulty falling asleep" to 3.0 for "waking up tired" indicating that these common sleep-related symptoms tend to represent a mild to moderate problem for patients with CRS. Each individual, patient-reported symptom improved significantly after ESS.

"Difficulty falling asleep" was the symptom with the highest percentage of patients reporting a preoperative score of 0. Further analysis also demonstrated that "difficulty falling asleep" was the symptom least likely to improve. These findings suggest that "difficulty falling asleep" may not be affected by CRS to the same degree as other sleep related symptoms leading to less predictable results after ESS. The impact of poor sleep hygiene, medications, and insomnia on sleep onset latency have been well documented in sleep literature and these confounding factors should be considered in patients reporting difficulty falling asleep.[14,15]

Several recent investigations have examined the impact ESS has on sleep in patients with CRS using sleep-specific instruments. In a study by Rotenburg et al., the Epworth Sleepiness Scale (EpSS) and Pittsburgh Sleep Quality Index (PSQI) were used to evaluate sleep outcomes after ESS.[5] Relative improvements in mean scores of 38% and 51% were noted postoperatively in the EpSS and PSQI, respectively, with 26% of patients reporting persistent poor sleep as indicated by a PSQI ≥ 5. Alt et al. also utilized the PSQI to assess postoperative improvements in sleep quality, noting a 57% prevalence of persistent poor sleep following ESS.[4] The rate of persistent sleep impairment in the current study is notably higher at 78%. This is consistent with rates reported by Benninger et al. who evaluated the impact of ESS on sleep using the Rhinosinusitis Disability Index (RSDI). Similar to our study, any degree of sleep dysfunction was assessed postoperatively with 78% of patients reporting persistent impairment.[3] We believe the larger percentage seen in Benninger et al. and our study is likely due to our analysis assessing for the persistence of symptom

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impairment to any degree rather than assessing for “abnormal” sleep as defined by a threshold using a validated sleep questionnaire with normative data.

The mechanisms underlying persistent sleep impairment in CRS are complex and incompletely understood due to the multi-factorial nature of sleep and its regulation. Certainly, one must consider that CRS is a chronic disorder that may continue to impact sleep quality if poorly controlled. Moreover, CRS exacerbations are often treated with oral steroids, a medication class well recognized for interfering with sleep quality, and persistent sleep impairment reported in the current study could certainly be influenced by oral steroid use. Alternatively, persistent sleep impairment may be secondary to an undiagnosed primary sleep disorder and the use of validated screening tools, such as the EpSS or PSQI, may be helpful in deciding if a formal sleep study or referral to a sleep specialist is warranted in patients reporting significant preoperative sleep impairment. Additionally, several chronic medical conditions (i.e. congestive heart failure, chronic obstructive pulmonary disease, chronic pain, etc.) and psychiatric illnesses (i.e. depression) are well known to affect sleep.[16-19] When these comorbid conditions are present, it becomes important to counsel patients pre-operatively regarding the potential impact of these conditions on sleep quality and treatment of these conditions should be optimized. This comprehensive approach to evaluating sleep quality in patients with CRS is essential in order to improve patient care and satisfaction. Further study evaluating comprehensive demographic and clinical data of patients who report persistent sleep impairment and comparing them to those who achieved resolution is a critical next step in identifying predictors of outcome following sinus surgery.

Although strongly linked to sleep, fatigue is differentiated from sleep impairment as it can be present despite adequate sleep and is characterized by both physical and mental exhaustion. Prior studies have examined the impact of ESS on fatigue in patients with CRS demonstrating significant improvements after surgery.[20] In a study by Sautter et al., visual analog scale (VAS) scores used to assess fatigue decreased by 39% after ESS.[21] In the current study, mean fatigue symptom scores similarly demonstrated significant post-operative improvements and decreased by a comparable 42%. Interestingly, fatigue was the symptom with the greatest percentage of patients reporting improvement and the symptom with the greatest increase in patients reporting resolution. The underlying rationale for these observations is unclear; however, one possibility is that ESS not only improves sleep but also improves physical and psychological symptoms leading to a higher likelihood of patient”s experiencing symptomatic improvement.

An important limitation of this current study is the method used to operationalize individual sleep symptoms. The validity of using single Likert scale items with limited discriminative ability and artificial response categories to describe a continuous, subjective health state is uncertain and all study findings should be interpreted with this in consideration.[22] Nevertheless, the measurement of pre-treatment sleep impairment using the SNOT-22 may help to spur patient-provider discussion about sleep related symptoms and facilitate proper evaluation. The inclusion of patients who underwent septoplasty or inferior turbinate reduction as well as patients with nasal polyposis may confound our analysis as these patient subsets would be expected to have a greater degree of mechanical nasal obstruction which alone could lead to sleep impairment and subsequent improvement when surgically

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addressed. Our results, however, are substantiated by the similarity in improvements seen with those from the Rotenberg et al. study, which excluded these patient subsets. While this study is strengthened by its prospective design and sample size, there is a lack of a comparison group of patients electing ongoing medical therapy, and therefore the impact of the placebo effect, cannot be fully excluded. Furthermore, although this study is multi-institutional in design, further external validity is required prior to implementation of these findings into clinical practice, as our results may only be a reflection of our patient cohort and may not be applicable to other patient populations.

CRS disease-specific QOL is a major determinant in a patient"s decision to continue medical therapy or pursue ESS.[23] To improve the shared patient-provider decision making process, knowledge regarding a patient"s motivation for electing a certain treatment modality as well as the expected outcome is paramount. Although sleep impairment may drive patients to elect ESS, based on the data presented, the impact of ESS on common sleep-related symptoms may or may not be in line with what patients are seeking. This study is expected to help providers address these challenging questions and frame expectations in a way that patients can understand.

CONCLUSIONS

Patients with CRS can expect significant and sustained improvements in common, sleep-related symptoms following ESS. Despite these significant improvements, some degree of persistent postoperative sleep impairment is common and patients with CRS seeking improvements in sleep quality should be counseled accordingly. Additionally, sleep onset may not be affected by CRS to the same degree as other sleep related symptoms leading to less predictable outcomes. Clinicians treating CRS must have a broad understanding of comorbid conditions affecting sleep quality so that patients requiring additional evaluation or management are identified and appropriate expectations are set. Further study to identify predictors of outcome is a critical next step in better understanding sleep quality improvements following sinus surgery.

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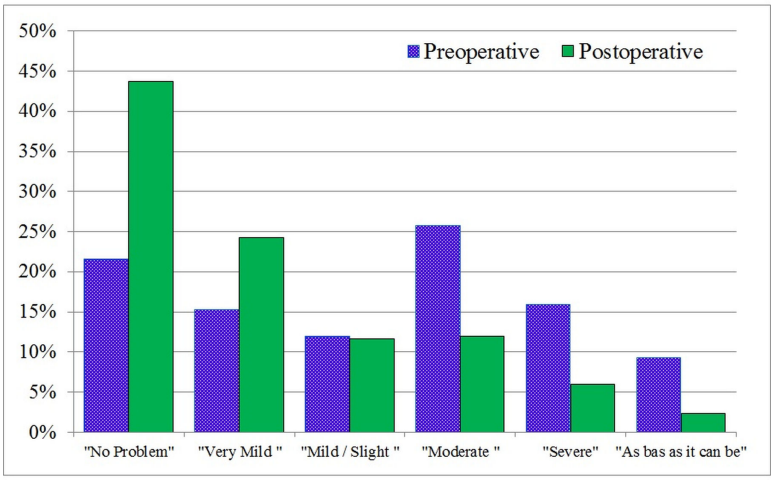

Figure 1.

Distribution of preoperative and postoperative SNOT-22 item scores evaluating “difficulty falling asleep”

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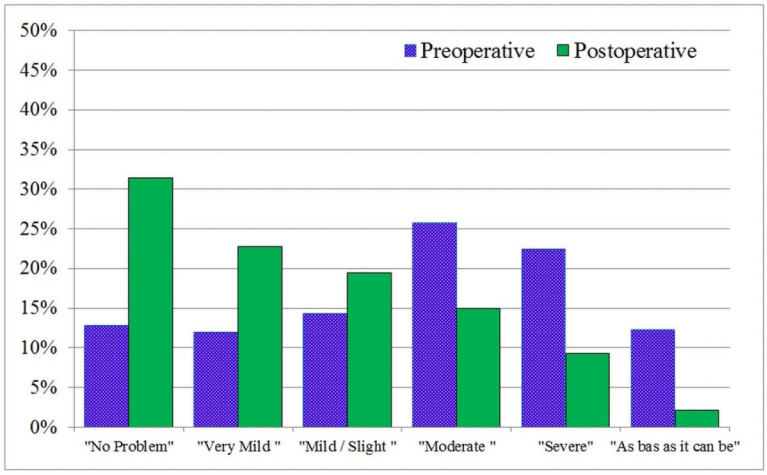

Figure 2.
Distribution of preoperative and postoperative SNOT-22 item scores evaluating “waking up at night”

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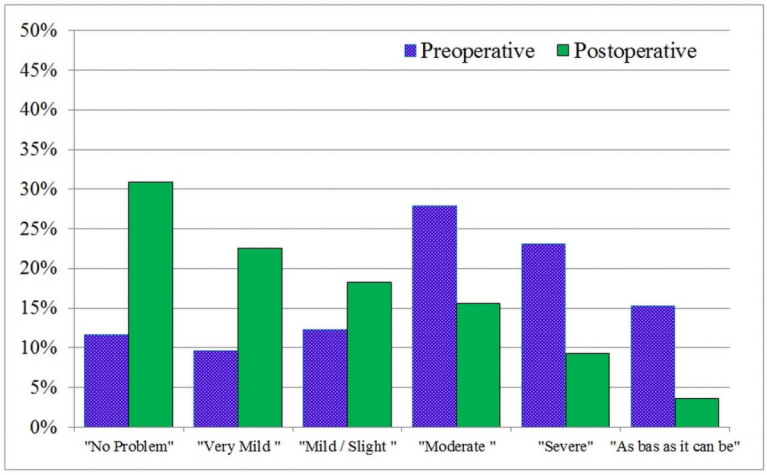

Figure 3.
Distribution of preoperative and postoperative SNOT-22 item scores evaluating “lack of a good night”s sleep”

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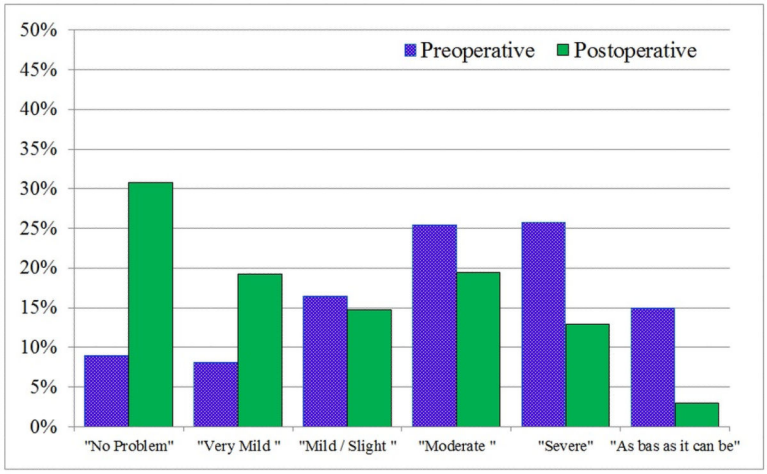

Figure 4.
Distribution of preoperative and postoperative SNOT-22 item scores evaluating “waking up tired”

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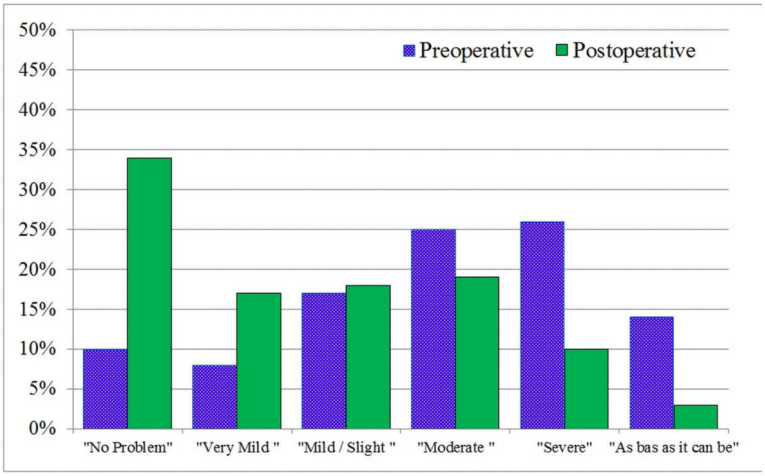

Figure 5.
Distribution of preoperative and postoperative SNOT-22 item scores evaluating “fatigue”

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Table 1

SNOT-22 sleep domain survey items used to operationalize sleep symptoms of CRS

SNOT-22 Survey Items:	Symptom Description:
Item #11	'difficulty falling asleep'
Item #12	'waking up at night'
Item #13	'lack of a good night's sleep'
Item #14	'waking up tired'
Item #15	'fatigue'

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Table 2

Cohort characteristics, preoperative clinical measures of disease severity, and mean quality of life measures (n=334); SD, standard deviation; LL, lower limit of range; UL, upper limit of range; mRAST, modified radioallergosorbent testing; CT, computed tomography; ASA, acetylsalicylic acid; QOL, quality of life; SNOT-22, 22-item SinoNasal Outcome Test;

Characteristics:	**Mean ± SD**	**Range [LL, UL]**	**N (%)**
Age (years)	50.7 ± 15.7	[18, 86]	
Male			150 (45%)
Caucasian			283 (85%)
African American			14 (4%)
Asian			14 (4%)
Hispanic / Latino			19 (6%)
Patient cofactors:			
Asthma			122 (37%)
Allergy (mRAST / skin prick)			147 (44%)
Prior sinus surgery			177 (53%)
Nasal polyposis			127 (38%)
ASA sensitivity			27 (8%)
Septal deviation			138 (41%)
Turbinate hypertrophy			51 (15%)
Depression			45 (14%)
Tobacco use			15 (5%)
Alcohol consumption			144 (43%)
Ciliary dyskinesia			10 (3%)
Diabetes mellitus (Type I or II)			26 (8%)
Clinical Measures of Disease Severity:			
Lund-Kennedy endoscopy scores	6.0 ± 3.8	[0, 18]	
Lund-Mackay CT scores	12.2 ± 6.1	[0, 24]	
Outcome Measures:			
SNOT-22 total score	53.0 ± 19.7	[4, 106]	
Rhinologic subdomain	16.5 ± 6.3	[0, 30]	
Extra-nasal rhinologic subdomain	8.4 ± 3.6	[0, 15]	
Ear / facial subdomain	9.2 ± 5.1	[0, 23]	
Psychological subdomain	15.9 ± 8.4	[0, 35]	
Sleep subdomain	13.7 ± 6.8	[0, 25]	

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Table 3

Prevalence of unilateral and bilateral surgical procedures

Surgical procedures:	**Left side N (%)**	**Right side N (%)**
Maxillary antrostomy	305 (91%)	301 (90%)
Partial ethmoidectomy	45 (14%)	46 (14%)
Total ethmoidectomy	257 (77%)	253 (76%)
Sphenoidotomy	235 (70%)	233 (70%)
Middle turbinate resection	38 (11%)	45 (14%)
Inferior turbinate reduction	66 (20%)	62 (19%)
Septoplasty	140 (42%)	
Frontal sinusotomy *Draf* I	31 (9%)	28 (8%)
Frontal sinusotomy *Draf* IIa	166 (50%)	164 (49%)
Frontal sinusotomy *Draf* IIb	25 (8%)	25 (8%)
Frontal sinusotomy *Draf* III	7 (2%)	

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Table 4

Mean improvement in sleep related symptom scores of the SNOT-22 instrument following endoscopic sinus surgery; SD, standard deviation

Sleep Related Symptom Items	Preoperative	Postoperative	
	Mean ± SD	Mean ± SD	
Item #11: 'difficulty falling asleep'	2.3 ± 1.6	1.2 ± 1.4	<0.001
Item #12: 'waking up at night'	2.7 ± 1.6	1.5 ± 1.4	<0.001
Item #13: 'lack of a good night's sleep'	2.9 ± 1.5	1.6 ± 1.5	<0.001
Item #14: 'waking up tired'	3.0 ± 1.5	1.7 ± 1.5	<0.001
Item #15: 'fatigue'	2.9 ± 1.5	1.6 ± 1.5	<0.001

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Table 5

Percentages of patients who reported improvement in sleep related symptoms following endoscopic sinus surgery (n=334)

SNOT-22 Survey Items:	Item #11: 'difficulty falling asleep'	Item #12: 'waking up at night'	Item #13: 'lack of a good night's sleep'	Item #14: 'waking up tired'	Item #15: 'fatigue'
Improved ≥1 point	58%	62%	66%	66%	66%
Worsened ≥1 point	12%	13%	11%	11%	9%
No change	30%	25%	23%	23%	25%