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Preoperative Lund-Mackay computed tomography score is associated with preoperative symptom severity and predicts quality-of-life outcome trajectories after sinus surgery

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Abstract

Background—Disagreement exists about the relationship between Lund-Mackay CT scores (LMCTS) and quality-of-life outcome (QoL) measures. We investigated whether preoperative LMCTS are associated with preoperative QoL, and whether LMCTS is predictive of postoperative QoL outcomes in chronic rhinosinusitis (CRS) patients.

Methods—Adult patients with medically recalcitrant CRS (n = 665) were enrolled in a prospective, observational cohort study. Preoperative LMCTS and pre- and postoperative self-reported QoL outcomes (22-item Sino-Nasal Outcomes Test [SNOT-22]) were collected and evaluated over 12 months. Five hundred sixty-eight patients met the inclusion criteria. Longitudinal linear mixed-effects modeling was used to investigate the effect of LMCTS on QoL after functional endoscopic sinus surgery (FESS).

Results—Preoperative LMCTS were significantly associated with preoperative SNOT-22 scores (p < 0.01) and postoperative SNOT-22 scores (p < 0.001), driven by Extranasal and Rhinologic subdomains of the QoL questionaire. Patients in the lowest preoperative LMCTS quartile had the lowest mean change in SNOT-22 scores at 12 months (16.8 points; 95% confidence interval [CI], 12.2–21.3). Patients in the second and third lowest preoperative LMCTS quartiles had mean changes at 12 months of 21.1 points (95% CI, 16.7–25.4) and 23.1 points (95% CI, 18.3–27.9). Patients in the highest preoperative LMCTS quartile had the greatest improvement in SNOT-22 scores after FESS (29.9 points; 95% CI, 24.9–34.8). The difference in QoL change at 12 months

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between the highest and lowest preoperative LMCTS quartiles was 13.1 points (95% CI, 6.0–20.2; p < 0.001).

Conclusion—Our study demonstrates that preoperative LMCTS correlate with preoperative extranasal and rhinologic symptom severity and that the LMCTS is an indicator of postsurgical QoL outcomes for medically recalcitrant chronic rhinosinusitis patients in a large tertiary otolaryngology setting.

Keywords

sinusitis; computed tomography; FESS; SNOT-22; quality of life; patient-reported outcome measure

Chronic rhinosinusitis (CRS) is a debilitating disease affecting more than 35 million Americans.^{1–3} Patients with CRS have a significantly decreased quality of life (QoL), both in disease-specific areas and in general health.⁴ Historically, the diagnosis of CRS was focused on patient-reported symptoms and clinical judgment rather than objective data, making standardization of the diagnosis of CRS challenging. Thus, the current clinical guidelines to diagnose CRS require both objective evidence of mucosal inflammation and a patients' subjective assessment of symptom burden. Although there are many scoring systems in place for sinonasal computed tomography (CT) analysis, the Lund-Mackay system has the best inter- and intraob-server agreement.^{5, 6} To measure subjective symptom severity in patients with CRS, the 22-item Sino-Nasal Outcomes Test (SNOT-22), a validated disease-specific survey for QoL, is commonly used.⁷

Several studies have concluded that there is little concordance between CT and total symptom–based scores,^{8–17} which implies that increased mucosal inflammation does not correlate with increased symptom severity. However, some of these same studies, as well as others, have shown significant correlation between CT scores and specific symptoms. ^{10, 13, 14, 18} For example, the 2015 study by Sedaghat et al¹³ demonstrated a significant association between preoperative Lund-Mackay CT scores (LMCTS) and a nasal component of the SNOT-22, which included symptoms such as nasal blockage/discharge and the need to blow nose. Finally, a study by Hopkins et al¹² showed no clinically significant correlation between LMCTS and SNOT-22 total score preoperatively, but did find a correlation between LMCTS and SNOT-22 and the change in total score at 12 and 36 months postoperatively.

The mixed findings in the literature indicate that more research is required to identify the relationship between these measures while highlighting the possibility that preoperative CT scores may have prognostic implications for QoL. In the current study, our aim was to investigate whether an association exists between preoperative LMCTS and pre-and postoperative SNOT-22 scores.

Patients and methods

At the time of the analysis, 665 patients had been recruited in an ongoing observational cohort study during visits at the Department of Otorhinolaryngology of the University of Pennsylvania Health System, between April 19, 2007 and February 25, 2017. Eligibility for

the study included age 18 years and having undergone functional endoscopic sinus surgery (FESS) for medically recalcitrant CRS. Exclusion criteria included having a known autoimmune disorder or immunodeficiency, primary ciliary dyskinesia, cystic fibrosis, history of radiation exposure to the paranasal sinuses, or a history of sinonasal trauma. Forty-eight patients were excluded due to these criteria. In addition, 1 patient underwent a revision FESS within the 12-month study period and was also excluded. The patient data from this study were used to address the research question of whether there exists a correlation between LMCTS and SNOT-22 scores.

All Lund-Mackay CT staging was done by a trained clinical research nurse who was blinded to the participating patient's identity, including their clinical and demographic characteristics. The LMCTS were then divided into quartiles for analysis. The first quartile (Q) had LMCTS of 1–8, the second Q had scores of 9–12, the third Q had scores of 13–16, and the fourth Q had scores of 17–24. The rationale for using quartiles in the model, as opposed to absolute score, was based on the understanding that a patient with an LMCTS of 4 is likely quite similar in degree of mucosal inflammation and sinus disease to a patient with an LMCTS of 5 or 6. Using quartiles thus allows us to have a more clinically useful interpretation of our results. The categorization of our predictor can also take into account a nonlinear response on the outcome variable. As a test of the model's sensitivity to this choice we ran the model using LMCTS both as a categorical and as a continuous variable, and checked for differences in results.

Lund-Mackay CT staging involves scoring 6 bilateral areas of sinus opacification from 0 to 2, for a possible range of scores between 0 and 24. A higher LMCTS indicates more opacity in the 6 measured areas of the sinus, as observed on CT imaging. Any patient who did not have a CT scan available at least 6 months prior to their surgery, either due to the scan not being accessible through the electronic medical record or because a scan had not been done during that period, was excluded (n = 48). In total, 568 patients were eligible for analysis. All study protocols and informed consent were collected and approved by the institutional review board of the University of Pennsylvania. There were no incentives, financial or otherwise, provided to the participating patients.

After providing consent to participate in the study, patients were followed for 1 year after undergoing FESS. The SNOT-22 was provided to every patient in the study before surgery and at each postoperative visit, but only completed questionnaires were included in the analysis. The SNOT-22 is a well-validated, disease-specific quality-of-life questionnaire, with a high Cronbach's α ($\alpha = 0.91$), and has a test-retest reliability of 0.93.⁷ Psychometric validity research by Hopkins et al showed the minimally important difference, which is the smallest change in SNOT-22 score that can be detected by a patient, to be 8.9 points.⁷ We used this 8.9-point change as our threshold for a clinically significant effect size. We also analyzed SNOT-22 domains to better understand which symptom areas are most important in our model. The 5 domains have been described previously, and consist of Rhinologic, Extranasal, Ear/Facial, Psychological, and Sleep symptoms.¹⁹ The point totals for each domain are different, and there are questions that are shared between domains.

We analyzed SNOT-22 scores at 5 predefined time periods: preoperatively (at least 6 months before surgery); at 1 month after surgery (0.5 month and <1.5 months); at 3 months after surgery (1.5 months and <4.5 months); at 6 months after surgery (4.5 months and <8.5 months); and at 12 months after surgery (8.5 months and <15 months). Of the 568 patients, there were a total of 2059 completed SNOT-22 forms over these 5 time-points, including 547 preoperatively, 388 at 1 month, 494 at 3 months, 326 at 6 months, and 304 at 12 months. The amount of completed SNOT-22s was well-balanced across all LMCTS quartiles, with no discernible pattern of missing data.

We examined baseline characteristics, including sociodemographic information and comorbidities, and compared their distributions across the LMCTS quartile groups (Table 1). Sociodemographic data were collected by a combination of chart review and patient self-report. Comorbidities were assessed by a combination of patient self-report and chart review of the anesthesiology report at the time of surgery. All chart review was independently entered by 2 different research assistants and then checked for agreement. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Pennsylvania.

Statistical analysis

Distributions for baseline characteristics and preoperative scores were compared using Fisher's exact test for categorical/dichotomous variables and general linear models for continuous variables (age, body mass index [BMI], and preoperative SNOT-22). Longitudinal linear mixed-effects modeling was used to examine the relationship between LMCTS quartiles and SNOT-22 scores. The distribution of the SNOT-22 measure follows a unimodal symmetric distribution and satisfies the assumptions for mixed-effects modeling. Mixed-effects modeling takes advantage of all available data (up to the point of loss to follow-up or withdrawal) and can also address missing data. Because the level of missingness was not excessive and patterns of missing-ness were not detected, the mixed-effects model relied on all available data.^{20–23} Both random slopes and intercepts were modeled to represent subject-level deviation from the average, or fixed-effect, slope over time and intercept. Restricted maximum likelihood estimation was used, along with an unstructured covariance structure. The outcome was analyzed as repeated observations. Time was measured as a categorical variable to account for nonlinearity in the SNOT-22 profile over time.

An unadjusted mixed-effects model was estimated by regressing the longitudinal outcome on time, LMCTS quartile group, and the time \times LMCTS quartile group interaction. We then stratified the unadjusted model by nasal polyp status and prior FESS status to determine whether the proposed effect of LMCTS on the SNOT-22s over time varied by these subgroups. An adjusted model was then built by including the fixed-effects of the nasal polyp and prior FESS covariates. The *a* was set at 0.050, all reported *p* values are 2-tailed, and all statistical analyses were carried out using Stata version 13.1/IC (StataCorp LP, College Station, TX).

Results

Baseline characteristics

Overall, our cohort was 89% white and 42% female (Table 1). The majority of the participants were never smokers (59%). Mean age for all 4 groups was 49.8 (\pm 14.4) years, and mean BMI was 28.0 (\pm 5.4). The 4 LMCTS quartiles were comparable across multiple comorbidities at the time of surgery, including allergic rhinitis (AR, defined as a diagnosis from the attending physician of both allergies and CRS at the time of presentation), diabetes mellitus (DM), gastroesophageal reflux disease (GERD), hypertension, and obstructive sleep apnea (OSA). Notably, there was no statistically significant difference between the 4 LMCTS quartiles with regard to primary vs revision FESS (p = 0.101). There were many covariates in which the 4 LMCTS quartile groups differed significantly. The fourth quartile of LMCTS (17–24) demonstrated a higher proportion of males and non-whites, and had greater numbers of allergic fungal sinusitis (AFS), aspirin-exacerbated respiratory disease (AERD), aspirin (ASA)-sensitive, CRS with nasal polyp (CRSwNP), and asthma patients.

Preoperative total SNOT-22 scores were significantly different by LMCTS quartile group, with higher LMCTS associated with higher SNOT-22 total scores (Table 2). This relationship was not seen in all 5 SNOT-22 domains—only the Rhinologic and Extranasal domains were statistically significant.

Longitudinal outcomes

Table 3 provides results from the unadjusted longitudinal linear mixed-effects model. Overall, all 4 quartile groups demonstrated significant improvement after FESS (mean change at 12 months vs preoperatively for all 4 quartile (Q) groups: 22.2 points; 95% confidence interval [CI], 19.9–24.4; p < 0.001).

The first Q of LMCTS was used as the reference group for both the unadjusted and adjusted models. In the unadjusted model, subjects in the fourth Q demonstrated a significantly greater decrease in SNOT-22 scores at 12 months post-FESS as compared with the reference group (difference, 13.9 points; 95% CI, 7.6–20.2; p < 0.001). In addition, the third Q also demonstrated a significantly greater decrease compared with the reference group. However, the difference seen in the third Q was smaller in magnitude, and did not reach clinical significance. The overall effect of LMCTS quartiles on SNOT-22 total score improvement over time in the unadjusted model was statistically significant (p < 0.001).

Stratifying the unadjusted model by nasal polyp status revealed a stronger effect of LMCTS on SNOT-22 scores at 12 months in the CRSwNP stratum than in the CRS without nasal polyp (CRSsNP) stratum (Table 4). However, most of the patients in the fourth Q of LMCTS were polyp patients (82%), so making inferences based on this stratification was difficult, especially at "12 months" when the amount of missing data was greatest. Patients in the primary FESS group had a weaker, yet still significant, effect of LMCTS on SNOT-22 score over time.

Figure 1 shows the trajectory of SNOT-22 scores over time after FESS by LMCTS Q group, along with 95% CIs at each time-point, for the adjusted model. The adjusted model included

the fixed effects of nasal polyps and previous FESS (Table 5). After controlling for these covariates, the independent effect of LMCTS on SNOT-22 trajectory over time was similar to that in the unadjusted model—subjects in the fourth Q still demonstrated a significantly greater decrease in SNOT-22 scores at 12 months post-FESS as compared with the first Q (difference, 13.1 points; 95% CI, 6.0–20.2; p < 0.001). Similar to the results in Table 2, the Rhinologic and Extranasal subdomains were driving most of the effect size seen in the change in total score after FESS (Table 5).

We investigated the relationship between LMCTS and SNOT-22 scores by grouping LMCTS into 4 quartiles. To determine whether this choice affected our results we also entered LMCTS as a continuous predictor of SNOT-22 scores into the final model. These data are presented in Table 6. In the adjusted model— including the fixed effects of nasal polyps and previous FESS—the continuous LM-CTS predictor did not demonstrate a different relationship between LMCTS and SNOT-22 score trajectory over time in this data set. For example, the coefficient for the effect of LMCTS on the Rhinologic subscale at the 12-month postoperative time-point was -0.36 (95% CI, -0.52 to -0.21; p < 0.001), indicating that, for every 1-point increase in LMCTS, there was a corresponding decrease in Rhinologic scores from baseline to 12 months of 0.36 point. This coefficient translates to an estimate of 5.8–8.3 points at LMCTS values of 17–24 (compared with a LMCTS of 1), in line with the estimate from the grouped analysis of 5.3 points (95% CI, 3.0–7.7) for the fourth Q of LMCTS scores (Table 5).

Discussion

CRS is a debilitating disease and its diagnosis is based on subjective and objective criteria. To date, studies are mixed regarding the correlation between inflammation, as seen on CT, and CRS symptoms.^{8–18, 24, 25} In this study we found evidence for an association between LMCTS and pre- and postoperative sinonasal quality of life, as measured by the SNOT-22.

Unlike other studies examining the correlation between LMCTS and SNOT-22 scores, this study utilized a longitudinal linear mixed-effects model to assess SNOT-22 surveys over a 1-year study period. This model is best suited for longitudinal data, in which each subject has repeated observations, because it accounts for the subjectivity of the SNOT-22 as it relates to an individual. The model therefore takes into consideration that an individual's answers on the SNOT-22 questionnaire are relative to their answers on previous questionnaires, allowing for a more accurate representation of the data. The model also can account for missing data, which is an important consideration for prospective cohort studies, where some patients will inevitably be lost to follow-up. To our knowledge, this is the first study on this topic to use a mixed-effects model for analysis, and is one of the largest studies to date to investigate the relationship between the LMCTS and SNOT-22.

Preoperative LMCTS and preoperative SNOT-22

Preoperative LMCTS were associated with preoperative SNOT-22 scores. When divided into symptom domains, this relationship was only seen in the Rhinologic and Extranasal domains. This finding suggests that increased mucosal inflammation has a limited impact on the QoL of patients outside of these 2 domains.

The Rhinologic and Extranasal domains reflect the majority of symptoms used to diagnose CRS. Similar to our study, others have identified a relationship between CT scores and nasal symptoms.^{8, 10, 13, 14, 18} Our findings, along with those from other studies, indicate that many of the symptoms we use to diagnose CRS are associated with LMCTS.

Preoperative LMCTS and postoperative SNOT-22 scores

All patients had a significant decrease in SNOT-22 score post-FESS. The patients with the most severe preoperative LMCTS (scores of 17–24) not only started with the highest preoperative SNOT-22 score, but also had the largest postoperative improvement. Thus, we have shown that higher preoperative LMCTS are predictive of better QoL outcomes after surgery. This finding once again raises the question of using preoperative LMCTS for purposes beyond just acquiring anatomic information.

Furthermore, preoperative LMCTS were strongly associated with the change in Rhinologic and Extranasal SNOT-22 score preoperatively to 12 months postoperatively. This finding indicates that there is a stronger relationship between LMCTS and many of the CRS-specific symptoms covered by the SNOT-22 *before and after* FESS than there is between LMCTS and the less CRS-specific areas measured by the SNOT-22 (such as the Psychological and Sleep domains).

These findings suggest a relationship between LMCTS and QoL that runs counter to some earlier publications that documented the surprisingly low symptomatology of patients with high CT score. We propose 3 factors to reconcile the difference between our finding of a clinically significant relationship and those studies suggesting the opposite. First, we utilized a longitudinal linear mixed-effects regression model. The aforementioned advantages of this model make it the superior choice when analyzing repeated-measures survey data, as compared with a "naive" regression, which does not address within-subject correlation. If the earlier studies that showed no clinically significant association between LMCTS and QoL were to be replicated using this model, it is possible their results would align more closely with ours. The second factor is that our study was carried out in a large, homogeneous cohort. QoL is inherently subjective, and can be influenced by culture, economics, and expectations. Therefore, a homogeneous cohort, although less generalizable to the country as a whole, does provide the researcher with a less variable set of data than a cohort comprised of patients with many different backgrounds and socioeconomic statuses. Finally, ours was one of the highest powered studies done to date. If earlier studies had utilized larger population sizes, it is possible that their findings would align more closely with ours.

Limitations

A potential source of error in this study is that preoperative SNOT-22s were not necessarily completed at the same time as preoperative CT imaging. However, given that this was true for all groups, it is unlikely that this biased our results in either direction.

Our study may be less generalizable to the general population as it was conducted with a homogeneous cohort (89% white) of medically recalcitrant CRS patients at a single, large tertiary rhinology clinic. It is possible that the proposed relationship does not exist or does

not exist as strongly among different patient groups and/or at different otolaryngology practices. Similarly, these patients met the criteria for CRS, and there are other indications for sinus surgery, such as recurrent acute infections, in which these data would not be generalizable given the fluctuating nature of the disease process.

Conclusion

Our study has shown that a higher degree of preoperative mucosal inflammation, as seen on CT scans, is associated with both a worse preoperative QoL and a greater improvement in QoL after FESS in a homogeneous cohort of medically recalcitrant CRS patients at a single, large tertiary rhinology clinic. We also found that this relationship was seen predominantly in the Rhinologic and Extranasal domains of the SNOT-22 questionnaire. Also, nasal polyp status and prior FESS status do not appear to be confounders in this proposed relationship.

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FIGURE 1.

SNOT-22 total score—adjusted mixed-effects model. Graph displays linear predictions of total SNOT-22 score for reach Lund-Mackay CT score quartile with 95% CIs based on the results of the adjusted mixed effects model. CI = confidence interval; CT = computed tomography; SNOT-22 = Sino-Nasal Outcomes Test.

TABLE 1

Patients' characteristics

	Total	Finet O (1 8)	Second O (0-13)	Thind O (13-16)	Ecurith O (17-34)	•
	IUUAI	LUSU (11-0)	(21-6) y ulugas	(ot-ct) D nint	1+7-11) 入 III.III0.J	μ
Patients [n (%)]	568 (100.0)	164 (28.9)	150 (26.4)	124 (21.8)	130 (22.9)	
Female [n (%)]	241 (42.4)	84 (51.2)	64 (42.7)	49 (39.5)	44 (33.9)	0.023 *
Race [n (%)] ^{<i>a</i>}						0.032^{*}
White	500 (88.8)	152 (92.7)	140 (93.3)	102 (84.3)	106 (82.8)	
Black	48 (8.5)	8 (4.9)	8 (5.3)	15 (12.4)	17 (13.3)	
Asian	15 (2.7)	4 (2.4)	2 (1.3)	4 (3.3)	5 (3.9)	
Ethnicity [n (%)]						0.465
Hispanic	6 (1.1)	2	0	2	2	
Non-Hispanic	562 (98.9)	162 (98.8)	150 (100.0)	122 (98.4)	128 (98.5)	
Smoker $[n (\%)]^{a}$						0.982
Never	329 (58.8)	92 (56.8)	86 (58.1)	70 (58.3)	81 (62.3)	
Former	184 (32.9)	56 (34.6)	50 (33.8)	39 (32.5)	39 (30.0)	
Current	47 (8.4)	14 (8.6)	12 (8.1)	11 (9.2)	10 (7.7)	
Comorbidities [n (%)]						
AERD	74 (13.0)	6 (3.7)	14 (9.3)	17 (13.7)	37 (28.5)	<0.001*
AFS	30 (5.3)	4 (2.4)	6 (4.0)	6 (4.8)	14 (10.8)	0.019^{*}
AR	392 (69.0)	106 (64.6)	108 (72.0)	80 (64.5)	98 (75.4)	0.125
ASA sensitivity	79 (13.9)	7 (4.3)	15 (10.0)	18 (14.5)	(0.05) 95	<0.001*
Asthma	282 (49.7)	43 (32.3)	77 (51.3)	55 (44.4)	97 (74.6)	<0.001*
DM	42 (7.4)	14 (8.5)	13 (8.7)	9 (7.3)	6 (4.6)	0.535
GERD	178 (31.3)	59 (36.0)	49 (32.7)	34 (27.4)	36 (27.7)	0.333
Hypertension	178 (31.3)	50 (30.5)	53 (35.3)	39 (31.5)	36 (27.7)	0.585
OSA	85 (15.0)	29 (17.7)	24 (16.0)	21 (16.9)	11 (8.5)	0.099
Nasal polyps [n (%)]	299 (52.6)	37 (22.6)	68 (45.3)	88 (71.0)	106 (81.5)	<0.001*
Previous FESS [n (%)]						0.101

Statistically significant difference $(p \quad 0.05)$.

 a Missing race data on 5 patients, and missing smoking data on 8 patients.

AERD = aspirin-exascerbated respiratory disease; AFS = allergic fungal sinusitus; AR = allergic rhinitus; ASA = aspirin; BMI = body mass index; DM = diabetes mellitus; FESS = functional endoscopic sinus surgery; GERD = gastroesophageal reflux disease; OSA = obstructive sleep apnea; Q = quartile; SD = standard deviation.

0.412 0.479

47.9 (13.5)

50.1 (14.7)

50.4 (15.3)

49.8 (14.4)

Age at surgery [mean (SD)]

Revision Primary

BMI [mean (SD)]

28.2 (5.2)

28.4 (5.4) 50.4 (13.7)

28.1 (5.3)

27.5 (5.8)

28.0 (5.4)

TABLE 2

Preoperative SNOT-22 scores

	First Q (1–8)	Second Q (9–12)	р	Third Q (13–16)	р	Fourth Q (17–24)	р
SNOT-22 total	40.9 (37.6–44.3)	45.5 (42.1–48.9)	090.0	46.2 (42.3–50.2)	0.045	50.7 (47.0–54.4)	<0.001
Subscales							
Rhinologic (0–35)	12.4 (11.4–13.4)	15.1 (14.1–16.2)	<0.001	16.3 (15.1–17.5)	<0.001	19.8 (18.7–20.9)	<0.001
Extranasal (0–15)	6.6 (5.9–7.2)	8.1 (7.5–8.7)	0.001	7.8 (7.1–8.5)	0.010	8.5 (7.8–9.2)	<0.001
Ear/Facial (0–25)	7.8 (6.9–8.6)	7.6 (6.8–8.5)	0.827	6.9 (6.0–7.9)	0.200	8.3 (7.4–9.2)	0.389
Psychological (0–35)	11.5 (10.1–13.0)	12.4 (11.0–13.9)	0.392	12.8 (11.1–14.5)	0.272	12.6 (11.0–14.2)	0.331
Sleep (0–25)	11.3 (10.1–12.4)	12.0 (10.8–13.2)	0.366	11.9 (10.5–13.3)	0.517	11.5 (10.2–12.8)	0.793

First Q (1-8) used as reference group for general linear model.

Q = quartile; SNOT-22 = 22-item Sino-Nasal Outcomes Test.

TABLE 3

SNOT-22 Unadjusted mixed-effects model-difference in change at 12 months between LMCTS quartiles with 95% CIs

	First Q (1–8)	Second Q (9–12)	р	Third Q (13–16)	р	Fourth Q (17–24)	р
SNOT-22 total score	Ref. group	-4.5 (-10.5 to -0.4)	0.148	-6.5 (-12.8 to -0.2)	0.042	-13.9 (-20.2 to -7.6)	<0.001
Subscales							
Rhinologic (0–35)	Ι	-2.7 (-4.7 to -0.7)	0.009	-3.6 (-5.7 to -1.5)	0.001	-6.2 (-8.3 to -4.1)	<0.001
Extranasal (0–15)	Ι	-1.5 (-2.7 to -0.2)	0.020	-1.5 (-2.8 to -0.2)	0.026	-2.2 (-3.5 to -1.0)	0.001
Ear/Facial (0–25)	Ι	-0.5 (-1.8 to 0.8)	0.457	-0.3 (-1.6 to 1.1)	0.708	-2.0 (-3.3 to -0.6)	0.005
Psychological (0–35)		-0.9 (-3.3 to 1.5)	0.445	-1.1 (-3.6 to 1.4)	0.385	-3.2 (-5.7 to -0.7)	0.011
Sleep (0–25)	Ι	-0.3 (-2.4 to 1.8)	0.809	-0.7 (-2.9 to 1.5)	0.515	-2.5 (-4.7 to -0.4)	0.023

CI = confidence interval; LMCTS = Lund-Mackay computed tomography score; Q =quartile; SNOT-22 = 22-item Sino-Nasal Outcomes Test.

SNOT-22 total score stratified mixed-effects models—difference in model estimates between fourth Q and first Q at 3-, 6-, and 12-month time periods *

CBCNII	SIMINI	р	6 months	р	12 months	d
-) 1771 1771 -	-19.1 to -5.0)	0.001	-14.7 (-23.4 to -6.0)	0.001	-20.6 (-31.2 to -10.1)	<0.001
CRSsNP18.0 (.27.2 to -8.9)	<0.001	-15.0 (-25.1 to -4.9)	0.004	-8.0 (-20.5 to 4.4)	0.207
Primary -12.7 (-	.20.7 to -4.8)	0.002	-12.7 (-21.9 to -3.5)	0.007	-12.3 (-23.2 to -1.3)	0.028
Revision –17.7 (–2	23.2 to -12.2)	<0.001	-13.9 (-20.6 to -7.3)	<0.001	-14.4 (-22.1, -6.7)	<0.001

* Refer to Table 1 for group sizes.

CRSwNP = chronic rhinosinusitis with nasal polyps; CRSsNP = chronic rhinosinusitis without nasal polyps; Primary = surgery performed during the study period was their first functional endoscopic sinus surgery; Revision = surgery performed during the study period was not their first functional endoscopic sinus surgery.

TABLE 5

SNOT-22 total score adjusted mixed-effects model—difference in change at 12 months between LMCTS quartiles with 95% CIs

	First Q (1-8)	Second Q (9-12)	р	Third Q (13–16)	d	Fourth Q (17–24)	d
SNOT-22 total score	Ref. group	-4.4 (-10.7 to 1.9)	0.171	-6.2 (-13.1 to 0.7)	0.078	-13.1 (-20.2 to -6.0)	<0.001
Subscales							
Rhinologic (0–35)		-2.4 (-4.5 to -0.3)	0.024	-3.0 (-5.3 to -0.7)	0.011	-5.3 (-7.7 to -3.0)	<0.001
Extranasal (0–15)		-1.4 (-2.7 to -0.1)	0.030	-1.4 (-2.8 to 0.05)	0.058	-2.1 (-3.5 to -0.6)	0.005
Ear/Facial (0–25)		-0.6 (-1.9 to 0.8)	0.397	-0.4 (-1.9 to 1.1)	0.596	-2.0 (-3.6 to -0.5)	600.0
Psychological (0–35)		-0.9 (-3.4 to 1.6)	0.466	-1.1 (-3.8 to 1.6)	0.436	-3.1 (-5.9 to -0.3)	0.030
Sleep (0–25)		-0.3 (-2.5 to 1.9)	0.799	-0.8 (-3.2 to 1.6)	0.533	-2.5 (-4.9 to 0.01)	0.051

 $\overset{*}{}_{\rm Adjusted}$ for the effect of both nasal polyps and previous functional endoscopic sinus surgery (revision vs primary).

CI = confidence interval; LMCTS = Lund-Mackay computed tomography score; Q =quartile; SNOT-22 = 22-item Sino-Nasal Outcomes Test.

TABLE 6

LMCTS continuous predictor adjusted mixed-effects model—difference in change of SNOT-22 scores (after the preoperative time period) for each point increase in LMCTS with 95% CIs*

	3 months	р	6 months	р	12 months	d
SNOT-22 total score	-1.02 (-1.35 to -0.70)	<0.001	-0.78 (-1.16 to -0.40)	<0.001	-0.87 (-1.32 to -0.42)	<0.001
Subscales						
Rhinologic (0–35)	-0.51 (-0.62 to -0.40)	<0.001	-0.37 (-0.50 to -0.24)	<0.001	-0.36 (-0.52 to -0.21)	<0.001
Extranasal (0–15)	-0.17 (-0.24 to -0.10)	<0.001	-0.14 (-0.22 to -0.06)	0.001	-0.15 (-0.24 to -0.05)	0.002
Ear/Facial (0–25)	-0.14 (-0.21 to -0.06)	<0.001	-0.10 (-0.18 to -0.01)	0.027	-0.13 (-0.23 to -0.03)	600.0
Psychological (0–35)	-0.20 (-0.34 to -0.07)	0.002	-0.20 (-0.35 to -0.05)	0.011	-0.21 (-0.39 to -0.03)	0.023
Sleep (0–25)	-0.17 (-0.29 to -0.5)	0.006	-0.10 (-0.24 to 0.04)	0.151	-0.13 (-0.29 to 0.03)	0.111
*						

Adjusted for the effect of both nasal polyps and previous functional endoscopic sinus surgery (revision vs primary).

CI = confidence interval; LMCTS = Lund-Mackay computed tomography score; SNOT-22 = 22-item Sino-Nasal Outcomes Test.