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Quality of life outcomes after endoscopic sinus surgery: How long is long enough?

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Abstract

Objective—Determine the time interval over which quality-of-life (QOL) outcomes stabilize after endoscopic sinus surgery (ESS).

Study Design—Multi-institutional, longitudinal cohort.

Setting—Tertiary rhinology centers.

Subjects and Methods—Adults with chronic rhinosinusitis from three medical centers were asked to provide responses to the Rhinosinusitis Disability Index (RSDI) and the Chronic Sinusitis Survey (CSS) at baseline and 6 months, 12 months, and 20 months after endoscopic sinus surgery. Repeated measures and post hoc analyses were used to compare QOL scores between follow-up time points. Subgroup analyses were done in a similar fashion for patients with and without nasal polyposis, asthma, allergies, acetylsalicylic acid intolerance, depression, and prior sinus surgery

Results—A total of 127 patients provided complete follow-up data for all three time points. Improvement in QOL scores was seen at 6 months after surgery for both the RSDI and CSS instruments. When comparing changes in mean QOL scores between all follow-up time points, there were no significant differences in either RSDI or CSS total scores (all $p \geq 0.853$) or subscale scores (all $p \geq 0.251$) between 6, 12, and 20 months. Each individual subgroup demonstrated stable QOL scores between 6 and 20 months follow-up, including patients with polyposis and those with ASA intolerance (all $p \geq 0.275$).

Conclusion—At a cohort level, improvements in QOL after ESS do not appear to change between 6 and 20 months. Clinical trial designs incorporating QOL outcomes after ESS should consider the six month time frame as an appropriate primary endpoint.

Keywords

Chronic rhinosinusitis; quality of life; outcomes; longitudinal; endoscopic sinus surgery; sinusitis

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Introduction

Over the last decade, several multidisciplinary panels have proposed designs for clinical trials that would allow appropriate evaluation of therapeutic options for chronic rhinosinusitis (CRS).^{1–3} One critical item missing from suggested study designs is an evidence-based recommendation regarding length of follow-up necessary after any specific intervention. The follow-up interval after a surgical intervention, such as endoscopic sinus surgery (ESS), is perhaps most important as postoperative healing may have a variable and prolonged time course which could impact outcomes. Practically speaking, the earliest follow-up point at which outcomes stabilize should be utilized as the primary time point for outcome measurement in a clinical trial.

Previously published studies have reported surgical outcomes for CRS after variable lengths of time, ranging from a few months to many years.^{4–6} Most of these studies are single institution, retrospective, and report only a single average follow-up time interval, making it difficult to draw firm conclusions regarding the ideal length of follow-up necessary. We have previously reported outcomes on a large multi-institutional cohort with a primary follow-up endpoint of approximately 18 months.⁷ In the current study, we present a subset of that cohort that was followed in a longitudinal fashion at multiple time points after ESS. The primary goal was to determine the time interval at which quality-of-life (QOL) outcomes stabilize after surgery.

Methods

Patient Population and Selection Criteria

Adult patients with CRS according to consensus guidelines were prospectively enrolled into a longitudinal, observational study at 3 medical centers (Oregon Health & Science University (OHSU), Medical College of Wisconsin (MCW), and Stanford University).² Patients were enrolled at the time they elected to undergo ESS after failing broad-spectrum or culture directed antibiotics in addition to a trial of oral and topical steroid therapy. The Institutional Review Board at each enrollment site provided approval for all research protocols. Voluntary, informed consent was obtained from all study participants at the initial enrollment meeting.

Data Collection

Demographic data was recorded as well as associated medical comorbidities, including presence of nasal polyposis, asthma, allergies (confirmed via skin prick test or mRAST), acetylsalicylic acid (ASA) intolerance, depression, and prior sinus surgery. Preoperative computed tomography (CT) scans in the coronal plane were obtained and assessed by Lund-Mackay scoring (score range: 0–24).⁸ Rigid sinonasal endoscopy was performed and graded according to the Lund-Kennedy system (score range: 0–20).⁹

Baseline disease-specific QOL was assessed using the Rhinosinusitis Disability Index (RSDI; score range: 0–120) and the Chronic Sinusitis Survey (CSS; score range: 0–120).^{10,11} The RSDI is composed of 30 questions in three separate subscales to monitor physical, functional, and emotional status. The CSS is comprised of two subscales concerning the impacts of sinonasal symptoms and prescribed medications during the previous 8-week period. Decreases in RSDI scores and increases in CSS scores indicate improvement in QOL outcomes over time.

Endoscopic sinus surgery was then scheduled and performed in accordance with established functional principles. All study patients completed postoperative follow-up at three time points after surgery: 6, 12, and 20 months. Postoperative RSDI and CSS scores were collected at each follow-up time point after surgery by a trained research coordinator at each enrollment site.

Lund-Kennedy rigid endoscopy scores were recorded at each postoperative visit by the treating physician.

Statistical Analysis

Data was collected on standard clinical research forms, manually scored, and entered into a protected database (Foxpro, Microsoft Corp., Redmond, WA.). All statistical analyses were completed using SPSS statistical software (SPSS v.17.0, SPSS Inc., Chicago, IL.). One-way repeated measures analysis of variance (ANOVA) and Friedman's test for non-parametric distributions were used to assess global changes in RSDI, CSS, and endoscopy scores where appropriate. The Tukey HSD test and Wilcoxon signed rank test with an adjusted α -level for multiple comparisons were used to compare QOL scores between follow-up time points. Subgroup analyses were done in a similar fashion for patients with and without nasal polyposis, asthma, allergies, ASA intolerance, depression, and prior sinus surgery.

The proportion of patients reporting a clinically significant change in QOL was reported for each time point. The minimal clinically important difference (MCID) was defined as one-half standard deviation of the baseline QOL score for both total and subscale survey scores, consistent with prior reports.¹² Chi-square tests were used to compare the proportion of patients reporting MCID's between follow-up time points. Means and standard deviations ($\pm$ SD) are reported for all analyses, with an α -level ≤ 0.05 considered statistically significant.

Results

Baseline Characteristics

A total of 127 patients were enrolled and each patient provided complete follow-up data for all three time points (OHSU: n=40, MCW: n=38, Stanford: n=49) between July, 2004 and September, 2009. The average age was 49.5 years (range: 18–78) with a slight majority of female patients. The prevalence of associated medical comorbidities is listed in Table 1. Baseline CT scores averaged 12.6 ± 6.2 (range: 0–24) and endoscopy scores 6.4 ± 4.6 (range: 0–18).

Quality-of-Life Trends

Statistically significant improvements in QOL were found between baseline and 6 month follow-up for the total and subscale scores of the RSDI ($p < 0.001$; Figure 1). Significant improvement was found for mean CSS total scores and the CSS symptom subscale scores between baseline and 6 months ($p < 0.001$; Figure 1). Mean scores of the CSS medication subscale did improve between baseline and 6 months (46.9 ± 25.0 to 54.1 ± 23.0 ; $p = 0.080$) however the magnitude of improvement only attained statistical significance at 12 months (46.9 ± 25.0 to 56.0 ± 25.2 ; $p = 0.015$).

When comparing changes in mean QOL scores between all follow-up time points, there were no significant differences in either RSDI or CSS total scores between 6, 12, and 20 months (all $p \geq 0.853$; Fig 1). Likewise, there were no statistically significant differences between follow-up intervals for mean subscale scores of the RSDI or CSS instruments (all $p \geq 0.251$; Figs 2 and 3).

The cohort at-large was divided into subgroups based on the presence or absence of medical comorbidities thought to influence QOL outcomes. As expected, some variability existed in QOL between different subgroups, with certain subgroups such as those with ASA intolerance having generally lower QOL throughout. However, each individual subgroup demonstrated stable QOL scores between 6, 12, and 20 month follow-up, including patients with polyposis and those with ASA intolerance (Table 2a, 2b; all $p \geq 0.275$).

Endoscopy Trends

As a secondary outcome, we examined trends in endoscopy scores following surgery as well. Endoscopy scores improved significantly between baseline and the 6 month postoperative time point (6.3 ± 4.6 to 3.9 ± 3.7 ; $p < 0.001$). When comparing mean endoscopy scores between all follow-up time points, there were no significant differences between 6, 12, and 20 months ($p = 0.550$; Fig 4).

Minimal Clinically Important Differences

A total of 64.6% of patients reported clinically significant improvement on the RSDI (≥ 9.85 unit decrease) and 67.7% on the CSS (≥ 9.20 unit increase) at the 6 month postoperative time point. Six patients (4.7%) reported worse RSDI total scores greater than the MCID at 6 months, while 11 patients (8.7%) reported clinically worse CSS total scores at 6 months. At the 20 month postoperative time point, 68.5% and 70.9% reported clinically significant improvement on the RSDI and CSS respectively. In comparing the proportions of patients with clinically significant improvement at the 6 month time point and 20 month time point, there were no significant differences identified for either outcome instrument ($p > 0.586$).

Discussion

In this large, multi-institutional longitudinal study, QOL outcomes after ESS were found to be stable between 6 month, 12 month, and 20 month follow-up time points. QOL outcomes were stable for both the RSDI and CSS instruments, including total scores and subscale scores. Subgroups within the cohort at large also demonstrated stable outcomes between 6 and 20 months, including those with and without comorbidities thought to adversely affect outcomes.

The results of this study have important implications for future clinical trials designed to evaluate comparative effectiveness of treatments for CRS. The recent national healthcare reform legislation has called for a rigorous evaluation of treatment options for any given condition, with the implicit goal of funding only those treatment options shown to be most effective.¹³ Although many studies have examined outcomes after sinus surgery, few have done so in a prospective fashion with control groups for comparison. There remains a need for prospective trials comparing ESS and available medical regimens.^{1,3,14} Although “long-term” outcome studies have traditionally been favored, our results suggest that a study of surgical outcomes beyond 6 months may be unnecessary if CRS-specific QOL is the primary outcome of interest. The ability to terminate a study at 6 months follow-up, rather than carrying it out to 20 months or beyond, can dramatically impact the feasibility of a clinical trial.

When designing this study, we originally hypothesized that QOL outcomes would be dynamic after 6 months and thus did not specifically evaluate time points prior to 6 months follow-up. It remains possible that QOL outcomes after ESS stabilize prior to 6 months. Future studies might longitudinally follow patients at 6 or 8 week intervals between surgery and 6 months in order to determine if outcomes stabilize at an earlier time point. This study also does not allow conclusions about QOL changes after 20 months. It is probable that certain subgroups of patients with CRS, likely those with severe phenotypes such as polyps and ASA intolerance, will develop recurrent disease over time and subsequent worsening of QOL measures. Although we did not see changes in subgroups between 6–20 months, we suspect that differences may surface if this longitudinal study is continued long enough. However, even if this is true, it probably has little bearing on the design of clinical trials, which are unlikely to be carried out beyond 20 months because of feasibility concerns (e.g., lost follow up and cost considerations for longer term studies).

Although QOL scores in this cohort were stable over time, it is important not to over-apply these findings to individual patients. CRS is, by definition, a chronic disease characterized by periods of exacerbation and relative remission.^{2,15} Therefore, any individual patient may experience improvement or worsening over time, even though the cohort at large will have stable QOL. This point is best illustrated by following the proportion of patients experiencing a clinically-significant change between 6 months and 20 months. If the RSDI is followed between 6 and 20 months, 60.6% of patients had stable QOL, 20.5% experienced a clinically-significant improvement, and 18.9% demonstrated a clinically-significant worsening of QOL. From a clinician's standpoint, these fluctuations are important and model what one will see when caring for individual patients with CRS. From a research standpoint, this dynamism is expected and essentially of no consequence as long as the overall QOL of the group is stable, as seen in this cohort.

In this study, we reported the proportion of patients whose QOL improved by at least one MCID (68.5% on RSDI, 70.9% on CSS) at 20 months postoperatively. We feel that reporting clinically significant improvement is important because small changes in QOL, even if statistically significant, might not be meaningful to patients. However, this data should not necessarily be interpreted as an overall success rate for the procedure. It is important to appreciate that some patients present with near-normal disease-specific QOL, but have one or more prominent symptoms which still drive them to elect surgical treatment of their disease. This group of patients in the top quintile for baseline QOL essentially has little room for improvement in QOL and thus will not reach the threshold of the MCID, even though surgery may have been clinically successful by other measures.

Conclusion

Endoscopic sinus surgery appears to result in significant improvements in CRS-specific QOL. At a cohort level, improvements in QOL and endoscopy do not appear to change between 6 and 20 months. Clinical trial designs focusing on QOL outcomes after ESS should consider the six month time frame as an appropriate primary endpoint.

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Figure 1.

Longitudinal trends in mean quality of life scores for both the Chronic Sinusitis Survey (CSS) and Rhinosinusitis Disability Index (RSDI). Decreases in RSDI scores and increases in CSS scores indicate improvement in QOL outcomes over time.

Figure 2. Longitudinal trends in mean quality of life scores for individual domains of the Chronic Sinusitis Survey (CSS).

Figure 3. Longitudinal trends in mean quality of life scores for individual domains of the Rhinosinusitis Disability Index (RSDI).

Figure 4.
Longitudinal trends in mean Lund-Kennedy endoscopy scores.

Table 1

Preoperative patient characteristics of cohort with CRS (n=127)

Characteristics:	mean(SD)	n(%)
Age	49.5 (14.0)	
Gender		
Male		61 (48.0)
Female		66 (52.0)
Polyposis		43 (33.9)
Previous sinus surgery		73 (57.5)
Asthma		52 (40.9)
ASA Intolerance		14 (11.0)
Allergy		27 (21.3)
Depression		17 (13.4)
Lund-Mackay CT score	12.6 (6.2)	
Lund-Kennedy endoscopy score *	6.3 (4.6)	

CRS=chronic rhinosinusitis. SD = standard deviation. ASA = acetylsalicylic acid. CT = computed tomography.

* Longitudinal data for endoscopy score available for 113 patients.

Table 2a

Mean postoperative total scores for the Rhinosinusitis Disability Index per comorbid status (n=127)

Characteristics:	6.1(1.5) mo. postop.	12.3 (2.1) mo. postop.	20.5 (4.5) mo. postop.	p-value *
	Mean(SD)	Mean(SD)	Mean(SD)	
Gender				
Male	31.5(22.2)	29.7(21.0)	29.1(20.5)	0.413
Female	29.2(23.8)	29.6(23.3)	29.2(23.0)	0.959
Polyposis	32.8(21.1)	30.3(20.6)	30.8(21.2)	0.426
Previous sinus surgery	33.9(24.0)	33.7(23.6)	34.4(21.8)	0.897
Asthma	32.4(23.4)	32.3(23.6)	31.6(21.9)	0.937
ASA Intolerance	42.6(24.9)	44.6(29.0)	40.6(20.4)	0.778
Allergy	22.5(20.5)	26.4(22.0)	27.5(20.3)	0.176
Depression	40.2(24.8)	34.7(25.9)	32.0(18.1)	0.182

mo. = months. SD=standard deviation. ASA=acetylsalicylic acid (aspirin).

* denotes a "global" p-value across all mean follow-up scores using one-way repeated measures ANOVA with a level 3 within-subjects design

Table 2b

Mean postoperative total scores for the Chronic Sinusitis Survey per comorbid status (n=127)

Characteristics:	6.1(1.5) mo. postop.	12.3 (2.1) mo. postop.	20.5 (4.5) mo. postop.	p-value *
	Mean(SD)	Mean(SD)	Mean(SD)	
Gender				
Male	57.5(19.8)	60.8(19.3)	59.1(21.9)	0.304
Female	58.0(18.6)	56.8(21.1)	60.3(18.9)	0.275
Polyposis	53.3 (19.8)	54.2 (19.1)	57.5(21.1)	0.304
Previous sinus surgery	55.5(19.8)	55.6(19.7)	57.0(20.6)	0.782
Asthma	53.0(18.4)	51.2(17.6)	52.8(18.8)	0.689
ASA Intolerance	46.7(14.4)	43.5(16.2)	43.7(14.7)	0.630
Allergy	59.4(15.1)	55.4(16.7)	56.8(19.6)	0.341
Depression	55.6(18.0)	57.4(20.5)	57.1(23.4)	0.941

mo. = months. SD=standard deviation. ASA=acetylsalicylic acid (aspirin).

* denotes a "global" p-value across all mean follow-up scores using one-way repeated measures ANOVA with a level 3 within-subjects design