



Prevalence of clinically significant worsening after endoscopic sinus surgery

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Abstract

Background: Chronic rhinosinusitis (CRS) can be managed both medically and surgically. Patients electing surgery for medically recalcitrant CRS must weigh the potential risks and benefits of surgery. A significant body of evidence has amassed establishing the frequency of achieving a clinically significant improvement and clinical factors associated with improvement, yet no studies to date have investigated the risk factors associated with significant worsening after surgery.

Methods: A secondary analysis of a prospective, multi-center cohort of adult patients undergoing surgery for medically recalcitrant CRSwNP and CRSsNP between March, 2011 and June, 2015 was performed. Clinically significant worsening has previously been associated with a 6-point decrement in the Sinonasal Outcome Test-22 (SNOT-22) from preoperative baseline. Regression analysis was used to identify risk factors for clinically significant worsening of SNOT-22 scores.

Results: A total of 440/565 (78%) of patients met inclusion criteria and had at least 6-month follow-up. Nine percent (38/440) of patients experienced clinically significant worsening after surgery. After adjustment for all final model covariates, prior sinus surgery (OR:4.65, 95%CI:1.95-11.08, p=0.001) and Hispanic/Latino ethnicity (OR:3.76, 95%CI:1.19-11.86, p=0.024) were associated with an increased risk of clinically significant worsening. All significant associations in the final model persisted even after manual adjustment and inclusion of socioeconomic variables including both household income and insurance provision covariates.

Conclusions: Although endoscopic sinus surgery has proven an effective treatment for medically recalcitrant disease, clinically significant worsening may occur in a small subset and disproportionately impacts patients who have experienced prior sinus surgery and those of Hispanic/Latino ethnicity independent of economic factors.

Introduction

Patients with chronic rhinosinusitis can be managed both medically and surgically. Patients that have failed appropriate medical therapy can elect to undergo sinus surgery or decide to continue medical therapy alone. Transparent informed consent is therefore especially critical as surgeons and patients help select the intervention that maximizes the likelihood of optimizing patient-reported outcome measures (PROMs). Reporting of minimal clinically important differences (MCIDs) for PROMs is an important way in which clinicians and patients can articulate the likelihood of achieving a given outcome. Frequently, clinical studies of endoscopic sinus surgery (ESS) report the rate of achieving an MCID when it comes to improvement after ESS (~80%)¹. Patients that do not achieve an improvement that reaches a MCID may either be longitudinally stable in their PROMs postoperatively or may actually experience worsening symptoms.

A large body of evidence has amassed demonstrating that patients with medically recalcitrant CRS, on average, improve after ESS; however, none has yet to explicitly examine clinical risk factors for a clinically meaningful worsening after endoscopic sinus surgery. Prior psychometric validation of the 22-item sinonasal outcome test (SNOT-22) in a United Kingdom National Health System prospective cohort study, using anchor questions, found that patients who report symptoms which are at least 'a little worse' corresponds to a mean decrement of 5.7 on the SNOT-22 aggregate score.² In fact, such a decrement, or more, was reported in 5.3% of patients in that cohort. Such prevalence is not an insignificant risk to patients and warrants explicit discussion during the informed consent process. No such data is available for patient populations with CRS in North American populations and no investigation into risk factors associated with postoperative symptom worsening have been performed to date.

The present study seeks to determine the rate of clinically significant worsening after ESS in a prospectively collected North American cohort of patients with CRS. Secondly, it seeks to identify baseline clinical factors associated with significant worsening of postoperative outcome measures.

Methods and Materials

Subjects: Prospectively enrolled cohort of adult (>18 years of age) subjects undergoing surgical procedures for CRS across four academic, tertiary care rhinology practices including: Oregon Health & Science University (OHSU, Portland, OR, USA), the Medical University of South Carolina (Charleston, SC, USA), Stanford University (Palo Alto, CA, USA), and the University of Calgary (Calgary, Alberta, Canada)

Inclusion Criteria:

- All study participants were diagnosed with CRS based on the Rhinosinusitis Task for criteria³ and were enrolled after failing medical therapy that entailed either broad-spectrum and/or culture-directed antibiotics and a trial of oral and topical steroid therapy. All subtypes of CRS were included in analysis including patients with aspirin sensitivity, mucociliary dysfunction and cystic fibrosis. Participants were excluded from final analyses if they failed to complete follow-up evaluations within 18 months after ESS.
- Sinus surgery was non-standardized and directed by the intraoperative discretion of the enrolling physician at each location per individual patient requirements and disease progression. Study participants were either primary or revision ESS cases.

Categorization and Comparison of Postoperative Improvements:

- The primary PROM of interest to this study was the interval change in SNOT-22 (≥6-months) after ESS (@2006, Washington University, St. Louis, MO, USA)²
- The postoperative change in SNOT-22 aggregate scores was operationalized to global improvement categories based upon a similar patient population with CRS from the United Kingdom as described in Table 1.²

Table 1. Categorization of postoperative symptom scores

Postoperative symptom transition categories:	Definition:	N (%)	SNOT-22 change scores Mean [SD]	95% Confidence Intervals (LL, UL)
"Much better"	(≤ -24)	231 (53%)	-40.7 [14.5]	(-42.6, -38.8)
"A little better"	(-23 through -9)	119 (27%)	-15.9 [4.6]	(-16.7, -15.0)
"About the same"	(-8 through 5)	51 (12%)	-2.1 [4.2]	(-3.3, -1.0)
"A little worse"	(6 through 7)	7 (2%)	6.7 [0.5]	(6.3, 7.2)
"Much worse"	(≥ 8)	31 (7%)	19.0 [11.0]	(15.0, 23.1)

Results

Final Study Cohort: A total of 565 patients were recruited and enrolled between March, 2011 and June, 2015 after meeting inclusion criteria. Postoperative evaluations were available for 440 (78%) of participants at least 6 months after ESS

Postoperative Improvements: Study participants (n=440) were observed longitudinally for an average of 14.8[5.1] month after endoscopic sinus surgery (range: 6-29). Significant improvement in postoperative mean endoscopy scores (3.4 [2.9]; p<0.001) were found for participants returning for standard clinical evaluation, however overall mean postoperative BSIT scores (8.9 [2.7]) did not significantly improve postoperatively (p=0.432). Average postoperative SNOT-22 total scores (28.9 [21.7]) were reported to significantly improve (p<0.001) at the last available follow-up evaluation.

Categorization and Comparison of Postoperative Improvements: Postoperative changes in SNOT-22 total scores were analyzed and categorized using predetermined guidelines, as described, and included PROM score change designations of "Much better" (n=232), "MCID" (n=119), "Unchanged" (n=51), "Little worse" (n=7), and "Much worse" (n=31; Figure 1). A total of ~9% of all participants reported some severity of worse patient functioning and/or symptom severity postoperatively.

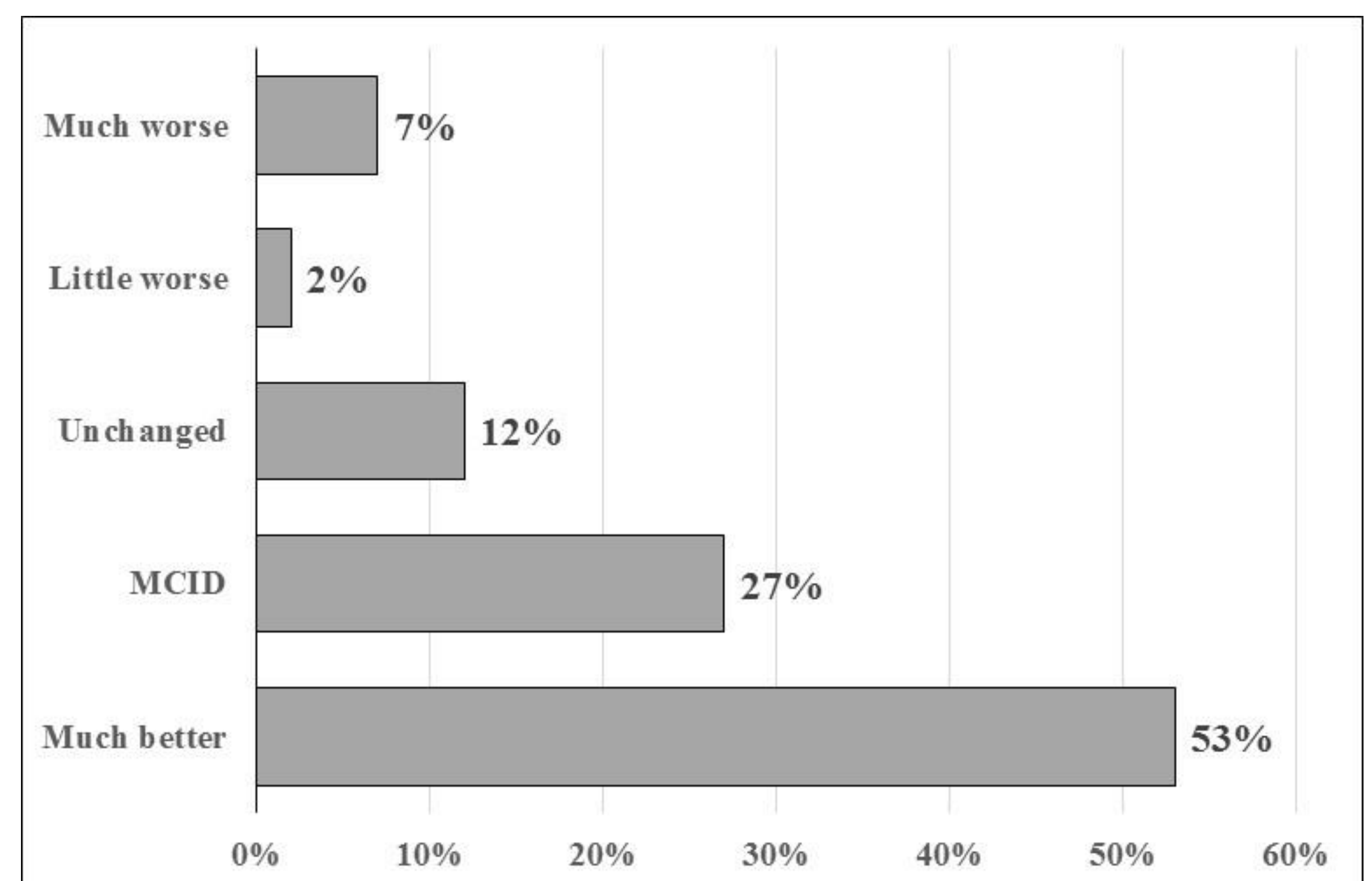


Figure 1: Prevalence of categorized postoperative change scores on the SNOT-22 survey. MCID, minimal clinically important difference.

Logistic modelling for clinically significant worsening: Logistic regression modeling was performed to identify potential predictive factors associated with clinically significant worsening after ESS. After both manual inclusion of enrollment site to control for treatment variation and preoperative QOL status, final regression model covariates associated with postoperative worsening of SNOT-22 aggregate scores are described in Table 2:

Table 2. Final logistic regression modeling for covariates associated with clinical worsening after ESS (n=440)

Covariate:	Unadjusted OR	Adjusted OR	95% CI	p-value
Enrollment site	0.82	0.67	[0.44 – 1.00]	0.050
Preoperative SNOT-22 score	0.97	0.96	[0.95 – 0.98]	<0.001
Hispanic / Latino	2.74	3.76	[1.19 – 11.86]	0.024
Previous sinus surgery	3.83	4.65	[1.95 – 11.08]	0.001

Discussion

While a significant body of evidence has accumulated demonstrating the effectiveness of ESS for medically recalcitrant CRS, a subset of patients actually experience clinically significant worsening after surgery. Failed prior surgery has consistently been associated with diminished gains after surgery.¹ The present study is consistent in that prior surgery independently increased the odds of worsening by a factor of 4.65 (95% CI: 1.95-11.08, p = 0.001). Patients with prior surgery may have surgically recalcitrant disease secondary to a variety of reasons including: inherent anatomic limitations, incomplete openings or scarring of prior openings, intrinsic mucosal inflammation/dysfunction independent of open sinuses with continued medical therapy. Extended sinusotomies may play a role in salvaging a portion of these patients,⁴ but there may be a subset that require novel medical therapies or biomarkers that could identify them prior to undergoing surgery.

After adjustment for all final model covariates, study participants of Hispanic / Latino ethnicity were found to be 3.76 times more likely to report significant postoperative worsening of QOL following ESS compared to participants of non-Hispanic/Latino ethnicities. Despite prior data demonstrating that minority ethnicity is associated with socioeconomic status,⁵ the discrepancy persisted after manual adjustment and inclusion of socioeconomic variables including both household income and insurance provision covariates. Further investigation into outcomes and underlying mechanisms by ethnicity will help to verify and clarify the observation that Hispanic / Latino ethnicity is a risk factor for significant worsening after surgery.

Conclusions

Although endoscopic sinus surgery has proven an effective treatment for medically recalcitrant disease, clinically significant worsening may occur in a small subset and disproportionately impacts patients who have experienced prior sinus surgery and those of Hispanic/Latino ethnicity independent of economic factors. Informed consent should include a discussion of the likelihood of clinically meaningful worsening after surgery.

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References

1. Smith TL, Litvack JR, Hwang PH, Loehrl TA, Mace JC, Fong KJ, et al. Determinants of outcomes of sinus surgery: a multi-institutional prospective cohort study. *Otolaryngol Head Neck Surg.* 2010 Jan;142(1):55-63.
2. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol.* 2009 Oct;34(5):447-54.
3. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Kumar KA, Kramper M, et al. Clinical Practice Guideline (Update) Adult Sinusitis Executive Summary. *Otolaryngology -- Head and Neck Surgery.* 2015 Apr 1;152(4):598-609.
4. Naidoo Y, Bassiouni A, Keen M, Wormald P-J. Risk factors and outcomes for primary, revision, and modified Lothrop (Draf III) frontal sinus surgery. *Int Forum Allergy Rhinol.* 2013 May;3(5):412-7.
5. Soler ZM, Mace JC, Litvack JR, Smith TL. Chronic rhinosinusitis, race, and ethnicity. *Am J Rhinol Allergy.* 2012;26(2):110-6.