Systematic Review and Meta-analysis of SNOT-22 Outcomes after Surgery for Chronic Rhinosinusitis with Nasal Polyposis

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. Wide variation exists regarding reported outcomes after endoscopic sinus surgery (ESS) for chronic rhinosinusitis with nasal polyps (CRSwNP). This study seeks to combine data across studies to generate a summary measure and explore factors that might lead to variation.

Data Sources. OVID Medline, Scopus, EbscoHost, Database of Abstracts and Reviews of Effects, Health Technology Assessment, and National Health Service Economic Evaluation Database.

Review Methods. A search was performed following the PRISMA guidelines. Two independent researchers conducted a search using the mentioned data sources. Studies published before August 29, 2016, that involved ESS to treat CRSwNP were included. Mean changes in Sinonasal Outcome Test–22 (SNOT-22) scores were determined through metaregression of the following independent variables: publication year, sex, age, allergy status, asthma, tobacco use, prior surgery, follow-up length, and preoperative SNOT-22.

Results. Fifteen articles with 3048 patients treated with ESS met inclusion criteria. Pooled analyses of SNOT-22 scores revealed a mean change of 23.0 points (95% CI, 20.2-25.8; \(P < .001\)). A metaregression of patient factor effects on the mean change of SNOT-22 scores demonstrated that age \((r = 0.71, P = .01)\), asthma \((r = 0.21, P = .01)\), prior ESS \((r = 0.29, P = .01)\), and preoperative SNOT-22 score \((r = 0.4, P < .01)\) correlated with greater improvement in SNOT-22 scores. Tobacco use \((r = -0.91, P = .01)\) and longer lengths of follow-up \((r = -0.45, P < .01)\) were associated with less improvement in SNOT-22 scores.

Conclusions. Quality-of-life outcomes are significantly improved after ESS among patients with CRSwNP. Patient-specific factors may affect the degree of SNOT-22 change after surgery.

Keywords

chronic rhinosinusitis, nasal polyps, meta-analysis, quality of life, 22-item Sinonasal Outcome Test, quality improvement

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The prevalence of chronic rhinosinusitis with nasal polyps (CRSwNP) ranges from 2.7% to 4.3% across Europe and the United States.\(^1\) Chronic rhinosinusitis (CRS) negatively affects quality of life (QOL), reduces economic productivity, and can increase the risk of depression and sleep dysfunction.\(^2,4\) The treatment of CRS consists of initial medical therapy, usually in the form of topical and systemic medicines such as antibiotics and corticosteroids. Patients who fail to sufficiently improve on appropriate medical therapy are candidates for endoscopic sinus surgery (ESS), which was shown across individual studies to improve symptomatology, QOL, and work productivity. The impact of ESS on QOL outcomes is generally positive, although it was reported that as many as 20% to 30% of patients who undergo ESS for CRS do not experience significant improvement.\(^5\) As compared with those without polyps, patients with CRSwNP may have higher rates of revision surgery, more frequent recurrences, and greater associations with other respiratory diseases, such as asthma and aspirin-exacerbated respiratory disease.\(^6,8\) Furthermore,
targeted biologics are being developed for CRSwNP that block specific aspects of the inflammatory pathway and could serve as alternatives to surgery. While these monoclonal antibodies hold early promise, they are likely to be costly. A better understanding of surgical outcomes may inform future decision making among different treatment modalities.

Meaningful improvement in CRS is typically measured in terms of patient-reported outcomes. Outcome measurement in the treatment of CRS is an area of ongoing investigation, without a single widely accepted metric to determine success. Several metrics have been proposed, but arguably the most important outcome measurement in CRS is how a patient feels after treatment. This type of subjective reporting of improvement is best captured with patient-reported outcome measures, which are tools that rely on patients’ subjective assessment of their health condition. These tools are at the forefront of the recent health care revolution surrounding patient-centered care. Multiple CRS-specific patient-reported outcome measures have been proposed over the past 20 years, but the 22-item Sinonasal Outcome Test (SNOT-22) is the most commonly used instrument and appears to have the highest quality of developmental methodology and psychometric performance.

To this end, we performed a systematic review and meta-analysis of all published English-language literature reporting pre- and postoperative SNOT-22 scores for patients with CRSwNP. The primary purpose of the study was to determine the mean change in SNOT-22 after ESS among patients with CRSwNP. Furthermore, the secondary goals were to ascertain impacts of various patient factors that influence SNOT-22 change after surgery.

**Methods**

**Literature Review**

A systematic review was performed following the methods of 2009 PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-analyses). Independent and comprehensive literature searches were performed by 2 reviewers using OVID Medline, Scopus, EbscoHost, Database of Abstracts and Reviews of Effects, Health Technology Assessment, and National Health Service Economic Evaluation Database in August 2016. A search strategy was employed with the following search strings: “chronic AND sinusitis” with “22-item Sinonasal Outcome Test OR snot-22 OR snot22 OR snot 22 OR Sinonasal Outcome Test.” Results were limited to English articles on adult human subjects. Once each reviewer completed the search, a total list of records was obtained; the results were cross-checked; and duplicates were removed. A final list of full-text articles was then compiled, and each article was then screened independently by 2 authors. Any article that was excluded by only 1 author but not the other was then brought up for discussion as a group. Potential articles that met inclusion criteria and were from the same institution were screened by dates of included patient cohorts. If similar dates were listed among studies, then the article with the largest and most complete data set was included. Once the list of articles was finalized, the reference lists from each study were examined to identify any other potential articles that may have met inclusion criteria. The National Institutes of Health quality assessment tool for before-after (pretest-posttest) studies was used to review all included studies.

**Data Extraction**

Data extraction was performed independently by 2 authors. Article review first involved verifying inclusion criteria. Patients were diagnosed with CRS per guidelines as stated in the articles (EPOS, American Academy of Otolaryngology—Head and Neck Surgery Foundation, other). Patient-reported outcome measurement with the SNOT-22 was required for pre- and postoperative data after ESS. Studies that involved only patients with polyps were included, as were studies that had separate patient cohorts with nasal polyps. Series were excluded if they reported on patients with CRS without nasal polyps or with mixed types of CRS, procedures involving balloon sinuplasty, or outcome measurements other than SNOT-22. Data collected for each article involved study characteristics such as study design, number of patients, and diagnostic criteria used to diagnose CRS. Patient characteristics from each study were also collected, such as age, sex, race, allergy status, asthma status, prior sinus surgery frequency, depression, and aspirin intolerance. Finally, objective examination data were collected, including computed tomography Lund-Mackay scores, Lund-Kennedy endoscopy scores, preoperative SNOT-22 scores, and postoperative SNOT-22 scores at the last follow-up.

**Statistical Analyses**

Statistical analyses involved using Comprehensive Meta-analysis Software 3.0 (Biostat Inc, Englewood, New Jersey) for univariate regression analyses. Data were inputted from the included studies. Meta-analysis was performed for this study that evaluated the impact of ESS on SNOT-22 with a continuous measure (comparison of means and standard deviations between pre- and post-ESS). For this analysis, the null hypothesis was that there was no difference in scores between pre- and post-ESS SNOT-22. The fixed effects model and the random effects model were both performed in this study. Under the fixed effects model, it was assumed that all studies come from a common population and that the effect size (mean difference) was not significantly different among the different studies. This assumption was tested by the heterogeneity test or $I^2$ statistic. If this test yields a low probability value ($P < .05$), then the fixed effects model was likely invalid. In this case, the random effects model is more appropriate, in which the random variation is not only within the studies but also incorporated among the studies. The random effects model was used in this study. Under the random effects model, the true effects were assumed to vary among studies, and the
The summary effect is the weighted average of the effects reported in the different studies. The random effects model provides a more conservative estimate (ie, with a wider confidence interval).\textsuperscript{15} Data were presented as mean difference with 95% CI. In addition, metaregression analyses examined the following independent variables, if available: publication year, sex, age, allergy status, asthma, tobacco use, prior surgery, Lund-Mackay score, Lund-Kennedy score, follow-up length, and preoperative SNOT-22. Data were presented with a funnel plot to visually assess whether bias from small-study effects may be present. Because visual inspection can be largely subjective, a regression test for funnel plot asymmetry was also performed as proposed by Egger et al.\textsuperscript{16}

## Results

### Study Selection

The literature search resulted in 420 abstracts, of which 306 records remained once duplicate studies were removed (Figure 1). After abstracts were screened for inclusion and exclusion criteria (Table 1), 205 records were excluded. Twenty-three articles were further identified through review of the references, leading to a total of 124 full-text articles eligible for review. Studies with the same cohort of patients were considered duplicates, leading to 31 excluded studies.\textsuperscript{17-47} An additional 78 studies failed to meet inclusion criteria, leading to a final list of 15 distinct patient studies.\textsuperscript{48-62}

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**Figure 1.** PRISMA-compliant literature review diagram.

<table>
<thead>
<tr>
<th>Table 1. Inclusion and Exclusion Criteria.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion criteria</strong></td>
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<tr>
<td>All patients must have CRS with nasal polyposis (diagnostic criteria can be from various sources)</td>
</tr>
<tr>
<td>≥16 y of age</td>
</tr>
<tr>
<td>All study types and levels of evidence</td>
</tr>
<tr>
<td>Includes 22-item Sinonasal Outcome Test for pre- and postoperative data for patients with CRS with nasal polyposis</td>
</tr>
<tr>
<td>Endoscopic sinus surgery procedures</td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
</tr>
<tr>
<td>Patients without rhinosinusitis or with non-CRS</td>
</tr>
<tr>
<td>Other patient-reported outcome measurements</td>
</tr>
<tr>
<td>Studies reporting balloon sinuplasty use</td>
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</tbody>
</table>

Abbreviation: CRS, chronic rhinosinusitis.
**Study Characteristics**

Fifteen studies were included with a total of 3048 patients (Table 2). In total, 45.9% of patients were female; 45.7% had allergies; 52.5% had asthma; 13.9% had current tobacco use; and 48.1% had prior sinus surgery. None of the 15 studies discussed the extent of the initial surgery if revision surgery was mentioned. Five studies did discuss the extent of their surgical techniques, with 1 study employing a modified Lothrop technique. The remaining 10 stated only that ESS was performed.48,51,53,57,61 Of the 15 studies, 6 documented allergy status. Of those 6 studies, 2 indicated that diagnosis was based on skin testing, while the other 4 were based on history.50,51,57,59,61,62 The average age of patients was 45 years. Baseline Lund-Mackay computed tomography score was 17.2. Mean follow-up time was 14.1 months, with a range of 1 to 36 months and an interquartile range of 21 months.

**Risk of Bias**

The risk-of-bias quality assessment of individual studies was assessed with the study quality assessment tool from the National Institutes of Health.12 The majority of the studies were deemed fair quality in terms of bias, and 2 studies were considered good (Table 3).49,51 Figure 2 presents a funnel plot of the studies. Sterne and Egger testing suggested a high likelihood of publication bias. These data were heterogeneous ($I^2 = 68\%$, $P < .001$).

**Results of Individual Studies**

Figure 3 displays the mean change of SNOT-22 for each study. The mean change after surgery ranged from 14.0 to 44.2. Two studies specifically examined the impact of patient factors upon change in SNOT-22 score. Hoseini et al found that patients with aspirin-exacerbated respiratory disease had less improvement, while revision surgery status did not have any correlation.53 Saedi et al did not find any correlation between change in SNOT-22 scores and allergic rhinitis, asthma, revision surgery, sex, or smoking status.59

**Synthesis of Results and Meta-analysis**

Pooled analyses revealed a mean SNOT-22 change of 23.0 points (95% CI, 20.2-25.8; $P < .001$). To understand the relationship between SNOT-22 and several variables, a metaregression was performed (Table 4). Age, a history of asthma, prior sinus surgery, and worse preoperative SNOT-22 scores all correlated with greater improvement in SNOT-22 scores with statistical significance. Age had the greatest positive correlation coefficient ($r = 0.71$, $P = .01$), followed by preoperative SNOT-22, prior sinus surgery, and asthma (Figure 4). On the contrary, current tobacco use status and the length of follow-up correlated with worse SNOT-22 outcomes. Length of follow-up had a negative correlation coefficient ($r = -0.45$), while current tobacco use had an even larger correlation coefficient ($r = -0.91$; Figure 5). Of the 15 studies, 7 had >1 postoperative visit with SNOT-22 scores recorded for extended follow-up.50,52,55-58,60 Endoscopy scores, depression, and race were reported in only 3 of the included studies, which was not sufficient to run a metaregression.

**Discussion**

The primary purpose of this study was to determine the mean change in SNOT-22 scores after ESS among patients with CRSwNP. Pooled analyses from 15 studies of SNOT-22 scores revealed a statistically significant mean change of 23 points postoperatively, which is greater than the commonly accepted minimal clinically important difference of 8.9.31 While previous studies determined various QOL outcomes among all patients with CRS, this is one of the first...
studies to systematically review SNOT-22 outcomes specifically for patients with CRSwNP. An understanding of expected outcomes and variables that will affect those outcomes is critical to better predict the patients who are most likely to benefit from ESS.

In regard to a negative influence on QOL scores, length of follow-up and tobacco use status both negatively correlated with SNOT-22 change scores after ESS. The average follow-up time for the 15 studies was 14.1 months, ranging from 1 to 36 months. Based on the metaregression, the mean change in SNOT-22 score is about 5 points less for each additional year of follow-up. Of the 15 studies in this review, 7 had >1 postoperative visit with documented SNOT-22 scores. Of those 7 studies, 6 demonstrated worse outcomes versus the first postoperative visit.

Figure 2. Funnel plot of standard mean difference (MD) of Sinonasal Outcome Test–22 scores from studies.

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and it is possible that physician recommendation for this therapy and patient compliance may affect postoperative SNOT-22 scores. Unfortunately, none of the studies reported sufficient data on these items for analysis.

Tobacco use was shown to affect ESS outcomes, with poorer symptom scores, worse patient-reported outcomes, and a higher proportion of smokers in revision surgery cases.68-71 This is consistent with this study’s findings, which exclusively focus on patients with nasal polyposis. Possible mechanisms that influence QOL potentially derive from changes in microbiome and tobacco-mediated induction of sinonasal microbial biofilms.72,73 Smoking can also suppress sinonasal innate immunity by altering toll-like receptors and inhibiting IL-8 and human B-defensin, which promote clearance of gram-negative and gram-positive bacteria.68

Not unexpectedly, worse preoperative SNOT-22 scores correlated with a larger change in SNOT-22 scores. This is consistent with a study by Levy et al.74 Patients with higher SNOT-22 scores at baseline have a greater opportunity for improvement than patients who are less symptomatic and have low preoperative SNOT-22 scores.

This review and analysis included patients down to age 16 years, as opposed to restricting it to a pure adult population. Inclusion criteria were based on prior knowledge that the English cohort (the largest) included some subjects down to this age.52 Nonetheless, the English cohort was still mostly adult patients, with the average age being 51.6 years, which is greater than the average patient age of the studies included in this review (45.01 years). Although an age of 16 years can classify patients as “pediatric,” it is commonly held that their condition more closely resembles adult CRS than pediatric CRS, as might be seen in a child aged 3 to 6 years. In this study, metaregression analysis demonstrated age as a positive predictor of outcomes. No study in the review examined age and outcomes of surgery, but pooled data revealed that older patients had greater improvements in their SNOT-22 scores. This may suggest that older patients with CRSwNP on average report worse preoperative SNOT-22 scores and have greater potential to improve after sinus surgery.

A history of asthma positively correlated with greater SNOT-22 improvement. The asthma prevalence among the

Figure 3. Studies included in meta-analysis for Sinonasal Outcome Test–22 mean change after functional endoscopic sinus surgery.

Table 4. Univariate Analysis of Patient Factors and Effect on Mean SNOT-22 Decrease.a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Studies, n</th>
<th>Coefficient, r</th>
<th>SE</th>
<th>95% Lower</th>
<th>95% Upper</th>
<th>2-Sided P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>15</td>
<td>0.89</td>
<td>0.53</td>
<td>-0.14</td>
<td>1.92</td>
<td>.09</td>
</tr>
<tr>
<td>Female sex</td>
<td>13</td>
<td>0.08</td>
<td>0.14</td>
<td>-0.19</td>
<td>0.36</td>
<td>.55</td>
</tr>
<tr>
<td>Age</td>
<td>13</td>
<td>0.71</td>
<td>0.27</td>
<td>0.19</td>
<td>1.23</td>
<td>.01</td>
</tr>
<tr>
<td>Allergy</td>
<td>6</td>
<td>0.13</td>
<td>0.22</td>
<td>-0.31</td>
<td>0.56</td>
<td>.57</td>
</tr>
<tr>
<td>Asthma</td>
<td>7</td>
<td>0.21</td>
<td>0.08</td>
<td>0.05</td>
<td>0.38</td>
<td>.01</td>
</tr>
<tr>
<td>AERD</td>
<td>7</td>
<td>0.33</td>
<td>0.52</td>
<td>-0.69</td>
<td>1.35</td>
<td>.52</td>
</tr>
<tr>
<td>Prior sinus surgery</td>
<td>6</td>
<td>0.29</td>
<td>0.11</td>
<td>0.08</td>
<td>0.50</td>
<td>.01</td>
</tr>
<tr>
<td>Current tobacco use</td>
<td>5</td>
<td>-0.91</td>
<td>0.36</td>
<td>-1.61</td>
<td>-0.21</td>
<td>.01</td>
</tr>
<tr>
<td>Baseline CT score</td>
<td>8</td>
<td>1.79</td>
<td>1.12</td>
<td>-0.40</td>
<td>3.99</td>
<td>.11</td>
</tr>
<tr>
<td>Preoperative SNOT-22</td>
<td>15</td>
<td>0.40</td>
<td>0.11</td>
<td>0.18</td>
<td>0.61</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>15</td>
<td>-0.45</td>
<td>0.13</td>
<td>-0.71</td>
<td>-0.19</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: AERD, aspirin-exacerbated respiratory disease; CT, computed tomography; SNOT-22, Sinonasal Outcome Test–22.

*Bold indicates P < .05.
pooled data of patients with CRSwNP ranged from 14.9% to 100%, while the mean was 52.5%. It is unclear why asthma is associated with greater SNOT-22 score improvement. No individual study demonstrated that patients with asthma had better surgical outcomes. However, when examined collectively in the metaregression, asthma appeared to be a factor for larger changes in postoperative SNOT-22 scores. A number of potential reasons may explain this association. ESS was shown to improve asthma-specific QOL for patients with CRS. QOL instruments often have overlapping domains, so it is not surprising that asthma is associated with greater SNOT-22 improvements. It is also possible that patients with asthma are more vested in their medical care, see more physicians, and are treated more comprehensively. They may receive adjuvant medical therapy, such as oral steroids, leukotriene antagonists, immunotherapy, and monoclonal antibodies, resulting in overall improvement in SNOT-22 scores.

Somewhat surprising is the positive association between change in SNOT-22 scores and history of sinus surgery. Of all the CRS-related factors that were previously studied, only prior sinus surgery was shown to have any significant association with outcomes after surgery, and that was a negative association. This discrepancy highlights the primary weakness of our analysis. The present study is a meta-analysis of pooled data, which means that one can compare the outcomes among only studies rather than individual patients. While this research was limited to serve as a

Figure 4. Metaregression of significant factors associated with positive mean change in Sinonasal Outcome Test–22 (SNOT-22): (A) age, (B) asthma, (C) prior sinus surgery, and (D) preoperative SNOT-22.

Figure 5. Metaregression of significant factors associated with negative mean change in Sinonasal Outcome Test–22: (A) tobacco use and (B) length of follow-up.
comparative study among surgical outcomes of patients with CRSwNP, future studies can be expanded to compare QOL outcomes among patients treated with ESS versus new biological medical treatments.

Several study strengths and limitations need mention. The number of studies and patients analyzed with various preoperative factors on a large scale were rarely seen in other reviews examining CRSwNP. In terms of limitations, publication bias from individual studies is a potential problem given the large number included in this review. Many studies also mix results from combined cohorts of CRS with and without nasal polyps, which prevented the data from being included in the analysis.

Future directions of research on the treatment of CRSwNP may lie within the context of QOL improvements and efficacy among different surgical and new biological therapies. New biological anti-IgE and anti-IL5 therapies for nasal polyps are currently being reviewed and have demonstrated promising benefits but at a large cost with ongoing maintenance. Therefore, this study provided a summative measure for outcomes of patients with CRSwNP after surgery to highlight the importance of surgery in the context of future comparative effectiveness and quality improvement initiatives.

Conclusion

ESS significantly improves QOL outcomes in CRSwNP. Pooled analyses revealed a mean change in postoperative SNOT-22 scores of 23 points. Through metaregression models, specific factors demonstrated a significant effect on patient QOL outcomes. Asthma, prior ESS, and preoperative SNOT-22 score correlated with greater improvement in SNOT-22 scores. Tobacco use and longer lengths of follow-up were associated with less improvement in SNOT-22 scores.

Author Contributions

Phong T. Le, acquisition, analysis, interpretation of data, revising and drafting manuscript, and final approval of manuscript; Zachary M. Soler, conception and design of study, analysis, interpretation of data, revising and drafting manuscript, and final approval of manuscript; Rabun Jones, acquisition, analysis, interpretation of data, revising and drafting manuscript, and final approval of manuscript; Jose L. Mattos, conception and design of study, acquisition, analysis, interpretation of data, revising and drafting manuscript, and final approval of manuscript; Shaun A. Nguyen, statistical analysis, interpretation of data, revising manuscript, and final approval of manuscript; Rodney J. Schlosser, conception and design of study, analysis, interpretation of data, revising and drafting manuscript, and final approval of manuscript.

Disclosures

Competing interests: Zachary M. Soler, Olympus, 480 Biomedical—consultant; Regeneron—advisory board. Rodney J. Schlosser, Olympus, Arrinex—consultant; Sanoﬁ, GlaxoSmithKline, Intersect, Entellus—grant support.

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