

# Revision Rates After Endoscopic Sinus Surgery: A Recurrence Analysis

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**Objectives:** Chronic rhinosinusitis with nasal polyposis is often refractory to medical and surgical management, especially in patients with asthma and aspirin intolerance. We used a contemporary database to investigate recurrence and revision surgery rates following endoscopic sinus surgery.

**Methods:** We performed a cohort study using a survival analysis technique. Records were reviewed of 549 patients with nasal polyposis who underwent endoscopic sinus surgery over a 10-year period. The main outcome measure was disease-free and surgery-free survival following endoscopic sinus surgery, investigated with Kaplan-Meier analyses.

**Results:** Patients with Samter's triad were significantly more likely to have a recurrence and undergo a second surgery following recurrence (risk-odds ratio, 2.7; 95% confidence interval, 1.5 to 3.2;  $p < 0.01$ ) than were patients without asthma or with only asthma from the triad. The presence of initial frontal sinus disease also increased the likelihood of revision surgery (risk-odds ratio, 1.6; 95% confidence interval, 1.2 to 1.8;  $p < 0.05$ ).

**Conclusions:** This is the first study to use survival analysis to document revision surgery rates following endoscopic sinus surgery. Revision surgery occurs at a high rate, especially in patients with asthma, Samter's triad, or frontal sinus disease. Patients should routinely be informed during clinical consultations about the likelihood of recurrence. Early intervention for frontal sinus disease may be considered.

**Key Words:** endoscopic sinus surgery, frontal sinus, nasal polyposis, revision surgery.

## INTRODUCTION

Chronic rhinosinusitis (CR) with nasal polyposis (NP) is a condition that affects up to 5% of the general population, causing nasal obstruction, anterior rhinorrhea, mucopurulent postnasal drip, and anosmia.<sup>1,2</sup> Several factors are known to be associated with inflammatory nasal polyps, including asthma and aspirin intolerance.<sup>1,3</sup> The clinical presentation of asthma, aspirin intolerance, and NP is labeled Samter's triad.<sup>4</sup> Nasal polyposis is present in 7% to 17% of patients with asthma alone<sup>1,2,5</sup> and in 36% to 96% of patients with the full triad.<sup>5</sup> Chronic sinusitis with NP is commonly managed with local and systemic steroid-based treatments, but a large proportion of patients fail to benefit from a purely medical approach.<sup>6,7</sup> Endoscopic sinus surgery (ESS) is often undertaken in this group, and generally has a very high initial success rate for symptomatic improvement in quality of life, as well as for clinical eradication of polyps.<sup>6</sup>

Unfortunately, a high rate of recidivism follow-

ing surgery makes the long-term management of this condition challenging for patients and clinicians.<sup>6,8</sup> Prior studies have suggested that recurrence rates are higher in patients with asthma alone or with Samter's triad,<sup>9-13</sup> but precise recurrence rates in these patients across time remain elusive. Moreover, a related unclear quantity is the proportion of patients with polyps who undergo revision surgery; how likely, and how soon, are important matters to address in counseling patients. At present, the literature does not supply the clinician with long-term data regarding the frequency of revision surgery and risk factors that might increase the likelihood thereof. The purpose of this study was therefore to use a contemporary database to conduct a recurrence analysis for polyposis revision surgery following primary ESS for CR with NP.

## MATERIALS AND METHODS

We conducted a review of prospectively gathered patient data from a preexisting departmental database. Records were available for review from 2,649

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patients who had undergone ESS performed by the study's senior surgeons (B.W.R., E.D.R.) from January 1999 to January 2009 at St Joseph's Health Care in London, Ontario. The Research Ethics Board at the University of Western Ontario approved this study (UWO Ethics No. 15545E).

**Inclusion and Exclusion Criteria.** Before we collected data, each record was assessed for completeness and suitability for inclusion. To be included in the study, each case needed to be consistent with the American Academy of Otolaryngology—established definition of CR with NP,<sup>14</sup> contain documentation regarding aspirin sensitivity and the presence or absence of asthma, and document the absence of extraneous systemic factors that could cause polyps (eg, cystic fibrosis). Each record must have been of a patient who underwent initial complete primary ESS (polypectomy, maxillary antrostomy, ethmoidectomy, sphenoidotomy, or frontal sinusotomy) after failed medical management (including intranasal and/or oral corticosteroid therapy and aspirin desensitization therapy in select cases). The senior surgeons (B.W.R., E.D.R.) used identical surgical techniques.

**Data Collection.** Once appropriate records were identified, they were abstracted for time until clinical recurrence of polyposis, time until revision surgery, and variables that could potentially influence polyp recurrence or the need for revision surgery: age, gender, asthma diagnosis, allergy to aspirin, specific sinuses involved, and the presence of fungal mucin during clinical examinations or at the time of surgery, preoperative and postoperative hyposmia or anosmia, environmental allergies, smoking history, and certain co-morbidities (cardiovascular disease, non-asthma respiratory disease, cancer history, and diabetes mellitus). Time until clinical recurrence was defined a priori as the first notation in the record of diagnosis of recurrent NP following surgery, as determined through endoscopic examination. Time until initial revision surgery was defined a priori as the time between the first and second surgeries.

**Statistical Analysis.** Differences in gender, sinus involvement (the total number of sinuses and bilateral or unilateral involvement), presence of mucin, preoperative and postoperative hyposmia or anosmia rates, environmental allergies, and the comorbidities investigated were compared with the Pearson  $\chi^2$  test. Age, total number of ESS procedures, and duration of follow-up were analyzed by use of analyses of variance with significance values determined via a Bonferroni correction for a final significance p value of 0.016. Post hoc Tukey tests were used to determine significant differences between groups.

#### PATIENT DATA

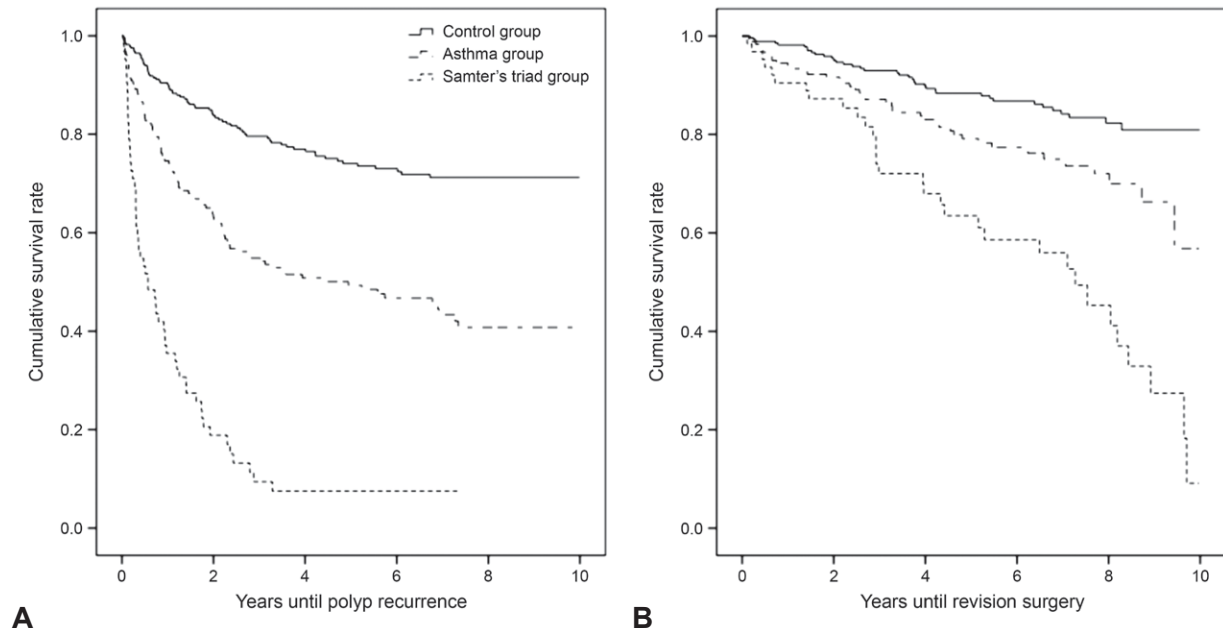
	Samter's		
	Control	Asthma	Triad
Median age (y)	54	56	55
Gender			
Male	29	83*	191*
Female	32	104*	101*
Mean No. of polypectomies	1.19	1.31	1.97*
Sinus involvement			
Median No. of sinuses	3	3	3
Unilateral	54*	18	4
Bilateral	241	173	59
Mucin			
Yes	25	14	13*
No	261	173	50*
Preoperative anosmia			
Yes	145	113	46
No	54	24	4*
Postoperative anosmia			
Yes	37*	59*	28*
No	70*	49*	19*
Mean duration of follow-up (y)	2.01	2.75	5.16*
Smoking (%)	41	38	35

\*p < 0.05.

The time periods between the first surgery and recurrence and between the first and second surgeries were analyzed by the Kaplan-Meier method and compared with the log-rank test. Cox proportional hazard models for both disease-free interval and interval to second surgery were constructed with the following predictor variables: patient group, age, gender, sinus involvement, presence of fungal mucin, preoperative and postoperative self-reported anosmia, environmental allergies, smoking history, and medical comorbidities. Statistical significance was set at a p level of less than 0.05 for all statistical tests (except analyses of variance, as mentioned above), and all tests were 2-tailed.

#### RESULTS

Of the 2,649 records, 549 met full inclusion criteria and were abstracted for analysis. This included 63 patients with Samter's triad, 191 patients with asthma but no aspirin sensitivity, and 295 patients with no asthma or aspirin sensitivity; this last group was defined as "control" for study purposes. The Table depicts demographics, risk factors, and disease severity information for the study population. Data regarding other tangential past health characteristics, such as non-asthma respiratory disease, cardiovascular disease, and diabetes, were often subject to incomplete recording that precluded meaningful analysis. These data were therefore excluded from the study. Most of the patients did not have formal



Kaplan-Meier curves for **A**) nasal polyp recurrence and **B**) revision surgery rates in patients with asthma, patients with Samter's triad, and controls.

allergy testing performed, and hence, without reliable data on the presence of true physiological allergies, we also excluded these data from the analysis.

Recurrence rates were significantly different between the groups. The Figure, A, illustrates Kaplan-Meier disease-free survival analysis for postoperative polyp recurrence, and the Figure, B, illustrates Kaplan-Meier survival analysis for the time period between the first and second surgeries. Patients with Samter's triad were the most likely to have a recurrence and did so the soonest ( $p < 0.001$ ). Patients with asthma were also more likely to have a recurrence and to do so sooner than control patients ( $p < 0.001$ ). Patients with Samter's triad also underwent a second surgery sooner and more often than did the other groups ( $p < 0.001$ ). Similarly, patients with asthma underwent a second surgery sooner and more often than control patients ( $p < 0.001$ ). The overall actuarial polyp-free survival rates at 5 years were 84%, 55%, and 10%, and the overall actuarial surgery-free rates at 5 years were 90%, 75%, and 63% for control patients, patients with asthma, and patients with Samter's triad, respectively. By the 10-year follow-up period, these numbers had dropped to polyp-free survival rates of 78% and 45% for control patients and patients with asthma, respectively, and surgery-free rates of 83%, 58%, and 11% for control patients, patients with asthma, and patients with Samter's triad, respectively. Note that 10-year follow-up data for polyp-free survival were not available for patients with Samter's triad, as every such patient followed in our study population had developed clinical disease recurrence by 3 years

after surgery.

A Cox proportional hazards analysis was conducted to determine which factors were predictive of either polyp recurrence or surgery recurrence. Of the possible predictive factors, patient group (control, asthma only, or Samter's triad) was significantly predictive for both outcomes: polyp recurrence (risk-odds ratio, 3.7; 95% confidence interval [CI], 2.5 to 5.5;  $p < 0.01$ ) and surgery recurrence (risk-odds ratio, 2.7; 95% CI, 1.5 to 3.2;  $p < 0.01$ ). With respect to sinus involvement, the presence of frontal sinus disease before the first surgery predicted polyp recurrence (risk-odds ratio, 1.4; 95% CI, 1.2 to 1.9;  $p < 0.01$ ) and surgery recurrence (risk-odds ratio, 1.6; 95% CI, 1.2 to 1.8;  $p < 0.05$ ). No other covariate was significantly predictive for either polyp or surgery recurrence, and all 2-way interactions were nonsignificant.

## DISCUSSION

A number of studies have investigated NP recurrence rates after ESS. However, the recurrence rates reported have varied substantially for several reasons, including the inherent disease heterogeneity of CR with NP, inconsistent research methods, non-differentiation of patient grouping (with and without asthma), variable duration of follow-up, different postoperative medical managements, variations in the surgeries performed, and differing definitions of recurrence (endoscopic, imaging, symptomatic, etc). In addition, the majority of recurrence studies have expressed relapse rates as a point estimate during a mean duration of follow-up; these are not rep-

representative of recurrence rates across time. Kaplan-Meier survival analysis enables estimation of instantaneous recurrence rates across time. A literature review shows only 2 prior studies of NP that used this technique; 1 excluded patients with Samter's triad,<sup>9</sup> and the other did not investigate clinical recurrence, but rather, the total number of ESS procedures that patients underwent across time.<sup>8</sup> Our study is therefore novel, in that it is the first study to include sufficient numbers of patients with Samter's triad to compare recurrence rates across time by use of survival analysis, and more importantly, is the first to document rates of revision surgery in all ESS patient groups over a long-term follow-up period.

We found that polyp recurrence rates at 5 years were 16%, 45%, and 90% for control patients, patients with asthma, and patients with Samter's triad, respectively, and that revision surgery rates at 5 years were 10%, 25%, and 37% for control patients, patients with asthma, and patients with Samter's triad, respectively; these grew higher at the 10-year time point. Prior studies have reported recurrence rates in shorter mean follow-up periods (less than 5 years) of between 21% and 66% for CR with NP, but most did not subdivide among patient groupings or did not comment on revision surgery rates, and all had shorter follow-up than the current study; hence, their results are difficult to compare to ours.<sup>13,15-21</sup>

Among the prognostic factors investigated, only asthma, Samter's triad, fungal mucin, and initial frontal sinus disease increased the rate of revision surgery. Given that fungal infections have been implicated in the pathogenesis of CR with NP,<sup>3</sup> the increased prevalence of fungal mucin in patients with Samter's triad may partially explain the increased recurrence rates in patients with Samter's triad. With respect to frontal sinus disease, frontal sinus involvement is believed to reflect a more severe disease phenotype,<sup>22,23</sup> although the frontal sinus appearance on computed tomographic scans appears to be unrelated to symptom severity.<sup>23</sup> The finding that frontal sinus disease presence increased the recurrence risk suggests that frontal sinus involvement is associated with increased disease severity. Surgical management of frontal sinus disease is controversial, with some surgeons suggesting avoidance of frontal sinusotomy at primary surgery, and others advocating early intervention.<sup>22</sup> In this practice, our general approach was to perform frontal sinusotomy in patients with symptoms (ie, headache) or patients with severe disease identified during clinical examination or by radiography. Given that our data suggest that frontal sinus disease may predict both disease and surgery recurrence, further inves-

tigation into this controversy is indicated. The role of early frontal sinus intervention may need better definition.

Interestingly, the rates of a second surgery lagged behind recurrence rates in all patient groups. There are several explanations for this finding. First, after recurrence, attempts at conservative management were often made. In addition, once patients experienced recurrence, they may have decided to delay a second surgery or not have one at all, perhaps because surgery was seen as futile if recurrence was perceived as inevitable. The time required to schedule a surgery might also explain the lag between recurrence and a second surgery. It is also possible that although endoscopic recurrence was recorded, some patients may have experienced minimal symptoms, lacking the need for revision operations.

This study has several limitations. Most notably, data were gathered prospectively for clinical purposes rather than for research, and thus, the information used in this study reflected the adequacy of documentation. The classification of patients by diagnosis and operative notes was well documented; however, the presence of fungal mucin, smoking history, and comorbid diagnoses may have been underreported or incompletely reported in some cases. The fact that patients with Samter's triad were followed up significantly longer than patients with asthma and control patients introduces the possibility that the increased revision surgery rates in this group were in part due to prolonged follow-up. However, given that increased recurrence rates are well known in patients with Samter's triad, the longer follow-up was likely attributable to the refractory nature of their disease. Our time-point definitions were based on the best possible data retrieved from the database, but may not precisely correlate with clinically significant disease. Last, our analysis of revision surgery may have been influenced by several factors unrelated to recurrence of NP, including wait-times for surgery and patients' preferences to delay surgery for personal reasons.

The results of this study, using contemporary data, demonstrate that management of CR with NP is currently inadequate. Although postoperative medical management with nasal steroids can reduce recurrence rates, revision surgery inevitably occurs in a significant proportion of patients. Although some studies suggest that postoperative oral corticosteroids may delay recurrence, the success rates reported for this method are still low.<sup>18</sup> Nasal polyposis is a recalcitrant condition, especially in patients with asthma and Samter's triad. Patients should be informed of the significant likelihood of revision sur-

gery. In citing a recurrence risk to a patient, rates should be stratified according to preoperative comorbidities, namely, asthma and Samter's triad.

Patients with these specific disorders in particular should be aware that ESS might provide only temporary relief of their symptoms.

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