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Impact of synechiae after endoscopic sinus surgery on long-term outcomes in chronic rhinosinusitis

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Abstract

Introduction—Synechiae are one of the most common unwanted outcomes after endoscopic sinus surgery (ESS) for chronic rhinosinusitis (CRS). However, there has been scant investigation into the true significance of synechiae formation after ESS. The aim of this study was to evaluate the impact of synechiae formation on quality-of-life (QOL) outcomes after ESS in patients with CRS.

Study Design—Prospective, multi-institutional cohort.

Methods—Rhinosinusitis Disability Index (RSDI) and Chronic Sinusitis Survey (CSS) scores were measured in adult patients before and after undergoing ESS for CRS. Differences in QOL were evaluated between those who developed sinonasal synechiae and those who did not, controlling for demographic factors, medical comorbidities, and measures of disease severity at baseline.

Results—A total of 286 patients underwent ESS, with 55 (19.2%) developing synechiae in the follow-up period. Patients developing synechiae reported significantly less improvement on the RSDI total scores (13.5 vs. 21.4, $p=0.008$), RSDI physical subscores (5.3 vs. 8.3, $p=0.007$), RSDI emotional subscores (2.9 vs. 5.8, $p=0.008$), CSS total scores (14.5 vs. 21.2, $p=0.093$) and CSS symptom subscores (19.9 vs 30.3, $p=0.069$) compared to those who did not develop synechiae postoperatively. These differences persisted even after controlling for baseline differences in disease severity.

Conclusions—Synechiae of the sinonasal cavity commonly occurs following ESS, particularly in those undergoing revision surgeries. Although both groups improve, the degree of QOL improvement appears to be less in those who form postoperative synechiae after surgery compared to those who do not.

Keywords

Chronic disease; sinusitis; cicatrix; outcomes assessment; tissue adhesions

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Conflict of Interest: None

INTRODUCTION

Approximately 500,000 patients per year undergo endoscopic sinus surgery (ESS) for the treatment of medical refractory chronic rhinosinusitis (CRS), a number that continues to rise each year^{1,2}. A wide body of literature supports the utility of ESS to improve health-related quality of life (HRQoL) in patients with CRS^{3,4}. However, not all patients improve to a similar degree and failures are still reported at a rate up to 26%⁴. When looking at patients requiring revision ESS, up to 50% present with synechiae in the middle meatus; a finding that has traditionally been implicated as a culprit of recurrent disease^{5,6}.

Synechiae are one of the most common unwanted outcomes after ESS, with an incidence ranging from 10% to 40%^{5,7}. Multiple studies have used the presence of synechiae after ESS as an outcome measure for various intraoperative interventions, including surgical techniques and middle meatal spacers/stents⁷⁻⁹. The focus on synechiae formation in clinical trials presupposes that their presence either contributes to or is associated with suboptimal outcomes. However, there has been scant investigation into the true significance of synechiae formation after ESS. The aim of this study was to evaluate the impact of synechiae formation on HRQoL outcomes after ESS in patients with CRS.

MATERIALS AND METHODS

Study overview

This study examined outcomes data from a previously performed observational cohort study of patients with CRS. Each patient failed comprehensive, initial medical management and selected ESS as the next treatment option^{10,11}. These patients were enrolled between July, 2004 and May, 2012. Patients underwent ESS and were then followed to a primary endpoint of at least 6 months to evaluate for improvement in HRQOL status.

Inclusion criteria and multi-institutional data collection

Adult patients (≥ 18 years) with CRS were enrolled into a prospective, observational cohort study from 5 tertiary rhinology practices across North America, including the Medical University of South Carolina, University of Calgary, Stanford University, Medical College of Wisconsin, and Oregon Health and Science University. All patients met diagnostic criteria for CRS according to the 2007 Adult Sinusitis Guideline endorsed by the American Academy of Otolaryngology-Head and Neck Surgery¹². Each patient completed at least one preoperative course of oral antibiotics (≥ 2 weeks duration) and topical nasal steroids (≥ 3 weeks duration) prior to surgery. In each instance, the treating physician determined the patient to be an appropriate candidate for ESS and offered the patient the option to pursue ESS or continue with medical management. Patient data from this cohort included age, gender, history of previous sinus surgery, sinonasal polyposis, a patient history of asthma, acetylsalicylic acid (ASA) intolerance, allergy, and tobacco use. Objective baseline measures of disease included computed tomography (CT) and endoscopy scores, which were recorded utilizing the scoring systems of Lund-Mackay (range: 0–24) and Lund-Kennedy (range: 0–20) respectively^{13,14}. All patients who returned for follow-up at 6 months or greater and completed all postoperative assessments were included in the study for final analysis. Informed consent and study protocols were independently monitored and approved by the Institutional Review Board at each enrollment site.

Extent of surgery

The specific sinonasal procedures performed on each patient at the time of surgery were recorded. These included sinus-specific procedures such as maxillary antrostomy, total or partial ethmoidectomy, sphenoidotomy, and frontal sinusotomy, as well as ancillary

procedures such as inferior turbinate submucous resection, partial middle turbinate resection, and septoplasty.

Primary outcomes: Post- ESS synechiae and HRQoL measures

Patients were divided into a subgroup which developed synechiae after surgery and a subgroup that did not. The presence or absence of synechiae was determined using the scarring component scores from the Lund-Kennedy endoscopic scale.¹⁴ The endoscopist (primary rhinologist) was blinded to all patient-reported data until the study's completion. Those with a bilateral scarring score of 0 were considered to not have synechiae and those with a score of 1–4 were considered to have synechiae.

All study patients were asked to complete two disease-specific HRQoL surveys during the initial enrollment meeting and at subsequent follow-up visits. The Rhinosinusitis Disability Index (RSDI) is a 30-question survey comprised of three individual subscales to measure the impact of sinus disease on the physical, functional, and emotional domains (range: 0–120)¹⁵. Higher RSDI total and subscale scores represent a higher impact of disease. The Chronic Sinusitis Survey (CSS) is a 6-question survey designed to measure sinusitis-specific symptoms and medication use within the preceding 8-week period (range: 0–100)¹⁶. Lower total and subscale scores indicate a greater impact of CRS on each patient. The primary outcome of interest was the mean change in HRQoL scores as measured by the RSDI and CSS total scores on a continuum (postoperative follow-up score minus baseline score) at the last available follow-up point.

Statistical analysis

Statistical analyses were conducted using commercially available statistical software (SPSS v.21; SPSS Inc., Chicago, IL). Patient characteristics were described with summary statistics to compare patient groups with and without synechiae after ESS (main independent variable) and compared across comorbid conditions using either Pearson χ^2 test for discrete variables and two-sample t-tests for continuous variables or their nonparametric equivalents. Paired *t* tests or Wilcoxon signed rank tests were used to compare improvement in HRQoL over time between patient groups with and without synechiae.

Simple stepwise multivariate linear regression was used to assess significance of the main independent variable while adjusting for independent covariates and confounding factors associated with changes in HRQoL. Final models were selected using a stepwise, manual forward selection ($p < 0.010$) and backwards elimination ($p < 0.050$) process. Reported results include crude and adjusted effect estimates for postoperative synechiae, 95% confidence intervals, and corresponding *p*-values.

RESULTS

Baseline cohort characteristics

A total of 286 patients with CRS undergoing ESS were included in this study. At 6 month follow up, 55 (19.2%) patients presented with synechiae and 231 patients (80.8%) had no evidence of scarring. Baseline characteristics for both groups are compared in Table 1. No significant differences in demographic characteristics were seen between groups, including age and gender. Also, no significance differences were seen in regards to amount of time for follow up between groups ($p = 0.089$). Similarly, there was no difference in comorbidities including asthma, allergy, ASA intolerance, tobacco use, and nasal polyposis. Patients who developed synechiae were more likely to have had prior ESS ($n = 44$; 80.0%) compared to those who did not develop synechiae ($n = 11$; 20.0% $p < .001$). The overall incidence of synechiae at baseline for the entire cohort was 36.7% ($n = 105$), with the vast majority of

these patients (95.8%) having undergone previous ESS. As expected, patients with postoperative synechiae were more likely to present with synechiae at baseline compared to patients with no postoperative synechiae (58.2 vs. 31.6%; $p<0.001$).

Baseline CT scores were slightly worse in patients who developed postoperative synechiae compared to those who did not, (12.7 (6.3) vs. 14.5 (6.1), $p=0.059$). Baseline endoscopy scores in the synechiae group were worse when compared with the non-synechiae group (8.4 (4.7) vs. 6.3 (4.4); $p=0.002$).

Baseline HRQoL

All patients in the cohort had available RSDI scores at baseline (Table 2). No significant differences in total or subdomain RSDI scores were noted between synechiae subgroups ($p=0.319$ for all). A total of 220 of 286 (76.9%) patients had baseline CSS scores available (Table 2). No significant differences in total or subdomain CSS scores were noted between both groups ($p=0.793$ for all).

Extent of surgery

In regards to extent of surgery, no significant differences were seen in the incidence of postoperative synechiae between patients undergoing unilateral or bilateral maxillary antrostomy, partial or total ethmoidectomy, sphenoidotomy, or frontal sinus surgery (Table 3). Similarly, no significant differences were seen either in patients undergoing inferior turbinate submucous resection or partial middle turbinate resection. However, patients undergoing concurrent septoplasty at the time of ESS had a decreased incidence of postoperative synechiae when compared with those who did not (10.4 vs 24.4%; $p=0.004$).

Changes in HRQoL following ESS

Both groups reported significant improvements in HRQoL after ESS, as measured by both the RSDI and CSS instruments ($p<0.050$). However, patients in the synechiae group had significantly less improvement in RSDI total scores (13.5 vs. 21.4; $p=0.008$), RSDI physical subscores (5.3 vs. 8.3; $p=0.007$), and RSDI emotional subscores (2.9 vs. 5.8; $p=0.008$) compared to those who did not develop synechiae postoperatively (Table 4). Similarly, those who developed synechiae after ESS had less improvement on CSS total scores (14.5 vs. 21.2; $p=0.093$) and CSS symptom subscores (19.9 vs. 30.3; $p=0.069$), although these did not quite reach statistical significance (Table 4).

Regression modeling

Patients who developed synechiae after ESS were more likely to have had prior ESS, synechiae present at baseline, worse CT and endoscopy scores prior to surgery, and were less likely to have had a concurrent septoplasty. Each of these factors were evaluated for independent significance and their potential confounding effect on the relationship between post-operative synechiae and HRQoL and controlled for where appropriate using linear regression modeling. Table 5 shows the regression coefficients before and after adjustment for these factors. After adjusting for differences at baseline, those patients who presented with postoperative synechiae were still found to have significantly less improvement as measured by total and subscores of the RSDI instrument and a trend toward less improvement on both the total CSS and symptom subscale scores.

DISCUSSION

Synechiae, or scarring, of the sinonasal cavity has traditionally been considered a complication of sinus surgery, or at least a poor outcome which should be avoided. This belief is evidenced by the numerous spacers and stents designed and marketed to prevent

synechiae formation after sinus surgery, as well as the many studies which include synechiae formation as a primary outcome measure. To date, there have been few studies designed to specifically evaluate the impact of synechiae on outcomes after sinus surgery. In this prospective, multi-institutional cohort study, 20% of patients had endoscopic evidence of sinonasal synechiae following ESS, an incidence which falls well within the range previously reported by other authors^{5,7}. The development of postoperative synechiae was associated with significantly less improvement in disease-specific HRQoL after ESS, even after controlling for potential confounding factors.

Only a handful of other studies have specifically reported outcomes after ESS with regard to synechiae formation. In a series of 182 patients undergoing ESS, Chambers et al. reported that synechiae at the natural maxillary ostium and ethmoid cavity were the only endoscopic findings which correlated with poor symptom outcomes⁵. Comparably, Musy and Kountakis reported on a series of 70 patients undergoing revision ESS in which half of the patients presented with synechiae at the frontal recess location⁶. Similarly, Ramadan reported on a series 52 patients undergoing revision ESS wherein slightly more than half had findings of synechiae. He made the argument that synechiae was the cause of failure when combined with other findings such as residual ethmoidal or frontal recess cells¹⁷. The current study lends strong additional evidence to the association between synechiae formation and suboptimal clinical outcomes following sinus surgery.

The question remains whether synechiae are directly responsible for worse outcomes (causative) or simply a marker of a more severe disease phenotype. The concept that synechiae could impair nasal airflow or contribute to ostial blockage and/or impair mucociliary movement is plausible and fits with traditional understandings of sinus physiology and the tenets of functional endoscopic sinus surgery. Perhaps synechiae could also impair delivery of topical medications to sinonasal mucosa. Another possibility is that synechiae are just a marker of a more severe disease phenotype and not causative per se. Certainly, it can be argued that some of the synechiae which form between the middle turbinate and lateral nasal wall appear to be of “cosmetic” importance only and would be unlikely to cause symptomatology. In this hypothesis, synechiae could represent the visible manifestations of excess inflammation and fibrosis. Recent studies which have identified an immunomodulatory role for airway fibroblasts lend support to the plausibility of this hypothesis¹⁸. A definitive answer to the role of synechiae has important implications to surgeons who must consider adjusting techniques or utilizing spacers/stents in attempt at preventing post-operative synechiae.

In this surgical cohort, patients who underwent concurrent septoplasty had a significantly lower incidence of synechiae than those who did not undergo septoplasty. This difference existed even after controlling for revision surgical status and presence of synechiae at baseline. Septoplasty in combination with ESS has been reported in the range of 27 to 48%^{10,19}. Traditional indications to perform concurrent septoplasty during ESS have included the presence of a septal deviation that impaired surgical access to the middle meatus and/or symptomatic nasal obstruction. In the case of the former, the nasal cavity would be expected to be narrower on at least one side. A possible explanation for our finding could be that surgeons may decide not to perform a septoplasty and “work around” a septal deviation during ESS, potentially causing greater mucosal trauma and hence greatest risk for synechiae formation. This study was unable to determine if postoperative synechiae were on the same side as septal deviations.

Strengths of this study include its prospective data collection, multi-institutional involvement, and use of validated outcome metrics. The main limitation of these analyses was the lack of site specific synechiae information. Given that the data from our cohort

came from a previously performed observational cohort study, we were bound by the limitations of the instruments by which the data was originally collected. The Lund-Kennedy endoscopic score grades bilateral synechiae as absent, mild, or severe by assigning a value of 0, 1, and 2 respectively with a possible maximal score of 4¹⁴. The staging system however, does not discriminate synechiae by location, nor does it explicitly define the difference between mild and severe. More quantifiable information regarding synechiae, including the location of involvement, would help determine true relationship between synechiae and clinical outcomes after sinus surgery.

CONCLUSION

Synechiae of the sinonasal cavity commonly occur following ESS, particularly in those undergoing revision surgeries. Although both groups improve, the degree of HRQoL improvement appears to be less in those who form postoperative synechiae after surgery compared to those who do not. Further study is required in order to determine whether a true causal relationship exists and to define the extent and nature of synechiae which are clinically relevant.

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TABLE 1

Baseline demographics and patients characteristics.

Characteristics:	Non-synechia cohort (n=231)		Synechia cohort (n=55)		p
	Mean (SD)	n(%)	Mean (SD)	n(%)	
Age	48.1 (14.0)		51.73 (14.7)		0.090
Gender					
Male		113 (81.3)		26 (18.7)	
Female		118 (80.3)		23 (19.7)	0.826
Follow up (months)	15.25 (6.57)		13.56 (6.61)		0.089
Previous sinus surgery		123 (53.2)		44 (80.0)	<0.001
Nasal polyposis		88 (38.0)		26 (47.2)	0.212
Asthma		95 (41.1)		28 (50.9)	0.188
ASA intolerance		26 (11.2)		4 (7.2)	0.386
Allergic rhinitis by history		30 (12.9)		4 (7.2)	0.239
Allergic rhinitis by testing*		62 (26.8)		13 (23.6)	0.627
Current smoker		10 (4.3)		4 (7.2)	0.363
Lund-Mackay CT score	12.73 (6.3)		14.51 (6.0)		0.059
Lund-Kennedy endoscopy score	6.25 (4.4)		8.36 (4.7)		0.002
Synechia		73 (31.6)		32 (58.2)	<0.001

* Either by skin prick or MRAST testing

ASA= acetylsalicylic acid; CT= computed tomography; SD= standard deviation

TABLE 2

Comparison of mean primary outcomes measures at baseline

Outcome measure:	Non-synechia cohort	Synechia cohort	<i>p</i>
	Mean (SD)	Mean (SD)	
RSDI physical	19.21 (7.6)	18.5 (7.5)	0.582
RSDI functional	15.82 (7.7)	15.20 (7.5)	0.589
RSDI emotional	13.7 (8.4)	12.45 (8.0)	0.319
RSDI total	48.7 (21.4)	46.24 (20.0)	0.432
CSS symptoms	30.22 (26.7)	28.95 (29.1)	0.793
CSS medication	45.24 (25.4)	45.17 (24.0)	0.989
CSS total	37.7 (19.9)	37.0 (24.6)	0.854

RSDI= Rhinosinusitis Disability Index, CSS = Chronic Sinusitis Survey, SD=standard deviation

TABLE 3

Rate of postoperative synechiae depending on the extent of surgery

Type of procedure:*	Patients undergoing the procedure	Patients not undergoing the procedure	p
	n (%)	n(%)	
<i>Maxillary antrostomy</i>	47(18)	8(32)	0.090
<i>Partial ethmoidectomy</i>	7(14.9)	48(20.1)	0.409
<i>Total ethmoidectomy</i>	42(18.4)	13(22.4)	0.491
<i>Sphenoidotomy</i>	36(20.1)	19(17.8)	0.625
<i>Frontal sinus surgery</i>	40(21.7)	15(14.7)	0.148
<i>Inferior turbinate submucous resection</i>	4(13.8)	51(19.8)	0.433
<i>Partial middle turbinate resection</i>	12(15.2)	43(20.8)	0.284
<i>Septoplasty</i>	11(10.4)	44(24.4)	0.004

* Unilateral or bilateral

TABLE 4

Comparison of absolute mean improvement in quality-of-life scores between cohort subgroups 6 months after endoscopic sinus surgery

Outcome measure:	Non-synechia cohort	Synechia cohort	<i>p</i>
	Mean (SD)	Mean (SD)	
RSDI physical	8.3 (7.4)	5.3 (7.6)	0.007
RSDI functional	7.18 (7.1)	5.3 (6.3)	0.750
RSDI emotional	5.8 (7.5)	2.9 (6.5)	0.008
RSDI total	21.4 (19.3)	13.5 (17.3)	0.008
CSS symptom	30.0(31.1)	19.9 (30.6)	0.069
CSS medication	12.5 (25.5)	9.2 (26.9)	0.475
CSS total	21.2 (21.3)	14.5 (24.9)	0.093

RSDI= Rhinosinusitis Disability, CSS = Chronic Sinusitis Survey, SD=standard deviation

TABLE 5

Crude and adjusted estimates of improvement in disease-specific quality-of-life for patients with and without postoperative synechia.

Outcome measures:	Synechia cohort	Non-synechia cohort		β	Adjusted β^*	[LL, UL]	p
	Mean $\pm$ SEM	Mean $\pm$ SEM	Mean $\pm$ SEM				
RSDI Physical	-5.31 $\pm$ 1.03	-8.36 $\pm$ 0.49	-7.19 $\pm$ 0.47	3.05	2.86	[0.65, 5.08]	0.012
RSDI Functional	-5.31 $\pm$ 0.86		-7.19 $\pm$ 0.47	1.77	1.72	[-0.38, 3.82]	0.109
RSDI Emotional	-2.91 $\pm$ 0.89		-5.87 $\pm$ 0.50	2.96	2.51	[0.27, 4.74]	0.028
RSDI Total	-13.53 $\pm$ 2.38		-21.41 $\pm$ 1.28	7.88	7.54	[1.86, 13.23]	0.017
CSS Symptom	19.96 $\pm$ 4.97		30.10 $\pm$ 2.32	-10.14	-8.53	[-19.87, 2.81]	0.140
CSS Medication	9.21 $\pm$ 4.36		12.50 $\pm$ 1.89	-3.29	-1.63	[-10.84, 7.59]	0.728
CSS total	14.58 $\pm$ 4.05		21.23 $\pm$ 1.59	-6.64	-5.98	[-13.63, 2.41]	0.170

* Final linear regression multivariate models adjusted for revision surgery, endoscopy staging, CT staging, baseline Scarring, and septoplasty where significant. P-values correspond with adjusted effect estimate (β) values. SEM=standard error of the mean. No evidence of any interaction effects between preoperative or postoperative scarring and revision surgery or septoplasty. Septoplasty was only significant as an independent predictor of change on the RSDI emotional subscale score.