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Endoscopic sinus surgery in cystic fibrosis: do patients benefit from surgery?☆

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Abstract

Objective: To examine the effects of endoscopic sinus surgery on the pulmonary status of cystic fibrosis (CF) patients through the objective parameters of steroid use, pulmonary function tests (PFTs), and inpatient hospital days (IHDs). *Methods:* Retrospective chart review of all patients with CF who underwent endoscopic sinus surgery from 1993 to 1999 at a tertiary care children's hospital. Preoperative pulmonary function, inhaler and steroid use, and IHDs were compared to postoperative parameters within a 1-year period. *Results:* Sixty-six patients, including eight lung transplant patients, underwent a total of 112 endoscopic sinus surgery procedures; 25 patients underwent more than one procedure. Patients were taking oral steroids preoperatively in 28% of procedures and inhaled steroids in 40%. Postoperatively, there was no statistically significant change in oral or inhaled steroid use, or in postoperative pulmonary function. If the index hospitalization, which was often for reasons not related to sinus disease, was considered part of the preoperative time period, endoscopic sinus surgery (ESS) was noted to result in a marked reduction (9.5 days (adjusted), $P = 0.001$) in hospital days during the subsequent 6 months. If the date of the procedure alone was used to define pre- and postoperative time periods, the reduction in postoperative days was more modest and not statistically significant (3.5 days (adjusted), $P = 0.21$). *Conclusions:* Although we found no statistically significant difference in PFTs, or steroid requirements following ESS, ESS may have resulted in a reduced need for hospitalization in the 6 months following the procedure. Future prospective studies in a larger number of patients and using more detailed outcome measures are needed to better evaluate the effects of endoscopic sinus surgery in pediatric patients with CF.

Keywords: Endoscopic sinus surgery; Cystic fibrosis

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1. Introduction

Sinus abnormalities are present in almost all patients with cystic fibrosis (CF) [1–3]. The etiology is felt to be related to abnormally viscous secretions and impaired mucociliary transport causing mechanical obstruction of the sinopulmonary tree [1,4,5]. Panopacification of the sinuses by imaging occurs in 90–100% of CF patients after 8 months of age [6]. Polypoid disease occurs in up to one-third of these patients [1]. Despite abnormal sinus CT scans in most CF patients, only $\approx$10–20% of patients are symptomatic from their sinus disease [4]. Imaging studies, therefore, are poor indicators for surgical intervention in patients with CF.

Most clinicians feel that there is little 'functional' component to endoscopic sinus surgery in CF patients. Many patients show no difference in pre- and postoperative sinus CT scans despite subjective improvement in symptoms after sinus surgery. The goal of surgery has become to debulk polypoid disease and irrigate out inspissated secretions with the hope of decreasing bacterial load, rather than to construct a functional sinus. Postoperative lavage protocols have also proven beneficial [7,8].

Otolaryngologists often base their decision to perform sinus surgery in the CF population on subjective sinus complaints. Some clinicians feel that sinus disease may also contribute to pulmonary exacerbations and declining pulmonary function in these patients. The intent of this review was to determine if one could identify objective measures, which support ESS in sinus disease in the CF population.

2. Materials and methods

We first identified all patients with the ICD-9 diagnosis of CF proven by a positive sweat test who had also undergone at least one endoscopic sinus surgery (ESS) procedure from 1993 to 1999. Records identified in administrative data were then screened manually to assure accurate case-identification.

Charts were then abstracted for each patient's steroid requirements, pulmonary function tests (PFTs), and inpatient hospital days (IHDs) during the 6-months period before and after each procedure. This time interval has been used in previous studies of sinus surgery in CF patients [9,10] and was developed in order to avoid difficulty in distinguishing between pre- and postoperative IHDs in patients undergoing multiple procedures in shorter time intervals. In keeping with these previous studies, patients who underwent multiple procedures greater than 6 months apart were included in the analysis. A minority of patients (37.8%) underwent more than one procedure during the study period.

Pediatric otolaryngology consultations, and subsequent ESS were performed in two general populations of patients, both of which were included in this study. The first group included patients with symptomatic disease who were evaluated as outpatients and set up for outpatient sinus surgery. The second group included patients hospitalized on the pulmonary service for pulmonary exacerbations but who were referred for symptomatic sinus disease at varying points of their hospital stay. ESS in these patients was performed semi-electively as an inpatient, and 25% (28/112) occurred in the midst of a 'clean-out' (7–14 days of intravenous antibiotics prescribed to treat subacute pulmonary exacerbations). In these cases, the majority of inpatient days during that admission was unlikely to be impacted by any positive or negative effect of ESS and was directed primarily by the primary service.

To account for this a priori theoretical difference, we collected data regarding IHDs using two methods. The first method counted all inpatient days accrued during the index hospitalization as being preoperative days, with any additional days due to rehospitalization during the 6-months followup period as postoperative days. The second approach counted pre- and postoperative days based on the date of the procedure alone.

If multiple sets of PFTs were obtained within each 6-months period, the highest percent predicted values were used for the study. If inhaled or oral steroids were prescribed at any time within the 6-months pre- or postoperative period, they were included in the data. Perioperative steroids prescribed by the surgeon specifically for sinus inflammation were not included in the analysis.

We used simple statistics to describe baseline characteristics of patients in this study. Univariate differences in pre- and postoperative PFTs and rates of hospitalization were performed using paired t-tests with a two-sided significance level of 0.05. We then fit multivariable mixed effects models adjusting for the possible confounding effects of age, gender, whether the patient had received a lung transplant, whether the patient underwent a clean-out, and whether more than one procedure was performed. Multivariable mixed effect analyses also included adjustment for clustering effects due to patient or procedure related factors, and are therefore, able to statistically account for whether patients preferentially underwent procedures because of factors (i.e. past clinical response to ESS) unmeasured in our data. All statistical analyses were performed using SAS 8.0 for Windows NT (SAS Institute, Cary, NC).

3. Results

3.1. Patient characteristics

Sixty-six CF patients, including eight (12.1%) who had received lung transplants, were identified. Twenty-five (37.9%) underwent more than one procedure, resulting in a total of 112 procedures being available for study. Of these, 102 (91.1%) had complete pre- and postoperative PFT data, 99 (88.4%) had complete IHD data. Thirty-four patients (51.5%) were male. Mean patient age at time of surgery was 17.0 years (S.D. 9.1 years).

3.2. Use of inhaled and oral steroids

Table 1 displays rates of use of steroids pre- and postoperatively for our patient cohort. Oral steroid usage before ESS was identified in 31 (28.7%) of cases; inhaled steroids were used preoperatively in 45 (41.7%). Seven (6.5%) discontinued or reduced oral steroid usage after ESS and six (5.6%) had oral steroids added. Inhaled steroids were changed postoperatively in equal numbers of cases, with these medications added and discontinued in three (2.8%) cases each. There were no statistically significant differences in steroid use in either adjusted or unadjusted analyses.

3.3. Changes in pulmonary function tests and hospital days

Table 2 displays pre- and postoperative percent predicted forced vital capacity (FVC), percent predicted forced expiratory volume in 1 s (FEV1), and IHDs for the patient cohort. Mean preoperative percent predicted FVC was 96.5 (S.D. 22.6); the mean postoperative percent predicted FVC was 96.1 (S.D. 21.7). The mean preoperative percent predicted FEV1 in this cohort was 86.7 (S.D. 29.3); the mean postoperative percent predicted FEV1 was 87.3 (S.D. 26.5). The unadjusted mean difference in percent predicted FVC was -0.30 (P for difference 0.78), and the unadjusted mean difference in percent predicted FEV1 was 0.23 (P for difference 0.86). After adjustment in multivariable models, no statistically significant differences in PFTs were observed, with an adjusted mean difference in pre- and postoperative FVC of -0.30 ($P = 0.53$), and an adjusted mean difference in FEV1 of 2.10 ($P = 0.52$).

Table 1
Use of steroids before and after ESS

	Preoperative (%)	Postoperative (%)	Discontinued postoperatively (%)	Added postoperatively (%)
Oral steroids	31 (27.9)	32 (28.8)	4 (3.6)	5 (4.5)*
Inhaled steroids	45 (40.5)	45 (40.5)	3 (2.7)	3 (2.7)*

All values displayed with n and % of procedures (total $n = 112$).
* P, NS.

Table 2
Changes in PFTs and hospitalization rates before and after ESS

	Preoperative value (mean, S.D.)	Postoperative value (mean, S.D.)	Unadjusted difference (mean, P for difference)	Adjusted difference (mean, P for difference)
FVC (% predicted)	96.5 (22.6)	96.1 (21.7)	−0.30 ($P = 0.78$)	−0.30 ($P = 0.53$)
FEV1 (% predicted)	86.7 (29.3)	87.3 (26.5)	0.23 ($P = 0.86$)	2.10 ($P = 0.52$)
Hospital days, method one[a] (days)	16.8 (16.8)	9.5 (15.9)	−7.4 ($P < 0.0001$)	−9.5 ($P = 0.001$)
Hospital days, method two[b] (days)	13.8 (15.6)	12.3 (17.1)	−1.5 ($P = 0.24$)	−3.8 ($P = 0.21$)

[a] Method one includes all hospital days for the index hospitalization and in 6 months prior to hospitalization as preoperative hospital days, postoperative days as all in hospital days in subsequent 6 months.

[b] Method two includes preoperative days defined as all hospital days in the 6 months preceding operative date, postoperative days as all days following (up to 6 months of followup).

When the entire index hospitalization is taken into account, the mean number of preoperative days was 16.8 (S.D. 16.8) and the mean number of postoperative days was 9.5 (S.D. 15.9). By our alternate method, the mean number of preoperative days was 13.8 (S.D. 15.6) and postoperative days was 12.3 (S.D. 17.1). These estimates result in a lower number of IHDs following ESS of 7.4 ($P < 0.001$) by our first method, and 1.5 ($P = 0.24$) by our second method.

After adjustment in multivariable mixed effects models, patients who underwent ESS had a marked reduction in hospital days following ESS (9.5 days fewer hospital days, 95% CI: 15.1 lower to 3.9 lower, $P = 0.001$). Although not statistically significant, we also noted a reduction in IHDs by our second method (3.8 fewer days, 95% CI: 9.9 lower to 2.3 higher, $P = 0.21$).

To explore the durability of our findings we performed subset and stratified analyses (not presented). Analyses limited to those patients undergoing their first procedure or among patients less than or equal to 9 years of age were not different than those presented. We chose this age from Mair's paper demonstrating immature bone in ESS specimens from patients less than 9 years of age and mature bone in ESS specimens from children greater than 9 years of age [19]. Additionally, analyses adjusting for changes in the use of inhaled or oral steroids were also not different from those presented. Analyses excluding patients who had received lung transplants were also not different than those presented.

4. Comments

In this retrospective chart review, ESS in patients with CF had no significant effect upon postoperative use of steroids, or in objective measures of pulmonary function. However, patients who underwent ESS had a decrease in rehospitalization rates versus their preoperative hospitalization rates, suggesting the possibility of cost savings and potential improved quality of life with appropriate use of ESS.

The risks and benefits of endoscopic sinus surgery in children are a topic of debate. Clinicians have not always agreed on the indications for surgical intervention in children with chronic sinus disease, although there is consensus regarding indications for surgical management of symptomatic CF patients with obvious polypoid disease [11–18]. Despite concerns regarding the effects of pediatric sinus surgery upon facial growth, no studies have been able to confirm clinically significant facial asymmetry due to ESS [19–21].

Historically, clinicians have favored aggressive treatment of sinus disease in patients with airway hyperreactivity, based on the assumption that bacterial seeding of the lower respiratory tract from the sinuses worsens pulmonary function [22]. ESS in patients with asthma results in reduced steroid requirements and bronchodilator use but, as in our study, no correlation with objective measures of pulmonary function has been demonstrated [23–26]. Previous studies have shown decreases in postoperative steroid requirements, in hospital admissions, and improved exercise tolerance after sinus surgery in CF patients [10,27]. Schulte and Kasperbauer even advocate ESS for asymptomatic CF patients as standard pre-lung transplant care [28]. Many of these previous studies involve small numbers of patients, however, and few include pediatric CF patients.

Evaluating the effects of sinus surgery in pediatric CF patients is difficult because standard outcome measures do not exist. Hebert and Bent attempted to quantify outcomes through their meta-analysis of pediatric ESS studies [29–32]. Most studies describe a ‘positive outcome’ based on subjective questionnaire data, although one small study (14 patients) did examine objective parameters, finding postoperative decreases in steroid use, IHDs, and school absenteeism [33]. Measurement of outcomes in patients with CF is further complicated because sinus disease is never entirely eradicated, and because objective measures (e.g. sinus CT scans and PFTs) do not necessarily correlate with clinical disease [34–36]. As a result, clinicians have depended upon subjective criteria as indicators for surgical intervention [37–40].

Our study has several limitations. Although our study represents one of the largest samples of pediatric CF patients treated in this fashion to date, our patient cohort remains relatively small and may therefore, be prone to sampling or selection biases. In addition, several different surgeons performed the procedures, possibly adding operator-specific biases.

Our study excluded patients who required more than one ESS procedure in a 6-months period using criteria taken from previous studies examining sinus procedures in patients with CF [9,10]. These exclusion criteria may have impacted our patient population in several ways. For example, excluded patients might represent a group who required procedures more often due to poor response to therapy or early recurrence of disease. Halvorson et al. reported that all CF patients who underwent ESS in their study had evidence of recurrent polyposis within 18 months [30]. Alternatively, these patients may have been chosen for ESS in a short-time period because they were considered good operative candidates, or because they had previous response to ESS. The true impact of these exclusion criteria on our findings is unclear, however, as these two biases may have selected for either sicker or healthier patients.

PFTs for our patients were near the predicted values for ‘normal’, suggesting that referral to ESS may have been biased in favor of healthier patients. This is in striking contrast to the patients in Umetsu’s study with a mean FVC of 43%, but is consistent with Madonna’s study with mean preoperative FVCs and FEV1s of 101 and 86%, respectively, in 14 children with CF undergoing ESS [9,10]. Although we have tried to adjust for confounding effects of patient related factors and severity of illness, it is possible that unmeasured severity may have affected our findings. Subset analyses excluding patients who had undergone lung transplantation—and might be considered the most chronically ill—were no different, however.

Lastly, the first method we used to define pre- and postoperative hospital days may have resulted in bias for increased preoperative IHDs because some patients underwent clean-out procedures. For this reason, all multivariable models adjusted for whether the patient was admitted for a clean-out prior to ESS. Our second definition of hospital days did not show a similar impact of ESS on IHDs and was likely to have been limited by a lack of accurate information regarding the coordination of medical and surgical care. Few other studies have explored the additive effect of ESS and preoperative clean-out protocols, however. In Umetsu et al.’s study, patients were admitted 5–15 days prior to surgical intervention for intravenous antibiotics, and it is unclear from their analyses whether they counted these days in the preoperative admission days data [9]. In Madonna’s study, all patients received 1 week of preoperative steroids and antibiotics [10]. In Reilly’s study of 30 CF patients undergoing polypectomy, all but two were scheduled as same day procedures without preoperative admission to maximize pulmonary status [20].

5. Conclusions

Our study, the largest to report effects of ESS on objective outcomes of patients with CF, suggests that ESS has little impact on pulmonary function, or use of oral and inhaled medications, but may result in fewer in hospital days in the 6 months following the procedure. Future research should seek to determine optimal coordination of medical and surgical therapies, and whether patient characteristics (such as CF genetic subtypes) may further identify patients who will benefit from ESS. Importantly, larger investigations should determine whether, in addition to reduced hospital stays, ESS results in improved quality of life among patients with CF and sinus disease.

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