Endoscopic Sinus Surgery in Adults With Cystic Fibrosis

Effect on Lung Function, Intravenous Antibiotic Use, and Hospitalization

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Objective: To ascertain the effect of endoscopic sinus surgery (ESS) on lung function, intravenous (IV) antibiotic use, and hospitalization in adults with cystic fibrosis (CF).

Design: Retrospective analysis.

Settings: Tertiary care center.


Main Outcome Measures: Twelve-month preoperative and 12-month postoperative pulmonary function testing (forced vital capacity [FVC] and forced expired volume in 1 second [FEV1]), number of IV antibiotic courses, total number of days of intravenous antibiotic use, and number of inpatient hospital days (IHDs) were assessed.

Results: Twenty-two adults with CF underwent ESS; 15 patients had adequate data for evaluation. No significant differences were found between mean preoperative and postoperative FEV1 (61.3% vs 59.9%; P = .41) or FVC (76.4% vs 76.1%; P = .97) or between best preoperative and postoperative FEV1 (67.4% vs 67.0%; P = .95) or FVC (84.2% vs 83.0%; P = .86) (paired samples t test). The number of IV antibiotic courses and the total number of days of IV antibiotic use did not differ between the preoperative and postoperative periods (Wilcoxon signed rank test P = .61 and P = .10, respectively). However, the number of IHDs was significantly lower in the 1-year postoperative period (36.7 days) vs the 1-year preoperative period (59.1 days) (Wilcoxon signed rank test, z = −2.20, P = .03).

Conclusions: This preliminary study of ESS in adult CF patients indicates significant reduction in the number of IHDs in the postoperative period. However, there is no evidence that ESS improved lung function or the need for IV antibiotics.

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Cystic Fibrosis (CF) is a systemic disease with autosomal recessive inheritance that affects exocrine gland function. Affecting more than 24,000 individuals in the United States as of 2006, CF is the most common life-shortening inherited disease in white populations. The CFTR gene (OMIM 602421), the gene responsible for changes seen in the disease, was identified in 1989 and is located on the long arm of chromosome 7. Its mutation results in abnormal synthesis of the CFTR protein, which functions as an ion channel across the apical surface of the epithelial cell membrane and is primarily found in tissues that produce sweat, mucus, saliva, tears, and digestive enzymes. This mutation results in abnormal chloride transport across the epithelium. Expression of mutant CFTR in the respiratory tract (including the sinuses) results in the triad of altered mucociliary clearance, a markedly exaggerated inflammatory response, and chronic bacterial infection. The most common cause of death (in >80% of cases) in CF patients today is progressive bronchiectasis and ultimately respiratory failure. Sinonasal disease in the form of chronic rhinosinusitis, with or without nasal polyposis, has a significant incidence in the CF population. Radiologic findings of paranasal sinus opacification on computed tomography can be found in almost every patient with CF, with a reported incidence of nasal polyposis between 33% and 57%. Exacerbations of rhinosinusitis in CF are thought to contribute to pulmonary exacerbations and frequently require treatment with intravenous (IV) antibiotics, especially in the adult CF population.
Therefore, adequate control of sinus symptoms in this population is necessary. Studies have reported a high degree of correlation between the microbial flora in CF paranasal sinus cultures and those in cultures of the lower airways. After endoscopic sinus surgery (ESS), CF patients frequently report subjective improvement in both upper and lower airway symptoms. These findings have led to the hypothesis that treatment of sinus disease in CF patients may improve their overall pulmonary health. On the basis of this hypothesis, other authors have compared preoperative and postoperative ESS outcomes in CF patients. Most of these studies have been performed in the pediatric CF population and have reported decreased symptoms and hospitalization days in the postoperative period, but significant improvement in postoperative pulmonary function test (PFT) results has not been demonstrated.

Because of advancements in CF diagnosis and treatment in recent decades, mean survival has increased markedly, with adults accounting for approximately 45% of patients with CF. Approximately 20% to 50% of CF patients will undergo surgical treatment for sinonasal disease in their lifetime. Assessment of the effect of ESS on adult CF patients is of great value in continuing to refine care strategies. The objective of this study was to assess the effect of ESS on lung function, inpatient hospital days (IHDs), and IV antibiotic use in adult CF patients.

We completed a retrospective review of the medical records of adult patients (≥18 years of age) with an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis of CF (277.xx) at Emory University Hospital who underwent at least 1 ESS between March 1, 2006, and June 31, 2008. All operations were performed by 1 of the 2 otolaryngology faculty authors (J.M.D. or S.K.W.). Data were obtained from the electronic medical record system of Emory University Hospital and The Emory Clinic and supplemented with information from the Cystic Fibrosis Foundation Registry. Approval for this study was granted by the institutional review board of Emory University.

The PFT data from spirometry were gathered for the 12-month preoperative period and the 12-month postoperative period. Specific PFT data included forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1), expressed as the percentage predicted for each patient. For both FVC and FEV1, mean 12-month preoperative and postoperative values were calculated. In addition, the highest FVC and FEV1 values for each patient’s 12-month preoperative and postoperative periods were noted. Each patient’s best FEV1 was used as his or her baseline pulmonary function measurement.

The total number of IHDs was calculated for each patient’s 12-month preoperative and postoperative periods. In cases in which the patient was an inpatient when the surgery was performed, the total number of days for that hospitalization was counted as part of the preoperative period.

In the same manner as in the 2 previous parameters, 12-month preoperative and postoperative periods were used to evaluate IV antibiotic use before and after ESS. The total number of courses and the total number of days of IV antibiotic use were calculated. For the total number of days of IV antibiotic use, both inpatient and home courses of antibiotics were included. Cases in which a patient was discharged from the hospital to continue taking antibiotics at home were considered 1 course of IV antibiotic therapy.

For demographic variables, standard descriptive statistics were used. The PFT values were compared using the paired samples t test. The Wilcoxon signed rank test was used to analyze preoperative vs postoperative IHDs and IV antibiotic use. Statistical analysis was performed with SPSS statistical software, version 11.0 (SPSS, Inc).

RESULTS

Twenty-two adults with CF underwent ESS throughout the study period. Of these, 2 patients died before the end of the 12-month postoperative period, and 5 patients had insufficient data for analysis. Adequate data were available for 15 patients. Eight patients were women (53%), and the mean age of the 15 patients was 34 years (range, 18-51 years). Eleven patients underwent at least 1 previous ESS other than the reference surgery for this study. Preoperative and postoperative FVC and FEV1 values for the 15 adult CF patients in this analysis are presented in Table 1. When comparing mean preoperative FVC (76.4%) with the mean postoperative FVC (76.1%), we found no statistically significant difference (P = .97). Similarly, mean preoperative FEV1 (61.3%) vs mean postoperative FEV1 (59.5%) revealed no significant difference (P = .41). Similar evaluations comparing the single best preoperative FVC (84.2%) and FEV1 (67.4%) and the single best postoperative FVC (83.0%) and FEV1 (67.0%) yielded no significant differences in PFT parameters before vs after ESS (P = .95 and .86, respectively). Evaluation of preoperative vs postoperative IV antibiotic use and inpatient hospital stay yielded 7 patients with sufficient data for analysis. When comparing preoperative vs postoperative IV antibiotic use in adult CF patients (Table 2), neither the total number of days of IV antibiotic use nor the total number of IV antibiotic courses demonstrated a statistically significant difference (P = .61 and P = .10, respectively). However, when comparing mean preoperative IHDs with postoperative IHDs, we found a statistically significant reduction in IHDs after ESS (P = .03, z = -2.20). Last, to assess whether the significant difference seen in IHDs was due to an increased use of outpatient IV antibiotic courses, we compared the difference between total days of IV antibiotic use minus the total number of preoperative inpatient days and postoperative inpatient days and found this to be statistically significant (P = .02).

COMMENT

The potential relationship between sinonasal disease and progression of pulmonary disease in CF patients remains unclear. A multicenter study by Dosanjh et al found a significant correlation in bacterial colonization between sinus cultures and endotracheal samples in CF patients. This finding raises the possibility of cross-infection from the sinus passages to the lower respiratory tract and, at the same time, raises the possibility that treatment of sinonasal disease could improve pulmonary disease, and hence survival, in CF patients.
Most studies evaluating ESS in CF patients have been restricted to the pediatric age group. Jarrett et al19 performed a retrospective review in 17 children with CF who underwent ESS and found no statistically significant difference in PFT results and ideal body weight preoperatively vs postoperatively. A study by Madonna et al,17 which also assessed the effect of ESS on postoperative PFT results up to a follow-up of 6 months after surgery. To our knowledge, only a few studies have addressed this variable in the adult CF patient population. A study by Kempainen et al20 that examined a series of adult CF patients reported no significant difference in PFT results after ESS, which is similar to our results. However, in regard to IHDs, their group also reported no significant difference, which is in contrast to our study findings. A mean decrease of 22 IHDs during a 1-year period, as was demonstrated in our study, could be considered a significant effect in the care of these adult CF patients. This finding has been shown in other series, such as the study by Rosbe et al,13 who found a significant decrease in hospitalization days after ESS. To explain these differences among studies, one could argue that the IHDs might have decreased as a result of more patients being treated with IV antibiotics in the outpatient setting during the postoperative period. By taking a closer look at our data, we found that the use of outpatient IV antibiotic courses in the postoperative period was significantly increased compared with preoperative use. We could then infer that, although the total number of days IV antibiotics were used did not change in the postoperative period, the clinical condition of the patients may have improved to a degree that would permit IV antibiotic treatment in the outpatient setting.

Another important variable to consider in the role of ESS in CF patients is relief of symptoms and quality-of-life improvement. A prospective study by Khalid et al21 used 2 validated disease-specific quality-of-life instruments (Rhinonasal Sinusitis Disability Index and the Chronic Sinusitis Survey) and found significant improvement in quality of life in adult CF patients that was comparable to adult non-CF patients also undergoing ESS. More recently, Virgin et al22 reported that adult CF patients undergoing ESS that included a modified endoscopic medical maxillectomy and comprehensive postoperative medical management had significant improvement in 1 validated disease-specific quality-of-life instrument (22-Item Sinonasal Outcome Test) up to 1 year postoperatively.

### Table 1. Preoperative and Postoperative FVC and FEV$_1$ for the 15 Adult Patients With Cystic Fibrosis

| Patient No. | Preoperative FVC | Postoperative FVC | Preoperative FEV$_1$ | Postoperative FEV$_1$
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>53.2 (59)</td>
<td>65.3 (68)</td>
<td>46.8 (50)</td>
<td>54.1 (57)</td>
</tr>
<tr>
<td>2</td>
<td>76.8 (86)</td>
<td>82.1 (92)</td>
<td>52.2 (59)</td>
<td>52.5 (63)</td>
</tr>
<tr>
<td>3</td>
<td>86.3 (91)</td>
<td>87 (87)</td>
<td>88 (93)</td>
<td>81 (81)</td>
</tr>
<tr>
<td>4</td>
<td>63 (81)</td>
<td>55.4 (62)</td>
<td>41.9 (54)</td>
<td>34.1 (42)</td>
</tr>
<tr>
<td>5</td>
<td>105.8 (116)</td>
<td>109.9 (124)</td>
<td>91 (101)</td>
<td>97 (112)</td>
</tr>
<tr>
<td>6</td>
<td>72.9 (79)</td>
<td>68 (70)</td>
<td>60.4 (66)</td>
<td>53 (57)</td>
</tr>
<tr>
<td>7</td>
<td>85 (96)</td>
<td>84.1 (89)</td>
<td>67.8 (77)</td>
<td>73.9 (86)</td>
</tr>
<tr>
<td>8</td>
<td>106.3 (111)</td>
<td>109.4 (113)</td>
<td>95.7 (101)</td>
<td>88.2 (102)</td>
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<tr>
<td>9</td>
<td>67.3 (73)</td>
<td>62.3 (73)</td>
<td>43.8 (48)</td>
<td>41.1 (44)</td>
</tr>
<tr>
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<td>91 (101)</td>
<td>75.9 (83)</td>
<td>78.3 (83)</td>
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<tr>
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<td>53.5 (61)</td>
<td>54.9 (60)</td>
<td>49.6 (55)</td>
</tr>
<tr>
<td>12</td>
<td>56 (62)</td>
<td>50.7 (58)</td>
<td>33.4 (36)</td>
<td>30.25 (30)</td>
</tr>
<tr>
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<td>84.7 (94)</td>
<td>71.2 (77)</td>
<td>59.7 (74)</td>
</tr>
<tr>
<td>14</td>
<td>38 (48)</td>
<td>42.6 (50)</td>
<td>26.5 (33)</td>
<td>26 (33)</td>
</tr>
<tr>
<td>15</td>
<td>93.5 (99)</td>
<td>95.1 (102)</td>
<td>69.5 (73)</td>
<td>72.9 (85)</td>
</tr>
<tr>
<td>Mean$^a$</td>
<td>76.4 (84.2)</td>
<td>76.1 (83.0)</td>
<td>61.3 (67.4)</td>
<td>59.5 (67.0)</td>
</tr>
</tbody>
</table>

Abbreviations: FEV$_1$, forced expired volume in 1 second; FVC, forced vital capacity.

$^a$For mean FEV$_1$ and mean FVC, $P = .41$ and .97, respectively. For best FEV$_1$ and best FVC, $P = .95$ and .86, respectively.

### Table 2. Mean Values for Preoperative and Postoperative IV Antibiotic Use and Inpatient Hospital Days

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of days of IV antibiotic use</td>
<td>65.6</td>
<td>70.6</td>
<td>.61</td>
</tr>
<tr>
<td>Total No. of antibiotic courses</td>
<td>3.4</td>
<td>2.9</td>
<td>.10</td>
</tr>
<tr>
<td>No. of Inpatient hospital days</td>
<td>59.1</td>
<td>36.7</td>
<td>.03</td>
</tr>
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</table>

Abbreviation: IV, intravenous.
Our study has a number of limitations that should be taken into account, including its retrospective nature, lack of a control group, and small sample size. Nonetheless, our study is one of the few studies investigating the adult CF population and the role of ESS. Furthermore, despite the small sample size, we found a significant decrease in IHDs after ESS in this group of adult CF patients.

In conclusion, our results indicate significant reduction in IHDs in the 1-year postoperative period after ESS in adult CF patients. However, no evidence is available from this small preliminary study that ESS improved lung function or the need for IV antibiotics in this patient group. Further investigation, in the form of a prospective study, is necessary for assessment of the definite role of ESS in the adult CF patient.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Henriquez, Wolfenden, DelGaudio, and Wise. Acquisition of data: Henriquez, Wolfenden, and DelGaudio. Analysis and interpretation of data: Henriquez, Wolfenden, Stecenko, DelGaudio, and Wise. Drafting of the manuscript: Henriquez and Stecenko. Critical revision of the manuscript for important intellectual content: Henriquez, Wolfenden, Stecenko, DelGaudio, and Wise. Statistical analysis: Wise. Administrative, technical, and material support: Stecenko. Study supervision: Wolfenden, DelGaudio, and Wise.

Conflict of Interest Disclosures: None reported.

Previous Presentation: This study was presented at the fall meeting of the American Rhinologic Society; October 3, 2009; San Diego, California.

Additional Contribution: Justin C. Wise, PhD, assisted with statistical analysis.

REFERENCES


