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What is This?
Long-term Sinonasal Outcomes of Aspirin Desensitization in Aspirin Exacerbated Respiratory Disease

Kyu-Sup Cho, MD, PhD1, Ethan Soudry, MD2, Alkis J. Psaltis, PhD, MBBS2, Kari C. Nadeau, MD, PhD3, Sean A. McGhee, MD3, Jayakar V. Nayak, MD, PhD2, and Peter H. Hwang, MD2

Abstract

Objective. This study aimed to assess sinonasal outcomes in patients with aspirin exacerbated respiratory disease (AERD) undergoing aspirin desensitization following endoscopic sinus surgery (ESS).

Study Design. Case series with chart review.

Setting. University hospital.

Subjects and Methods. A retrospective review of sinonasal outcomes was conducted for 30 AERD patients undergoing aspirin desensitization and maintenance therapy following ESS. Sinonasal outcomes were prospectively assessed by the Sinonasal Outcomes Test-22 (SNOT-22) and endoscopic polyp grading system. Data were collected preoperatively, 1 and 4 weeks postsurgery (before desensitization), and 1, 6, 12, 18, 24, and 30 months after aspirin desensitization.

Results. Twenty-eight of 30 patients (93.3%) successfully completed aspirin desensitization, whereas 2 of 30 (6.7%) were unable to complete desensitization due to respiratory intolerance. Of the 21 patients who successfully completed a minimum of 24 weeks of follow-up, 20 (95.2%) patients demonstrated sustained endoscopic and symptomatic improvement for a median follow-up period of 33 months. After surgical treatment but before desensitization, patients experienced significant reductions in SNOT-22 and polyp grade scores. In the first 6 months after aspirin desensitization, patients experienced further significant reductions in SNOT-22 scores, whereas polyp grade remained stable. The improvements in symptom endoscopic scores were preserved throughout the follow-up period after desensitization. No patients required additional sinus surgery. One patient had to discontinue aspirin therapy due to gastrointestinal side effects. No other adverse reactions to aspirin were noted.

Conclusion. Aspirin desensitization following ESS appears to be a well-tolerated and effective adjunctive therapy for long-term control of nasal polyposis in patients with AERD.

Keywords

aspirin exacerbated respiratory disease, asthma, desensitization, endoscopic sinus surgery, nasal polyps, sinusitis

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Introduction

Aspirin exacerbated respiratory disease (AERD) is a well-documented condition characterized by the triad of nasal polyps, bronchial asthma, and aspirin intolerance.1 Aspirin exacerbated respiratory disease is associated with 1 of the more severe forms of chronic rhinosinusitis2,3 marked by a larger polyp burden and higher rates of recurrence after endoscopic sinus surgery (ESS).4-7 Adjunctive medical treatments such as topical nasal steroids, leukotriene-modifier drugs, and oral steroids have all demonstrated some benefit in preventing polyp recurrence after ESS.8,9

Another adjunctive intervention that has been shown to improve sinonasal outcomes is oral aspirin desensitization.4,10-12 Aspirin desensitization has been associated with prolonged time to revision sinus surgery.13,14 However, previous published studies have had various limitations, including small sample size, limited documentation of symptoms and endoscopic findings, nonvalidated outcome measures, or a mixed population of preoperative and postoperative ESS patients.4,10,11

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This study examines our institution’s long-term outcomes of post-ESS aspirin desensitization in a population of AERD patients. We assessed sinonasal outcomes using endoscopic scoring systems and validated sinonasal symptom questionnaires.

**Subjects and Methods**

After receiving Stanford University Institutional Review Board approval, we conducted a retrospective review of all patients who had undergone aspirin desensitization at Stanford University from December 2009 through December 2011.

The following inclusion criteria were applied: (1) a diagnosis of asthma according to the Global Initiative on Asthma guidelines, present for at least 12 months; (2) medically refractory chronic rhinosinusitis, as defined by the consensus report of the Rhinosinusitis Task Force; (3) endoscopic evidence of bilateral nasal polyposis; (4) aspirin or nonsteroidal anti-inflammatory drug intolerance as indicated by a documented history of acute exacerbation of upper and/or lower airway symptoms after ingestion of either medication; and (5) postdesensitization follow-up of at least 24 months. Exclusion criteria included age younger than 18 years, pregnancy, immunodeficiency, and cystic fibrosis.

All patients underwent ESS, with the extent of surgery determined by the extent of disease based on endoscopy and imaging. The goal of surgery was removal of all visible polyps and clearing of all sinuses showing opacification or mucosal thickening on computed tomography (CT). No preoperative steroids were given, and intraoperatively, patients received a single intravenous dose of 8 mg of dexamethasone. Postoperatively, all patients received an oral prednisone taper (30 mg/day × 4 days, then 20 mg/day × 4 days, then 10 mg/day × 4 days) and topical steroid irrigation (budesonide 0.5 mg/250 cc saline bid), which was continued postdesensitization. Patients were also placed on oral zileuton in preparation for desensitization, if not already on the medication.

**Aspirin Challenge and Desensitization**

Four to 6 weeks following ESS, oral aspirin challenge and desensitization were performed. Patients were premedicated with montelukast, prednisone, and zileuton. Patients took 40 mg prednisone 24 hours prior to desensitization. Patients also underwent nasal endoscopy to ensure that there was no active infection and no gross recurrence of polyposis. Patients began with a 20.25-mg oral aspirin challenge, followed by escalating doses of aspirin, progressing through 40.5 mg, 81 mg, 162 mg, and 325 mg, administered at 90-minute intervals under intensive monitoring in an outpatient procedure room in the Department of Otolaryngology. Flow/volume spirometry, chest auscultation, and review of respiratory, nasal, and ocular symptoms were assessed every 30 minutes after dose administration. If nasal, ocular, or pulmonary symptoms occurred, the dosing interval was lengthened to 3 hours and dose escalation was resumed, provided that the symptoms had stabilized within the 3 hours.

Aspirin desensitization was discontinued if respiratory distress occurred and the patient’s peak expiratory flows remained 15% below baseline for more than 3 hours from the last dose despite treatment. The target cumulative dose for aspirin was 650 mg. If the target dose could not be achieved in 12 hours, patients were maintained on their highest tolerated dose until a second stage desensitization could be performed. Patients who attained the target dose of 650 mg were considered eligible for long-term maintenance therapy. At home, patients escalated their dose from 650 mg qd to 650 mg bid and returned for follow-up after 1 month. If a significant improvement in upper and lower airway symptoms was observed, the dose of aspirin was tapered as tolerated to either 650 mg qam and 325 mg qhs, or 325 mg bid. After reaching maintenance dose, some patients underwent a trial of discontinuation of zileuton at the discretion of the treating allergist. If no worsening of upper and lower airway symptoms was noted, the patients were allowed to remain off of the leukotriene inhibitor.

**Data Collection**

The following data were collected: age, sex, atopic status, comorbidities, number of prior surgeries, and preoperative Lund-Mackay CT. Patients were considered to be atopic if they had at least 1 positive skin test or in vitro blood test.

Subjective and objective sinonasal outcomes were prospectively acquired. Subjectively, patients’ symptoms were assessed using the Sinonasal Outcomes Test-22 (SNOT-22). The SNOT-22 assessed 12 nasal- and sinus-related symptoms and 10 psychological and behavioral symptoms on a scale of 0 (absent) to 5 (severe) for a total score between 0 and 110. Objectively, the extent of polyposis was determined with nasal endoscopy according to an established polyp grading system. Polyps were graded as follows: 0 if no polyps were present, grade 1 if polyps resided within the middle meatus (MM) but did not reach the inferior edge of the middle turbinate (MT), grade 2 if polyps existed within the MM and reached the inferior border of the MT, and grade 3 for polyps extending into the nasal cavity below the edge of the MT but not below the inferior edge of the inferior turbinate. Grade 4 was reserved for extensive polyposis filling the entire nasal cavity. The polyp grades from each side were added together for a total endoscopic polyp score, which was used for outcomes analysis.

The Sinonasal Outcomes Test-22 and endoscopic polyp scores were recorded within 3 months before surgery to establish the pretreatment baseline. Scoring was repeated between surgery and desensitization at 1 and 4 weeks post-surgery. Scores were also taken at 1, 6, 12, 18, 24, and 30 months after aspirin desensitization.

A successful response to aspirin desensitization treatment was defined as (1) successful completion of the aspirin desensitization protocol, (2) tolerance of daily aspirin dosing throughout the follow-up period, and (3) maintenance of the symptomatic and endoscopic score improvement achieved by ESS throughout the follow-up period. A postsurgical reduction of SNOT-22 score by at least 9 points was considered of clinical significance.
Statistical Analysis

Mean differences in objective and subjective scores pre- and post-ESS were analyzed by a paired t test using SPSS for Windows (version 16.0; SPSS Inc, Chicago, Illinois, USA). Preservation of subjective and objective outcomes after desensitization was statistically determined with a repeated-measures analysis of variance (ANOVA). A value of $P < .05$ was considered to be significant. Data are presented as mean ± standard deviation (SD).

Results

In the review period, 36 patients underwent aspirin desensitization for aspirin intolerance related to any medical indication. Six (16.7%) were excluded from this analysis because they had undergone aspirin desensitization for treatment of nonrhinologic disease such as coronary artery disease and thrombocytosis. Of the remaining 30 patients, all of whom had AERD, 2 (6.7%) were unable to complete desensitization because of aspirin-induced respiratory reactions during aspirin challenge. In addition, 3 were lost to follow-up and 4 were excluded due to insufficient postdesensitization clinical data. Twenty-one patients constituted the final study population for which sinonasal outcomes were analyzed (Figure 1).

Demographics and Baseline Characteristics

There were 11 men and 10 women from 24 to 70 years of age, with a mean age of 49.9 years. The median follow-up period for the study was 33 months (range, 24-45 months). All patients had a minimum of 24 months of follow-up, and 13 patients had at least 30 months of follow-up. Whereas 4 of 21 patients were undergoing ESS for the first time, the majority of the patients (17/21) had undergone prior ESS, with a mean ± SD of 2.0 ± 1.1 prior surgeries. Three patients had undergone prior aspirin desensitization at an outside institution without sinus surgery and presented to our clinic with persistent nasal polyposis and symptomatic, medically refractory chronic rhinosinusitis. The aspirin had been discontinued in all 3 patients at the time of presentation to our clinic.

Thirteen patients (61.9%) were atopic as demonstrated by positive allergy testing. The mean ± SD preoperative Lund-Mackay CT scores were 22.5 ± 2.6 on a 24-point scale. The most common presenting symptoms were nasal obstruction (90.5%) and hyposmia (76.2%). There were no perioperative or intraoperative surgical complications.

Subjective Outcomes

The mean ± SD preoperative SNOT-22 scores were 53.4 ± 12.4. After ESS but before desensitization, SNOT-22 scores significantly decreased to 14.5 ± 4.5 ($P = .042$) at 1 week postsurgery and 11.6 ± 2.5 ($P = .046$) at 4 weeks postsurgery. After completion of aspirin desensitization, SNOT-22 scores further decreased to 11.0 ± 2.3, 9.2 ± 2.1, 8.9 ± 1.7, 8.6 ± 1.8, 8.7 ± 1.6, and 8.9 ± 1.7 at 1, 6, 12, 18, 24, and 30 months postdesensitization, respectively (Table 1).

Compared to the best predesensitization score, the postdesensitization scores remained significantly improved at all time points throughout the follow-up period.

Nasal blockage and hyposmia subscores of the SNOT-22 were independently analyzed as these were the most common presenting symptoms. A significant improvement in symptom score was noted following ESS. The mean ± SD postsurgical SNOT-22 scores for nasal blockage and sense of smell were significantly decreased to 0.7 ± 0.6 and 1.2 ± 0.9 from 3.9 ± 1.2 and 4.1 ± 1.3, respectively ($P = .009$ and $P = .019$, respectively). This improvement was maintained postdesensitization throughout the follow-up period (Table 1).

**Objective Outcomes**

Compared to a mean ± SD preoperative endoscopic polyp score of 5.6 ± 1.2, postoperative endoscopic scores (before desensitization) were significantly decreased to 0.3 ± 0.5 at 1 week and 0.6 ± 0.8 at 4 weeks ($P < .001$ and $P = .001$, respectively). Following desensitization, endoscopic scores continued to remain low with values of 0.5 ± 0.9, 0.3 ± 0.7, 0.6 ± 0.7, 0.8 ± 0.5, 0.7 ± 0.5, and 0.6 ± 0.4 at 1, 6, 12, 18, 24, and 30 months, respectively. There was no significant worsening or further improvement of polyp score noted after desensitization, and no statistical differences were seen between the right and left sides (Table 2).
Success Rate of Aspirin Desensitization and Maintenance Dose

After successful completion of desensitization, all patients began aspirin therapy with 650 mg daily and subsequently decreased to the lowest effective dosage to minimize adverse effects while maintaining symptomatic improvement. The mean ± SD timing from initial to final maintenance dose was 4.3 ± 1.1 months. Final maintenance doses of aspirin ranged from 325 mg daily to 650 mg twice daily with a mean daily dosage of 845 mg. There was no significant correlation between final maintenance doses of aspirin and successful control of polyps or sinonasal symptoms (Table 3). After reaching maintenance dose, 18 of 21 patients (85.7%) had their zileuton successfully discontinued without a decline in subjective or objective scores. However, there was no significant difference in success rate according to discontinuation of zileuton.

Of the 21 patients, 20 patients (95.2%) were considered to have a successful response to aspirin desensitization following ESS according to the criteria outlined in the methods. One patient discontinued aspirin therapy at 13 months for gastrointestinal intolerance despite clinical improvement. Although a recurrence of grade 2 nasal polyposis was observed in this patient, her symptoms did not require additional surgery during the entirety of her follow-up period. She was classified as failing aspirin desensitization.

Adverse Reactions and Complications

The adverse reaction rate related to the desensitization procedure itself was 5.6% (2/36). Postprocedure, the adverse reaction rate of maintenance aspirin therapy was 4.8% (1/21). One patient, discussed in the previous section, experienced gastric pain and easy bruising during the first 2 months of therapy at a dose of 1300 mg/day. The patient’s symptoms diminished with a decrease in dosage to 650

Table 1. Changes in Sinonasal Outcomes Test-22 (SNOT-22) during Aspirin Desensitization following Endoscopic Sinus Surgery (n = 21).a

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Nasal Blockage Subscore</th>
<th>Sense of Smell Subscore</th>
<th>Total SNOT-22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>3.9 ± 1.2</td>
<td>4.1 ± 1.3</td>
<td>53.4 ± 12.4</td>
</tr>
<tr>
<td>POD 7</td>
<td>0.7 ± 0.6b</td>
<td>1.2 ± 0.9c</td>
<td>14.5 ± 4.5d</td>
</tr>
<tr>
<td>POD 28/AD day 0</td>
<td>0.3 ± 0.7e</td>
<td>0.8 ± 1.1ae</td>
<td>11.6 ± 2.5e</td>
</tr>
<tr>
<td>Post-AD 1 month</td>
<td>0.5 ± 0.8</td>
<td>1.3 ± 0.9</td>
<td>11.0 ± 2.3</td>
</tr>
<tr>
<td>Post-AD 6 months</td>
<td>0.4 ± 0.5</td>
<td>0.9 ± 0.4</td>
<td>9.2 ± 2.1</td>
</tr>
<tr>
<td>Post-AD 12 months</td>
<td>0.5 ± 0.7</td>
<td>1.1 ± 0.7</td>
<td>8.9 ± 1.7</td>
</tr>
<tr>
<td>Post-AD 18 months</td>
<td>0.3 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>8.6 ± 1.8</td>
</tr>
<tr>
<td>Post-AD 24 months</td>
<td>0.4 ± 0.5</td>
<td>1.4 ± 0.5</td>
<td>8.7 ± 1.6</td>
</tr>
<tr>
<td>Post-AD 30 months</td>
<td>0.4 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>8.9 ± 1.7</td>
</tr>
</tbody>
</table>

Abbreviations: AD, aspirin desensitization; POD, postoperative day; SD, standard deviation.

aData are expressed as mean ± SD.

bP = .009.
cP = .019.
dP = .042.
eP < .001.
fP = .046.
gData are based on a subcohort of 13 patients.

Table 2. Changes in Endoscopic Polyp Grade during Aspirin Desensitization following Endoscopic Sinus Surgery (n = 21).a

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Right</th>
<th>Left</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>2.8 ± 1.2</td>
<td>3.1 ± 1.1</td>
<td>5.6 ± 1.2</td>
</tr>
<tr>
<td>POD 7</td>
<td>0.2 ± 0.4b</td>
<td>0.1 ± 0.3b</td>
<td>0.3 ± 0.5b</td>
</tr>
<tr>
<td>POD 28/AD day 0</td>
<td>0.4 ± 0.5c</td>
<td>0.2 ± 0.4d</td>
<td>0.6 ± 0.8d</td>
</tr>
<tr>
<td>Post-AD 1 month</td>
<td>0.3 ± 0.5</td>
<td>0.3 ± 0.5</td>
<td>0.5 ± 0.9</td>
</tr>
<tr>
<td>Post-AD 6 months</td>
<td>0.2 ± 0.4</td>
<td>0.1 ± 0.3</td>
<td>0.3 ± 0.7</td>
</tr>
<tr>
<td>Post-AD 12 months</td>
<td>0.4 ± 0.5</td>
<td>0.3 ± 0.5</td>
<td>0.6 ± 0.7</td>
</tr>
<tr>
<td>Post-AD 18 months</td>
<td>0.5 ± 0.6</td>
<td>0.3 ± 0.5</td>
<td>0.8 ± 0.5</td>
</tr>
<tr>
<td>Post-AD 24 months</td>
<td>0.5 ± 0.3</td>
<td>0.3 ± 0.4</td>
<td>0.7 ± 0.5</td>
</tr>
<tr>
<td>Post-AD 30 months</td>
<td>0.4 ± 0.3</td>
<td>0.3 ± 0.4</td>
<td>0.6 ± 0.4</td>
</tr>
</tbody>
</table>

Abbreviations: AD, aspirin desensitization; POD, postoperative day; SD, standard deviation.

aData are expressed as mean ± SD.

bP < .001.
cP = .002.
dP = .001.

data are based on a subcohort of 13 patients.

Success Rate of Aspirin Desensitization and Maintenance Dose

Table 3. Success Rate of Aspirin Desensitization following Endoscopic Sinus Surgery According to Final Maintenance Dose of Aspirin.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Response</th>
<th>325 mg qd</th>
<th>325 mg bid</th>
<th>650 mg bid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success, No.</td>
<td>4</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Failure, No.</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Success rate, %</td>
<td>100.0</td>
<td>88.9</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice a day; qd, once a day.

After successful completion of desensitization, all patients began aspirin therapy with 650 mg twice daily and subsequently decreased to the lowest effective dosage to minimize adverse effects while maintaining symptomatic improvement. The mean ± SD timing from initial to final maintenance dose was 4.3 ± 1.1 months. Final maintenance doses of aspirin ranged from 325 mg daily to 650 mg twice daily with a mean daily dosage of 845 mg. There was no significant correlation between final maintenance doses of aspirin and successful control of polyps or sinonasal symptoms (Table 3). After reaching maintenance dose, 18 of 21 patients (85.7%) had their zileuton successfully discontinued without a decline in subjective or objective scores. However, there was no significant difference in success rate according to discontinuation of zileuton.

Of the 21 patients, 20 patients (95.2%) were considered to have a successful response to aspirin desensitization following ESS according to the criteria outlined in the methods. One patient discontinued aspirin therapy at 13 months for gastrointestinal intolerance despite clinical improvement. Although a recurrence of grade 2 nasal polyposis was observed in this patient, her symptoms did not require additional surgery during the entirety of her follow-up period. She was classified as failing aspirin desensitization.

Adverse Reactions and Complications

The adverse reaction rate related to the desensitization procedure itself was 5.6% (2/36). Postprocedure, the adverse reaction rate of maintenance aspirin therapy was 4.8% (1/21). One patient, discussed in the previous section, experienced gastric pain and easy bruising during the first 2 months of therapy at a dose of 1300 mg/day. The patient’s symptoms diminished with a decrease in dosage to 650
mg/day; however, she ultimately chose to cease aspirin therapy after 13 months due to ongoing gastric discomfort. There were no other adverse complications or discontinuations of aspirin in the remainder of the cohort.

Discussion

Aspirin desensitization has been recognized as a useful adjunct to ESS in the treatment of AERD patients. Although studies generally have reported benefit, the degree of improvement has varied according to different dosing protocols. Furthermore, there has been inconsistency in the outcome variables measured, with many studies using nonstandard outcomes measures for subjective and/or objective criteria. In 1996, Stevenson et al reported on 65 patients with AERD who were desensitized to aspirin and maintained on 1300 mg/day for a mean of 3.1 years. They showed a decrease in number of sinus infections per year, a decrease in number of revision surgeries required, and improvement in airflow after desensitization. However, symptomatic improvements were not assessed with validated instruments, and there were no endoscopic assessments. Furthermore, the postdesensitization clinical data were collected at a single time point by phone interview, up to 7 years postdesensitization, introducing potential recall bias. In contrast to our findings, Stevenson et al found that 17 of 65 patients required revision sinus surgery despite desensitization. It is notable that it was not specified that surgery was required immediately before desensitization as part of the treatment protocol. Berges-Gimeno et al reviewed a larger series of 172 patients followed for at least 1 year after desensitization and also found improvements in the number of sinus infections and ESS. Nasal symptoms and olfaction were also reported to be improved, but again, nonvalidated assessments were used, and no objective endoscopic data were collected.

In this study, we report prospectively acquired subjective and objective sinonasal outcomes for an extended follow-up period postdesensitization. In our cohort, the most significant symptomatic and endoscopic improvements occurred as a result of ESS to remove the inflammatory burden and anatomic obstruction of diseased tissue. Three patients in our study had a history of unsuccessfully undergoing prior aspirin desensitization without antecedent sinus surgery; all 3 were successfully re-treated in our study with surgery first followed by desensitization. Our findings are consistent with the general best-practice consensus from the literature that aspirin desensitization should be immediately preceded by surgical treatment of polyps. It is generally agreed that aspirin desensitization can reduce the regrowth of polyps in a sinus that has been surgically cleared of polyps, but it has no effect on the size of preexisting polyps that have not been surgically removed or have already recurred.

In our series, post-ESS aspirin desensitization was associated with an additive benefit to ESS as evidenced by a further 6-point reduction in SNOT-22 scores in the 4 weeks postdesensitization (in addition to the 9-point reduction observed between the time of surgery and desensitization). Although some of the postdesensitization symptom improvement could potentially be attributed to continued beneficial effects of the ESS, it is notable that aspirin desensitization was associated with a sustained preservation of the postsurgical improvements for the duration of the follow-up period. No significant decline was observed in either endoscopic or SNOT-22 score between 1 month and 30 months postdesensitization. Our findings are consistent with a recently published report by Havel et al, who reported favorable subjective and objective long-term outcomes using validated instruments in 56 patients followed for an average of 35 months. Using a target maintenance dose of 500 mg/day, Havel et al found very good tolerance with minimal attrition due to untoward side effects of aspirin.

The appropriate maintenance dose of aspirin remains a controversial issue. Although a dose as low as 81 mg of aspirin has been reported to maintain the desensitized state, it is usually considered suboptimal with respect to blocking lower respiratory tract inflammation. Although some reports have shown promising results with maintenance doses of 100 mg, a prospective clinical trial has shown worse outcomes versus a 300-mg maintenance dose. Our institution uses the more classic maintenance dose of 325 to 650 mg twice daily. This study showed no significant difference in the success rates achieved between patients using either maintenance dose, although the small sample size and low number of failures may partly explain this finding. Although not assessed in this study, previous evidence does suggest that aspirin maintenance therapy may need to be administered indefinitely to prevent polyph relapse. The patient in our study who discontinued aspirin therapy at 13 months did demonstrate polyp recurrence on interval follow-up examination. However, her symptoms remained adequately controlled, and therefore, revision ESS was not required through the duration of our study period.

Our successful completion rate of aspirin desensitization (93.3%) is consistent with prior literature indicating a 10% to 15% rate of unsuccessful desensitization due to lower respiratory intolerance. For those who successfully complete the desensitization process, there is some concern in the literature that chronic dosing of aspirin may lead to untoward side effects or complications, with an early study suggesting that up to 30% of patients using aspirin long term had to discontinue it due to gastric irritation. A more recent study reported a lower discontinuation rate of 9%, with use of protective medications such as proton pump inhibitors and misoprostol cited as a possible reason for improved tolerance.

In our relatively small series, we observed an even lower rate of gastric irritation (4.8%) and no other serious adverse effects, suggesting that higher maintenance doses of aspirin can be well tolerated on a long-term basis and can be titrated to the patients’ symptoms and endoscopic findings. One of the relative shortcomings of our study is the lack of a robust comparison group of patients not undergoing desensitization. Although we did not have a comparison nontreatment group in our study, there is abundant evidence that AERD patients show a strong propensity for recurrent polyposis after sinus surgery in the absence of desensitization. Historical cohort studies indicate that the natural course of polyp regrowth in AERD...
without desensitization typically begins around 6 months post-
surgery.3 In the 1 patient in our study who had to stop main-
teinance therapy, polyps in fact began to recur within 6 months
after discontinuation of aspirin. Havel et al12 compared their
desensitization cohort to a control cohort consisting of AERD
patients who underwent surgery without subsequent desensiti-
зation. They found significantly worse quality-of-life measures
and endoscopic polyp scores in the nondesensitized control
cohort at 1 year and 31 months posttreatment.

Although this study has the inherent limitations of a ret-
rospective review, we believe that our prospectively col-
lected data composed of validated outcomes measurements
do offer further support to the benefit of aspirin desensitiza-
tion following ESS in AERD patients. Although a placebo-
controlled, blinded study design would be ideal, such a trial
would not be practical given the inability to blind patients
being desensitized from the clinical effects of the aspirin
challenge.10,11,27

Conclusion
In patients with AERD, ESS clears gross nasal polyp burden
but does not address the underlying metabolic eicosanoid
derangement. Therefore, postoperative adjunctive therapy with
aspirin desensitization is an important component of the care
of patients with AERD and symptomatic nasal polyposis. Our
study demonstrates that aspirin desensitization following ESS
is well tolerated and efficacious. The majority of patients who
successfully complete ESS and aspirin desensitization can
expect improved control of polyyp recurrence and sustained
improvements in sense of smell and nasal obstruction in the
first 30 months postdesensitization. Longer term outcomes
data can be expected as this cohort continues to be followed
closely over time.

Author Contributions
Kyu-Sup Cho, analysis and interpretation of data, drafting and
revision, final approval, responsibility for content of manuscript;
Ethan Soudry, analysis and interpretation of data, revision, final
approval, responsibility for content of manuscript; Alkis J. Psaltis,
analysis and interpretation of data, revision, final approval, respon-
sibility for content of manuscript; Kari C. Nadeau, acquisition of
data, revision, final approval, responsibility for content of manu-
script; Sean A. McGhee, acquisition of data, revision, final
approval, responsibility for content of manuscript; Peter H. Hwang,
conception and design, drafting and revision, final approval, responsibility for content of manuscript.

Disclosures
Competing interests: Alkis J. Psaltis received an honorarium from
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