Standalone balloon dilation versus sinus surgery for chronic rhinosinusitis: A prospective, multicenter, randomized, controlled trial

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ABSTRACT

Background: A prospective randomized controlled study was conducted on patients with chronic rhinosinusitis (CRS) to test the hypotheses that symptom improvement after balloon dilation was noninferior to functional endoscopic sinus surgery (FESS) and balloon dilation was superior to FESS for postoperative debridements.

Methods: Adults with uncomplicated CRS of the maxillary sinuses with or without anterior ethmoid disease who met criteria for medically necessary FESS were randomized 1:1 to office balloon dilation or FESS and followed for 6 months. A minimum of 36 patients per arm were required to test the hypotheses with 90% power. Symptom improvement using the validated 20-item Sino-Nasal Outcome Test (SNOT-20) survey, debridements, recovery outcomes, complications, and revision surgeries were compared between groups.

Results: Ninety-two patients (50 balloon dilation; 42 FESS) were treated. Mean SNOT-20 improvement was 1.67 ± 1.10 and 1.60 ± 0.96 in the balloon and FESS arms, respectively. Both groups showed clinically meaningful and statistically significant (p < 0.0001) improvement and the balloon arm was noninferior (p < 0.001) to FESS. The mean number of postprocedure debridements per patient was 0.1 ± 0.6 in the balloon arm versus 1.2 ± 1.0 in the FESS arm, with the balloon group showing superiority (p < 0.0001). Occurrence of postoperative nasal bleeding (p = 0.011), duration of prescription pain medication use (p < 0.001), recovery time (p = 0.002), and short-term symptom improvement (p = 0.014) were all significantly better for balloon dilation versus FESS. No complications occurred in either group and one revision surgery was reported in each arm.

Conclusion: Balloon dilation is noninferior to FESS for symptom improvement and superior to FESS for postoperative debridements in patients with maxillary and anterior ethmoid disease. Balloon dilation is an effective treatment in patients with uncomplicated CRS who meet the criteria for medically necessary FESS.

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Chronic rhinosinusitis (CRS) is one of the most common diseases in the United States affecting an estimated 29.8 million adults.1 It has a significant negative impact on quality of life (QOL), and with an economic burden estimated to be as high as $8.6 billion annually in the United States it ranks as one of the 10 costliest physical health conditions.2 Medical management is the first line of therapy for patients presenting with CRS. If medical management fails and symptoms persist, functional endoscopic sinus surgery (FESS) is commonly performed.

Over the past 10 years, balloon dilation of sinus ostia and ethmoid infundibula has been shown to be safe and effective in the treatment of CRS.3–8 Although there is consistency in outcomes between case series and single arm studies, the absence of adequately powered, prospective, multicenter, randomized controlled trials (RCTs) comparing balloons with conventional surgery has prompted a call for an RCT to compare balloon ostial dilation to FESS.9–10 The objective of this RCT was to prospectively compare outcomes of office balloon dilation with FESS in the treatment of patients with uncomplicated CRS who met the requirements of medically necessary FESS. The study was designed to test two primary endpoint hypotheses; long-term symptom improvement after balloon dilation is noninferior to FESS and the number of postoperative debridements after balloon dilation is superior to FESS.

MATERIALS AND METHODS

Study Design and Oversight

This study (randomized evaluation of maxillary antrostomy versus ostial dilation efficacy through long-term follow-up [REMODEL]) was designed as a prospective, multicenter, open-label, RCT. The randomization was one-to-one between balloon dilation and control (FESS). All balloon devices used in the study were manufactured by Entellus Medical, Inc. Institutional Review Board approval was obtained for each investigational site and all patients provided voluntary informed consent before enrollment. Each investigator was board certified in otolaryngology and had experience with both balloon dilation and FESS procedures. An independent physician who was blinded to treatment assignment performed Lund-Mackay scoring of the baseline computed tomography scans and reviewed postoperative debridement details for consistency. Two additional independent physicians conducted an audit of the original case report forms, data management processes, and quality control measures to verify data outputs and results accurately reflected the case report forms received from the investigators. The Methods and Results sections were written in accordance with current randomized clinical trial reporting guidelines Consolidated Standards of Reporting Trials.11

Randomization assignments were generated by an independent statistician and stratified by clinical site using randomly permuted blocks to optimize balance at each site. The clinical sites, the treating physician, and the sponsor were blinded to the randomization assignments and the block sizes.

Inclusion and Exclusion Criteria

Eligible patients were at least 18 years of age and were diagnosed with either chronic or recurrent acute rhinosinusitis per the 2007 adult...
All patients had maxillary sinus disease with or without anterior ethmoid disease. Each patient also met the criteria for medically necessary FESS for uncomplicated rhinosinusitis per either the Anthem Coverage Guideline (CG-SURG-24; December 2011) or BlueCross BlueShield of North Carolina Medical Policy (August 2011) as described in Fig. 1. Patients with posterior ethmoid, sphenoid, or frontal rhinosinusitis requiring FESS or balloon dilation, as well as those with fungal sinusitis, severely deviated septum causing complete obstruction, or gross sinonasal polyposis were excluded. Patients who had previously undergone sinus surgery, those who underwent nasal surgery within 3 months before randomization, and anyone requiring concomitant sinonasal surgery at the time of the study procedure (e.g., septoplasty) were not eligible. Patients with ciliary dysfunction or Samter’s triad along with individuals either undergoing chemotherapy in the head/neck region or who were pregnant were also excluded from study participation.

Primary Endpoints
The first primary endpoint was long-term improvement in sinus symptoms as assessed by the mean change in overall 20-item Sino-Nasal Outcome Test (SNOT-20) score between baseline and 6-month follow-up. The SNOT-20 is a validated QOL outcome measure specifically for patients with rhinosinusitis. Patients rate the severity of 20 different symptoms on a scale of 0 (no problem) to 5 (problem as bad as it can be). A decrease of 0.8 of the mean SNOT-20 score is considered clinically meaningful. The second primary endpoint was the mean number of postoperative debridements defined as transnasal maneuvers performed within the nasal cavity to remove dead, contaminated, or adherent tissue or foreign material that may promote infection and impede healing occurring throughout the study period.

Secondary Endpoints
Secondary end points included recovery outcomes (postdischarge nausea, nasal bleeding, duration of analgesic use, and recovery time), short-term improvement in sinus symptoms, complication rate, and revision rate. Postdischarge recovery time was reported by each patient as the time to return to normal daily activities (i.e., baseline activity level before surgery). Short-term improvement in sinus symptoms was computed using the combined 1-week and 1-month changes in SNOT-20 scores from baseline. A complication was defined as a serious device-related or procedure-related adverse event. Revision surgery was defined as surgery on any sinus initially treated during the study procedure or surgery on a previously untreated sinus. Nasal surgeries performed over the duration of the study were also reported but not included in the calculation of revision rate.

Sample Size and Statistical Analysis
Sample size for both primary endpoints was calculated using PASS 2008. The minimum required sample size was driven by the long-term symptom improvement (SNOT-20) endpoint. A minimum of 36 subjects was required in each study arm to have 90% power to show noninferiority of balloon dilation with a margin of 0.8 compared with FESS at a one-sided \( \alpha \)-level of 0.025. The margin was established as the clinically meaningful difference from the developer of the validated SNOT-20 instrument (Piccirillo et al.\(^{15}\)). A minimum of 23 subjects was required in each arm to have 90% power to show superiority of balloon dilation over FESS for postoperative debridement rate at a one-sided \( \alpha \)-level of 0.025.

One-sided Student’s \( t \)-test was used to compare symptom improvement between study arms and a Wilcoxon signed-rank test was used to compare postoperative debridements per patient between study arms. Values of \( p < 0.025 \) were considered statistically significant. Repeated measures regression modeling was used to compare short-term symptom improvement between study arms. Two-sided Student’s \( t \)-tests were used to compare other continuous measures and Fisher’s exact tests were used to compare other categorical measures. For the secondary endpoint measures evaluated, a Benjamini-Hochberg\(^{17}\) adjustment for multiple comparisons was used to determine statistical significance and control the overall \( \alpha \) for the family of tests at 0.05. For other statistical tests, values of \( p < 0.05 \) were deemed statistically significant. An independent statistician calculated the required sample sizes and performed all statistical analyses. All analyses were performed using SAS Version 9.3 (SAS Institute, Cary, NC).

RESULTS

Patients and Procedures
Between December 2011 and December 15, 2012 a total of 105 adults at 10 sites were enrolled and either underwent treatment or withdrew before the study procedure. No study center contributed >20% of patient enrollments and results were consistent across sites. Of the 105 patients enrolled, 52 were randomly assigned to undergo balloon dilation and 53 to undergo FESS (Fig. 2). A total of 13 patients who underwent randomization withdrew their consent for treatment (2 in the balloon dilation arm and 11 in the FESS arm). Eight of the 11 patients who withdrew from the FESS group were unwilling to undergo sinus surgery. Ninety-two (50 balloon dilation and 42 FESS) patients were treated and 91 (98.9%) completed 6-month follow-up. There were no significant differences in any of the baseline characteristics between treatment study arms (Table 1).
A total of 98 balloon dilations of the maxillary ostia and ethmoid infundibula were attempted in the 50-patient balloon dilation group and 97 were successfully completed (3 unilateral and 47 bilateral) for a technical success rate of 99.0%. The balloon could not be placed into one maxillary ostium in a bilateral procedure. In the 42-patient FESS arm, 81 maxillary antrostomies with uncinctomies were attempted and 80 were successfully completed (98.8%), (4 unilateral and 38 bilateral). One FESS patient was treated under local anesthesia and the planned bilateral procedure was converted to a unilateral procedure because of uncontrolled sneezing and patient...
discomfort. A total of 41 concomitant anterior ethmoidectomies (3 unilateral and 19 bilateral) were performed in 22 patients. Accessory ostia were observed in 17 balloon patients and 9 FESS patients. All accessory ostia in the FESS group were joined to the primary maxillary ostia during surgery.

Primary Endpoints

Figure 3 shows the first primary endpoint of mean change in SNOT-20 symptom score between baseline and 6-month follow-up by study arm. The mean (±SD) SNOT-20 score improvement was 1.67 ± 1.10 in the balloon arm and 1.60 ± 0.96 in the FESS arm. Comparison of these changes between groups confirmed the mean symptom improvement for patients undergoing balloon dilation was noninferior to that of patients undergoing FESS (p < 0.001). Both study groups experienced clinically meaningful (mean change in score of ≥0.8) and statistically significant (p < 0.0001) improvement.

The results for the second primary endpoint of mean number of postoperative debridements per patient are shown in Table 2. There was a mean of 0.1 ± 0.6 postoperative debridements per patient in the balloon arm compared with 1.2 ± 1.0 in the FESS arm. This difference was significant (p < 0.0001) for balloon superiority. A total of 92.0% (46/50) of patients in the balloon dilation arm did not require a postoperative debridement and only 26.2% (11/42) of FESS patients did not require a postoperative debridement (p < 0.0001). In the FESS group, physicians removed clots in 55% (23/42) of patients, removed scabs in 43%, cleared early synechiae in 26%, removed crusting in 14%, and removed scar tissue in 5% of patients. In the balloon group, scabs were removed in 4% (2/50) of patients, synechiae were cleared in 2%, and scar tissue was removed in 2% of patients.

Secondary Endpoints

Postoperative recovery outcomes by study group are provided in Table 3. A total of 28.0% of the balloon dilation patients were discharged with nasal bleeding compared with 54.8% of the FESS patients (p = 0.011). On average, balloon dilation patients were able to return to normal daily activities faster (1.6 days) than FESS patients (4.8 days; p = 0.002). The balloon dilation patients took prescription pain medications for fewer days (0.9 days) compared with the FESS patients (2.8 days; p < 0.001). The mean short-term improvement in SNOT-20 score was better for patients in the balloon dilation arm than for patients undergoing FESS (p = 0.014; Table 4).

No (0%) complications occurred in either the balloon dilation arm or the FESS arm. One (2.0%) patient in the balloon dilation arm received revision sinus surgery on postoperative day 89 and one (2.4%) patient in the FESS arm received revision surgery on postoperative day 147. In the balloon patient, unilateral, left-sided endoscopic sinus surgery including maxillary antrostomy, uncinctomy, ethmoidectomy, and frontal sinusotomy was completed without issue. In the FESS patient, septoplasty, resection of a concha bullosa, bilateral maxillary antrostomy, and bilateral sphenoethmoidectomy were completed. Separately, two other FESS patients underwent additional nasal surgery during the study. One patient underwent bilateral turbinate reduction 98 days after the study procedure and the other

Table 2  Mean number of postoperative debridements per patient by study arm

<table>
<thead>
<tr>
<th></th>
<th>Balloon Dilation</th>
<th>Control (FESS)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>50</td>
<td>42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total No. of Debridements</td>
<td>7</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>0.1 ± 0.6</td>
<td>1.2 ± 0.9</td>
<td></td>
</tr>
</tbody>
</table>

*Based on a one-sided two-sample Wilcoxon test for superiority. Statistical significance is determined by comparing the p value to 0.025. In conclusion, the mean number of debridements for patients undergoing balloon dilation is superior (i.e., less debridements) to that for patients undergoing FESS. FESS = functional endoscopic sinus surgery.

Figure 3. Long-term change in 20-item Sino-Nasal Outcome Test (SNOT-20) score from baseline by study arm. The p value is based on a one-sided Student's t-test, with a noninferiority margin of 0.8. Statistical significance is determined by comparing the p value at the 6-month time point to 0.025. In conclusion, the mean 6-month improvement in SNOT-20 score for patients undergoing balloon dilation is noninferior to that for patients undergoing functional endoscopic sinus surgery (FESS).
underwent lysis of a scar band in the right nostril on postoperative day 218.

Subgroup and Subscale Analyses
Subgroup analyses of mean SNOT-20 score improvement at 6 months postprocedure were performed for the following characteristics: diseased sinuses (maxillary only or maxillary and anterior ethmoid), presence or absence of accessory ostia, presence or absence of septal deviation, and CRS diagnosis (chronic or recurrent acute; Table 5). Results were similar within and between study arms for all subgroups. That is, clinically meaningful (mean change in score of ≥0.8) and statistically significant (p < 0.0001) improvement was shown for each subgroup and there was no difference in improvement in any of the subgroups between the two study arms (p > 0.05). Analyses of mean SNOT-20 score improvement at 6 months postprocedure were performed for the following subscales: rhinological symptoms, ear/facial symptoms, sleep function, and psychological function.21,22 Both study arms experienced clinically meaningful and statistically significant (p < 0.0001) improvement in each of the four subscales and there was no difference in improvement in any of the subscales between the two study arms (p > 0.05).

DISCUSSION
This is the first prospective, multicenter, RCT with sufficient statistical power to compare sinus ostial balloon dilation to FESS for the treatment of medically refractory CRS. In this study examining patients with maxillary and anterior ethmoid disease, we found that balloon dilation is noninferior to FESS with respect to long-term symptom improvement and that balloon dilation is superior to FESS in terms of number of postoperative debride ments. Four secondary endpoints including postoperative occurrence of nasal bleeding, prescription pain medication use, recovery time, and short-term symptom improvement were statistically lower or quicker for balloon dilation patients compared with FESS patients. No differences in complication and revision rates were observed between the two groups.

Subgroup analyses showed that dilation of maxillary ostia and ethmoid infundibula resulted in symptom improvement for patients with maxillary and anterior ethmoid disease that was as good as improvement in those with maxillary-only disease, suggesting the importance of infundibular dilation. In addition, the similar magnitude of symptom improvement obtained for balloon patients presenting with an accessory ostium and FESS patients presenting with an accessory ostium in which all ostia were connected to the primary ostium, suggests it may be acceptable to leave accessory ostia untreated when sinus ostial dilation is performed. Although these favorable trends in both groups are useful because they have not been previously shown in a randomized trial, the sample sizes are too small to draw definitive conclusions. Our study results and conclusions are strengthened by the fact that 98% of treated patients returned for 6-month follow-up and by the absence of any differences in baseline characteristics between the study groups.

We used the validated SNOT-20 survey to assess the primary endpoint because it is one of the most commonly used instruments to measure patient sinus symptom status before and after FESS or balloon dilation procedures.20 Because rhinosinusitis symptoms have been linked to depression, fatigue, poor sleep, and anxiety, QOL instruments like the SNOT-20 can also help physicians tailor patient treatment to achieve clinically meaningful improvements and optimal outcomes.21 Although QOL surveys are subject to patient recall bias, this was mitigated in our study by the frequency of follow-up survey use. In addition, assessment of QOL at 6 months has been established as an acceptable long-term primary endpoint for use in rhinosinusitis clinical trials.22

Postoperative debridement rate was chosen as a relevant second primary endpoint because these procedures are uncomfortable for patients, require return trips to the office, and add to the overall cost of sinus surgery. Because physicians performing debride ments in this study can not be blinded to treatment arm, the frequency of performing debridement could be influenced by prior habits or beliefs of the surgeon, representing a potential limitation of the study. The reasons for debridement were documented and an external reviewer determined that the reasons for debridement appeared clinically appropriate to verify debridement was performed as a medical necessity rather than standard policy. Despite these limitations, a recent evidence-based review recommended debridement as an early postop-
erative intervention and debridement after FESS may be necessary to reduce crusting and adhesion formation. In a survey of otolaryngologists who perform postoperative debridement, it was found that 87.1% performed between one and three debridements per each FESS patient. Earlier studies reported debridement rates per patient following standalone balloon dilation procedures that ranged from 0.15 to 0.8. Because debridement rates reported in our study were low (balloon, 73%; FESS, 62.5%) at 12 months and consistency of outcomes relative to other published data show the REMODEL study design has sufficient rigor to support its statistical findings and conclusions.

**CONCLUSION**

Adult patients with maxillary and anterior ethmoid sinus disease who fail medical management and meet surgical criteria for uncomplicated CRS experience long-term symptom improvement after balloon dilation that is noninferior to the improvement also occurring after FESS. Balloon dilation results in fewer postoperative debridements than FESS, indicating superiority of the balloon arm. In addition, the number of patients discharged with nasal bleeding, duration of prescription pain medication use, recovery time, and short-term symptom improvement are all significantly better in patients who undergo balloon dilation compared with FESS. Balloon dilation and FESS are both safe because neither procedure produced any serious adverse events and the durability of each has been established via very low reported rates of revision surgery within each treatment arm.

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**Table 5** Subgroup analyses of long-term change in SNOT-20 score from baseline

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Balloon Dilation</th>
<th>Control (FESS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean Change ± SD</td>
</tr>
<tr>
<td>Diseased sinuses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillary only</td>
<td>30</td>
<td>−1.62 ± 1.15</td>
</tr>
<tr>
<td>Maxillary and anterior ethmoid</td>
<td>18</td>
<td>−1.74 ± 1.03</td>
</tr>
<tr>
<td>Accessory ostium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17</td>
<td>−1.76 ± 1.38</td>
</tr>
<tr>
<td>No</td>
<td>31</td>
<td>−1.62 ± 0.93</td>
</tr>
<tr>
<td>Septal deviation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28</td>
<td>−1.67 ± 1.15</td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>−1.67 ± 1.05</td>
</tr>
<tr>
<td>CRS diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic (&gt;12 wk duration)</td>
<td>32</td>
<td>−1.72 ± 1.12</td>
</tr>
<tr>
<td>Recurrent acute (≥4 episodes in 1 yr)</td>
<td>16</td>
<td>−1.57 ± 1.08</td>
</tr>
</tbody>
</table>

*The p value from paired t-test, testing if change between baseline and 6-mo follow-up statistically different from zero.
#The p value from two-sample t-test, comparing changes from baseline between study arms.

CRS = chronic rhinosinusitis; FESS = functional endoscopic sinus surgery; SNOT-20 = 20-item Sino-Nasal Outcome Test.
REFERENCES


15. Piccirillo J, Merritt MG Jr, and Richards ML. Psychometric and clini-


