Two-year results: transantral balloon dilation of the ethmoid infundibulum

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Background: Multiple prospective and retrospective studies have reported results from balloon-only procedures and hybrid balloon sinus surgeries through intermediate follow-up periods of up to 1 year. Long-term durability results beyond 2 years are limited.

Methods: One-year results from the original study of standalone transantral balloon dilation in patients with computed tomography (CT) evidence of chronic inflammation in the maxillary sinuses alone or maxillary and anterior ethmoid sinuses combined were previously reported. Revision rate, symptom improvement, and productivity improvement were prospectively evaluated after a minimum follow-up of 2 years.

Results: Fifty-nine patients (107 maxillary ostia) underwent balloon dilation of the maxillary sinus outflow tract and completed postprocedure follow-up assessment at 27.0 ± 3.6 months. Patient 20-item Sino-Nasal Outcome Test (SNOT-20) score improved from 2.65 ± 0.97 at baseline to 0.79 ± 0.71 at long-term follow-up (p < 0.0001). Improvement in work productivity and activity due to sinus-related health issues for all patients was statistically significant across all survey instrument characteristics (p range, <0.0001 to 0.02). An analysis of the outcomes in a subgroup of patients with maxillary and anterior ethmoid disease (20; 34%) showed similar significant improvement in symptoms (SNOT-20 decrease = −2.1; p < 0.0001). Approximately 92% of all patients reported satisfaction with the balloon procedure. Four (6.8%) patients underwent revision sinus surgery at 11.1 ± 7.3 months after treatment.

Conclusion: Patients with chronic rhinosinusitis and radiographic evidence of isolated maxillary disease with or without anterior ethmoid disease have reported clinically meaningful and statistically significant improvement in symptoms, productivity, and activity through a minimum of 2 years following standalone balloon dilation.

Key Words: balloon; dilation; transantral; ostia; maxillary; infundibulum

How to Cite this Article: Stankiewicz J, Truitt T, Atkins J, et al. Two-year results: transantral balloon dilation of the ethmoid infundibulum. Int Forum Allergy Rhinol, 2012; 00:X–XX

Endoscopic sinus surgery (ESS) is the current standard of care to treat chronic rhinosinusitis (CRS) after failure to respond to maximum medical therapy and is intended to reestablish normal aeration and mucociliary outflow of the paranasal sinuses. The primary reasons conventional sinus surgeries fail include scarring and stenosis, adhesions, residual air cells, mucous recirculation, and polyps/polypoidal tissue. Balloon dilation makes it possible to safely widen the sinus outflow tract without removing tissue, and postoperative debridements to facilitate healing have been reported to be less frequent following balloon dilation.1,2 Feasibility, safety, and outcomes studies using balloon catheters to dilate the drainage pathways of the sinuses alone or in conjunction with traditional techniques (ie, “hybrid” procedures) have successfully demonstrated that balloon catheters have a role in the treatment of persistent and recurring rhinosinusitis.1–9

Despite encouraging results from a growing number of studies designed to evaluate balloon-based interventions in rhinology, physicians and healthcare payers alike continue to acknowledge the need for prospective comparative studies and longer-term follow-up data to better assess the sustainability of the improvement. In addition, there may be potential cost implications if the effectiveness of this

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Potential conflict of interest: J.S., T.T., and P.C. are paid consultants for Entellus Medical; T.T. and J.A. are paid consultants and stock shareholders for Entellus Medical.

Received: 15 August 2011; Revised: 29 November 2011; Accepted: 19 December 2011

DOI: 10.1002/alr.21024

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technology is not durable and leads to a higher rate of repeat sinonasal procedures as compared to traditional ESS. This prospective study records patient outcomes between 2 and 3 years after successful completion of standalone balloon dilation. The primary objective of this long-term analysis is to provide further evidence that ostial dilation without tissue removal can provide chronic symptom relief and significant improvement in quality of life (QOL) with a rate of revision surgery similar to those reported for standard of care endoscopic surgical methods.

Patients and methods
This multicenter Balloon Remodeling Antrostomy Therapy (BREATHE) Long-Term Follow-Up Study (NCT01319305) was designed to prospectively collect QOL (e.g., sinus symptoms; work productivity, and activity) and revision sinus surgery data through a minimum of 2 years after patients underwent balloon dilation with FinESS™ sinus treatment. This study supplements previously reported 1-year results from the original BREATHE I (NCT00645762) study population and extends the durability assessment of transantral balloon dilation through at least 2 years.4 The study was conducted under a common protocol with approval from a central Institutional Review Board (IRB) and all patients voluntarily agreed to participate. Patient demographic data, the balloon procedure itself, operative data, and 1-year results from the BREATHE I study have been previously reported.4–6 Adults aged 18 years and older diagnosed with CRS and radiologic evidence of infundibular narrowing and at least 2 mm of mucosal thickening or an air/liquid level in the maxillary sinus antrum were enrolled in the study. Patients with concurrent disease in the anterior ethmoid sinuses were also eligible to participate whereas those with evidence of any combination of posterior ethmoid, frontal, or sphenoid sinus disease were excluded. Patients with fungal sinusitis or a history of any of the following conditions were also ineligible: previous sinus surgery, primary ciliary dysfunction, Samter’s triad, cystic fibrosis, midfacial/orthognathic surgery, significant polyp disease, severe septal deviation, known sinonasal tumors/obstructive lesions, or insulin-dependent diabetes. BREATHE I patients who remained active through the end of the study and were not lost to follow-up at 1 year were asked to complete 1 additional assessment at a minimum of 2 years after the date of balloon dilation of the maxillary ostia and ethmoid infundibula. This assessment could be completed either in the clinic or via mail. The following validated QOL instruments were included in the long-term follow-up evaluation: 20-item Sino-Nasal Outcome Test (SNOT-20),10 Work Productivity and Activity Impairment (WPAI) Questionnaire,11 and Work Limitation Questionnaire (WLQ).12 Medical records and patient data were also reviewed to capture the occurrence of any revision surgeries. The long-term follow-up study was initiated after the last patient enrolled in the BREATHE I study completed 1-year follow-up. Therefore, patients who were enrolled early on in the BREATHE I study completed long-term follow-up evaluation more than 2 years after balloon dilation; in some cases, assessment in this long-term study was performed approximately 3 years after the BREATHE I study procedure.

A repeated measures regression model was fit to compare the overall SNOT-20 scores at 6- and 12-month follow-up in those patients who participated in this long-term study vs those who did not. All available SNOT-20 scores from the 6- and 12-month visits were used as the outcome in the model. The following were used to adjust the model: baseline SNOT-20 score, follow-up visit, and an indicator for whether or not the patient continued in the long-term study. A compound symmetry covariance structure was used to model within patient variability.

Standard summary statistics were calculated for all study variables by an independent statistician. Categorical variables were summarized using frequency distributions, and continuous variable statistics included means, standard deviations, and ranges. Paired t tests were used to evaluate whether the change in outcomes from baseline to follow-up were statistically different from zero. All statistical tests were 2-sided, with p values less than 0.05 deemed statistically significant. All analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

Results
A total of 71 patients (131 maxillary sinus ostia) were previously enrolled and treated with standalone balloon dilation in the BREATHE I study across 11 study centers. Sixty-seven patients completed 1-year follow-up requirements per protocol while 4 patients voluntarily withdrew or were lost-to-follow up after the index procedure. Three study centers (5 patients) did not participate in this BREATHE I long-term follow-up study due to lack of study coordinator resources, physician interest, or length and cost of local IRB approval. Therefore, a total of 62 patients were eligible to participate in this long-term follow-up study and 59 patients (107 ostia) successfully completed the 2-year evaluation (95% patient retention). The average duration between the study procedure and long-term follow-up evaluation was 27.0 ± 3.6 (range, 21.9–34.4) months.

The average age of the 59 patients who enrolled in the long-term outcome study was 48.0 ± 14.4 years. Females (68%) and Caucasians (93%) made up a majority of the study population and 88% never smoked or stopped smoking before study participation. Approximately 37% of the patients suffered from respiratory allergies all year long while 42% had no history of allergies. Sixty-six percent (39) of the population presented with radiologic evidence of chronic maxillary-only sinusitis while 34% (20) of the patients also had evidence of anterior ethmoid disease. Inflammation in the left and right maxillary antrums where the ostia were treated with balloon dilation measured 5.4 ± 4.8 mm and 6.7 ± 6.1 mm, respectively. In the
A 20-patient cohort characterized as having concurrent anterior ethmoid disease, less than 25% of the anterior ethmoid cells showed opacification in a majority (60%) of the patients. Also enrolled and treated were 6 patients (30%) with 25% to 50% of the anterior ethmoid cells opacified and 2 patients with 50% to 75% of these air cells opacified. None of the patients had greater than 75% of the anterior ethmoid cells showing opacification. Forty-five (76%) of the patients underwent balloon dilation in the operation room whereas 14 (24%) were successfully treated in the clinic setting.

There were 12 BREATHE I patients who did not continue on to participate in this long-term follow-up study. Eleven of these patients had 6-month SNOT-20 score data available and 8 patients had 12-month data available. To address the potential issue that only patients with the most improved SNOT-20 scores were selected to participate in long-term follow-up (N = 59), a repeated measures analysis was done using 6- and 12-month SNOT-20 scores. Among the 12 patients who did not continue in BREATHE I through long-term follow-up, average SNOT-20 scores at 6 and 12 months were 0.93 ± 0.65 and 1.18 ± 0.80, respectively. Patients who participated in the long-term follow-up assessment had average SNOT-20 scores of 0.79 ± 0.91 and 0.82 ± 0.79, at 6 and 12 months, respectively. There was no statistical evidence of a difference in SNOT-20 scores between those who were included in the long-term follow-up cohort and those who were not (p = 0.35).

Sinonasal symptom improvement
Patient symptoms were measured with the SNOT-20 survey instrument. The aggregate data were analyzed for all patients as well as for the following cohort groups: (1) patients with isolated maxillary disease; (2) patients with maxillary and anterior ethmoid disease. For all patients (N = 59), the average symptom score improved from 2.65 ± 0.97 at baseline to 0.79 ± 0.71 (p < 0.0001) at long-term follow-up. Figure 1 shows the symptom improvement by sinuses affected from baseline through long-term (ie, 2-year minimum) follow-up. The 20 questions of the survey were also grouped into symptom categories to further assess the severity of rhinological symptoms, ear/facial symptoms, sleep function, and psychological issues (eg, concentration, frustration, sadness, embarrassment) related to each patient’s sinus disease. At baseline assessment each patient was asked to specify which 5 of the 20 questions were most important to him or her. The improvement, or lack thereof, of these 5 symptoms was also evaluated over the study duration. Table 1 provides the average and change in SNOT-20 scores by category. Symptom improvement was confirmed by a reduction in the average symptom score (ie, negative Δ) and the absolute value of the difference between follow-up and baseline scores remained clinically meaningful (Δ ≥ 0.8) (Table 2). Patients were also asked upon completion of the long-term assessment if they were satisfied with the study procedure. Fifty-four patients (91.5%) responded that they were satisfied with the balloon procedure whereas only 5 answered that they were dissatisfied.

Productivity and activity improvement
Limitations on patient activity, on-the-job productivity, and other workplace demands due to sinusitis before and up to 1 year after balloon dilation have been previously reported. Statistically significant improvement in all work

![FIGURE 1. Average SNOT-20 scores by sinuses affected.](image-url)
productivity and activity metrics as measured by the WPAI questionnaire and the WLQ was sustained through long-term follow-up. Figure 2 shows the WPAI results at each study follow-up interval and included an assessment of on-the-job productivity (ie, presenteeism) and overall productivity loss due to sinus-related problems. Similarly, Figure 3 shows the WLQ results where cognitive and social interaction skills were included in the “mental/interpersonal” metric and “output” measured the quality, quantity, and timeliness of an employee’s work. The \( p \) values in each figure show the level of significance between long-term follow-up and pretreatment baseline values. The level of significance is similar to those \( p \) values computed at all of the previous study intervals and further demonstrates consistent and sustained improvement for a minimum of 2 years after balloon dilation.

**Revision surgery**

A total of 4 patients (6.8%) underwent a revision ESS at an average of 11.1 ± 7.3 months after balloon dilation. One patient underwent a bilateral maxillary antrostomy plus unilateral balloon sinuplasty on the left sphenoid sinus 5.4 months after the study procedure to treat
persistent maxillary sinus/infundibular disease and exacerbation of sphenoid sinus disease. A septoplasty was also performed at the time of the revision sinus surgery. Another patient failed to improve and underwent a bilateral maxillary antrostomy and anterior ethmoidectomy approximately 5.6 months after balloon dilation. Two additional patients were also revised using traditional ESS techniques at 12.9 and 20.7 months postprocedure to treat chronic sinusitis. One patient had a bilateral maxillary antrostomy, total ethmoidectomy, frontal sinusotomy, septoplasty, and bilateral turbinate coblation, while the other patient had a bilateral maxillary antrostomy, total ethmoidectomy, and frontal sinusotomy.

**Discussion**

One of the objections to the adoption of balloon catheters as either a potential tool or procedure to treat sinus disease has been the absence of long-term durability data to confirm acute posttreatment improvement is sustained over time and without the need for additional surgery. In 1 multicenter study that was conducted to evaluate the point in time in
which QOL outcomes stabilize following ESS, the results demonstrated that QOL improvements did not fluctuate between 6 and 20 months after surgery. Although early symptom improvement following balloon dilation may be insufficient to evaluate the long-term benefit, the significant improvement that was observed in the BREATHE I study population as early as the 1-week postoperative visit was sustained through 2 years. Interestingly, in this study population the average SNOT-20 score for all 59 patients at 6-month follow-up was 0.79 ± 0.91 (p < 0.0001) and 0.79 ± 0.71 (p < 0.0001) at 27.0 ± 3.6 months post-procedure. This data further supports the conclusion that 6-month follow-up may be sufficient to adequately assess QOL endpoints and future clinical trial designs may consider shorter follow-up duration when aiming to prove primary QOL-based primary study hypotheses.

Another challenge when reporting aggregate QOL improvements across a controlled, prospective trial is the potential disparity between improvement that is statistically significant but not clinically meaningful to the patient. To address this, the SNOT-20 survey was selected in part because the authors of the instrument specified the minimum numeric change in symptom score between preoperative and postprocedure values that is considered clinically meaningful to the patient (ie, Δ ≥ 0.8). In the BREATHE long-term follow-up study population, 56 of 59 (95%) patients had symptoms scores greater than 0.8 at baseline and were therefore capable of a potential improvement ≥ 0.8. Of this subgroup, 48 (86%) demonstrated clinically meaningful improvement through a minimum of 2-year follow-up.

In addition to the classic symptoms of chronic sinusitis (ie, facial pain/pressure; thick nasal discharge; postnasal discharge), the collateral impact of sinusitis on QOL due to increased fatigue and other ancillary factors has also been well-documented.5,14 Not surprisingly, when the average numeric symptom score from each SNOT-20 survey question at baseline is ranked in order from most to least severe, the 5 largest changes in symptom severity from the BREATHE population of 59 patients demonstrated clinically meaningful improvement through a minimum of 2-year follow-up.

There have been several published reviews that have summarized the clinical evidence of balloon dilation in the treatment of CRS. One of the cited methodological limitations of a majority of these studies is the absence of a prospective comparative arm, and the BREATHE I 1-year and long-term follow-up trials are no different. However, the paucity of level 1 data is not unique to these trials and is also true for the large volume of ESS literature describing the benefits of ESS in the treatment of persistent and recurring sinus disease. There are, however, several design elements of the study presented here that warrant elaboration.

To date, this is 1 of the largest prospective long-term evaluations of standalone balloon dilation to treat CRS and the results are strengthened by a high patient retention rate (59/71; 83%) through a minimum of 2 years after the study procedure. Another prospective ostial dilation study of 115 patients was conducted with follow-up through 2 years, and of the 61 patients from the original cohort who completed 2-year follow-up, almost 50% (29) underwent ESS in conjunction with balloon dilation of at least 1 sinus (ie, hybrid procedure).3 The mean SNOT-20 scores for the 32 balloon-only patients improved from 2.09 at baseline to 1.09 at 2-year follow-up (Δ = −1.00; p < 0.001) compared to the change of −1.83 (p < 0.0001) in symptom status from the BREATHE population of 59 patients.

It is recognized that the results from balloon studies that allow traditional endoscopic sinonasal surgical procedures in conjunction with sinus ostial dilation may limit the ability to determine which intervention(s) contributed most to patient improvement. Treatment in the BREATHE I study was restricted to transantral balloon dilation of the maxillary sinus outflow tract. It has been suggested by Batra et al.16 that 2 simultaneous treatments, transantral access and balloon dilation, were performed, but there is no data on standard of care practice within rhinology today to suggest 1-time, transantral access is a treatment for CRS nor is there any anatomic or physiologic rationale to suggest antral puncture alone would provide therapeutic benefit for a disease linked to obstruction in the osteomeatal complex.

Because patients who participated in this study were counseled on the 2 primary surgical options that could be performed to treat their chronic disease (ostial dilation, ESS) but volunteered to undergo balloon dilation rather than the surgical alternative, it is possible those who consented to the study did so to avoid conventional surgery or a general anesthesia procedure. It is also possible that patient preference for a less-invasive procedure may have influenced the self-reported severity of his/her sinus symptoms. Although it is possible this bias could have affected perceived symptomatic improvement at the early follow-up visits, because all patient-completed QOL surveys at long-term follow-up were collected via mail and without any contact with the study physician, it is less likely that long-term symptom severity was influenced by patient bias or the physician investigator.

One of the most important goals of any surgical intervention to treat CRS is improvement of QOL.13 With this in mind, and because the BREATHE I study evaluated balloon dilation in patients with isolated disease in the maxillary and anterior ethmoid sinuses, radiological assessment at 2-year follow-up was not performed. Although Lund-Mackay grading is recognized as 1 of most established classification systems to quantify the extent of sinus disease present on CT scan, published data indicate radiographic evidence...
does not correlate to patient symptoms. In addition, patients with low Lund-Mackay scores have been shown to experience significant improvement in QOL after undergoing ESS even though their CT scans suggested disease was minimal. Therefore, despite the absence of 2-year radiological scans, the results presented here support the clinical rationale for offering patients with mild to moderate mucosal thickening in the maxillary and anterior ethmoid sinus the option to undergo an interventional procedure to treat their sinus symptoms and improve QOL.

Preservation of sinus mucosa and natural ciliary function has influenced the evolution of sinus surgery techniques over the past 30 years. Postoperative scarring, stenosis, and obstruction of sinus mucociliary flow are the primary causes of failed sinus surgery. The reported revision rate for traditional ESS has ranged between 8% and 13% with a slightly lower rate of repeat surgery (6%–7%) when the frontal sinuses were not involved. In 1 prospective cohort study, revision rates in CRS patients with and without nasal polyps were reported at 1, 3, and 5 years following sinus surgery and showed the rate of revision surgery increased at all time points in both groups. At 5-year follow-up, 15.5% of the CRS patients underwent revision surgery compared to 20.6% of the CRS patients with polyps. Disease severity and the extent of baseline surgery reported in these studies was highly variable. Some excluded patients with severe polyposis, Samter’s triad, or ciliary dysfunction, while others included patients with more advanced disease and severe polydisease. In addition, postoperative care including nasal cavity debridement was variable.

Balloon dilation studies of the sinus ostia, on the other hand, have historically excluded patients with a history of extensive nasal polyps, Samter’s triad, ciliary dyskinesia, immune disorders, facial fractures, aberrant sinonasal anatomy, or failure of previous sinus surgery. Postoperative care was also different. For patients who only underwent balloon dilation procedures, the average number of postoperative debrideents ranged from 0.43 to 0.8 per patient as compared to approximately 1.5 debridements per patient in those patients who underwent conventional sinus surgery combined with ostial dilation. Revision rates reported from these balloon studies have varied between 2.4% and 9.2%.

In this BREATHE I long-term study, patients with a comorbid history of similar to the other balloon studies were excluded and enrollment was limited to those patients with mucosal inflammation contained within the maxillary/anterior ethmoid sinuses and the bony outflow tract. Treatment was restricted to balloon dilation alone and only 2 postprocedure debridements were performed throughout the duration of the study (average 0.03 debridements per patient). Although a randomized study of patients with similar sinus disease severity and extent of sinonasal surgery is required to compare postoperative wound care and subsequent long-term surgery success (ie, absence of revision surgery, sustained symptom improvement) between balloon dilation and conventional ESS, the BREATHE I revision rate at 2-year follow-up is within the range reported from the other balloon dilation and ESS studies.

Conclusion
Ostial dilation in patients with less-advanced disease who have not previously undergone sinonasal surgery has been shown to be safe whether performed under general anesthesia in an operating room or in the clinic setting with a combination of topical and local anesthesia only. Patients with persistent sinusitis unresponsive to medical therapy and isolated to the maxillary and anterior ethmoid sinuses may also experience sustained, clinically meaningful improvement in their sinus symptoms following balloon dilation of the maxillary ostia and ethmoid infundibulum. Significant improvement in QOL after standalone balloon dilation remains durable through a minimum of 2 years and the rate at which patients require additional surgical interventions (ie, repeat ostial dilation, conventional ESS) to treat their ongoing sinus disease is relatively low and within the range of published revision rates following other surgical interventions.

Acknowledgments
James Atkins, Jr., MD, Paul Cink, MD, Diana Henderson, MD, Brent Lanier, MD, Howard Loveless, MD, Joseph Raviv, MD, Theodore Truitt, MD, and Bradford Winegar, MD, along with their study staffs, collected the long-term follow-up data.

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