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Balloon Dilation of the Eustachian Tube: 12-Month Follow-up of the Randomized Controlled Trial Treatment Group

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Abstract

Objective. Obstructive eustachian tube dysfunction (OETD) affects up to 5% of adults; however, available treatment strategies have limitations. It was previously reported that balloon dilation of the eustachian tube (BDET) with the eustachian tube balloon catheter + medical management (MM) results in a significantly higher proportion of subjects with normalized tympanograms versus MM alone at 6- and 24-week follow-up. The current analysis extends these initial findings by investigating the durability of BDET + MM treatment outcomes through 52 weeks.

Study Design. Prospective cohort follow-up study from the treatment group in a previously reported multicenter randomized controlled trial.

Setting. Twenty-one investigational sites across the United States.

Subjects and Methods. Here we report on secondary and exploratory endpoints for patients with OETD who previously failed MM and were randomized to the BDET + MM cohort. Analyses of tympanogram outcomes are reported by ear, unless specified otherwise, as a more accurate measure of durability of the procedure over time.

Results. Among subjects randomized to BDET + MM, the overall number with normalized tympanograms and ETDQ-7 scores (Eustachian Tube Dysfunction Questionnaire–7) remained comparable to those reported at 6- versus 52-week follow-up: tympanograms, 73 of 143 (51.0%) versus 71 of 128 (55.5%); ETDQ-7, 79 of 142 (55.6%) versus 71 of 124 (57.3%). The overall number of ears with normalized tympanograms also remained comparable, with 117 of 204 (57%) versus 119 of 187 (63.6%).

Conclusions. The present study suggests that the beneficial effects of BDET + MM on tympanogram normalization and symptoms of subjects with refractory OETD demonstrate significant durability that is clinically relevant through 52 weeks.

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Eustachian tube dysfunction (ETD) refers to failure of the functions of the eustachian tube (ET): middle ear ventilation, clearance of secretions, and protection from reflux of nasopharyngeal pathogens, gastric contents, and voice/breath sounds.[1] ETD can be broadly characterized as a spectrum from obstructive dysfunction (ie, insufficient opening of the ET) to patulous dysfunction (ie, abnormally patent ET).[2] The incidence of obstructive ETD (OETD) has been estimated to range from 0.9% to 5% among adults, although prevalence may be significantly higher.[3-5]

Limitations of current treatment strategies include the following: (1) medical management (MM) has limited efficacy in the absence of a clear etiology[6]; (2) insertion of tympanostomy tubes does not reduce ET inflammation, can cause other complications, and only temporarily addresses OETD; and (3) surgical widening of the cartilaginous ET by laser or microdebrider results in limited reduction of inflamed tissue.[7,8] Recently, a relatively new treatment strategy has emerged: balloon dilation, which involves the longitudinal and circumferential crushing of inflamed mucosa and submucosal adenoid-like lymphoid hyperplasia within the cartilaginous ET lumen.[9,10] Cadaver studies provide support for the safety, procedural efficiency, and effectiveness of balloon dilation of the ET (BDET).[11]

A recent prospective multicenter randomized controlled trial tested the superiority of BDET with ET balloon catheter + MM versus MM alone to treat OETD among adult subjects. Results from the second interim analysis were reported, and the primary endpoint was met: there was a significantly higher proportion of subjects who experienced normalization of tympanograms in the treatment cohort versus the control cohort at 6-week follow-up.[12] Based on ETDQ-7 (Eustachian Tube Dysfunction Questionnaire–7)[13] to assess OETD symptoms, normalization of scores was significantly higher in the BDET + MM group versus the MM group. This analysis extends these findings to 52-week follow-up to evaluate the durability of treatment effects.

Methods

This study (NCT02087150) sought to demonstrate the superiority of BDET + MM versus MM alone to treat OETD among adult subjects. Inclusion and exclusion criteria, treatment details, study endpoints, and statistical analyses were described previously.[12] Briefly, adults aged ≥22 years with OETD who had failed MM and had chronic, persistently abnormal tympanograms for at least 1 ear and abnormal ETDQ-7 scores were randomized to either BDET + MM or MM alone in a 2:1 ratio. Subjects were followed up at 2, 6, 12, 24, and 52 weeks postprocedure. The current analysis focuses on secondary and exploratory endpoints; therefore, tympanogram outcomes are reported by subject and by ear to provide a more detailed and ear-specific assessment of durability of the procedure over time. ETDQ-7 outcomes will continue to be reported by subject. After week 6, subjects randomized to the MM group could elect BDET with additional follow-up visits at 2, 6, and 12 weeks postprocedure. Crossover was allowed after 6 weeks, as study recruitment would have been challenging if a longer period had been mandated for the control subjects who had already endured persistent ETD for several months or years, having failed MM. Control subjects were not allowed access to tympanostomy tubes or other appropriate management, but to deny such therapy for a prolonged period would be below the standard of care. The crossover period is consistent with standard-of-care follow-up for ETD and published clinical literature.[11,14] Crossover subjects were analyzed separately.

Here we report secondary and exploratory outcomes assessing the durability of the treatment through 52-week follow-up within the randomized BDET + MM group only, including tympanogram normalization, improvement in tympanogram (ie, type B to type C, B to A, or C to A), ETDQ-7 normalization (ie, mean <2.1), change from baseline in absolute ETDQ-7 score, ETDQ-7 minimally important difference (MID)–level improvement (ie, mean reduction ≥0.5 points), positive modified Valsalva maneuver ability, work productivity and activity impairment,[15] and safety. Regarding MID, Norman et al[16] evaluated numerous quality-of-life instruments for a range of disease conditions and determined that there is consistency in the magnitude of MID estimates. They determined that with 7-point response scales, the MID is consistently close to 0.5 points on the 7-point scale. Because the MID for the ETDQ-7 has not been determined, an improvement of symptoms ≥0.5 points as compared with baseline was selected as the MID.

All adverse events that occurred in either arm were included in the safety analysis and summarized by frequency, seriousness, and relationship to the study device, procedure, and medical therapy. A high percentage of subjects randomized to the control arm elected to undergo BDET; therefore, a traditional intention-to-treat analysis was not appropriate in evaluating the long-term data collected. The analyses within this report include per-protocol subjects who were randomized to the BDET + MM arm. Data from the 52-week follow-up visit were evaluated against baseline data where appropriate and descriptive statistics provided. The study was approved by an Institutional Review Board for each participating study site.

Results

Patient Flow

A total of 323 subjects (465 ears) were included in this study: 162 (235 ears) were randomized to BDET + MM, 80 (115 ears) to MM only, and 81 (115 ears) as nonrandomized lead-in subjects.

Table 1. Baseline Demographics and Medical History for the Randomized BDET + MM Cohort.

	%
Female	47.5
Caucasian	90.7
Age, y[a]	55.6 ± 14.3
Unilateral ETD	54.9
Allergic rhinitis	45.7
Adenoid hypertrophy	12.4
Mild	9.9
Moderate	2.1
Severe	0.4
Mucosal inflammation	60.5
Mild	45.5
Moderate	12.4
Severe	2.6
Tympanogram	
Type A	0.9[b]
Type C	64.3
Type B	34.9
≥1 prior ear surgery	62.3

Abbreviations: BDET, balloon dilation of the eustachian tube; ETD, eustachian tube dysfunction; MM, medical management.
[a]Mean ± SD.
[b]Three patients had 1 ear with a type A tympanogram and were treated bilaterally; this was a protocol deviation.

Of the 323 enrolled subjects, 1 lead-in and 13 randomized BDET + MM subjects did not pass surgical screening and were not treated with a BDET procedure. Of the 80 treated lead-in subjects, 6 were lost to follow-up; 2 withdrew; and 1 did not complete the study for unspecified reasons. Of the 149 treated BDET + MM subjects, 13 were lost to follow-up; 5 withdrew from the study; 1 moved out of town; 1 died (unrelated to the procedure); and 1 exited from the study per physician discretion. Of the 80 randomized MM subjects, 7 were lost to follow-up; 3 withdrew from the study; and 70 received a BDET procedure. As stated in the Methods section, these 70 crossover subjects did not complete the 52-week follow-up visit but were followed for 12 weeks postprocedure instead. Of the 149 treated BDET + MM subjects, 128 (85.9%) completed the 52-week follow-up visit. Subject demographics and baseline characteristics[12] are summarized in **Table 1**.

Efficacy Outcomes

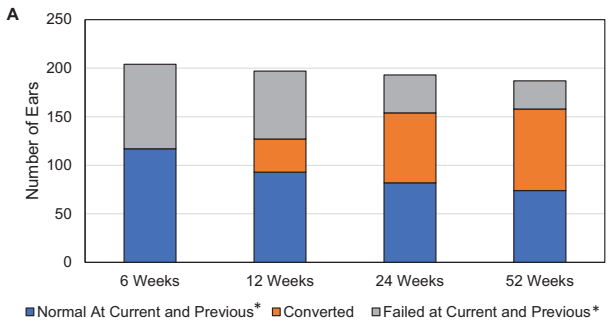
At 52-week follow-up, the overall number of randomized BDET + MM subjects with normalized tympanograms and those with normalized ETDQ-7 scores remained comparable to those at 6 weeks: tympanograms (6 vs 52 weeks), 73 of 143 (51.0%) versus 71 of 128 (55.5%); ETDQ-7 (6 vs 52 weeks), 79 of 142 (55.6%) versus 71 of 124 (57.3%). At 6 weeks, follow-up was completed for 204 treated ears. Of these, 117 (57%; 73 subjects) had normalized tympanograms. By 52 weeks, 74 of 187 ears (39.6%) had remained normal at all subsequent follow-up visits (12, 24, and 52 weeks); 45 of 187 ears had normalized tympanograms at 52-week follow-up but recorded an abnormal tympanogram at ≥1 prior follow-up visits (ie, ''converted'' from abnormal to normal by 52 weeks; **Figure 1A**). For example, 1 of these subjects had a type B at baseline, had A at 6 weeks, relapsed to C at 12 weeks, and was A at 24 and 52 weeks in the left ear. This subject's right ear had type B at baseline and 6 weeks, C at 12 weeks, and A at 24 and 52 weeks. In total, 87 of 182 (47.8%) ears were type A at 6 and 52 weeks, either continually through the study or having failed once during the study period but subsequently recovered.

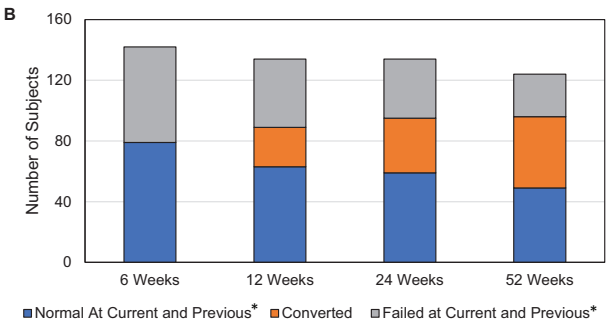
Additionally, 15 ears failed to normalize tympanograms at the 6-week visit but became normal at 12 weeks. The number of ears that normalized after failure at 6 weeks further increased to 44 at 24 weeks and 45 at 52 weeks. In aggregate, 119 of 187 (63.6%) ears had type A tympanograms at 52 weeks, either remaining normal throughout the study or converting to normal (failure becoming normal or temporary failure but return to normal). All other outcomes of interest were either comparable or improved at 52-week follow-up when compared with the proportion of subjects/values at 6-week follow-up (**Table 2**).

While 117 of 204 (57.4%) ears had normalized tympanograms at 6-week follow-up, 128 of 204 (62.8%) showed improvement in tympanogram from baseline to 6-week follow-up. Of these ears, 86 of 187 (46.0%) remained improved at each subsequent follow-up visit, and an additional 45 ears demonstrated improvement at 52-week follow-up but did not meet this criterion at ≥1 of the visits between 6 and 52 weeks. In summary, at 52 weeks, 86 of 187 (46.0%) showed improvement that persisted throughout the study, and overall 131 of 187 (70.1%) were improved at study end (**Figure 2A**).

Of those subjects (n = 71) who exhibited normalized ETDQ-7 scores at 6-week follow-up and were followed through 52 weeks, 39.5% (49 of 124) remained normal at each subsequent follow-up visit, and 22 had normalized ETDQ-7 scores at 52-week follow-up but recorded an abnormal ETDQ-7 score at ≥1 of the visits between 6 and 52 weeks (**Figure 1B**). Regarding those subjects who achieved an MID-level improvement of 0.5 at 6 weeks posttreatment and were followed through 52 weeks, 98 of 124 (79.0%) remained normal at each subsequent follow-up visit, and 13 achieved a MID-level improvement of 0.5 at 52-week follow-up but did not meet this criterion at ≥1 visits between 6 and 52 weeks (**Figure 2B**).

Normalization of tympanograms and ETDQ-7 in the treatment arm tended to agree (**Table 3**). Specifically, both were either normal or abnormal in the majority of cases at all time points: 6 weeks, 90 of 142 (63.4%); 12 weeks, 84 of 134 (62.7%); 24 weeks, 84 of 134 (62.7%); and 52 weeks, 78 of 124 (62.9%). In those subjects with a nonnormalized tympanogram, ETDQ-7 scores were normalized in 29 of 69 (42.0%), 32 of 71 (45.1%), 25 of 56 (44.6%), and 23 of 53 (43.4%) at 6-, 12-, 24-, and 52-week follow-ups, respectively. At 52 weeks, 75.8% of subjects experienced either tympanogram or ETDQ-7 normalization.





Visit	6 weeks	12 weeks	24 weeks	52 weeks
Total N	204	197	193	187
Failed at Current and Previous*	87/204 (42.6%)	70/197 (35.5%)	39/193 (20.2%)	29/187 (15.5%)
Converted	0/204 (0%)	34/197 (17.3%)	72/193 (37.3%)	84/187 (44.9%)
Success at visit	N/A	15/34 (44.1%)	44/72 (61.1%)	45/84 (53.6%)
Fail at visit	N/A	19/34 (55.9%)	28/72 (38.9%)	39/84 (46.4%)
Normal at Current and Previous*	117/204 (57.4%)	93/197 (47.2%)	82/193 (42.5%)	74/187 (39.6%)

* "Previous" does not apply to 6 weeks data

Visit	6 weeks	12 weeks	24 weeks	52 weeks
Total N	142	134	134	124
Failed at Current and Previous*	63/142 (44.4%)	45/134 (33.6%)	39/134 (29.1%)	28/124 (22.6%)
Converted	0/142 (0%)	26/134 (19.4%)	36/134 (26.9%)	47/124 (37.9%)
Success at visit	N/A	14/26 (53.8%)	19/36 (52.8%)	22/47 (46.8%)
Fail at visit	N/A	12/26 (46.2%)	17/36 (47.2%)	25/47 (53.2%)
Normal at Current and Previous*	79/142 (55.6%)	63/134 (47.0%)	59/134 (44.0%)	49/124 (39.5%)

* "Previous" does not apply to 6 weeks data

Figure 1. Sustainability of treatment effects over 52-week follow-up with normalization of (A) tympanogram (by ear) and (B) ETDQ-7 (by subject). ETDQ-7, Eustachian Tube Dysfunction Questionnaire–7.

Table 2. Outcomes at 6- and 52-Week Follow-up in the BDET + MM Cohort.[a]

	Follow-up	
Outcome	6 wk	52 wk
Normalized tympanogram		
Subjects	73 of 143 (51.0)	71 of 128 (55.5)
Ears	117 of 204 (57.4)	119 of 187 (63.6)
Improvement in tympanogram (B to A, B to C, or C to A), ears	128 of 204 (62.7)	131 of 187 (70.1)
ETDQ-7 <2.1, subjects	79 of 142 (55.6)	71 of 124 (57.3)
Absolute change from baseline ETDQ-7 scores		
Subjects	–2.3 ± 1.4 (142)	–2.4 ± 1.6 (124)
Subjects whose tympanograms were not normalized	–1.9 ± 1.4 (69)	–1.9 ± 1.7 (55)
ETDQ-7 <2.1, subjects whose tympanograms were not normalized	29 of 69 (42.0)	23 of 55 (41.8)
Positive Valsalva, ears	173 of 220 (78.6)	185 of 230 (80.4)
Work productivity and activity impairment due to problems in the last 7 d, subjects	16.6 ± 23.6 (141)	9.1 ± 18.2 (124)

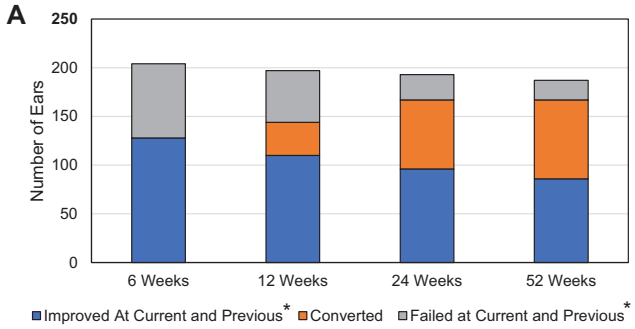
Abbreviations: BDET, balloon dilation of the eustachian tube; ETDQ-7, Eustachian Tube Dysfunction Questionnaire–7; MM, medical management.
[a]Values are presented as n (%) or ± SD (n).

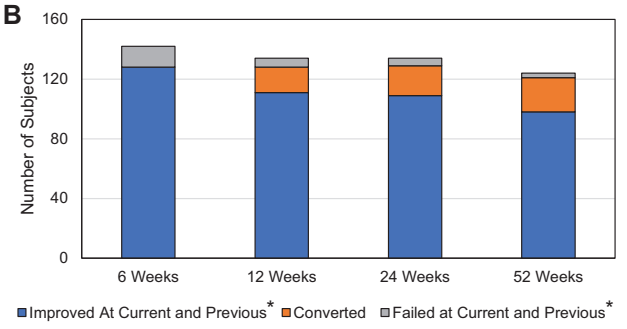
Safety Data

There were no device- or procedure-related serious adverse events reported through last follow-up in either the BDET + MM group (including lead-in; randomized BDET + MM and MM crossover subjects) or the MM group. Two occurrences of patulous ET were reported, both of which were described as mild. At 52-week follow-up, 1 subject's patulous symptoms had resolved without sequelae, and the other subject was still experiencing patulous symptoms. There was 1 case in which a false passage occurred during BDET and was recognized by the surgeon. The catheter was replaced into the true lumen, and dilation was successfully carried out without sequelae.

Discussion

The results of the present analysis demonstrate a clinically significant degree of durability of BDET + MM through 52 weeks for the treatment of OETD in adult subjects. The subjects had a baseline of persistent (documented to be nonfluctuating) chronic OETD for a minimum of 90 days but, in





Visit	6 weeks	12 weeks	24 weeks	52 weeks
Total N	204	197	193	187
Failed at Current and Previous*	76/204 (37.3%)	53/197 (26.9%)	26/193 (13.5%)	20/187 (10.7%)
Converted	0/204 (0%)	34/197 (17.3%)	71/193 (36.8%)	81/187 (43.3%)
Success at visit	N/A	21/34 (61.8%)	44/71 (62.0%)	45/81 (55.6%)
Fail at visit	N/A	13/34 (38.2%)	27/71 (38.0%)	36/81 (44.4%)
Improved at Current and Previous*	128/204 (62.7%)	110/197 (55.8%)	96/193 (49.7%)	86/187 (46.0%)

* "Previous" does not apply to 6 weeks data

Visit	6 weeks	12 weeks	24 weeks	52 weeks
Total N	142	134	134	124
Failed at Current and Previous*	14/142 (9.9%)	6/134 (4.5%)	5/134 (3.7%)	3/124 (2.4%)
Converted	0/142 (0%)	17/134 (12.7%)	20/134 (14.9%)	23/124 (18.5%)
Success at visit	N/A	7/17 (41.2%)	14/20 (70%)	13/23 (56.5%)
Fail at visit	N/A	10/17 (58.8%)	6/20 (30%)	10/23 (43.5%)
Improved at Current and Previous*	128/142 (90.1%)	111/134 (82.8%)	109/134 (81.3%)	98/124 (79.0%)

* "Previous" does not apply to 6 weeks data

Figure 2. Sustainability of treatment effects over 52-week follow-up with improvement of (A) tympanogram (by ear) and (B) ETDQ-7 (minimally important difference improvement; by subject). ETDQ-7, Eustachian Tube Dysfunction Questionnaire–7.

Table 3. Normalization of Endpoints among the Subjects Who Underwent BDET + MM.

	Time Point, n (%)			
	6 wk (n = 142)	12 wk (n = 134)	24 wk (n = 134)	52 wk (n = 124)
Normal tympanogram				
Normal ETDQ-7	50 (35.2)	45 (33.6)	53 (39.6)	48 (38.7)
Nonnormal ETDQ-7	23 (16.2)	18 (13.4)	25 (18.7)	23 (18.6)
Nonnormal tympanogram				
Normal ETDQ-7	29 (20.4)	32 (23.9)	25 (18.7)	23 (18.6)
Nonnormal ETDQ-7	40 (28.2)	39 (29.1)	31 (23.1)	30 (24.2)

Abbreviations: BDET, balloon dilation of the eustachian tube; ETDQ-7, Eustachian Tube Dysfunction Questionnaire–7; MM, medical management.

most cases, over a duration of months to years and the majority with previous tympanostomy tubes.[12]

In contrast to this baseline of unremitting presenting symptoms, the outcomes show a clinically significant percentage of subjects who had enduring normalization of results—tympanogram (6 vs 52 weeks), 117 of 204 (57.4%) versus 74 of 187 (39.6%); ETDQ-7 (6 vs 52 weeks), 79 of 142 (55.5%) versus 49 of 124 (39.5%)—and an even greater number of enduring improvement: tympanogram (6 vs 52 weeks), 128 of 204 (62.8%) versus 86 of 187 (46.0%); ETDQ-7 (6 vs 52 weeks), 128 of 142 (90.1%) versus 98 of 124 (79.0%). The criterion that we used to define MID—a convention that is felt to represent the smallest detectable difference in symptoms as experienced by patients[16]—was the least stringent of our data endpoints, and this appeared to be reflected in the higher rates of improvement of ETDQ-7 scores versus tympanograms. Including the ears (tympanograms) and subjects (ETDQ-7) that converted between success and failure at intermediate time points, the overall 52-week results were similar to the 6-week results: at 52 weeks—tympanogram normalization, 119 of 187 (63.6%); tympanogram improvement, 131 of 187 (70.1%); ETDQ-7 normalization, 71 of 124 (57.3%); ETDQ-7 improvement, 111 of 124 (89.5%).

There was a growing percentage of subjects during the study that showed fluctuation in outcomes between success and failure. There were 15 ears that failed to normalize tympanograms at 6 weeks but improved to type A at 12 weeks

and an additional 30 ears that subsequently improved. It is possible that there could be a delayed onset of benefit with BDET that might account for these improvements, particularly for those that improved by 12 weeks. It is possible that BDET may have made sufficient improvement to convert persistent OETD to fluctuating OETD. Certainly, the improvements could also be explained by the natural history of the disease. In the absence of long-term controls for comparison, this issue cannot be resolved in the present study and should be examined in future studies.

The proportion of subjects who had normalized or improved ETDQ-7 symptom scores exceeded the outcomes for tympanograms, suggesting that some symptomatic benefits may occur that are not entirely dependent on tympanogram status. In nearly half of subjects who did not achieve normal tympanograms, ETDQ-7 scores were normal (<2.1). In general, however, the success or failure of tympanogram and ETDQ-7 tended to agree. Overall, at 52 weeks, 75.8% of subjects experienced normalization of either tympanogram or ETDQ-7.

While the primary endpoint was normalization of tympanogram, in clinical practice, improvement short of normalization criteria may be sufficient to achieve satisfaction. In this study, tympanograms improved in 131 of 187 (70.1%) of ears at 52 weeks, including normalization and type B baseline tympanograms that improved to C. Many such subjects with a mild type C tympanogram might be entirely asymptomatic, possibly accounting for some of the discrepancy between failure to normalize tympanograms and normalizing ETDQ-7 score.

The durability of the results following a 2-minute dilation of the cartilaginous ET is encouraging. Given that the lumen is flexible and not rigidly fixed circumferentially (other than the portion adjacent to the isthmus), the mechanism of effect has not been fully established. Data from a histologic study from Kivekäs et al[9] suggest that the mechanism may be the result of balloon dilation causing a combination of crushing and excoriation of injured/inflamed mucosa and crushing of the submucosal inflammatory lymphoid infiltrate and follicular hyperplasia. Postoperative biopsies ($\geq$5 weeks) from 3 subjects all showed thinner mucosa and submucosa with restoration of normal ciliated epithelium and a thin layer of submucosal scar devoid of any lymphoid follicles. The histologic demonstration of reduction in inflammation agrees with the endoscopic mucosal inflammation scores that were shown to statistically improve in the analysis of the present cohort out to 24 weeks.[12] It appears that the noncompressible balloon may accomplish benefits similar to adenoidectomy within the lumen of the ET where conventional techniques would not be accessible to treat the adenoid-like tissue present within the lumen.

In the current study, there were 9 subjects who were considered a success at 6-week follow-up but converted to a nonnormalized tympanogram in at least 1 ear at a subsequent visit and then converted back to a type A tympanogram before the end of the study. Of these subjects, 7 had at least 1 ear tube placement procedure (range, 1-7 tubes) prior to enrollment in the study. The 2 who did not have prior ear surgery had type B or C in at least 1 ear $>$12 weeks prior to enrollment. By protocol, subjects were deemed treatment failures for the remainder of the study if they reverted to a type B or C tympanogram,[12] but in the present study examining longer-term outcomes, temporary failure and return to normal might represent a clinical success, allowing subjects to recover when their prior history indicated a more protracted and persistent course of disease.

The addition of adjunctive procedures was not allowed in conjunction with BDET, even when it may have appeared to be possibly clinically indicated. ETD is not a disease in isolation in most cases, and inflammation within the ET is often associated with inflammatory disease elsewhere within the upper aerodigestive tract. Surgeons should assess the burden of inflammatory disease, especially regarding its potential effect on the ET and determine whether adjunctive procedures may be indicated to improve outcomes. The placement of tympanostomy tubes (even $\leq$1-mm inner diameter) when an effusion is present may resolve the effusion and allow air to pass through the ET more quickly in the postoperative period.[17] Other procedures may be indicated, such as turbinate reduction, nasal or sinus surgery, adenoidectomy (possibly including removal of the lateral portion from proximity to the Torus tubarius), and cautious reduction of the tubal tonsil tissue from the medial one-half of the Torus tubarius. When indicated, adjunctive procedures might potentiate or sustain the beneficial impact of BDET + MM, despite a greater burden of inflammatory disease preexisting within the upper aerodigestive tract.[18] We consider that it is important to optimize medical treatment for the source of the inflammation when appropriate and to continue that MM following BDET when indicated to prevent recurrence of inflammatory disease and subsequent return of OETD.

Huisman et al recently evaluated the effect of BDET in reducing symptoms of OETD. Of the 15 eligible studies, consisting of retrospective case series and prospective case series, no randomized controlled trials were included.[19] The authors concluded that while the available literature supported the use of BDET for OETD, placebo-controlled trials were necessary. Although there was heterogeneity in the indications, balloon devices, protocols, and outcome measures, the results were similar to the overall 52-week results for improvement of outcomes in this study: tympanogram, 131 of 187 (70.1%); ETDQ-7, 111 of 124 (89.5%). Not only is the present study the first randomized controlled trial comparing BDET + MM and MM only, but it is one of the first randomized controlled trials to study any procedure on the ET that uses an objective measure of success, tympanogram normalization assessed by a blinded reader, which can reduce and/or eliminate any bias or placebo effect that might otherwise confound the study.

Several limitations follow: First, because crossover to the BDET + MM group was allowed after 6-week follow-up, the remaining MM group became self-selected, and this

limited the ability to perform meaningful comparisons with the control group after 6-week follow-up. Moreover, because the subjects in the treatment cohort were used as their own historical control, the extent of improvement specifically attributable to treatment remains unknown. Subjects were not blinded to treatment. General anesthesia was used only in the treatment cohort and not in the control cohort and therefore is a potential confounding variable.

There were no serious adverse effects in the study, but 2 subjects did develop mild symptoms of patulous ET, 1 of which resolved by the completion of the study. This serves as a reminder that histologic changes that reduce the volume of soft tissue within the functional valve of the ET likely do occur because of BDET. Candidates for BDET should have a demonstrable burden of inflammatory disease visible within the lumen of the ET on preoperative endoscopic examination. A lack of inflammatory disease might increase the risk of patulous ET. In the case of limited inflammatory disease, a reduction in duration of balloon inflation may be appropriate, and the effect of duration needs to be studied.

Conclusion

This study suggests that the beneficial effects of BDET + MM on tympanogram normalization and symptoms of subjects with refractory OETD demonstrate a significant degree of durability that is clinically relevant through 52 weeks.

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Author Contributions

Vijay Anand, co–primary investigator with Dr Poe, had the responsibility for the study design, oversight, participating in the study as contributing study centers, interpretation of the data, writing and editing of the manuscript and approval of the manuscript; **Dennis Poe**, co–primary investigator with Dr Anand, had the responsibility for the study design, oversight, participating in the study as contributing study centers, interpretation of the data, writing and editing of the manuscript and approval of the manuscript; **Marc Dean**, collaborated in study design/conduct updates, collection of data, manuscript review and approval; **William Roberts**, investigator, manuscript review and approval; **Pablo Stolovitzky**, acquisition of data, manuscript review and approval; **Karen Hoffmann**, substantial contribution to the acquisition of data, revising he intellectual content, and final approval of the data; **Nathan Nachlas**, investigator, manuscript review and approval; **Joshua Light**, investigator, manuscript review and approval; **Mark Widick**, investigator, manuscript review and approval; **John Sugrue**, performed research, manuscript review and approval; **C. Layton Elliott**, investigator, contributed to results of procedures, manuscript review and approval; **Seth Rosenberg**, collect data, manuscript review and approval; **Paul Guillory**, investigator, manuscript review and approval; **Neil Brown** , investigator, manuscript review and approval; **Charles Syms**, investigator, manuscript review and approval; **Christopher Hilton**, data collection and interpretation, manuscript review and approval; **John McElveen**, investigator, manuscript review and approval; **Ameet Singh**, investigator, manuscript review and approval; **Raymond Weiss**, original concept/design, data acquisition, manuscript review and approval; **Moises Arriaga**, data acquisition, manuscript review and approval; **John Leopold**, data analysis, data interpretation, manuscript review and approval.

Disclosures

Competing interests: Dennis Poe, consultant for Acclarent Inc for reimbursement of expenses and time. No equity interest in the company, no royalties from products, no financial interests. **Marc Dean**, consultant for Acclarent Inc, BioInspire, Biosense Webster. **Pablo Stolovitzky**, Acclarent Inc: consultant, clinical research; IntersectENT: consultant, clinical research, speaker's bureau; Spirox: consultant, clinical research. **Karen Hoffmann**, consultant for Acclarent Inc since September 2017. **John Sugrue**, consultant 1.5 to 2 years ago (no recent consulting for >1 year) for Acclarent Inc. **Charles Syms**, Earlens Corp, Tusker Medical, Arrinex: advisory board and stock options; Audigy Medical: consultant; Cochlear Corp: does audiologic support for implant patients at author's institution. **Ameet Singh**, Intersect ENT: consultant, grant. **Raymond Weiss**, rhinology consultant for Acclarent Inc. **Moises Arriaga**, Elsevier: royalties on textbook editing. **John Leopold**, employee of DePuy Synthes.

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