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Balloon Eustachian Tuboplasty—A Feasible Double-Blinded Sham Surgery Randomized Clinical Trial Protocol to Study Efficacy

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Introduction: Balloon Eustachian tuboplasty (BET) is used to treat obstructive Eustachian tube dysfunction (OETD) and recurrent otitis media with effusion (OME). However, there are no indisputable evidence of its efficacy. Here, we present a multicenter, double-blinded, randomized, placebo-controlled trial (MDRCT) design to evaluate the efficacy of BET, and the results of a pilot trial with 3- and 12-months' follow-up.

Material and Methods: This was a prospective MDRCT. For a pilot study, OETD ($n = 10$) and OME ($n = 5$) patients were recruited and followed. Detailed inclusion and exclusion criteria were used. Participants were randomized at beginning of the operation to active or sham surgery. All procedures were performed under local anesthesia. Controls were performed in double-blinded manner (both patient and physician), at 3 and 12 months after the procedure.

Results: Altogether, 20 ears were treated and followed for 12 months, including 14 active BETs and 6 sham surgeries. Both the active and sham surgery were performed under local anesthesia without problems or deviations from the protocol. There were no differences in the preoperative symptoms (ETDQ-7) or objective measures (tympanometry, Valsalva and Toynbee maneuvers, tubomanometry, Eustachian tube score) between active and sham surgery arms. During follow-up, we noticed largely similar reduction in subjective symptoms and improvement in Eustachian tube score both in active and sham surgery arms.

Conclusions: The pilot study demonstrates that our MDRCT protocol is feasible, and that blinded RCTs are dearly needed to objectively measure the efficacy of BET.

Key Words: balloon Eustachian tuboplasty, Eustachian tube dysfunction, placebo-controlled trial, sham surgery.

Level of Evidence: 2

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INTRODUCTION

Eustachian tube dysfunction (ETD) may significantly impair the quality of life.[1] Diagnosis should be based on consensus criteria.[2] ETD may be divided to different categories based on the underlying pathology.[2,3] The most common form is functional obstructive ETD (later OETD). Otitis media with effusion (OME) is usually considered to result from chronic OETD.[2,4]

Possible treatments for OETD and OME include nasal corticosteroids and decongestants, antihistamines, and tympanostomy tube placement (TTP), but these usually offer short-term or insufficient relief.[5] More recently, balloon Eustachian tuboplasty (BET) was introduced in clinical use in 2010[6] to gain long-term benefit[7] and today, it is part of established clinical care world-wide.[8] The procedure is straight-forward, it may be carried out under general or local[9,10] anesthesia, and complications are rare and usually minor.[7] Although BET is considered safe for both adult and pediatric patients,[11,12] its efficacy has been questioned. Recent systematic reviews[12,13] and meta-analyses[7,14] suggest overall benefit in both subjective symptoms and objective findings in a majority of OETD patients, but heterogeneity of studies in diagnostic criteria and study endpoints makes it difficult to draw clear-cut conclusions. Also, almost all the studies lack proper control groups. Thus far, the best proof on effectiveness of BET in adults has been provided by a few randomized controlled trials where BET was compared to medical treatment.[15–18] Another type of comparison was made with OME patients with no significant difference between BET + TTP and BET alone.[19] BET has more recently been used also in children[20] where colleagues showed that BET reduced the need for repeated TTPs in children when compared to matched control patients.[21]

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The optimal method to study the effectiveness of any treatment is a placebo-controlled trial because placebo interventions does not have significant clinical effects in general.[22] The purpose of the placebo-controlled study is to reduce the bias,[23] which is likely to play a major role in the perceived symptoms and discomfort caused by diseases. When considering the harm caused by sham surgery, it should be borne in mind that it is unethical to provide a treatment which efficacy has not been conclusively demonstrated.[23] To our knowledge, there are no previously published multicenter double-blind placebo-controlled randomized trials (MDRCT) on the efficacy of BET. To this end, we designed a study using our previously published local anesthesia method[9,10] to allow ethical randomization to active and sham surgery arms and carried out a pilot study in a double-blinded manner. The study design, its implementation, and the results of the pilot study are presented. Goal of the study was to recruit altogether 120 patients in the three study centers, but due to COVID-19 pandemic and changes in balloon dilation devices and their availability in Europe, we managed to recruit and follow-up only 15 patients. For the common interest, we decided to publish the study design and the results as a pilot study.

MATERIALS AND METHODS

Ethics

The study protocol was approved by the ethical review board of the Tampere University Hospital (ref: R17040) and a research permit was obtained for each research center. The study was registered at the ISRCTN (a clinical trial registry recognized by WHO and ICMJE) registry with ID ISRCTN50406162. Written Informed consent was obtained from all participants.

Study Design

This was a MDRCT. All patients were operated in operation room under local anesthesia. Patients were randomized either for active or sham surgery. One out of five received sham surgery and four out of five received conventional BET. Both the patient and the otologist on postoperative visits were blinded to the randomization (Fig. 1). In a systematic review, Eustachian tube score (ETS) improved in 66% of the patients undergone BET.[7] Placebo treatment was estimated to yield better results in 20% of the patients.[24] Power analysis using the generally applied power value of 0.8 resulted in a cohort of 44 patients in the active arm and 11 patients in the sham surgery arm. This yielded target population of 60 subjects in both conditions.

The primary outcome was the change in the total value of objective measurements (objective ETS) at the 12-month postoperative visit. The secondary outcomes were the change in subjective symptoms (ETDQ-7), outcomes of the individual components of the ETS, the need for tympanostomy tubes during follow-up and visual changes in tympanic membrane.

Participants

There were two separate study conditions: (1) chronic OETD and (2) long-lasting OME. Adult patients (age ≥18 years) were recruited. All the patients had to be suitable and compliant to surgery under local anesthesia. Inclusion and exclusion criteria for both conditions are presented in Figure 1. Altogether, 17 patients were recruited. Two patients declined to participate in control visits, and their data were excluded from the analysis.

Recruiting Process

Patients were recruited from ENT outpatient clinics in three University Hospitals in Finland (Helsinki, Turku and Tampere). Patients were recruited from specialist ETD outpatient visits with tubomanometry (TMM) available. At the visits, all the examinations mentioned below were performed on all patients. Our diagnostic criteria were based on symptoms and findings explained in detail below. The recruitment process included a detailed explanation of the randomization process and its impact on patient's treatment. It was explained to the patients that currently, there are no definite evidence for the efficacy of BET, and thus sham surgery controls are needed. Patients understood and accepted the need for the trial and gave their informed consent. It was agreed that patients randomized in the sham surgery would receive active treatment after 12-month postoperative visit if patient wished so at that point.

Outpatient Tests

All subsequent examinations and measurements were performed before recruiting process, as well as at 3-month and 12-month postoperative visits.

Eustachian tube dysfunction questionnaire (ETDQ-7)[25] was used to evaluate burden caused by ETD. Patients responded separately for both ears.

Tympanometry was performed on both sides using MAICO easyTymp Pro (Illinois, USA) and Titan by Interacoustics (Middelfart, Denmark). Results were scored as 2 points for type A curve, 1 point for type C, and 0 points for type B.[26]

Otomicroscopy was performed on both ears. Tympanic membrane (TM) condition was recorded (normal, retraction, effusion etc.). See exclusion criteria (Fig. 1).

Valsalva and ***Toynbee maneuvers*** were performed in sitting position with simultaneous otomicroscopy. Valsalva was evaluated as on-time, delayed or negative, and the result was scored with 2, 1 or 0 points, respectively. Toynbee was evaluated either positive or negative and scored 2 or 0 points.

Nasoendoscopy was performed through both nostrils to ensure normal anatomy of the nasopharynx and the ET orifice, and to ensure that nasal anatomy was suitable for local anesthesia procedure. Special attention was paid to the mucosal inflammation around tubal orifice. Gross inflammation or other abnormality led to exclusion.

Oral cavity was examined to exclude patients with cleft palate or other abnormalities in the palate.

Tubomanometry (TMM)[27,28] was performed with 30, 40, and 50 mbar pressures on both ears (Eustachian Tube Diagnostic Tubomanometer, La Diffusion Technique Francaise, Saint Etienne, France). To equalize middle ear pressure between measurements, the patients closed their nostrils and swallowed twice after which they were asked to yawn. Results were scored as 2 points for on-time opening ($R \leq 1$), 1 point for delayed opening ($R > 1$) or 0 points for no ET opening. TMM score was a sum of points from all different pressures (0–6 points).

Objective ETS was modified from the original ETS[6] and ETS-7[26] scores by using only objective measurements of tympanometry, Valsalva, and Toynbee results together with TMM 30, 40, and 50 mbar results. The score range was 0–12.

Audiometry Pure tone audiometry was obtained all subjects prior to recruiting.

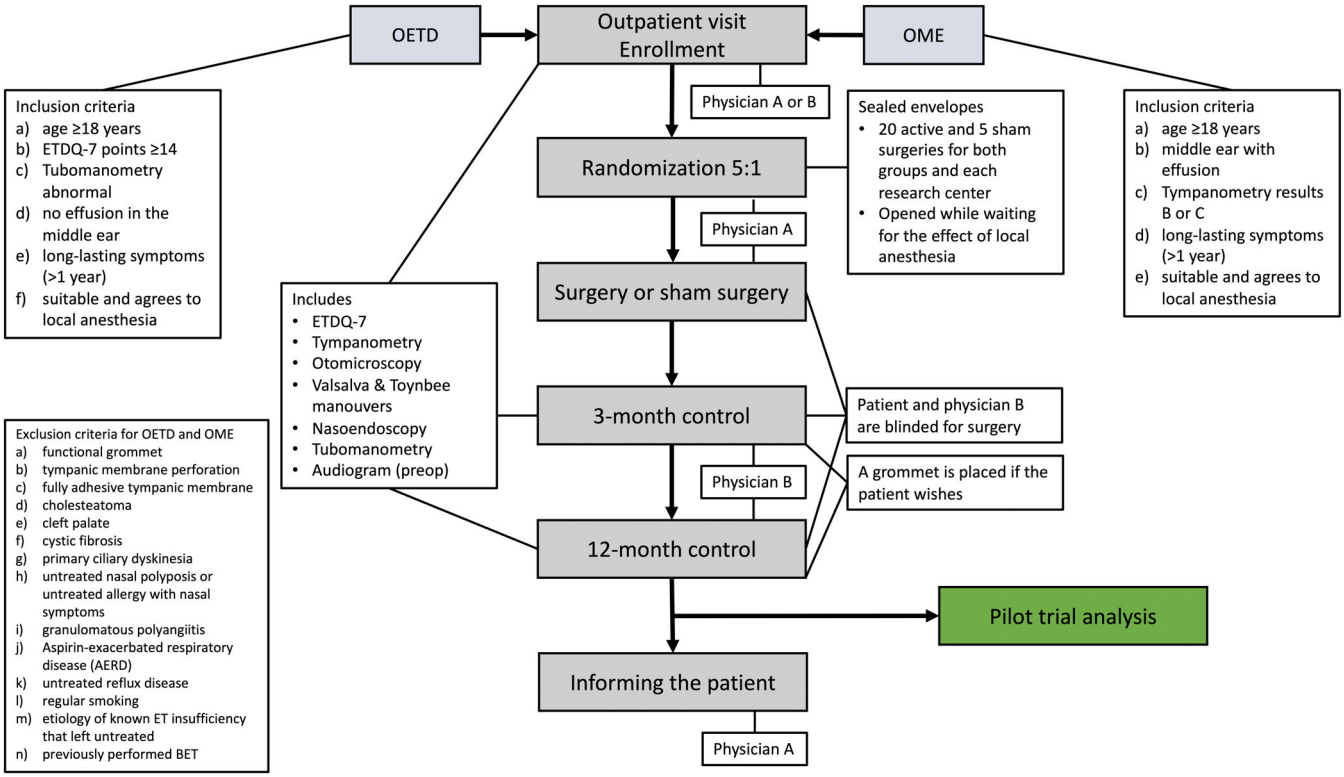

Fig. 1. Study protocol. ETDQ-7 = Eustachian tube dysfunction questionnaire; OETD = obstructive Eustachian tube dysfunction; OME = otitis media with effusion. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Randomization Method

Sealed randomization envelopes were prepared. Each center had 20 envelopes for active and five for sham surgery for both conditions. The sealed envelopes were mixed and then numbered with respective recruitment numbers.

Surgery and Sham Surgery

The patient was blinded to the procedure. The surgeon opened the randomization envelope right before going to the operating room. At operating room, patient was given small doses of intravenous opioids and sedation if needed. During the procedures, the patient's eyes were under coverings. Patient received regional nerve block anesthesia with cotton patches moisturized in cocaine-epinephrine solution for 10 min. For ET local anesthesia,[9] 1 mL lidocaine-prilocaine cream was applied to the ET lumen orifice under endoscopic control for 5 min.

For active BET treatment, after 15 min' local anesthesia, TubaVent® short balloon dilator (Spiggle & Theis Medizintechnik GmbH, Overath, Germany) and TubaInsert® (Spiggle & Theis) was used in Helsinki (9 ears) and Turku (2 ears). The inflation pressure was 12 ATM for 2 min whereby the diameter of the balloon was 3.3 mm. The Acclarent AERA® (Acclarent Inc., California, United States) was used in Tampere (3 ears). The inflation pressure was 12 ATM for 2 min whereby the diameter of the balloon was 6 mm.

In case of sham surgery, local anesthesia was like active BET group, but TubaInsert® catheter (6 ears, in Helsinki) was placed at the opening of ET. Although keeping the catheter at the ET opening, the surgeon asked the assisting nurse to raise the pressure to 12 ATM. The nurse called gradual increase in pressure until 12 ATM. The TubaInsert tool was kept in place for 2 min after which the surgeon asked the nurse to deflate the balloon. Thereafter, the operation was finished.

Information about the patient participating in the study and possible surgery or sham treatment in a ratio of 5:1 was entered into the medical records. At the recovery room, the staff did not know whether the patient had undergone active or sham surgery. Sick leave was written for the operation day in all cases. All patients were discharged within 3 h of operation.

Postoperative Visits

Postoperative visits were performed in a double-blinded manner for both the patient and physician (Fig. 1) at 3 and 12 months after the procedure. Visit included ETDQ-7, tympanometry, otomicroscopy with Valsalva and Toynbee maneuvers and TMM. If patient had major OETD symptoms or OME, TTP was offered on symptomatic side at the request of the patient. All examinations took place prior to possible TTP. After 12-month control, the surgeon informed the patient whether he/she had received active or sham surgery. If the patient wished, he/she was scheduled for standard BET.

Statistics

Statistical analyses were performed using IBM SPSS Statistics for Macintosh version 27 (Armonk, NY) and GraphPad Prism 9 (GraphPad, San Diego, CA). The significance level was

TABLE I.
Patient Characteristics.

	All, $n = 15$	All Active, $n = 11$	All Sham, $n = 4$	OETD Active, $n = 7$	OETD Sham, $n = 3$	OME Active, $n = 4$	OME Sham, $n = 1$
Age (y), mean (SD)	47.3 (15.0)	44.9 (13.7)	55.2 (18.3)	38.7 (8.83)	48.8 (16.1)	53.4 (15.5)	74.1
BMI, mean (SD)	25.6 (4.3)	26.3 (4.68)	23.3 (2.2)	25.0 (4.2)	24.0 (2.0)	27.1 (3.1)	21.2
Duration of symptoms (y), mean (SD)	15.9 (12.3)	18.3 (12.7)	8.5 (8.1)	19.9 (11.7)	10.0 (9.2)	16.2 (15.1)	4
Gender, *n* (%)							
Female	7 (47)	5 (45)	2 (50)	3 (43)	2 (67)	2 (50)	0 (0)
Male	8 (53)	6 (55)	2 (50)	4 (57)	1 (33)	2 (50)	1 (100)
Treated reflux disease, *n* (%)	3 (20)	3 (27)	0 (0)	2 (29)	0 (0)	1 (25)	0 (0)
Occasional smoking, *n* (%)	4 (27)	3 (27)	1 (25)	3 (43)	1 (33)	0 (0)	0 (0)
Pollen allergy, *n* (%)	2 (13)	2 (18)	0 (0)	2 (29)	0 (0)	0 (0)	0 (0)
Side, *n* (%)							
Right	7 (47)	6 (55)	1 (25)	5 (71)	0 (0)	1 (25)	1 (100)
Left	3 (20)	2 (18)	1 (25)	0 (0)	1 (33)	2 (50)	0 (0)
Both	5 (33)	3 (27)	2 (50)	2 (29)	2 (67)	1 (25)	0 (0)

n = number of patients. OETD = obstructive Eustachian tube dysfunction; OME = otitis media with effusion. Only patients with complete follow-up were included in the table.

TABLE II.
Preoperative and Postoperative Results.

	All Active, $n = 14$	All Sham, $n = 6$	OETD Active, $n = 9$	OETD Sham, $n = 5$	OME Active, $n = 5$	OME Sham, $n = 1$
ETDQ-7						
Preop.	30.14 (11.10)	25.83 (9.13)	31.44 (10.83)	26.80 (9.86)	27.80 (12.46)	21
3 mo	19.86 (8.59)*	19.33 (8.31)	19.33 (9.53)	18.20 (8.76)	20.80 (7.53)	25
12 mo	17.93 (5.69)***	12.50 (12.06)**	20.11 (5.65)*	12.60 (13.48)*	14.00 (3.39)*	12
Tympanometry						
Preop.	1.07 (0.92)	0.83 (0.98)	1.44 (0.73)	1.00 (1.00)	0.40 (0.89)	0
3 mo	1.21 (0.83)	0.67 (1.03)	1.67 (0.71)	0.80 (1.10)	0.60 (0.55)	0
12 mo	1.21 (0.89)	1.17 (0.98)	1.44 (0.73)	1.00 (1.00)	0.80 (1.10)	2
Valsalva						
Preop.	0.71 (0.73)	0.67 (0.82)	0.89 (0.78)	0.80 (0.84)	0.40 (0.55)	0
3 mo	1.14 (0.86)	1.17 (0.75)	1.22 (0.83)	1.40 (0.55)	1.00 (1.00)	0
12 mo	1.29 (0.91)	1.00 (1.10)	1.11 (1.05)	1.20 (1.10)	1.60 (0.55)	0
Toynbee						
Preop.	0.43 (0.85)	0	0.67 (1.00)	0	0	0
3 mo	0.57 (0.94)	0.33 (0.82)	0.89 (1.05)	0.40 (0.89)	0	0
12 mo	0.71 (0.99)	0	0.89 (1.05)	0	0.40 (0.89)	0
TMM score						
Preop.	1.64 (1.45)	1.17 (1.83)	1.56 (1.59)	0.80 (1.79)	1.80 (1.30)	3
3 mo	2.71 (2.05)	2.67 (1.75)	2.78 (2.33)	2.40 (1.82)	2.60 (1.67)	4
12 mo	2.79 (2.01)	2.84 (1.47)	3.00 (2.29)	2.60 (1.52)	2.40 (1.52)	4
ETS						
Preop.	3.86 (2.89)	2.67 (1.37)	4.56 (3.13)	2.60 (1.52)	2.60 (2.07)	3
3 mo	5.71 (3.67)	4.83 (2.79)	6.56 (4.39)	5.00 (3.08)	4.20 (0.84)	4
12 mo	6.00 (3.53)	5.00 (1.90)*	6.44 (4.10)	4.80 (2.05)	5.20 (2.39)	6

N = number of ears. Data are mean (SD). ETDQ-7 = Eustachian tube dysfunction questionnaire 7 (score 7–49 points); OETD = obstructive Eustachian tube dysfunction; OME = otitis media with effusion. Tympanometry was scored as 2 points for type A curve, 1 point for type C, and 0 points for type B. Objective Valsalva maneuver was scored in sitting position as on-time (2 points), delayed (1 point), or negative (0 points). Objective Toynbee maneuver in sitting position was scored either positive (2 points) or negative (0 points). TMM was scored as 2 points for on-time opening ($R \leq 1$), 1 point for delayed opening ($R > 1$), or 0 points for no ET opening at three different pressures. ETS = Eustachian tube score, combines results from objective Valsalva and Toynbee maneuvers, tympanometry and TMM score (total 0–12 points). *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$ for the difference from the preoperative values. No statistical differences were detected between 3- and 12-month controls in any group. Only patients with complete follow-up were included in the table.

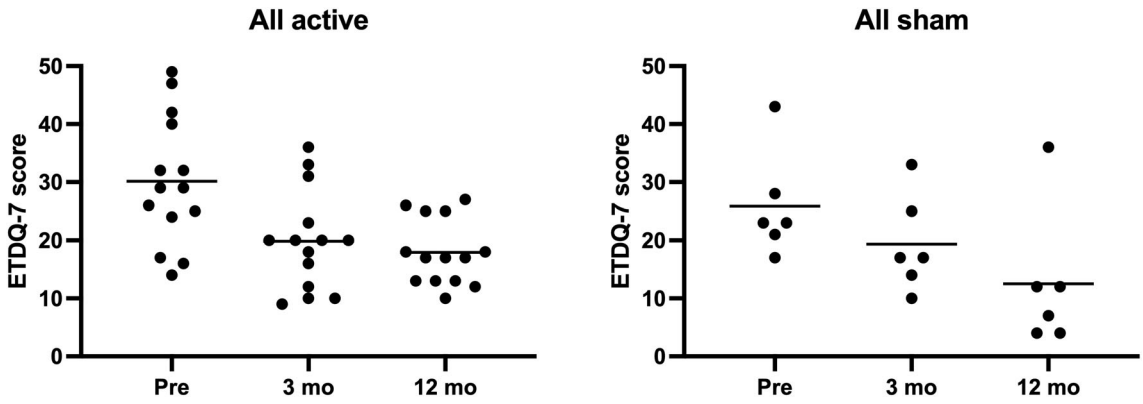

Fig. 2. ETDQ-7 (Eustachian tube dysfunction questionnaire) results.

set at $p \leq 0.05$. In Table I, independent samples t-test was used between active and sham surgery arms. In Table II, differences between active and sham surgery arms in ETDQ-7 scores were tested with ANOVA followed by Dunnet's multiple comparison post-hoc test, for all the other variables with Friedman test followed by Dunn's multiple comparison post-hoc test. Differences in variables between preoperative and control visits were examined with repeated measures ANOVA and Friedman test.

RESULTS

Altogether, 17 patients were recruited (11 OETD and 6 OME patients, Table I and Supplementary Table 1) and 23 ears (16 OETD and 7 OME ears) participated in the study. Sham surgery was performed to 5 OETD and one OME ears. Two patients declined to participate in postoperative visits, and their data were excluded from the analysis. One patient with OETD in active arm (two ears participated) refused to attend the postoperative visits due to fear of the COVID-19 infection. One patient with OME in active arm (one ear in the study) did not attend 12-month visit. Thus, at the end of study, complete follow-up data were available for 14 OETD and 6 OME ears. Keeping in mind the small sample size in this pilot study, there was no statistical difference in age, BMI, duration of symptoms, gender, reflux disease, smoking status or pollen allergy between groups or arms. When comparing preoperative active and sham surgery arms (All, OETD, OME), there were no differences in symptoms (ETDQ-7), tympanometry, Valsalva or Toynbee maneuver performance, TMM score or ETS (Table II, patients with complete follow-up).

Both the active and sham surgery were performed under local anesthesia without problems or deviations from the protocol. No adverse events were noticed. Patients were asked at 12-month visit whether they had an idea if they had received active or sham treatment. Some patients had a feeling of belonging to the active surgery arm. Many were unable to judge between the options. One active surgery patient was convinced to be in the sham surgery arm. Despite the uncertainty of being in active or sham surgery arm, patients were generally eager to attend the postoperative visits.

ETDQ-7 symptom scores were reduced at 12-month both in active and sham surgery arms (Table II, Fig. 2). No differences were detected between active and sham surgery arms between different time-points. In OETD and OME conditions, similar trend in reduction of ETDQ-7 points during follow-up was detected in both active and sham surgery (Fig. 2).

No differences from preoperative values were detected during follow-up in either active or sham surgery arms in tympanometry, Valsalva or Toynbee maneuver performance, or TMM score (Table II). Also, no differences in these variables were detected in any time point between active or sham surgery arms.

There was a statistically significant increase in ETS score only in sham surgery arm at 12 months (Table II, Fig. 3). No differences were detected between active and sham surgery arms between different time-points. Due to low patient number in this pilot study no differences in preoperative and postoperative ETS scores were detected when patients were divided to OETD or OME conditions either in active or sham surgery arms.

At 3-month, three out of five OME ears still had effusion in the active treatment arm and as well as the only patient in the sham surgery arm. One of the patients in the active surgery arm requested and got TTP. At 12-month visit one patient from the active surgery arm still had effusion but did not' want TTP.

Preoperatively, 11 out of 14 ears in OETD condition had pars tensa retraction. At 12-month, pars tensa retraction persisted in three out of nine ears in active surgery arm and two out of five in sham surgery arm. Preoperatively, six out of 14 ears in OETD condition had pars flaccida retraction and at 12-month there was one, and one patient in the active surgery arm who had preoperative pars tensa and pars flaccida retractions, developed adhesive TM seen at 12-month visit. At 3-month, two patients got TTPs in the active treatment arm. At 12-month, grommet were inserted to one OETD patient in sham surgery arm.

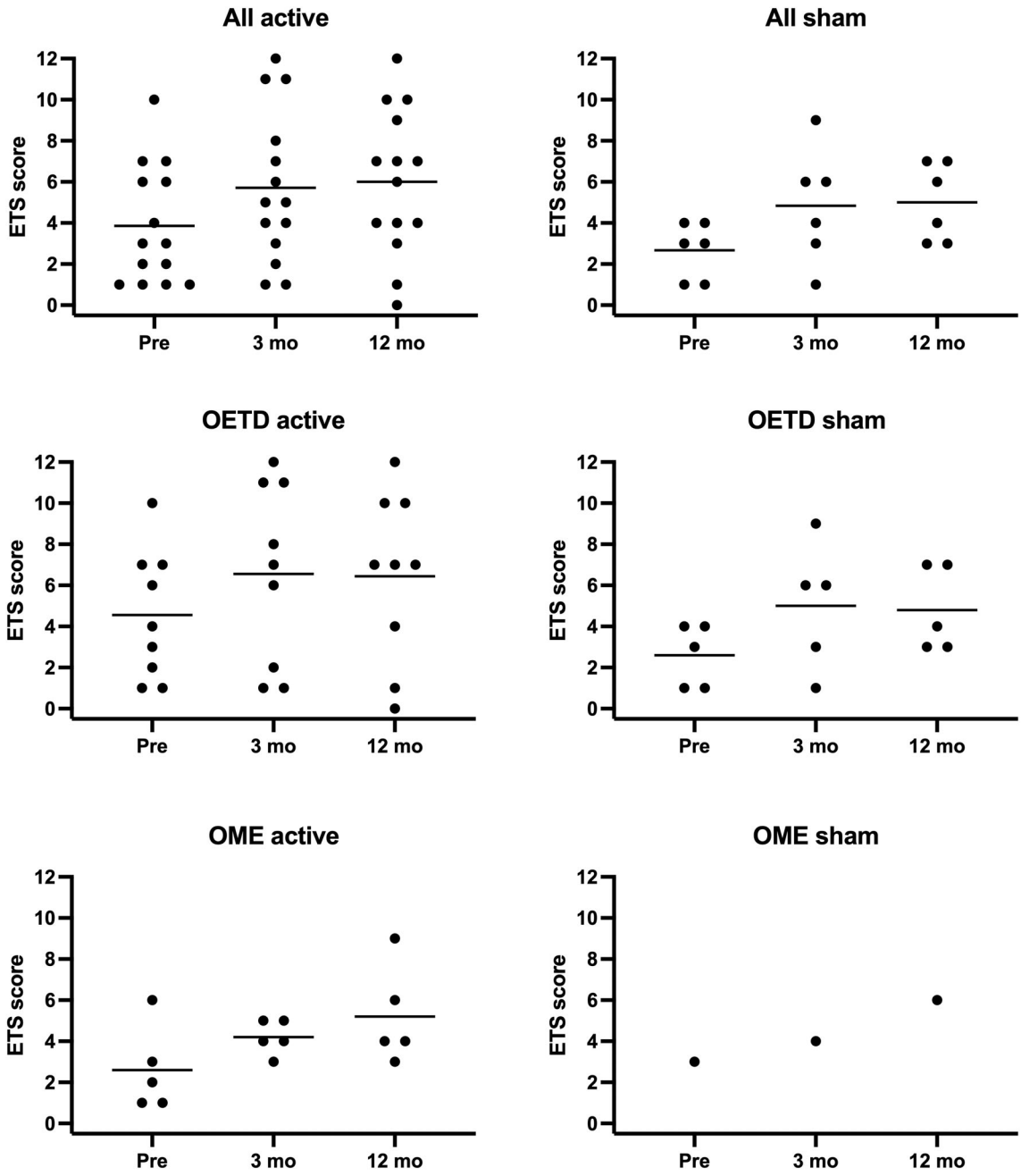

Fig. 3. ETS results. ETS = Eustachian tube score, combines results from objective Valsalva and Toynbee maneuvers, and TMM score (total 0–12 points). Objective Valsalva maneuver was scored in sitting position as on-time (2 points), delayed (1 point), or negative (0 points). Objective Toynbee maneuver in sitting position was scored either positive (2 points) or negative (0 points). TMM was scored as 2 points for on-time opening ($R \leq 1$), 1 point for delayed opening ($R > 1$), or 0 points for no ET opening at three different pressures. Tympanometry results were scored as 2 points for type A curve, 1 point for type C, and 0 points for type B.

DISCUSSION

Here, we present the design and implementation of the first a multicenter double-blinded randomized placebo-controlled (sham surgery) trial to study the effectiveness of BET in OETD and OME patients. Goal of the study was to recruit altogether 120 patients in the three study centers, but due to COVID-19 pandemic and changes in balloon dilation devices and their availability in Europe, we managed to recruit and follow-up only 15 patients. For the common interest, we decided to publish the study design and the results of the 15 patients as a pilot study. Although the study population is small, the study protocol proved feasible, and the preliminary results demonstrate clear need for placebo-controlled studies in future to prove BETs efficacy.

Blinded randomized clinical trials (RCTs) are considered to provide the most relevant information on the effectiveness of the surgery.[29] There is indisputable

evidence of the usefulness of blinded RCTs, also in operative field.[30–32] However, the legitimacy of sham surgery shares the views of colleagues, especially on risks.[33] To minimize these risks in our study, the procedures were carried out under local instead of general anesthesia. We have previously developed the local anesthesia protocol for BET for both the types of balloon catheters used in the study.[9,10] With these protocols, local anesthesia is as feasible in BET as in medial antrostomy in endoscopic sinus surgery.

At the beginning of the study, we had two types of BET catheters in Finland, the Spiggle & Theis TubaVent short (3.3 × 20 mm at 12 ATM) and the Acclarent AERA (6 × 16 mm at 12 ATM). The COVID-19 pandemic slowed down the initial recruiting process as less patients could be treated in the hospitals worldwide. Thereafter, Acclarent AERA was withdrawn from the European market and was used for three patients only. After Spiggle & Theis came to market with TubaVent® wide catheter (5.1 × 20 mm at 12 ATM), the study group judged that it would be unethical to continue the trial using smaller TubaVent catheter, as using wider balloon would most likely benefit the patient. Because TubaVent® wide catheter has not been shown to be feasible under local anesthesia, recruiting for the study had to be stopped. For these reasons, we could not' meet our original goal in the study population size. However, we felt it is important to publish the study protocol and preliminary results as a proof-of-concept report.

During the study period, there were no problems in patient care or deviations from the study protocol. None of the active or sham surgeries needed to be stopped because of pain or discomfort caused by the local anesthesia. No differences in patient demographics or preoperative symptoms or findings were detected, which suggested successful randomization process. Double-blinding setup worked as planned, as none of the patients nor any of the doctors taking care of the postoperative visits were aware of patient's randomization status at the end of the study. In fact, ETDQ-7 symptom score was reduced at 12-month both in active and sham surgery arms confirming successful blinding process. All the patients that participated in the 12 months' control visit (15/17) expressed their satisfaction in being regularly monitored, and none of them were disappointed in their decision to participate. Several patients also mentioned that they were proud to have participated in a randomized sham surgery controlled study.

Due to a small study population, it is impossible to draw conclusions of the effectiveness of BET in OETD or OME. Patients' symptoms were reduced during follow-up both in active and sham surgery arms demonstrating that there might be a placebo effect in BET, and at 12 months', sham surgery patients seemed to be even less symptomatic (Table II, Fig. 2). Although all patients had long lasting symptoms and findings of OETD or OME, we do not know the natural course of these diseases. Thus, the fluctuations in patients' symptoms may explain the changes instead of the placebo effect. Also, one cannot rule out the possible effect of the lidocaine-prilocaine cream applied to the tubal orifice. Toivonen et al. noted no statistically significant difference in the need for additional interventions between BET performed under local or general anesthesia and both groups showed statistically significant improvements in otoscopy findings, tympanogram, and the ability to perform a Valsalva maneuver using tetracaine-lidocaine cream to the ET orifice for local anesthesia procedure only.[34] Objective measures (tympanometry, objective Valsalva or Toynbee maneuver performance, TMM) did not reveal clear changes during follow-up between active and sham surgery arms, possibly due to the small study population. ETS combining objective Valsalva, Toynbee maneuver, tympanometry, and TMM score was increased in both active and sham surgery arms (Table II, Fig. 3, Supplementary Table 2), again suggesting the need for sham surgery controls in future studies.

CONCLUSIONS

Based on our experience, a MDRCT on the efficacy of BET is feasible. This study shows the possibility for designing a sham-controlled trial to study the efficacy of BET. Such multicenter studies could shed light on the true effect of BET.

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