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Systematic Review

Treatment of Eustachian Tube Dysfunction With Balloon Dilation: A Systematic Review

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Objective: Balloon dilation is a new entity in the therapeutic approach of Eustachian tube dysfunction. The aim of this systematic review is to evaluate the success of balloon dilation of the tuba auditiva in reducing symptoms in adult patients with Eustachian tube dysfunction.

Data Sources: Embase, PubMed, and Cochrane Library.

Review Methods: The systematic literature search was conducted independently by two authors based on title and abstracts, and resulted in 36 articles. These articles were screened as full text, 15 of them were eligible for critical appraisal. Data were extracted from selected studies and presented in this article. A meta-analysis was conducted for four subgroups. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used as a writing guideline for this systematic review.

Results: All 15 included studies were case series. A total of 1,155 patients were treated with balloon dilation of the tuba auditiva. Outcome parameters were relief of symptoms, otoscopy, Valsalva maneuver or Toynbee test, audiometry, tympanometry, Eustachian tube dysfunction classification, and Eustachian tube score. All articles showed short-term improvement of original symptoms; some showed further improvement over time. Follow-up ranged from just after therapy to 50 months. Relatively mild and self-limiting complications were described in 36 patients.

Conclusion: All current studies suggest that balloon dilation of the Eustachian tube can be a helpful treatment in patients with Eustachian tube dysfunction. However, placebo controlled trials are still warranted.

Key Words: Eustachian tube dysfunction, balloon dilation of the tuba auditiva, adults, systematic review.

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INTRODUCTION

Eustachian tube dysfunction (ETD) has a major impact on the general population, with a prevalence of 0.9%.[1,2] The function of the Eustachian tube is to equalize pressure, clear mucociliary secretions, and protect the middle ear.[3] Dysfunction of the Eustachian tube can be caused by a variety of diseases that interfere with the mucosal function or cartilaginous structures, resulting in a diminished possibility to open the Eustachian tube. ETD's exact pathophysiology has not yet been elucidated, and one simple standardized test to objectify ETD is lacking.[4] Negative pressure in the middle ear seems to be the key factor and may coincide with contributing factors such as microbial overload or obstruction of the nasopharynx, for example, in case of adenoid hypertrophy or nasopharyngeal cancer.[5–7] The negative pressure in the middle ear may lead to tympanic membrane retraction and fluid accumulation in the middle ear.[3,5] ETD causes symptoms, especially during barometric changes, such as aural fullness, otalgia, tinnitus, and/or temporary hearing loss.[2,4,5] Similar symptoms also are observed in chronic otitis media, cholesteatoma, (allergic) rhinitis, chronic rhinosinusitis, and laryngopharyngeal reflux.[2,8] Conventional medical treatment aimed at improving mucosal conditions of the nasal cavity and Eustachian tube, includes nasal steroids, decongestants, or antihistamines. Unfortunately, it remains challenging to predict the effectiveness of these treatments, partly due to the difficulty to objectify ETD.[2,9] Well-known invasive symptomatic treatments are paracentesis and ventilation tubes, in order to equalize pressure via the tympanic membrane.[2,9]

Until now, no gold standard treatment for ETD has emerged.[4] Therefore, a safe, easily performable, and effective treatment option would be welcomed in the otolaryngological armamentarium. The new Eustachian tube

Additional supporting information may be found in the online version of this article.

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balloon dilation (ETBD) technique, first described in patients in 2010, comprises the inflation of a balloon in the cartilaginous part of the Eustachian tube to cause local dilation.[10] Some consider ETBD to be a new promising entity in therapeutic options for patients with complaints of tuba dysfunction. However, ETBD also has been referred to as a "gizmo" and an unproven procedure.[11] Therefore, we systematically reviewed the current literature on balloon dilation therapy, adverse events, outcome parameters, and results in adults with Eustachian tube dysfunction and herein present our critical appraisal.

MATERIALS AND METHODS

Search and Selection

A systematic literature search in PubMed, Embase, and the Cochrane library was conducted on May 1, 2016. Search terms used were "Eustachian tube," "balloon," and "dilation," as well as relevant synonyms (see Appendix 1, available online). No terms were included in the search for patient characteristics to avoid publication bias. No search terms were included for outcome because there is no reference standard. Titles, abstracts, and full texts were screened independently by two authors (J.M.L.H. and F.J.V.) on predetermined inclusion and exclusion criteria. Inclusion criteria were balloon dilation of Eustachian tube and adults with tuba dysfunction. Exclusion criteria were studies in other than human, cadaver studies, non-English and children studies, editorial articles, conference abstracts, case reports, comments or opinions, (systematic) reviews, when no balloon dilation was performed, and if balloon therapy was performed as part of more profound middle ear surgery. Cross-referencing was performed through Scopus after full text screening. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used as the writing guideline for this systematic review.[12]

Study Assessment

Because ETD has no clear definition, not all investigators use the same criteria to diagnose ETD. We classified the relevance of articles based on three criteria: 1) patient characteristics, 2) therapy, and 3) ETD measurements before and after therapy. Quality outcome parameters were objective and/or subjective evaluation of complaints, additional diseases (such as cholesteatoma), and other therapy besides ETBD. Objective measurements were tympanometry, Valsalva maneuver, Toynbee test, otoscopy, tuba manometry, histopathology, mucosal inflammation, the Eustachian Tube score (two types of scoring systems), and the Eustachian tube classification (see Appendix 2). Studies used retrospective data from patient files, and two studies used questionnaires to evaluate symptoms. The two questionnaires were the 7-item Eustachian Tube Dysfunction Questionnaire (ETDQ-7), and the Glasgow Benefit Inventory (GBI).

Studies were considered of high relevance if they complied with all three criteria, moderate relevance when two or more criteria were met, and low if fewer than two criteria were met (see Table I). Risk of bias was measured by seven criteria: study population, standardization of outcome, blinding, missing data, selection bias, confounders, and follow-up. Missing data were subdivided into less than 10%, between 10 % to 20%, more than 20%, or not reported. Finally, follow-up was scored satisfactory if measurements were performed more than 6 months after treatment. If studies complied with six or more criteria, they were classified as having low risk of bias, with four or five as moderate risk of bias, and less than four as high risk of bias.

Data Extraction and Statistical Analysis

Study characteristics and outcome data were extracted from selected articles independently by two authors (J.M.L.H. and F.J.V.). No selection was made on type of outcome.

To perform the meta-analysis, we calculated the relative risk with a 95% confidence interval (CI) and random effects modelling using RevMan 5.3.[13] Articles that described the results pre- and post-ETBD were included for meta-analysis. We assessed the heterogeneity among the studies by calculating the I^2 statistic.

RESULTS

Search and Study Selection

As illustrated in Figure 1, 103 articles were retrieved from the PubMed, Embase, and Cochrane Library search. Removal of duplicates and screening on title and abstract resulted in 36 articles; these were screened in full text, and 15 remained for critical appraisal. Cross-referencing through Scopus did not result in additional articles.

Assessing Quality of Studies

The critical appraisal of the 15 articles on relevance and risk of bias is shown in Table I. All studies were case series evaluating the effect of ETBD on patients with ETD without a control group. In several studies, patients received additional conventional treatment apart from ETBD.[6,10,14–19] Three articles[20–22] were considered to be of high relevance; the remaining studies were of moderate relevance, for example, due to additional treatment next to ETBD (such as nasal corticosteroid spray or functional endoscopic sinus surgery) or patients with additional illnesses (such as chronic otitis media with cholesteatoma). One study blinded the caretakers after treatment to prevent influence on the test results[23]; one study[6] treated both children and adults; and all studies had a moderate-to-high risk of bias.

Data Extraction and Statistical Analysis

A descriptive analysis is provided. The conducted meta-analysis was made per subgroup. Inclusion criteria varied between studies, and not all studies described their population baseline characteristics. In addition, heterogeneity existed between follow-up times and the types of provided data at the outpatient clinic visits. Pooling of data was therefore difficult, and not for all types of outcome a meta-analysis could be provided. The outcome "reported symptoms" presented either no data before ETBD, or the inclusion of the symptoms differed too much between studies and therefore this parameter had to be excluded from analyses. The outcomes "audiometry," "tubamanometry," "mucosal inflammation," "Eustachian tube score 2," and "ETD classification" also had to be excluded because no data before ETBD were reported or because one or two studies remained to conduct the meta-analysis. The remaining four subtypes that could be analyzed over time include the Valsalva test, otoscopy, tympanometry, and the Eustachian tube score. Three subgroups used dichotomous data (relative

TABLE I.
Critical Appraisal.

Study (year)	Study Design	Sample Size* (years)	Mean Age in Years* (range)	Relevance				Validity							
				Patients	Therapy	Outcome	Verdict	Study Population	Standardization of Outcome	Blinding	Missing Data	Follow-up	Selection Bias	Confounders	Risk of Bias
Bast (2014)	RCS	30 (?)	49.7 (24–73)	●	●	◐	M	○	◐	○	?	●	●	○	H
Catalano (2012)	RCS	70 (100)	45 (18–73)	●	◐	●	M	○	◐	○	●	●	●	●	M
Dai (2016)	RCS	8 (12)	53 (45–62)	◐	●	●	M	●	◐	○	◐	●	●	○	M
Dalchow (2016)	PCS	217 (324)	45.6 (6–88)	●	◐	●	M	○	◐	○	●	●	●	●	M
Gürtler (2015)	RCS	21 (?)	37.5 (19–67)	●	●	●	M	●	◐	○	●	●	○	○	H
Jurkiewicz (2013)	RCS	4 (7)	45.8 (23–61)	●	●	●	H	●	◐	○	●	○	○	●	H
Kivekas (2015)	RCS	13 (26)	46 (18–74)	●	◐	●	M	●	◐	○	●	○	○	○	H
McCoul (2012)	PCS	22 (35)	55.1 (46.4–63.8)	●	●	●	H	●	●	○	●	●	○	◐	M
Ockermann (2010)	PCS	8 (13)	44.1 (21–81)	◐	◐	●	M	●	◐	○	●	○	○	○	H
Poe (2011)	PCS	11 (11)	51.8 (33–76)	◐	◐	●	M	●	◐	○	●	●	●	◐	M
Schröder (2015)	RCS	622 (1076)	? (7–84)	●	◐	●	M	●	◐	○	◐	●	●	◐	M
Silvola (2014)	PCS	37 (42)	48 (15–38)	◐	◐	●	M	●	◐	○	●	●	●	●	M
Wanscher (2014)	PCS	34 (50)	45 (20–74)	◐	◐	●	M	●	◐	○	●	○	○	◐	H
Williams (2016)	RCS	18 (25)	40.6 (18–68)	◐	●	●	M	●	◐	◐	●	●	○	◐	M
Xiong (2016)	RCS	40 (58)	42 (21–70)	●	●	●	H	●	◐	○	●	●	○	◐	M

Patients	● Adults with tuba dysfunction |◐ Pathology that can be caused by tuba dysfunction |○ Symptoms not related to tuba dysfunction Verdict = level of relevance
Therapy	● Balloon tuba dilation without combination treatment | ◐ Combination treatment | ○ No balloon tuba dilation (M)oderate or (H)igh relevance
Outcome	● Clinically relevant objective measures | ◐ Subjective measures | ○ No clinically relevant measures
Study population	● Patient characteristics well described | ○ Patient characteristics not reported or incompletely described Risk of bias = level of validity
Standardization of outcome	● Validated test | ◐ Validated test not specific for condition | ○ No validated test (M)oderate or (H)igh validity
Blinding	● Blinding | ◐ Partial blinding | ○ No blinding
Missing data	● <10% of missing data | ◐ 10–20% missing data | ○ >20% missing data | ? not reported
Follow-up	● ≥ 6 months | ○ < 6 months
Selection bias	● No selection bias |○ Susceptible to bias
Confounders	● There are no confounders, or they are corrected in the analysis | ◐ Confounders are only mentioned | ○ Confounders are not mentioned

*Sample size: number of patients (number of ears treated, if mentioned). Mean age: in years (range of age).
PCS = prospective case series; RCS = retrospective case series.

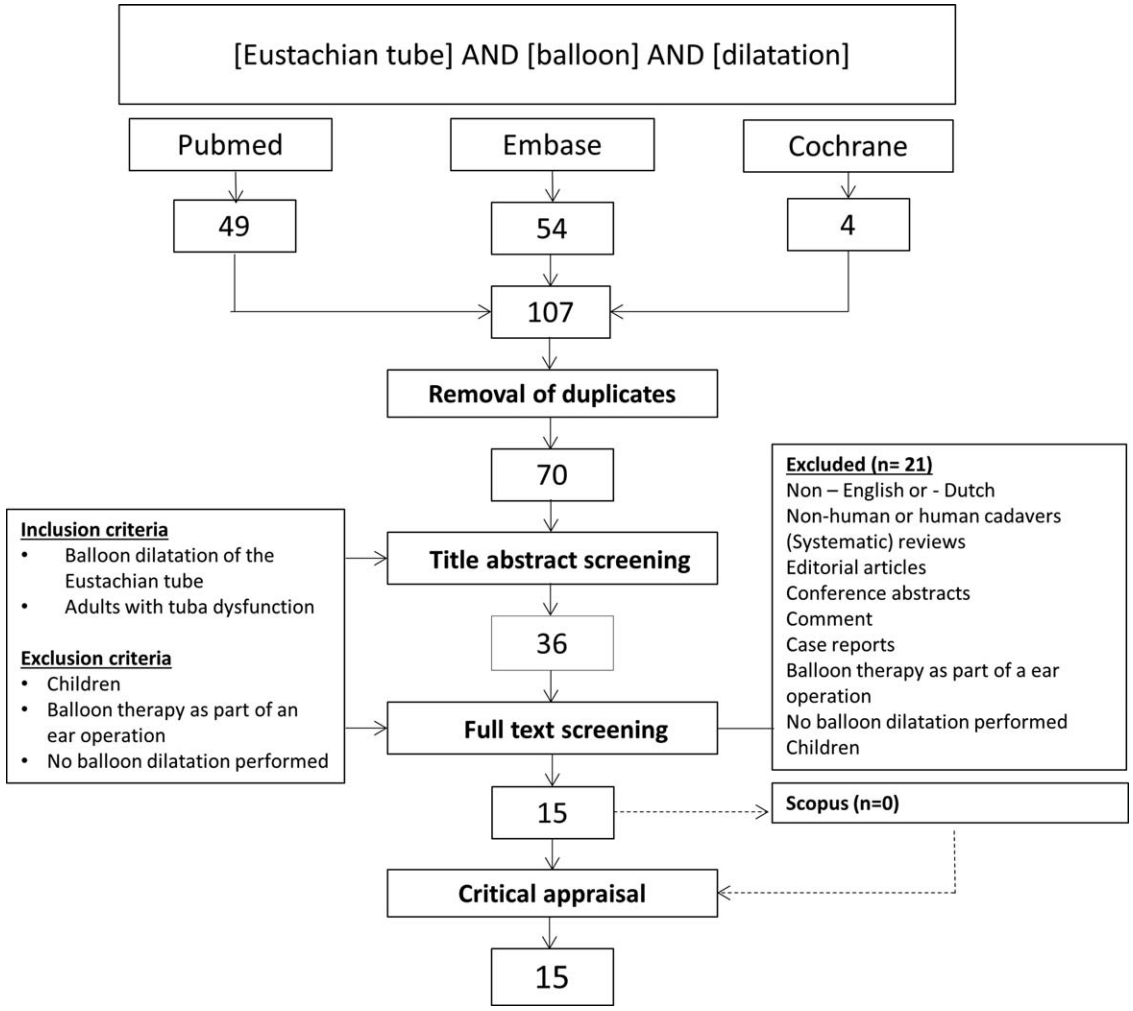

Fig. 1. Flow chart.

risk [RR]) and one continuous data (mean score and standard deviation [SD]). Two studies in which these subgroups were mentioned had to be excluded due to the absence of data before the ETBD procedure.[18,24]

Study Characteristics

The study characteristics are presented in Table II. In this table, several aspects are highlighted: number of patients, mean age, tests, follow-up, comorbidities, other therapy, and anesthesia. The 15 included studies concern 1,155 patients who suffered from ETD, although it was not always further specified how ETD was diagnosed. Patients often had coexisting disease or comorbidity such as cholesteatoma, sinusitis, or mucosal hypertrophy of the turbinates, and some patients previously underwent radiotherapy. Mostly, subjects were included if they did not respond to conventional treatment such as nasal steroids and antihistamines. Some underwent tympanoplasty or ventilation tubes. Exclusion criteria varied; patients with anatomical variations such as severe nasal septal deviation or patients who did not show an intact bony wall of the internal carotid canal by means of computed tomography (CT). In order to assess potential dehiscence of the bony wall of the internal carotid artery or anomalies of the tuba auditiva, a preoperative (high-resolution) CT scan of the temporal bone was performed in nine studies[6,14,17,18,21,22,25–27] and a digital volume tomography in one.[15] The remaining five studies refrained from imaging.[14,16,19,23,24]

Every patient underwent clinical examination, tympanometry, audiometry, and sometimes tubamanometry. All studies used either Spiggle & Theis (Overath, Germany),[6,10,15,19,20,22–26] or Acclarent (Acclarent, Inc.; Irvine, CA)[14,16–18,21] for balloon dilation. Spiggle & Theis uses a balloon of 20 mm in length and 3 mm in width, which is inflated to 10 bars for 2 minutes, whereas Acclarent (Acclarent, Inc.) is 16 mm in length and 5 to 7 mm in width and inflated to 12 bars for 1 to 2 minutes. Patients received general anesthesia in 10 studies. In three studies, both general (n = 82) and local (n = 30) anesthesia was used.[14,19,24] Two studies did not report their way of providing anesthesia.[10,17]

Outcome

In the 15 appraised studies, a total of 1,155 patients received at least 1,830 and up to 1,881 ETBD

TABLE II.
Study Characteristics.

Study (year)	Number of Patients (men:women)	Mean Age in Years (range)	Tests	Follow-up (months)	Comorbidities	Other Therapy	Anaesthesia: Number of Operators*
Bast (2014)	30 (11:19)	49.7 (24–73)	GBI questionnaire	6–18	NR	NR	0: 1
Catalano (2012)	70 (26:44)	45 (18–73)	Subjective symptoms and tympanometry	3 and 34	NR	39 sinonasal procedures, 5 otologic procedures	0 and 1: NR
Dai (2016)	8 (NR)	53 (45–62)	Subjective symptoms, tympanic membrane, audiometry, tympanometry	3, 6, and 12	NR	NR	0: NR
Dalchow (2016)	217 (119:98)	45.6 (6–88)	ETS 2	1, 3, 6, 9, and 12	NR	Cefuroxime and prednisolone, 124 tympanoplasty	0: NR
Gürtler (2015)	21 (14:7)	37.5 (19–67)	Subjective symptoms, audiometry, otoscopy, tympanometry, tubamanometry, ETS	1 week, 3 and 26	6 cholesteatoma, 1 carcinoma nose (not specified where)	6 cholesteatoma operations, 1 irradiated carcinoma of the nose	0: NR
Jurkiewicz (2013)	4 (3:1)	45.8 (23–61)	Valsalva, air–bone gab audiometry, tympanometry	1 and 6 weeks	1 rhinitis, 2 mucoserous otitis	Rhinitis treatment	0: NR
Kivekas (2015)	13 (10:3)	46 (18–74)	Otoscopy (tympanic membrane retraction), tympanometry, histopathology	5–12 weeks	NR	2 tympanoplasty, nasal steroids and antihistamines continued if patients were on it chronically	0: NR
McCoul (2012)	22 (NR)	55.1 years (46.4–63.8)	ETDQ-7, tympanometry	3, 6, 12 weeks, and 6	NR	7 tympanoplasty	0: NR
Ockermann (2010)	8 (NR)	44.1 (21–81)	Valsalva, tubamanometry, ETS	1, 2, and 8 weeks	NR	2 tympanostomy tubes (in 3 patients removed)	0: NR
Poe (2011)	11 (5:6)	51.8 (33–76)	Valsalva, tympanic membrane, tympanometry, mucosal biopsy	directly after, and 7–14	11 tympanoplasty or perforation, 6 CRS	Nasal steroids	0: NR
Schroder (2015)	622 (ratio ± 1:1)	? (7–84)	Subjective symptoms, ETS	2, 12, 24, and 36	NR	Nasal steroids, tympanostomy	0: NR
Silvola (2014)	37 (ratio ± 1:1)	48 years (15–38) -> probably a typo	Valsalva, otoscopy, tympanometry, mucosal biopsy	mean 2.5 years (1.5–4.2)	16 CRS, 12 perforated tympanic membranes/ tubes	Decongestant, nasal steroids, antibiotics	0: NR
Wanscher (2014)	34 (18:16)	45 (20–74)	Subjective symptoms, Valsalva/Toynbee, audiometry, tympanometry, ETD classification	2	6 tubes	5 ventilation tubes	0 and 1 (3): 2
Williams (2016)	18 (NR)	40.6 (18–68)	Tympanometry	2–3, 6–9, and 12–15	NR	6 ventilation tubes, 4 patients previously mastoid surgery or tympanoplasty	0: at 2 different centers
Xiong (2016)	40 (21:19)	42 (21–70)	Subjective symptoms, Valsalva, otoscopy, tympanometry, tubamanometry, ETS	1 week, 3 and 12	NR	NR	0: NR

*0 = general anesthesia
1 = local anesthesia.
CRS = chronic rhinosinusitis with/without nasal polyps; ETBD = Eustachian tube balloon dilation; ETD = Eustachian tube dysfunction; ETDQ-7 = Eustachian tube dysfunction questionnaire; ETS = Eustachian tube score; GBI = Glasgow Benefit Inventory; NR = not reported.

TABLE III.
Outcome: Reported Symptoms, Valsalva Test, and Complications.

Study (year)	Reported Symptoms Follow-up (months): symptom relief in % or scores, *P* value	Valsalva Follow-up (months): ability to perform in % or scores, *P* value	Complications number, classification (type and treatment)*
Bast (2014)	6–18: scores NR, $P = 0.001$	NR	NR
Catalano (2012)	3: 71%.	NR	1, mild (1A)
	34: 88% (n = 8)		
Dai (2016)	3: 83%	NR	0
	6: 86% (7 ears)		
	12: 100% (3 ears)		
Dalchow (2016)	NR	NR	0
Gürtler (2015)	1/4: 71%	NR	11, mild (1x 2A, 10x 3A)
	3: 76%		
Jurkiewicz (2013)	NR	1/4: 29% improvement	0
		1 1/2: 71% improvement	
Kivekas (2015)	NR	NR	11, mild (4A)
McCoul (2012)	Before: mean 4.5 (SD 1.2), $P < 0.001$	NR	1, severe (2B)
	3/4: mean 2.7 (SD 1.5), $P < 0.001$		
	1/2: mean 2.6 (SD 1.1), $P < 0.001$		
	3: mean 2.8 (SD 1.7), $P < 0.001$		
	6: mean 2.8 (SD 1.3), $P < 0.001$		
Ockermann (2010)	NR	Before: 23%	0
		2: 92%	
Poe (2011)	NR	Directly after: 100%	5, mild (2A)†
		7–14: 63–100%, $P < 0.001$	
Schroder (2015)	24: 74% (n = 30)	NR	3, mild (1A, 2A, 5A)
Silvola (2014)	NR	Mean 30: from 0% to 80%, $P < 0.001$	0
Wanscher (2014)	2: 55% (only concerning aural fullness) and 48% (only concerning otalgia), $P < 0.05$	2: 66%, $P < 0.05$	4, mild (6?)
		Toynbee: 2: from 7% to 77%	
Williams (2016)	NR	NR	0
Xiong (2016)	1/4: 88%	Before: 0%	0
	3: 95%	1/4: 62%	
	12: 98%	3: 83%	
		12: 98%	

*mild = symptoms resolved spontaneously; severe = symptoms did not resolve spontaneously without treatment; 1 = preauricular emphysema; 2 = self-limiting bleeding at site of balloon dilation; 3 = mild rhinitis; 4 = diffuse (sub)mucosal crush injury; 5 = increased tinnitus; 6 = otitis media acuta; A = resolved spontaneously; B = resolved with myringotomy; ? = not reported.

†1 patient had temporary C6-7 contralateral radiculopathy due to neck extension.

Ears = number of ETBD procedures; ETBD = Eustachian tube balloon dilation; NR = not reported; SD = standard deviation; TM = tympanic membrane.

procedures (for 51 patients, it was not clear whether the procedure was done unilaterally or bilaterally). The sample sizes ranged from seven ETBD procedures in four patients to 1,076 ETBD procedures in 622 patients, and average follow-up was 6.9 months (range 0 to 50 months). In Tables III to V, all outcome parameters are subdivided per type of measurement of ETD. Almost all parameters showed an improvement, mostly qualified as significant, which remained during the follow-up time or even ameliorated further over time.[9,10,14–17,19–26,28] Two studies reported diminished results over time. More specifically, Poe showed an improved Valsalva maneuver at all follow-up times, but there was a decline in percentage from 100% positive Valsalva maneuver directly after ETBD to 63% after a period of 7 to 14 months.[18] Schröder measured a decline of improvement in mean Eustachian tube score; only at 3 years of follow-up.[6] Revisions due to failure of the first ETBD procedure were reported in three out of the 15 studies; out of at least 1,830 procedures performed, 122 needed a revision.[6,14,21] However, specific outcomes for these patients were not separately described.

Mucosal Inflammation

Three studies reported mucosal inflammation in the tuba auditiva as one of their outcome parameters.[16–18]

TABLE IV.
Outcome: Otoscopy, Audiometry, Tympanometry, and Tubamanometry.

Study (year)	Otoscopy F: normal TM in % or scores, *P* value	Audiometry F: reduction of anion gab in % or scores, *P* value	Tympanometry F: improvement of graph type in % or scores, *P* value	Tubamanometry F: improvement of ventilation in % or scores, *P* value
Bast (2014)	NR	NR	NR	NR
Catalano (2012)	NR	NR	3: 90% (28 ears)	NR
Dai (2016)	3: 83%, $P < 0.05$ 6: 100% (7 ears), $P < 0.05$ 12: 100% (3 ears), $P < 0.05$	3: 83% 6: 86% 12: 100% (3 ears)	3: 83% 6: 86%. 12: 100% (3 ears)	NR
Dalchow (2016)	NR	NR	NR	NR
Gürtler (2015)	1/4–3: 18%	1/4–3: 5 dB, $P < 0.01$	1/4–3: 55%	1/4–3: 30 mbar: from 15.81 to 1.20, $P < 0.01$ 40 mbar: 4.10 to 0.98, $P < 0.001$ 50 mbar: 1.66 to 0.83, $P < 0.001$
Jurkiewicz (2013)	NR	1/4: 43% 1 1/2: 86%	1/4: 0% 1 1/2: 86% PST 1/4: 0% 1 1/2: 86%	NR
Kivekas (2015)	1 1/4–3: from 22% to 72%	NR	1 1/4–3: from 25% with normal graph to 58%	NR
McCoul (2012)	1 1/2: from 5.7% to 100%, $P < 0.001$	NR	1 1/2: from 0% to 97% normal graph, $P < 0.001$	NR
Ockermann (2010)	NR	NR	NR	1/4: 30 mbar: from 37.5% tubes opening to 87.5% 40 mbar: from 25% tubes opening to 87.5% 50 mbar: from 12.5% tubes opening to 87.5%
Poe (2011)	7–14: from 0% to 45%	NR	7–14: 36%	NR
Schroder (2015)	NR	NR	NR	NR
Silvola (2014)	Mean 30: from 0% to 90%, $P < 0.001$	NR	Mean 30: from 2% type A curve to 56%, $P < 0.001$	NR
Wanscher (2014)	NR	2: 10 dB, $P < 0.05$	2: from 0% type A curve to 28%. Positive change in 58% (38 ears)	NR
Williams (2016)	NR	NR	Before: −295 DaPa (SD 77.38) 2–3: −164 (SD 105.09) 6–9, 14% −255 (SD 90.08) 12–15: −213 (SD 124.64) In total 68% improvement, $P < 0.05$	NR
Xiong (2016)	Normal pre- and postoperatively	NR	Before: 74% type A curve 1/4: 83% 3: 86%, 12: 98%	1/4, 3, 12: 30 mbar: from 36% tubes opening to 67%, 71%, and 79% respectively, $p<0.05$ 40 mbar: from 43% tubes opening to 71%, 78%, and 86%, $P <0.05$ 50 mbar: from 50% tubes opening to 74%, 84%, and 90%, $P <0.05$

Ears = number of ETBD procedures; ETBD = Eustachian tube balloon dilation; NR = not reported; PST = pressure swallow test; SD = standard deviation; TM = tympanic membrane.

TABLE V.
Outcome: Eustachian Tube Score, Eustachian Tube Score 2, and ETD Classification.

Study (year)	Eustachian Tube Score Follow-up (months): improvement in % or scores, *P* value.	Eustachian Tube Score 2 Follow-up (months): improvement in % or scores, *P* value	ETD Classification
Bast (2014)	NR	NR	NR
Catalano (2012)	NR	NR	NR
Dai (2016)	NR	NR	NR
Dalchow (2016)	NR	Before: mean 2.23 (SD 1.15)	NR
		1: mean 2.07 (SD 1.14)), NS	
		3: mean 2.31 (SD 1.23)), NS	
		6, mean 2.32 (SD 1.26)), NS	
		9: mean 2.33 (SD 1.29)), NS	
		12: mean 2.68 (SD 1.01)), $P < 0.05$	
Gürtler (2015)	1/4–3: mean score from 3 raised to 7, $P = 0.0001$	NR	NR
	26: mean score similar to 3 months		
Jurkiewicz (2013)	NR	NR	NR
Kivekas (2015)	NR	NR	NR
McCoul (2012)	NR	NR	NR
Ockermann (2010)	Before: 1.077 (SD 0.605)	NR	NR
	1/4: 4.154 (SD 63.023), $P < 0.05$		
	1/2: 5.846 (SD 62.609), $P < 0.05$		
	2: 7.539 (SD 61.391), $P < 0.05$		
Poe (2011)	NR	NR	NR
Schroder (2015)	Before: mean 3.15 (SD 2.54).	NR	NR
	2: mean 5.37 (SD 2.71) (n = 506), $P < 0.001$		
	12: mean 5.75 (SD 2.76) (n = 188), $P < 0.001$		
	24: mean 6.26 (SD 3.07) (n = 34), $P < 0.001$		
	36: mean 5.27 (SD 3.82) for n = 11, $P < 0.032$		
Silvola (2014)	NR	NR	NR
Wanscher (2014)	NR	NR	75% moved to a lower class.
Williams (2016)	NR	NR	NR
Xiong (2016)	Before: mean 3.3 (SD 1.4)	NR	NR
	1/4: mean 6.2 (SD 1.6)		
	3: mean 7.1 (SD 0.8)		
	12: mean 7.9 (SD1.2)		

Ears = number of ETBD procedures; ETBD = Eustachian tube balloon dilation; ETS = Eustachian tube score: history and tubamanometry (ETS 2: tubamonometry and tympanometry, ETD classification: Valsalva performance with help); NR = not reported; SD = standard deviation.

Kivekas et al. obtained biopsies of the Eustachian tube mucosa; postoperative biopsies demonstrated a thinner layer of fibrous tissue and restoration of epithelium at 5 to 12 weeks follow-up.[16] Two studies rated mucosal inflammation by means of nasendoscopy, which was assessed by various physicians.[17,18] Scores ranged from 1 to 4, where 1 was an open Eustachian tube, and 4 severe edema and inability to dilate the lumen. The mean preoperative score was either 2.91 (SD 0.83)[17,18] or 2.8 (SD 1.2),[12] and ameliorated postoperatively to 1.73 (SD 0.79) at a follow-up of 7 to 14 months and 1.4 (SD 0.8) after 30 months, respectively.[17] Both showed a significant ($P < 0.01$) decline of mucosal inflammation.

Adverse Events

Complications were mild, few, and self-limiting; of all the procedures in the 1,830 to 1,881 procedures, 36 minor adverse events were encountered (2%) (see Table III). Most often, a diffuse crush injury or local bleeding of the mucosa at the site of the Eustachian tube was reported (n = 20). One study described a severe side effect; a hematotympanum and

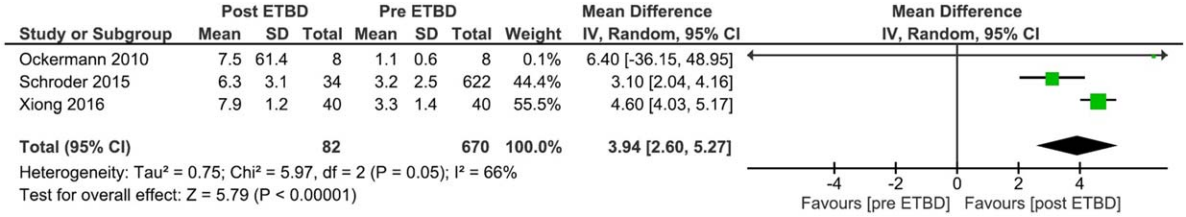

Fig. 2. Forest plot of the Eustachian tube score. A higher score correlates with fewer symptoms. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

myringotomy was necessary to relieve symptoms.[21] Four patients suffered from temporary otitis media acuta after ETBD,[19] and three patients had preauricular emphysema that spontaneously resolved over a few days.[6,14] Rhinitis complaints were reported in five patients during 1 to 5 days after ETBD.[26] One patient had a temporary increase in tinnitus complaints.[6]

Meta-Analysis

For four subgroups, a meta-analysis could be conducted: Valsalva, otoscopy, tympanometry, and Eustachian tube score (see Figs. 2–5). The subgroup Valsalva included five studies with 153 procedures in total and showed a decline of inability to perform the Valsalva maneuver after ETBD (RR: 0.13, 95% CI: 0.04–0.38, P = 0.0002, I^2 = 78%).[10,17,19,20,22]

Otoscopy showed either a normal tympanic membrane or not. An abnormal tympanic membrane usually implied either a retracted membrane, tubes or perforation. Six included studies with 166 procedures all showed a decline of otoscopic abnormal tympanic membranes after ETBD (RR: 0.38, 95% CI 0.07–2.05, P = 0.26, I^2 = 99%).[16–18,21,22,26]

In nine included studies accounting for 255 procedures tympanometry was described, showing a decline in the inability to dilute the Eustachian tubes (RR: 0.47, 95% CI 0.32–0.70, P = 0.0002, I^2 = 84%).[16–23,26]

Last but not least, the Eustachian tube score showed a mean improvement of 3.94 (95% CI:2.60–5.27, P < 0.00001, I^2 = 66%,) across three included studies, with up to 670 procedures.[6,10,22]

DISCUSSION

We conducted a systematic review aimed to evaluate balloon dilation as a treatment of ETD in adults and reviewed 15 articles, including 1,155 patients, undergoing 1,830 to 1,881 procedures. Although we may assume that all patients underwent ETBD procedure bilaterally, this was not specifically mentioned in 51 patients. Evaluation of the effect of ETDB was performed by a combination of prospective and retrospective collection of patient data (ETDQ-7 and GBI questionnaires), the Eustachian tube score, the Valsalva maneuver/Toynbee test, otoscopy, tympanometry, audiometry, ETD classification, and/or histopathology and mucosal inflammation by means of biopsies and nasendoscopy. All types of evaluation of ETD showed an improvement in short-term follow-up. In general, treatment provided symptom relief, which either remained stable over time or improved even further during an average follow-up time of 6.9 months (range 0–50 months). Furthermore, the number of complications was classified as relatively low and self-limiting. Revisions had to be performed in a total of 122 out of the 1,830 to 1,881 procedures. Overall, every published case study concludes ETBD to be a useful treatment of ETD, although further controlled studies are warranted. Supporting this claim is the meta-analysis provided in this review. The meta-analysis was restricted to four subgroups: the Valsalva maneuver, otoscopy, tympanometry, and the Eustachian tube score. All showed a decline of symptoms in favor of treatment. The heterogeneity ranged between 66% to 99% with a RR ranging from 0.13 to 0.47, showing a significant decline of symptoms.

All studies reported short-term symptom relief, although two studies reported a relative decline of this improvement over time (at 7–14 and 36 months).[6,18] Because follow-up ranged between 0 and 50 months postoperatively, no definite conclusion can be drawn on the long-term effectiveness of ETBD.

Overall risk of bias of the included studies was high because all studies were case series, without a control

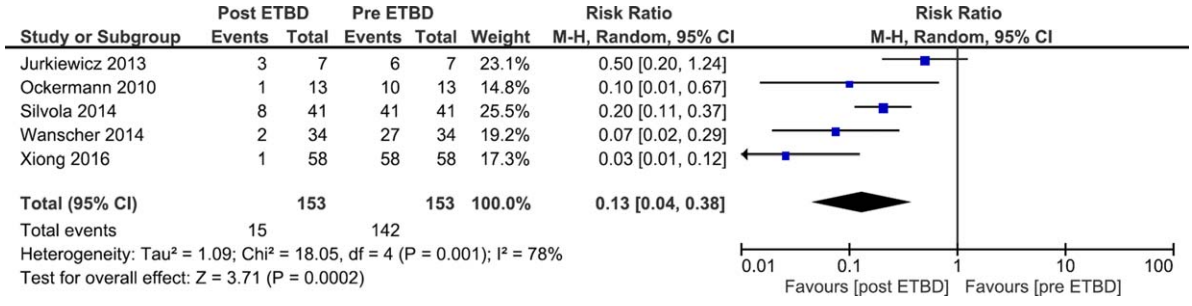

Fig. 3. Forest plot of the Valsalva maneuver. The lower the score, the more patients can perform a successful Valsalva maneuver. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

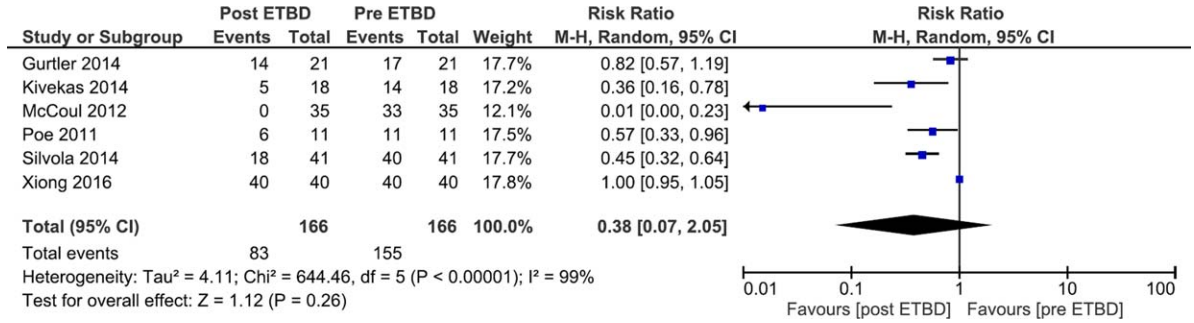

Fig. 4. Forest plot of otoscopy. The lower the score, the smaller the number of patients with an otoscopic tympanic membrane classified as abnormal. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

group or blinding, and susceptible to selection bias. Moreover, data needed for adequate comparison between studies and patient populations were not alike in all studies. Importantly, only relatively mild and few complications were reported, but not all studies mentioned side effects or complications in the first place. In addition, patient groups were not homogenous: some patients were preoperatively treated with decongestive nose spray; others received a ventilation tube; and some patients received other therapy (nasal steroids, decongestants, antibiotics, and tympanoplasty) during or after ETBD. In data analysis, there was no correction for confounders such as additional treatment and comorbidities.

Our meta-analysis was hampered by a high heterogeneity. As stated above, the inclusion criteria were not homogenous among studies, the manner of reporting differed, and the presence of simultaneous other therapies are all factors that might influence the reported outcome. Furthermore, the follow-up times differed between studies, which we could not correct for in the analysis.

With respect to radiological assessment, 10 studies performed imaging before EBTD in order to detect dehiscence of the carotid artery in the temporal bone. It may seem obvious that exclusion of these patients can prevent potential severe side effects, but no data were provided on how many patients were excluded for this reason. Abdel-Aziz et al.[29] previously questioned whether CT imaging is necessary and conclude that imaging does not predict intra- or postoperative difficulties in balloon dilation, and that fear of injury to the internal carotid artery might be disproportionate.[29] This is concomitant with a radiological study in which one thousand CT scans from the archives of the Military Hospital Ulm (Ulm, Germany) were evaluated and no dehiscence of the bony wall of the carotid was found.[30]

For future research on evaluating this promising ETBD therapy, three points need to be addressed. Primarily, it would be challenging to measure the effectiveness of balloon dilation more objectively.[9] The relationship between symptoms and the extent of measurable tuba dysfunction is not always linear. Several authors designed tools in order to assess ETD; one study used a self-designed externally validated Eustachian tube dysfunction questionnaire (ETDQ-7),[21] reaching both a high sensitivity (91%–100%) and specificity (95%–100%).[31–33] However, until now no other studies have used this test. Tubamanometry can be very useful, although it is not specific enough to diagnose ETD.[34] The combination of tubamanometry and symptoms by means of the Eustachian tube score may provide a more objective modality to assess ETBD severity. In a systematic review from 2014, the Eustachian tube score was reported to reach a sensitivity of 72% to 91% and a specificity of 53% to 86%.[9] Adding tympanometry to the Eustachian tube score raises both sensitivity and specificity to 96%.

Secondly, some argue that comparison of ETBD to other treatment should be performed before clinical

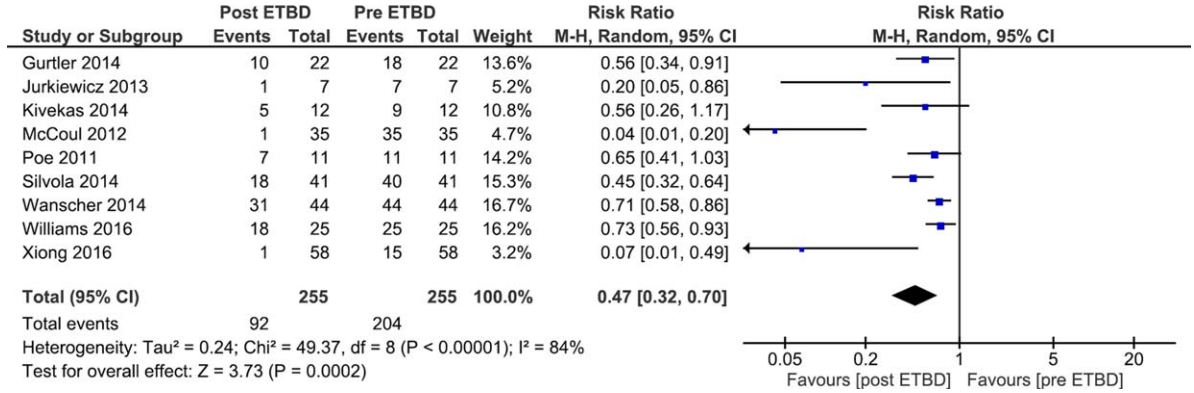

Fig. 5. Forest plot of tympanometry. The lower the score, the smaller the number of patients with a tympanogram type B or C. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

broad-scale implementation. Although this study design is the gold standard to demonstrate the effectiveness of a treatment, some treatments can have such a clear response that background noise has a subordinate effect.[35] As a result, randomized controlled trails not always are necessary. The least we can conclude is that treatment of ETD with balloon dilation seems favorable to reduce symptoms of ETD.

Thirdly, it is pivotal to select the appropriate study population. Not all patients with ETD complaints are hampered in the same manner. For some patients, ETD may be a leisurely problem, and for other patients such as pilots and divers who are exposed to relatively large changes in barometric pressure, it can severely affect their job capabilities.[2] It is recommended to provide a clear definition and standard measurements for ETBD in order to compare studies and outcome parameters, and a potential overlap with coinciding pathologies or comorbidities such as otitis media with effusion and atelectasis should be clearly described.

CONCLUSION

The Eustachian tube balloon dilation technique comprises the inflation of a balloon in the cartilaginous part of the Eustachian tube to cause local dilation. This procedure results in reduction of symptoms and diminished ETD severity scores in all the included studies. We recommend future research in randomized, homogenous populations, using a solid combination of the available diagnostic instruments and symptom scores to evaluate pre- and postoperative severity of tuba dysfunction.

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