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Type I Tympanoplasty Meta-Analysis: A Single Variable Analysis

Short running head:

Type I Tympanoplasty Meta-Analysis

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Acknowledgement:

Dr Noweed Ahmed and Dr Guy Watts contributed to the review of the studies included in the analysis, and Ms Charley Budgeon and Miss Chrianna Bharat contributed to the statistical analysis.

There was no funding received for this project.

ABSTRACT

Objective: To determine which independent variables influencing the efficacy of type I tympanoplasty in adult and pediatric populations.

Data Sources: A search of the PubMed database and Cochrane Database of Systematic Reviews using the key words “tympanoplasty OR myringoplasty” from January 1966 to July 2014 was performed.

Study Selection: Studies reporting outcomes of myringoplasty or Type I tympanoplasty in primary non-cholesteatomatous chronic tympanic membrane perforation were included.

Data Extraction: Of 4,698 abstracts reviewed, 214 studies involving 26,097 cases met our inclusion criteria and contributed to meta-analysis.

Data Synthesis: The primary outcome of success was defined as closure rate at 12 months. The independent variables analyzed were age, follow-up period, approach, graft material, perforation cause, size, location, ear dryness, and surgical technique. Only those studies providing data on a given parameter of interest could be included when comparing each variable.

Conclusion: The weighted average success rate of tympanic closure was 86.6%. Based on this meta-analysis, pediatric surgery has a 5.8% higher failure rate than adults and there is no correlation between follow-up period and success. Other variables associated with improved closure rates include perforation with a size less than 50% of total area (improved by 6.1%) and the use of cartilage as a graft (improved by 2.8% compared to fascia), while ears that were operated on while still discharging, those in different locations of the pars tensa, or using different surgical approaches or techniques did not have significantly different outcomes.

Key Words:

Myringoplasty, Meta-analysis, Tympanoplasty, Tympanic membrane perforation

INTRODUCTION

Type I tympanoplasty is a relatively common procedure in otolaryngology. The history of the management of a perforated tympanic membrane (TM) can be traced back to 1644, when Banzer used a tube of elk's claw covered in pig's bladder to close the perforation in a TM. (1) It was not until the nineteenth century that the British otologists, James Yearsley and Joseph Toynbee, targeted an improvement in hearing with their innovative devices. (2,3) Berthold introduced the term "myringoplasty", when he performed the first surgical closure of a TM perforation in 1878. (4) However, myringoplasty was not widely accepted until Wullstein and Zollner, utilizing the operative microscope, re-introduced it in 1951. (5) Tympanoplasty is the surgical repair of the TM and/or the middle ear ossicles. Horst Wullstein classified it into five types as described first in 1956. (6) Type I tympanoplasty, involving an intact ossicular chain, involves the grafting of TM alone onto an intact ossicular chain. The difference between type I tympanoplasty and myringoplasty is that tympanoplasty involves the raising of a tympanomeatal flap whereas myringoplasty does not, although the terms are often used interchangeably. (7) To avoid confusion for the remainder of this analysis both type I tympanoplasty and myringoplasty will be referred to as tympanoplasty. Two previous meta-analyses investigate outcomes in pediatric populations only. (8,9) This study aims to identify and analyze the variables that influence the success of TM repair in terms of closure rates and hearing outcomes in both the adult and pediatric population.

METHODS

This meta-analysis was performed in accordance with the PRISMA guidelines. (10)

Search method and study selection

All observational and experimental studies reporting closure rates were eligible for inclusion. Using the key words of tympanoplasty or myringoplasty a systematic literature search of the PubMed database and Cochrane Database of Systematic Reviews for studies published, in the English language, from January 1966 to July 2014 was conducted (July 2nd 2014), yielding 4698 articles. The search strategy for PubMed was ("myringoplasty"[MeSH Terms] OR "myringoplasty"[All Fields]) OR ("tympanoplasty"[MeSH Terms] OR "tympanoplasty"[All Fields]) AND ("1966/01/01"[PDAT] : "2014/07/01"[PDAT]). The primary author reviewed all abstracts of studies found with the above search strategy before two other independent authors selected studies for inclusion based on the defined criteria. If there were any abstracts that lacked clarity or adequate detail in their methodology or results, the full manuscript was read to assess suitability for inclusion. The inclusion and exclusion criteria were only applied after detailed assessment of full-text manuscripts. Duplicate reporting of results by authors were discarded. Studies were classified by a particular variable if at least 90% of the population fitted into that category, otherwise the options of unclassified, mixed or other were used and therefore being excluded in data analysis.

Study Inclusion Criteria

The inclusion criteria for individual studies were any observational (retrospective or prospective) or treatment (randomized or non-randomized clinical trials) study reporting the outcome of tympanoplasty in adult and pediatric

populations. Only studies reporting clinically diagnosed, primary non-cholesteatomatous chronic TM perforations were included. Studies were excluded if they reported patients who had tympanoplasty for acute perforations, for conditions other than perforation, revision surgery (if >10% of study population required revision surgery), other types of tympanoplasty (non-type I), ossicular chain pathology or mastoidectomy.

Variables

Variables examined included: the patient's age (at the time of surgery), follow-up period (months from surgery to the latest follow-up appointment), surgical approach (endaural or postaural), perforation cause (otitis media or traumatic – as defined by individual studies), graft material (cartilage, fascia, fat or other materials), perforation size (above or below 50% of TM surface area), perforation location (anterior, central or posterior), ear status (dry ear or 'wet' ear – defined as discharge from the middle ear at time of preadmission surgery appointment or a history of discharge within three months before surgery) and surgical technique (underlay, inlay or overlay graft positioning). For clarification, only chronic perforations were included and traumatic or other perforations that were not chronic were not included. Age and follow-up period were analyzed as a continuous variables with the range of ages, mean age and mean follow-up period extracted from each study.

Outcome measures

The primary outcome measure was the complete closure of the TM perforation, defined as an intact neo-membrane at 12 months follow-up. Secondary outcome measures were the presence of adverse events (re-perforation, re-operation / revision surgery, blunting, lateralization) and degree of improvement of conductive hearing loss (by pure tone audiometry).

Assessment of risk of bias in included studies

Risk of bias was assessed at the individual study level at time of first appraisal and in the finally included studies, using the studies own summary assessment of the risk of bias. No studies were excluded on this basis.

Data synthesis

A meta-analysis applying the methodology of Einarson was performed using S-PLUS 2000 (Insightful Corporation, Seattle, WA, USA). (11) An overall success rate was calculated, as well as rates for each variable. For each category, the number of studies that the results were based on was recorded, and the homogeneity of the studies ($p < 0.05$ indicates a non-homogeneous population), the meta-analytic average success rate, the standard error, and 95% confidence intervals were calculated. A p value less than 0.05 was considered statistically significant. Linear regression technique was used to analyze the correlation between follow-up period and success rate.

RESULTS

The search strategy identified 4704 articles after duplicates were removed. Figure 1 shows the method of study identification according to PRISMA. (10) Following screening, 321 full-text articles were assessed for eligibility and 107 articles were excluded. A total of 214 studies were included in quantitative analysis (see supplementary table). Of the 214 studies, two were randomized control trials and the rest were observational retrospective or prospective cohort studies. Across 214 included studies, there were 26,097 cases and the mean number of patients in each study was 122 (121.92 ± 149.51 , range of 7 to 1298 cases). The mean closure rate was 86.6% (range of 46.8% to 100%, 95% CI [85.3, 87.9]) and the mean age of patients in the included studies was 28 (27.63 ± 13.59 , range of 5.50 to 70.70 years of age). Figure 2 demonstrates the increasing trend in the number of articles published concerning Type I tympanoplasty or myringoplasty since 1970.

The results of the meta-analysis are plotted in Figure 3 and summarized in Table 1, showing that the overall meta-analytic average success rate for closure of perforations was 86.6%. Highest failure rates were detected in studies with follow-up periods greater than 12 months (4.38% worse with follow-up periods >12 months compared to ≤ 6 months). Though a decreasing success rate is observed with average longer follow-up times (≤ 6 months: 87.15%, ≤ 12 months: 85.61%, >12months: 82.77%), simple linear regression analysis calculated no correlation between success rate and follow-up period (Pearson's $r = 0.037$, $p = 0.625$, after adjusting for outlier studies). The adult population (defined as 18 years and above) had 5.8% better closure rates compared to the pediatric population (defined as 17 years old and below) (adult: 89.25%, pediatric: 83.42%). Within the pediatric population, children < 12 years had the worst closure rate of all age groups (≤ 12 years: 83.11%, >12 years 88.23%, 13 to 17 years: 92.81%). Patients with otitis media pre-operatively had 3.4% worse closure rates compared to patients with traumatic perforations (otitis media: 83.86%, traumatic: 87.25%). Patients with actively discharging ears had 3.6%

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)(10) flowchart summarizing the search results and the application of eligibility criteria.

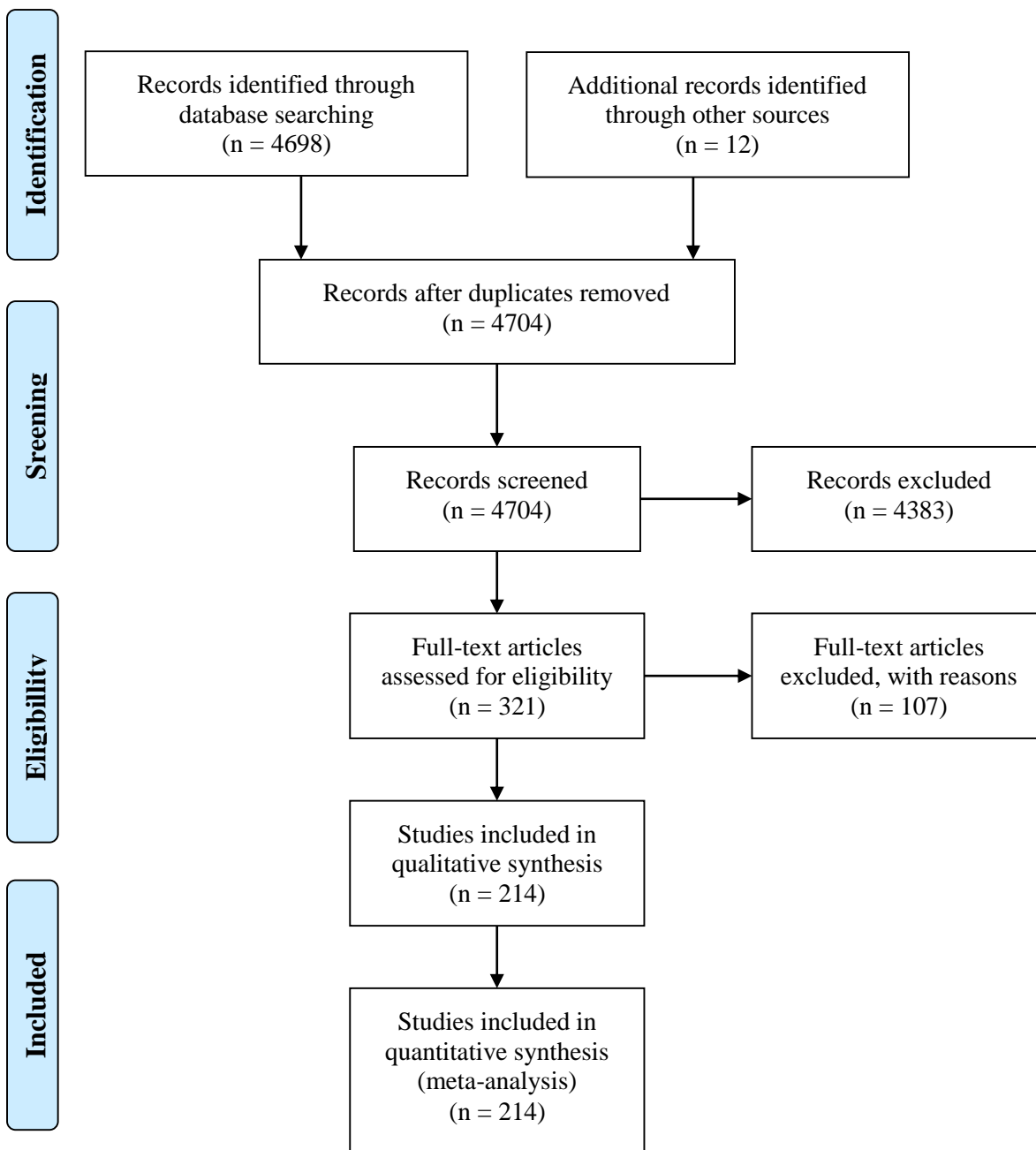


Figure 2: Graph demonstrating the number of studies regarding Type I tympanoplasty or myringoplasty published since 1970 per 5-year interval.

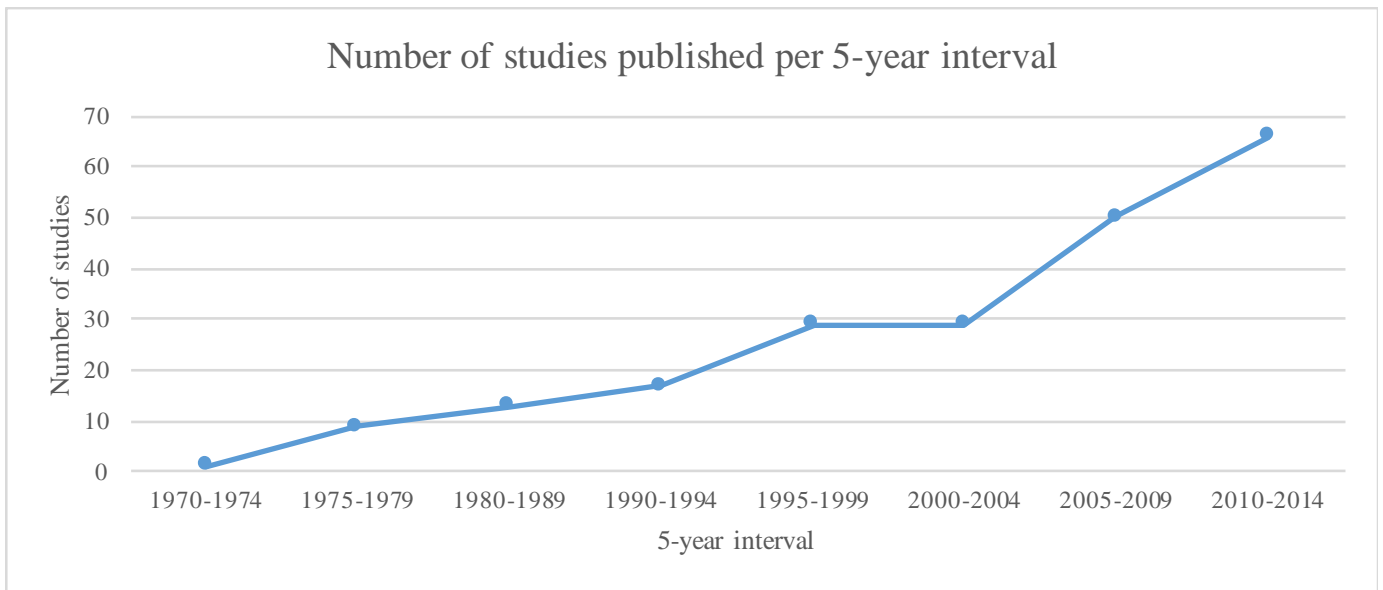


Figure 3: Graph of results depicting the overall closure rate and success rates stratified by each variable.

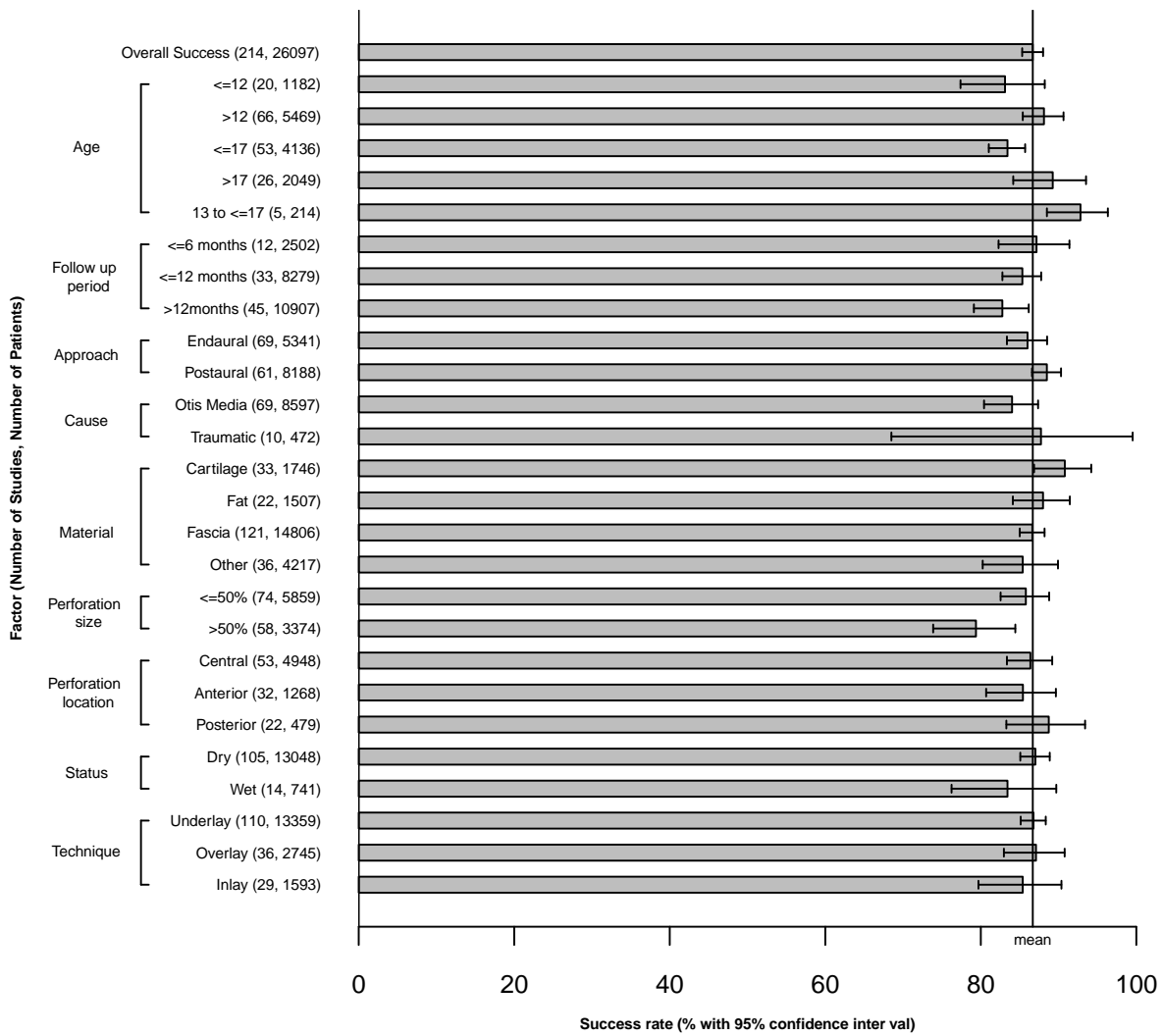


Table 1: Variables and their effects on the primary outcome of success of tympanoplasty.

Variable	Type	No. Studies	No. Patients	Success (%)	95% CI Range	<i>p</i> value*
	Overall Success	214	26097	86.62	85.27 – 87.92	-
Age	≤12	20	1182	83.11	77.38 – 88.21	0.075
	>12	66	5469	88.23	85.55 – 90.68	
	≤17	53	4136	83.42	81.01 – 85.70	<u>0.017</u>
	>17	26	2049	89.25	84.17 – 93.52	
	13 to ≤17	5	214	92.81	88.49 – 96.33	-
Follow-up period	≤6 months	12	2502	87.15	82.28 – 91.38	-
	≤12 months	33	8279	85.61	83.07 – 87.98	0.320
	>12months	45	10907	82.77	79.11 – 86.15	
Approach	Endaural	69	5341	86.02	83.35 – 88.51	0.112
	Postaural	64	8188	88.06	86.12 – 89.88	
Perforation cause	Otitis Media	69	8597	83.86	80.33 – 87.12	0.8610
	Traumatic	10	472	87.25	70.21 – 98.62	
Graft material	Cartilage	33	1746	90.80	86.85 – 94.19	<u>0.048</u>
	Fascia	121	14806	88.00	84.13 – 91.44	
	Fat	22	1507	86.52	84.91 – 88.05	0.469
	Other	36	4217	85.39	80.23 – 89.92	
Perforation size	≤50%	74	5859	85.56	82.39 – 88.48	<u>0.019</u>
	>50%	58	3374	79.44	74.06 – 84.40	
Perforation location	Central	53	4948	86.03	83.08 – 88.77	0.822
	Anterior	32	1268	85.42	80.68 – 89.66	
	Posterior	22	479	88.72	83.28 – 93.41	
Ear status	Dry	105	13048	87.02	85.09 – 88.85	0.155
	Wet	14	741	83.44	76.24 – 89.69	
Surgical technique	Underlay	110	13359	86.71	85.09 – 88.26	0.712
	Overlay	36	2745	86.83	82.78 – 90.45	
	Inlay	29	1593	85.39	79.69 – 90.36	

worse closure rates compared to pre-operatively dry ears (dry: 87.02%, wet: 83.44%). Perforations greater than 50% have a 6.1% lower success rate than those less than 50% in size ($\leq 50\%$ perforation size: 85.56%, $>50\%$ perforation size: 79.44%). Anterior perforations had lower closure rates than central or posterior perforations by 0.6% and 3.3% respectively (anterior: 85.42%, central: 85.42%, posterior 88.72%). The postaural approach had an increased closure rate of 2.0% compared to endaural approach, but the difference was not statistically significant. The underlay technique was the most commonly used graft technique (used in 75.5% of patients: 13,359 of 17,697 total patients where surgical technique was specified). The overlay technique was only 0.1% better in achieving successful closure compared to the underlay technique, and the inlay technique was the least common and successful (underlay: usage 75.5%, success 86.71%, overlay: usage 15.5%, success 86.83%, inlay: usage 9.0%, 85.39%). Cartilage had superior closure rates compared to temporalis fascia, fat, and ‘other’ materials such as paper, alloderm, perichondrium, other synthetic materials (cartilage: 90.80%, fascia 88.00%, fat: 86.52%, other 85.39%). Pairwise comparisons of graft materials showed that cartilage compared to fascia as the only significant pair comparison with a p value of 0.048. When cartilage was compared to fat or to ‘other’ materials, there was no significant advantage (p value 0.366 and 0.110 respectively). Likewise, fascia compared to fat and to ‘other’ materials was not significant (p value 0.581 and 0.560 respectively). Lastly, fat compared to ‘other’ materials was not significant (p value 0.4692). Audiometry data was inconsistently reported, and a mean improvement in ABG post operatively could not be ascertained. However, data at the 10dB, 20dB and 30dB postoperative ABG thresholds was available in 29, 32 and 30 studies respectively. Looking at the postoperative ABG within these studies, 42.5% of cases ($n = 1380/3247$) were within 10dB, 68.6% ($n = 2428/3540$) within 20dB and 95.5% ($n = 2797/2928$) within 30dB.

DISCUSSION

The overall closure rate for this meta-analysis was 86.6%, with an adult population success rate of 89.2% and a pediatric population success rate of 83.4%, which is the same success rate identified in a 2015 meta-analysis of pediatric tympanoplasty. (9)

Follow-up period does not correlate to graft success rate

Through linear regression analysis, this study demonstrates that there is no correlation between follow-up period and success rate. In some series, the follow-up period is as little as two months while in others it was as high as 12 years. (12-15) Some authors have suggested that late graft failure is relatively rare, therefore stating that a graft follow-up period of six months is sufficient. (16,17) However, others have compared short and long-term follow-up periods and demonstrated that a significant number of failures occur after one year. (18,19) It has been observed that regardless of any factors that can be controlled, a 10% deterioration in closure rate occurs within the first two years post-operatively. (13) These late re-perforations are attributed to either underlying Eustachian tube dysfunction or to avascularity and inappropriate thickness of the graft. (20) Future studies should aim to follow-up graft success for a minimum of 12 months.

Adult populations have superior closure rates

In our analysis, it was demonstrated that adults had a better closure rate than the overall pediatric population. Interestingly, the teenage subgroup (13 to 17 years of age) had the highest success rate (92.81%), 9.7% higher than for children ≤ 12 years (83.11%) and 9.4% higher than success rate for children ≤ 17 years (83.42%) suggesting

within children, better outcomes are found in older children. However, direct comparison of age groups above and below 12 years was not significant, and no comparative analysis could be made between <12 years and 13 to 17 years. Our findings are consistent with a meta-analysis of pediatric tympanoplasty performed in 1997, which identified that age was a significant factor, and that in children better outcomes are found with increasing age. (8) However, a more recent meta-analysis of pediatric tympanoplasty has found through subgroup analysis that age was not a significant factor affecting the closure rate. (9) The lower success rate of tympanoplasty in children is thought to be related to Eustachian tube function and its relationship with otitis media. (21-25) There remains debate as to whether there should be a minimum age for tympanoplasty or not, with some studies suggesting it should be performed after the Eustachian tube is at adult development after seven years of age. (22,26-31) The decision to perform tympanoplasty in children remains a balance of the risks and benefits within the individual patient with the additional added risk of an increased rate of failure. In order to determine a recommended minimum age for tympanoplasty, future studies should aim to report age-specific closure rates.

Discharging ears and perforations due to otitis media do not significantly affect closure rates

Closure rates in tympanoplasty performed in perforations due to otitis media and in those perforations that were still discharging were not significantly affected. It is important to recognize that discharging ears may not necessarily be infected, with multiple factors including tympanomastoid space mucosa, ventilation and Eustachian tube dysfunction influencing the occurrence and presentation of infection. (28) Individual studies looking at this specific issue have reported mixed results. (15,17,22,26,32-36) Given that this meta-analysis and no individual study claims that perforations that are wet have a higher success rate for closure, it would seem reasonable to attempt to create a dry perforation but not make this a necessary condition for surgery.

Perforation size matters, but location does not

This meta-analysis indicates that perforations greater than 50% have a lower success rate, while the location of the perforation had no significant effect on success rate. Several individual studies also found a significantly higher rate of failures in larger perforations. (9,17,20,26,32,34,37,38) There are also individual studies where perforation size was not observed to affect overall results. (16,22,24,36,39-46) The major reasons thought to be responsible for graft failure in larger perforations are increased technical difficulty, reduced visibility, reduced graft overlap with the residual TM, a poor vascular bed for the graft and poor graft support or fixation. (16,34) Some studies have claimed that anteriorly placed perforations are associated with a poorer outcome, possibly due to reduced vascularity or exposure of the anterior TM. (13,15,47,48) While our meta-analysis did not demonstrate statistical significance with the location of the perforation, it is important to acknowledge that large-sized perforations often include the anterior segment, as anterior-only perforations are uncommon. (49) Anteriorly located perforations also had the lowest success rate (85.42% vs. 86.03% for central and 88.72% for posterior) and so the site of the perforation while not proving to be significant for success rate remains an important factor.

No surgical approach has an advantage

The type of surgical approach did not have an impact on outcomes. Surgical approach depends on many factors including the perforation size, location, visualization and the individual surgeon's preference. Typically an endaural or transcanal approach is used for smaller, more posterior perforations in wider canals. Because there are a number of variables that contribute to the decision of approach and these are biased by the individual surgeon's preferences it is not surprising that this meta-analysis did not detect a difference.

There is no superior graft placement technique

This meta-analysis demonstrates that there is no significant difference between the grafting techniques used (underlay, overlay and inlay). While the underlay technique was the most commonly used graft technique (75.5% of patients in this meta-analysis), there was no significant benefit of any individual technique. Some individual studies have claimed superiority in closure rates for the overlay technique. (50,51) Others have reported no difference; however, there is an identified increased risk of blunting of the anterior tympanomeatal angle and lateralization of the TM are more common when utilizing the overlay technique. (52-54) Blunting may result in a persistent conductive hearing loss. (16) The inlay technique was initially used for small perforations utilizing a plug of adipose tissue. (4,55) More recently, this technique has been applied using cartilage. (56-58) There does not appear to be a definitive indication for each technique, so to a large extent the choice usually depends on the surgeon's view of each technique's relative advantages or disadvantages. (59,60) As each surgeon has personal preferences, it is almost impossible to compare grafting techniques performed by the same surgeon and excellent outcomes are achieved with all techniques. (16,51,61-64)

Cartilage has superior closure rates

The most commonly used graft materials are temporalis fascia, cartilage and fat, which are all readily accessible at the surgical site. Over the years many other natural and synthetic materials have been trialed, but there are very few published studies on outcomes. Our meta-analysis shows that cartilage (90.80%) has a small but significant superior closure rate to temporalis fascia (88.00%), with pairwise comparisons of other material choices demonstrating no significance. A small randomized prospective clinical trial comparing fascia (20 ears) to cartilage (18 ears) found the graft uptake rates and hearing outcomes were not significantly different at 24 months (84.2% and 80% respectively). (65) Since the literature review date of this meta-analysis one other randomized control trial showed a

benefit for cartilage in closure rate at 12 months, while another reported a reduced post-operative infection rate with cartilage. (57,66,67) One possible suggested explanation of this difference in cartilage success, between these two trials, is that poorer results may occur with cartilage thickness over 500 micrometers. (67) While graft choice ultimately depends on the perforation type, size and surgeon preference, our meta-analysis has shown that cartilage, as an independent variable, is a superior graft choice compared to temporalis fascia in both the pediatric and adult populations in terms of perforation closure. Cartilage is also often used as a graft material for smaller sized perforations, which innately have higher healing rates, and this may account for the increased closure rate with cartilage compared to other graft material. Different graft materials can also be used in different situations and the superiority of cartilage must still be balance for an individual patient's situation and the surgeon's experience with a particular material.

Hearing outcomes were inconsistently reported

Hearing outcomes following tympanoplasty are inconsistently reported which limits the conclusions that are able to be made. In this meta-analysis 39% (83 of 214 studies) of the studies recorded post-operative hearing results. Due to inconsistency in reporting the overall mean hearing gain could not be calculated. The range of mean postoperative air-bone gap (ABG) closures in individual studies was 1.2dB to 25.5dB. A total of 32 studies in this meta-analysis contributed data with complete reporting of postoperative ABG. (20,24,43,48,56,57,61,64,68-91) Data at the 10dB, 20dB and 30dB postoperative ABG thresholds was available in 29, 32 and 30 studies respectively. Looking at the postoperative ABG within these studies, 42.5% of cases (n = 1380/3247) were within 10dB, 68.6% (n = 2428/3540) within 20dB and 95.5% (n = 2797/2928) within 30dB, demonstrating that only a minority of patients achieved the best postoperative ABG (<10dB). While the ideal outcome in Tympanoplasty is the complete closure of the postoperative ABG to 0 dB (indicating no hearing loss), achieving a postoperative ABG

<10dB should be considered good clinical outcome as an ABG greater than 10dB indicates a conductive hearing loss. Though data was collected on pure-tone air conduction thresholds, very few studies documented findings in adequate detail for a meaningful analysis. When examining other individual studies' ability to achieve a postoperative ABG within 20dB there are reports ranging from 60% to 90%, consistent with our finding of 69%. (12,35,48,51,70,72,92,93) The impact of variables on hearing outcomes could not be determined due to the poor quality of reporting. Future studies should report audiometric outcomes in accordance to the American Academy of Otolaryngology, Head and Neck Surgery's Hearing Committee and with audiometry test results before and after surgery. (94)

Secondary outcomes and complications

The complications detected in this meta-analysis are reported in Table 2. Complication rates were reported in only 21% of studies (44 of 214 studies). The most commonly reported complications were reperforation (11.9%), revision surgery (11.4%), blunting (6.7%) and lateralization (4.2%). Re-operation or revision surgery was defined as any operation caused by an event requiring return to theatre, or as defined by the individual study. Future studies should aim to report complications in greater details to help future analysis of specific complications.

The effect of mastoidectomy

Mastoidectomy or other surgical adjunctive procedures were not included as a variable as the majority of studies did not discriminate between cholesteatoma and non cholesteatoma etiology when considering mastoidectomy. The current body of literature has been unable to demonstrate a clear benefit for TM healing when mastoidectomy is performed concurrently with tympanoplasty. Several studies retrospectively compared tympanoplasty alone to

Table 2: Complication rates as reported by individual studies included in this meta-analysis.

Complication	Number of studies	Mean (%)	Range (%)	SD
Reperforation	22	11.88	2.25 - 31	7.72
Reoperation	14	11.43	1 - 87%	23.25
Blunting	17	6.65	1 - 54%	12.36
Lateralization	17	4.24	1 - 13%	3.75

tympanoplasty with mastoidectomy for TM perforation repair and did not find any statistical difference in repair success or hearing outcomes for adults or children. (95-98) A large prospective randomized study of adults with CSOM compared graft success rate and mean postoperative-ABG between tympanoplasty only to tympanoplasty with cortical mastoidectomy and concluded there was no significant difference. (99) Regarding non-cholesteatomata CSOM perforations, a literature review examining 26 articles concluded that there was no additional benefit to performing mastoidectomy with tympanoplasty for uncomplicated TM perforations. (100)

Limitations

Any meta-analysis is limited by the quality of the primary data. In the 214 included studies, there were only three experimental studies, with the majority of studies being retrospective cohort studies. Most studies did not report hearing outcomes adequately, or were inconsistent with outcome reporting. We relied on individual studies to determine the chronicity of perforations, as well as their definition of a 'chronic traumatic' perforation. Differences in surgical technique were not accounted for as these are highly variable between individual surgeons, difficult to define and mostly unreported.

CONCLUSION

Based on this meta-analysis, the weighted average success rate of tympanic closure was 86.6%. Pediatric surgery has a larger failure rate than adults. Poorer outcomes are found in those perforations with a size over 50% of the total area. Perforations discharging around the time of surgery and those perforations of different locations of the pars tensa did not have significantly different outcomes. The length of follow-up period does not correlate to graft success. Surgical factors that led to improved closure rates include the use of cartilage whilst other factors such as

surgical approach or technique of graft placement did not influence the closure rate overall. Future studies should, at a minimum, report closure rates, hearing outcomes, complications and report follow-up of at least 12 months.

ACKNOWLEDGEMENTS

We thank Dr Noweed Ahmed and Dr Guy Watts for contributing to the review of the studies included in the analysis, and Ms Charley Budgeon and Miss Chrianna Bharat for contributing to the statistical analysis.

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SUPPLEMENTARY TABLE – INCLUDED STUDIES

Reference	Author(s)	Year	Title
1	Abdelghany, A.M.	2013	The button graft technique for perforations affecting less than 25% of the tympanic membrane: a non-randomised comparison of a new modification to cartilage tympanoplasty with underlay and overlay grafts
2	Acar, M., et al.	2015	Fat-plug myringoplasty of ear lobule vs abdominal donor sites
3	Adkins, W.Y., et al.	1984	Type I tympanoplasty: influencing factors
4	Ahmed, S., et al.	2013	Chondroperichondrial clip myringoplasty: a new technique for closure of tympanic membrane perforations
5	Ahmed, Z., et al.	2005	Over-under myringoplasty
6	Ajulo, S.O., et al.	1993	Peri-umbilical superficial fascial graft myringoplasty--a simple alternative
7	Al-Khtoum, N., et al.	2009	Myringoplasty in children: retrospective analysis of 35 cases
8	al-Shaikh, A.M., et al.	1998	Underlay tympanoplasty with anterior and posterior flaps for subtotal perforations
9	Albera, R., et al.	2009	Equine versus bovine pericardium in transmeatal underlay myringoplasty
10	Albera, R., et al.	2006	Tympanic reperforation in myringoplasty: evaluation of prognostic factors
11	Albera, R., et al.	1998	[Myringoplasty in children: a comparison with an adult population]
12	Albirmawy, O.A.	2010	Comparison between cartilage-perichondrium composite 'ring' graft and temporalis fascia in type one tympanoplasty in children
13	Alkan, S., et al.	2009	Effect of the use of dry (rigid) or wet (soft) temporal fascia graft on tympanoplasty
14	Altuna, X., et al.	2010	[Island cartilage myringoplasty. Anatomical and functional results in 122 cases]
15	Alzahrani, M., et al.	2015	Hyaluronic acid fat graft myringoplasty vs fat patch fat graft myringoplasty
16	Alzoubi, F.Q., et al.	2010	Comparison between transtympanic and elevation of tympanomeatal flap approaches in tympanoplasty
17	Anderson, O., et al.	2007	Tri-adcortyl ointment ear dressing in myringoplasty: an analysis of outcome
18	Attallah, M.S., et al.	1996	Hearing results in tympanoplasty in Riyadh
19	Aviles Jurado, F.J., et al.	2009	[Myringoplasty: auditory follow-up and study of prognostic factors]
20	Ayache, S.	2013	Cartilaginous myringoplasty: the endoscopic transcanal procedure
21	Ayache, S., et al.	2003	Adipose graft: an original option in myringoplasty
22	Bajaj, Y., et al.	1998	Tympanoplasty in children--a prospective study
23	Balaguer Garcia, R., et al.	2011	[Myringoplasties. A retrospective analysis of our surgical outcomes]
24	Becker, J., et al.	2011	Success rate of myringoplasty at Groote Schuur Hospital
25	Benson-Mitchell, R., et al.	1996	Day-stay myringoplasty

26	Berger, G., et al.	1983	Myringoplasty in children
27	Bhat, N.A., et al.	2000	Retrospective analysis of surgical outcome, symptom changes, and hearing improvement following myringoplasty
28	Black, J.H., et al.	1995	An analysis of the results of myringoplasty in children
29	Black, J.H., et al.	1995	Myringoplasty--effects on hearing and contributing factors
30	Blanshard, J.D., et al.	1990	A long term view of myringoplasty in children
31	Borkowski, G., et al.	1999	[Autologous perichondrium-cartilage graft in the treatment of total or subtotal perforations of the tympanic membrane]
32	Boronat-Echeverria, N.E., et al.	2012	Prognostic factors of successful tympanoplasty in pediatric patients: a cohort study
33	Brandow, E.C., Jr.	1976	Homograft tympanic membrane myringoplasty
34	Buchwach, K.A., et al.	1980	Serous otitis media and type I tympanoplasties in children. A retrospective study
35	Callanan, V.P., et al.	1993	Xenograft versus autograft in tympanoplasty
36	Castro, O., et al.	2013	Myringoplasties in children: our results
37	Caye-Thomasen, P., et al.	2007	Bilateral myringoplasty in chronic otitis media
38	Caylan, R., et al.	1998	Myringoplasty in children: factors influencing surgical outcome
39	Chanvimalueng, W.	2000	A clinical comparison of outpatient and standard myringoplasty
40	Claes, J., et al.	1990	Allograft tympanoplasty: predictive value of preoperative status
41	Cody, D.T., et al.	1973	Tympanoplasty: long-term results
42	Coskun, B.U., et al.	2006	The effects of the incision types in myringoplasty operations on cosmesis
43	Couloigner, V., et al.	2005	Inlay butterfly cartilage tympanoplasty in children
44	D'Eredita, R., et al.	2009	Anterior tab flap versus standard underlay myringoplasty in children
45	Dabholkar, J.P., et al.	2007	Comparative study of underlay tympanoplasty with temporalis fascia and tragal perichondrium
46	De, S., et al.	2004	Myringoplasty using a subcutaneous soft tissue graft
47	De Seta, E., et al.	2013	Type I tympanoplasty with island chondro-perichondral tragal graft: the preferred technique?
48	Deddens, A.E., et al.	1993	Adipose myringoplasty in children
49	Deenadayal, D.S., et al.	2011	Graft uptake rates with isoamyl-2-cyanoacrylate in myringoplasty procedures: a 10-year retrospective study
50	Demirpehlivan, I.A., et al.	2011	Comparison of different tympanic membrane reconstruction techniques in type I tympanoplasty
51	Denoyelle, F., et al.	1999	Myringoplasty in children: predictive factors of outcome
52	Dursun, E., et al.	2008	Comparison of paper-patch, fat, and perichondrium myringoplasty in repair of small tympanic membrane perforations

53	Eavey, R.D.	1998	Inlay tympanoplasty: cartilage butterfly technique
54	Effat, K.G.	2005	Results of inlay cartilage myringoplasty in terms of closure of central tympanic membrane perforations
55	Eisenbeis, J.F., et al.	2004	Areolar connective tissue grafts in pediatric tympanoplasty: a pilot study
56	el-Guindy, A.	1992	Endoscopic transcanal myringoplasty
57	Emir, H., et al.	2007	Success is a matter of experience: type 1 tympanoplasty : influencing factors on type 1 tympanoplasty
58	Emmett, J.R.	1999	Age as a factor in the success of tympanoplasty: a comparison of outcomes in the young and old
59	Eren, S.B., et al.	2014	A randomized prospective trial of a novel device for measuring perforation size during inlay 'butterfly' myringoplasty
60	Fadl, F.A.	2003	Outcome of type-1 tympanoplasty
61	Feilen, S.E., et al.	1996	[Long-term outcome of tympanoplasty in chronic suppurative middle ear infection in childhood]
62	Fernandes, S.V.	2003	Composite chondroperichondrial clip tympanoplasty: the triple "C" technique
63	Fouad, T., et al.	2010	Utilization of amniotic membrane graft for repair of the tympanic membrane perforation
64	Francois, M., et al.	1985	[Miringoplasty in children]
65	Fukuchi, I., et al.	2006	Tympanoplasty: surgical results and a comparison of the factors that may interfere in their success
66	Gamra, O.B., et al.	2008	Cartilage graft in type I tympanoplasty: audiological and otological outcome
67	Gavriel, H., et al.	2013	Inferior flap tympanoplasty: a novel technique for anterior perforation closure
68	Gedikli, O., et al.	2011	Efficacy of octyl-2-cyanoacrylate in type I tympanoplasty
69	Gersdorff, M., et al.	1995	Myringoplasty: long-term results in adults and children
70	Ghosh, L.M., et al.	1991	Paediatric myringoplasty in India
71	Gibb, A.G., et al.	1982	Myringoplasty (A review of 365 operations)
72	Golz, A., et al.	2003	Paper patching for chronic tympanic membrane perforations
73	Goyal, N., et al.	2002	Myringoplasty for chronic otitis media
74	Gross, C.W., et al.	1989	Adipose plug myringoplasty: an alternative to formal myringoplasty techniques in children
75	Gupta, S.C.	2000	Myringoplasty with a single flap
76	Habesoglu, T.E., et al.	2011	Effect of type I tympanoplasty on the quality of life of children
77	Habib-ur-Rehman, et al.	2011	Otitis Media: Comparison of outcome of underlay versus overlay myringoplasty
78	Hagemann, M., et al.	2003	[Tympanoplasty with adipose tissue]
79	Haksever, M., et al.	2015	Inlay butterfly cartilage tympanoplasty in the treatment of dry central perforated chronic otitis media as an effective and time-saving procedure
80	Halim, A., et al.	2009	Pediatric myringoplasty: postaural versus transmeatal approach
81	Hamans, E.P., et al.	1996	Allograft tympanoplasty type 1 in the childhood population

82	Harterink, E., et al.	2014	Results of myringoplasty in children with cleft palate: a patient-matched study
83	Harugop, A.S., et al.	2008	A comparative study of endoscope assisted myringoplasty and microscope assisted myringoplasty
84	Harvinder, S., et al.	2005	Underlay myringoplasty: comparison of human amniotic membrane to temporalis fascia graft
85	Hicks, G.W., et al.	1988	A review of 925 cases of tympanoplasty using formaldehyde-formed-fascia grafts
86	Hod, R., et al.	2013	Inlay "butterfly" cartilage tympanoplasty
87	Hung, T., et al.	2004	Anterosuperior anchoring myringoplasty technique for anterior and subtotal perforations
88	Iacovou, E., et al.	2012	Effect of type I tympanoplasty on the resonant frequency of the middle ear: comparison between chondrotympanoplasty and temporalis fascia grafting
89	Jung, T., et al.	2009	Medial or medio-lateral graft tympanoplasty for repair of tympanic membrane perforation
90	Jung, T.T., et al.	2005	Mediolateral graft tympanoplasty for anterior or subtotal tympanic membrane perforation
91	Jurovitzki, I., et al.	1988	Miringoplasty: long-term followup
92	Kaddour, H.S.	1992	Miringoplasty under local anaesthesia: day case surgery
93	Kane, R.J., et al.	1980	Out-patient myringoplasty
94	Karela, M., et al.	2008	Miringoplasty: surgical outcomes and hearing improvement: is it worth performing to improve hearing?
95	Karkanavatos, A., et al.	2003	Day-case myringoplasty: five years' experience
96	Kartush, J.M.	2000	Tympanic membrane Patcher: a new device to close tympanic membrane perforations in an office setting
97	Kazikdas, K.C., et al.	2007	Palisade cartilage tympanoplasty for management of subtotal perforations: a comparison with the temporalis fascia technique
98	Kessler, A., et al.	1994	Type 1 tympanoplasty in children
99	Khan, M.M., et al.	2011	Primary cartilage tympanoplasty: our technique and results
100	Kim, D.K., et al.	2011	Clinical efficacy of fat-graft myringoplasty for perforations of different sizes and locations
101	Kim, H.J., et al.	2014	Functional and practical outcomes of inlay butterfly cartilage tympanoplasty
102	Knapik, M., et al.	2011	Pediatric myringoplasty: a study of factors affecting outcome
103	Koch, W.M., et al.	1990	Tympanoplasty in children. The Boston Children's Hospital experience
104	Komune, S., et al.	1992	Interlay method for myringoplasty
105	Konstantinidis, I., et al.	2013	Fat myringoplasty outcome analysis with otoendoscopy: who is the suitable patient?
106	Kumar, S., et al.	2010	Pediatric myringoplasty: definition of "success" and factors affecting outcome
107	Kwong, K.M., et al.	2012	Fat graft myringoplasty using umbilical fat
108	Kyrodimos, E., et al.	2014	Cartilage tympanoplasty: a reliable technique for smokers
109	Lai, P., et al.	2006	Lateral graft type 1 tympanoplasty using AlloDerm for tympanic membrane reconstruction in children
110	Landsberg, R., et al.	2006	Fat graft myringoplasty: results of a long-term follow-up

111	Lee, P., et al.	2002	Myringoplasty: does the size of the perforation matter?
112	Lee, S.H., et al.	2008	Paper-patch myringoplasty with CO2 laser for chronic TM perforation
113	Li, P., et al.	2010	The selection and strategy in otoendoscopic myringoplasty with autogenous adipose tissue
114	Lima, J.C., et al.	2011	Evaluation of the organic and functional results of tympanoplasties through a retro-auricular approach at a medical residency unit
115	Lin, Y.C., et al.	2011	Predictors of surgical and hearing long-term results for inlay cartilage tympanoplasty
116	Loock, J.W., et al.	2008	A randomised controlled trial comparing fresh, dried, and dried-then-rehydrated temporalis fascia in myringoplasty
117	Lou, Z.C., et al.	2011	Prognosis and outcome of the tympanic membrane flap at traumatic tympanic membrane perforation edge
118	Lubianca-Neto, J.F.	2000	Inlay butterfly cartilage tympanoplasty (Eavey technique) modified for adults
119	MacDonald, R.R., 3rd, et al.	1994	Fasciaform myringoplasty in children
120	Maeta, M., et al.	1998	[A clinical comparison of orthodox myringoplasty and a simple method with fibrin glue]
121	Mak, D., et al.	2004	Outcomes of myringoplasty in Australian Aboriginal children and factors associated with success: a prospective case series
122	Mauri, M., et al.	2001	Evaluation of inlay butterfly cartilage tympanoplasty: a randomized clinical trial
123	Mendel, L., et al.	1985	A clinical comparison of the results of two different methods of closing tympanic membrane perforations
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