

## Main Article

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## Abstract

**Objective.** To determine the outcomes of tympanoplasty surgery using porcine-derived small intestinal submucosa.

**Method.** A retrospective audit was conducted in a hospital setting. Thirty-five adult and paediatric patients who received a small intestinal submucosa graft as part of tympanoplasty surgery were retrospectively reviewed. Patients underwent either simple tympanoplasty ( $n=26$ ) or complex tympanoplasty as part of a concurrent otological procedure such as atticotomy and mastoidectomy. The main outcome measures were rate of tympanic membrane closure and change in four-frequency mean air–bone gap.

**Results.** Thirty-one patients had a follow-up period of longer than two months. Closure was obtained in 22 patients (71 per cent). The mean air–bone gap improved from 20.7 to 12.3 dB HL in the simple tympanoplasty group and from 22.3 to 12 dB HL in the complex tympanoplasty group.

**Conclusion.** Tympanoplasty surgery with small intestinal submucosa is a viable option for patients where autologous graft is not available or in order to minimise donor site morbidity.

## Introduction

Chronic tympanic membrane perforations continue to be a challenge for modern otolaryngologists and present morbidity for their patients. Type I tympanoplasty (or myringoplasty) for tympanic membrane perforation repair is a commonly performed otological procedure. The procedure involves placement of a graft material under the tympanic membrane perforation, which acts as a framework for the native tympanic membrane epithelium to grow over and close the perforation. The largest meta-analysis of type I tympanoplasty reported a surgical success rate of 86.6 per cent at one year post-operatively.<sup>1</sup>

Traditional tympanoplasty techniques involve the harvest of an autograft, with associated donor site morbidity. In revision cases, graft material may be limited. A Biodesign xenograft (Cook Medical, Bloomington, Indiana, USA) consists of acellular porcine small intestinal submucosa, providing an alternative to an autograft. This material was granted Therapeutic Goods Association approval in 2016 for 'implantation to reinforce soft tissue in the head and neck in applications of otological repair, nasal repair and facial reconstruction'.

The largest study examining the outcomes of this graft for tympanoplasty, by D'Eredità,<sup>2</sup> compared Biodesign with temporalis fascia in a randomised, controlled trial in a paediatric population. Six-month outcomes were comparable between the two grafts, and 24-month outcomes with Biodesign were reported as a 91.2 per cent tympanic membrane perforation closure rate. Yawn *et al.*<sup>3</sup> described a heterogeneous series of patients undergoing different otological surgical procedures, making appreciation of the success rate of the Biodesign graft challenging. Yawn used a cartilage graft as well as the Biodesign graft to repair the tympanic membrane in the majority of cases, with a closure rate of 87 per cent. The paediatric study by D'Eredità<sup>2</sup> is the only paper in the literature describing the success rate of the graft in microscopic tympanoplasty, indicating a significant gap in our knowledge of the utility of this graft.

This study aimed to evaluate our surgical and audiological outcomes from using small intestinal submucosa in type I tympanoplasty surgery, both as a single procedure and as part of more complex otological surgery.

## Materials and methods

Following institutional board approval, a retrospective chart review of all cases of porcine-derived small intestinal submucosa tympanoplasty performed at a single institution between April 2017 and September 2018 was undertaken. All procedures were performed by two senior staff otolaryngologists (PB and JK). Data were obtained from review of all clinical notes and operation reports, as well as pre- and post-operative audiograms.

The primary outcome measure was perforation closure as defined by otoscopic examination. This was deemed to be either complete closure, a residual pinhole perforation, a reduction in residual perforation size or surgical failure. Where the tympanic membrane could not be visualised, particularly in children, the tympanogram and audiogram were used as surrogates of tympanic membrane closure. The time point at which closure was observed was noted.

The secondary outcome measures were audiological, and included tympanometry and the change in air–bone gap (ABG), the difference between air conduction pure tone thresholds (in dB HL), and bone conduction pure tone thresholds (in dB HL), averaged across four frequencies (0.5, 1, 2 and 4 kHz).

Pertinent patient details recorded included: demographics, age at the time of surgery, cause of the perforation, location of the perforation, whether surgery was primary or revision, the surgical approach, and whether other otological procedures were performed concurrently with the small intestinal submucosa tympanoplasty.

When small intestinal submucosa tympanoplasty surgery was performed as the only procedure with no other middle-ear or mastoid surgery, this was a type I Wullstein tympanoplasty or ‘simple tympanoplasty’. When small intestinal submucosa tympanoplasty was performed in conjunction with other otological procedures such as mastoidectomy or atticotomy surgery, this was deemed ‘complex tympanoplasty’. In both groups, a small intestinal submucosa graft was used as the only graft material.

Statistical outcome measures included means, standard deviations (SDs) and percentages. Statistical analysis was performed using paired *t*-tests to compare pre- and post-operative changes within groups. Intergroup comparisons were performed using the Mann–Whitney U test. A *p*-value lower than 0.05 was considered statistically significant.

## Results

A total of 35 patients met the inclusion criteria. Twenty-six patients underwent ‘simple tympanoplasty’ surgery using porcine-derived small intestinal submucosa. Nine patients underwent ‘complex tympanoplasty’ surgery using small intestinal submucosa as part of other otological procedures performed. In both groups, the small intestinal submucosa graft was handled and prepared in the same manner. The mean age of all patients was 25.7 years, with a range of 5–79 years. There were 18 male patients and 17 females.

The surgical approach was either endaural or transcanal. An underlay technique was used in all cases, with the small intestinal submucosa graft pre-soaked in saline just prior to being placed under the tympanic membrane. The medial aspect of the graft was filled with absorbable gelatine compressed sponge (Gelfoam; Pfizer, New York, USA), and in the lateral aspect of the graft the same was used with Kenacomb ointment (Bristol-Myers Squibb, New York, USA), comprising triamcinolone acetonide, neomycin sulphate, gramicidin and nystatin.

### Simple tympanoplasty

The simple tympanoplasty group ( $n = 26$ ) had a mean age at surgery of 18.6 years (range, 5–63 years). The surgery was performed on the right ear in 15 cases and on the left ear in 11 cases; 23 cases were primary surgical procedures and 3 were first revisions. The cause of the perforation in the 23 primary

procedures was: residual perforation following grommet insertion in 13 cases (56 per cent), trauma in 3 cases, chronic suppurative otitis media (CSOM) in 2 cases and recurrent acute otitis media in 1 case. The cause of the perforation was unknown in four cases (17 per cent). The median follow-up time was 133 days (4.4 months; range, 17–731 days). The mean size of the perforations was 36 per cent, with a range of 10–99 per cent (subtotal perforation). The surgical approach was transcanal in half the cases and endaural in the remainder. A canalplasty was performed in three cases in order to improve visualisation of the tympanic membrane perforation.

Given the variability in follow-up time intervals, the primary outcome of tympanic membrane closure was recorded at the last post-operative follow-up appointment, provided the patient was seen more than two months after surgery. Of the 26 patients, 23 had longer than two months’ follow up. In 3 of the 23 cases, the tympanic membrane could not be visualised because of an uncooperative child and wax occluding the tympanic membrane on otoscopy. In two cases, the child had a normal audiogram and tympanometry, and the perforation was inferred to be closed and included in the analysis. In 1 of the 23 cases, audiological outcomes were not available and the case was excluded, leaving a final cohort of 22 patients in whom both audiological and closure rates could be analysed.

The overall closure rate in the simple tympanoplasty group was 68 per cent (15 out of 22 patients). A persistent similar-sized perforation was present in three cases (13.6 per cent), a persistent but smaller-size perforation in two cases (9.1 per cent) and a pinhole perforation in two cases (9.1 per cent). These results are shown in [Table 1](#). When the persistent similar-sized perforation patients were excluded, the mean pre-operative four-frequency ABG improved from 20.7 dB HL (SD = 13.3) to 12.3 dB HL (SD = 11.5). This improvement in ABG was statistically significant ( $p = 0.004$ ) ([Figure 1](#)).

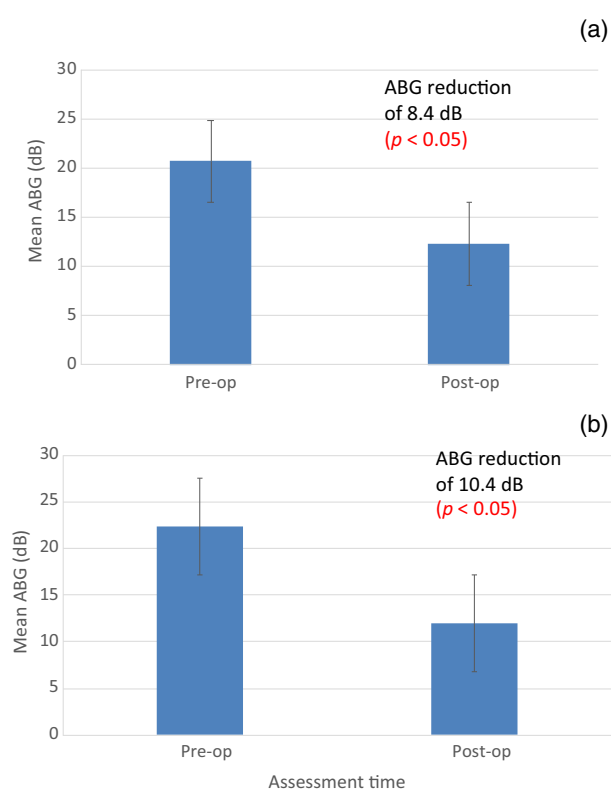
### Complex tympanoplasty

In the complex tympanoplasty group ( $n = 9$ ), the small intestinal submucosa graft was utilised in a second-look tympanotomy in one case, atticotomy in six cases and revision modified radical mastoidectomy in two cases. The mean age of this group at time of surgery was older, at 46 years, with a range of 16–79 years. Six patients were male and three were female. Six of the nine cases were performed on the right ear. The surgery was primary in five cases and a revision procedure in four. A post-auricular surgical approach was used in 78 per cent of cases and an endaural approach was used in the remainder. The surgical indication was cholesteatoma in four cases, cholesteatoma recurrence in two, CSOM in two cases, and a single case of tympanic membrane perforation with conductive hearing loss resulting from lateral ossicular chain fixation. The median duration of follow up was longer, at 371 days, with a range of 161–926 days.

The closure rate in this group was 78 per cent (seven out of nine cases), where the tympanic membrane was intact at last review. In one case, there was a persistent perforation and in one case a smaller-sized perforation remained. These results are listed in [Table 2](#). When the persistent similar-sized perforation patient was excluded, the mean pre-operative four-frequency ABG among the remaining eight patients was 22.3 dB HL (SD = 6.9), which decreased to 12 dB HL (SD = 9). This improvement in ABG was statistically significant ( $p = 0.02$ ) ([Figure 1](#)).

**Table 1.** Simple tympanoplasty outcomes

Age (years)	Perforation size (%)	Primary or revision surgery	Follow-up duration (days)	Outcome
5	99	Primary	134	Smaller perforation
5	99	Primary	260	Residual pinhole
5	10	Primary	340	Perforation closure
5	10	Primary	340	Perforation closure
6	10	Primary	91	Perforation closure
6	90	Primary	653	Perforation closure
7	15	Primary	583	Smaller perforation
8	10	Primary	93	Failure
8	60	Primary	148	Perforation closure
9	10	Primary	94	Perforation closure
10	50	Primary	388	Failure
11	15	Primary	114	Perforation closure
12	50	Primary	374	Perforation closure
12	20	Primary	549	Failure
13	30	Primary	71	Perforation closure
18	10	Revision	731	Perforation closure
20	40	Primary	133	Perforation closure
25	30	Primary	127	Perforation closure
52	99	Primary	99	Perforation closure
53	70	Primary	273	Residual pinhole
62	40	Primary	70	Perforation closure
63	20	Primary	413	Perforation closure

**Fig. 1.** Mean change in air–bone gap (ABG) after (a) simple and (b) complex tympanoplasty surgery. Pre-op = pre-operatively; Post-op = post-operatively.

When both simple and complex tympanoplasty groups were combined ( $n = 31$ ), the overall closure rate was 71 per cent (22 out of 31).

## Discussion

Tympanoplasty surgery is one of the most common surgical procedures performed by otolaryngologists. A wide variety of options are available to the surgeon to reconstruct the tympanic membrane, and some of those most commonly utilised are autologous grafts. These include temporalis fascia, perichondrium, cartilage, fat, fibrous tissue or a combination of these materials.<sup>4–7</sup> Whilst these are readily available within the operative field and are therefore biocompatible, with low antigenicity and cost-effectiveness, the availability of autologous tissue is dependent upon the condition of the donor site, and harvesting tissue results in donor site morbidity.

These issues have led to the consideration of non-autologous tissue, which has the advantage of no donor site morbidity, less time required to harvest the tissue, and theoretically an unlimited amount available. Drawbacks of non-autologous tissue include the cost of purchasing the graft and the fact that use of xenografts, such as porcine grafts, may not be acceptable to some community groups.

Small intestinal submucosa material is one such material that has shown promise. A large randomised, controlled trial compared small intestinal submucosa with autologous temporalis fascia grafts in 414 children undergoing tympanic

**Table 2.** Complex tympanoplasty outcomes

Age (years)	Indication	Surgical procedure	Follow-up duration (days)	Outcome
16	Recurrent cholesteatoma	Second-look tympanotomy	246	Smaller perforation
17	Cholesteatoma	Atticotomy	325	Perforation closure
32	Perforation + ossicular chain fixation	Atticotomy	386	Failure
35	Cholesteatoma	Atticotomy	581	Perforation closure
39	CSOM	Atticotomy	287	Perforation closure
42	CSOM	Atticotomy	926	Perforation closure
76	Cholesteatoma	Atticotomy	500	Perforation closure
78	Cholesteatoma	Revision modified radical mastoidectomy	371	Perforation closure
79	Recurrent cholesteatoma	Revision modified radical mastoidectomy	161	Perforation closure

CSOM = chronic suppurative otitis media

membrane perforation repair over an 11-year period.<sup>2</sup> A single surgeon performed all procedures, utilising a post-auricular approach and underlay grafting with small intestinal submucosa. A small percentage of patients were lost to follow up (4 per cent), leaving 432 ears for analysis. No statistical difference was observed in six-month closure rates, with a closure rate of 96.3 per cent using small intestinal submucosa and 94.8 per cent using temporalis fascia. The two-year closure rate for small intestinal submucosa was reported as 91.2 per cent; again, no statistical difference from temporalis fascia was observed. It is unclear what percentage of patients reached this follow-up point, although the median follow-up time was 7.7 years. That study provides compelling evidence for the use of small intestinal submucosa, although these closure rates or patient numbers have not been replicated to date in the literature.

James<sup>8</sup> used small intestinal submucosa and AlloDerm<sup>®</sup> grafts in endoscopic tympanic membrane repair, reported in a series describing a single-surgeon transition from microscopic to totally endoscopic ear surgery. The combined success rate for the non-autogenous grafts was 88 per cent at 12 months. Redaelli De Zinis *et al.*<sup>9</sup> also used small intestinal submucosa for endoscopic myringoplasty with a holding system in 10 cases. A 100 per cent success rate at six months was reported. These last two studies again reported high success rates, but with significantly smaller numbers of patients than the original study by D'Eredità,<sup>2</sup> the success rates are also higher than those reported in published meta-analyses.<sup>1</sup>

In contrast to these studies, we examined both simple tympanoplasty and complex tympanoplasty groups of patients. Our cohort is similar to that of Yawn *et al.*,<sup>3</sup> who studied a heterogeneous case series of 37 patients undergoing tympanic membrane repair, with or without more extensive otological surgery, with 27 per cent having undergone concomitant mastoidectomy; 40 per cent of the cases were revision cases and 46 per cent were for cholesteatoma. The tympanic membrane was repaired using an underlay tympanoplasty technique with small intestinal submucosa placement lateral to the malleus. However, in that study, cartilage graft was also used in 92 per cent of cases, whereas in our study, small intestinal submucosa was used in all cases as the sole graft material. The overall perforation closure rate was 87 per cent. The closure rate of cases with small intestinal submucosa graft alone (three cases) was 33 per cent. Given the composite nature of the small intestinal submucosa graft in conjunction with cartilage in that study, it is difficult to draw

conclusions about the success of the small intestinal submucosa graft alone. In addition, because type I tympanoplasty surgery was not analysed separately, direct comparisons with our study are difficult. Patients undergoing a concurrent otological procedure such as atticotomy or mastoidectomy arguably have abnormal Eustachian tube function, and the surgical exposure to graft placement is very different.

Our study was limited by the retrospective nature of the review and the loss to follow up, which limits data interpretation. The senior author (JK) performed the procedures in 23 cases and reported a learning curve with the graft, which may have affected the success rates obtained. Small intestinal submucosa graft is less pliable and less prone to deforming; therefore, the graft must be sized and positioned appropriately to ensure there are no gaps between the graft and the perforation edges, whilst also avoiding buckling of the graft. The senior authors in our study also utilised Kenacomb ointment, which may have affected the permeability of the material, being an oil-based preparation (established via communication with the company). Minimal rehydration of the graft, which is no longer recommended, may have also resulted in delamination of small intestinal submucosa. This was in contrast to the experience of D'Eredità,<sup>2</sup> who used a long period of hydration to 'obtain maximal hydration' prior to using the graft.

The theoretical benefits of small intestinal submucosa are multiple. There is a lack of donor site morbidity as no allograft harvesting is required, reducing operative time.<sup>2</sup> This is a clear advantage in cases where graft options are limited, such as in revision cases. A number of square and circle grafts of different sizes are available, hence there is theoretically unlimited graft material. The obvious additional advantage of small intestinal submucosa in endoscopic ear surgery is that no incisions are needed for graft harvest. In paediatric patients, where donor sites such as the tragus or temporalis muscle are much smaller in size, small intestinal submucosa is also advantageous.

- A wide range of graft material is available for reconstructing the tympanic membrane during otological surgery, with autografts being most common
- Biodesign xenograft consists of acellular porcine small intestinal submucosa – an alternative to autograft
- Overall tympanic membrane closure rate for simple tympanoplasty using underlay porcine-derived small intestinal submucosa graft was 68 per cent
- Biodesign can reduce donor site morbidity as no autograft is harvested, and it may be useful in revision surgery where donor sites are limited

Our early experience with small intestinal submucosa in otological procedures has been encouraging, although our outcomes are not comparable to large series or to standard myringoplasty outcomes. Despite this, in our experience, small intestinal submucosa has an important place in the otological reconstructive armamentarium, and its benefits should not be understated. Further research is required to assess long-term outcomes with small intestinal submucosa.

**Competing interests.** None declared

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