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Tympanic Membrane Perforation Repair Using Porcine Small Intestinal Submucosal Grafting

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Objective: To evaluate the use of porcine small intestinal submucosal grafts for tympanic membrane repair.
Patients: Adult and pediatric patients with tympanic membrane perforations with and without chronic otitits media, and perforations after removal of cholesteatoma.
Intervention: Endoscopic or microscopic tympanic membrane repair using porcine small intestinal submucosal grafts (Biodesign).
Main Outcome Measure(s): Perforation closure, bone and air pure-tone averages (PTA), air-bone gap (ABG), and word recognition scores (WRS) were recorded as outcome measures.
Results: Thirty-seven patients were included with a mean age of 25.4 years (range, 6–75), 57% men. Twenty-six cases (70%) were performed endoscopically and 34 (92%) had concomitant cartilage grafting. Three patients (8%) had postoperative pinpoint (<1% surface area) perforation, and two patients (5%) had postoperative perforation, with an overall success rate of 86.5%. The mean improvement in air-bone gap was 7.6 dB and ($p = 0.006$). There were no statistically significant differences in closure rates when comparing primary versus revision cases, endoscopic versus microscopic cases, size of perforation, cholesteatoma, concomitant mastoidectomy, age, tobacco exposure, or comorbid diabetes mellitus. Patients with concomitant cartilage graft were more likely to be successful when compared with those without cartilage graft ($p = 0.04$).
Conclusions: Porcine small intestinal submucosal grafts are effective in the repair of the tympanic membrane. These grafts are an excellent choice in total endoscopic cases as it avoids incisions necessary for allograft harvest. **Key Words:** Biodesign—Bioscaffold—Endoscopic—Hearing loss—Porcine small intestinal submucosa—Surgisis—Tympanoplasty.

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Tympanic membrane perforation is a common otologic problem. A variety of techniques have been described to repair perforations including lateral/overlay, medial/underlay, and lateral to malleus underlay (1–3). A common theme of all repair techniques is that a graft is used as a scaffold to promote ingrowth of the native tympanic membrane. A variety of materials have been used, including autologous temporalis or loose areolar fascia, human acellular dermal allograft (AlloDerm, LifeCell Corporation, Branchburg, NJ), vein grafts, and scar tissue (4–7). Autologous grafts can be advantageous because they are non-immunologic and can be readily accessed through a postauricular incision. However, in second look procedures or endoscopic cases an additional incision is necessary for harvest of these materials. In these cases, the availability of other allografts or xenografts can be useful to avoid unnecessary morbidity from an extra incision. Other materials have also been investigated to promote the non-surgical healing of tympanic membrane perforations, including epidermal growth factor and fibroblast growth factor (8,9).

Porcine small intestinal submucosal grafts (PSISG) can be commercially processed into an acellular matrix that promotes epidermal differentiation of cells and basement proteins (10). It is rich in glycosaminoglycans that promote wound healing (11). Animal studies in chinchillas showed good success of repair of induced tympanic membrane perforations when compared with cartilage grafting (12). The graft is commercially available in sterile packaging in 2.5×2.5 cm and 5×5 cm sizes (Fig. 1). One randomized controlled trial has been performed in pediatric patients comparing autologous

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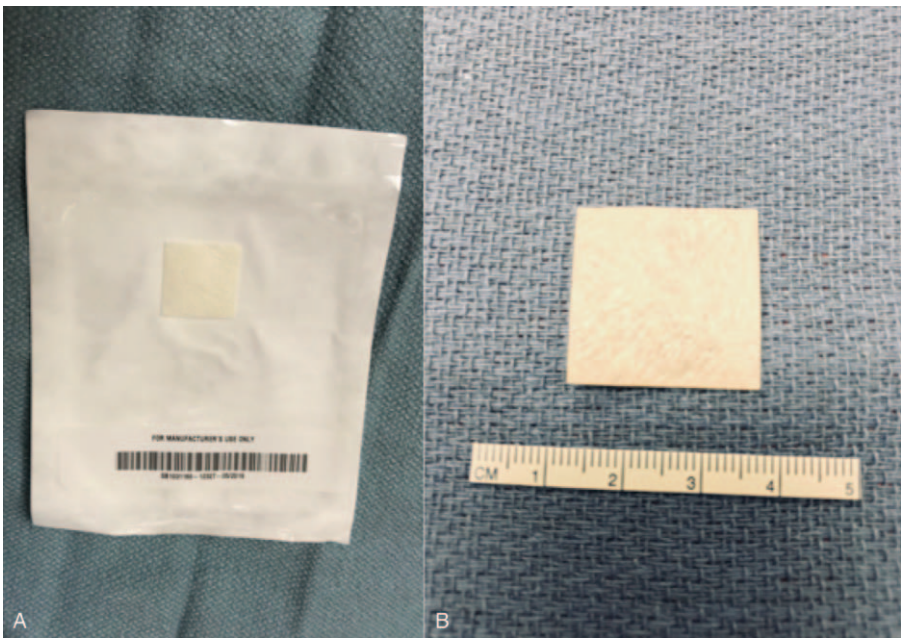

FIG. 1. *A*, Packaging of the implant. *B*, The 2.5 cm implant once opened.

fascia versus porcine small intestinal submucosal grafts that showed excellent closure rates at 6 months (13). Of note, the study excluded children with cholesteatoma, revision cases, and children with history of myringotomy tubes. Because relatively few studies have investigated this material in a variety of patients with tympanic membrane perforations, further study is needed to evaluate its performance. Herein the authors report their experience using PSISG allografts either endoscopically or microscopically in a lateral-to-malleus underlay fashion.

MATERIALS AND METHODS

After institutional review board approval, a retrospective chart review was conducted at a single tertiary otologic referral center and all patients that underwent tympanoplasty using porcine small intestinal submucosal grafts, specifically Biodesign (Cook Medical, Bloomington, IN) were identified. Only patients that underwent underlay tympanoplasty with graft placement lateral to the malleus as described previously by the senior author (A.R.) were included to minimize confounding from different tympanoplasty techniques. The primary outcome measured was graft failure (either primary or delayed) as confirmed through postoperative otomicroscopic examination. Secondary outcomes investigated included change in air-bone gap and bone conduction thresholds. Initial data collection included baseline demographic data, pertinent otologic history, preoperative, immediate postoperative and most recent postoperative audiometric data, notable intraoperative findings, postoperative complications, and durability of repair. Patients were excluded for incomplete records. Audiometric data are presented according to the 1995 American Academy of Otolaryngology–Head and Neck Surgery, Committee on Hearing and Equilibrium consensus guidelines (14).

Features were summarized with means, medians, ranges, and standard deviations or frequency counts and percentages where applicable. Statistical analyses were performed with GraphPad Prism 7.0 (GraphPad Software, La Jolla, CA). Fisher's exact tests were used to compare categorical data, paired *t* tests were employed to evaluate audiometric performance over time within a group, and Mann–Whitney *U* tests were used to compare means between study populations. *p*-values of less than 0.05 were considered statistically significant.

RESULTS

Baseline Clinical Data

This study included 37 patients who underwent tympanoplasty using PSISG as graft material between 2016 and 2017. The mean age of included patients was 25.4 years (range, 6–75). 57% of patients were male. Twenty-six cases (70%) were performed endoscopically and 34 (92%) had concomitant cartilage grafting. Mastoidectomy was performed in 10 patients (27%). Indication for surgery was perforation in 20 patients (54%) and cholesteatoma in 17 patients (46%). The most common involved sites of cholesteatoma were the epitympanum (five patients, 29%) and mesotympanum (five patients, 29%). Four patients (24%) had holotympanic cholesteatomas. Two patients (12%) had hypotympanic cholesteatomas, and one patient (6%) had cholesteatoma in the protympanum. Twenty-two cases (59%) were primary versus 15 (41%) revision cases. The mean perforation size as estimated by otomicroscopy was 39% (range, 15–90%). Ossiculoplasty with titanium prosthesis was performed in four patients and a partially eroded incudostapedial joint was reinforced with hydroxyapatite in three patients.

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Clinical Outcome Data

Of 37 patients that underwent tympanoplasty using Biodesign, two patients (5.4%) had microperforation (<1% tympanic membrane surface area) and three patients (8%) had persistent perforation at mean follow-up of 4 months. Secondary analysis summarized in Table 1 showed no significant difference in perforation rates in primary and revision patients, endoscopic versus microscopic approach, concomitant mastoidectomy or ossiculoplasty with titanium prosthesis, presence of cholesteatoma, tobacco status, or history of diabetes mellitus. There was a significant difference in graft take rate in patients that had concomitant cartilage grafting versus those that did not ($p = 0.04$).

The mean preoperative bone conduction (BC) puretone average (PTA) was 11.8 dB HL, the mean air conduction (AC) PTA was 33.4 dB HL, and the average air-bone gap (ABG) was 22.1 dB HL. The average postoperative BC PTA was 11.7 dB HL, AC PTA was 27.2 dB HL, and the mean ABG 16.3 dB HL. There was a statistically significant improvement in postoperative ABG (Fig. 2) ($p = 0.006$). Surgery was not associated with a BC threshold shift, evidenced by less than a 1 dB threshold shift in the average postoperative BC PTA. Furthermore, there were no statistically significant differences in the preoperative and postoperative word recognition scores.

DISCUSSION

Our results indicate that porcine small intestinal submucosal grafts are effective for tympanic membrane repair in the setting of chronic perforation and cholesteatoma. The primary advantage of this as a graft material is that it avoids extra incisions for the harvest of fascia or other autologous tissues in the setting of transcanal microscopic or endoscopic surgery. In revision cases where sufficient autologous graft material may not be available through a previous postauricular incision, it affords the surgeon another option for tympanic membrane repair. Furthermore, graft take rates in this series are similar to rates seen in a previous report at our center using autologous tissue grafts (2).

TABLE 1. *Surgical outcomes*

	Success Rate (%)	*p*-Value
Primary surgery	17/22 (77.3)	0.07
Revision surgery	15/15 (100)	
Endoscopic	22/26 (84.6)	0.99
Microscopic	10/11 (90.9)	
Concomitant mastoidectomy	9/10 (90)	0.99
No concomitant mastoidectomy	23/27 (85.2)	
Cholesteatoma	16/17 (94.1)	0.99
No cholesteatoma	16/20 (80)	
Cartilage graft	31/34 (91.2)	**0.04**
No cartilage graft	1/3 (33.3)	
(+) Tobacco exposure	7/7 (100)	0.56
(−) Tobacco exposure	25/30 (83.3)	
(+) History of diabetes mellitus	4/4 (100)	0.99
(−) History of diabetes mellitus	28/33 (84.8)	

$p < 0.05$ are displayed in bold.

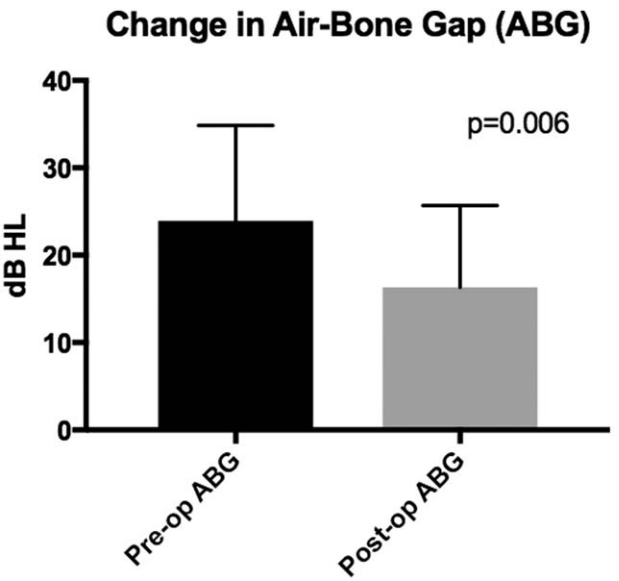

FIG. 2. Graph depicting mean air-bone gap change postoperatively after tympanoplasty using Biodesign.

Subgroup analysis did not show any difference in graft take rate with regards to primary or revision, microscopic or endoscopic, age, size, and comorbidities including diabetes or tobacco exposure. A statistically significant difference in graft take rate was seen in patients that underwent concomitant cartilage grafting versus those that did not. These results, while statistically significant, should be interpreted with caution, as the sample size that did not undergo cartilage grafting was only 8% of included patients, as it is the general practice at our center to place thin cartilage grafts to prevent long-term retraction. In the case of small perforations it is reasonable to use perichondrial grafts from the tragus as graft substrate, however this may be inadequate in larger defects, making PSISG a reasonable alternative to additional incisions for autologous tissue harvest. Additionally, it is the authors' hypothesis that the cartilage graft may provide additional scaffolding promoting the in-growth of the native tympanic membrane, although this study was not designed to evaluate this phenomenon.

Audiologic results were included as a secondary analysis and showed a statistically significant improvement in postoperative air-bone gap in patients with sufficient follow-up data. The primary reason for including this as a secondary analysis was that the patients in this study were heterogeneous with regard to ossicular status and reconstruction.

A recent study by D'Eredità (13) has shown the porcine small intestinal submucosal grafts to be comparable to autologous fascia grafts in pediatric patients. Our study corroborates these findings in a smaller, but expanded patient population. The previously mentioned

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study did not include revision cases or patients with cholesteatoma. Additional benefits proposed by D'Eredità are improved operative time in patients with PSISG. Furthermore, patients and clinicians with cultural concerns should know that the product has been reviewed by Jewish and Muslim faiths and has been classified as kosher and halal, respectively, because of the positive medical benefits of its use (15). The price of PSISG is affordable when considered in the context of reduced operating room costs, usually in the range of a few hundred United States dollars. Individual prices are negotiated between the manufacturer and the provider.

The study has several limitations. There are inherent limitations to retrospective review and the sample size, while adequate statistically, is relatively small. Additionally, graft-take rate was shown to be influenced by the presence of concomitant cartilage grafting. Despite these limitations, the series does show that PSISG is a reasonable option for grafting material, especially in patients where autologous material is not readily available (multiple revision surgeries) or an incision is not desired.

CONCLUSION

PSISG are an effective grafting material in tympanic membrane repair for perforation or after cholesteatoma surgery. Surgeons may consider concomitant cartilage grafting as this impacted success rates in this series.

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