

ORIGINAL RESEARCH

Anatomic and audiometric outcomes of porcine intestinal submucosa for tympanic membrane repair

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Abstract

Objective: Surgical repair of tympanic membrane perforations has been traditionally performed with autologous soft-tissue grafts with high success rates. Newer allografts such as porcine small intestine submucosa (pSIS) have been employed as alternatives to minimize donor morbidity and surgical time, and in cases where autologous tissue may not be available. The comparative anatomic and audiometric success rates of these tissues is still unclear.

Study design: Retrospective case-control series of anatomic and audiometric outcomes of autologous soft tissue versus pSIS graft for primary, isolated transmeatal tympanic membrane repair.

Methods: Analysis of patients undergoing primary transmeatal tympanic membrane repair with autologous soft tissue or pSIS. Patients with otorrhea, cholesteatoma or retraction pockets, those who had cartilage grafts or ossicular reconstruction, and revision procedures were excluded. Pre- and post-surgery air-bone gaps (ABG) and pure tone averages (PTA) were compared. Graft success was defined as closure of the perforation at 2-month follow-up visit.

Results: The success rate for both the autologous soft tissue and the pSIS arm is 93.8%. There was no statistical significance ($p < .05$) between the post-op ABG, change in ABG, post-op PTA, change in PTA, or graft success rate between the two groups with either lumped cohort or matched-pairs analysis.

Conclusions: pSIS grafts are effective for repair of tympanic membrane perforations with hearing outcomes and graft success rates comparable to autologous soft tissue.

Lay summary: Repair of tympanic membrane perforations is traditionally done using a soft-tissue graft harvested from the patient at the time of surgery. pSIS is a newer graft material that is equally effective in terms of anatomical and audiometric outcomes.

Level of evidence: Level 3b.

KEYWORDS

autologous soft tissue graft, porcine small intestine submucosa graft, tympanic membrane, Tympanoplasty

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1 | INTRODUCTION

Tympanic membrane (TM) perforations can result in hearing loss and tinnitus, and increase the risk of middle ear infections.¹ Surgical management with tympanoplasty is necessary for the repair of chronic perforations when mitigation of these complications is desired. This surgery is commonly performed by either transmeatal or post-auricular approaches with autologous fascia or loose areolar tissue harvested from the temporalis muscle through the same or separate incision, or with tragal perichondrium, when soft tissue grafting alone is employed.² It can also be performed from an endoscopic approach with comparable closure rates and hearing results.^{3–5} Autologous grafts have had high success rates, but may not always be the ideal choice due to the inconsistency in quality between patients and their nonoptimized structural properties for sound conduction and prevention of TM retraction.^{6,7} Furthermore, with transmeatal approaches, autologous tissues require a separate, additional incision for harvest, with risk of increased pain, scarring, hematoma formation, and infection.⁸

There are many types of non-autologous grafts and graft adjuncts available to the surgeon, including paper patch, gelatin sponge, growth factors, acellular dermal matrix, and acellular porcine small intestine submucosa (pSIS) (BioDesign Otologic Repair Graft, Cook Medical, <https://www.cookmedical.com/products/96f4b36f-75f7-4ebf-ae0-611faca117c8/>).^{7,9} pSIS is an extra-cellular membrane tissue graft of type I collagen and fibronectin that includes glycosaminoglycans, chondroitin sulfate, hyaluronate, heparin, and dermatan sulfate.^{10,11}

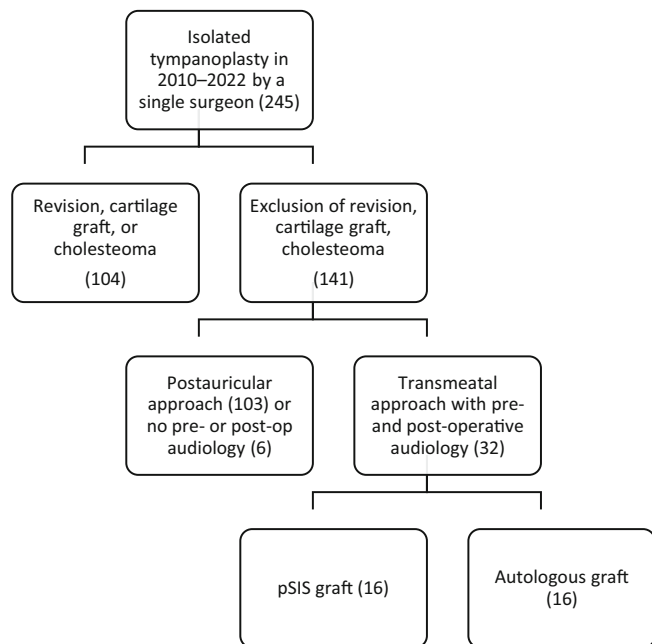


FIGURE 1 Flowchart of patient inclusion and exclusion criteria starting with a list of 245 patients who had an isolated tympanoplasty performed by a single surgeon. The included patients were separated into two arms by the type of graft they received. Number of patients in each group are displayed in parentheses. pSIS, porcine small intestine submucosa

pSIS has been proven to be an effective repair option for tympanoplasty in both animal and human studies.^{6,7,12,13} It has been utilized as graft material for vascular, skin, bladder, dura, and abdominal wall sites and is shown to be well tolerated and easily integrated.^{10,12,14,15} The main benefits of this non-autologous graft are that it is available without the need for an incision, has no special storage requirements, and is consistent and uniform.¹⁵ Additionally, the current manufacturer supplies these in 6 or 9 mm diameter circular pieces and a 2.5 × 2.5 cm piece, giving multiple options for different surgical findings while minimizing graft waste.¹⁶

There is still no universally accepted “best” option for tympanoplasty, as many of the graft materials have not been directly compared to each other. A recent review article looked at the literature on non-autologous graft materials for tympanoplasty including paper patch, silk fibrin patch, steri-strip tape, gelatin, hyaluronic acid, growth factors, bacterial cellulose, protease-solubilized collagen, pSIS, and silicone foil.⁷ This review concluded that available data suggests that of these grafts, pSIS has one of the highest success rates for chronic perforation closure. However, the authors noted that there is a need for

TABLE 1 Patient characteristics

Characteristics	Autologous soft tissue arm, n (%)	pSIS arm, n (%)
Total patients	16	16
Race		
White	8 (50%)	9 (56%)
Black	3 (19%)	4 (25%)
Other	5 (31%)	3 (19%)
Sex		
Male	7 (44%)	6 (38%)
Female	9 (56%)	10 (62%)
Age		
< 18 y/o	7 (44%)	7 (44%)
≥ 18 y/o	9 (56%)	9 (56%)
Mean, years	31.9 (8.5, 55.4)	30.8 (8.0, 53.5)
Size of perforation		
< 50%	13 (81%)	14 (88%)
≥ 50%	3 (19%)	2 (12%)
Etiology		
Tubes	6 (38%)	9 (56%)
Traumatic	2 (12%)	2 (12%)
Infectious	2 (12%)	0 (0%)
Unknown	6 (38%)	5 (31%)

Note: Continuous variables are described by mean (standard deviation) and categorical variables are described by number (%). Sex refers to biological sex at birth. Size of perforation was determined by subjective visual measurement on physical exam. Etiology from tubes indicates failure of spontaneous closure after tympanostomy tubes were extruded. There is no statistically significant difference between the two groups, with $p > .05$ in all categories.

Abbreviation: pSIS, porcine small intestinal submucosa.

TABLE 2 Pre- and postoperative tympanoplasty outcomes variables

	Autologous (n = 16)	pSIS (n = 16)	MD	p*
Pre-op ABG (dB)				
Mean	27	22	4	.30
(95% CI)	(21, 33)	(17, 28)		
Pre-op PTA (dB)				
Mean	35.0	33.3	1.7	.71
(95% CI)	(27.9, 42.1)	(27.6, 39.0)		
Post-op ABG (dB)				
Mean	6	6	0	>.99
(95% CI)	(2, 11)	(1, 12)		
Post-op PTA (dB)				
Mean	23.0	20.7	2.3	.63
(95% CI)	(15.5, 30.4)	(15.7, 25.8)		
ABG change (dB)				
Mean	20	16	4	.38
(95% CI)	(13, 27)	(9, 22)		
PTA change (dB)				
Mean	12.0	12.6	0.6	.86
(95% CI)	(7.4, 16.7)	(9.2, 15.9)		
Success rate (%)	93.8	93.8	0.0	>.99

Note: ABG was measured at 500 Hz and PTA was measured as an average of pure tone frequency at 500, 1, 2, and 3 kHz. Abbreviations: ABG, air-bone gap; CI, confidence interval; MD, mean difference; pSIS, porcine small intestinal submucosa; PTA, pure tone average. *p-Value considered statistically significant <.05.

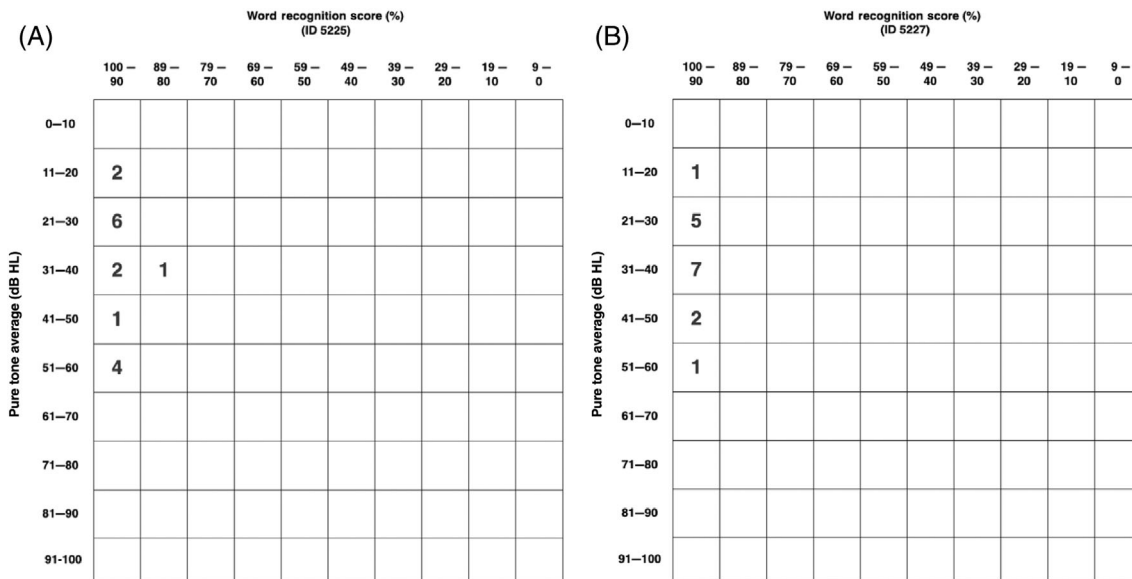


FIGURE 2 (A) Preoperative audiometric data for patients who received an autologous soft tissue graft. (B) Preoperative audiometric data for patients who received a pSIS graft. Pure tone average as calculated as the average of pure tone frequency at 0.5, 1, 2, and 3 kHz. Word recognition score measured at 40 dB above the patient's speech recognition threshold or at their most comfortable level above that. dB, decibels; pSIS, porcine small intestinal submucosa

future pSIS studies that rigorously report pre- and postoperative audiometric thresholds. One study included in this review compared pSIS to autologous temporalis fascia for tympanoplasty in a

randomized control trial in a pediatric population. Comparable closure rates were found between the two groups. Audiometric data were not reported, but the author stated that there were no statistically

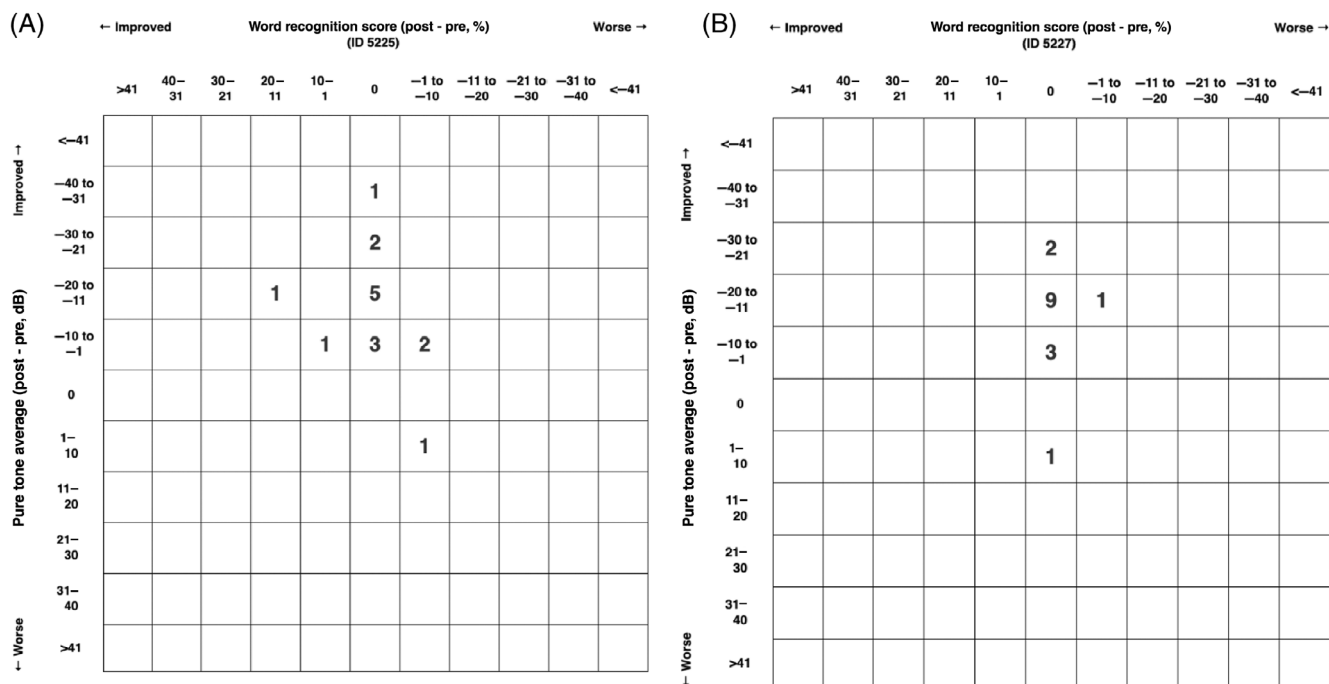


FIGURE 3 (A) Postoperative audiometric outcomes for patients who received autologous soft tissue grafts compared to preoperative data. (B) Postoperative audiometric outcomes for patients who received pSIS grafts compared to preoperative data. Pure tone average as calculated as the average of pure tone frequency at 0.5, 1, 2, and 3 kHz. Word recognition score measured at 40 dB above the patient's speech recognition threshold or at their most comfortable level above that. dB, decibels; pSIS, porcine small intestinal submucosa

significant audiometric differences between the groups.¹⁷ Two studies have reported the outcomes of the TM perforation repair in a single pSIS graft arm. Yawn et al. found a 77.3% closure rate for primary surgery and 100% after a single revision in a group of 37 adult and pediatric patients. The patient group had heterogeneity in presentation and surgical approach. The majority of patients also received a concomitant cartilage graft, which may have influenced the graft take rate.⁶ Chen and Hsieh also found a high closure rate with pSIS in an adult population with TM perforation related to simple chronic otitis media.¹⁸ Both of these studies reported significant improvement in postoperative air–bone gap (ABG).^{6,18}

While Yawn and Chen reported strong audiometric data in support of pSIS, neither study included a comparison group. D'Eredita's study was a direct comparison between pSIS and autologous fascia and found that the two groups had similar outcomes, but it was limited to a pediatric population and did not include the specific audiometric data. This study focuses on a patient population of both children and adults to compare the effectiveness of pSIS with autologous soft tissue grafts for chronic TM perforation repair regarding anatomical and audiometric outcomes. We hypothesize that pSIS is equally effective in both outcome measures for tympanoplasty.

2 | MATERIALS AND METHODS

The charts of all patients who underwent a primary isolated tympanoplasty performed by a single surgeon at a tertiary care institute

between December 2010 and April 2022 were reviewed. The protocol was determined to be exempt from institutional review board (IRB) approval under 45 CFR 46.101(b) from IRB review. Patients were selected by a record search for a sole CPT code of 69631. Patients undergoing simultaneous mastoidectomy were excluded. A total of 245 patients were retrieved. Revisions, use of cartilage or composite cartilage-perichondrial grafts, and patients with cholesteatoma were excluded, as were patients with active otorrhea, leaving 141 patients. The patient pool was then narrowed further to only include surgeries performed via a transmeatal approach. Of those final 38 patients, 18 of the repairs were grafted with Biodesign pSIS (Cook Medical) and 20 with autologous soft tissue. Autologous grafts included temporal fascia and tragal perichondrium. All grafts were placed with an underlay technique. Only patients with follow-up at least 2 months post-operatively and available pre-operative and post-operative audiologic testing results were evaluated, which included 16 pSIS patients and 16 autologous soft tissue patients. (Figure 1). For each patient, data on the patient's age at surgery, approximate size of their perforation, pre-operative audiology data, post-operative audiology data at their 2-month follow-up, and success of the surgery at the 2-month post-operative follow-up were collected. Audiology outcomes were measured by ABG at 500 Hz, pure tone average (PTA) of 500, 1000, 2000, and 3000 Hz, and word recognition score (WRS). Pre-operative WRS that were not calculated during audiometric testing were reported as the same percentage as the post-operative finding. Audiometric data were presented according to 2012 American Academy of Otolaryngology

– Head and Neck Surgery consensus guidelines.¹⁹ Anatomic success was defined as no perforation visible on otomicroscopic exam of the TM.

The primary outcome was defined as graft take success rate, and secondary outcomes were the audiometric variables of post-operative ABG, change in ABG between pre-operative and post-operative testing, post-operative PTA, and change in PTA difference between pre-operative and post-operative testing. The success rates between the groups were compared by two-tailed Z-test. The variables and mean audiometric outcomes between the two groups were compared by a two-tailed, unpaired Student's *t* test. Differences were considered statistically significant at $p < .05$.

A matched pairs analysis was also performed for each outcome measure. Thirteen pSIS patients were matched to 13 autologous soft tissue patients by age group <18 versus >18 years old, perforation size of <50% versus >50% of the TM, and pre-operative ABG within 10 units. The outcomes from the matched groups were compared by a two-tailed paired *T* test.

3 | RESULTS

The study group included 32 patients—16 in the autologous soft tissue arm and 16 in the pSIS arm. The patients ranged from 5 to 65 years old and had perforations ranging from 20% to 55% of their total TM area. Patient and TM perforation characteristics are shown in Table 1. Audiometric data are summarized in Table 2 and Figures 2–4. There were no statistical difference between the success rate or audiometric outcomes between the two graft groups.

For the matched pairs analysis, 13 autologous soft tissue patients were individually paired with the 13 pSIS graft patients based on age,

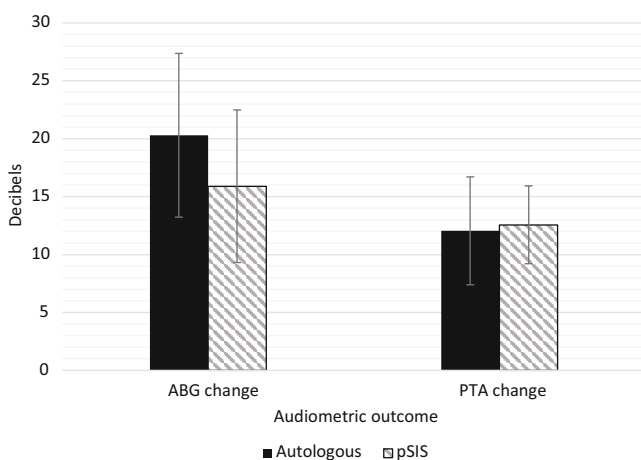


FIGURE 4 ABG change and PTA change from pre- to postoperative audiometric testing for the autologous soft tissue (solid) and pSIS (striped) graft groups. ABG was measured at 500 Hz and PTA was measured as an average of pure tone frequency at 0.5, 1, 2, and 3 kHz. Error bars represent 95% confidence interval. ABG, air-bone gap; pSIS, porcine small intestinal submucosa graft; PTA, pure tone average

size of perforation, and pre-operative audiometric testing. The results (not shown) were comparable to the results by lumped cohort analysis with no significant differences between the two groups.

4 | DISCUSSION

This study investigated the use of pSIS graft through a retrospective, case-control series of anatomic and audiometric outcomes of autologous soft tissue versus pSIS grafts for primary, isolated transmeatal TM repair. The two groups had similar characteristics with comparable age, size of perforation, etiologies, and pre-op ABG. The data from the current study show that there is no statistically significant difference between post-op ABG, post-op PTA, change in ABG, or change in PTA between the two graft groups. There is also no significant difference between success rate, as defined as no evidence of perforation at follow-up. The success rate for autologous soft tissue was 93.8% and the success rate for pSIS was 93.8%, with one unsuccessful repair in each group.

Compared with using autologous soft tissue, there is no additional incision or harvest time required for the pSIS graft. It is immediately accessible off the shelf with no special storage requirements, and is of a consistent thickness, which is not the case with autologous soft tissue grafts. Acellular dermal matrix (AlloDerm, Allergan Aesthetics, AbbVie, <https://hcp.alloderm.com/portfolio>), is another commonly used manufactured graft.⁹ This graft option is available in a more limited number of sizes, often resulting in graft waste when used for small surgical sites such as the TM, and can vary in thickness. The pSIS grafts are supplied in 6 or 9 mm diameter circular pieces and a 2.5 × 2.5 cm piece, allowing for more flexibility in choosing an appropriate size while limiting waste.¹⁶ Compared with the commercially available acellular dermal matrix graft, pSIS is of uniform thickness, has easier handling characteristics, can be used dry or rehydrated, and can be stored on a shelf in the OR suite rather than a blood bank. It is a reliable and advantageous graft option.

Overall, this study found similar success rates for pSIS compared to previously published studies. D'Eredita had a closure rate of 96.3% in the pSIS arm at 6 months post-op in a pediatric population. Surgical time was found to be decreased with the use of pSIS.¹⁷ Yawn et al. had a 77.3% closure rate for primary surgery with pSIS and 100% after a single revision in a group of adult and pediatric patients, the majority of whom had concomitant cartilage grafting.⁶ Additionally, Chen et al. similarly noted a closure rate of 94.7% with pSIS in an adult population.¹⁸ Similarly high closure rates were found in both the pediatric and adult populations for primary isolated tympanoplasty.

Ghanad et al. highlighted the need for studies that rigorously report pre- and post-operative audiometric thresholds with the pSIS graft.⁷ They noted that the inclusion of these data can help surgeons factor in the expected hearing outcomes when making a graft selection. Both arms in this study showed improvement in audiometric testing post-operatively with comparable mean reductions in PTA and ABG.

The patients included in the autologous soft tissue and pSIS arms had similar characteristics. They were almost equivalent in group demographics of age, etiology, and size of perforation, and had no statistically significant difference in pre-operative ABG measures. The analysis was also repeated and conducted as a matched pairs analysis and a paired statistical test, with 13 patients in each arm matched by age, size, perforation, and pre-operative ABG. The matched pairs analysis showed similar results with no difference in any of the outcomes between the two groups. Comparability of the study cohorts was ensured with aggressive exclusion of any patients with potential confounding factors to isolate graft related effects on outcomes of primary TM repair. Furthermore, by limiting the study groups to isolated, primary transmeatal surgery, uniformity of technique and underlying otopathology was maximized.

The main limitation of this study is the small sample size. Based on the aggressive exclusion criteria and data collection from a single institution by a single surgeon, 32 patients were included in the study, increasing the possibility of type 2 error. To achieve a power of 80% with a confidence level of 95% under the assumption that a 20% difference in graft success rate is clinically significant, a sample size of approximately 60 patients in each study group would be needed. The restrictive inclusion criteria were set and upheld despite the unfavorable effect on power in an effort to isolate graft related effects on the anatomical and audiometric outcomes by eliminating confounders associated with patients having a higher Bellucci classification, and to optimize comparability between the two study groups. Another limitation is the use of a single surgeon, which, while limiting the discrepancy between surgeon performance, lowers the generalizability of the results.

This study should be conducted with a larger sample size of patients to confirm the similarity in anatomical and audiometric outcomes between autologous soft tissue and pSIS grafts in tympanoplasty surgeries. In addition, it can be repeated with multiple surgeons at multiple institutions. A prospective randomized control trial comparing the two graft options would of course be helpful to increase the strength of the evidence. Furthermore, sub-analyses can be conducted based on the etiology of the perforation to identify if etiology should play a role in the decision between the graft options, and the graft comparison can be repeated for use in revision cases.

5 | CONCLUSION

This retrospective case-control study at a single institution, shows that pSIS grafts are as effective as autologous soft tissue for repair of TM perforations based on anatomic and audiometric outcomes. There is no statistically significant difference between the pSIS and autologous soft tissue outcomes as measured by audiometric data and closure rates after tympanoplasty in the patient population ranging from 5 to 65 years old. Pre- and postoperative audiometric data showed significant improvement postoperatively for both graft groups, with no statistical difference.

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CONFLICTS OF INTEREST

The authors declare that there is no conflicts of interest to disclose.

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