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Original Article

Human Acellular Dermal Allograft Patch on Traumatic Tympanic Membrane Perforation

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BACKGROUND: This study aimed to investigate the outcome of using the human acellular dermal allograft patch compared with the conventional paper patch in traumatic tympanic membrane perforation.

METHODS: This was a retrospective study including 41 patients (42 ears) treated with 22 human acellular dermal allografts and 20 paper patches for acute traumatic tympanic membrane perforation from April 2013 to June 2020. The procedure was performed by applying human acellular dermal allograft or paper patches after trimming of perforation margins under local anesthesia. Patient's age, sex, cause, duration, side, location, size of perforation, and the result of healing was analyzed. The audiologic or computed tomography data were also investigated when available.

RESULTS: There was no significant difference in sex, age, affected side ratio, size and duration of perforation, recovery confirmation time, and audiogram results between the two groups. There was no significant difference in the size or duration of perforation between the success and failure groups. The human acellular dermal allograft and paper-patch groups showed no significant difference in the recovery confirmation time (70.7 ± 42.3 vs. 89.9 ± 119.4 days, $P = .486$) and recovery rate (95.5% vs. 85.0%, $P = .333$). However, the patch maintenance time of the human acellular dermal allograft group was statistically longer than the paper-patch group (32.9 ± 14.9 vs. 15.6 ± 19.9 days, $P = .001$). On multivariable regression analysis, patch material was the only parameter associated with patch maintenance time ($P = .002$).

CONCLUSION: Treatment outcomes of traumatic tympanic membrane perforation using human acellular dermal allograft showed better or similar therapeutic efficacy compared to paper patch. The important advantage of this material is to stay in situ for a sufficient time without being detached until successful healing.

KEYWORDS: Trauma, tympanic membrane perforation, acellular dermal graft tissue, paper, myringoplasty

INTRODUCTION

Traumatic tympanic membrane perforation (TTMP) is caused primarily by beating, sports activity, blast injury, or careless ear picking[1,2] with an annual incidence of 1.4–8.6 per 100,000.[3] It usually causes a conductive hearing loss and in cases of inadequate management, it can result in chronic inflammation due to secondary infection.[4] It is usually managed conservatively with spontaneous healing or minimally invasive procedures such as paper patching which is widely used because of its cost-effectiveness and convenience.[1,3] However, the presence of TTMP after long-term conservative observation may require surgical correction. Furthermore, the use of medically non-approved material in paper patching may be disputable, as it is usually obtained from cigarette rolling paper.[5] The paper patches often escape before the complete healing of the tympanic membrane due to the short period of attachment to the tympanic membrane.

There have been several studies on the techniques and materials used for TTMP management.[1,5-11] Cigarette paper,[5,12,13] eggshell membrane,[10] silk,[9] gel foam,[11] and various kinds of materials have been tried and reported. Human acellular dermal allograft (HADA) derived from donated human skin undergoes a process of separation or inactivation of cells, antigens, and potential viruses but maintains the structural integrity of the collagen. It has been found effective in various clinical applications such as management of gingival recession,[14] breast reconstruction,[15] closure of meningomyelocele defects,[16] and augmentation rhinoplasty.[17] It has been

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reported to be effective in the treatment of tympanic membrane perforation as a patch material in animal study,[18] or graft material for tympanoplasty in humans.[19]

Despite various trials for clinical applications with HADA, the treatment outcomes of HADA patch for the treatment of TTMP in humans have not been reported. This study was conducted to compare and analyze the therapeutic effects of HADA and paper patches in acute TTMP.

MATERIALS AND METHODS

Study Population and Patch Material

This study was a retrospective review of the electronic medical records of 41 patients (42 ears) with acute TTMP who underwent early patch procedure at the otolaryngology–head and neck surgery clinic of a tertiary referral hospital from April 2013 to June 2020. All patients underwent an early patch procedure using paper or HADA by a skilled otologist and were retrospectively divided into two groups according to the patch material used (paper vs. HADA). Of the 41 patients (42 ears), 20 received a paper patch and 21 patients (22 ears) a HADA patch. Patients with chronic tympanic membrane perforation or incomplete data were excluded. Ethical committee approval was received from the Institutional Review Board of the Seoul National University Hospital (Approval no: IRB-10-2020-1). Written informed consent was obtained from all participants who participated in this study.

In this study, freeze-dried type (thickness range: 0.1–0.3 mm) of MegaDerm® (L&C BIO, Seongnam-si, Korea) was used in the HADA patch group. MegaDerm® is one of HADA, which is provided by the U.S. tissue banks, according to the guidelines of the American Association of Tissue Banks and U.S. Food and Drug Administration (FDA).[19] In the paper-patch group, traditionally marketed cigarette rolling paper after sterilization with ethylene oxide gas was used.

This study was approved by the Institutional Review Board of our hospital (IRB-10-2020-1) and was conducted in accordance with the Declaration of Helsinki.

Patch Procedures for Tympanic Membrane Perforation

The common patch procedure applied to the two groups is as follows (Figure 1). Under microscopic view, the external auditory canal (EAC) was sterilized with a cotton swab soaked with 70% ethanol, and local anesthetic (lidocaine mixed with epinephrine) was injected into the inlet of EAC, followed by elimination of the foreign material or blood clot around the perforated tympanic membrane and ear canal. Through the ear speculum under the microscopy, the perforated area of the tympanic membrane was identified and the irregular margins of the perforation were trimmed using micro-instruments such as sharp picks or cup forceps. Blood clots or foreign materials inside the middle-ear cavity were removed through the perforation hole and the presence of middle-ear infection or ossicular disruption was checked. The HADA (0.1–0.3 mm thickness) or cigarette paper was designed according to the appropriate shape and size about 2 mm larger than the actual perforation size, as sufficient to cover the perforated area completely. The patch material was soaked with quinolone antibiotic otic drops and placed on the outside of the perforated tympanic membrane to cover the entire perforation area. The patch was confirmed for the attachment without deviation outside of the perforation, then the procedure was finished without packing

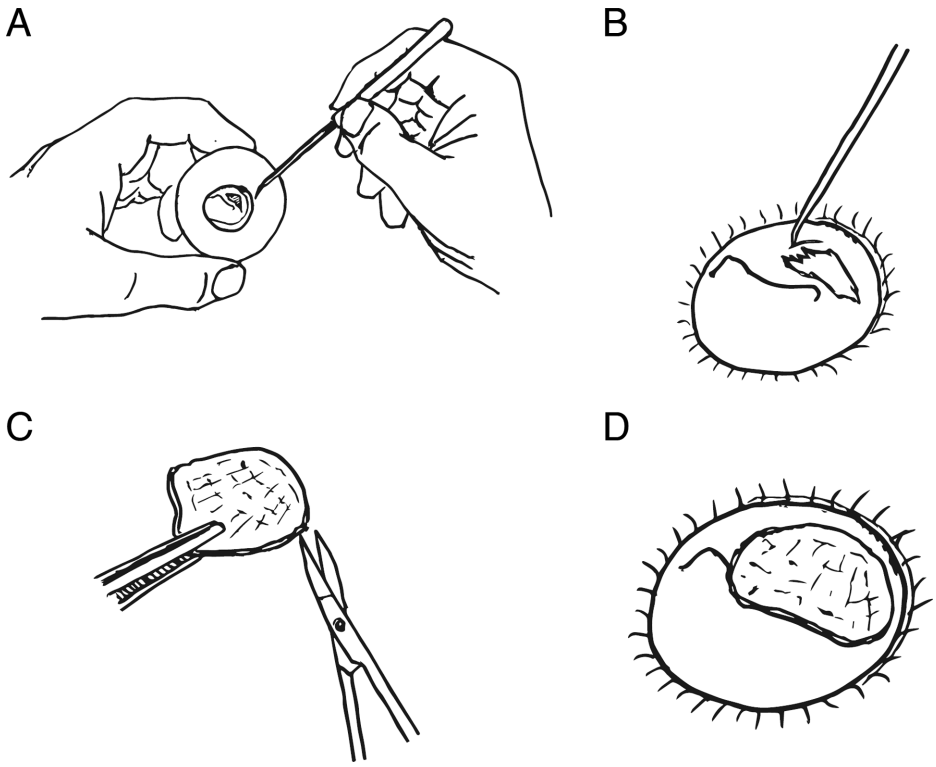

Figure 1. a-d. Procedures of patch technique. (a) Identification of tympanic membrane perforation with ear speculum; (b) trimming of perforation margin; (c) design of material to patch; (d) application of patch.

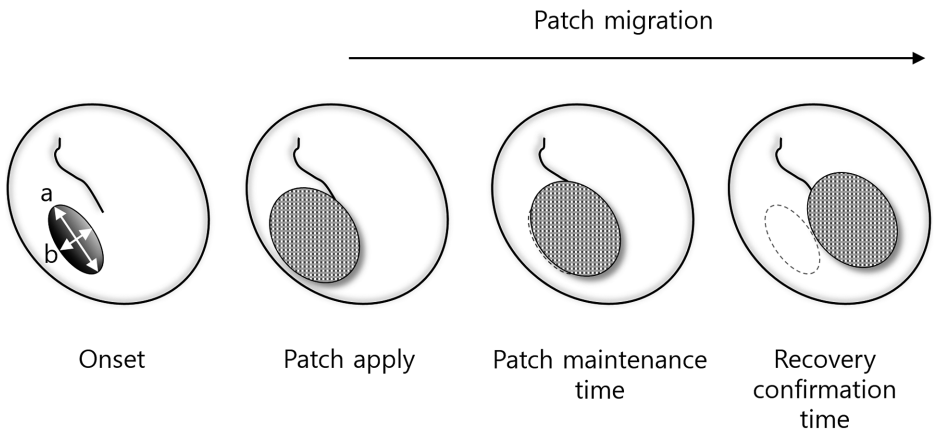

Figure 2. Variables and its definitions. Perforation size: average of a and b; patch maintenance time: keep covering the perforated area; recovery confirmation time: after total spontaneous migration or removal; failure of recovery: failure of healing within 3 months.

the EAC. The patients were instructed to avoid blowing their noses and prevent water from getting into their ears.

Variables and Definitions

Complete medical history was recorded, and all patients' information was obtained including age, sex, time of onset, symptoms, mode of injury, affected side, perforation size and location, patch materials, and follow-up data (Figure 2). In most patients, pre-procedural audiologic examination and temporal bone computed tomography evaluation were performed, otoscopic examination was serially performed and recorded at every visit, and final audiologic examination was performed after the complete healing of perforation. Usually, the regular follow-up protocol included the first visit within a week after the patch procedure followed by a visit every 2–3 weeks until the recovery was completed. However, since this was a retrospective study without strict control over the visit intervals, the actual follow-up intervals were found to be heterogeneous.

Perforation Size

The average length of the longest and shortest diameters of perforation was defined as the size of the perforation.

Patch Maintenance Time

After the patch procedure, the duration of the maintenance of the patch to cover the initial perforated area was defined as the patch maintenance time.

Recovery Confirmation Time

After the patch procedure, when the patch completely escaped from the initial perforated area and complete healing of the perforation was confirmed, the duration was defined as the recovery confirmation time. The recovery confirmation time was collected only for patients who showed complete recovery.

Failure of Recovery

If the perforation did not recover within 3 months post-procedure, it was considered as a failure of recovery.

As the main outcomes, patch maintenance time, recovery confirmation time, and success rate were compared between the two groups (paper vs. HADA). Sex, age, affected side, size, and duration of perforation were also compared between the two groups. All audiologic results were compared using the average hearing thresholds of 500 Hz, 1 kHz, 2 kHz, and 4 kHz.

Statistical Analysis

Demographical and clinical features were compared between paper and HADA patch groups. Continuous variables (i.e., age, size and duration of perforation, patch maintenance time, recovery confirmation time, and hearing thresholds) were compared by Mann–Whitney U-test. Categorical variables (i.e., sex ratio, affected side ratio, and success rate) were compared by Pearson's Chi-square test or Fisher's exact test. Correlation between several outcomes and potential confounding factors was examined by univariable and multivariable regression analysis or logistic regression analysis. Continuous outcome variables (e.g., patch maintenance time, recovery confirmation time, and air-bone gap reduction) were analyzed by univariable and multivariable regression method, and categorical outcome variable (recovery or not) was analyzed by univariable and multivariable logistic regression method. For multivariable analysis, relatively significant potential confounding variables ($P < .3$) in the univariable analysis were selected. All statistical analyses were performed using SPSS version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) and illustrated using GraphPad Prism version 7.00 (GraphPad Software, Inc. San Diego, Calif, USA). A *P*-value <.05 was considered statistically significant.

RESULTS

Patient Characteristics

There were 9 males and 11 females (mean age, 36.8 ± 20.2 years) in the paper-patch group and 9 males (10 ears) and 12 females (mean age, 36.3 ± 17.2 years) in the HADA patch group. The perforation side was on the right in 4 patients in the paper-patch group and 8 patients in the HADA patch group. It was on the left in 16 patients of the paper-patch group and 14 patients in the HADA patch group. There was no significant difference between the two groups according to sex, age, left and right ratio of the perforation side, perforation size, and duration of perforation (Table 1).

Table 1. Demographics and Clinical Characteristics of the Paper and Human Acellular Dermal Allograft Patch Groups

	Paper Patch (n = 20, 20 ears)	HADA Patch (n = 21, 22 ears)	*P*
Sex (male : female)	9 : 11	9 : 12	.890†
Age (mean ± SD, years)	36.8 ± 20.2	36.3 ± 17.2	.910‡
Side (right : left)	4 : 16	8 : 14	.315§
Duration of perforation (days)	6.3 ± 9.7	4.2 ± 4.0	.694‡
Perforation size (mean ± SD, mm)	2.88 ± 1.01	2.85 ± 0.81	.818‡
Perforation location (dominant quadrant)			
Anterior inferior	11	13	
Anterior superior	4	5	
Posterior inferior	5	4	
Posterior superior	0	0	
Patch maintenance time (mean ± SD, days)	15.6 ± 19.9	32.9 ± 14.9	**.001**‡
Recovery confirmation time (mean ± SD, days)	89.9 ± 119.4 (n = 17)	70.7 ± 42.3 (n = 21)	.486‡
Success vs Failure cases	17 : 3	21 : 1	
Success rate (%)	85.0	95.5	.333§

†Pearson's chi-square test.
‡Mann–Whitney *U*-test.
§Fisher's exact test.
HADA, human acellular dermal allograft; SD, standard deviation.

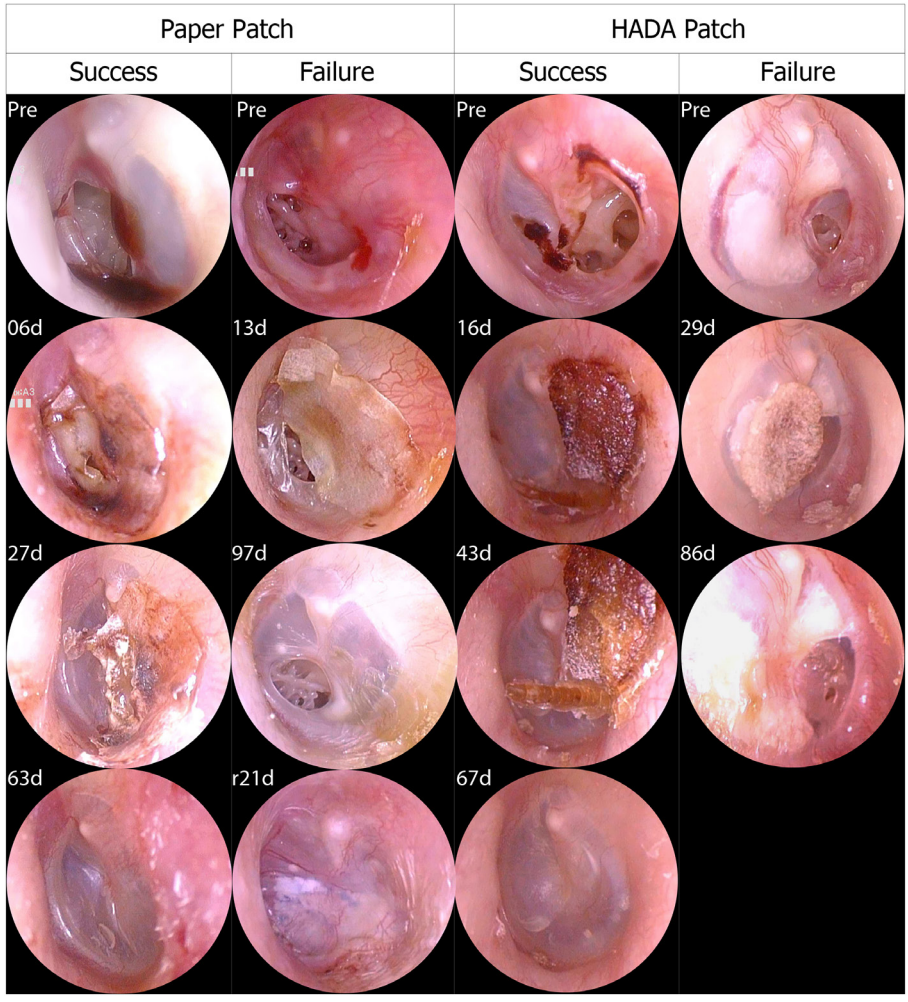

Figure 3. Examples of results in paper patch and human acellular dermal allograft patch groups. One of the patients who failed to heal in paper patch group underwent myringoplasty and perforation was healed. One patient with remained micro-perforation in HADA patch group wanted observation with no additional surgery. HADA, human acellular dermal allograft; Pre, pre-procedural; d, days; r, revision surgery.

Table 2. Demographics and Clinical Characteristics of the Recovery and Failure Groups

Total (n = 41, 42 ears)	**Recovery (38 ears)**	**Failure (4 ears)**	***P***
Age (mean ± SD, years)	36.2 ± 18.4	40.0 ± 21.5	.764†
Duration of perforation (days)	4.1 ± 3.7	16.0 ± 19.5	.188†
Perforation size (mean ± SD, mm)	2.82 ± 0.91	3.25 ± 0.87	.349†
Perforation location (dominant quadrant)			
Anterior inferior	21	3	
Anterior superior	9		
Posterior inferior	8	1	
Posterior superior			
Paper patch (n = 20, 20 ears)	**Recovery (17 ears)**	**Failure (3 ears)**	
Perforation size (mean ± SD, mm)	2.74 ± 1.03	3.67 ± 0.29	.160†
Duration of perforation (days)	3.9 ± 3.1	19.3 ± 22.5	.312†
Age (mean ± SD, years)	35.5 ± 19.9	44.0 ± 24.4	.427†
Perforation location (dominant quadrant)			
Anterior inferior	9	2	
Anterior superior	4		
Posterior inferior	4	1	
Posterior superior			
HADA patch (n = 21, 22 ears)	**Recovery (21 ears)**	**Failure (1 ear)**	
Perforation size (mean ± SD, mm)	2.89 ± 0.81	2.00	.223†
Duration of perforation (days)	4.1 ± 4.1	6.0	.426†
Age (mean ± SD, years)	36.7 ± 17.5	28.0	.693†
Perforation location (dominant quadrant)			
Anterior inferior	12	1	
Anterior superior	5		
Posterior inferior	4		
Posterior superior			

†Mann–Whitney *U*-test.
SD, standard deviation; HADA, human acellular dermal allograft.

Patch Maintenance Time, Recovery Confirmation Time, and Success Rate

HADA patch group showed a significantly longer patch maintenance duration compared to the paper-patch group (32.9 ± 14.9 vs. 15.6 ± 19.9 days, $P = .001$) (Table 1). However, there was no significant difference in the recovery confirmation time and recovery rate between the two groups (Table 1, Figure 3).

In addition, there was no significant difference in perforation size, duration, and age between the perforation recovery and the failure groups in the patients who underwent paper-patch procedures; which was also the same in the patients who underwent HADA patch procedures (Table 2).

Audiologic Results

Audiologic results were analyzed in patients with both the pre-procedural and post-recovery pure tone audiogram data in the paper (n = 14) and HADA (n = 15) patch groups. There was no significant difference between the paper and HADA patch groups in the hearing threshold of pre-procedural bone conduction, air conduction, air-bone gap, post-recovery bone conduction, air conduction, air-bone gap, and air-bone gap reduction (Table 3, Figure 4).

Factors Associated with Outcomes

Table 4 provides the results of univariable and multivariable regression analysis for continuous outcome variables (e.g., patch maintenance time, recovery confirmation time, and air–bone gap reduction) in relation to potential predictors (e.g., patch material,

Table 3. Audiologic Results of the Paper and Human Acellular Dermal Allograft Patch Groups

Hearing Threshold (Mean ± SD, dB HL)	**Paper Patch (n = 14, 14 ears)**	**HADA Patch (n = 14, 15 ears)**	***P***
Pre_BC	20.8 ± 16.0	18.6 ± 8.8	.948†
Pre_AC	32.6 ± 26.4	29.9 ± 11.6	.570†
Post_BC	16.0 ± 16.5	11.2 ± 6.0	.743†
Post_AC	22.0 ± 28.8	12.6 ± 6.3	.471†
Pre_AB_Gap	11.8 ± 12.6	11.4 ± 7.3	.570†
Post_AB_Gap	6.0 ± 13.4	1.4 ± 1.7	.313†
AB_Gap_Reduction	5.8 ± 4.4	9.9 ± 6.4	.077†

†Mann–Whitney *U*-test.
SD, standard deviation; HADA, human acellular dermal allograft; pre, pre-procedural; post, post recovery; BC, bone conduction; AC, air conduction; AB, air-bone.

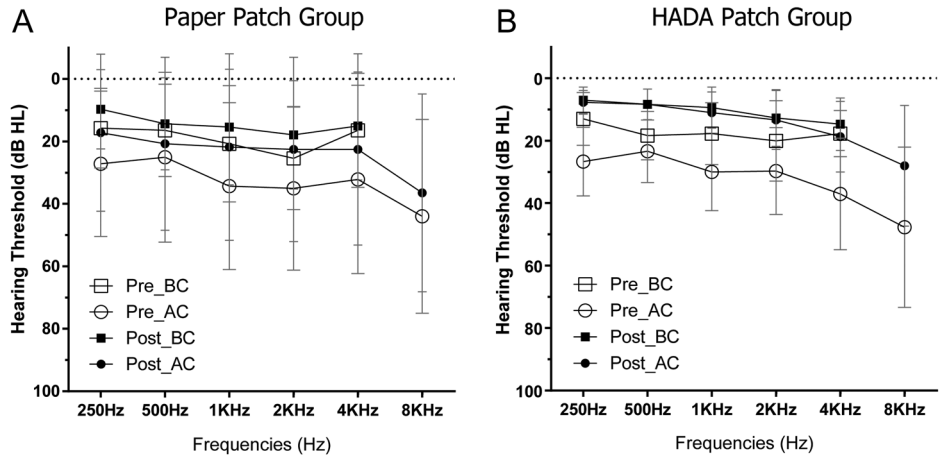

Figure 4. a,b. Audiologic results in paper patch and human acellular dermal allograft patch groups. Pre-procedural and post-recovery audiologic results show no significant differences between (a) paper patch group and (b) HADA patch group. However, both bone and air conduction were significantly improved in two groups after recovery of perforation. *The error bar represents the mean and standard deviation of each variable. HADA, human acellular dermal allograft; Pre, pre-procedural; Post, post recovery; BC, bone conduction; AC, air conduction; AB, air-bone.

Table 4. Factors Affecting the Outcomes after Patching Procedure in Traumatic Tympanic Membrane Perforation (by Univariable and Multivariable Regression Analysis)

Patch Maintenance Time (Dependent Variable)		**Univariable Regression**			**Multivariable Regression (R squared = 0.256, *P* = .003)**		
	Explanatory variables	**B**	**SE**	***P***	**B**	**SE**	***P***
	Patch material (HADA = 1)	17.309	5.386	0.003*	17.208	5.279	**.002***
	Sex (female = 1)	−4.069	6.028	0.504			
	Age (years)	−0.241	0.161	0.143	−0.235	0.145	.112
	Affected side (left = 1)	−4.317	6.644	0.520			
	Perforation size (mm)	2.722	3.362	0.423			
	Duration of perforation (days)	−0.401	0.416	0.341			
Recovery Confirmation Time (Dependent Variable)		**Univariable Regression**			**Multivariable Regression (R squared = 0.111, *P* = .100)**		
	Explanatory variables	**B**	**SE**	***P***	**B**	**SE**	***P***
	Patch material (HADA = 1)	−8.995	26.271	0.734			
	Sex (female = 1)	18.551	26.236	0.484			
	Age (years)	−1.208	0.695	0.090	−1.086	0.694	.125
	Affected side (left = 1)	−43.300	28.268	0.133	−37.560	28.010	.188
	Perforation size (mm)	5.777	14.734	0.697			
	Duration of perforation (days)	0.045	1.834	0.981			
Air–Bone Gap Reduction (Dependent Variable)		**Univariable Regression**			**Multivariable Regression (R squared = 0.314, *P* = .022)**		
	Explanatory variables	**B**	**SE**	***P***	**B**	**SE**	***P***
	Patch material (HADA = 1)	4.169	2.058	0.053	3.396	1.924	.09
	Sex (female = 1)	1.472	2.201	0.509			
	Age (years)	−0.020	0.060	0.738			
	Affected side (left = 1)	0.142	2.469	0.955			
	Perforation size (mm)	2.605	1.084	0.023*	2.411	1.040	**.029***
	Duration of perforation (days)	−0.363	0.328	0.278	−0.367	0.289	.216

Univariable and multivariable linear regression analyses were performed. The variables that were relatively significant ($P < .3$) in the univariable analysis were involved in the multivariable analysis. The dependent variables were outcomes (patch maintenance time, recovery confirmation time, and air-bone gap reduction). The explanatory variables were patch material (paper = 0, HADA = 1), sex (male = 0, female = 1), age, affected side (right = 0, left = 1), perforation size, and duration of perforation.

*Represents statistical significance ($P < .05$).

R squared, coefficient of determination; B, unstandardized regression coefficient; SE, standard error; HADA, human acellular dermal allograft.

Table 5. Factors Affecting the Recovery after Patching Procedure in Traumatic Tympanic Membrane Perforation (by Univariable and Multivariable Logistic Regression Analysis)

	Univariable Logistic Regression				Multivariable Logistic Regression			
	B	SE	*P*	OR (95% CI)	B	SE	*P*	OR (95% CI)
Patch material (HADA = 1)	1.310	1.200	0.275	3.706 (0.353–38.927)	0.963	1.289	.455	2.619 (0.209–32.758)
Sex (female = 1)	0.211	1.052	0.841	1.235 (0.157–9.708)				
Age (years)	–0.011	0.028	0.690	0.989 (0.937–1.044)				
Affected side (left = 1)	0.201	1.209	0.868	1.222 (0.114–13.065)				
Perforation size (mm)	–0.597	0.665	0.369	0.550 (0.150–2.026)				
Duration of perforation (days)	–0.163	0.108	0.132	0.850 (0.688–1.050)	–0.163	0.117	.165	0.850 (0.676–1.069)

Univariable and multivariable logistic regression analyses were performed. The variables that were relatively significant ($P < .3$) in univariable analysis were involved in the multivariable analysis. The dependent variable was recovery or not (failure = 0, recovery = 1). The explanatory variables were patch material (paper = 0, HADA = 1), sex (male = 0, female = 1), age, affected side (right = 0, left = 1), perforation size, and duration of perforation.
B, unstandardized regression coefficient; SE, standard error; OR, odds ratio.

age, sex, affected side, perforation size, and duration of perforation). Based on the multivariable regression analysis, patch material was the only parameter significantly associated with patch maintenance time ($P = .002$), and perforation size was significantly associated with air–bone gap reduction ($P = .029$), whereas none of other parameters reached statistical significance (Table 4). Table 5 provides the results of univariable and multivariable logistic regression analysis for recovery in relation to potential predictors, and no parameter showed significant correlation with recovery (Table 5).

DISCUSSION

According to the literature, the spontaneous recovery rate of TTMP is fairly high (79%-94%), and if the size of the perforation is less than 50%, natural healing occurs in most cases.[3,20,21] The factors lowering the spontaneous recovery rate of TTMP are old age, large-sized perforation, penetrating injury, perforation of posterosuperior quadrant, and interventional treatments such as external ear saline irrigation.[3,20,21] Although the spontaneous recovery rate of TTMP is high, the early application of a patch has multiple benefits. First, the persistence of air–bone gap in the audiogram after patch application can indicate a probability of ossicular disruption. Second, otological symptoms such as hearing loss and ear fullness can be immediately reduced. Third, recent studies including meta-analysis showed that the recovery rate of TTMP in the paper patching group was statistically higher than that in the observation group.[22,23] Therefore, it may lower the necessity of future surgical treatment for tympanic membrane perforation compared to the watchful observation.

Surgical treatment requires higher cost, longer hospitalization period, more difficult operative skills with strict aseptic management, and complex postoperative managements than patch technique, and it has issues of defects in donor site and a risk under general or local anesthesia, which increases the burden on both the surgeons and patients.[24] The patch technique is technically simple, cost-effective, and safe to perform requiring less time, therefore suitable to be performed in an outpatient setting.

The ideal graft material must meet the following requirements: it should (1) be thin but pliable with sufficient physical solidity, (2) allow the new epithelium to overgrow on the graft material, (3) be degradable but survive until the overgrowing epithelium meets with the opposite margin of the perforation, and (4) not cause an inflammatory reaction or a rejection by the host tissue.[25] Historically, various graft materials have been used for the treatment of tympanic membrane perforation. They were autograft materials such as vein, perichondrium, periosteum, earlobe fat, cheek mucosa, and fascia;[26] homograft (i.e., allograft) materials such as amnion, cornea, pericardium, perichondrium, periosteum, vein, arteria umbilicalis, cardiac valves, dura, fascia, omentum, and tympanic membrane;[27] heterograft (i.e., xenograft) materials which were fish's skin and air bladder along with the previously mentioned materials obtained from animals; and artificial materials such as cigarette paper, cotton wool, India rubber, eggshell membrane, silver, cellophane, and silicone rubber.[28]

Before the 1950s, the modern era of middle-ear surgery including myringoplasty and tympanoplasty using microscopes, Blake introduced the first paper-patch graft technique for the treatment of tympanic membrane perforation in 1887,[29] and this technique is still widely used to treat acute and TTMP. In recent years, various patch materials such as eggshell membrane,[10] silk,[9] gel foam,[11] collagen film,[8] Steri-Strips(3M®),[7] and calcium alginate[6,30] have been reported.[31] Paper patches act as scaffolds inducing epithelial growth over the attached patches, with high success rates, but limited to the cases with small-sized perforation.[13] Cigarette rolling paper is the most widely used material for patch procedure because of its availability and cost-effectiveness.[32] However, it leaves controversy in terms of biocompatibility, with the limitation of not being approved for medical purposes. Moreover, sometimes the paper patches early migrate before the complete recovery of the perforation, adversely affecting the successful results.

HADA is a processed human cadaveric skin, and one of its commercialized products, AlloDerm® (LifeCell Corporation, The Woodlands, Tex) has been approved by the FDA for human use.[33] It is a cell-free dermal matrix with preserved collagen structures and elastic fibers. The absence of cell components, antigens, or potential viruses do not raise unwanted inflammatory reaction or immune rejection by host cell.[34] Therefore, HADA meets the abovementioned requirements of the ideal graft material. The cigarette paper and HADA are similar in that they are initially dry and thin, easy to handle, and be trimmed to the desired size and contour. They both act as scaffolds promoting the growth of the tympanic membrane epithelium; however, HADA is superior to the exogenous paper material in terms of biocompatibility. Unlike the cigarette paper that requires an additional disinfection process before use, HADA is provided in a sterile state, and as

confirmed in this study, may stay longer without leaving the perforation site, reflecting its excellent adhesive property to the tympanic membrane.

HADA is effective in various clinical applications such as surgical reconstruction or implantation, and also in the treatment of tympanic membrane perforation. In 2001, Laidlaw et al[4] reported that HADA patch and rice paper patch showed no statistically different recovery rates (78% vs. 66%, respectively) in 28 chinchillas with chronic subtotal tympanic membrane perforation, and histopathological evaluation showed that the HADA was integrated into the middle fibrous layer of the tympanic membrane. In 2012, Qin et al[18] performed an animal study using 50 guinea pigs with subtotal tympanic membrane perforation and reported that acellular dermal matrix (ADM) patch technique and ADM underlay technique showed no statistically different recovery rates (89.3% vs. 90.9%, respectively), but a significantly higher recovery rates compared to the non-treated controls (6.0%). In 2018, Lee et al[19] performed a prospective randomized controlled study where 60 patients with tympanic membrane perforation were enrolled, and reported no difference in the perforation recovery rate between two groups who underwent tympanoplasty using HADA and autologous perichondrium (85.2% vs. 75.8%, $P = .519$), with the shorter surgical time in the HADA group (27.4 min vs. 35.2 min, $P = .039$). Although there have been animal studies using the HADA patch and human studies using the tympanoplasty technique, patients with acute TTMP treated with HADA patch and a comparison of its outcomes with those of the paper patch have not been reported.

During the patching procedure, the following factors should be considered to improve the success rate. The key element is to trim the edge of the tympanic membrane perforation to remove all medially inverted edges and prevent the ingrowth of the epithelial layer while inducing epithelial overgrowth. This enables the patch material to attach completely to the entire perforation area without detaching, and prevents the development of middle-ear cholesteatoma. The difference in adhesive property to the tympanic membrane between the patch materials can affect the patch maintenance time after the procedure. Because of the cone-shaped structure of the eardrum, the pliability of the patch material is required to ensure its tight attachment, especially when the perforation area includes the concave center of the tympanic membrane, umbo. For better attachment, patch materials can be applied with soaking in saline solution or ointment (Mupirocin 2% ointment).[12]

Generally, if the perforation is not fully healed within 3 months after the patching procedure, surgical intervention other than the patch technique is recommended.[35] Among 41 patients (42 ears) who underwent patching procedures in this study, one patient in the HADA patch group left small perforation (0.5 × 0.5 mm) after the procedure, but the patient did not want additional surgery and no special side effects were observed for more than 6 months post-procedure. For 3 cases that failed to recover in the paper-patch group, myringoplasty using autologous temporalis muscle fascia was performed after 3.5 months, 5 months, and 12 months of observation, respectively, followed by full recovery and maintenance until 4–24 months of follow-up.

Limitations

This is the first study comparing therapeutic efficacy between using HADA and paper-patch materials in acute TTMP, but it has a few limitations. First, it was difficult to accurately estimate the duration of patch maintenance and complete recovery, since it was a retrospective study with various follow-up intervals. Second, the average size of perforation in 2 groups was generally small (2.88 ± 1.01 mm in the paper-patch group, 2.85 ± 0.81 mm in the HADA group, respectively). Third, due to a relatively small number of patients, the present study may have failed to reveal statistically significant differences in some results. Therefore, it may be necessary to evaluate the effectiveness of the HADA patch in a larger cohort study in the future, including cases with large perforations.

Despite these limitations, the HADA patch was significantly superior to the paper patch in terms of the maintenance duration of the patch.

CONCLUSION

In this study, the HADA patch was found to be an alternative to a traditional paper patch for acute TTMP treatment. Paper patches are limited in that the source of the material was not developed for medical uses. Paper patches have the disadvantages of non-biocompatible characteristics, tendency to be early detached or migrated, and potential vulnerability to infections. On the contrary, HADA is FDA-approved material with accumulated experience in many clinical fields, and it may partially compensate for these disadvantages. HADA showed a non-inferior or partly superior therapeutic performance as patch material for the treatment of TTMP. Although HADA patches may require increased costs compared to the existing paper patches, unapproved materials need to be replaced considering the safety required for medical materials.

Ethics Committee Approval: Ethical committee approval was received from the Institutional Review Board of the Seoul National University Hospital (Approval no: IRB-10-2020-1).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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