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The Long-Term Stability of Fat-Graft Myringoplasty in the Closure of Tympanic Membrane Perforations and Hearing Restoration

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Keywords
Ear surgery · Myringoplasty · Autologous fat

Abstract
Background/Aims: This study was conducted to evaluate the long-term stability of fat-graft myringoplasty (FGM) for chronic tympanic membrane perforations, analyzing the perforation closure rate and re-gained hearing outcome with respect to the size and location of the perforations. ***Methods:*** Between August 2007 and June 2018, a total of 193 patients who underwent FGM due to chronic tympanic membrane perforation at a tertiary referral center were enrolled and analyzed. ***Results:*** The mean follow-up was 14.6 months (range 6–39). The complete perforation closure rate after FGM was 89.6%, with no statistical difference among the perforation size groups. The mean postoperative air-bone gap (ABG) was 11.0 dB and mean ABG improvement was 4.9 dB. ***Conclusion:*** Our FGM technique had a favorable tympanic closure rate for small to large perforations, and yielded relatively good hearing improvement in the mid-size perforation cases over long-term follow-up periods. According to the topographic evaluation of FGM, this procedure resulted in a reliable perforation closure rate and audiological results regardless of the perforation site.

Introduction

Tympanic membrane (TM) perforation is a frequent diagnosis in otologic clinics worldwide. TM perforations mainly result from middle ear infections, trauma, or are the sequelae of ventilation tube insertion. Most acute perforations heal spontaneously when there is no other pathology, but about 10–20% become a chronic process without healing [1]. Chronic perforations can cause recurrent otorrhea, conductive hearing loss, acquired cholesteatoma, and middle ear infection [2]. Therefore, surgical closure is generally recommended for persistent TM perforation. A myringoplasty, which closes TM perforation without middle ear evaluation, is considered to be a simple but most effective surgery in the otology field [3].

First introduced in 1962 by Lingenberg, fat-graft myringoplasty (FGM) is a simple, cost-effective, and minimally invasive procedure with a short surgery time, so it has advantages over conventional myringoplasty using temporalis fascia. It is a great advantage to be able to perform the surgery with local anesthesia in an outpatient clinic [4, 5].

The primary goal of myringoplasty is to permanently close the TM perforation and restore hearing, and successful surgical results of FGM have been reported, especially for small perforations [5–7]. Furthermore,

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recent literature reported a high success rate ranging from 85 to 90% including selected cases of quite large perforations [8–10]. However, reports of audiological evaluations according to perforation size and FGM are limited. Consequently, the purpose of this study was to evaluate the long-term perforation closure rate and graft failures of FGM performed in patients with chronic TM perforations. We also aimed to assess hearing outcomes in successful cases in relation to perforation location and size.

Materials and Methods

Patients

After obtaining approval from the institutional review board (KC14RISI0048), we retrospectively reviewed the charts of the patients who underwent FGM from August 2007 to June 2018 at Seoul's St Mary's Hospital. This involved a total of 193 patients (134 female and 59 male subjects). The patients were selected consecutively and were included in the study according to the following criteria: perforation at pars tensa and non-marginal localization; perforation size <50% of the total TM; perforations present for >6 months; at least 6 months have elapsed since an otologic surgery; no clinical evidence of cholesteatoma; absence of ossicular or mastoid pathology (checked by otoendoscopy and temporal bone computed tomography [CT] scan), and absence of major Eustachian tube dysfunction was indirectly confirmed as seen on the CT scan of mastoid air cells. In addition, any patient who had active discharge or acute inflammatory change of the middle ear within the last 3 months was excluded from this study. All patients received a full description of the procedure and signed an informed consent form.

FGM Surgical Techniques

Based on the patient's preference, anesthesia was either general or local. All surgical procedures were performed by 1 senior surgeon (K.H.P.). A short incision was made posterior to the ear lobule on the same side as the operated ear, and adequate fat tissue was extracted using a 15-blade scalpel. Care was taken to harvest a graft that was at least 2 times the estimated size of the perforation. The margins of the perforation were de-epithelialized circumferentially with a pick and cup forceps under the microscope. The harvest fat tissue was then inserted through the perforation using a standard "champagne cork" technique. The fat graft was placed, and it was gently pulled back until at least half of the graft was above the perforation to ensure eversion of the TM edges. Finally, the fat graft and the TM remnant were covered by a fibrin sealant, Beriplast® combi-set (CSL Behring LLC, King of Prussia, PA, USA). The external ear canal was packed with gelfoam pieces soaked in antibiotic drops.

Postoperative Care and Outcome Measures

Patients were discharged the day after surgery and instructed to keep their ears dry. The gelfoam pieces in the ear canal were removed at the end of the third week. Postoperative follow-up was arranged every week for the first month, and then 2, 4, and 6 months and annually postoperatively. Preoperative and postoperative otoendoscopy was performed with the use of a 4-mm diameter, 0° otoendoscope (Karl Storz Co., Tuttlingen, Germany). All obtained images of the TM were transferred as JPEG files to our workstation. Successful closure was confirmed when the complete healing of the perforation was observed under otoendoscopy and the intact membrane was maintained for a follow-up period of >6 months without the occurrence of re-perforation. On the contrary, graft failure was defined as incomplete closure of the perforation or re-perforation during the follow-up period.

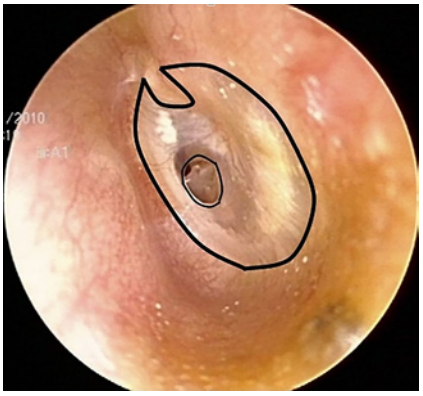

Fig. 1. The areas of total TM (thick outer line) and perforation site (thin inner line) were measured using the image analysis program after manual drawing of the margins.

Audiometric measurements used in this study were based upon the preoperative and the last evaluation of each patient. This included the pure tone audiogram (PTA) in which preoperative and postoperative air-bone gap (ABG), air conduction (AC), and bone conduction (BC) thresholds at 500 Hz, 1, 2, and 3 kHz were obtained. Hearing improvement was assessed using audiogram results obtained at 6 months postoperatively after discarding the graft failure cases, and "ABG improvement" was defined as the difference between the pre- and postoperative mean ABG. Furthermore, the postoperative status of the TM, the improvement of hearing, and the incidence of complications were recorded thoroughly at each follow-up visit to measure outcomes.

The TM perforation closure rate and audiological outcome were analyzed as a function of perforation size and location with the use of otoendoscopy. The perforation size was measured by morphometric analysis of the stored TM photograph using the image analysis program Paint.net (version 3.5.11; dotPDN LLC, Kirkland, WA, USA). After outlining the margins of total TM and perforation area manually by an investigator who was blinded to operations, the percent of the area of the perforation with respect to that of the entire TM-perforation area index (PAI, %) was calculated by automatically counting the number of pixels in the outlined area (Fig. 1). Accordingly, the patients were divided into 4 groups depending on the size of the perforation (<10%, 10–20%, 20–30%, >30%) and into 2 groups depending on its location (anterior and posterior). The data were analyzed using the software program SPSS version 24.0 (SPSS Inc., Chicago, IL, USA) and $p < 0.05$ was considered statistically significant.

Table 1. Perforation closure rate according to size group

	No perforation	Residual perforation	Total
Perforation size			
PAI <10%			
Count	99	8	107
% within group	92.5	7.5	100.0
PAI 10–20%			
Count	52	8	60
% within group	86.7	13.3	100.0
PAI 20–30%			
Count	15	2	17
% within group	88.2	11.8	100.0
PAI >30%			
Count	7	2	9
% within group	77.8	22.2	100.0
Total			
Count	173	20	193
% within group	89.6	10.4	100.0

PAI, perforation area index.

Table 2. Perforation closure rate according to location group

	No perforation	Residual perforation	Total
Location			
Anterior group			
Count	122	15	137
% within group	89.0	11.0	100.0
Posterior group			
Count	51	5	56
% within group	91.1	8.9	100.0
Total			
Count	173	20	193
% within group	89.6	10.4	100.0

Results

In total, 193 patients who met the inclusion criteria were operated. The age (mean ± SD) of the patients at the time of FGM was 55.3 ± 17.4 years and mean follow-up was 14.6 months (range 6–39). Of the 193 perforations, 93 (48%) were right sided and 100 (52%) were left sided. The patients' histories revealed 29 with previous otologic surgery: 12 with ventilation tube insertion, 2 with FGM, 9 with tympanoplasty, and 6 with canal wall up tympanomastoidectomy on the same side. The mean AC threshold, BC threshold, and ABG in preoperative PTA were 33.0 ± 17.6, 17.1 ± 14.6, and 15.9 ± 8.7 dB, respectively. The preoperative mean PAI was 10.1 ± 9.7%, ranging from 2.3 to 53.4%, and in most cases (167, 86.5%) PAI was <20%. The perforation was most frequently located in the anteroinferior quadrant (81 cases, 42.1%), with 137 perforations (71.0%) involving the anterior part of the TM.

Perforation Closure Rate

Complete closure was achieved in 173 of 193 ears, with an overall success rate of 89.6%. No statistical difference was found between the 4 size groups; however, the mean closure rate in the group with PAI >30% (77.8%) was lower than in the other groups (Table 1). Regarding the location of perforation, the distribution of failed cases was 15 anteriorly and 5 posteriorly, with the success rate being 89.0 and 91.1%. The difference in the closure rate between the 2 groups was not significant (Fisher's exact test, $p = 0.753$; Table 2). Figure 2 shows the representative endoscopic findings of various TM perforations and completely healed status at 2 months after FGM.

Audiological Outcome

The mean follow-up was 14.6 months and follow-up PTA at 3 months postoperatively was available for all 173 patients who had the TM with complete closure after FGM. The mean postoperative AC threshold, BC threshold, and ABG were 27.8 ± 18.8, 16.8 ±14.3, and 11.0 ± 8.4 dB, respectively. Thus, the mean AC threshold and ABG improved significantly after FGM (Student *t* test, $p < 0.001$) and the mean "ABG improvement" (defined as the value of preoperative ABG minus postoperative ABG) was 4.9 ± 4.2 dB. However, no difference of BC threshold was found postoperatively ($p = 0.632$). Regarding ABG improvement among the different size groups, patients with PAI <10% and PAI >30% had poor postoperative results, and the ABG of the PAI <10% group showed significantly less improvement compared with the other groups (Kruskal-Wallis test, $p = 0.003$). In addition, the mean ABG improvement of the PAI >30% group was smaller than the PAI <10% group, but there was no statistical significance compared with the 3 other groups (Fig. 3a).

The difference in mean ABG improvements of the 2 groups depending on the location of the perforation (anterior and posterior) was not significant, but the ABG of the posterior group was more improved compared with the anteriorly located perforation group (Student *t* test, $p = 0.097$; Fig. 3b). Analyzing 173 patients, we confirmed an almost complete closure of the postoperative ABG

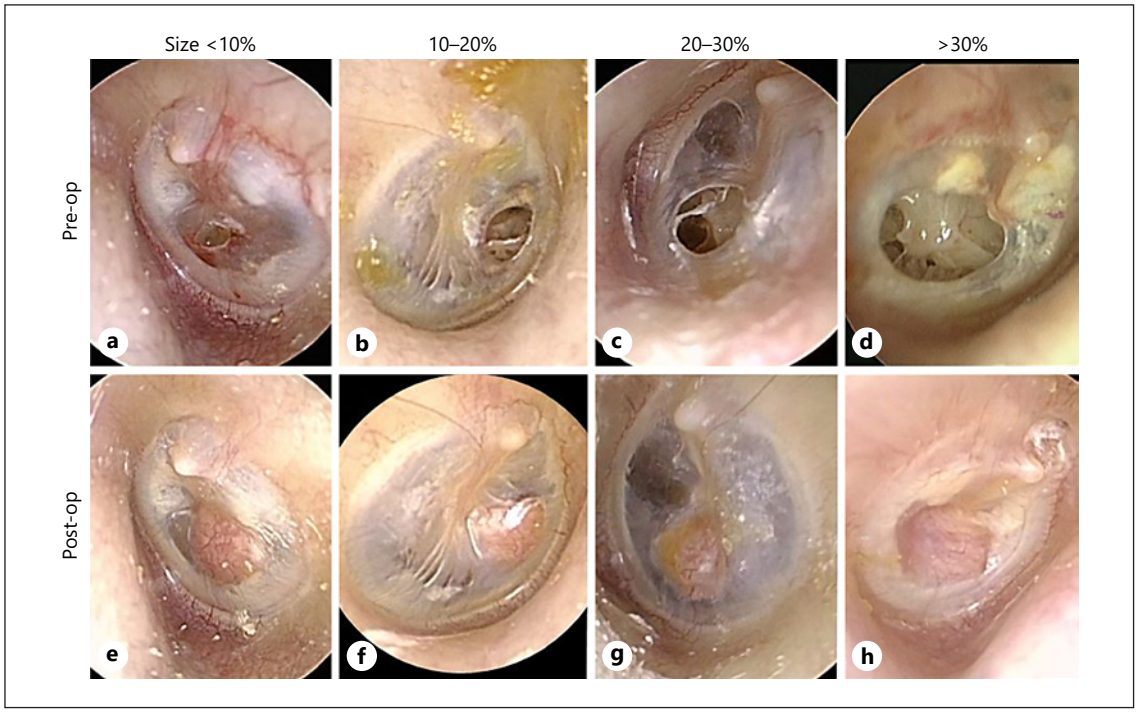

Fig. 2. Representative endoscopic findings of the TMs preoperatively and at 2 months after FGM. **a–d** Any type of chronic TM perforations, including various sizes and locations, could be a good indication for FGM. **e–h** Complete healing of the perforation and the revascularization of the newly formed TM after surgery is evident. Pre-op, preoperative; Post-op, postoperative.

Table 3. Characteristics of the graft failures (n = 20/193) and additional otologic procedures according to the size of residual perforation

Size of residual perforation	Patients, *n*	Size of preoperative perforation (PAI)	Localization of residual perforation	Additional otologic procedure
Pin-point perforation	12	<10% (5); 10–20% (6); >30% (1)	Anterior (9); Posterior (3)	None (spontaneous healing with regular dressing)
PAI <10%	5	<10% (2); 10–20% (1) 20–30%(2)	Anterior (3); Posterior (2)	4 with paper patching; 1 surgical tympanoplasty
PAI 10–20%	2	10–20% (1) >30% (1)	Anterior (2)	Surgical tympanoplasty
PAI 20–30%	0	–	–	–
PAI >30%[a]	1	<10% (1)	Anterior (1)	Surgical tympanoplasty

PAI, perforation area index; FGM, fat-graft myringoplasty.
[a] The only case with a larger residual perforation than at preoperative assessment.

(PTA <5 dB) in only 12.7% (22 of 173). Almost 64.7% (112 cases) remained within 10 dB, whereas an insufficient result (>20 dB) was seen in 9.2% (16 cases) despite the successful closure of the TM.

Analysis of Graft Failure Cases

Residual perforation remained in 20 ears with a graft failure rate of 10.4% (20 of 193). The analysis of the 20 failed cases showed that 1 had a size >30% of the pars

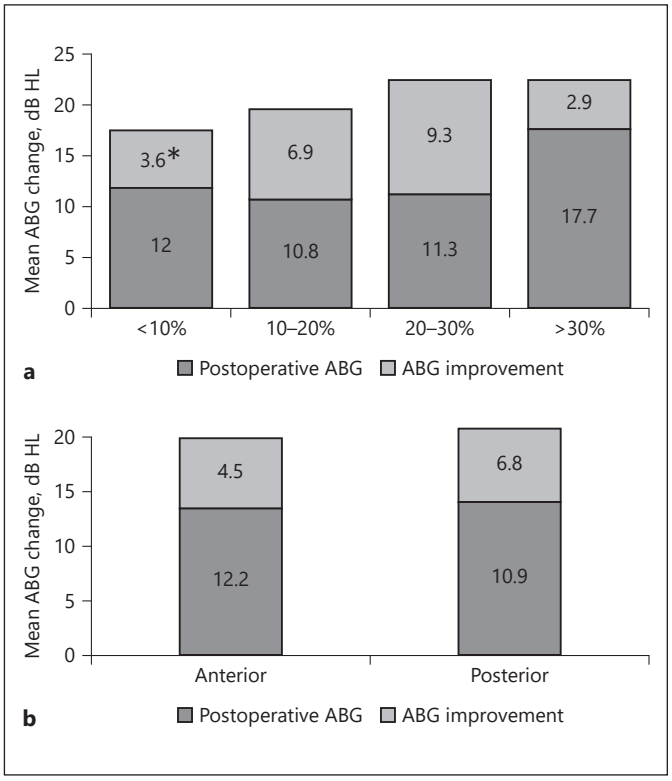

Fig. 3. Mean postoperative ABG and ABG improvement according to perforation size group (**a**) and location group (**b**). No statistically significant differences were observed except for the PAI <10% group, which showed less ABG improvement. Kruskal-Wallis test, * $p = 0.003$.

tensa and the other 12 had <20% of the pars tensa (12 with pin-point perforation, 5 with PAI <10%, and 2 with PAI 10–20%). Most residual perforations occurred at an anterior location (15 of 20, 75%). Postoperative assessment of these cases showed smaller perforations in 16 patients, no change in size in 3 patients, and a larger perforation in only 1 patient (who had a residual perforation with PAI >30%; Table 3). Regarding the time of failure, no residual perforation was identified within 3 weeks postoperatively. However, 8 residual perforations were found at the 1-month follow-up visit, 4 at 2 months, and 8 at 4 months, but there was no perforations at >6 months.

Of the 29 patients who previously had ear surgery, graft failure developed in 6 patients. In the failure group, 6 patients had previous otologic surgery, 3 had tympanoplasty, and 3 had canal wall up tympanomastoidectomy. While the perforation closure rate in patients without a prior otologic intervention was 90.3% (130 of 144), those patients with a previous otologic surgery had a closure rate of 79.3% (23 of 29), but no significant correlation was observed between previous operation and successful closure (Fisher's exact test, $p = 0.098$).

In 12 cases, the residual perforation was pin-point in size and did not require additional treatment. In 4 cases in which the size of the perforation was quite large (PAI <10%), 4 residual perforations could be healed by trimming the margin and applying a paper patch in an outpatient clinic, but the perforation of the other 1 patient was closed completely after tympanoplasty. Moreover, in 3 cases in which the perforation size was larger than 10%, successful closure was achieved after standard surgical tympanoplasty (Table 3).

No definite causes of failure were identified, with the exception of 1 case of active infection (mucoid otorrhea with localized fungal hyphae were identified on otoendoscopy; the size of residual perforation in that patient was 36%). We noted the absence of complications during the follow-up period, such as cholesteatoma development, TM lateralization, marginal blunting, or retraction pocket formation in all of the 193 operated ears, including the failure cases.

Discussion

The spontaneous healing rate of chronic TM perforations is low because squamous epithelium grows from the perforated margin to the medial mucosal layer, preventing the spontaneous closing of the perforation [11]. The following 3 principles have been reported to be required for the TM perforations: first, the margin of the perforation should be de-epithelialized and everted; second, the inflammatory reaction resulting from mechanical or chemical irritants to activate cell proliferation; and third, the graft should lie on the perforation as a scaffold of re-epithelization [12]. Using the best available evidence, the gold standard remains a tympanoplasty using temporalis fascia [13]. However, this surgery results in a cost and time-consuming burden on both the patient and the healthcare system [14], and an increasing number of patients want minimally invasive procedures.

FGM and inlay butterfly cartilage tympanoplasty is one of the alternative options for conventional tympanoplasty [15, 16]. Compared to inlay butterfly cartilage tympanoplasty, which usually uses tragal cartilage as a graft material, FGM is relatively less invasive, and fat has some advantages in that it can be harvested easily and several times, unlike tragal cartilages. In this respect, FGM is preferred as a day-stay surgical procedure for the repair of chronic TM perforation in suitable patients.

The overall graft success rate was 89.6% and is similar to the 85–90% success rate reported in other recent studies [6]. Fat plug myringoplasty was first introduced by Ringenberg [4] and the success rate was reported as 87% for small perforations. Afterwards, Deddens et al. [17] found the TM perforation size to be an important factor in predicting the success rate of myringoplasty. In their series, a good prognosis was considered for 5–30% TM perforations, while larger perforations were more prone to failure. Konstantinidis et al. [10] showed similar results; the success rate was shown to be higher in perforations not greater than 30% of the pars tensa, and the central and the posterior parts of the TM are considered optimal locations for successful FGM. In contrast with previous reports, our study did not reveal a significant difference in the closure rate according to the size of the perforation. However, the number of patients in the group with PAI >30% (n = 9) was too small to provide statistical power and clinical implications. That is because we preferred a standard tympanoplasty to FGM for the patients with a large perforation on the basis of the well-established stability of that surgical procedure. To be free from selection bias and to confirm the reliability of FGM in the closure of large TM perforations, further investigation in a large series is needed prospectively.

We also observed no significant difference in closure rate between the 2 groups with a distinct location of TM perforation (anterior vs. posterior). In general, the anterior perforation closure of traditional tympanoplasty is limited due to a poor surgical view of anterior margin, insufficient vascular supply, and inadequate graft support [5, 6]. However, FGM overcomes some of these technical challenges. First, no supports are required for fat plugging at the level of the anterior annulus. Second, fat is an incredibly active substance that promotes cicatrization as well as revascularization of adjacent tissue. With these advantages of FGM, we could expect a high closure rate of anterior perforation as well as that of posterior perforation. Moreover, in the present study, the mean ABG improvement of the patients with anterior perforated TM was not significantly different from that of posterior perforation patients. With this result, we may confirm the usefulness of FGM in anterior perforation in terms of not only the TM closure rate, but also the audiological outcome.

In view of the audiological outcome, the mean AC threshold and ABG improved significantly regardless of the perforation size and location. A significant correlation between the preoperative size of the TM perforation and the postoperative ABG was reported in a recent study [16], and it was easy to predict that the patients with larger perforations would show bigger postoperative ABGs. To evaluate the exclusive effect of FGM among different size and location groups, we analyzed our hearing gain of FGM based on "ABG improvement" rather than postoperative ABG. The mean "ABG improvement" was 4.9 dB; however, hearing gain was comparatively poor in the PAI <10% and PAI >30% groups (3.3 and 2.9 dB, respectively). We believe that a low hearing gain in the smallest perforation group (PAI <10%) reflected the smallest preoperative ABG among the 4 patient groups. The poor outcome of the largest perforation group (PAI >30%) occurred because even after FGM the TM in this group remained thicker than that in other groups. As mentioned in our previous study [18], larger perforations needed a much larger amount of fat tissue proportionally. Thus, it is readily speculated that non-absorbed fat tissue or fibrous tissue generated during the remodeling process of the fat graft would thicken the postoperative TM much more in this group. Additionally, as noted in the study by Pfammatter et al. [19], it can be assumed that the random arrangement of collagen fibers in the intermediate layer of the neo-TM may have a slight effect on the sound-induced travelling wave motions of the TM that can cause incomplete ABG closure, especially after closing large perforations [19, 20]. Probably, this is one of the feasible explanations for incomplete closure of the ABG after FGM, as seen in our study; an insufficient hearing result (postoperative ABG >20 dB) was noted in 16 patients despite the successful closure. Again, these hypotheses remain to be validated in future research.

Comparing the perioperative BC thresholds, we could not observe any deterioration in the present study. Since tympanotomy is not performed in FGM, the risk of iatrogenic trauma of the middle ear structures is very low. For the same reason, the risk of sensorineural hearing loss occurring in FGM is low, which is thought to be the reason why not a single sensorineural hearing loss occurred in our study [12]. Thus, we could verify the safety of FGM with our collected data.

To date, only a few reports analyzing the factors contributing to graft failure of FGM have been published. As well as the preoperative size and location of TM perforation, we examined the graft failure cases regarding the time of failure, the presence of a previous otologic procedure, and any other complications, including infection. In our study, all 20 residual perforations occurred in the first 4 postoperative months, and after the fourth month, no re-perforation of a new TM was observed during a mean follow-up period of 14.6 months. These results illustrate the stability of the newly developed TM and are consistent

with the results in the previous literature [8]. However, Jurovitzki and Sade [21] reported that TM perforations can recur for years, with initial success turning into failure in 7.6% of patients who underwent traditional myringoplasty. Accordingly, regular follow-up otoendoscopic examinations over the years after the confirmation of successful closure are crucial and we also need more long-term follow-up periods for patients who underwent FGM.

Analyzing the failure group, 6 patients had previous otologic surgery. Compared with the success group, we could determine that there was no significant effect of previous operation on the complete closure of TM. However, it is essential to check the status of middle ear space and mastoid air cells by CT scan preoperatively. This is because the Eustachian tube function is thought to impact on the success rate of TM graft and hearing gain [22], especially in patients with prior otologic intervention.

During the follow-up period, a sign of active infection was detected in only 1 patient even among the failure group. Actually, he was lost to follow-up for 3 months, and visited again in the fourth month with a mucoid discharge in the operated ear. Furthermore, he was the only case with a larger residual perforation (PAI = 36%) than at the preoperative assessment, maybe due to the infectious condition. After the administration of proper antibiotics, a successful closure was achieved by underlay tympanoplasty without other complications. On the other hand, almost all residual perforations (16 of 20, PAI <10%) were managed with simple outpatient procedures. Regular follow-up examinations and early detection of postoperative problems is imperative for the first 4 months after FGM.

Conclusion

Our FGM technique revealed a favorable TM closure rate for small to large perforations, and relatively good hearing improvement results in the moderate sized (PAI 10–30%) perforation cases over long-term follow-up periods. The topographical assessment of FGM showed that the procedure resulted in a reliable perforation closure rate and audiological outcomes regardless of perforation location. Because a significant ABG improvement in the present study reflects the excellent repair of the TM and serves as evidence for hearing restoration, our results suggest that we can accomplish the stability of newly developed TM through FGM in both aspects. However, the clear-cut suitability of FGM for chronic large TM perforations (PAI >30%) should be established by evenly distributed trials in a large series.

Statement of Ethics

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki and was approved by the institute's committee on human research (KC14RISI0048).

Conflict of Interest Statement

All authors approved this manuscript, and there are no conflicts of interest to report.

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Author Contributions

K.H.P.: conceptualization and supervision. J.S.H. and J.J.H.: data collection and analysis, and manuscript draft. J.S.H., J.M.P., and J.-H.S.: revision of the manuscript. All authors approved the final manuscript.

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