

Fibrinogen-Based Collagen Fleece Graft Myringoplasty for Traumatic Tympanic Membrane Perforation

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Background and Objectives: The aim of this study was to investigate how fibrinogen-based collagen fleece (Tachocomb[®]) graft myringoplasty (FCGM), performed under microscopic guidance, improves both hearing and tympanic membrane tissue repair in patients with traumatic tympanic membrane perforation (TMP). **Subjects and Methods:** Between August 2009 and March 2015, a total of 52 patients with traumatic TMP visited the department of otorhinolaryngology at a secondary medical center. Twenty-nine of these underwent FCGM under microscopic guidance in our outpatient clinic. For each patient, we recorded the location and size of the perforation, the time elapsed from the onset of TMP until the myringoplasty, and the hearing level both before and after myringoplasty. **Results:** The TMP closed completely in all cases (29 of 29 patients). After myringoplasty, the postoperative air-bone gap (ABG) differed significantly from the preoperative ABG. Three of the 29 patients (10.3%) experienced complications. Specifically, 2 presented with otorrhea after FCGM, but conservative management led to improvement without recurrence of perforation. One patient showed delayed facial palsy 1 week after the procedure. The condition of this patient also improved and the palsy was not permanent. **Conclusions:** FCGM may be an effective treatment option in case of traumatic TMP. The procedure requires no hospitalization, and can be used to avoid traditional tympanoplasty. **J Audiol Otol 2016;20(3):139-145**

KEY WORDS: Tympanic membrane perforation · Fibrinogen-based collagen fleece · Myringoplasty · Conductive hearing loss · Patch.

Introduction

The tympanic membrane perforation (TMP) can be classified according to their duration, in acute and chronic (more than 3 months), and by the presence or absence of drainage, in wet and dry perforation [1]. In recent times, the number of patients presenting with chronic otitis media has been decreasing rapidly due to advances in antibiotic treatment. For this reason, trauma has become one of the main causes of TMP. While most patients of traumatic TMP recover spontaneously without complications [2], some suffer middle ear infections and develop conductive hearing problems caused by unhealed perforations [3]. Although physicians often at-

tempt a suitable non-surgical treatment of TMP at an early stage, invasive surgery such as tympanoplasty or myringoplasty is nonetheless required in cases with insufficient healing. Such surgery is more expensive, involves more effort, and entails higher risks than non-surgical treatments. Therefore, treatment using substances that facilitate membrane regeneration has recently been considered as an alternative to surgical TMP repair [4].

The fibrinogen-based collagen fleece (Tachocomb[®], Nycomed Austria GmbH, Linz, Austria) is a collagen-bound fibrinogen sealants. It consists of a sponge-like patch composed of equine collagen and coated with a mixture of human fibrinogen, bovine thrombin, and bovine aprotinin [5]. It has been used both to stop bleeding and to treat leakage of cerebrospinal fluid, bile, saliva, pleural effusion, and lymph. It is also well known that the fibrinogen-based collagen fleece adheres strongly to tissue and thereby forms a waterproof mem-

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brane. Collagen types I to IV are the most abundant collagens in animals. For example, muscular fascia, which is commonly used to repair perforated tympanic membrane (TM) tissue during myringoplasty, consists primarily of collagen type I [6]. In addition, collagen types I and III have been found at the perforation border and around dilated blood vessels early in the healing phase after myringotomy in rats [7]. We decided to use the fibrinogen-based collagen fleece as a patch material because it has 1) good tissue affinity, 2) water-proofing properties, and 3) abundant type I collagen.

The aim of this study was to present the clinical outcomes of fibrinogen-based collagen fleece graft myringoplasty (FCGM) in traumatic TMP patients. The procedure was performed under microscopic guidance in our outpatient clinic.

Subjects and Methods

Subjects

Between August 2009 and March 2015, 52 patients with traumatic TMP visited the department of otorhinolaryngology at a secondary medical center. Of these, 29 underwent FCGM under microscopic guidance at the outpatient clinic. Ten patients were loss to follow-up after diagnosis of TMP, and 3 patients discontinued to visit the hospital after FCGM. Six patients were excluded because of the small TMP (less than 30% of the entire TM area), and 4 patients were young age (3–8 years old). For each patient, we recorded the location and size of perforation, the time elapsed from the onset of TMP until the myringoplasty, and the hearing level both before and after myringoplasty. There were 17 male and 12 female patients ranging in age from 13 to 69 years (mean age, 33.3 ± 16.6 years). Indications for FCGM under microscopic guidance were as follows: patients 1) had a direct injury to the TM wherein the perforation area measured more than 30% of the entire TM area, and 2) the size of TMP was more than half of its original size after 2 weeks of observation. We also included patients in whom TMP had recurred despite their having undergone the paper patch procedure. All patients included in this study consented to participate in the study after hearing the merits and demerits of FCGM. We evaluated the patients using pure tone audiometry (PTA) both before the procedure and after the TMP had completely healed.

Surgical technique

The surgical procedure, FCGM under microscopic guidance, was carried out as follows.

1) The external auditory canal (EAC) was cleaned and, along with the TM, locally anesthetized using a 10% lidocaine spray (Xylocaine® 10 mg spray, Astra Zeneca, Södertälje,

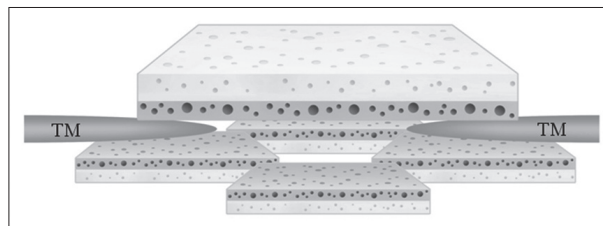


Fig. 1. Schematic illustration of how to place the pieces of the fibrinogen-based collagen fleece. The smaller pieces of the fibrinogen-based collagen fleece were inserted into the middle ear cavity, and the larger piece was placed onto the lateral side of TM. TM: tympanic membrane.

Sweden). Ten minutes were allowed to pass between application of the spray and continuation of the surgery.

2) We divided the fibrinogen-based collagen fleece into pieces of about the size of the perforation, and one piece of about twice the size.

3) The TM was inspected, and the edge of the perforation was unfolded using the ear hook if necessary.

4) We inserted the smaller pieces of the fibrinogen-based collagen fleece into the middle ear cavity, and placed the larger piece onto the lateral side of TM (Fig. 1). Fibrinogen-based collagen fleece patch was not removed until it was detached from the TM by itself.

Audiological test

PTA was performed before and after FCGM, and the frequencies 250, 500, 1,000, 2,000, and 4,000 Hz were used for analysis. The mean air-bone gap (ABG) was defined as the arithmetical average derived from the analysis of these frequencies. After the patch was removed and the TMP was examined the PTA measurements of each patient were recorded.

Statistical analyses

The data were analyzed using PASW® statistics 18 software (SPSS Inc., Chicago, IL, USA). The Wilcoxon signed rank test was used to compare the preoperative with the postoperative mean ABG, calculated from the PTA recordings. p -values < 0.05 were considered statistically significant.

Institutional review board approval

This retrospective study was approved by the Institutional Review Board of Jeju National University Hospital for data collection and analysis (IRB No. JEJUNUH 2014-05-022). The requirement for informed consent was waived.

Results

The location of the TM perforation was classified as anterior, central, posterior, or in multiple positions. Thirteen (44.8%)

Table 1. Demographic and clinical data of patients

No. of patient	Sex	Age (years)	Side	Location of TMP	Size of TMP (%)*	TMP to FCGM (days)	Duration of follow-up (days)	Causes of TMP	Previous history	Postoperative complication
1	F	69	Rt	Central	20	15	123	Cotton swab		
2	M	24	Lt	Central	25	17	414	Slap		
3	F	27	Lt	Posterior	40	23	93	Slap		
4	F	33	Lt	Anterior	20	17	50	Slap		
5	M	16	Rt	Central	20	20	29	Slap		
6	F	54	Lt	Anterior	30	360	116	Ear pulling	Tympanoplasty [†]	
7	F	32	Lt	Central	30	66	63	Cotton swab	Patch [†]	
8	M	18	Lt	Central	80	62	30	Slap		
9	F	49	Lt	Central	35	23	95	Slap		
10	F	32	Lt	Posterior	25	19	56	Slap	Patch [†]	
11	M	16	Lt	Posterior	50	23	332	Slap		
12	F	50	Lt	Central	30	20	28	Cotton swab		
13	M	15	Lt	Central	40	22	28	Slap		Otorrhea
14	M	27	Lt	Central	60	22	27	Slap		
15	M	13	Lt	Central	35	24	22	Slap		
16	M	59	Lt	Central	20	300	784	Cotton swab		
17	F	38	Lt	Central	40	20	89	Slap		Otorrhea
18	M	64	Lt	Multiple	30	24	28	Slap		
19	M	45	Lt	Anterior	30	17	129	Barotrauma [§]		
20	M	22	Rt	Anterior	30	21	880	Swimming		
21	M	39	Lt	Anterior	25	365	260	Slap		
22	M	18	Lt	Anterior	30	15	62	Slap	Patch [†]	
23	M	29	Lt	Central	60	15	89	Slap		
24	F	55	Lt	Posterior	20	30	34	Slap		
25	M	38	Lt	Anterior	40	23	131	Cotton swab		
26	F	17	Rt	Posterior	40	22	106	Cotton swab		
27	F	38	Rt	Posterior	20	23	63	Cotton swab		
28	M	13	Lt	Posterior	40	22	50	Slap	Patch [†]	
29	M	15	Lt	Multiple	60	22	65	Slap		Facial nerve palsy

*the size of TMP was measured when patients underwent FCGM under microscopic guidance, [†]the patient has history of the tympanoplasty operation in another hospital, [‡]the patient has history of the paper patch procedure in another hospital, [§]barotrauma during the flight have made the TMP to the patient. TMP: tympanic membrane perforation, FCGM: fibrinogen-based collagen fleece graft myringoplasty, F: female, M: male, Rt: right, Lt: left

perforations occurred in the central position; 7 (24.1%) in the posterior position; 7 (24.1%) in the anterior position; and 2 (6.9%) in multiple positions. The average perforation area, expressed as a proportion of the entire TM, was $35.3 \pm 14.8\%$. The elapsed time between the onset of the TM perforation and the hospital visit ranged from 15 days to 12 months (57.0 ± 99.6 days).

In 19 patients (65.5%), the TM was perforated after others had slapped the face. Cotton swabs perforated the TM in a further 7 patients (24.1%), and 4 patients (13.8%) visited our hospital after failure of the paper patch procedure at another hospital.

The overall technical success rate was 100%. That is, all 29 patients showed complete healing of the TM. The complication rate was 10.3% (3 of 29 patients). Specifically, otorrhea occurred in 2 patients, but they improved without recurrence of perforation. One patient developed delayed facial palsy 1 week after the procedure, but the patient improved and no permanent facial palsy occurred. The mean follow-up period was 147.5 ± 210.9 days (28–784 days, Table 1).

When the postoperative audiological outcomes in all patients were compared with the preoperative, there was signifi-

cant difference with regard to the mean ABGs of patients ($p < 0.001$). When calculated using frequencies of 500–4,000 Hz, the mean preoperative ABG was 12.9 dB HL, whereas the mean postoperative ABG was 2.4 dB HL. Moreover, ABGs differed significantly at each frequency from 250 Hz to 4,000 Hz ($p < 0.001$) (Fig. 2). Fig. 3 shows a representative example of both PTA results and TM findings taken from one of 29 patients.

Discussion

Both the pars flaccida and the pars tensa of the TM consist of an epidermal layer, a lamina propria, and a mucosal epithelial layer. The fibrils of the fibrous layer contain a large amount of type II and type III collagens, and a small amount of type I collagen. It has been suggested that such an unusual collagen composition is the underlying reason for the unique physical features of the pars tensa of the TM [8]. TMP heals often into a thin atrophic scar which lacks the lamina propria, having only an outer epidermal layer and inner mucosal epithelial layer. This may rupture easily by external trauma, forcible inflation of the Eustachian tube and in otitis media

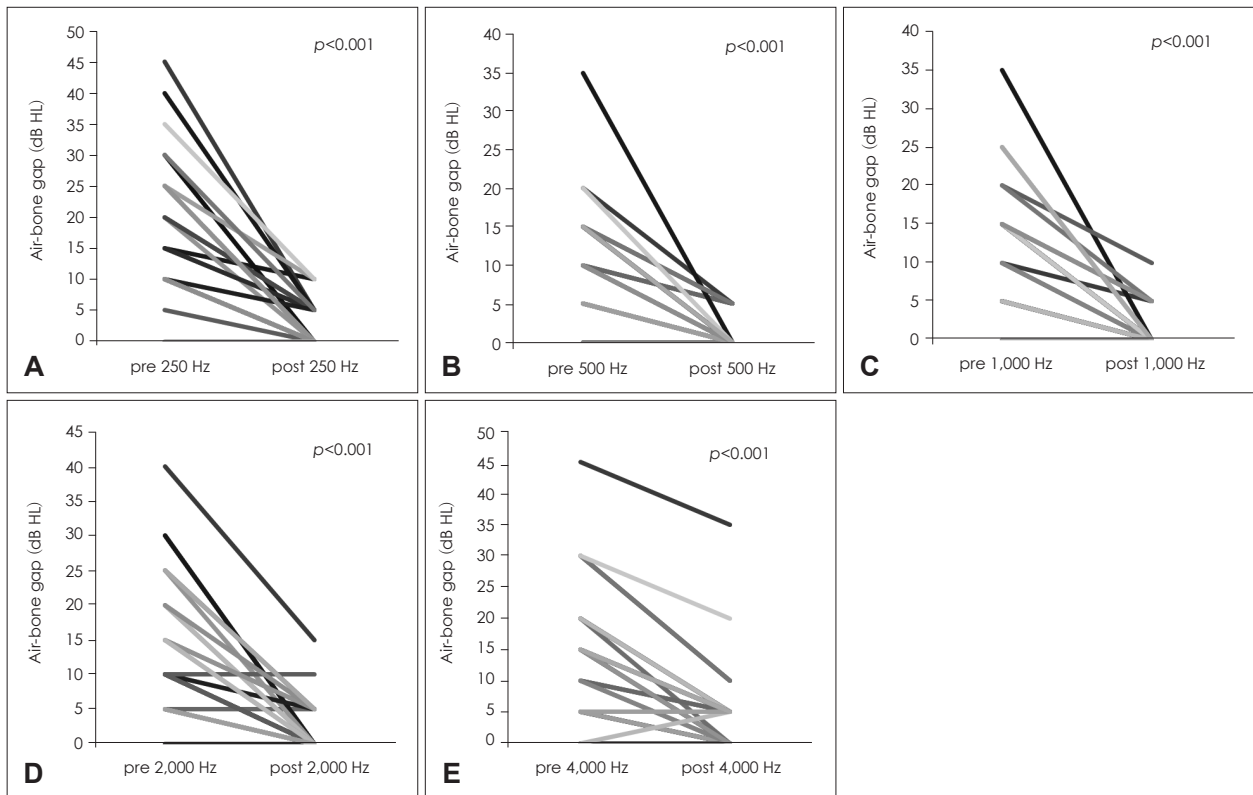


Fig. 2. The change of air-bone gap (ABG) before and after the fibrinogen-based collagen graft myringoplasty (FCGM) at each frequency. ABGs differed significantly at each frequency from 250 Hz to 4,000 Hz. Twenty-nine patients are represented by each line. A: The change of ABG before and after the FCGM at 250 Hz. B: The change of ABG before and after the FCGM at 500 Hz. C: The change of ABG before and after the FCGM at 1,000 Hz. D: The change of ABG before and after the FCGM at 2,000 Hz. E: The change of ABG before and after the FCGM at 4,000 Hz. ABG: air-bone gap, pre: preoperative, post: postoperative.

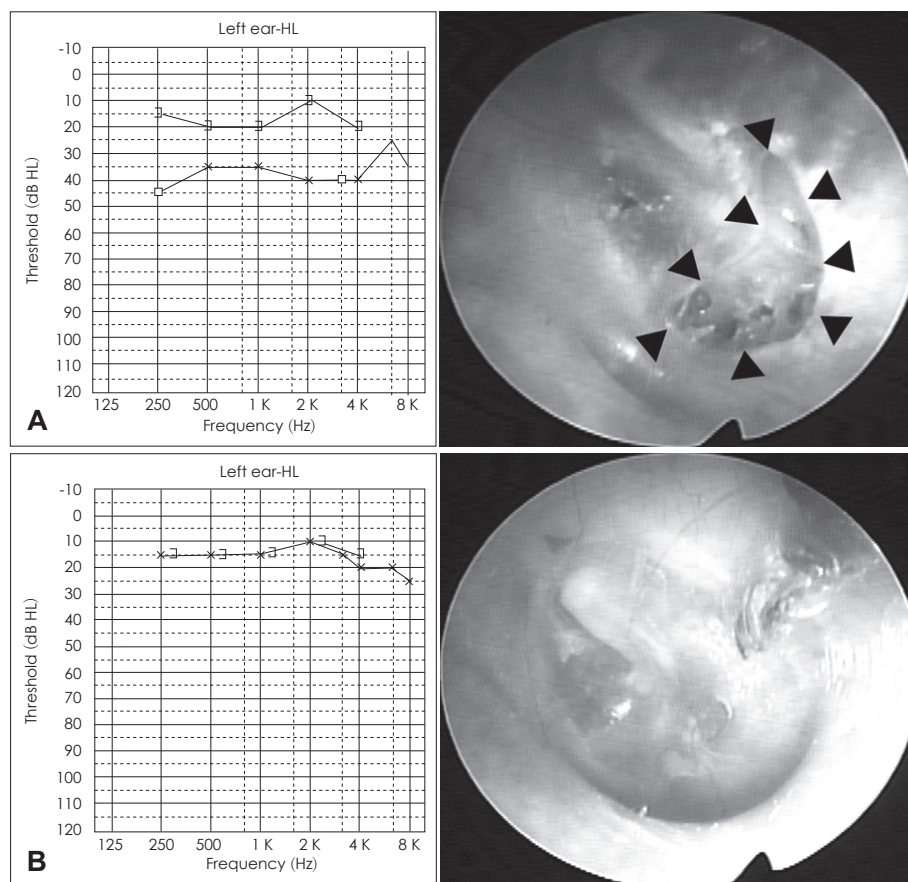


Fig. 3. The PTA results and TM findings of a patient before (A) and after (B) the FCGM. The arrowheads indicate the perforation of TM. PTA: pure tone audiometry, TM: tympanic membrane, FCGM: fibrinogen-based collagen fleece graft myringoplasty.

[9]. Histopathological study of a newly formed TMP shows proliferation of squamous epithelium within 12 hours at the edge of the perforation, granulation formation within 18 hours, while the inner mucosa of the membrane takes several days to regenerate [10]. This is one of contributing factors for a perforation to persist. The hypothesis of FCGM is that when on application, the fibrinogen-based collagen fleece may provide collagen for new tissue formation of the lamina propria and act as a splint to bridge the margins of the perforation.

Collagen type I and III are present in the acute healing phase after myringotomy and infection, and the collagen content of the TM is modified during the inflammatory and healing processes [7]. TMP is generally located in the pars tensa. Type II collagen is a main constituent of the lamina propria of the pars tensa, whereas type I collagen is mainly found in the pars flaccida. It follows that graft material in which type II collagen is abundant may more effectively treat TMP in the pars tensa than does our fibrinogen-based collagen fleece, which contains type I collagen. Unfortunately however, we were unable to find commercially-available product containing type II collagen that could be used as a graft material in myringoplasty. Instead of the material with type II collagen, the fibrinogen-based collagen fleece contain-

ing type I collagen were used for myringoplasty. The fibrinogen-based collagen fleece is at hand, manageable, and easily stored. It is well known that the commercially-available fibrinogen-based collagen fleece have very few side effects, because it have been widely used. In addition, for FCGM, clinicians need little preparation because of the commercially-available products. Furthermore, in a study involving a model of pleural defect, the fleece seemed to have had completely dissolved after 12 weeks [11].

There was no control group in this study. However, the results of FCGM are better than those of conventional myringoplasty or paper patching in the literatures (overall success rate of 88.9–90.9%) [3,12]. The audiological outcomes of paper patching procedure showed the mean preoperative ABG of 23.6 dB HL, whereas the mean postoperative ABG of 1 dB HL [3]. In addition, the overall success rates of “no therapy” are lower than 80% in previous studies [3,12-14]. Those patients with no therapy showed a preoperative ABG was 26.1 dB HL, whereas the mean postoperative ABG was 5 dB HL [3]. Some studies of patch materials to treat the TMP are listed in Table 2 [3,15-20].

In the follow-up visit, facial palsy (grade IV according to House-Brackmann facial nerve grading system) occurred in

Table 2. Studies of patch materials for TMP treatment

Author, year	Country	Model	TMP duration	Cause of TMP	Patch material (patients number)	Control group	Assessment methods	Result
Lee, et al., 2008 ¹⁵⁾	South Korea	Human	Chronic	COM	Paper patch after trimming with CO2 laser (90)	None	Endoscopy, audiometry	Healing rate (%): 52.2 Improvement of ABG in all the cases where the TM healed to normal status
Hakuba, et al., 2010 ¹⁶⁾	Japan	Human	Chronic	COM	Silicone film with bFGF and atelocollagen (87)	None	Endoscopy, audiometry	Healing rate (%): 92 Hearing threshold improvement by 10 dB or more in 51 patients, 13.4 dB HL of average hearing improvement
Lou and He, 2011 ¹⁷⁾	China	Human	Acute, ≤ 3 days	Trauma	Gelfoam patch (30), Perforation edge-approximation with gelfoam patch (30)	No treatment	Endoscopy, healing time, infection rate	Healing rate (%): 97, 97 (study groups), 85 (control group) (p>0.05) Healing time (days): 16 ± 5.6, 18 ± 4.7 (study groups) & 30 ± 10.1 (control group) (p<0.05) Infection rate (%): 3, 3 (study groups), 7 (control group)
Saliba and Woods, 2011 ¹⁸⁾	Canada	Human	Chronic, > 6 months	COM	Hyaluronic acid fat graft myringoplasty (131)	Underlay technique with TF/TP, overlay technique with TF/TP	Endoscopy, audiometry	Healing rate (%): 92.7 (study groups), 92.2 & 92.6 (control groups) (p>0.05) ABG (dB HL): clinically and statistically significant improvement in hyaluronic acid fat graft myringoplasty
Araujo, et al., 2012 ¹⁹⁾	Brazil	Human	Chronic	COM	Myringoplasty with polylysine latex biomembrane (39)	Myringoplasty only, myringoplasty with silicone film	Endoscopy, audiometry	Healing rate (%): 74.4 (study group), 70 & 57.1 (control groups) (p>0.05) Vascularization: significantly greater in myringoplasty with polylysine latex biomembrane ABG (dB HL): 23.5 → 12.9* (study group), 25.2 → 11.9* & 28.5 → 10.1* (control groups) (p>0.05)
Jun, et al., 2014 ²⁰⁾	South Korea	Human	Acute, ≤ 3 months	Trauma	Egg shell membrane (39)	Perforation edge-approximation	Endoscopy, healing time	Healing rate (%): 92.3 (study group), 89.7 (control group) (p=0.74) Healing time (days): 42.8 ± 19.8 (study group), 87.2 ± 41.3 (control group) (p=0.02)
Simsek and Akin, 2014 ²¹⁾	Turkey	Human	Acute, ≤ 10 days	Trauma	Paper patch (33)	No treatment	Endoscopy, audiometry	Healing rate (%): 90.9 (study group), 76.7 (control group) (p>0.05) ABG (dB HL): 23.6 → 1* (study group), 26.1 → 5* (control group) (p<0.001)
Present study	South Korea	Human	Acute & chronic, > 14 days	Trauma	Fibrinogen-based collagen fleece (29)	None P"	Endoscopy, audiometry	Healing rate (%): 100 ABG (dB HL): 12.9 → 2.4*

*preoperative average ABG → postoperative average ABG. TMP: tympanic membrane perforation, COM: chronic otitis media, ABG: air-bone gap, TM: tympanic membrane, TF: temporalis fascia, TP: tragal perichondrium, bFGF: basic fibroblast growth factor

a patient 15 days after FCGM. Methylprednisolone was prescribed for 2 weeks and the patient recovered completely. Two patients had otorrhea after myringoplasty. Bacterial culture of otorrhea showed no growth, and otorrhea disappeared after using oral antibiotics (levofloxacin 250 mg twice a day) in both patients.

The main conclusion of this study is that FCGM may be a viable treatment option in cases of traumatic TMP. However, based on our results, we cannot say that the same procedure may be useful in cases of chronic otitis media. In a recent trial investigating the treatment of chronic and dry TMP, hyaluronic acid fat graft myringoplasty (HAFGM) was an effective technique for TMP treatment. The success rate of HAFGM in this trial was comparable to that of both the underlay and the overlay techniques [18]. However, it was necessary to locally anesthetize via injection and to make an incision in order to harvest fat. In the present study, patients whose perforation had persisted for more than 60 days, or had recurred in spite of the paper patch procedure, showed remarkable improvement. In addition, EAC incisions or injections were not necessary for the procedure, which is simpler and less painful than the HAFGM. We are currently attempting to treat patients with chronic otitis media with dry TMP using FCGM.

In this study, we found that FCGM may be an effective treatment option in traumatic TMP. The postoperative ABG differed significantly from the preoperative. Furthermore, the technique requires no hospitalization, and can be used to avoid traditional tympanoplasty.

Acknowledgments

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Conflicts of interest

The authors have no financial conflicts of interest.

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