Original Article

Impact of Titanium-Prepared Platelet-Rich Fibrin in Type 1 Fascia Graft Tympanoplasty on Graft Survival and Hearing Outcomes

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Abstract

Background: Type 1 fascia graft tympanoplasty (T1FGT) is the mainstay surgical approach for the treatment of tympanic membrane perforations. The most widely used graft material is temporal muscle fascia, and graft take rates are reported differently. The methods to enhance graft take are still being investigated. **Aim:** The aim of our study was to investigate the effect of titanium-prepared platelet-rich fibrin (T-PRF) on graft take and hearing outcomes in T1FGT. **Materials and Methods:** Fifty-seven ears eligible for T1FGT were involved in the study and prospectively evaluated. T-PRF was applied with T1FGT in 27 ears. Thirty ears in the other group underwent only T1FGT. The patients underwent an otomicroscopic and audiometric examination in preoperative and postoperative 2nd week, 1st month, and 6th month. Both groups were evaluated in terms of hearing levels, infection, and graft take rates. **Results:** Two patients in the T1FGT + T-PRF group and seven patients in the T1FGT group had postoperative perforation (graft take rate: 92.6% versus 76.7%). The graft take rate was found to be increased in the T-PRF group although the difference was not statistically significant. In the T1FGT group, the percentage of infection was higher than in the T1FGT + T-PRF group. When the preoperative and postoperative 6th-month audiometry was compared, a statistically significant hearing gain was obtained for both groups. **Conclusion:** In the treatment of tympanic membrane perforations, T-PRF applied over the fascia graft was shown to increase graft take rates and decrease the probability of infection. Further studies with larger samples are needed to demonstrate the effects of PRF.

Keywords: *Chronic otitis media, platelet-rich fibrin, temporal muscle fascia, titanium, type 1 tympanoplasty*

Introduction

Chronic suppurative otitis media (CSOM) is a chronic inflammation of the middle ear and mastoid mucosa, characterized by tympanic membrane perforation, ear discharge, and hearing loss.[1] The aims of surgical treatment are to prevent recurrent infections and improve hearing by closing the tympanic membrane perforation.[2] Treatment failures necessitate repeated surgeries, which increase morbidity and cost. Additional costs can be avoided by reducing repetitive surgeries.

To increase the success rate of tympanoplasty, there is a need to investigate methods to promote the healing of the tympanic membrane. It is thought that platelet concentrations would accelerate wound healing and increase the success rates in repairing tympanic membrane perforations because of its ingredients, such as growth factors and cytokines.[2-4]

Platelet-rich fibrin (PRF) was first described in 2001 and PRF is often referred as second-generation platelet-rich plasma (PRP).[5,6] In 2006, Dohan *et al*. made a detailed biochemical analysis of PRF. They reported that PRF is surrounded by a polymerized fibrin network, containing

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cytokines, glycolic chains, and structural glycoproteins. In addition to a high platelet concentration, PRF contains various growth factors.[7-9] PRF also contains white blood cells, phagocytic cells, vasoactive amines, and chemotactic agents with high fibrinogen concentration. These biochemical components have a well-known synergistic effect on the healing process.[7-9] Unlike other studies, we prepared the PRF in a titanium-coated tube [Figure 1]. We provided tighter fibrin network formation with the effect of titanium in the form of platelet-rich fibrin prepared in the titanium-coated tube (T-PRF).

In light of this information, we investigated the effects of T-PRF on graft take success in tympanic membrane perforations repaired with temporal muscle fascia graft. In this way, we predict that morbidity and additional costs caused by repetitive surgeries and drug treatments can be prevented by increasing the graft take rates in tympanoplasty.

Material Methods

The research was carried out at the Department of Otolaryngology-Head and Neck Surgery with the approval of the Scientific Research Local Ethics Committee with the protocol number 2017/0207. This study was carried out between July 2017 and August 2018. Fifty-seven ears of 55 patients who underwent type 1 fascia graft tympanoplasty (T1FGT) with CSOM diagnosis were included. The patients were randomized and divided into two groups. T1FGT was performed with T-PRF in 27 ears, and T1FGT was performed without T-PRF in 30 ears in the control group. All patients were informed about the purpose of surgical treatment and possible complications before the operation, and their informed consent was obtained. Runny ears that have not been provided with a dry period for at least 3 months, adhesive otitis, ears with an air–bone gap (ABG) of 40 dB and above those considered as having ossicular chain pathology, patients under 15 years and older than 65 years of age, patients with osseous chain movement restriction or damaged ossicular chain, patients with cholesteatoma, and patients with systemic diseases, such as diabetes, which decrease recovery, were excluded.

Preoperative patient histories of each patient were taken, and a detailed physical examination was performed for each patient in terms of otolaryngology. First, in the preoperative stage, pathologies, such as septum deviation, adenoid vegetation, and nasal polyp, which cause upper respiratory tract obstruction, and chronic allergic bacterial rhinosinusitis, which may be a source of infection, were treated medically and surgically. These patients were excluded from the study.

Audiological measurements

Audiometric measurements of all patients were made before the operation and in the first and sixth months after the operation in a soundproofed cabin in the audiovestibular unit of our clinic. The Interacoustics AD629 (Interacoustics A/S Audiometer, Denmark) device was used. Air pathway and bone pathway hearing thresholds were recorded at frequencies of 500, 1000, 2000, and 4000 Hz. Preoperative and postoperative 6th-month results were evaluated and compared.

Preparation of the T-PRF

At the beginning of the operation, 10 cc of venous blood was collected into two titanium-coated tubes without any additives. They were centrifuged at 3000 RPM for 15 minutes. After centrifugation, the blood samples were divided into three layers. Red blood cells were accumulated in the lower layer, platelet-poor plasma in the top layer, and PRF in the middle layer. The PRF layer was removed and pressed [Figure 2].

In the first group, after fascia grafting was applied to 27 ears, pressed T-PRF was laid on the fascia graft as a double layer [Figure 3]. It was supported with absorbable gelatin sponges, and one ear wick tampon was placed in the external ear canal. In the second group, T1FGT was performed in 30 ears by laying the temporal muscle fascia as an over-underlay technique. It was supported with absorbable gelatin sponges without T-PRF, and one ear wick tampon was placed in the external ear canal.

Statistical analysis

SPSS 16 (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0, Chicago, SPSS Inc.) program was used for statistical analysis. The suitability of all interval parameters to parametric distribution was evaluated by the Shapiro–Wilk analysis. The nominal/interval data were compared using the Chi-square test, Wilcoxon signed-rank test, and Mann–Whitney U-test, which were used for continuous variables. A $P < 0.05$ value was considered statistically significant.

Results

It was seen that all interval parameters were distributed nonparametrically. 54.4% (n = 31) of the patients included in the study were male, and 45.6% (n = 26) were female. The median age of all patients was found to be 30.91 ± 14.13 years (between 15 and 61 years). The demographic characteristics of the cases are shown in Table 1. When the two groups were compared, there was no statistically significant difference between the gender and age distributions and the operation sides [Table 1].

In preoperative automicroscopic examination, tympanic membrane perforations were divided into

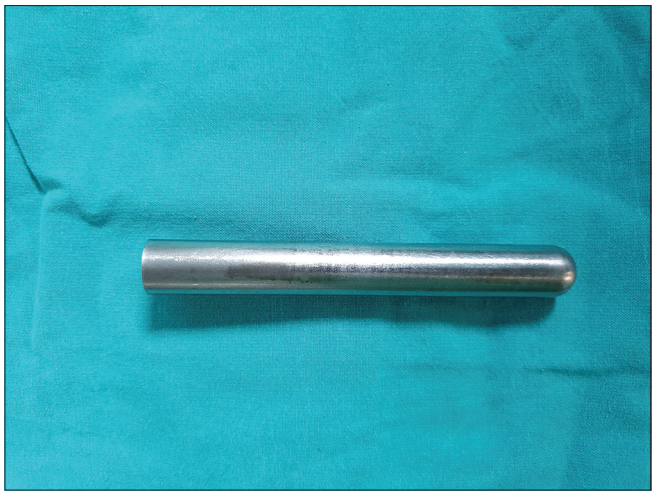

Figure 1: Titanium-coated tube

Figure 2: Pressed platelet-rich fibrin

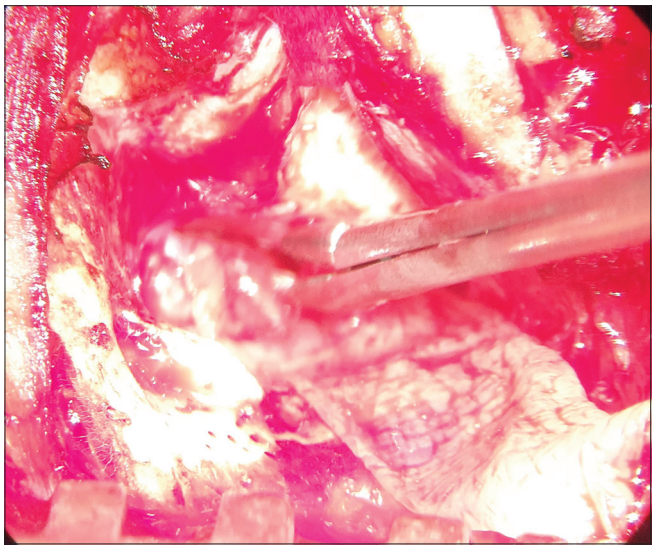

Figure 3: Application of platelet-rich fibrin

three groups: anterior (n = 8), posterior (n = 11), and malleolar central (n = 38) perforations.

Table 1: Demographic data and operation sides of groups

	T1FGT with T-PRF		T1FGT alone		*P*
	n	%	*n*	%	
Sex					
Female	11	40,75%	15	50%	0.483*
Male	16	59,25%	15	50%	
Mean age	31.67±14.00		30.23±14.69		0.708**
Age range	15.0–61.0		15.0–59.0		
Operation side					
Right	10	37%	13	43.33%	0.629*
Left	17	63%	17	56.67%	

T1FGT: 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin. *: Chi-square test. **: Mann–Whitney U-test

Table 2: Preoperative and postoperative 6th-month tympanic membrane status

Grade	Preoperative		Postoperative 6th month		*P*
	n	%	*n*	%	
T-PRF + T1FGT					
Intact	0	%0.0	25	%92.59	**$P<0.001$
1	0	%0.0	1	%3.70	
2	9	%33.33	1	%3.70	
3	17	%62.96	0	%0.0	
4	1	%3.70	0	%0.0	
T1FGT alone					
Intact	0	%0.0	23	%76.67	**$P<0.001$
1	2	%6.67	2	%6.67	
2	13	%43.33	3	%10.0	
3	13	%43.33	2	%6.67	
4	2	%6.67	0	%0.0	
	*P=0.237		*P=0.165		

T1FGT: Type 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin. **: Preoperative and postoperative membrane perforation sizes, Wilcoxon signed-rank test. : Differences between groups, Mann–Whitney U-test

Table 3: Postoperative graft take and infection rates

Graft status	T-PRF + T1FGT		T1FGT alone		*P*
	n	%	*n*	%	
Intact	25	%92.6	23	%76.7	0.149*
Perforation	2	%7.4	7	%23.3	
Infection					
Yes	1	%3.7	5	%16.7	0.197*
No	26	%96.3	25	%83.3	

T1FGT: Type 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin. *Fisher's exact test

The effect of preoperative perforation site on postoperative graft take rates was investigated in all patients regardless of the use of T-PRF. The postoperative 6th-month graft take rate of the ears with preoperative anterior perforation (62.5%) was lower than posterior and malleolar central perforations (%81.8 and %89.5, respectively).

Table 4: Postoperative 6th-month air–bone gap

	T-PRF + T1FGT (*n*(%))		T1FGT alone (*n*(%))		AAO-HNS scale
0–10 dB	6	% 22.22	7	% 23.33	Class A
11–20 dB	19	%70.37	18	%60.0	Class B
21–30 dB	2	%7.41	5	%16.67	Class C
31–40 dB	0	%0.0	0	%0.0	Class D
Mean±SD	13.48±3.96 dB		14.87±5.01 dB		*P=0.255

T1FGT: Type 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin. AAO-HNS scale: Hearing evaluation scale of the American Academy of Otorhinolaryngology-Head and Neck Surgery. *: Mann–Whitney U-test

Table 5: Preoperative and postoperative 6th-month air–bone gap gain

ABG (dB)	T-PRF + T1FGT (*n*(%))		T1FGT alone (*n*(%))		*P*
0–9 dB	10	% 37.03	14	% 46.67	
10–19 dB	15	%55.55	15	%50.0	
>10 dB	17	%62.96	16	%53.33	
>20 dB	2	%7.41	1	%3.33	
Mean±SD	11.11±5.12 dB		8.10±6.75 dB		*P=0.065

T1FGT: Type 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin, ABG: Air–bone gap. *: Mann–Whitney U-test

Table 6: Audiogram mean values of all patients

	T-PRF + T1FGT	T1FGT alone	*P*
Preoperative air conduction thresholds/bone conduction thresholds	32.89±14.89 dB/ 8.30±10.28 dB	31.57±10.66 dB/ 8.60±7.06 dB	*P=0.699/ P=0.896
Preoperative ABG	24.59±5.59 dB	22.97±6.09 dB	*P=0.300
1st-month air conduction thresholds/bone conduction thresholds	20.89±8.82 dB/ 5.74±7.03 dB	25.43±10.90 dB/ 7.70±6.56 dB	*P=0.091/ P=0.281
1st-month ABG	15.15±4.04 dB	17.73±7.46 dB	*P=0.115
6th-month air conduction thresholds/bone conduction thresholds	18.85±9.43 dB/ 5.37±7.37 dB	21.83±9.00 dB/ 6.97±6.26 dB	*P=0.277/ P=0.380
6th-month ABG	13.48±3.96 dB	14.87±5.01 dB	*P=0.255

T1FGT: Type 1 fascia graft tympanoplasty, T-PRF: Titanium-prepared platelet-rich fibrin, ABG: Air–bone gap. *: Mann–Whitney U-test

The preoperative perforation sizes of the ears were divided into four groups according to Saliba's perforation classification: 0%–25% = grade 1, 25%–50% = grade 2, 50%–75% = grade 3, and 75%–100% = grade 4.[10] There was no statistically significant difference between the groups with and without T-PRF in terms of preoperative perforation size and postoperative graft status (P = 0.237 and P = 0.165, Table 2). It was observed that the tympanic membrane perforation of both groups closed significantly at the postoperative 6th-month control (P < 0.001, Table 2). When all patients were examined, it was seen that the grafts of nine patients did not retain. It was observed that seven of these nine patients had perforations greater than 50% (grades 3–4) preoperatively. No statistically significant difference was detected, but it was observed that the graft take rate was lower in perforations larger than 50% (graft take rate in grade 1–2 perforations = 91.7%, graft take rate in grade 3–4 perforations = 78.8%).

It was observed that grafts were not retained in two of 27 ears (7.4%) with T1FGT + T-PRF and seven of 30 ears (23.3%) with T1FGT only. Although graft take rates were different from each other, there was no statistically significant difference between the groups (Table 3, P = 0.149). The infection finding was found in the first month after the operation was evaluated as a postoperative infection. Postoperative infection was observed in one of 27 ears that underwent T1FGT + T-PRF and in five of 30 ears with T1FGT only. There was no statistically significant difference between the two groups (P = 0.197), but it was observed that the infection rate decreased with the T-PRF (3.7% -16.7%, Table 3).

Preoperative and postoperative 1st-month and 6th-month pure tone audiometry was performed. The mean of air and bone pathway thresholds and ABG at 500, 1000, 2000, and 4000 Hz frequencies were compared. There was no statistically significant difference in all audiometry values between the groups with and without T-PRF. The mean 6th-month pure sound ABG was 13.48 ± 3.96 dB in the T1FGT+T-PRF group and 14.87 ± 5.01 dB in the T1FGT-only group [Table 4].

The difference between ABG values in the preoperative and postoperative 6th-month audiograms was calculated, and the gain in ABG was found. The gain was found as 11.11 ± 5.12 dB in the T1FGT+T-PRF group and 8.10 ± 6.75 dB in the T1FGT-only group [Table 5]. When the two groups were compared, there was no statistically significant difference. However, the P value was found to be so close to the limit of significance (P = 0.065). More than 10 dB improvement was observed in the postoperative ABG value in 17 of 27 patients (62.96%) who underwent T1FGT+T-PRF. In 16 of 30 patients (53.33%) who underwent T1FGT alone, more than 10 dB improvement was observed in postoperative ABG [Table 5]. All values are shown in Table 6.

Discussion

Temporal muscle fascia has been the most used graft material for many years in tympanoplasty surgery.[11]

Variable results regarding the success rates of T1FGT have been reported.[3] Since T-PRF is obtained from the patient's own blood and does not contain any additives, it does not carry the risk of infectious disease and has no allergic properties. It is easy to obtain and low in cost. Its usage in otolaryngology operations has been increasing in recent years. Stavrakas *et al.*[12] examined 11 studies on the use of PRP in otorhinolaryngology surgery and stated that PRP is promising and that more studies should be carried out. In addition to the graft material, there are also studies reporting that it is used with an enhancing and accelerating effect and higher success rates in eardrum perforation repairs.[2,3,5]

Different results have been reported on perforation location and success rates. In a study, it was shown that the rate of graft take of anterior perforations was 34%; inferior and posterior perforations were 91 to 100%, respectively.[13] In anterior perforations, the failure of the graft to be supported by sponges in the anterior mesotympanum causes the graft to detach from the membrane residue and decrease the graft take rate of the anterior perforations. In our study, statistical analysis could not be performed to evaluate the rate of graft take at the perforation site since the distribution of patients was not sufficient. However, anterior perforations were found to have lower graft take rates. In addition, when the perforation areas and graft take rates were examined according to the groups, although the number of preoperative anterior perforations was higher in the T1FGT+T-PRF group, postoperative graft take rates were better.

In a study, it was found that the rate of graft take was lower in perforations with more than half of the membrane surface.[14] In another study, it was stated that graft take success was higher in perforations less than half of the membrane surface.[15] Although there was no statistically significant difference in our study, it was observed that the rate of graft take was lower in perforations greater than 50%.

In the literature, there are experimental and clinical studies showing that PRF increases graft take rates in tympanoplasty. Considering that PRF contains components that accelerate healing, it can be expected to increase graft take rates. The efficacy of PRP products has been demonstrated in experimental animal studies in which tympanic membrane perforation models are created. Erkilet *et al.*[4] suggested that PRP was effective in accelerating the healing of membrane perforation in rats. In another study, in the tympanic membrane perforations created experimentally in rats, the mean recovery time was 10.3 days in the group in which PRF was used and 17.0 days in the group that was left to spontaneous recovery. It has been shown that PRF significantly accelerates the recovery of tympanic membrane perforation.[16]

The effectiveness of PRF has been demonstrated in tympanic membrane repairs performed with graft materials other than temporal muscle fascia.[3,17] El-Anwar *et al.*[3] performed a study, PRF + type 1 tympanoplasty using the perichondrium of the conchal cartilage. Graft take rates were found to be 100% and 81.25% in the groups with and without PRF, respectively, and a statistically significant difference was shown. Hosam *et al.*[17] performed inlay butterfly myringoplasty with central perforations. In the groups that used PRF and not used it, they found the rate of graft take to be 96% and 76%, respectively.

In the literature, there are clinical studies showing that PRF application in addition to fascia graft tympanoplasty statistically increases the graft take rates.[3,5,18] Gökçe Kütük *et al.*[2] performed T1FGT with PRF and T1FGT only. At the end of 6 months, graft take rates were found to be 94.4% and 74.5%, respectively, and a statistically significant difference was observed. Gopalakrishnan *et al.*[5] used PRF who underwent tympanoplasty. Graft take rates were found to be 96% in the tympanoplasty + PRF group and 80% in the tympanoplasty group, and the difference was statistically significant.[5] In a study, Nair *et al.*[18] used PRF with fascia myringoplasty and only fascia myringoplasty. After 3 months, the rate of graft take in the group with PRF was 97.7% and 81% in the other group and there was a statistically significant difference. In addition, in a study on PRF use in myringoplasty, the surgical success rates in patients with and without PRF were 96% and 85%, respectively.[19] In these studies, the PRF prepared in plastic tubes was laid on the graft by the onlay technique. Graft take rates were found to be statistically significantly higher in the PRF groups.

In our study, although there was no statistically significant difference in graft take rates between the groups with and without T-PRF, the rate of graft take was higher in the T-PRF group. The *P* value was observed close to the significance limit. It was thought that this may be due to the small sample size, and T-PRF increased the graft take rates, as in other studies.

There are authors stating that the success of graft take in tympanoplasty operations has decreased because of graft necrosis due to postoperative infections.[11] Since the temporal muscle fascia is transparent, thin, and structurally more similar to the tympanic membrane, various studies have reported that it provides better hearing gain when compared with cartilage

grafts.[11] However, due to its thin structure, it is thought that the fascia is more prone to atrophy and is more easily necrotic with infections.[20] Therefore, it is more important to reduce the infection rate in tympanoplasty performed with temporal muscle fascia.

In a study conducted by El-Anwar *et al*.,[3] no postoperative infection was observed in the group in which PRP was used, but the postoperative infection was observed in four patients in the control group, and a statistically significant difference was found between the two groups. Nair *et al*.[18] observed no postoperative infection in patients who underwent fascia myringoplasty with PRF, while 12.9% of patients had a postoperative infection in the group without PRF and found a statistically significant difference. In our study, although it was not statistically significant, the rate of infection was found to be low in the T-PRF group. These data suggest that T-PRF can also be protective against infection.

In our study, no statistically significant difference was found in hearing values between the patient groups with and without T-PRF. Postoperative 6th-month ABG averages were evaluated according to the hearing evaluation scale of the American Academy of Otorhinolaryngology-Head and Neck Surgery. The values between 0 and 10 dB were accepted as "class A—excellent" and between 11–20 dB as "class B—successful."[21] Accordingly, 92.59% operation success (class A+B) was observed in the T1FGT + T-PRF group and 83.33% in the T1FGT alone group [Table 4].

In addition, the hearing gain was calculated by the ABG difference between the preoperative and postoperative 6th month. In the T-PRF group, 17 patients (62.96%) had a hearing gain of 10 dB or more. In the group where only T1FGT was applied, 16 (53.33%) patients had hearing gain of 10 dB or more. Although there was no statistically significant difference between the two groups, the better hearing gain was achieved in the T-PRF group due to a higher graft take rate.

El-Anwar *et al*.[3] obtained better postoperative ABG values with the use of PRF in their study. They accepted the change of 10 dB and above in ABG as hearing gain. They achieved hearing gain in 65.6% of the perichondrium myringoplasty+PRF group and 40.6% of the perichondrium myringoplasty alone group. There was no statistically significant difference between the two groups.

Kütük *et al*.[2] compared the patient groups with and without PRF, and they found no statistically significant difference in 0.5, 1, 2, and 4 kHz frequency-specific hearing results. In another study, 108 patients who used PRP in middle ear surgery were examined retrospectively and at least 10 dB improvement was observed at 1–2 and 4 kHz in 93.8% of patients one year after surgery.[22]

In our study, titanium-coated tubes were used instead of silica tubes. Thanks to the effect of titanium on platelet activation, a tighter fibrin structure is formed. As a result, the resorption time of T-PRF is prolonged.[23] However, many clinicians use silica-coated plastic tubes to prepare the PRF. These silica-coated tubes are approved for diagnostic use only. Many manufacturers warn about the use of silica-coated plastic tubes in the preparation of PRF. It is stated that the prepared fibrin is contaminated with silica and that the silica has side effects, such as cytotoxicity, mutagenicity, skin irritation, and hemolysis.[24-26] Also, there are studies indicating that silica has cytotoxic effects and has the possibility of adversely affecting tissue regeneration through inflammation induction.[25] In addition, there is clear evidence that silica microparticles obtained from blood collection tubes induce apoptosis and have toxic effects on human periosteal cells, and silica completely impairs cell growth and viability.[24,25]

We believe that the effectiveness of T-PRF can be demonstrated more clearly in studies conducted with more patients. We anticipate that the use of this material in the repair of tympanic membrane perforation will become more widespread in the future and may be used in different areas because of its contribution to wound healing.

In conclusion, the use of T-PRF in type 1 tympanoplasty performed with temporal muscle fascia can potentially increase the rate of graft take. We think that the effectiveness of T-PRF can be demonstrated more clearly in studies with larger samples. We anticipate that the use of this material in the repair of tympanic membrane perforation will become more widespread in the future and may be used in different areas because of its contribution to wound healing.

Ethics approval

This retrospective study was conducted according to the World Medical Association Declaration of Helsinki and was approved by the ethical committee of Karadeniz Technical University (2017/0207).

Consent to participate

Written informed consent was obtained.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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