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Original Article

A Comparative Study: Platelet-Rich Fibrin Packing as an Alternative to the Absorbable Gelatine in Tympanoplasty

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BACKGROUND: We aimed to investigate platelet-rich fibrin's potential role as packing material in both the middle ear and external auditory canal.

METHODS: Twenty-nine patients undergoing transcanal endoscopic type 1 cartilage tympanoplasty were included in this controlled prospective clinical study. Patients were randomly assigned to platelet-rich fibrin (n = 14) or absorbable gelatine (n = 15) groups. Preoperative and postoperative pure-tone audiometry results, graft healing rates, tympanometry values, and Glasgow Benefit Inventory scores were compared.

RESULTS: No significant postoperative complications were observed and the graft intake rate was 100% in both groups. Mean air-bone gap gain was 9.82 ± 4 dB HL in the postoperative first month and 10.08 ± 4.91 dB HL in the sixth postoperative month in the platelet-rich fibrin group. There was no statistically significant difference between the postoperative air-bone gap gains of the groups in the first ($P = .537$) and sixth month ($P = .723$) controls. There was no statistically significant difference in compliance ($P = .453$) between groups. The physical benefit scores of the Glasgow Benefit Inventory were significantly higher in the platelet-rich fibrin group ($P = .01$). There was no difference in general and social benefit scores ($P > .05$).

CONCLUSION: As a middle and external auditory canal packing agent, platelet-rich fibrin was as successful as absorbable gelatine in transcanal endoscopic cartilage tympanoplasty with similar functional results and graft healing rate.

KEYWORDS: Cartilage, endoscopic tympanoplasty, gelfoam, platelet-rich fibrin

INTRODUCTION

Reconstruction of the perforated tympanic membrane (TM) with a graft is the tympanoplasty procedure's primary purpose. The healthy middle ear without chronic inflammation and infection can only be achieved with a totally healed TM. The contact between the TM residue and the graft is an essential condition for healthy epithelization and healing. Antibiotic ointments and absorbable gelatine are used in the external auditory canal (EAC) to provide a healthy medium for epithelialization and contact between the graft and TM remnant. Also, absorbable gelatine buffers are commonly used in the middle ear to prevent grafts' medialization.[1]

More than a decade ago, Dohan et al introduced platelet-rich fibrin (PRF), which is a second-generation autologous platelet concentrate that induces soft tissue regeneration and wound healing.[2] Platelet-rich fibrin contains a polymerized natural fibrin matrix and acts like favorable physiologic architecture in open cavities and induces micro vascularization and epithelial cell migration.[3] In recent years, PRF and another platelet concentrate platelet-rich plasma (PRP) have been commonly used in many treatment procedures.

The positive effects of the autologous platelet concentrate on tissue healing is a well-known entity. Erkilet et al[4] reported that the PRP accelerates tympanic membrane perforation healing in rats.[4] Recently, Ozgursoy et al[5] published a similar article that shows

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the positive effects of the PRP in the healing process of the acute TM perforations in a rabbit model. Nowadays, the use of PRP and PRF is a hot topic in otology. Many recent studies reported better functional and surgical results in tympanoplasty with the use of PRP and PRF.[6-8] Plasma-derived platelet-rich biomaterials have encouraging results in tympanoplasty, and we believe that they can be an alternative to non-autologous materials. So, controlled clinical studies are mandatory to conclude their potential roles in otology.

This study aimed to assess the use of PRF as a packing agent in both the middle ear and EAC. Our primary aim was to investigate PRF buffers' effect on healing in the patients diagnosed with subtotal or total TM perforation and who underwent type 1 tympanoplasty. We also planned to investigate the PRF's potential benefits on the functional, surgical, and overall health-related outcomes with a comparison with gelatine sponges.

METHODS

This study was designed as a randomized controlled prospective study and was conducted between February 2018 and March 2019 at a tertiary academic center. All procedures that we performed in the study were in concordance with the institutional and/or national research committee's ethical standards and the Declaration of Helsinki in 1964 and its subsequent amendments or comparable ethical standards. The ethics committee approval was received for this study from the Ege University Ethical Committee (IRB No: 20-11.1T/12). We obtained written informed consent for both surgical procedures and study participation from all of the participants in the study. Ethical approval was obtained from the ethical committee in September 2020 (IRB No: 20-11.1T/12).

Twenty-nine patients diagnosed with total undergoing transcanal endoscopic type 1 cartilage tympanoplasty were included. Patients with PRF (n = 14) (PRF group) and absorbable gelatine (n = 15) (control group) were randomly divided into 2 groups. Randomization was sequential in a one-by-one manner. Selection criteria were subtotal/or total TM perforation with a history of at least 1 year, the presence of intact ossicular chain, the absence of clinically or radiologically demonstrated cholesteatoma, and no evidence of purulent discharge at the time of surgery. All of the data were prospectively collected. These included demographic data, date of the surgery, preoperative and postoperative first and sixth-month pure-tone audiometry (PTA) results, first-month tympanometry values, type of the packing material, graft healing success, and first-month subjective health status scores.

Standard PTA (InteracousticVR AC-40, Middelfart, Denmark, headphone: TDH39) was measured before surgery and pre- and postoperative PTA thresholds at 0.5, 1, 2, and 4 kHz were noted. Here, 226 Hz standard tympanometry was performed on the patients who had complete graft healing in the first-month control, and air volume and compliance values of the 2 groups were noted and compared.

Glasgow Benefit Inventory (GBI) was used to assess the overall health benefit at the first-month control. The GBI consists of an 18-item questionnaire. Patients answered the questions using a 5-point Likert scale that asks directly about the change in health status resulting from an intervention. Twelve questions show general health status changes, the next 3 questions are related to social support, and the remaining 3 questions address changes in the physical health status.[9]

The same senior surgeon performed all operations. All patients were primary cases, and transcanal cartilage type 1 tympanoplasty was performed on all patients. Selection criteria were TM perforations with a history of at least 1 year, the presence of intact ossicular chain in the perioperative evaluation, the absence of clinically or radiologically demonstrated cholesteatoma and pathological middle ear mucosa, no evidence of inflammation or infection at the time of surgery, and the absence of smoking. The PRF and absorbable gelatine sponges were removed from EAC during the first postoperative week in both groups.

Instrumentation and Procedure

A high definition monitor and camera (Karl StorzVR®, Germany) were used, and videos were recorded on a computer hard disc. Xenon light source (Karl Storz® Xenon. Nova 175, Tuttlingen, Germany) and a 4-mm (18 cm length) Hopkins-rod lens rigid 0° endoscope (Karl Storz® Endoscopes, Tuttlingen, Germany) were used during the procedures. We performed an over-underlay cartilage tympanoplasty procedure for both groups. First, the margins of the TM perforation were freshened. Then, an anteriorly based tympanomeatal flap and the annulus were raised. Tympanomeatal flap was elevated and TM remnant was dissected from malleus handle. The graft was placed using the over-underlay technique, lateral to the handle of the malleus and medial to the tympanic membrane and annulus. One piece of tragal-perichondrial single island cartilage graft was used and thinned to 0.2-0.5 mm with a Storz® cartilage cutting device.

In the PRF group, we used PRF for both EAC and middle ear packing. We performed the PRF protocol that was defined by Choukroun et al.[2] A venous blood sample was taken during operation in 10-mL sterile tubes without anticoagulant, which was immediately centrifuged at 3000 rpm (approximately 400 g) for 10 minutes. After collecting the PRF as a fibrin clot, it was sliced into pieces shaped like 2-3 mm pieces with a scalpel. Platelet-rich fibrin pieces were placed in the middle ear to support cartilage graft medially, especially medial to the graft's anterior half. After stabilising the cartilage graft, the tympanic membrane remnant was placed back to its position, and PRF pieces were used in EAC packing. In the control group, absorbable gelatine sponges were used for packaging EAC and supporting graft. The PRF clot and PRF buffers were shown in Figure 1 and Figure 2. Platelet-rich fibrin pieces placed in EAC and middle ear were shown in Figure 3 and Figure 4.

Statistical Analysis

Statistical analysis was done using computer software, v.22 (IBM SPSS Corp.; Armonk, NY, USA), and descriptive statistics were used for analyzing demographic data and graft healing rates. The Shapiro–Wilk test was used for determining the distribution pattern of the data. Independent and paired sample *t*-tests were used to analyze parametric variables, while Wilcoxon and Mann–Whitney *U* tests were used to analyze non-parametric variables based on the distribution pattern of the data. Pure-tone audiometry measurements, tympanometry values, and GBI scores were expressed as "mean ± standard deviation."

RESULTS

The mean age of the 29 patients (19 female and 10 male) was 33.18 ± 11.08 years (range: 22-56 years). The mean ages were 35.21 ± 11.69

Figure 1. Collection of platelet-rich fibrin as fibrin clot.

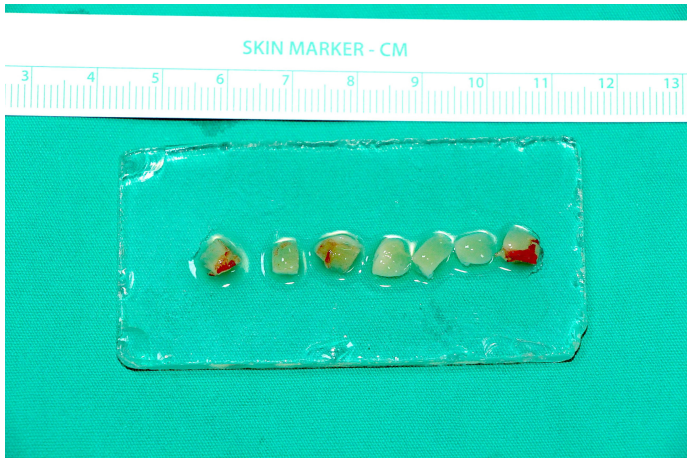

Figure 2. Preparation of platelet-rich fibrin buffers.

years in the PRF group (8 right ears and 6 left ears) and 36.2 ± 10.85 in the control group (8 right ears and 7 left ears), respectively. Patient demographics did not statistically differ between the groups.

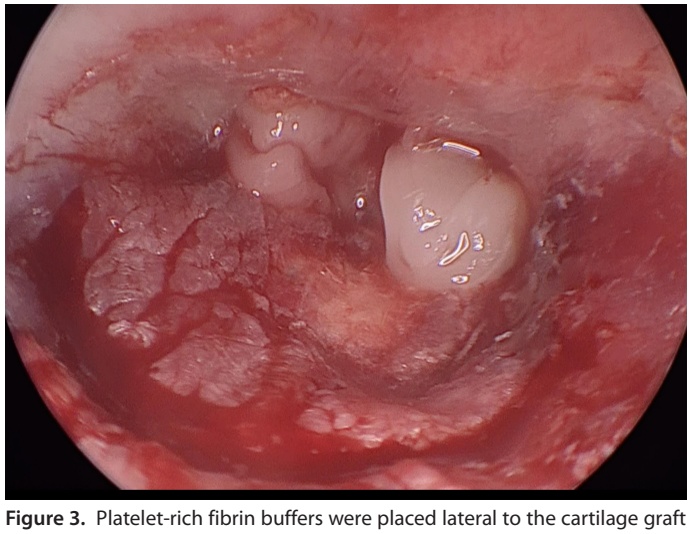

Figure 3. Platelet-rich fibrin buffers were placed lateral to the cartilage graft in external auditory canal.

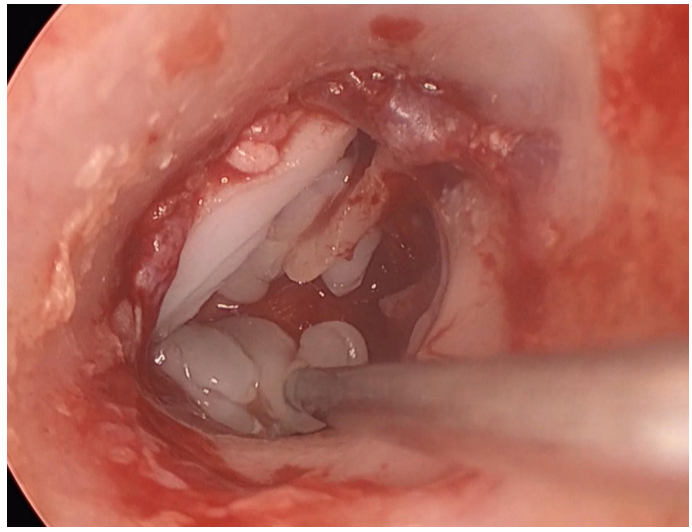

Figure 4. Platelet-rich fibrin buffers were used in middle ear to prevent cartilage graft medialization.

No significant postoperative complications were observed in both groups during the 6 months follow-up period and no patient was excluded from the study. Complete cartilage graft healing without perforation or medialization was observed in all patients in the first and six-month controls. No patient suffered from purulent discharge in both groups during the six-month follow-up period. When the first-month tympanometry values were compared, there were no statistically significant differences in compliance or EAC volume values between the 2 groups ($P = .453$ and .383, respectively). In the PRF group, 8 patients had type A (compliance >0.5 mL), 3 patients had type S (compliance <0.5 mL), and 4 patients had type B (no compliance) tympanograms. In the control group, 5 patients had type A, 5 patients had type S, and 5 patients had type B tympanograms. None of the patients had a type C tympanogram. First-month tympanometry values and mean postoperative ABG gains of the groups and their comparison are shown in Table 1.

Preoperative, postoperative first, and six-month PTA results of the groups are presented in Table 2. In the PRF group, the mean ABG gain (dB HL) of 0.5, 1, 2, and 4 kHz frequencies was 9.82 ± 4 dB HL in the postoperative first month and 10.08 ± 4.91 dB HL in the sixth postoperative month. There was a significant difference between

Table 1. First-Month Tympanometry Values and Mean Postoperative Air-Bone Gap Gains of the Groups

	PRF Group (n = 14)		Control Group (n = 15)		
	Mean	Standard Deviation	Mean	Standard Deviation	*P*
Air-bone gap gain (dB HL)					
First month	9.82	4	8.91	6.26	.537
Sixth month	10.08	4.91	10.25	4.48	.723
Tympanometry					
Compliance (mL)	0.53	0.41	0.4	0.42	.453
Ear canal volume (mL)	1.80	0.78	1.69	1.04	.383

Table 2. Preoperative First- and Sixth-Month Mean Pure-Tone Audiometry Hearing Levels of the Groups

	Value	Preoperative	Postoperative First Month	*P*	Postoperative Sixth Month	*P*
PRF group	Bone conduction (dB)	12.85 ± 9.87	13.48 ± 10.2	.151	13.125 ± 10.14	.648
Control group		16.16 ± 9.05	14.33 ± 10.53	.02	14.16 ± 10.5	.09
PRF group	Air conduction (dB)	35.53 ± 11.69	26.33 ± 9.55	.00	25.71 ± 8.65	.00
Control group		39.16 ± 14.37	28.41 ±13.37	.00	26.91 ±13.69	.00
PRF group	Air-bone gap (dB)	22.67 ± 4.72	12.85 ± 5.17	.00	12.58 ± 4.98	.00
Control group		23 ± 5.95	14.08 ± 5.35	.00	12.75 ± 5.04	.00

pre- and postoperative mean ABG levels ($P = .00$). There was no statistically significant difference between the postoperative first and sixth-month ABG gains ($P = .766$).

In the control group, the mean ABG gain (dB HL) of 0.5, 1, 2, and 4 kHz frequencies was 8.91 ± 6.26 dB HL in the postoperative first month and 10.25 ± 4.48 dB HL in the postoperative sixth month. There was a significant difference between pre- and postoperative mean ABG ($P = .00$). There was no statistically significant difference between the postoperative first and sixth-month ABG gains in the control group ($P = .112$). There was no statistically significant difference in ABG gains in the first- ($P = .537$) and sixth-month ($P = .723$) controls between PRF and control groups.

Preoperative first-month GBI scores of the groups are presented in Table 3. The physical benefit scores were significantly higher in the PRF group ($P = .01$). There was no difference in general and social benefit scores ($P > .05$).

DISCUSSION

Healthy epithelialization in the early postoperative period after tympanoplasty is a crucial factor in graft intake. Since cartilage grafts are rigid, they usually provide enough support for the perforated TM in underlay tympanoplasty, but in some cases, surgeons use Gelfoam (absorbable gelatine sponge) for preventing graft medialization. Since the 1960s, many studies have reported potential harmful effects like fibrosis and adhesions regarding the absorbable gelatine sponges in the middle ear.[10,11] However, today, Gelfoam is regarded as a safe, non-toxic, and well-tolerated material in the middle ear mucosa, and Gelfoam is a widely accepted middle ear packing material compared to other biomaterials.[1,12]

Many clinical studies favored platelet-rich biomaterials in otology to accelerate healing and healthy epithelization. Gür et al[13] published the use of PRF membranes in traumatic tympanic membrane perforation repair as a successful method. They reported that the PRF membrane provided more rapid healing with more successful audiological results than the conventional paper patch group. Mandour et al[14] published the comparison of fat graft enriched with PRP and cartilage perichondrium graft in myringoplasty. They found similar hearing and healing results in both groups, and they suggested the fat graft enriched with PRP as an alternative to the cartilage perichondrium. Nair et al[15] reported that PRF in myringoplasty with temporalis muscle fascia resulted in a better graft intake rate. They used PRF as a plug over perforation sealed with temporalis muscle fascia and reported the superiority of PRF plugs in TM healing. Also, Kütük et al[6] reported the superiority of the PRF with temporal fascia graft compared to temporal fascia alone with better functional outcomes in their retrospective controlled study.

In our study, we observed that PRF provided healthy epithelization and successful graft intake without complication. However, unlike mentioned studies that reported better functional outcomes with PRF or PRP, we found no statistically significant difference between PRF and control groups regarding ABG gains and tympanometry values. Tympanometry results showed that the mean compliance was higher in the PRF group, but it was not statistically significant. Eight of 14 patients (57.1%) in the PRF group and 5 of 15 (33.3%) patients in the control group had natural TM compliance higher than 0.5 mL. It is impossible to conclude on the limited group of patients without a statistical significance. But we observed that PRF offers adequate time for supporting the graft medially, and after degradation, it creates a natural middle ear cavity without effusion.

The graft intake success depends on many factors. The type of graft material and surgical procedure is more crucial than using platelet-rich biomaterials. Cartilage grafts are considered as successful materials in TM grafting with minimum resorption and retraction rates in the postoperative period.[16] We used a composite cartilage graft with perichondrium as graft material, and all of the patients in both groups had a graft intake rate of 100%.

Recently, Taneja[7] published a controlled study on 82 patients that compares the efficacy of PRP-soaked Gelfoam in the middle ear and EAC packing, similar to our study. Better graft intake rate and hearing improvement were observed in the PRP-soaked Gelfoam group. We used PRF in the EAC for packing and in the middle ear to support the cartilage graft's position as an alternate to absorbable gelatine

Table 3. Preoperative First-Month Glasgow Benefit Inventory Scores of the Groups

	Total Score (Mean ± Standard Deviation)	Overall Benefit Score (Mean ± Standard Deviation)	Social Benefit Score (Mean ± Standard Deviation)	Physical Benefit Score (Mean ± Standard Deviation)
PRF group	24.53 ± 14.49	21.00 ± 18.30	32.63 ± 15.26	30.55 ± 13.45
Control group	22.56 ± 9.56	20.13 ± 10.25	30.55 ± 11.96	24.30 ± 15.26
P	>.05	>.05	>.05	.01

sponges. Platelet-rich fibrin has a rigid structure due to the polymerized fibrin, and it can be prepared in 15 minutes with a simple centrifugation procedure without any specific tube or agent that increases the cost of surgery unlike Gelfoam. We followed a total of 14 patients in PRF group for 6 months and observed complete graft healing in all of them. Also, we did not observe any graft medialization in any patient. Functional outcomes showed that PRF was as successful as Gelfoam packing in tympanoplasty. The limited number of patients is the major limitation of our study, and to obtain both statistically and clinically valuable conclusion, long-term controlled and high patient numbered studies that investigate the role of platelet-rich biomaterials such as PRP and PRF on graft healing are mandatory.

Platelet-rich fibrin was introduced as a fibrin clot that induces wound healing and tissue regeneration. It releases growth factors with diffusion and degrades in a cavity within a week or 2.[3] In a study that assesses the blood derivate biomaterials' mechanical properties, the PRF was found to be tough enough to serve as a barrier in open cavities.[17] On the other hand, the degradation time of Gelfoam in the middle ear cavity was found to be within 2-9 weeks.[10] It provides mechanical support for a longer time than PRF. In our study, we did not observe graft medialization in both groups in the first month controls. Platelet-rich fibrin can be considered a successful packing agent in middle ears in the early postoperative time.

We reported the benefits and the results of the PRF buffers in tympanoplasty procedure. Our study is the first study that introduces and encourages the use of PFR buffers as a packing agent in otology. We selected a small group of patients with non-complicated TM perforation. Platelet-rich fibrin buffers can be used for healthy epithelization also in mastoid cavity and further studies can be conducted on other pathologies.

We evaluated patients' overall health status in the first-month controls. During the first month after the surgery, a change in physical health status was significantly better in the PRF group. The significant difference was seen in the 16th and 17th questions of the GBI that state physical benefit status. Patients in the PRF group significantly needed less medication and professional help during their recovery period after surgery. We think that as an autologous material, PRF provides a healthy environment without significant inflammation or foreign body reaction during the early postoperative time in both the middle ear and EAC. Also, it degrades itself without a need for EAC aspiration. These factors can be related to better physical outcome in the early postoperative time period.

CONCLUSION

We discussed the potential role of PRF as a packing agent in tympanoplasty. Using PRF in the middle ear and EAC as a support material for cartilage graft was feasible and resulted in a satisfactory graft intake rate. Platelet-rich fibrin was successful as absorbable gelatine sponges with similar functional outcomes, graft healing rates, and better physical health-related outcomes. It is suggested that PRF can be used as an alternative to Gelfoam sponges as packing material in tympanoplasty.

Ethics Committee Approval: The ethics committee approval was received for this study from the Ege University Ethical Committee (IRB No: 20-11.1T/12).

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

Peer-review: Externally peer-reviewed.

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