Effect of topical use of platelet-rich fibrin in repairing central tympanic membrane perforation using the endoscopic inlay butterfly cartilage myringoplasty technique

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Objective
The aim of this study was to determine the effectiveness of inlay butterfly cartilage myringoplasty and to assess the importance of topical use of autologous platelet-rich fibrin (PRF) in this technique.
Patients and methods
Fifty patients with dry central perforation were classified into two groups: group A included 25 patients who had undergone endoscopic inlay butterfly myringoplasty with the use of autologous PRF, and group B consisted of 25 patients who had undergone the same technique but without the use of autologous PRF. The study was performed during the period between 2013 and 2016. The follow-up period ranged from 1 to 14 months. All patients were assessed clinically to evaluate healing of tympanic membrane, postoperative air-bone gap, and complications.
Results
The overall graft take rate was 96% (24 cases) in group A, whereas the graft take rate in group B was 76% (19 cases) with a statistically significant difference between the two groups. The hearing results were satisfactory and compatible with previous studies in the literature. No postoperative complications were reported.
Conclusion
Inlay butterfly cartilage myringoplasty is a simple technique for repairing small-to-medium-sized tympanic membrane perforation. The success rate of this technique has improved with topical application of PRF. The autologous PRF not only enhances healing of the graft but also protects it from infection.

Keywords:
cartilage, inlay butterfly, myringoplasty, platelet-rich fibrin

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Introduction

Patients having chronic suppurative otitis media with central perforation suffer from hearing loss as well as recurrent discharge. Therefore, several trials were carried out to close the tympanic membrane (TM) perforations and restore hearing loss. These procedures involve the use of different graft materials, such as fat, perichondrium, temporalis muscle fascia, and synthetic materials [1,2].

Several authors have suggested that cartilage should take the upper hand among most of the graft materials. Cartilage is well incorporated with TM layers; it provides firm support to prevent retraction. It also has a very low metabolic rate and receives its nutrients through diffusion [3]. However, many otologists prefer fascia over cartilage, as the thickness of the cartilage graft may affect the hearing results. Moreover, it creates an opaque TM, which could potentially hide a residual cholesteatoma [4].

To simplify the closure of the TM defect, Eavey [5], introduced the inlay butterfly cartilage tympanoplasty. He performed this technique using a tragal cartilage–perichondrium graft covered with a split-thickness skin graft.

Many studies were conducted to evaluate this procedure, and the results vary from poor to excellent.

In 2001, Choukroun *et al.* [6] developed platelet-rich fibrin (PRF), the new generation of platelet agglutination. The initial concept of this preparation was to concentrate platelets and their growth factors in a plasma solution and to activate it into a fibrin gel applied to a surgical site to improve local healing. It offers inflammatory protection to grafts and accelerates cell proliferation and matrix remodeling. Moreover, it has the advantage of ease formation and manipulation during the surgical procedure with no undesirable

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tissue reaction [7]. However, there are limited studies on the effect of PRF in the otology field.

The aim of this study was to determine the effectiveness of inlay butterfly cartilage myringoplasty and to assess the importance of topical use of autologous PRF in this technique.

Patients and methods

This prospective, comparative study included 50 patients who presented to the Ear, Nose, and Throat Department of Assiut University Hospital, Egypt, from May 2013 to September 2016.

Patients with dry central perforation being inactive for at least 1 month with air-bone gap (ABG) of less than or equal to 30 dB regardless of sex and age were included in our study.

We excluded the following patients: patients who presented with active discharging central perforation and patients with atticoantral disease and large perforations according to Saliba's subdivision [8]. (The TM was divided preoperatively into four quadrants, and perforations involving more than two quadrants were excluded.) Moreover, patients having wide ABG suggesting ossicular pathology and patients with narrow or extra kinked ear canals that could not be treated surgically using the transcanal approach were excluded. Finally, we excluded patients refusing the research procedure.

The study protocol was approved by the local ethics committee and written informed consent was obtained from each patient. For all patients, the following were carried out: history taking, general and ENT examination with particular concern on the ear, and otoscopic examination. Pure tone audiometry (PTA) and tympanometry, explanation of the surgical procedure, and then surgical intervention were carried out after routine preoperative investigations.

We classified our patients into two groups: group A included 25 patients who had undergone endoscopic inlay butterfly myringoplasty with the use of autologous PRF, and group B consisted of 25 patients who had undergone the same technique but without the use of autologous PRF.

Surgical procedure

The surgical procedure was carried out under general anesthesia with the utilization of an endoscopic zero lens telescope (9 cm long, 2.7 mm wide) and endoscopic camera. Infiltration of the tragus with a mixture consisting of lidocaine 0.05% and 1 : 1 00 000 epinephrine was carried out to facilitate dissection and harvesting of the tragal cartilage. After exposing the tragal cartilage, an incision was made on the medial side 2–4 mm away from the cartilage dome so that a small strip of cartilage is left in place to maintain tragal contour postoperatively. The cartilage was harvested with intact perichondrium on both sides. It is necessary to avoid peeling off of the perichondrium. No stitches were necessary for the tragal incision. The margins of the perforated drum were freshened with a pick and then the dimensions and shape of the perforation were estimated using a 4-mm right-angled surgical hook. The cartilage graft was designed according to the size of the perforation – that is, ~2 mm larger in diameter – using a sharp scissor. Thereafter, the cartilage graft was carefully grooved midway between the two perichondrial layers all around using a surgical blade no. 15 (Fig. 1).

The graft was inserted into the perforation similar to the insertion of grommet tube – that is, one surface of the cartilage with its perichondrium lies in the middle ear and the other on the lateral side of the margin of the perforation (Fig. 2). The final step was the application of medicated gelfoam, and a sterile gauze was inserted in the external meatal opening.

Preparation of the autologous platelet-rich fibrin

We usually start the preparation of the PRF in the operating theater during induction of anesthesia. A volume of 10 ml of blood was drawn with a syringe into a 10 ml glass test tube from the saphenous vein without application of anticoagulant. Usually, blood begins to coagulate in less than a minute when it comes in

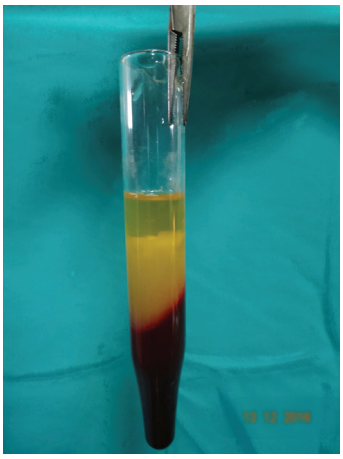
Figure 1

The grooved tragal cartilage graft with its perichondrial layers.

Figure 2

Intraoperative endoscopic view shows the graft is fitted into the perforation.

Figure 3



Blood was separated out into three layers in the test tube.

Figure 4

The PRF clot after centrifugation.

contact with the glass surface, and hence quick blood collection and centrifugation was necessary. Blood was centrifuged using a tabletop centrifuge (Zhengji Model No. 80-1; Jiangsu Zhengji Instruments Co., Ltd., China) machine for 12 min at 2700 rpm. Consequently, the resultant product consisted of three layers: the top layer was composed of acellular platelet poor plasma, the layer in the middle was the PRF clot, and the last layer comprised red blood cells at the bottom (Figs 3 and 4). The PRF was taken and applied to the fitted graft as the final step of surgery, and then a sterile gauze was inserted in the external meatal opening.

Postoperative instructions and follow-up

All patients were instructed not to blow their nose for at least 1 month. In addition, they were instructed to avoid wetting of the ear and to keep it dry.

The first postoperative visit was at 1 week, when the dressing and pack were removed. Local drops (a mixture of antibiotic with steroid) were administered twice daily.

Endoscopic evaluation of the graft was performed on a weekly basis for at least 1 month and then once monthly until the end of the first year. The postoperative clinical assessment included the healing of TM, the presence of discharge, granulation tissues, development of complications, and subjective hearing improvement.

Postoperative hearing assessment

Postoperative PTA was carried out by the end of the third and sixth months. We used the postoperative ABG as the parameter for hearing evaluation. We also calculated the average PTA increase. Success as regards hearing was considered if there was an improvement of 10 dB or greater at 6 months postoperatively, as used by Sergi *et al.* [9].

Recording and statistical analysis of the data

Data analysis was carried out to obtain the following data: personal data, clinical characteristics of the patients, postoperative graft taking, hearing improvement, and postoperative complications.

We analyzed the data using statistical package for the social science for Windows 19.0 (SPSS Inc., Chicago, Illinois, USA). Categorical variables were compared using the χ^2-test for sex, and the paired t-test was used for other outcome results.

Results

A total of 50 patients were involved in this study and divided into two groups: group A (25 patients) and

group B (25 patients). Each group comprised 14 (56%) male and 11 (44%) female patients with a statistically nonsignificant difference between the two groups (P=1.000).

The mean age of the patients was 24±5.8 years in group A and 26.9±12.8 years in group B, with a statistically nonsignificant difference (P=0.304) (Table 1).

The follow-up period postoperatively ranged from 1 to 14 months. The mean follow-up interval for both groups was 11.4±2.1 months.

The overall graft take rate was 96% (24 cases) in group A, whereas the graft take rate in group B was 76% (19 cases) with a statistically significant difference between the two groups (P=0.041).

The time of graft failure was on the second week postoperatively in one patient due to upper respiratory tract infection in group A. However, in group B, the time of failure was on the second week postoperatively in three patients due to infection of the graft, on the third week in two patients due to upper respiratory tract infection, and lastly on the fourth week in one patient due to acute otitis media.

As regards the postoperative hearing gain we found the following.

In group A, the postoperative hearing gain was 5–10 dB in 11 patients, 11–15 dB in eight patients, 16–20 dB in four patients, more than or equal to 21 dB in one patient, and one patient did not improve at all. In group B, the postoperative hearing gain was 5–10 dB in seven patients, 11–15 dB in six patients, 16–20 dB in five patients, more than or equal to 21 dB in one patient, and seven patients did not improve at all. Audiometric results are presented in Tables 2–4.

During the follow-up period, no graft lateralization or medialization was reported. There were no postoperative complications such as sensorineural hearing loss, tympanosclerosis, facial nerve paralysis, or thin atrophic areas.

Discussion

Various techniques have been developed and refined. Moreover, many grafting materials are used to simplify the closure of the TM. They include refreshing the perforation edges and then inserting a graft. However, results with the utilization of these materials were inferior to those achieved with the use of conventional methods because the graft was not stably fixed and required support with a material inserted into the middle ear [10].

In 1998, Eavey [5] described a minimally invasive technique for repairing TM perforation in children

Table 1 Baseline characteristics of patients in both groups

	Group A [*n* (%)]	Group B [*n* (%)]	*P* value
Age (years)			
Mean±SD	24±5.85	26.92±12.79	0.304 (NS)
Range	16–45	13–65	
Sex			
Female	11 (44.0)	11 (44.0)	1.000 (NS)
Male	14 (56.0)	14 (56.0)	
Diagnosis			
Bilateral CSOM	6 (24.0)	3 (12.0)	0.499 (NS)
Left CSOM	9 (36.0)	9 (36.0)	
Right CSOM	10 (40.0)	13 (52.0)	
Operated ear			
Left myringoplasty	12 (48.0)	10 (40.0)	0.776 (NS)
Right myringoplasty	13 (52.0)	15 (60.0)	
Size of perforation			
Small (≤25%)	12 (48.0)	13 (52.0)	1.000 (NS)
Medium (≤50%)	13 (52.0)	12 (48.0)	

CSOM, chronic suppurative otitis media.

Table 2 Comparison between the studied groups as regards preoperative and postoperative audiogram

	Group A	Group B	*P* value
Preoperative audiogram (mean±SD)	21.76±5.07	22.4±6.14	0.737 (NS) (t=0.3402)
Postoperative audiogram (mean±SD)	8.88±3.30	14.8±10.2	0.0069 (S) (t=2.9552)
Improvement in ABG (mean±SD)	12.48±4.78	7.40±10.78	0.0597 (NS) (t=1.9764)

Paired t-test. ABG, air-bone gap; S, significant.

Table 3 Average of preoperative and postoperative air-bone gap (dB)

	Audiogram		*P* value
	Preoperative	Postoperative	
Group A (*N*=25)	21.76±5.07	8.88±3.30	<0.001*
Group B (*N*=25)	22.4±6.14	14.8±10.2	0.001*

Student's *t*-test. *$P<0.01$, statistically significant difference.

Table 4 Success rates according to hearing gain more than or less than 10 dB gain

	Group A [*n* (%)]	Group B [*n* (%)]	*P* value
Graft taking			
Failure	1 (4.00)	6 (24.00)	0.041*
Success	24 (96.00)	19 (76.00)	
Hearing gain in all cases			
0–10 dB gain	5 (20.00)	10 (40.00)	0.217 (NS)
≥10 dB gain	20 (80.00)	15 (60.00)	

Paired *t*-test. *$P<0.05$, statistically significant difference.

(10 patients) using a tragal cartilage graft, which resembled butterfly wings with a successful take rate and improvement in hearing in 100% of patients.

Lubianca-Neto [11] had modified this technique to be used for adults (20 patients) under local anesthesia and without the application of the split-thickness skin graft with a take rate of about 90%.

Mauri *et al.* [12] compared the results between patients treated with the inlay butterfly cartilage technique and patients treated with the underlay fascia technique. The take rates were 85% with the inlay technique and 83% with the underlay fascia technique. There were no significant differences in the hearing results between the two methods.

Couloigner *et al.* [13] also compared the results of the transcanal inlay butterfly technique in 59 children, of whom 29 were previously operated with an underlay fascia graft technique. The 'take' rate was 71% with the inlay butterfly myringoplasty and 83% in the underlay fascia myringoplasty with no statistically significant difference in taken rates or hearing gain between the groups.

Omran [14] conducted his study on 30 patients; their ages ranged from 9 to 57 years. Successful closure of TM defect was achieved in 73.3%.

Effat [15] obtained inconsistent results in that only 43% showed closure of the perforation using the inlay butterfly cartilage technique in 21 (28 ears) patients. He noticed lack of epithelialization of the cartilage graft. The presence of unepithelialized cartilage–perichondrium may be an ideal site for the development of a bacterial biofilm on the surface.

Previous studies have shown that the main cause of graft failure was infection. This usually occurs within the first 2 weeks postoperatively. In this study, we preferred to cover the tragal graft with the PRF instead of the split-thickness skin graft to assess its importance in improving the success rate of this technique.

In 1974, platelets' regenerative potentiality was introduced, and Ross *et al.* [16] were first to describe growth factors from platelets. Blood-derived products were started to be used to seal wounds and to improve local healing in surgical procedures in the form of fibrin glues. However, their use remains limited due to the complexity of their production protocols and their high cost as well as the risk for disease transmission.

Therefore, the use of autologous platelet-rich plasma (PRP) for the repair and regeneration of different tissues was proposed. This was followed by the development of PRF as a second-generation platelet concentrate, which is widely used to accelerate soft and hard tissue healing in different medical fields.

In 2009, Erkilet *et al.* [17] reported that PRP is effective in speeding up the healing of perforated TMs in rats and leads to shortening of the healing period. Therefore, they suggested that PRP might be effective in humans as it is an autologous material.

El-Anwar *et al.* [18] reported favorable results (100%) with the use of topical autologous PRP on the lateral surface of a conchal perichondrial graft in 32 patients with large dry central TM perforations. Myringoplasty was performed through the postauricular approach.

In 2016, Gur *et al.* [19] published a study to evaluate the effects of PRF membrane in the repair of traumatic TM perforations, and to compare the use of a PRF membrane with the paper patch technique. Closure was achieved in 28 (93%) perforations in group 1 and in 25 (83%) perforations in group 2.

We reported few studies that had used PRF for the closure of TM perforations. From these studies and our study, we concluded that the application of PRF improved the success rate and proved the role of PRF in enhancing healing and preventing infection of the graft. We believe that PRF could become a valuable material for repairing TM perforation.

In our current study, the overall graft take rate was 96% with the use of PRF (group A), which is higher than that in the other group (group B) that was operated without the application of PRF (only 76%).

Postoperative hearing gain is reported to be about 10 dB for inlay butterfly myringoplasty in many studies. Our study showed similar results and the hearing results were satisfactory and compatible with these studies. Moreover, the results are comparable to those studies in which temporalis fascia grafts were used [20].

We noticed that hearing gain (≥10 dB) was achieved in 20 (80%) patients of group A, which is better than the hearing gain achieved in group B (15 patients; 60%), with a statistically nonsignificant difference (P=0.217). There was no effect of application of PRF on hearing gain in the taken graft cases as the hearing gain was related to the closure of TM.

Inlay butterfly cartilage myringoplasty was originally designed for small perforations in children. Later, indications were expanded by using such graft to involve small-to-medium sized perforations through a transcanal route and even for large perforations using a postauricular approach. The technique has many advantages: no postaural incision and therefore no need for postoperative wound care with risk for neither inflammation nor keloid formation.

There was no tympanomeatal flap elevation with no risk for granulation tissue formation. The procedure is well tolerated by all patients with no or minimal pain in most of the cases.

The procedure needs shorter time (30–40 min) than the usual conventional tympanoplasty; this leads to reduced operative costs. It is considered as 1-day surgery where the patient can leave the hospital after recovery from anesthesia; the patient can go back to work and the child can go back to school the next day after surgery.

As regards the disadvantages of this technique, cartilage usually creates an opaque TM at the site of repair, which leads to inability to inspect possible development of middle ear diseases through otoscopic examination, and hence we recommend using the technique in small-to-medium-sized perforations and not in large ones as recommended by Ghanem *et al.* [4].

Another disadvantage of the procedure is that it does not allow for examination of ossicular chain integrity. Hence, we should not depend on the size of perforation only. Cases with wide ABG that cannot be attributed to the perforation should be excluded.

As regards the use of PRF, we found that it offers both mechanical and inflammatory protection to the graft with no undesirable tissue reaction. It can be easily prepared and obtained from the blood of patients with easy handling during the surgical procedure. We recommend it instead of PRP as, during the preparation of PRP, calcium chloride and bovine thrombin could lead to the development of antibodies to the factors V, XI, and thrombin, which results in the risk for life-threatening coagulopathies [21]. Other advantages over PRP include the ease of preparation/application, minimal expense, more efficient cell migration and proliferation, and no requirement of bovine thrombin or anticoagulant.

Conclusion

Inlay butterfly cartilage myringoplasty is a simple technique for repairing small-to-medium-sized TM perforation. The success rate of this technique has improved with topical application of PRF. Topical PRF application is safe and highly efficient and successful with no reported complications. It not only enhances healing of the graft but also protects it from infection.

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Conflicts of interest

There are no conflicts of interest.

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