

REVIEW

# Platelet-Rich Fibrin in Otorhinolaryngology

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## ABSTRACT

**Background:** Platelet-rich fibrin is a second-generation platelet concentrate. It is rich in platelets, cytokines, growth factors and leukocytes. Compared to platelet-rich plasma, it releases growth factors for a more extended amount of time.

**Methods:** A literature review was conducted on the applications of platelet-rich fibrin in otolaryngology. Only articles written in English were further considered for the study; all others were excluded. Also, articles relating to oral and maxillofacial surgery were removed. Results: Twenty-five studies were deemed appropriate for inclusion in the present review.

**Conclusion:** Based on the current data, platelet-rich fibrin appears to be a safe, healing-promoting material. It is a cost-effective, autologous material with enormous therapeutic application potential in the future. However, further clinical research is required before conclusive conclusions can be drawn about its usefulness.

**Keywords:** platelet-rich fibrin, otolaryngology, ear, nose, pharynx, larynx.

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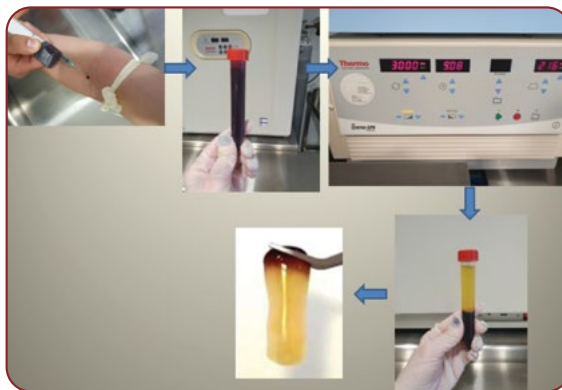
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## INTRODUCTION

**P**latelet-rich fibrin (PRF) is a second-generation platelet concentrate rich in platelets, cytokines, growth factors, and leukocytes (1). Platelet-rich plasma (PRP) is created by blood centrifugation at two stages, a soft spin stage and a hard spin stage (2). The mechanism of PRP therapy is based on the release of growth factors from platelet alpha granules. PRF represents the next generation of autologous platelet treatment. Platelet-rich fibrin is comparable to PRP except that PRF naturally contains fibrin for clot scaffolding and localisation of mesenchymal stem cells and releases platelet-related therapeutic granules for a longer period than PRP (3). It was first described by Choukroun *et al* in 2000 (4). Platelet-rich fibrin consists of cytokines, glycemic chains, and structural glycoproteins integrated into a fibrin network that is slowly polymerized (5). These components promote tissue regeneration via synergistic processes. Platelets secrete several cytokines and growth factors such as tumor growth factor (TGF-), platelet-derived growth factor (PDGF), insulin-like growth factor-1 (IGF-1) and vascular endothelial growth factor (VEGF) (3). Platelet-rich fibrin stimulates cell proliferation, promotes wound healing and hemostasis, reduces scarring, and protects grafts from inflammatory damage (6). Platelet-rich products have been widely recognized as an established therapeutic intervention that has favorable results for a range of clinical problems. Nevertheless, the utilization of PRF in the field ENT remains uncommon, indicating the necessity for additional research and exploration of its potential applications. This study provides an overview of the existing evidence regarding the utilization of PRF in the field of ear, nose and throat surgery.

### Preparation of PRF

In contrast to PRP, PRF is produced by centrifuging pure whole blood without adding anticoagulants (Figure 1). Platelet-rich fibrin spontaneously generates a fibrin matrix gelatinous clot that limits growth factor secretion to the clotting (1). Venipuncture of 10 to 100 cc of blood is the standard process according to each protocol. Glass containers stimulate coagulation factors more than their plastic counterparts. Blood must be immediately transported to the centrifuge to



**FIGURE 1.** Platelet-rich fibrin preparation by centrifugation of blood sample collected without anticoagulant

prevent premature coagulation (1). Transport times over 60 seconds are related to early clotting before adequate blood component separation has occurred (1). After the blood sample has been centrifuged, the supernatant or coagulated layer on top is removed from the red blood cells at the bottom. Solid PRF can be cut or molded into the desired shape based on the requirements of the method in which it will be used. In contrast to PRP's quick growth factor release, PRF's growth factor release is prolonged: up to seven days for the majority of growth factors. In addition, PRF is simple to shape, manipulate, and tailor to the needs of each surgical treatment. It is a simple, inexpensive, safe, autologous material with regeneration capabilities. □

## MATERIALS AND METHODS

**A** literature search of the PubMed database was conducted using the terms 'platelet-rich fibrin' and/or 'platelet-rich fibrin in otorhinolaryngology', 'platelet-rich fibrin in ENT', 'platelet-rich fibrin in otolaryngology', 'platelet-rich fibrin in otology', 'platelet-rich fibrin in laryngology', 'platelet-rich fibrin in rhinology' from database inception to April 2023. Articles related to oral surgery and maxillofacial surgery were excluded. Only total access articles written in English were further considered for the present study; all others were excluded. Randomized controlled trials and human clinical trials in adults were preferred, thus, animal trials were excluded. □

## RESULTS

**A** total of 146 articles were obtained after searching databases and 121 articles were

TABLE 1. PRF in laryngology surgery

Study	Year	Number of patients/type of surgery	Results
Mostafa Eid <i>et al</i> (7)	2020	67/total laryngectomy	After total laryngectomy, PRF accelerates the healing process and reduces the occurrence of PCF. PCF was found in 5.7% of subjects in the PRF group compared to 31.3% of those in the control group.
Reksodiputro <i>et al</i> (8)	2021	20/total laryngectomy	PRF application improved postoperative wound healing (edema and discomfort) in total laryngectomy patients. In the PRF-treated group, early fistula was not observed, although five patients in the control group have developed fistulas.
Reksodiputro <i>et al</i> (9)	2021	18/injection laryngoplasty	After laryngoplasty for vocal cord paralysis, there was no statistically significant difference between the two groups.

PRF=platelet-rich fibrin, PCF=pharyngocutaneous fistula

excluded because they did not meet the selection criteria. A total of 25 studies fulfilled the inclusion and exclusion criteria. They were categorized according to their specialism. Three articles in the field of laryngology, twelve articles in the field of rhinology and skull base and ten articles in the field of otology were chosen for review.

### Platelet-rich fibrin in laryngology surgery (Table 1)

In 2020, Eid *et al* (7) evaluated the potential role of PRF application in pharyngeal healing after total laryngectomy. A total laryngectomy was performed on 67 individuals with advanced laryngeal cancer who participated in their clinical trial. Platelet-rich fibrin was administered to the pharyngeal closure line to promote healing in the PRF group. There was a statistically significant difference between groups regarding the occurrence of pharyngocutaneous fistula (PCF). Their findings demonstrated that PRF promotes healing after total laryngectomy by lowering the rate of PCF. As a result, it reduces postoperative morbidity and hospital length of stay. In 2021, Reksodiputro *et al* (8) reached the same conclusion on the utility of PRF in total laryngectomy. The PRF group received PRF around the oesophageal stroma, and both groups were monitored for two weeks after surgery. The PRF matrix releases growth factors during the first week. In this study, the PRF group did not develop an early fistula, but five patients in the control group did. Overall, the study indicates that PRF administration in total laryngectomy accelerates postoperative wound healing, particularly in terms of edema and pain. The same author evaluated the impact of PRF on autologous adipose tissue after injection laryngoplasty for vocal cord paralysis (9). Computerized acoustic analysis/Multidimensio-

nal Voice Program (MDVP) parameters and maximum phonation time were utilized for the postoperative evaluation. After surgery, both groups demonstrated clinical improvement with no statistically significant differences.

### Platelet-rich fibrin in rhinology surgery (Table 2)

There were ten publications describing the use of PRF in rhinology. Most of them investigated the use of PRF in rhinoplasty. In 2017, Kovacevic *et al* proposed PRF as a scaffold for rhinoplasty, employing a combination of cartilage scales and cartilage paté embedded in platelet-rich fibrin (10). They hypothesized that their technique would result in increased graft survival and greater precision in avoiding superficial imperfections. Follow-up notes as well as pre- and postoperative photographic documentation were evaluated to determine the success of the surgery. According to them, PRF cartilage scales appear to be a potential and dependable alternative to present dorsal nose augmentation techniques. In 2021, the same author presented the results of a case series involving 107 rhinoplasties involving fat transfer mixed with platelet-rich fibrin (11). In the follow-up clinical examination, there were no symptoms of skin shrinkage, significant scarring, or color changes, with positive skin mobility test in all patients. Ultrasonography and magnetic resonance imaging have demonstrated the survival of fat. In the same year, Dan Yan *et al* reported the results of their clinical trial evaluating the use of platelet-rich fibrin in conjunction with autologous fat transplantation in augmentation rhinoplasty (12). Seventy patients, separated into two groups, had rhinoplasty and were monitored for over a year. Platelet-rich fibrin with autologous highdensity fat transplantation resulted

TABLE 2. PRF in rhinology and skull base surgery

Study	Year	Number of patients/type of surgery	Results
Kovacevic <i>et al</i> (10)	2017	48/rhinoplasty	No evidence of dorsal abnormalities, resorption, erythema, or irritation. No patient expressed complaints.
Rasmussen <i>et al</i> (20)	2018	12/transhenoidal approach to the sellar region	Early regeneration of the sphenoid sinus mucosa, absence of with no reported complications postoperatively
Khafagy <i>et al</i> (21)	2018	40/repair of CSF leakage	L-PRF has been identified as a beneficial supplementary substance in the repair of endoscopic spontaneous CSF leaks. It facilitates the reduction of the required number of layers for defect closure.
Gode <i>et al</i> (14)	2019	40/rhinoplasty	The control group experienced a notable volume reduction. PRF was able to reduce the rate of resorption of diced cartilage on the nasal dorsum by either enhancing its viability or preserving its shape
Gode <i>et al</i> (13)	2019	38/rhinoplasty	In the first week, the mean skin thickness over the supratip region was considerably greater in the control group. There were no significant variations in the nasal dorsum mean skin thickness measurements between the first-week and third-month control groups
Santos <i>et al</i> (15)	2020	200/rhinoplasty	PRF offers superior long-term aesthetic results.
Manoel Neto <i>et al</i> (16)	2020	23/rhinoplasty	No patient experienced immediate or delayed problems following surgery. Leukocyte- and platelet-rich fibrin (L-PRF) was sufficient for camouflage and filling in all patients, and patients reported satisfaction.
Tutar <i>et al</i> (17)	2020	67/septoplasty	In the early postoperative period, the results of the PRF group on the sniffin' sticks test were superior to those of the non-PRF group. Patients' pain scores at one week and three weeks; statistically significant differences between groups.
Sari <i>et al</i> (18)	2021	50/ESS	After ESS, there are fewer instances of adhesion, infection, hemorrhage, granulation, and frontal ostium stenosis.
Chang <i>et al</i> (19)	2021	2/endonasal microplasty for empty nose syndrome	The combination of PRF scaffolds with diced cartilage permitted the reestablishment of the neoturbinate in an effective manner.
Kovacevic <i>et al</i> (11)	2021	107/rhinoplasty	Positive skin mobility test in all patients with good skin quality, no symptoms of shrinkage, significant scarring or color changes, and no signs of skin atrophy. Ultrasonography and magnetic resonance imaging have demonstrated the survival of fat.
Yan <i>et al</i> (12)	2021	70/rhinoplasty	The nasal shape was stable six months after the operation, the contour was higher and more stereoscopic than before, and the average rise in nasal height was 3.0 mm in the PRF group and 2.0 mm in the control group. During the one-year follow-up, no problems such as fat embolism, infection, or necrosis occurred. The difference between the two groups' satisfaction rates is statistically significant.

ESS=endoscopic sinus surgery, CSF=cerebrospinal fluid

in a much higher fat-retention rate than the control group, with no clear long-term side effects.

In 2019, Gode *et al* reported the outcomes of two clinical investigations utilizing PRF in rhinoplasty. In one of them, the effect of PRF on nasal skin thickness during rhinoplasty was investigated (13). Rhinoplasty was performed on 38 patients divided into two groups: nasal dorsal PRF group and control group. Preoperative and postoperative ultrasound examinations revealed no significant changes between the two groups. In the other clinical experiment, the impact of injectable PRF on the viability of diced cartilage in rhinoplasty was investigated (14). In both groups, the thickness of the cartilage transplant was evaluated by linear superficial tissue ultrasonography during the first week and third month following surgery. In the control group, considerable volume loss was seen. Platelet-rich fibrin reduced the rate of resorption of diced cartilage on the nasal dorsum by either enhancing its viability or preserving its shape.

In 2020, Santos *et al* conducted a prospective study of 200 patients who underwent primary reduction rhinoplasty; the authors examined the

long-term impacts of PRF and found that PRF provided superior long-term aesthetic outcomes (15). Neto *et al* have used PRF in 23 patients undergoing rhinoplasty, noting that this membrane was a great surgical option for the camouflage and filling in rhinoplasty that can enhance tissue regeneration (16).

Except for rhinoplasty, the impact of PRF on healing has been explored in septoplasty and endoscopic sinus surgery as well. Tutar *et al* investigated the effect of PRF on olfactory function and discomfort following septoplasty (17). 148 patients participated in this clinical study; based on the Sniffin' Sticks test scores, the PRF group performed better in the early postoperative period than the non-PRF group. In terms of olfactory function, there were no differences at six weeks and six months. At one week and three weeks following septoplasty, there were statistically significant variations in pain scores across groups. Sari *et al* conducted a clinical investigation with 50 endoscopic sinus surgery patients (18). In terms of adhesion, infection, bleeding, granulation, and frontal ostium stenosis, improved outcomes were observed following ESS due to the



TABLE 3. PRF in otology surgery

Study	Year	Number of patients/type of surgery	Results
Habesoglu <i>et al</i> (22)	2014	32/myringoplasty	In the study group, the rate of eardrum closure was 64.3%, compared to 22.2% in the control group.
Gur <i>et al</i> (23)	2016	60/tympanoplasty	Compared to the paper patch approach, PRF resulted in faster healing and more successful audiological results.
Kumar <i>et al</i> (30)	2017	25/myringoplasty	The closure rate for traumatic tympanic membrane perforation was 92%, and hearing improvement was statistically significant (88%).
Hosam <i>et al</i> (24)	2017	50/myringoplasty	The overall graft acceptance rate in the PRF group was 96% (24 instances), compared with control group where it was 76% (19 instances).
Nair <i>et al</i> (25)	2018	86/tympanoplasty	4.7% of patients in the study group experienced postoperative infection, compared to 19% of patients in the control group. The success rate of graft uptake was reported to be 97.7% in the study group and 81.0% in the control group.
Kutuk <i>et al</i> (26)	2019	91/tympanoplasty type I	PRF plus temporal fascia graft was related with better postoperative outcomes in terms of tympanic membrane healing and graft survival; outcomes regarding hearing restoration were comparable.
Shukla <i>et al</i> (31)	2020	41/transcanal myringoplasty	In 85.4% of patients, holes of the tympanic membrane were successfully healed with PRF membranes.
El Awady <i>et al</i> (28)	2021	40/myringoplasty	Six months after surgery, the PRF group's success rate (95%) was much greater than the control group's (70%) success rate. Nineteen patients (95%) in the PRF group and 14 patients (70%) in the control group were successful in closing the air-bone gap by more than 10 decibels.
Riaz <i>et al</i> (27)	2021	50/tympanoplasty	After three months of follow-up, graft uptake was reported at 78% for patients and 52% for controls. The average improvement in hearing was 18 dB in cases and 6 dB in controls. Infection following surgery occurred in 8% of cases and 32% of controls.
Turhal <i>et al</i> (29)	2022	29/tympanoplasty	PRF proved to be just as effective as absorbable gelatine as a middle and external auditory canal packing agent, providing comparable functional outcomes and graft healing rates.

effects of PRF on wound healing. Two patients with empty nose syndrome (ENS) were treated with endonasal microplasty and cartilage implants by Chang *et al* in 2021 (19). For establishing the neoturbinate on the lateral wall of the nasal cavity, PRF scaffolds with diced cartilage transplant were employed. The findings of that study imply that the combination of PRF scaffolds with diced conchal cartilage grafts is appropriate for endonasal microplasty in the treatment of ENS.

#### Platelet-rich fibrin in skull base surgery (Table 2)

Two studies have examined the healing effects of PRF in endoscopic approaches to the base of the skull. Rasmussen *et al* utilized PRF in 12 patients undergoing transsphenoidal endoscopic sellar area procedures (20). Their findings revealed an early regeneration of the sphenoid sinus mucosa with no problems during the first 30 days after surgery. Khafagy *et al* employed PRF as a novel graft material for the endoscopic repair of spontaneous cerebrospinal fluid (CSF) leakage (21). In their study, 40 patients were separated into two groups, and PRF was discovered to be an in-

expensive, autologous graft that was simple to manufacture and manage, hence reducing the number of repair layers. When utilized in underlay procedures where CSF washes away the grafts, PRF creates an instantaneous watertight barrier, rapid clotting, and speeds mucosalization and postoperative healing.

#### Platelet-rich fibrin in otology surgery (Table 3)

In 2014, Haseboglul *et al* demonstrated the healing effects of PRF on acute eardrum perforation (22). They concluded that PRF accelerated eardrum repair. Two years later, the same conclusion was reported by Gur *et al*, who conducted a clinical trial of 60 patients treated for traumatic tympanic membrane perforations and separated into two groups (23). In their research, PRF resulted in quicker healing and better audiological outcomes with no need for a second surgery compared to the control group.

Many studies have assessed the impact of PRF mixed with perichondrium grafts in myringoplasty over the past five years. In terms of tympanic membrane healing and graft survival, all studies found that PRF was related to improved

postoperative results. In 2017, Hosam *et al* studied the effects of PRF application in patients who underwent endoscopic inlay butterfly myringoplasty. The overall graft acceptance rate in the PRF group was 96 versus 76% in the control group (24). In 2018, Nair *et al* conducted a clinical trial with 86 individuals who received myringoplasty and were observed for three months by a blinded observer (25); 4.7% of patients in the study group experienced postoperative infection, compared to 19% of controls. The success rate of graft uptake was reported to be 97.7% in the study group and 81.0% in the control group. In a total of 91 patients, Gokse Kutuk *et al* discovered that graft survival rates were much greater in the PRF group, but there was no difference in hearing gain between the two groups (26). In 2021, Riaz *et al* presented the results of their study involving 50 people who underwent myringoplasty with and without PRF (27). After three months of follow-up, graft uptake was reported at 78% for patients in the study group and 52% for controls. The average improvement in hearing was 18 dB in cases and 6 dB in controls. The incidence of postoperative infection was 8% in the study group and 32% in the control group. El Awady *et al* conducted a clinical trial on 20 patients who underwent myringoplasty and were divided into two groups. Six months after surgery, the success rate of the PRF group (96%) was much greater than that of the control group (70%), with no statistically important difference on hearing gain between the two groups (28). In 2022, Turhal *et al* found no statistically significant difference between the PRF group and the control one in patients who underwent myringoplasty in terms of graft intake rates and postoperative air-bone gap gains (29).

Kumar *et al* investigated the effectiveness of PRF in 25 patients with small central tympanic membrane perforation. Closure was observed in 23 subjects (92%) and hearing improvement was statistically significant as well (88% air-bone gap closure) (30). In 2020, Shukla *et al* have also investigated the use of PRF in 41 patients with tympanic membrane perforation. All patients underwent surgical repair of their perforation using PRF membrane and the closure rate was 85.4% (31). □

## DISCUSSION

Various types of research describing the use of PRF in ENT surgery were included in the literature review. The majority of those studies assessed the application of PRF in rhinology and otology surgery. Regarding the regeneration of the tympanic membrane following myringoplasty, all investigations have indicated excellent closure rates with the application of PRF. Many of them imply that the use of PRF may minimize the healing time of acute perforations and the incidence of infections in comparison to controls. Some of the selected studies reported the contribution of PRF to tympanoplasty-related hearing improvement. The majority of studies in rhinology have focused on the use of PRF in rhinoplasty. As with other rhinology treatments such as septoplasty and endoscopic sinus surgery, the results appear promising. PRF appears to promote the repair of nasal mucosa and has a good effect on postoperative olfactory function and pain. Few studies have been conducted on the subject of laryngology. However, it appears that PRF may be advantageous for the treatment of vocal cord paralysis and reduces the occurrence of pharyngocutaneous fistula after total laryngectomy by promoting recovery. □

## CONCLUSION

Each article utilized different experimental and control groups as well as different procedures, evaluation methods and follow-up periods. As a result, it is impossible to draw safe conclusions about the value of platelet-rich fibrin in ENT surgery. However, all studies included in the present review indicate that PRF is generally beneficial to the healing process, and no harmful side effects have been reported. Although it appears that PRF is a safe and useful material for use in ENT surgery, additional research is necessary to corroborate this idea. □

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