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Platelet-Rich Fibrin in Oral Surgery and Implantology: A Narrative Review

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Keywords

PRF · Oral surgery · Bone augmentation · Third molar extraction · MRONJ

Abstract

Background: The application of blood concentrates has gained popularity in dentistry in recent years. Platelet-rich fibrin (PRF) has been discussed frequently due to a high content of growth factors and the option of chair-side manufacturing in a simple centrifugation process. PRF is free from adjuvants and inexpensive to produce. The number of studies reporting beneficial effects of PRF in various clinical applications such as alveolar ridge preservation, sinus floor elevation, management and prevention of medical-related osteonecrosis of the jaw, third molar extractions, and guided bone regeneration in dentistry has increased recently. However, to date, neither clinical recommendations nor guidelines are available. The present narrative review aims to summarize the level of evidence on the clinical application of PRF within the field of oral surgery and implantology. ***Summary:*** A literature search in Pubmed and Medline has identified 34 articles as a basis for this narrative review. The effectiveness of the clinical application of PRF has been analyzed for five indications within dentistry: medical-related osteonecrosis of the jaw, wisdom tooth extraction, guided bone regeneration, sinus floor elevation, and alveolar ridge preservation. The amount of data for third molar extractions, socket preservation, and guided bone regeneration is extensive. Less data were available for the use of PRF in combination with sinus floor elevations. There is a lack of studies with scientific evidence on PRF and medical-related osteonecrosis of the jaw; however, studies positively impact patient-related outcome measures. Most studies report on beneficial effects when PRF is additionally applied in intrabony defects. There is no evidence of the positive effects of PRF combined with bone graft materials during sinus floor elevation. However, some benefits are reported with PRF as a sole filling material. ***Key Messages:*** Many recently published studies show the positive clinical impact of PRF. Yet, further research is needed to ensure the validity of the evidence.

Introduction

Blood concentrates have a lengthy history in dentistry and started with fibrin glues. The idea of this product is simple. Blood presence and its contents around the wound have always been the key to proper healing. Thus, establishing a blood clot at surgical sites appears to support natural healing processes [1–3].

The first described autologous platelet product used in dentistry was platelet-rich plasma (PRP) [4, 5]. It is produced in two centrifugation steps, depending on the applied protocol [6]. Platelets get activated by adding throm-

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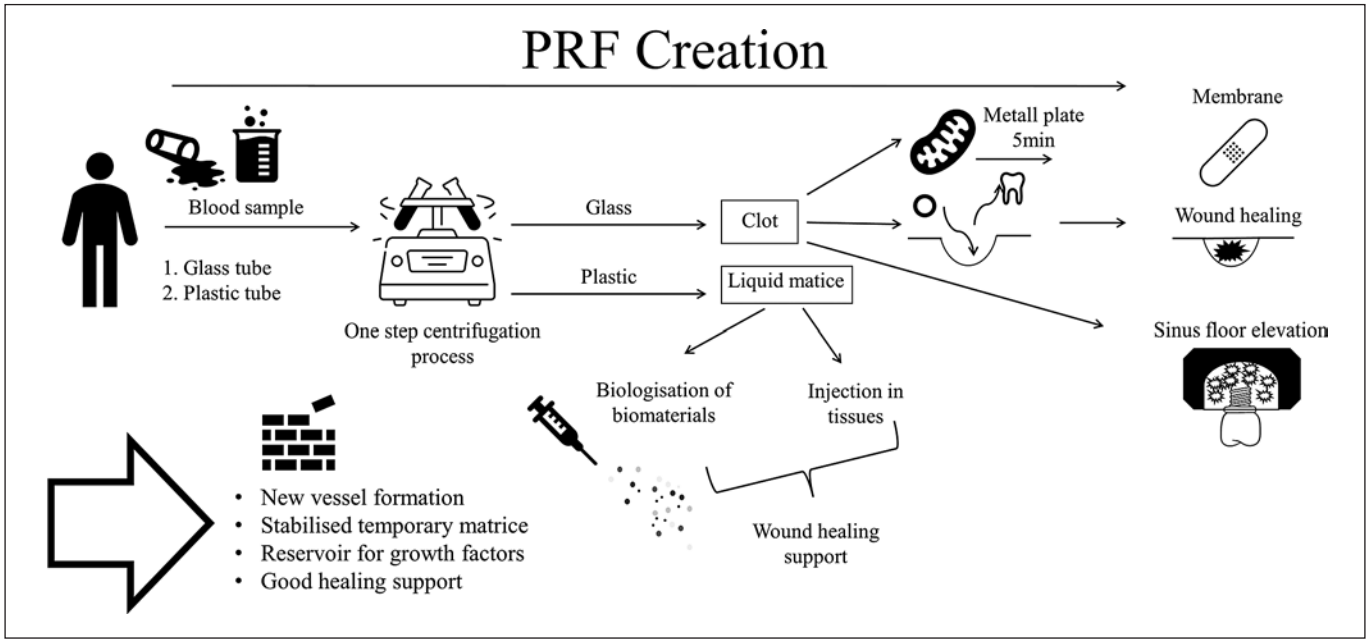

Fig. 1. PRF creation.

bin, usually of bovine descent, as well as calcium chloride or a combination of both. As a result, a liquid substance is fabricated. With certain technologies, its viscosity can be changed [6]. It contains approximately 5 times more platelets than noncentrifuged, natural blood and a variety of key growth factors that accelerate wound healing and tissue remodeling [7]. PRP stimulates certain cells' proliferation and differentiation, such as osteoblasts [4, 8]. It supports healing processes [9] and interacts with physiological processes, especially in the first days after surgeries, to prevent serious complications, like ankylosis [10]. PRP has been considered safe in clinical application with a low-risk of infections and allergies [11]. PRP further allows bleeding management during the treatment of patients with anticoagulant medications [12]. Despite all these positive effects, there are some limitations. In the literature, there are opposing results reported on the effects of PRP, especially on the promotion of bone healing [13–15]. In addition, PRP releases growth factors only once, right when it is applied [2]. Another disadvantage is its preparation, which requires time due to the two-step centrifugation process. As a result, PRP seems rather unlikely to become a routine clinical practice in the future [13].

More than 10 years ago, Choukroun et al. [16] introduced platelet-rich fibrin (PRF). PRF is the first platelet concentrate easily generated in a single-stage centrifugation process free of anticoagulants [17] (see Fig. 1). PRP clots' size is rather small compared to PRF [13]. The matrix of PRF tends to be more penetrable than the one of PRP. This might ease the release of growth factors and other important substances of the wound healing cascade. Also, its permeability for cells simplifies the organization of the wound healing process [1, 3, 18]. There are two consistencies of PRF-solid [19] and liquid [20]. In oral surgery, the solid version of PRF is preferably often and specially used as a membrane, for example, to cover bone substitute in bone augmentation procedures. Membranes can be created by pressing PRF-clots with a plate [21]. With certain centrifugation protocols using glass tubes or silica-coated tubes, PRF forms as a solid clot. Being weighted with a panel PRF turns into a stable membrane used for guided bone regeneration (GBR) procedures in various trials [22, 23]. Further cylindric clots are frequently used for alveolar ridge preservation techniques or as filling material in cyst cavities [23]. Due to the centrifugation process, three fractions are visible: acellular plasma, fibrin, and erythrocytes on the bottom [21]. PRF consists of various blood cells, growth factors, and fibrinogen which play a crucial role in natural healing processes [21, 23]. The cell composition of PRF includes: platelets, lymphocytes, monocytes, neutrophils, and basophiles [24].

The complex process of wound healing can be partitioned into several overlapping phases. After the immediate excess of blood to flush out the wound, the hemostasis and coagulation cascade are initiated. Surrounding vessels contract for a few min and platelets initiate the formation of a clot as a temporary matrix. This active matrix involving fibrin acts as a storage for invading cells. Vessels dilate, leukocytes enter the wound stimulated by activated platelets and their growth factor release. The inflammatory phase is initiated by release of IL-1 and IL-6 [25]. TGF-β1 regulates inflammatory processes and the

synthesis of collagen type III [25–27], and VEGF leads to new blood vessel formation and stabilization. VEGF further supports the proliferation and division of fibroblasts and endothelial cells. New bone formation seems to be enhanced [28, 29]. Neutrophils perform wound cleansing during inflammatory phase by phagocytosis and secretion of proteinases. Monozytes differentiated to macrophages participate in the process of wound debridement and trigger the proliferative phase through the release of TGF-β, PDGF, and VEGF. Additionally, they act as antigen-presenters [25, 30] with the aim of granulation tissue formation; vessels grow in the proliferative phase. Collagen synthesis is aiming to close the wound in the first place and to decrease again as keratinocytes start re-epitheliazation. Finally, collagenases and elastases are released to dissolve intercellular bonds and restore the permeability of the tissue. Dense new formed vascular nets, granulocytes, macrophages, fibroblasts, and collagen bundles are the main components of the granulation tissue developed. During remodeling, collagen type III is exchanged to more robust collagen type I [25].

The PRF-clots head describes the part which is abutted in the red blood cells after the centrifugation process. Along the border, authors describe a high leukocyte content [28].

Complications stimulate the development of new methods. In recent years, the topic of PRF has reached interest in the field of clinical research. The number of published articles in dentistry has grown. Ghanaati et al. have summarized the first 15 years of PRF in a systematic review [31], The quantity of publications and reports on the application of PRF in dental surgery and tissue regeneration has significantly increased and deepened. The number of articles indexed in Pubmed related to the keyword combination "platelet-rich fibrin" AND "oral surgery" has expanded exponentially since 2006 from 8 publications to 125 publications in 2021. However, no clinical recommendations or guidelines for indications and clinical protocols can be extracted. Therefore, the present narrative review aims to give an overview of the current level of evidence on the application of PRF within the field of dentistry and the regeneration of oral tissues.

Main Text

Materials and Methods

Literature search has been conducted via Pubmed and Medline. The following keywords have been used: "PRF" AND "Third molar" OR "SOCKET PRESERVATION" OR "SINUS FLOOR ELEVATION" OR "STICKY BONE" OR "GUIDED BONE REGENERATION" OR "ALVEOLAR RIDGE PRESERVATION" OR "MRONJ."

PICO approach has been applied to verify the current knowledge effect of PRF in oral surgery.

Population

Adult human beings receiving third molar extractions, socket preservation, alveolar ridge preservation, sinus floor elevation, GBR, or a surgical intervention due to osteonecrosis of the jaw.

Intervention

Randomized clinical trial (RCTs)/case series/cohort studies/prospective studies or retrospective studies with additional application of PRF in oral surgery.

Comparison

RCTs/case series/cohort studies/prospective studies or retrospective studies without application of PRF in oral surgery.

Outcome

Healing of soft tissue, healing of hard tissue, the patient-centered outcome such as pain.

Inclusion Criteria

In vivo studies, RCTs, case series, cohort studies, prospective studies, retrospective studies, only studies published between 2018 and 2021. Ghanaati et al. summarized relevant clinical data about PRF in the field of dentistry up to 2017 [31].

Exclusion Criteria

Reviews, animal studies, in vitro studies, studies published in languages other than English (see Fig. 2).

Scientific evidence, according to the US Agency for Healthcare Research and Quality, has been classified (see Table 1).

Third Molar Extractions

The extraction of wisdom teeth is a frequently performed oral surgical intervention potentially causing distress in patients. This may be related to possible postoperative complications such as trismus, pain, and severe swelling, which are usually more frequent than infections, alveolar osteitis, and sensibility disorders [33]. In order to improve patients' postsurgical outcomes in regard to swelling, trismus, and pain, filling the defect with a PRF clot has been described in the literature [34].

Out of 22 articles published since 2018, only eight studies have been selected for this review. This selection is due to the number of patients, follow-up rate, and examination parameters. Studies with at least 20 patients were included. In total, a number of 315 patients were involved in the mentioned articles. Follow-up in the first week to report pain and swelling results up to 6 months to assess bone healing was included. Parameters investigated in the use of PRF for wisdom tooth removals are most likely pain assessment [29, 35–41], level of swelling

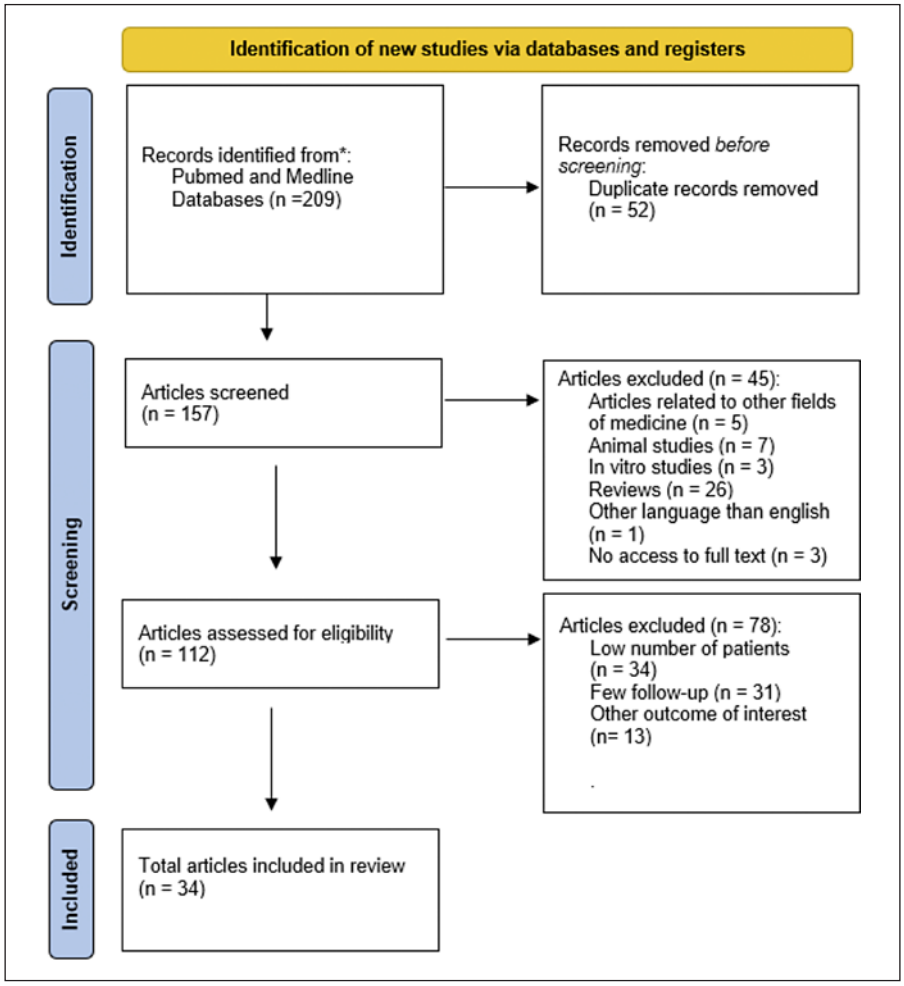

Fig. 2. Adapted after: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71.

Table 1. Level of scientific evidence adjusted according to the US Agency for Healthcare Research and Quality [32]

Level of scientific evidence adjusted according to the US Agency for Healthcare Research and Quality
Ia…. Systematic reviews/Meta-analyses of RCTs
Ib…. A minimum of one RCT
IIa…. A minimum of one controlled study, well-designed, without randomization
IIb…. A minimum of one other type of quasi-experimental study, well-designed
III…. Descriptive studies such as comparative, correlation or case-control studies, nonexperimental, and well-designed
IV…. Repot/opinions from expert committees

[29, 35–37, 39, 41], effect on trismus [29, 41], the incidence of alveolar osteitis [38], soft tissue healing [29, 35, 39–41], and bone healing [29, 35–37, 39–41]. A follow-up to evaluate pain, swelling, trismus has been reported within the first postsurgical week. Incidence of alveolar osteitis and soft tissue healing has been examined in the first 3 months. Evaluation of bone healing has been performed generally after three to 6 months [29, 35–41]. All included studies are designed as split-mouth studies. Lower impacted third molars have been extracted, and in test groups, the alveolus has been filled with PRF, and control sides have been left for conventional healing. Gupta et al. [29] found significantly better results concerning pain, trismus, swelling, and soft tissue healing at day 3 in the PRF group ($p < 0.05$). Several other groups also observed reduced pain in the test group [29, 36–39, 41]. Multiple research teams examined less swelling in the first postsurgical week [36–39, 41]. Only one group, Ritto et al. [40] notified no statistically significant difference between test and control group related to pain and soft tissue healing. Additionally, Gupta et al. [29] showed that bone healing seemed to be influenced positively in the

PRF group significantly ($p < 0.05$) measured radiographically. Five studies confirm these results with similar results [35, 37, 39–41]. In contrast, Sybil et al. [36] reported no statistically significant influence in bone height between the groups. One of the included studies [38] evaluated the presence or absence of alveolar osteitis showing more infectious events in the control groups.

Six studies with scientific evidence type Ib [29, 36–38, 40, 41] and two studies type IIa [35, 39]were taken in account. The extraction of wisdom teeth is a frequently performed intervention in oral surgery. Distinct advantages regarding patient-related outcome measures emerge from the studies listed above. In most of the studies, PRF appears to be a valuable supplement with clinical effect, especially in soft tissue healing [29, 36–39, 41], There are some limitations. Publications with small case numbers predominate in this field. Studies about simultaneous upper and lower third molar extractions would be closer to practical relevance. Additional data reflecting these frequently occurring interventions are still missing.

Alveolar Ridge Preservation

Alveolar ridge preservation techniques are usually performed by filling the extraction socket with autogenous bone or substitute materials. An autogenous or exogenous barrier membrane can be applied to protect the bone graft particles from soft tissue ingrowth and dislocation [42]. Soft tissue closure is recommended in some cases [43]. To ensure the emergence profile around implants and to maintain a natural appearing gingival margin, the preservation of sufficient soft tissue is mandatory. In this field, PRF is used to support the preservation of soft tissues around extracted teeth. At the same time, these surgical interventions are also associated with postoperative discomforts such as pain, swelling, and the risk of inflammation. These could be reduced by the use of PRF [23]. The application in the included studies was performed either with PRF as a sole filling material [44–49] or PRF in combination with bone graft materials and a collagen plug compared to spontaneous healing of the alveolus [49–51]. Eight out of 32 articles dealing with this topic were included in our analysis. Excluded articles had a low number of participants or little follow-up. A total of 294 patients were treated in the studies included. Follow-up is reported up to 6 months.

For this purpose, studied parameters were defined as dimensions of alveolar bone and its changes [44–51], new bone formation [44, 46, 47, 51], pain [49–51], swelling [51], soft tissue healing [48, 49, 51–53]. Follow-up for soft tissue healing was documented in the first postsurgical week [44, 45, 47, 48] and for hard tissue healing between up to 6 months [44–51]. Statistically, significant less reduction in bone dimension using PRF in combination with bone graft material was described in four articles [46, 47, 50, 51]. In addition, improved soft tissue healing due to PRF application could be detected in three included articles [45, 47, 48]. Ahmed et al. compared PRF as a sole filling material to natural healing as well as to PRF in combination with a collagen plug [45]. They found that PRF combined with a collagen plug was superior to socket preservation with PRF alone. These findings were reflected in the examination of bone dimensions [45]. Histomorphometric analyses were carried out by two groups and showed significantly higher percentages of new bone formation after 3 months using PRF as a sole graft material in clinical studies [46, 47]. In contrast, Aravena et al. [44] could not find significant differences in wound healing or bone formation and bone dimension [$p = 0.78$] between socket preservation using PRF as a sole graft material and natural healing. Pain in the first postsurgical week was slightly lower in the group treated with PRF, according to Kumar et al. [49]. Santhanakrishnan et al. and Yewale et al. [50, 51] reported no statistically significant differences in pain values between the groups. No statistically significant differences were observed in the study of Yewale et al. [51] evaluating patients' swelling.

Six studies at a level of evidence Ib [44–46, 49–51] and two studies at a level IIa were included in the analysis [47, 48]. Results on the application of PRF for the indication of alveolar ridge preservation are controversial. In the absence of evidence, no firm recommendation for the use of PRF can be made in this area.

Guided Bone Regeneration

PRF has been used for GBR to treat defects. With this type of intervention, success is particularly dependent on the healing readiness of the surrounding tissue. Inflammatory tissue is removed as thoroughly as possible and, if feasible, a restitutio ad integrum should be aimed for by creating ideal healing conditions. The application of PRF is intended to additionally support the formation of new tissues, both bone and soft tissue. Seven studies out of 31 have been analyzed in detail. Follow-up after 6 months is reported in each of the included studies. In total, 318 patients received treatment with PRF. Parameters examined in the seven studies were probing depth [52–55], clinical attachment loss [52–55], gingival recession [52, 55], bone fill [52–54, 56], bone height [53, 54, 57], percentage of vital bone [58], intrabony component [54], pain, bleeding [56], wound healing, and tooth mobility [53]. Intrabony defects have been treated with a variety of treatment options. Sun et al. [56] compared PRF and bone powder covered with PRF membranes and a flap curettage combined with GBR. Pain evaluation has been reported during 24 h postsurgical; however, bleeding was reported after 7 days. Both parameters were statistically significantly lower in the PRF group. After 60 days and 120 days, degrees of bone defects and bone density have been reexam-

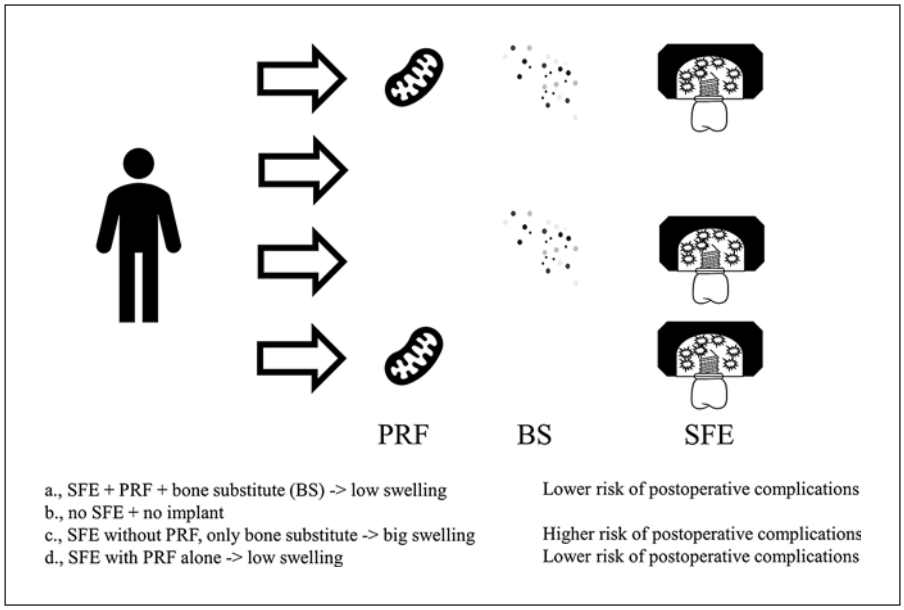

Fig. 3. Sinus floor elevation with and without PRF.

ined. The PRF group had significantly lower values in bone defect measurements ($p < 0.05$) after 60 days. The level of bone density was significantly higher after 60 days as well as after 120 days ($p < 0.001$). The study was carried out in patients with bone defects caused by peri-implantitis [56]. In the split-mouth, designed study of Bodhare et al. [52] bioactive glass has been either combined with PRF or applied as a sole filling material. Three-month follow-up and 6-month follow-up showed a significantly greater clinical attachment level, bone fill, and a reduction in probing depth in the PRF group [52]. Lei et al. [54] have compared three groups. Guided tissue regeneration used PRF, concentrated growth factors [CGF], and a control group treating periodontal intrabony defects. After 6 months, there was no difference in pocket depths, clinical attachment level gain, or bone height between PRF and CGF. However, both PRF and CGF achieved significantly better results concerning intrabony component depth and percentage of bone fill at the defect side than the control group [54]. A histological examination was performed by Hartlev et al. [58] six months after the surgical intervention. The group investigated the percentage of vital respectively nonvital bone and the number of blood vessels.

The test group was treated with autologous bone graft and PRF, the control group with bovine bone and a resorbable collagen membrane. In this article, no statistically significant difference of the examined parameters was found [58]. Similarly, Işik et al. like Hartlev et al. [57] conclude that both bovine bone graft alone and bovine bone graft combined with PRF deliver success used for GBR. Treatment of intrabony defects was compared by Pham et al. trying three different approaches. Open flap debridement combined with PRF, guided tissue regeneration, and open flap debridement alone. Periodontal parameters such as probing depth, clinical attachment level, tooth mobility, and bone defect fill were superior when defects were treated with open flap debridement and PRF, respectively, guided tissue regeneration [53]. Gingival recession defects were handled applying sticky bone, a mixture of bone allograft and liquid PRF, covered with collagen membranes coated with liquid PRF by Kapa et al. [55]. According to the case series, 6 months after the surgical intervention, positive effects in root coverage and increase of gingival thickness were noted [55].

The level of scientific evidence of the studies mentioned was Ib [52, 53, 55, 57, 58] and III [54, 55]. The evidence levels of the cited studies in this field appear to be high. The present studies included indicate potential benefits when using PRF during GBR procedures compared to control groups. However, also for this indication, no clear guideline can be extracted from the literature.

Sinus Floor Elevation

When jawbone loses its function after tooth removal, it recedes. However, a certain height and width of bone is a prerequisite for placing dental implants. Bone height can be reconstructed in the upper jaw using GBR techniques such as sinus floor elevation [59–61]. Sinus floor elevation is usually either performed through a lateral window or transcrestal approach [61, 62]. The cavity between the Schneiderian membrane and the bony sinus floor is usually filled with autogenous bone and or bone substitutes (see Fig. 3). When using a lateral window, the bone substitute is usually covered with a synthetic or xenogenic membrane [63]. In order to facilitate the integration of bone substitute in patients' maxilla, PRF has been used for a biologicalization of bone substitutes.

This review includes only one study in which transcrestal sinus floor elevations were performed [64]. Three other studies with lateral sinus floor elevations were also analyzed [65–67]. One study examined lateral and transalveolar sinus floor elevations [68]. Studies included in this review consider 147 patients in total. Molemans et al. Cho et al. and Barbu et al. [64, 66, 68] used PRF as a sole filling material. Pichotano et al. and Irdem et al. [65, 67] combined PRF with deproteinized freeze-dried bovine bone mineral (DBBM) in the test group, whereas in control groups, SFE was performed with DBBM alone. Cho et al. [64] compared PRF as a sole filling material with saline as a control. The studies of Pichotano et al. Cho et al., and Irdem et al. [65, 67] were designed as split-mouth randomized controlled clinical trials. The case series of Barbu et al. [66] report about large sinus membrane perforation preserved with PRF as a sole filling material and simultaneous implant placement. Molemans et al. [68] did twenty-two transcrestal and six lateral SFE using a prospective, single-cohort study design. Most likely, newly formed bone was measured as a parameter. Histological analysis, radiographs, or Micro-CT were made after three to 12 months [65–68]. Pichotano et al. observed implant survival, as did Cho et al. at a 1-year follow-up [64, 65] and Barbu et al. [66] at a 4-year follow-up. Two groups collected histological samples to detect the amount of vital bone [66, 67], fibrous tissue, and residue from bone graft [69]. PRF as a sole filling material in simultaneous SFE showed clinically integrated implants [68, 70]. A significantly higher intrasinusoidal bone level could be measured using PRF (2.6 ± 1.1 mm) as a sole filling material in comparison to a saline filling (1.7 ± 1.0 mm) ($p < 0.5$) [68]. Pichotano et al. reported statistically significant higher percentages of vital bone in the test group with PRF and DBBM ($p = 0.0087$). The amount of residual graft was higher in the control group with DBBM as a sole filling material ($p = 0.0111$) [71]. Using PRF as a filling material in surgeries with a large perforation of the Schneiderian membrane was tested by Barbu et al. [72]. The case series observed nine complicated sinus floor elevations resulting in successfully osseointegrated implants after 4 years of follow-up [72]. Surprisingly Irdem et al. found no statistically significant difference in none of the investigated parameters. Neither new bone formation was more, nor residual graft amount was lower, in the test group using PRF additionally to DBBM instead of DBBM alone in the control group [69]. The low number of cases may have had an influence on the result.

There are three studies about sinus floor elevation and PRF at a scientific evidence level Ib [68, 69, 71]. One study with scientific evidence level IIa [70] and one study at a level of III were included in this narrative review [72].

The results obtained from the involved studies report controversial data on the application of PRF during sinus floor elevation. However, potential clinical benefit and new pathways in bone augmentation might arise, that have to be confirmed in further investigations.

This applies to both transcrestal and lateral SFE. Especially, the use of PRF combined with bone substitutes and as sole filling material might to be a promising alternative to the use of bone substitute alone [64, 68].

Medication-Related Osteonecrosis of the Jaw

Medication-related osteonecrosis of the jaw is a big challenge in oral surgery. The necrosis usually occurs as a side effect in patients under i.v. or oral antiresorptive therapy to treat osteoporosis and osteoclastic metastasis. This group of patients requires particularly careful treatment. There are great difficulties in mucosal healing. Patients often suffer from dehiscence and exposed bone for weeks after extraction or surgical debridement of necrotic bone. Quality of life can be reduced dramatically, and treatment can be easily accompanied by complications [71]. Since oral surgery may sometimes be necessary during antiresorptive therapy, it is important to support fast and natural healing as much as possible in order to avoid dehiscence and wound healing disorders and necrosis. Covering wounds with PRF membranes might compensate healing disturbances.

To illuminate the effect of PRF used at surgical interventions for the treatment of osteonecrosis of the jaw, six of thirteen studies were reviewed in detail [73–78]. Four studies compared surgical treatment with additional use of PRF and conventional treatment [73–75, 78]. Three studies observed management of preexisting MRONJ using PRF [74, 75, 77]. Overall, 443 patients were observed in the studies mentioned above. Giudice et al. [70] compared a test group adding PRF to the conventional surgical treatment of MRONJ to a control group. Guidice et al. [75] could show that the PRF group had a statistically significant better mucosal integrity, no infection and less pain after 1-month follow-up. However, after 6 months and 1 year, no differences were found. Zelinka et al. concluded a success rate of 85% after 12 months of treating patients with early stages of MRONJ. Early stages are defined as necrosis which could be removed completely [77]. Pain, exposed bone, mucosal closure, and signs of inflammation were defined as outcome parameters. Zelinka et al. [77] assumed additional PRF application in surgical therapy of early stages of MRONJ is effective. Comparing three different treatments, Tenore et al. investigated healing, a transition from higher to lower stage of MRONJ, and persistence of pain and bone exposure. In the test groups, surgery was performed, and antibiotics and PRF were applied. In a second control group, additional photobiomodulation was performed. As a consent of this article, therapy with PRF, surgery, antibiotics, and photobiomodulation via low-level laser therapy (LLLT)

Table 2. Stages of MRONJ after [80]

Stage 0	Non-specific clinical signs such as difference in bone density, tooth mobility without periodontal disease, pain in mandibular, no exposed necrotic bone
Stage 1	Necrotic bone exposed but asymptomatic, no infection
Stage 2	Infected exposed necrotic bone accompanied by symptoms
Stage 3	Infected exposed necrotic bone accompanied by symptoms additionally to severe signs of MROJ such as fracture, extra-oral fistula or extended osteolysis

contribute to the management of MRONJ [74]. Nica et al. described a heterogenous patient cohort consisting of low-risk patients, patients suffering from MRONJ stage zero, and patients suffering MORNJ stage 1–3 for whom an extraction was necessary (see Table 2). Low-risk patients were treated with sutures and LLLT, stage 0 patients took antibiotics, sutures, and LLLT, stage 1–3 patients received a perioperative antibiosis and were treated with piezo-surgery and additional LLLT and PRF were applied at the wound. The study concluded a high rate of success in all groups and a total healing rate of 91.66% in the third group using PRF [73]. Two studies investigated the possible prevention of MRONJ followed by oral surgeries in patients at risk [76, 78]. The study participants received antiresorptive therapy for up to 6 months [73, 74, 78]. Pain [78], exposed bone, mucosal healing, symptoms indicating inflammation were the assessed outcomes [73, 74, 78]. Miranda et al. treated patients under antiresorptive or antiangiogenic agents requiring acute dental extraction. In the control group, extractions were performed carefully and minimally invasive to prevent postoperative complications such as MRONJ. Test group extractions sockets were filled with a PRF plug. In the control group, 19.23% of patients suffered from MRONJ, whereas none of the test group patients developed necrosis [78]. Şahin et al. analyzed 63 dental extractions treated with PRF in 44 patients with a risk of MRONJ. They reported uneventful healing in all cases and success preventing MRONJ after 6 months of follow-up [79].

One study with scientific evidence level Ib was included [75]. One study was at level IIa [77] and four studies at level III [73, 74, 76, 78].

In conclusion, PRF could provide notable improvements for patients suffering from MORNJ. In the presented clinical studies, it seems that the prevention and management of MRONJ could benefit from a PRF application.

Discussion

PRF is created from whole blood samples without additional ingredients [75]. Thus, a low risk of side effects can be assumed. Another advantage is the simplicity of its preparation process [76] and by that the intervention it is not associated with high costs [77]. PRF is applicable as liquid as well as solid matrix [19, 78] and seems to encounter a range of reasonable clinical applications. A variety of different manufacturing protocols have been published in the literature; however, the lack of a standardized protocol creates confusion and difficulty in the comparison of data [31]. Various parameters are required for the definition of a protocol. In the literature, this was often not fully specified, which hindered the reproducibility of study protocols. The different devices and protocols used for PRF-creation seem to have an influence on the quality of the blood product [28]. In particular, the literature suggests that the reduction of centrifugal force has a positive effect on the release of growth factors in vitro [19, 20, 24]. According to the available data on the application of PRF within field of dentistry, the following conclusion seems to be plausible:

A considerable number of RCTs report beneficial outcomes when using PRF in third molar extractions. Focusing on patients' comfort and avoiding complications during postoperative care, supplemental use of PRF could be a valuable treatment option.

Results on the application of PRF for the indication of alveolar ridge preservation are controversial. There is a lack of evidence to make a clear statement for the benefit of PRF in this field of application.

In the prevention and therapeutic management of MRONJ, potential benefits might derive from an application of PRF. However, to date, the degree of scientific evidence is rather low. Larger RCTs are urgently needed to confirm or otherwise reject these preliminary observations since in this area any benefit for the patients seems to be most crucial.

Results on PRF application during sinus floor elevation and GBR are also heterogeneously. PRF might be a promising supplement to bone substitutes or even sole filling material during SFE justifying further clinical investigations. In addition, PRF obviously represents a possibility for managing perforated sinus membranes.

Conclusion

There is a tendency that the available data on PRF in dentistry may have a positive impact on patient-related postoperative outcomes. However, there is a huge heterogeneity of protocols and a lack of guidelines for clinical application for PRF. Further studies are urgently needed to justify the standardized use of PRF within oral surgery.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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