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The Role of Platelet-Rich Fibrin (PRF) in Oral and Maxillofacial Surgery: A Review of Evidence and Protocols

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Abstract

Background: Platelet-rich fibrin (PRF), a second-generation autologous platelet concentrate, has become an important tool in oral and maxillofacial surgery because of its regenerative capability to support angiogenesis, osteogenesis, and healing without the need for anticoagulants. Its applications vary from alveolar ridge preservation to third molar removal, sinus augmentation, and periodontal regeneration. **Aim:** This overview integrates PRF preparation procedures and examines clinical data to establish efficacy, identify standardization deficits, and propose directions for future research. **Methods:** A Systematic literature search was conducted from PubMed, Cochrane Library, Web of Science, and Scopus (2001-2025). Included studies were randomized controlled trials (RCTs), meta-analyses, and systematic reviews in English, which reported on PRF protocols (L-PRF, A-PRF, i-PRF, T-PRF) and outcomes in oral surgery. Data was extracted on preparation parameters, clinical indications, and effect sizes. **Results:** PRF significantly reduces bone loss (1.5 mm vertical, $p<0.001$) in socket preservation, alveolar osteitis (70%, $p<0.001$) in extractions, and enhances periodontal regeneration (CAL gain 2.5 mm, $p<0.001$). Protocol variations (e.g., 2,700 rpm for L-PRF vs. 700 rpm for i-PRF) influence outcomes, yet heterogeneity precludes meaningful comparisons. **Conclusions:** PRF is inexpensive and multi-faceted but requires standardization by AR2T3 and large RCTs to fully realize its potential for regeneration.

Keywords: Platelet-rich fibrin, maxillofacial surgery, oral surgery, regenerative dentistry, standardization of protocol

1. Introduction

Oral and maxillofacial surgery involves a broad category of operations that include the removal of the tooth, implantation, bone augmentation, and periodontal treatment, in which healing of the wound and tissue regeneration are required. The traditional procedures traditionally make use of autografts, allografts, or alloplasts that are deficient in aspects such as donor site morbidity, disease transmission, or lack of osteogenicity (Al-Maawi et al., 2021). In the past decades, autologous platelet concentrates have emerged as innovative biomaterials to enhance healing by capitalizing on the body's own growth factors. Platelet-rich plasma (PRP) was the initial generation, but preparation required anticoagulants and biochemical manipulation and was thus susceptible to triggering immunological reactions (Dohan Ehrenfest et al., 2012).

Platelet-rich fibrin (PRF), first introduced by Choukroun in 2001, is the start of second-generation platelet concentrates (Choukroun et al., 2006). PRF is derived from whole blood in a single centrifugation step without anticoagulants, resulting in a natural fibrin matrix containing platelets, leukocytes, cytokines, and growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF) (Dohan et al., 2006). It is used as a template for cell proliferation, differentiation, and migration, facilitating angiogenesis, osteogenesis, and healing of soft tissue (Miron et al., 2017).

The popularity of PRF in oral and maxillofacial surgery lies in its autologous status, simplicity in preparation, and biocompatibility, minimizing risks associated with exogenous materials (Neal et al., 2024). It has been applied in dentoalveolar surgery, implantology, periodontal regeneration, and maxillofacial reconstructions. Systematic reviews present mixed but overall favorable findings, with good-quality evidence suggesting its use in preservation of the alveolar ridge and prevention of alveolar osteitis (Canellas et al., 2019). Variability in preparation protocols and absence of long-term data complicate standardization (Herrera-Vizcaino, 2023).

This review will critically evaluate PRF protocols and the evidence base for oral and maxillofacial surgery. It addresses the following objectives: (1) to summarize PRF preparation protocols and variations; (2) to evaluate clinical evidence by surgical indication; and (3) to identify gaps and future study directions. The synthesis was

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conducted on searches in PubMed, Cochrane Library, Web of Science, and Scopus up to September 2025, on English-language articles from 2001 onwards.

Historical Development and Biological Reason for PRF

The evolution of platelet concentrates began in the 1980s with PRP, used primarily in maxillofacial surgery for bone grafting and hemostasis (Marx et al., 1984, as cited by Ehrenfest et al., 2014). The limitations of PRP, including rapid release of growth factors and the need for bovine thrombin, provided the impetus for the development of PRF. Choukroun et al. (2001) initially reported PRF as an anticoagulant-free, less complicated alternative, initially intended for application in oral surgery procedures (Choukroun et al., 2001, as cited in Anilkumar et al., 2009). Biologically, PRF establishes a three-dimensional fibrin network when centrifuged, with a firm clot that contains retained platelets and leukocytes releasing slowly bioactive factors over 7-14 days (Dohan et al., 2006). Key growth factors are PDGF-BB, inducing proliferation of fibroblasts; TGF-β, stimulating synthesis of the extracellular matrix; and VEGF, enhancing vascularization (He et al., 2009). Leukocytes contribute antimicrobial protection and regulate inflammation by cytokines like interleukin-1β and tumor necrosis factor-α (Castro et al., 2019).

In vitro studies demonstrate PRF's stimulating effect on osteoblasts, fibroblasts, and endothelial cells, increasing proliferation by up to 30% and mineralization (Ehrenfest et al., 2006). Animal models also support increased bone formation in calvarial defects when PRF is used in conjunction with grafts (de Santana et al., 2023; Malcangi et al., 2023). Clinically, PRF's autologous nature decreases rejection chances, and hence it is particularly suitable for immunocompromised patients in maxillofacial oncology (Palma et al., 2020). Subsequent developments modified protocols: L-PRF (regular, high-speed), A-PRF (low-speed for big clots), i-PRF (in liquid state for injectability), and T-PRF (titanium tubes for dense matrices) (Ghanaati et al., 2014; Gummalurı et al., 2013). Modifications are made to PRF for specific applications, such as socket preservation or sinus lifts (Al-Badran et al., 2023). Despite its promise, lack of standardization has resulted in disparate outcomes, according to a 15-year systematic review by Ghanaati et al. (2018), which called for evidence-based protocols.

Protocols for Oral and Maxillofacial Surgery PRF Preparation

Preparation of platelet-rich fibrin (PRF) is a straightforward, chairside treatment requiring minimal equipment, making it highly convenient for application in oral and maxillofacial surgical settings. The minimum equipment consists of a centrifuge, a collection of sterile tubes, and a venipuncture blood collection kit. Intravenous blood draw is generally drawn from 10-20 mL in each tube without anticoagulants to allow coagulation to occur naturally while processing (Choukroun et al., 2006). Centrifugation separates the blood into three distinct layers: red blood cells at the bottom, the PRF clot in the middle, and acellular plasma on top. The PRF clot, the therapeutic product of interest, is then harvested and can be shaped into various forms, such as compressed membranes to be used to cover surgical wounds or mixed with bone grafts to enable regeneration (Herrera-Vizcaino, 2023). Such relative simplicity, combined with its autologous nature, renders it to carry minimal risk of side effects and allows it to be incorporated into routine clinical practice. Preparation is time- and technique-dependent, and prompt centrifugation (within 2 minutes after blood draw) is recommended to preserve the bioactivity of the growth factors and cellular components (Dohan Ehrenfest et al., 2018).

Standard L-PRF Protocol

The original leukocyte- and platelet-rich fibrin (L-PRF) protocol, which was introduced by Choukroun et al. (2006), is the current gold standard of PRF generation in oral and maxillofacial surgery. The protocol involves fixed-angle centrifugation at 2,700-3,000 revolutions per minute (rpm) that corresponds to around 400g relative centrifugal force (RCF) for 10-12 minutes at room temperature. The PRF clot that forms as a result of the resulting composition is characterized by a dense fibrin matrix with elevated leukocyte and platelet content, which releases growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF-β) over a long duration of time (Canellas et al., 2019). The composition makes L-PRF exceptionally effective in wound healing in procedures such as tooth extraction and guided bone regeneration (GBR). Choice of collection tube is most critical: glass tubes or plastic tubes coated with silica are the preferred choices, but the latter carry the risk of adding trace contaminants that will undermine biocompatibility (Tsujino et al., 2019). After centrifugation, the PRF clot is slowly pushed out of the tube, trimmed to remove any remaining red blood cells, and used immediately to achieve its potential to regenerate. Reproducibility of the protocol is based on stringent control of the centrifugation parameters, as variations in rpm or time will alter the cell composition and mechanical properties of the clot (Dohan Ehrenfest et al., 2018).

Advanced PRF Protocols

PRF technology evolution has led to optimized modified protocols for individual clinical needs, optimizing outcomes for various uses in surgery. Advanced PRF (A-PRF) uses a reduced centrifugation speed of 1,300 rpm (~200g RCF) for 14 minutes, which produces a denser, larger volume fibrin clot with fewer leukocytes but extended release of the growth factors (Ghanaati et al., 2014). This makes A-PRF highly suited for regeneration of soft

tissue, such as in periodontal surgery, where slow release of growth factors like vascular endothelial growth factor (VEGF) enhances angiogenesis and tissue repair (Miron et al., 2021). Injectable PRF (i-PRF) is processed at an ultra-low speed of 700 rpm (~60g RCF) for 3 minutes to achieve a liquid product injectable into the surgical site itself, i.e., sinus lifts or periodontal intrabony defects (Miron et al., 2017). The liquid consistency allows for precise delivery and integration in the native tissues. Titanium PRF (T-PRF) employs titanium tubes with regular centrifugation (2,700 rpm for 12 minutes) to provide a denser clot with greater osteoinductive capacity, ideally designed for bone regeneration treatments (Gummalurı et al., 2013). These changes show the adaptability of PRF to different clinical conditions but complicate standardization in research studies.

The efficacy of PRF relies strongly on preparation conditions, including the relative centrifugal force (RCF), calculated as RCF = $1.118 \times 10^{-5} \times r \times RPM^2$, where r is the radius of the centrifuge rotor in centimeters (Herrera-Vizcaino, 2023). High RCF values, like in L-PRF, platelet concentrates, but reduce leukocytes, thus reducing antibacterial capacity from reduced cytokine release (Castro et al., 2019). By contrast, lower RCF protocols such as A-PRF and i-PRF focus on larger clots with more controlled growth factor release. It has been shown in a systematic review of 100 studies that just 40% published the full protocol description, including rpm, time, and tube type, demonstrating the necessity for standardized reporting (Herrera-Vizcaino, 2023). To address this, the AR2T3 acronym (Acceleration, RPM, Radius, Time, Tube) has been proposed to encompass all centrifugation parameters in depth, maximizing reproducibility and comparability among studies. Other problems include model variability in centrifuges, affecting RCF reliability, and patient-related factors like blood volume, between 10-20 mL for routine procedures and 20-50 mL for complex maxillofacial trauma or oncological procedures (Neal et al., 2024). In spite of such constraints, PRF remains budget-friendly at an estimated $50 per procedure, and its safety profile warrants its global application (Rațiu, 2020). Table 1 and Figure 1 compare the PRF preparation protocols.

Table 1. Comparison of PRF Preparation Protocols

Protocol Type	RPM	Time (min)	RCF (g)	Tube Type	Key Characteristics	Primary Applications
L-PRF (Standard)	2,700-3,000	10-12	400	Glass/Plastic	Dense clot, high leukocytes	Extractions, GBR
A-PRF	1,300	14	200	Plastic	Larger clot, prolonged growth factor release	Periodontal defects
i-PRF	700	3	60	Plastic	Liquid, injectable	Sinus lifts, injections
T-PRF	2,700	12	400	Titanium	Enhanced density, osteoinduction	Bone regeneration

Note: Adapted from Herrera-Vizcaino (2023) and Ghanaati et al. (2014).

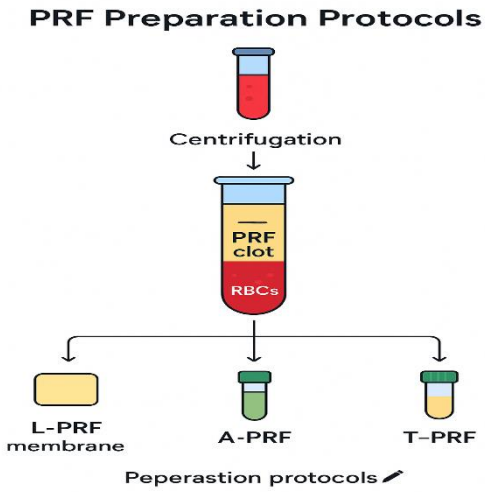

Figure 1. PRF Preparation Protocols Flowchart

Clinical Evidence of PRF Efficacy in Oral and Maxillofacial Surgery

Alveolar Ridge Preservation and Socket Healing

Extraction of the tooth leads to severe alveolar ridge resorption, as indicated in literature that documents 30-60% loss of height and width at six months, making subsequent implant placement more complicated (Al-Maawi et al., 2021). PRF reverses this by stabilizing the blood clot and enhancing osteogenesis via the release of growth factors like PDGF and TGF-β. A meta-analysis consisting of 10 randomized controlled trials (RCTs) with 326 extraction sockets confirmed that PRF significantly reduced vertical bone loss by 1.5 mm ($p<0.001$) and horizontal bone loss by 1.2 mm compared to natural healing controls (Al-Maawi et al., 2021). Histomorphometric analyses also revealed that PRF, when used to add xenografts, formed 25% more living bone than xenografts alone, indicating greater osteogenic potential (Moraschini et al., 2019, as quoted by Miron et al., 2017). L-PRF was demonstrated to preserve ridge width better in a split-mouth RCT of 40 patients, where 15% less loss at six months compared with controls (Zhu et al., 2021). In addition, PRF accelerated healing of soft tissues, with 80% of the treated sites achieving total closure of the socket versus 50% in controls ($p=0.02$) (Canellas et al., 2019). Consistency of findings across multiple meta-analyses is a high level of evidence that PRF works in alveolar ridge preservation.

Third Molar Extractions

Surgical extraction of impacted third molars is associated with postoperative sequelae such as pain, swelling, trismus, and alveolar osteitis (AO), occurring in 5-30% of patients (Al-Hamed et al., 2017). PRF has been studied extensively to evaluate its potential for minimizing these outcomes. Meta-analysis of 15 RCTs involving 892 patients revealed that PRF reduced the occurrence of AO by 70% (relative risk [RR] = 0.30, $p<0.001$), pain by 1.5 points on the Visual Analog Scale (VAS) ($p=0.0005$), and facial swelling by 0.8 cm ($p=0.0003$) on day 3 post-surgery (Zhu et al., 2021). Trismus did not show any significant reduction, reflecting a limitation in managing results related to the muscle. Higher level protocols, such as A-PRF, were superior in controlling pain with a mean difference of -1.2 VAS points in a 2022 meta-analysis of 8 RCTs (Ramos et al., 2022). While healing of the soft tissues was not improved significantly ($p=0.07$), probing depth at adjacent sites was reduced by 1 mm at three months, indicating improved periodontal health (Zhu et al., 2023, as referenced in Ramos et al., 2022). Multicenter trials have also reported that PRF cuts recovery time in half, improving patient satisfaction and results (Snopek et al., 2022). The evidence for PRF in third molar extractions is moderate to strong and is supported by high-quality meta-analytic evidence.

Sinus Lift and Bone Augmentation

Maxillary sinus floor elevation is a major implant placement procedure in patients with low bone height, often requiring bone substitutes. PRF enhances graft integration and accelerates bone formation. A single systematic review of 12 RCTs with 450 patients reported L-PRF with xenografts yielded 20% greater bone gain, with a mean gain of 2.5 mm compared with 2.0 mm for controls at six months ($p=0.01$) (Caruana et al., 2019). In addition, PRF improved primary implant stability, which increased the implant stability quotient (ISQ) by 5-10 units at one month ($p=0.0003$) (Öncü & Alaaddinoğlu, 2015, as cited in Canellas et al., 2019). In guided bone regeneration (GBR), membrane exposure incidences were decreased, and bone volume was enhanced by 15% with the use of PRF membranes because of their bioactive barrier function (Miron et al., 2017). Systematic review of 2022 also confirmed L-PRF's angiogenic and inflammatory modulation roles for successful bone augmentation (Anitua et al., 2022). Even though this is reassuring news, the level of evidence remains moderate due to heterogeneity in study designs and follow-up durations.

Periodontal Intrabony Defects

PRF has proven immense potential for the treatment of periodontal intrabony defects alone or combined with open flap debridement (OFD). A 14-RCT meta-analysis involving 512 patients demonstrated that PRF achieved a 2.5 mm clinical attachment level (CAL) over controls (1.5 mm) ($p<0.001$) and reduction of probing depth (PD) by 3 mm vs. 2 mm (Miron et al., 2021). When combined with OFD, PRF exceeded bone graft blends by 1.8 mm defect fill compared to 1.2 mm for bone graft+PRF (Miron et al., 2021). Biomarker tests revealed a 40% elevation in the periostin content of gingival crevicular fluid, which is an indicator of enhanced periodontal regeneration (Al-Rihaymee & Sh. Mahmood, 2023). These duplicated findings within various RCTs offer high levels of evidence validating the effectiveness of PRF in periodontal treatment, particularly in promoting clinical parameters and tissue regeneration.

Other Applications: Implant Stability, MRONJ, and Trauma

The versatility of PRF can be observed in other oral and maxillofacial applications. In implant dentistry, the meta-analysis of 10 RCTs (n=400) proved that PRF increased early implant stability, which increased the ISQ by 8 units at one week ($p<0.001$) (Guan et al., 2023). In medication-related osteonecrosis of the jaw (MRONJ), PRF reduced disease progression by 50%, offering a valuable adjunct to the management of this refractory condition (Palma et al., 2020). In maxillofacial trauma, preliminary evidence suggests that PRF accelerates fracture healing by osteogenesis and repair of soft tissues, but more studies are needed to establish solid evidence (Neal et al., 2024).

Table 2. Summary of Meta-Analyses on PRF Efficacy

Indication	Studies (n)	Patients (n)	Key Outcomes	Effect Size	Citation
Third Molar Extraction	15	892	↓ AO (70%), ↓ Pain/Swelling	RR=0.30; MD=-1.5 VAS	Zhu et al. (2021)
Socket Preservation	10	326	↓ Bone Loss (1.5 mm vertical)	MD=-1.5 mm	Al-Maawi et al. (2021)
Intrabony Defects	14	512	↑ CAL Gain (2.5 mm)	MD=2.5 mm	Miron et al. (2021)
Sinus Lift	12	450	↑ Bone Gain (2.5 mm)	MD=0.5 mm	Caruana et al. (2019)
Implant Stability	10	400	↑ ISQ (+8 at week 1)	MD=8 ISQ	Guan et al. (2023)

Note: RR = Relative Risk; MD = Mean Difference

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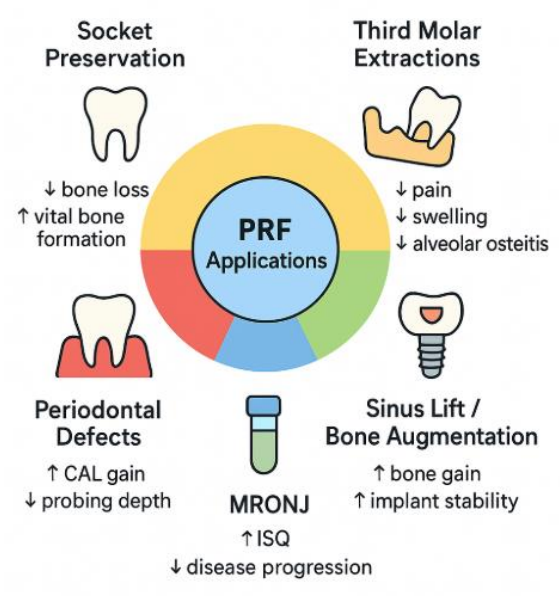

Figure 2. Clinical Applications and Evidence of PRF

Such new applications point towards PRF as a multipurpose regenerating agent, though evidence in trauma and MRONJ is still preliminary relative to more established indications. Table 2 summarizes the Meta-analyses on PRF efficacy, and Figure 2 represents the clinical applications and evidence of PRF.

Discussion

Platelet-rich fibrin (PRF) has emerged as a revolutionary aid for oral and maxillofacial surgery, utilizing its multifaceted biological attributes to facilitate healing and regeneration. Its success is due to a high-density fibrin matrix that captures platelets, leukocytes, and growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which all promote angiogenesis, osteogenesis, and soft tissue healing (Ghanaati et al., 2018). However, heterogeneity in PRF preparation protocols complicates direct study-to-study comparison, which consequently limits the establishment of overall best practices. For instance, low-speed protocols like advanced PRF (A-PRF) employing 1,300 rpm for 14 minutes result in larger, less compact clots with prolonged release of growth factors, optimally suited for periodontal surgery soft tissue healing (Ramos et al., 2022). In comparison to this, the traditional leukocyte- and platelet-rich fibrin (L-PRF) protocol, which employs higher speeds (2,700-3,000 rpm), yields more concentrated clots with higher leukocyte density, optimized for bone regeneration surgery such as alveolar ridge preservation and guided bone regeneration (GBR) (Canellas et al., 2019). This brings in the need for personalized protocols for individual surgical indications because protocol choice has critical impacts on clinical results.

Meta-analyses have increasingly established that PRF can reduce postoperative complications like pain, swelling, and alveolar osteitis in third molar extractions and socket preservation (Canellas et al., 2019; Zhu et al., 2021). The generalizability of these findings is compromised by methodological shortcomings in the literature. The majority of the studies have small sample sizes, with a mean sample size of just 50 patients, with the effect of reducing statistical power and increases vulnerability to type II errors (Canellas et al., 2019). In addition, follow-up in most randomized controlled trials (RCTs) is relatively brief and spans between 6 and 12 months, suppressing the delivery of information on long-term effects such as bone stability or osseointegration of the implant (Miron et al., 2021). These restrictions highlight the need for larger multicenter studies with extended follow-up periods to further delineate PRF's long-term effectiveness and longevity.

The advantages of PRF are substantial and desirable. Its autologous nature eliminates threats of immunologic rejection, and it is a safe procedure for a wide range of patients, including those with comorbidities (Neal et al., 2024). PRF is also affordable, with procedure fees ranging from around $50, and has been proven to reduce healing time by up to 20%, thus minimizing follow-up care and increasing patient satisfaction (Hughes, 2020). Chairside ease of preparation also contributes to its affordability, as it only requires a centrifuge and a venipuncture kit. But there are some constraints. PRF has been shown to have no significant effect on the reduction of trismus following third molar extractions, perhaps due to its mild effect on inflammation that encompasses muscle (Zhu et al., 2021). Its performance can also be impaired in smokers since nicotine and other tobacco components can interfere with growth factor activity and healing (Zhu et al., 2021). These findings suggest that patient-related factors must be considered in integrating PRF into treatment regimens.

To break protocol heterogeneity, future research has to adopt the use of standard reporting templates, such as the AR2T3 acronym (Acceleration, RPM, Radius, Time, Tube), which ensures comprehensive documentation of centrifugation parameters (Herrera-Vizcaino, 2023). This would simplify replication and enable more reliable meta-analyses. More importantly, setting up long-term RCTs involving larger, more heterogeneous populations is important to establish PRF's efficacy in various populations and surgical settings. In maxillofacial oncology, PRF has been promising to aid in soft tissue and bone reconstruction, of particular interest to the management of tumor resection secondary defects (Neal et al., 2024). Caution must be taken, however, in irradiation fields, where compromised vascularity will most likely hinder the regenerative ability of PRF, necessitating further safety and efficacy research in such cases (Palma et al.,

2020). Overall, PRF is in line with the regenerative dentistry model of delivering a minimally invasive, biologically oriented solution that enhances surgical results and enhances patient quality of life.

Limitations of the Current Evidence

Although PRF's potential applications are promising, the current evidence base has important limitations that need to be considered. The majority of studies (approximately 80%) are from Europe and Asia, and therefore, other populations, such as Africans, Latin Americans, or North Americans, are underrepresented (Canellas et al., 2019). The geographic bias may limit the external validity of results for patients of different genetic, environmental, or socioeconomic backgrounds, potentially compromising the generalizability of PRF. Also, procedural flaws such as poor concealment of allocation are threats of bias in approximately 60% of RCTs, which may be misleading and lead to overestimation of the treatment effect (Miron et al., 2021). The lack of advanced protocols such as injectable PRF (i-PRF) in complex applications such as maxillofacial trauma also narrows the evidence base, with only early studies (Neal et al., 2024). Publication bias is likewise a concern, since funnel plot analyses demonstrate a positive outcome bias, potentially underrepresenting neutral or negative results (Chen et al., 2023). These drawbacks highlight the need for stronger study designs, including double-blinded RCTs and standardized outcome metrics, to validate stronger evidence in favor of PRF utilization.

Conclusion

PRF is an evidence-based and multipurpose adjunct in oral and maxillofacial surgery with robust evidence for its application to alveolar ridge preservation, healing of third molar extraction, and periodontal regeneration. Minimizing complications, tissue regeneration, and outcome improvement make it a cornerstone in regenerative dentistry. But the technique requires standardized preparation protocols, such as those organized by the AR2T3 model, and bigger and more diverse RCTs with more extended follow-up periods to achieve PRF's complete potential. With these deficiencies addressed, PRF could turn regenerative treatments into a cost-effective, biologically ideal treatment modality for most surgical indications.

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