

# Effectiveness Of A-Prf, I-Prf And L-Prf In Enhancing Bone Regeneration In Oral And Maxillofacial Surgery : A Systematic Review

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## ABSTRACT

**Background :** Platelet-rich fibrin (PRF) is commonly used in dental surgical procedures. As a second-generation autologous platelet concentrate, PRF plays a crucial role due to its regenerative potential. Nowadays, 3 types of PRF are often used: A-PRF, I-PRF, and L-PRF. This review aims to evaluate the effectiveness of A-PRF, I-PRF, and L-PRF in enhancing bone regeneration and tissue healing within the field of oral and maxillofacial surgery.

**Methods:** A review of scientific articles was conducted using PubMed, Web of Science, and the Cochrane Library. The search was restricted to reviewed articles published between January 1st 2016, and April 30th 2026.

**Results:** Eight RCTs fulfilled the inclusion criteria. Four of eight studies reported that PRF significantly preserved alveolar bone height or volume compared to controls, while three found no macro-dimensional superiority. Crucially, PRF consistently improved early qualitative aspects of bone and accelerated soft tissue healing across the majority of the literature.

**Conclusions:** A-PRF, I-PRF, and L-PRF have demonstrated potential in oral and maxillofacial surgery. However, their ability to preserve long-term macro-structural dimensions remains variable due to significant methodological heterogeneity and an elevated risk of bias in the current literature.

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## INTRODUCTION

Oral and maxillofacial surgical procedures, including tooth extraction, dental implant placement, bone augmentation, and periodontal surgery, depend on effective wound healing and tissue regeneration to achieve successful clinical outcomes. Platelet concentrates, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), have been widely examined in promoting bone regeneration, improving graft integration, and enhancing postoperative healing.<sup>1,2,3</sup>

Platelet-rich fibrin (PRF), introduced by Choukroun in 2001, represents the second generation of autologous platelet concentrates, which is prepared from whole blood using a single centrifugation process. PRF with no anticoagulants produces a three-dimensional fibrin matrix enriched with platelets, leukocytes, cytokines, and numerous growth factors, containing platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF- $\beta$ ), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). This fibrin network serves as a natural scaffold for cell migration, proliferation, and differentiation while providing the sustained release of bioactive molecules that stimulate angiogenesis, osteogenesis, extracellular matrix formation, and soft tissue regeneration.<sup>4,5</sup>

This systematic review focuses particularly on three major PRF formulations: L-PRF, A-PRF, and I-PRF. Advanced platelet-rich fibrin (A-PRF) is acquired from the patient's venous blood without anticoagulants, providing a minimal risk of immune reactions after placement and tissue integration. Injectable platelet-rich fibrin (I-PRF) is a modified platelet concentrate enriched with liquid formulation that can be injected directly into the target area and needs to be applied shortly after centrifugation within approximately 15 minutes, thereby delivering concentrated regenerative cells and bioactive

molecules. I-PRF will rapidly polymerizes into a fibrin clot enriched with blood-derived growth factors, providing a sustained, gradual release of regenerative mediators throughout the healing process.<sup>7,8</sup> Leukocyte and platelet-rich fibrin (L-PRF) is a second-generation platelet concentrate characterized by a natural fibrin matrix formed through centrifugation of whole blood without anticoagulants added or artificial clotting agents. L-PRF exhibits osteoinductive properties by stimulating the migration, proliferation, and activity of various cell types, including osteoblasts, fibroblasts, and dental pulp cells. These biological effects contribute to enhanced angiogenesis, tissue maturation, bone formation, and overall improvement of the wound healing process.<sup>6-9</sup>

Although numerous clinical applications of PRF have been proposed due to its regenerative potential, evidence-based evaluation is necessary to demonstrate reliable clinical effectiveness. Therefore, this systematic review aimed to assess the effectiveness of clinical applications of A-PRF, I-PRF, and L-PRF following oral and maxillofacial surgical procedures, with particular focus on their ability to enhance bone regeneration and wound healing. The objective of this systematic review was to answer the following focused question: To what extent are A-PRF, I-PRF and L-PRF effective in potentially improving hard and soft tissue outcomes after oral and maxillofacial procedures?

## METHODS

The study was registered with the International PROSPERO (Registration Number: CRD420261452013). A systematic search was performed across three major databases: PubMed, the Cochrane Library, and Web of Science, limited to published articles from January 1st 2016, to April 30th 2026. This systematic review was conducted and reported in strict accordance with the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.<sup>10</sup> PRISMA flowchart show in figure 1. The inclusion criteria for this systematic review were defined using the PICOS framework. The population was comprised of humans who required bone regeneration or augmentation procedures in oral and maxillofacial surgery, excluding animal studies. The intervention was A-PRF, I-PRF, and L-PRF application along with information on centrifugation principles. Studies using PRP or other alternative materials were excluded. The comparison with the conventional healing, alternative biomaterials, different approaches, or comparisons among the three PRF types were included. Studies lacking a control group were excluded. The primary outcomes measured were divided into bone dimensional stability (height/width measurement) and bone quality (bone density/bone formation), with tissue healing as the secondary outcome. Studies that evaluated only soft tissue healing outcomes without hard tissue parameters were excluded.

This review considered only randomised controlled trials (RCTs) and controlled clinical trials that employed the specified PRF types (A-PRF, I-PRF, and L-PRF). Case studies, case series, and in vitro studies were excluded.<sup>10</sup> The study selection was carried out independently by two reviewers using the Covidence systematic review platform. Both reviewers screened independently to ensure consistency and reduce bias. Any disagreements during screening or assessment were resolved through discussion with a third reviewer to reach consensus. Data were independently extracted by reviewers using a standardised format, and the third reviewer resolved any differences. The risk of bias (RoB) was assessed using the Cochrane Collaboration's RoB tool (RoB 1). This tool was used to evaluate bias across seven domains:

sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias.

## RESULTS

This systematic review included randomised controlled trials (RCTs) that met the inclusion criteria and evaluated the effectiveness of different generations of platelet-rich fibrin (PRF) in promoting bone regeneration following oral and maxillofacial surgery. Thorough study selection provided the inclusion of relevant, high-quality evidence, and a comprehensive overview of the clinical performance of A-PRF, I-PRF, and L-PRF. Following the predefined eligibility standards, from forty-three studies, only eight met the inclusion criteria for this review (shown in Table 1).

### Interpretation of Findings

- **Bone Dimensional Stability**

A total of 7 studies evaluated the effect of platelet-rich fibrin (PRF) on alveolar bone dimensional stability after tooth extraction.<sup>11-13,15-18</sup> Three studies reported that PRF maintained alveolar bone height and width better than the control group or conventional methods.<sup>15,17,18</sup> Canellas et al. showed that L-PRF significantly reduced buccal bone resorption and increased new bone volume compared to spontaneous healing (p-value <0.05).<sup>15</sup> Furthermore, Konbar et al.<sup>18</sup> reported that the combination of I-PRF with xenograft resulted in the smallest bone height loss after 12 weeks (p-value <0.05), while Huang et al. showed that A-PRF provided comparable results to xenograft in maintaining bone height during sinus floor elevation procedures (p-value >0.05).<sup>17</sup> In contrast, three studies found no significant differences in bone height or width changes between the PRF group and the control group (p-value > 0.05).<sup>11-13</sup>

Meanwhile, the study by Chary et al. did not

evaluate changes in bone dimensions, as it focused primarily on bone quality and insertion torque values.<sup>14</sup>

### • Bone Quality

Six studies assessed bone quality through bone density, bone formation, or histological examination.<sup>11,13-16,18</sup> Two studies showed that PRF use improved bone quality compared to the control group.<sup>14,15,18</sup> Canellas et al. reported a higher percentage of new bone formation in the L-PRF group compared to the control group (p-value < 0.05).<sup>15</sup> Chary et al. also found that implant placement at week 8 after A-PRF application resulted in higher bone quality, as measured by histomorphometry and insertion torque compared to week 6.<sup>14</sup> Similar results were reported by Konbar et al. who showed that the I-PRF and A-PRF groups had higher bone density than the xenograft-only group.<sup>18</sup> Conversely, no significant dissimilarities in bone quality results between the PRF and comparison groups were reported by Amer et al. (2025), Aravena et al. (2021), and Demirok et al. (2024). However, all groups indicated good bone healing.<sup>11,13,16</sup>

### • Wound Healing

Five studies evaluated the wound-healing process following PRF application.<sup>11,12,15,17,18</sup> The majority of studies demonstrated that PRF has positive effects on soft tissue healing, such as reducing postoperative pain, accelerating wound healing, and reducing the risk of complications. Amer et al. reported that the group receiving the combination of ADDG and i-PRF experienced a smaller loss of keratinised tissue width than the control group.<sup>11</sup> Alasqah et al. also showed that PRF significantly reduced pain in the first 24 hours to the third day after extraction.<sup>12</sup> In addition, Konbar et al. reported that all sockets in the i-PRF and A-PRF groups had experienced complete healing by the fourth week, whereas in the

xenograft-only group, only 40% of sockets achieved this condition (p-value < 0.05).<sup>18</sup> On the other hand, Aravena et al. found no significant difference in wound healing between the L-PRF and blood clot groups (p-value > 0.05). At the same time, Demirok et al. reported that L-PRF and photobiomodulation produced similar soft-tissue healing outcomes.<sup>13,16</sup>

### Heterogeneity Across Study

Understanding the results reveals inconsistencies in the data across studies due to diverse methodological approaches to PRF utilisation, including centrifugation protocols, evaluation parameters, additional materials, and control comparators.

The essential distinction between L-PRF centrifugation and A-PRF or I-PRF centrifugation lies in the physics of cell separation.<sup>19</sup> Miron et al. demonstrated that reducing the centrifugal force leads to a significant increase in the leukocyte and platelet number, and stimulates osteoid formation.<sup>20,21</sup> This mechanism directly contributes to the enhanced bone quality and dimensional stability observed in the I-PRF by Konbar et al., in contrast to the insignificant findings by Aravena et al. and Alasqah et al.<sup>12,13,18</sup> However, Canellas et al. found differently, showing L-PRF significantly reduced bone resorption and produced greater volume and quantity of new bone.<sup>15</sup> Despite all of the studies utilising the same centrifugal parameters, the clot architectures were fundamentally affected by the type of tubes. Silica-coated tubes showed favourable trends in clot and growth factor release, as demonstrated by Canellas et al. and Demirok et al., resulting in significant outcomes from the L-PRF group, while Aravena et al. and Alasqah et al. were not using glass-covered tubes for the PRF preparation.<sup>12,13,15,16</sup>

The conflicts among these studies are reflected in their selected evaluation parameters. Specifically, Aravena et al. relied on periapical

radiography to assess linear ridge height and width, alongside superficial 3D scanning to track volumetric changes.<sup>13</sup> Alasqah et al. utilised cone-beam computed tomography (CBCT) exclusively to measure pre- and post-operative changes in ridge dimensions.<sup>12</sup> Conversely, Canellas et al. similarly utilised CBCT for volumetric screening; hence, they also harvested bone specimens for direct histomorphometric analysis to identify bone formation that remained hidden through radiographic and volumetric parameters.<sup>15</sup> Demirok et al. further investigated by implementing digital Fractal Dimension (FD) analysis in ImageJ, which identified internal structural volume shifts and qualitative bony maturation that standard macro-linear measurements failed to detect. The investigation proves that the documented results of L-PRF protocols depend on the investigative metrics employed.<sup>16</sup>

A distinct approach is reported by Chary et al., using A-PRF-assisted healing without a non-PRF comparison in socket healing, and comparing the timing of implant placement by evaluating bone formation; therefore, the observation window itself is a source of heterogeneity across this literature. Even though this study cannot speak to PRF's efficacy relative to unassisted healing, it underscores that grafting timelines may also influence PRF outcomes across studies, since 6-week and 8-week windows do not evaluate the same phase of bone maturation.<sup>14</sup>

Furthermore, Demirok et al. (2024) demonstrated a different approach within a scaffold-free framework, comparing L-PRF directly with photobiomodulation. Far from a failure, standalone L-PRF meets a non-inferiority clinical threshold, matching the hard-tissue outcomes of the alternative modality via its own highly active tissue-remodelling pathway.<sup>16</sup> This approach is also observed in Huang et al. (2025), who assessed the

effectiveness of standalone A-PRF by comparing it with deproteinized bovine bone mineral (DBBM) in sinus floor elevation procedures. Although Huang et al. found no statistically significant difference in bone regeneration between the two groups at 6 and 12 months post-surgery, their results indicate that advanced platelet-rich fibrin can serve as an effective substitute in sinus lift surgeries.<sup>17</sup>

Unlike Huang et al., Konbar et al. documented a high rate of success in bone regeneration utilising A-PRF combined with other materials. This apparent contradiction highlights the critical interpretation of the relationship between the specific surgical application and the addition of graft co-materials. The procedural protocol by Konbar et al. combined A-PRF and I-PRF with a xenograft for socket preservation. This combination fulfils the dual structural and biological requirements for accelerated bone regeneration: the xenograft serves as a rigid, osteoconductive framework, while the PRF serves as a bioactive matrix rich in leukocytes that regulate immune responses, exert anti-infectious effects, and guide matrix remodelling via sustained growth factor release.<sup>17,18,24</sup>

On the other hand, Amer et al. also used I-PRF in combination with an ADDG (autogenous demineralised dentin graft). They found no significant difference compared with the ADDG group alone. ADDG demonstrated radiologic and histologic outcomes equivalent to those of bone grafts, as it alone showed promising osteoinductive properties histologically. Because the ADDG matrix natively provides optimal bone-mimicking signalling molecules, adding liquid I-PRF introduces biochemical redundancy. This local receptor saturation explains why adding I-PRF does not substantially improve macro-dimensional ridge preservation beyond the high baseline already achieved by ADDG alone.<sup>11,18, 25,26,27</sup>

## DISCUSSION

A-PRF has demonstrated favourable clinical outcomes in promoting soft tissue healing and bone regeneration. In addition to its regenerative potential, A-PRF has been shown to reduce postoperative complications following tooth extraction. I-PRF has shown promising clinical benefits in alveolar ridge preservation (ARP), particularly in the esthetic zone. It effectively minimised soft tissue changes by significantly reducing the loss of keratinised tissue width. These results suggest that the primary clinical benefit of I-PRF may lie in preserving soft-tissue architecture rather than in preventing post-extraction bone resorption. L-PRF has also demonstrated beneficial effects on postoperative healing following tooth extraction. Histomorphometric analyses have reported increased numbers of CD34-positive cells and von Willebrand factor expression following L-PRF application, indicating enhanced angiogenesis during socket healing.<sup>9, 28-30</sup>

These findings corroborate and distinctively expand upon the existing secondary literature evaluating PRF. Our conclusion regarding the limited capacity of standalone PRF to preserve alveolar ridge volume aligns closely with the systematic reviews by Castro et al. and Del Fabbro et al., both of which highlighted that while PRF accelerates early soft-tissue closure and enhances radiographic bone density, it fails to completely arrest horizontal and vertical bone resorption without a rigid graft material.<sup>31,32</sup> However, a critical distinction sets the present review apart from historical syntheses by Miron et al. and Stumbras et al., which evaluated platelet-rich fibrin as a monolithic entity or pooled older protocols together.<sup>33,34</sup> By contrast, this review provides a differentiation by isolating the specific structural and biological boundaries of A-PRF, I-PRF, and L-PRF.

While comprehensive reviews frequently included retrospective cohort studies or case series, our strict adherence to randomised controlled trials (RCTs) reflects the elevated standards advocated in Cochrane-aligned oral health overviews. Consequently, by addressing these challenges rather than overlooking them, this review avoids overstating the clinical efficacy of these biomaterials. The study provides clinicians with a more secure, internally valid, and protocol-specific baseline for regenerative oral surgery.<sup>31-35</sup>

### Impact of Risk of Bias on the Evidence

Of the eight included randomised controlled trials (RCTs), seven (87.5%) were assessed as having a high overall risk of bias, with Aravena et al. (2021) being the sole study demonstrating a low risk of bias across all seven evaluated domains, caused by its double-blind, split-mouth design, which facilitated blinding of both participants and assessors despite the surgical nature of the intervention. The predominant factor contributing to the high-risk classification was performance bias: blinding of participants and personnel was rated as high risk in five of the eight trials (Amer et al., Alasqah et al., Demirok et al., Konbar et al., Canellas et al.).<sup>11,12,15,16,18</sup> This issue largely reflects inherent structural limitations in platelet-rich fibrin (PRF) research rather than shortcomings in trial conduct, given that the complicated method attempts to blind the operating clinician in most parallel-arm designs.<sup>17,18</sup> Missing data were rated as low risk in seven of the eight studies; the sole exception, Konbar et al., reflects an unresolved inconsistency between the reported sample size, warranting clarification from the study authors.<sup>18</sup> Collectively, the bias profile indicates that conclusions regarding objective bone regeneration outcomes can be synthesised with moderate confidence, since the domains most significant to outcome data were predominantly low risk across the review.

Confidence in subjective or patient-reported outcomes should be further downgraded owing to the general lack of blinding of participants and personnel. Because the current primary literature is so highly heterogeneous and plagued by high risk of performance bias, a quantitative meta-analysis was not statistically feasible. Therefore, future clinical trials must standardise their evaluation parameters so that future reviews can finally perform a robust pooled meta-analysis. Risk of Bias Assessment show in Table 2.

### Strength and Limitation of the Review

One of the principal strengths of this review is its broad scope, encompassing the A-PRF, I-PRF, and L-PRF across various oral and maxillofacial surgical procedures. This approach enables a comprehensive synthesis of the available evidence and comparison of the regenerative potential of different PRF protocols in diverse clinical settings. Additionally, using the Cochrane Risk of Bias (RoB1) tool added strong methodological rigour, ensuring a highly transparent and critical evaluation of the literature. A limitation of this study is the number of articles that meet the inclusion criteria. This relatively limited number means that the synthesis results cannot yet represent all scientific evidence. Furthermore, methodological differences across studies contributed to heterogeneity in the results, which can influence the interpretation of the findings. Most importantly, the RoB analysis

### CONCLUSION

In conclusion, these findings shared the biological properties of A-PRF, I-PRF, and L-PRF: their fibrin matrices and sustained growth factor release are beneficial for soft tissue healing. A-PRF, I-PRF, and L-PRF have demonstrated potential in bone regeneration following oral and maxillofacial surgery procedures. However, their effects remain less uniform due to significant methodological

highlighted an 87,5% risk of bias. However, because measurement bias and missing data were well-controlled, we can still confidently rely on objective outcomes.

### Implications and Recommendations for Future Research

It is recommended that similar studies be conducted again when the number of scientific publications meeting the inclusion criteria has increased. With more articles meeting the inclusion criteria, future systematic literature reviews are expected to produce more comprehensive and representative evidence. Furthermore, prospective clinical trials must standardise their domain parameters so that forthcoming reviews can finally perform a robust pooled meta-analysis.

Merupakan bagian yang menyajikan esensi hasil penelitian dan analisa statistik yang telah dilakukan. Data yang ditampilkan disajikan menggunakan tabel atau grafik. Narasi data disampaikan dengan singkat dan jelas, tidak direkomendasikan untuk melakukan pengulangan data. Penomoran tabel atau gambar ditulis dengan angka arab dan spasi tunggal. Untuk mencegah terjadinya penurunan kualitas gambar atau tabel, sebaiknya dilampirkan dalam file terpisah (format JPEG min 300 dpi untuk gambar dan format doc atau xls untuk tabel). Contoh format penulisan gambar dan tabel:

heterogeneity and an elevated risk of bias in the current literature, a variability explored further below.

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