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SYSTEMATIC REVIEW

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Does platelet-rich fibrin enhance the outcomes of peri-implant soft tissues? A systematic review

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Abstract

Background Improving soft tissue quality and quantity around dental implants is crucial for successful outcomes. Platelet-Rich Fibrin (PRF) is showing promise in enhancing wound healing and implant stability. This systematic review aims to evaluate the clinical benefits of PRF in soft tissue regeneration around dental implants compared to standard methods.

Methods This systematic review adhered to the PRISMA guidelines and utilizing the PICO methodology, investigated the use of Platelet-Rich Fibrin (PRF) in soft tissue augmentation during implant therapy. The primary outcomes assessed include the width of keratinized mucosa and soft tissue thickness, comparing PRF interventions to standard techniques.The study included randomized controlled trials (RCTs) and comparative studies, focusing on human patients needing implant therapy with or without PRF. An extensive search of databases and manual references was conducted; data extraction involved assessing study quality and risk of bias, but due to high heterogeneity among studies, a meta-analysis was not feasible, leading to a systematic review of the available literature.

Results A total of 766 references were initially identified, with 29 being eligible after screening. Nine studies were included for detailed review. The findings revealed that PRF is effective in increasing the width of keratinized mucosa (KT) and soft tissue thickness (STT) around implants. Even if free gingival grafts (FGG) sometimes performed better. However, the differences between PRF and FGG were not clinically significant, and PRF offers lower cost, ease of use, and reduced morbidity. There was limited information on the esthetic outcomes of PRF, with only two studies addressing this aspect, showing mixed results.

Conclusion Overall, PRF demonstrated positive effects on KT width and STT, but further research with rigorous methodology and larger sample sizes is needed to better understand its impact on implants health and esthetics.

Keywords Platelet-rich fibrin, Dental implants, Systematic review, Soft tissues, Autologous platelets concentrates

Background

It is clinically advisable to ameliorate the quantity and quality of soft tissues at sites of immediate or delayed implant placement [1–3]. In fact, despite the lack of consensus regarding the need for a minimum amount of keratinized tissue around implants, it seems clinically reasonable to aim for well-represented peri-implant mucosa. Additionally, correct management of soft tissues is very important at each surgical entry, whether it be tooth extraction, alveolar bone augmentation, the

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implant placement, or the implant uncovering [4–6]. In recent decades, the *ad modum*Bränemark staged approach has been rapidly overtaken by immediate placement and immediate loading protocols [7–9]. Consequently, there has been a growing number of new surgical-prosthetic approaches aimed at promoting faster bone healing, better soft tissue sealing, and accelerating wound closure.

The local application of growth factors and biological scaffolds is believed to enhance wound healing [10–12]. Various preparations of platelets and respective fibrin-rich matrix (PRF) have gained recognition because they provide a mature clot rich in growth factors and a protective barrier against early mechanical and microbiological insults to the surgical wound [13–16]. PRF is enriched in growth factors like platelet derived growth factor or PDGF and transformation growth factors (TGFs) alpha and beta. The enriched growth factors are released in a sustained manner for a minimum of one week, possibly extending up to 28 days [17, 18].

Platelet-rich fibrin (PRF) is easily prepared from plasma after centrifugation of whole venous blood [19]. Plasma containing platelets undergoes spontaneous coagulation, and like a natural blood clot, activated platelets and white cells become entrapped in the fibrin-rich matrix [20]. PRF can be processed into a PRF membrane or also mixed with grafts and biomaterials to form "sticky bone" [21, 22].

The platelet fibrin plexus is an excellent medium for proliferation as well as migration of cells, thus its regeneration potential has been increasingly investigated in different clinical scenarios. Various authors have demonstrated the efficacy of PRF in aiding bone regeneration within the maxillary sinus, and it appears to be correlated with improved implant stability [23, 24]. The 2018 systematic review by Strauss concluded that there is moderate evidence supporting the clinical benefits of PRF in ridge preservation and in the early phase of osseointegration [25]. Importantly, PRF is strongly associated with positive patient outcomes, such as reduced pain, faster healing, and lower discomfort [26, 27].

The use of PRF has been most extensively investigated in periodontology for the treatment of periodontal intrabony defects and gingival recessions, where most studies have demonstrated favorable results in soft tissue management and repair [28, 29]. It remains unclear whether PRF can improve soft tissue healing around dental implants as well. In their 2017 systematic review on the regenerative properties of PRF, Miron and colleagues highlighted that PRF's reparative potential favors soft tissue formation and ligament regeneration [23]. The authors further recommended discussing the role of PRF in improving implant therapy outcomes.

Therefore, the purpose of the present systematic review is to report the current state of knowledge and clinical potential of PRF in regenerative soft tissue therapy around dental implants when compared to standardized controls from human clinical randomized trials, prospective comparative studies, and controlled clinical trials.

Materials and methods

Protocol development and eligibility criteria

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The review follows the PRISMA guidelines for developing a focus question and defining inclusion and exclusion criteria. The PICOS framework was applied to guide the formulation of the research question:

Population (P)

Description: Humans in need of implant therapy with soft tissue augmentation requirements.
Details: Studies involving adult patients who require or are undergoing implant therapy, specifically where there is a need for augmentation of peri-implant soft tissue, whether due to insufficient tissue quantity or quality, or to enhance esthetic outcomes.

Intervention (I)

Description: Platelet-Rich Fibrin (PRF) as an adjunct for soft tissue enhancement.
Details: PRF used either alone or in combination with other graft materials, applied during soft tissue augmentation techniques associated with implant therapy. Studies utilizing any variation of PRF (e.g., L-PRF, P-PRF, T-PRF, A-PRF) were included.

Comparison (C)

Description: Surgical procedures without the use of PRF.
Details: Comparison to standard soft tissue augmentation methods such as free gingival grafts (FGG), connective tissue grafts (CTG), or no intervention. This also includes cases where soft tissue procedures were performed with the sole use of traditional graft materials or non-PRF biomaterials.

Outcomes (O)

Primary outcomes

Width of KT (KT): Measurement of the increase in keratinized mucosa around the implant site, a crucial factor for implant success and esthetic outcomes. This outcome was assessed in alignment with the STA-COSM (Soft Tissue Augmentation Core Outcome Set for Implant Dentistry) framework, as proposed by Tonetti et al. in 2023 [30]. This framework highlights the importance of KT as a key metric for evaluating the effectiveness of soft tissue augmentation interventions.

Soft Tissue Thickness (STT): Assessment of the increase in soft tissue thickness around the implant site, important for tissue stability and long-term esthetic results. The measurement of STT follows the guidelines established in the STA-COSM, ensuring a standardized approach to evaluating soft tissue augmentation outcomes in implant therapy [30].

Secondary outcomes

Esthetic Outcome: Evaluation of visual improvements in peri-implant soft tissue, including color, contour, and papilla height.

Clinical Significance: Assessment of the practical significance of observed differences between PRF and non-PRF interventions, including long-term implant success and tissue stability.

Cost-Efficiency: Comparison of the cost-effectiveness and ease of use of PRF relative to traditional methods, considering both clinical and economic perspectives.

Morbidity: Evaluation of patient discomfort, complications, and post-operative outcomes associated with PRF versus traditional techniques. This includes measures of pain, healing time, and complication rates.

Study design (S)

Types of studies:

Randomized Controlled Clinical Trials (RCTs): High-quality studies with random assignment of participants.

Comparative Studies: Studies comparing PRF to other techniques or no treatment.

Split-Mouth Studies: Studies where one side of the mouth receives PRF, and the other receives a comparative treatment for within-subject comparisons.

Parallel Arms Studies: Studies where participants are divided into different groups, each receiving different treatments for inter-group comparisons.

Research question

Based on the PICOS framework, the following question was formulated:

Is there any additional benefit of using PRF on soft tissue healing in implant therapy when compared to traditional approaches (such as free gingival grafts or connective tissue grafts)?

Search strategy

An electronic search of three databases (MEDLINE, EMBASE, CENTRAL) was performed. Articles published from December 31, 2017 were considered. An additional hand search was carried out including the bibliographies of the selected papers and collateral papers suggested by the databases.

Search terms

The electronic search strategy included terms related to the intervention and used the following combination of keywords, MeSH and Emtree terms: ((((((((((((((((((((dental implants) OR (tooth implant)) OR (alveolar ridge augmentation)) OR (socket preservation)) OR (tooth extraction)) OR (alveolar ridge preservation)) OR (immediate implant)) OR (postextractive implant)) OR (alveolar process)) OR (soft tissue)) OR (keratinized tissue)) OR (periimplant mucosa)) AND (platelet-rich fibrin)) OR (autologous platelet concentrate)) OR (thrombocyte rich plasma)) OR (leukocyte platelet-rich fibrin)) OR (pure platelet-rich fibrin)) OR (LPRF)) OR (l prf)) OR (advanced platelet-rich fibrin)) OR (APRF)) OR (A-PRF). Cochrane search filters for RCTs and CCTs were implemented, with cohort trials also included. The results were limited to human studies.

Inclusion criteria

Randomized clinical trials (RCT) or controlled clinical trials (CCT) or comparative studies (CS) including at least 10 patients/sites per group.

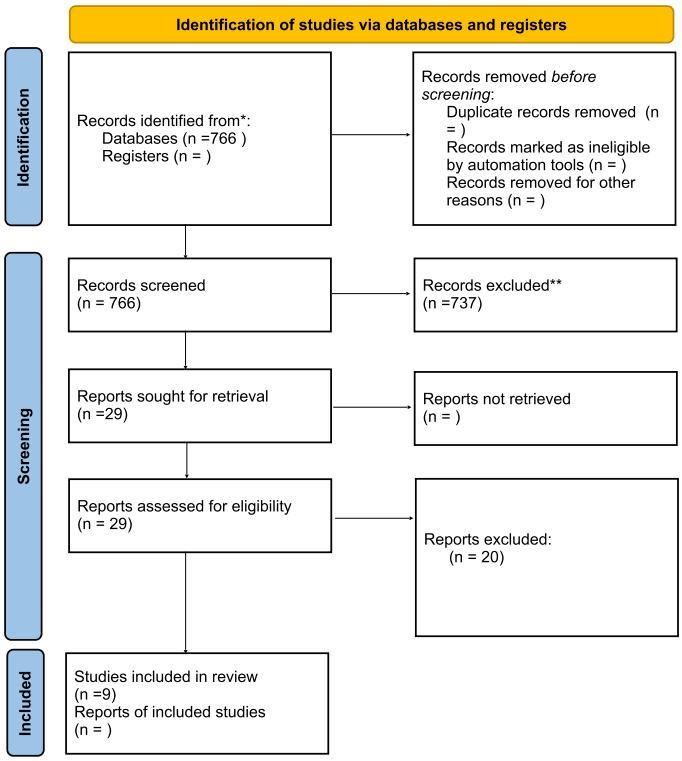
Studies reporting the outcomes of soft tissue healing around dental implants in combination with the use of platelet-rich fibrin. Long term inflammatory parameters were not considered.

Exclusion criteria

In vitro and preclinical studies, cohort studies, case series, case reports, retrospective studies, RCTs or CCTs, with less than 10 patients/sites per group, studies not reporting soft tissue outcomes, and studies not meeting all inclusion criteria.

Data extraction

The search process is shown in Fig. 1. The included studies presented high heterogeneity regarding the timing of PRF usage, outcome measures, PRF preparation, or



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Fig. 1 PRISMA flow-diagram

study duration. Therefore, a meta-analysis was not feasible. Instead, the data are reported in a systematic fashion characterizing all available literature to date. PROSPERO does not accept scoping reviews, literature reviews or mapping reviews, thus this review was not registered.

Screening and selection of studies

Publication records and titles identified by the electronic search and hand search were independently screened by two reviewers (EG and SM) based on the inclusion criteria. Discrepancies were solved by discussion. Cohen's Kappa- coefficient was used as a measure of agreement between the readers. Thereafter, full texts of the selected abstracts were obtained. Where full texts could not be obtained authors and editors of the respective journal were contacted. The two reviewers independently performed the screening process, that is, from the MeSH/Emtree term search through the full-text examination. Then, articles that met the inclusion criteria were processed for data extraction.

Data extraction and quality assessment

The inclusion criteria were applied for data extraction. The studies were classified according to study design and type of intervention. Then, outcomes were compiled in tables. All extracted data were double-checked, and any questions that came up during the screening and the data extraction were discussed among the authors to reach consensus. Two reviewers (EG and SM) independently evaluated the methodological quality of all included studies using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials [31]. All included studies were assessed based on the following criteria: (a) sequence generation, (b) allocation concealment, (c) blinding of participants and personnel, (d) blinding of outcome assessment, (e) incomplete outcome data, (f) selective

reporting, and (g) other potential biases. Any disagreements were resolved through discussion until consensus was reached. Each study was categorized into one of the following groups: low risk of bias if all quality criteria were rated as"present,"moderate risk of bias if one or more key domains were"unclear,"and high risk of bias if one or more key domains were deemed"not present"(Fig. 2).

Results

Selection of studies

The literature search identified 766 potential references in Medline, of which 29 were eligible after title and abstract screening (inter-reviewer agreement $\kappa > 0.90$). Of the 29 full- text articles, 20 articles were excluded based on their lack of controls or appropriate endpoints matching the search criteria. Nine studies did meet the inclusion criteria and therefore were assessed, eight randomized clinical trials and one prospective comparative study. The included studies are summarized in Table 1 [32–40].

The effect of PRF on keratinized mucosa width (KT)

The evaluation of PRF on the keratinized soft tissue regeneration and/or healing has been investigated in eight studies. In all studies, PRF was associated with an increase of the width of peri-implant keratinize tissue, the increase was significantly greater when compared with a negative control group, but smaller when compared with a free gingival graft (FGG). Studies were divided according to the timing of implant placement, either immediate or delayed.

In their split-mouth, randomized, controlled pilot clinical study, Temmerman and colleagues tested L-PRF membranes against a FGG harvested from the palate in eight patients in need for bilateral widening of the KT around implants in the lower jaw presenting less than 2 mm buccal KT [34]. In both groups, a buccal split-thickness flap was raised and repositioned apically in order to receive either PRF or the FGG. The authors set the cut-off from clinical efficacy at ≥ 2 mm gain in buccal KT. The total bucco-lingual width of KT was significantly increased in both groups; the mean gain of KT varied from 6.0 mm ± 0.8 for the test group to 7.3 mm ± 1.2 for the control group, with 1.3 mm ± 0.9 extra gain ($P < 0.05$) for the FGG sites. The mean amount of KT vestibular for the implant at the test site was 3.3 mm ± 0.9 and 3.8 mm ± 1.0 at the control site. Shrinkage of the augmented sites 6 weeks later were slightly higher at the test site (32.1%) than at the control side (23.6%). However, this difference was not statistically significant.

In their split mouth randomized controlled clinical trial, Patnaik and colleagues tested the efficacy of the L-PRF membrane using Sohn's poncho technique over implants placed in the mandibular posterior region in peri-implant mucosal enhancement at second stage surgery [35]. At control sites, a conventional healing abutment was placed. While there was a consistent increase in the width of KT from baseline (2.25 ± 0.44 mm),

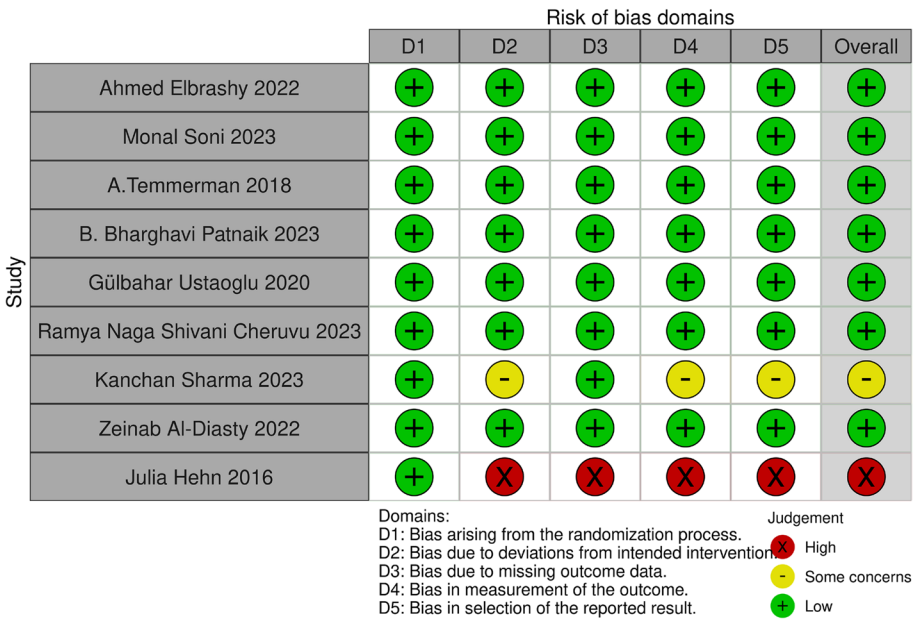


Fig. 2 Plot of the risk of bias domains for each included study

Table 1 Included studies

Author (year)	Study design	Sample size	Test treatment	Control treatment	Follow up	PRF preparation	Outcome measures	Conclusion
Ahmed Elbrashy 2022 [32]	Randomized clinical trial	20	The PRF plug was packed into the buccal gap space the PRF plug was maintained in place with approximating sutures using 4–0 resorbable suture material	Xenograft	6 months	700 RPM for 12 min	Pink esthetic score (PES)	There was no statistically significant difference between control and the test groups
Monal Soni 2023 [33]	Randomized controlled clinical trial	18	The L-PRF membrane was placed to fill the gap between the implant and the socket wall	Natural healing	6 months	2700 RPM for 12 min	Tissue biotype assessment	L-PRF does offer benefits when placed in the extraction sockets for immediate implant placement sites in terms of a thicker tissue biotype
A.Temmerman (2018) [34]	Randomized controlled clinical trial	8	The L-PRF membranes were fixed using resorbable sutures over a superficial, split-thickness flap preparation at the moment of implant uncovering	Free gingival graft	6 weeks	2700 rpm for 12 min	KT, shrinkage of KT	L-PRF can increase the width of KM around implants. Furthermore, the use of LPRF results in a lower surgical time with less postoperative discomfort and pain for the patients in comparison to the FGG
B. Bharghavi Patnaik (2023) [35]	Randomized controlled clinical trial	10	The L-PRF was placed over the surface in the form of a poncho and the rest of the surrounding membrane was tucked in to the surrounding mucosa	Natural healing	6 weeks	NA	KT, thickness of peri-implant mucosa STT (biotype), healing	Sohn's poncho technique in combination with L-PRF has the poten- tial to improve the thickness of peri-implant mucosa and the width of keratinized mucosa around implants
Gülbahar Ustaoglu (2020) [36]	Randomized controlled clinical trial	30	The titanium prepared (T-PRF) membrane was inserted in the prepared mucoperiosteal flap at the facial site and secured with horizontal mattresses	Connective tissue graft	3 months	2,700 rpm for 12 min Titanium PRF	KT, STT	Both groups experienced a greater increase in peri-implant STT at the OAC level, and T-PRF can be considered as an autogenous alternative to CTG

Table 1 (continued)

Author (year)	Study design	Sample size	Test treatment	Control treatment	Follow up	PRF preparation	Outcome measures	Conclusion
Included studies- 2								
Ramya Naga Shivani Cheruvu (2023) [37]	Randomized controlled clinical trial	40	The PRF membrane was placed along with the healing abutment, using the poncho technique to cover the implant	Natural healing	6 months	2,700 rpm for 12 min	width of keratinized tissue (WKT), and the thickness of keratinized tissue (TKT)	The PRF membrane enhances periimplant tissue wound healing, with gains in soft tissue width and thickness around nonsubmerged implants
Kanchan Sharma (2023) [40]	Comparative study	15	PRF membrane in the osteotomy site and over it	Natural healing	9 months	10-min centrifugation at 3000 RPM	Jemt papilla index	Statistically significant differences for the papilla index score at baseline and six and nine months of loading
Zeinab Al-Diasty 2022 [38]	Split mouth randomized clinical study	15	At the moment of implant exposure, a partial thickness flap was reflected and apically displaced to receive either a PRF membrane or a FGG	Free gingival graft	3 months	3,000 rpm for 10 min	KT, graft shrinkage	The Onlay PRF membrane increased the KT width with the advantages of a lower surgical time and less postoperative pain in comparison to the FGG. FGG had a significantly higher ability to augment and increase KT
Julia Hehn 2016 [39]	Randomized controlled clinical trial	31	PRF membrane over a recipient bed created with splitthickness flap	Natural healing	6 months	NA	Tissue thickness	Soft tissue augmentation with PRF performed with a split-flap technique cannot be recommended for thickening thin mucosa

4 weeks (3.52 ± 0.62 mm) to 6 weeks (3.65 ± 0.64 mm) in the test group, there was a slight and non-significant decline from the 4 weeks' to 6 weeks' time point in the control group. The comparative analysis of healing scores between test and control groups led to a significant difference in healing at 1 week and 2 weeks' time points, with L-PRF group denoting faster healing.

Ustaoglu and al compared Titanium-Prepared PRF (T-PRF) versus connective tissue graft (CTG) contextual with implant placement in thin soft tissue areas [36]. Both the CTG and the T-PRF were inserted in the prepared mucoperiosteal flap at the facial site and secured with horizontal mattresses. Comparison of the baseline and 3-month measurements from the 2 groups showed a significant increase in KTW. Compared with the test group, the control group performed better.

Cheruvu et al. reported the outcomes of a randomized controlled clinical trial comparing the effects of PRF around non submerged implants against a negative control [37]. The PRF membrane was placed along with the healing abutment, using the poncho technique to cover the implant. The authors reported a gain in KT w in the test group vs the negative control at 6 months post-op: on average, 1.25 ± 0.67 mm were gained in the test group and 0.59 ± 0.35 mm in the control group.

Zeinab Al-Diasty and colleagues compared the use of PRF versus the FGG during the second stage to increase the amount of KT split-mouth randomized clinical study with fifteen patients [38]. In both groups, a partial thickness flap was reflected and apically displaced to achieve an adequate recipient site. There was a significant increase in KT after 1 and 3 months in both groups. The KT in the FGG group was significantly higher than that in the PRF group after 1 and 3 months and PRF group showed a significantly higher mean shrinkage percentage in the PRF group compared to the FGG group.

In summary, the collected RCTs have demonstrated that the use of PRF leads to significant KT gain around both submerged and non-submerged implants. While free gingival grafts performed better, the difference was not clinically relevant *as per* the a priori success parameters defined by the authors (KT ≥ 2 mm and peri-implant soft tissue health or bone levels). Within 3- to 6-month observation period, the shrinkage of KT in PRF group was higher than FGG group, but eventually became moot thereafter.

The effect of PRF on soft tissue thickness (STT)

The evaluation of PRF on soft tissue thickness has been investigated in six studies. In all studies, PRF was associated with a significant increase of the soft tissue thickness. Only CTG placed under the muco-periosteal flap outperformed PRF, but the difference was not clinically relevant.

The RCCT by Soni and colleagues explored the outcomes of a PRF membrane secured over immediate implants when compared with a negative control [33]. The study included tissue biotype or STT assessment amongst primary outcome measures. The tissue thickness was measured using an endodontic reamer and, on average, PRF group outperformed the negative control group.

Patnaik and colleagues, in their split mouth RCCT exploring outcomes for PRF with Sohn's poncho technique, showed a statistically significant increase in soft tissue thickness at 4 weeks (3.73 ± 0.34 mm vs 2.21 ± 0.37 mm) and 6 weeks (4.20 ± 0.37 mm vs 2.4 ± 0.48 mm) at the buccal site for the test group [35].

In the study by Ustaoglu and colleagues comparing titanium-prepared PRF (T-PRF) and CTG, both groups experienced an increase in peri-implant STT at the crestal level, still, the CTG group achieved better results, but the difference was not significant [36].

In the RCCT by Cheruvu and colleagues on non-submerged implants comparing a PRF poncho over the healing abutment with a negative control, the mean facial STT scores between the 2 groups, significant gains were observed in test group vs control group at 3 and 6 months post-op: on average, 0.97 ± 0.12 mm were gained in the test group and 0.59 ± 0.57 mm in the control group [37]. Thus, compared to natural healing, in the case of non-submerged implants, the use of a PRF poncho led to a double the thickness of facial soft tissues.

In their studies, Hehn and colleagues randomized 31 patients in the lower mandible using a split-flap technique [39]. In the test group, mucosa was treated with a PRF membrane. In the control group, implantation was realized without soft tissue augmentation. Soft tissue augmentation with PRF led to a significant tissue loss. In the test group, the crestal tissue thickness dropped from 2.20 mm ± 0.48 SD at baseline to 0.9 mm ± 1.02 SD at reentry, whereas crestal mucosa in the control group showed higher stability (2.64 mm ± 0.48 SD at baseline to 2.62 mm ± 0.61 SD at reentry). The authors decided to interrupt test group allocations.

In summary, with the exception of Hehn's study, the collected RCTs have demonstrated that the use of PRF leads to a significant increase of soft tissue thickness around implants. While in one study the CTG performed better, the difference was not clinically relevant.

The effect of PRF on the esthetic outcome

Only two studies included the esthetic outcome in the analysis of PRF performance around implants.

In their RCT, Ahmed Elbrashy and colleagues compared the effect of xenograft or PRF to graft the jumping gap in immediate implant placement in the maxillary premolar region [32]. No significant differences in pink esthetic score could be observed by the authors.

In their comparative study, Kanchan Sharma and colleagues compared implant placement with or without the use of PRF as an osteotomy site healing enhancer [40]. The authors reported significant better outcomes for the test group in terms of interdental papilla representation (measured with the Jemt index).

In summary there is little information regarding the effect of PRF on the esthetic outcome of implants. The lack of information seems to be related to lack of reporting from authors.

A graphic summary of the results is presented in Fig. 3 (R version 4.3.2 (2023–10–31) –"Eye Holes").

Discussion

In this systematic review, randomized clinical trials and comparative studies assessing the role of PRF in peri-implant soft tissue healing were analyzed. PRF's performance was compared either to a negative control or to conventional treatments, such as connective tissue grafts and free gingival grafts. The studies revealed considerable heterogeneity in surgical techniques; however, the overall evidence supported PRF's effectiveness in enhancing the amount of keratinized tissue and the thickness of the peri-implant mucosa, which were the primary outcomes of this review. Despite the clear need for further research, PRF shows potential for regenerating and improving soft tissues around dental implants. To our knowledge, this is the first systematic review investigating the benefits of PRF for peri-implant soft tissues.

PRF's ability to enhance soft tissue healing has already been demonstrated in other clinical contexts, such as tooth extractions, management of oro-antral communications, and osteonecrotic lesions of the jaws [41–43]. A recent review evaluated the use of autologous platelet concentrates as adjuvant therapies for the surgical management of medication-related osteonecrosis of the jaws (MRONJ), analyzing 58 articles [44]. Compared to surgical treatment alone, PRP and L-PRF applications appear to improve healing outcomes in MRONJ management.

Despite its versatile and promising results, there is still a lack of consensus on the optimal use of PRF, particularly regarding the type of PRF (P-PRF, L-PRF, A-PRF, T-PRF, H-PRF). Future research should categorize results based on these PRF variants to standardize applications and improve comparative analyses.

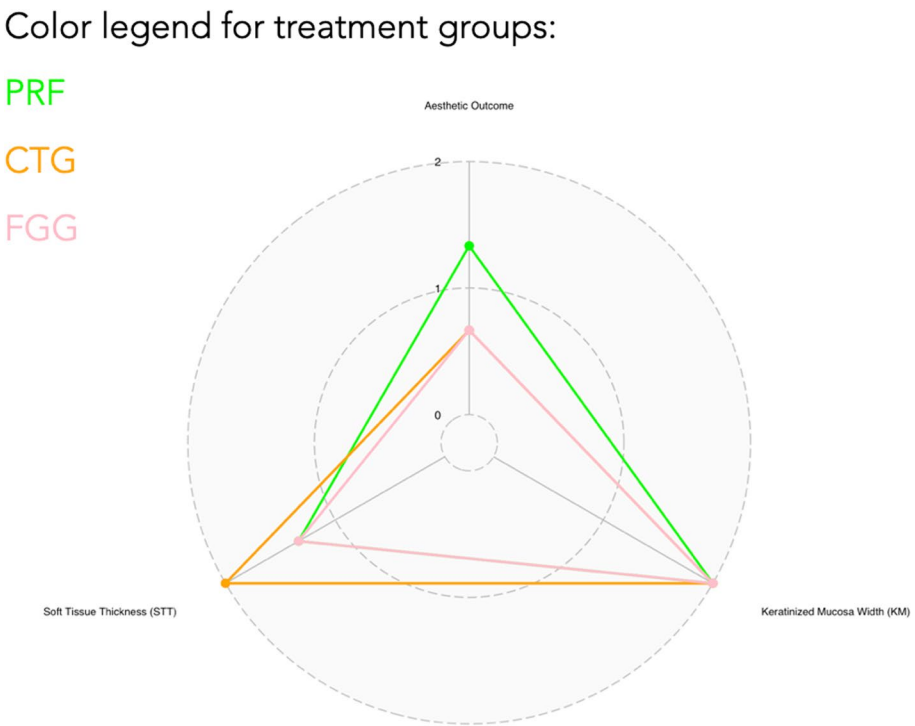


Fig. 3 Radar graphic summary of the systematic review on the effectiveness of PRF against CTG and FGG. Values closer to 2 describe more desirable outcomes. 0: Indicates the least desirable outcome or no observed benefit. 1: Represents an intermediate or moderate level of benefit. 2: Denotes the most desirable or optimal outcome

PRF offers a biotechnological solution capable of releasing growth factors (GFs) essential for tissue repair over time. Recent studies have also explored PRF's potential in cancer treatment. Indirect PRF treatment of tumor cells led to a significant reduction in viable cancer cells, particularly with low-RCF PRF, suggesting potential future applications in localized tumor management [45].

However, the histoconductive properties of PRF and other natural biomaterials warrant critical examination, as they may be ineffective or even inhibitory for keratinized tissue promotion at the implant level. The studies included in the present review consistently demonstrated that PRF significantly increased the width of peri-implant keratinized tissue compared to negative control groups, although the increase was less pronounced when compared to results from free gingival grafts (FGG). The positive effect of PRF was evident regardless of whether implant placement was immediate or delayed.

These clinical outcomes align with numerous proof-of-concept, in vitro, and preclinical studies that have demonstrated PRF's efficacy in enhancing soft tissue regeneration. L-PRF can accelerate wound healing by stimulating fibroblast wound closure in vitro and enhancing fibroblasts'ability to promote endothelial tube formation [46, 47]. It has also been shown to boost cell proliferation in various cells involved in soft tissue repair, stimulate the mitogenic activity of endothelial cells vital for angiogenesis, and release a range of growth factors into the surrounding microenvironment [48, 49]. These growth factors serve as chemotactic agents for various cell types, such as monocytes, fibroblasts, endothelial cells, and stem cells, creating favorable tissue microenvironment and directly influencing the proliferation and differentiation of progenitor cells [50]. This is primarily due to the increased angiogenesis at defect sites, driven by enhanced microvascularization [28]. For this reasons, clinically, L-PRF has been used to protect resorbable barrier membranes in guided bone regeneration (GBR) procedures in cases of flap dehiscence after bone augmentation. Talon et al. reported higher cell adhesion and spreading on expanded polytetrafluoroethylene (e-PTFE) membranes when coated with L-PRF [51]. This is significant for this type of membrane due to the high rate of flap dehiscence or perforation. The same principle applies when L-PRF is used at the palatal donor site after harvesting a free gingival graft or connective tissue graft [52]. Various studies have shown faster wound healing and less postoperative discomfort when applying L-PRF to wounds [53, 54].

It is important to notice that its ease of use, combined with its low cost and low morbidity, and the autologous source, makes PRF an ideal biomaterial for peri-implant soft tissue establishment and enhancement. Thus, studies reporting no differences with the standard comparison, FGG or CTG, are actually testifying the potential of PRF even more, as both FGG and CTG are associated with greater patients' morbidity. Also, the same studies reporting greater outcomes in terms of soft tissue keratinization and thickening in FGG and CTG groups are also disclosing the absence of a real clinical differential between the techniques, as 6 months after surgeries, no patient displayed signs of tissue inflammation or crestal bone loss.

The greater thickening of peri-implant soft tissues with CTG could be related to the significant histoconduction of this biomaterial once implanted in the recipient area [55]. The same could be inferred for tissue keratinization and FGG; nevertheless, studies have been pointing out the ability of PRF to induce keratinization and this phenomenon is consistently reported in the case of second intention healing scenarios [56]. All studies that implemented a PRF membrane versus a negative control denoted better results in terms of both KT and STT. The PRF group also demonstrated faster healing of the wound.

In contradiction with the rest of the studies, the RCT by Hehn and colleagues found that PRF led to significant tissue loss, prompting them to halt PRF allocations due to better stability in the control group [39]. The authors themselves recognized that the possible explanation for their failure relied in the flap design, which was a split thickness flap. It is likely that flap release maneuvers may have masked the final outcome as they are poorly forgiving when compared to a negative control. Also, the PRF membrane might perform better when left exposed and induce granulation tissue formation and cells diapedesis and differentiation [57, 58]. Biological information for tissue thickening is associated with periosteal detachment and following granulation tissue accumulation [59].

While aesthetic outcomes are important, they have not been widely studied in relation to PRF in peri-implant tissues. Future research should prioritize uniformity in aesthetic measurements and follow-up periods to draw more definitive conclusions on PRF's impact on esthetics.

Most authors failed to assess the esthetic outcome, so it is likely that the evidence is already there, but only a few cared to share.

The authors of 2024 Consensus Statements and Recommended Clinical Procedures Regarding Optimizing Esthetic Outcomes in Implant Dentistry made a general observation, that the available data on esthetic outcomes were predominantly represented by case series studies [60]. The authors belief is that given the importance of the prevention of esthetic complications, it is difficult to construct a RCT around a technique that may increase the risk of adverse esthetic outcomes. In the specific case of soft tissue augmentation procedures, the authors conclude that

future research in soft tissue augmentation should focus on standardized outcomes and long-term studies to assess the stability and esthetic impact of various techniques, including innovative materials like PRF. Comparative trials and patient-centered metrics are essential to refine protocols and improve predictability, ensuring optimal esthetic results in implant-supported therapies.

When comparing all the articles included in this review, there were biases related to the study type, patient characteristics, and variations in medical and surgical protocols. These factors can potentially confound the evaluation of treatment outcomes. Typical confounding factors included the type of jaw involved, location of the implant within the jaw, PRF method of preparation, the position of the PRF membrane/plug within the implant site -over it, around it, secured to the flap, in a poncho fashion-). Another confounding factor affecting treatment outcomes, that is the moment for soft tissue augmentation—either at the time of implant insertion or during the second surgical procedure -, was not homogeneous among studies. Factors that may have affected soft tissue outcomes such as the vertical bone height, the number of implants, and muscle hyperactivity (level of muscle attachment) were not considered by most studies.

The present review has a few specific limitations: studies were not categorized based on the type of PRF used. Also, the nine studies differed for the implant placement protocol (immediate post-extraction or delayed), as well as for the implant healing approach (submerged or tissue-level). The heterogeneity of the included studies prevented a meta-analysis of the results for any of the explored soft tissue outcome measures; thus, a quantitative analysis was not feasible. Also, the included studies differed in the type of indexes and success criteria applied, making a comparison difficult.

Future research directions

Standardization of surgical procedures aimed at ameliorating peri-implant soft tissue outcomes with PRF membrane/plug is needed to facilitate clinical implementation of the technique and the comparison between studies. There is need of randomized clinical trials with long follow-up period assessing the soft tissue outcomes of PRF in combination with implant therapy. Future studies on PRF should standardize methodologies to enable meta-analysis. Well-designed randomized clinical trials or prospective case series studies of consecutively enrolled subjects with clearly defined inclusion and exclusion criteria could provide important information to validate surgical procedures and materials associated with PRF preparation and use.

Conclusion

Within the limitation of this systematic review, the following conclusions can be drawn:

1. PRF significantly enhances the width of keratinized mucosa () and soft tissue thickness (STT) around implants compared to negative controls.
2. While PRF shows promising results, free gingival grafts (FGG) often yield slightly better outcomes, though these differences are not clinically significant.
3. Clinically, PRF stands out due to its ease of use, low cost, low morbidity, and autologous nature. Even studies reporting no significant differences between PRF and traditional grafts (e.g., FGG, CTG) emphasize PRF's potential, as traditional methods are associated with higher morbidity. At six months post-surgery, studies revealed no signs of tissue inflammation or crestal bone loss in either group, supporting PRF as a viable alternative.
4. The impact of PRF on esthetic outcomes remains underreported and requires further investigation.
5. Overall, PRF appears to be a beneficial adjunct in soft tissue management for implant therapy, with further research needed to fully elucidate its effects on esthetic results.

Abbreviations

A-PRF	Advanced Platelet-Rich Fibrin
CCT	Controlled Clinical Trials
CTG	Connective Tissue Graft
FGG	Free Gingival Graft
ID-COSM	Implant Dentistry Core Outcome Set and Measurement
KT	Keratinized Tissue
L-PRF	Leukocyte-Platelet-Rich Fibrin
PICO	Population, Intervention, Comparison, Outcome
PICOS	Population, Intervention, Comparison, Outcome, Study Design
PRF	Platelet-Rich Fibrin
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
RCT	Randomized Controlled Trial
RCCT	Randomized Controlled Clinical Trial
STA-COSM	Soft Tissue Augmentation Core Outcome Set for Implant Dentistry
STT	Soft Tissue Thickness
T-PRF	Titanium-Prepared Platelet-Rich Fibrin

Supplementary Information

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Additional file 1

Clinical trial number

Not applicable.

Authors' contributions

EG: Concept/Design, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article, Data collection; NB: Drafting article, Critical revision of article, Approval of article; UC: Drafting article, Critical revision of article, Approval of article; MM: Drafting article, Critical revision of article, Approval of article; PP: Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article; SM: Concept/Design, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article, Data collection.

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Data availability
All the data that supports the findings of this study are available in the cited publications. No new data were generated for this study.

Declarations

Ethics approval and consent to participate
Not applicable.

Competing interests
The authors declare no competing interests.

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