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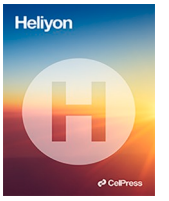

Research article

Clinical application of platelet-rich fibrin to enhance dental implant stability: A systematic review and meta-analysis

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ABSTRACT

Objective: To investigate the effect of platelet-rich fibrin application on implant stability.
Study design: Five databases, namely, PubMed, Embase, Web of Science, Wiley, and China National Knowledge Infrastructure, were searched for reports published up to November 20, 2022. Randomized controlled trials (RCT), including parallel RCTs and split-mouth RCTs, with at least 10 patients/sites were considered for inclusion.
Results: After screening based on the inclusion criteria, ten RCTs were included. Low heterogeneity was observed in study characteristics, outcome variables, and estimation scales ($I^2 = 27.2\%$, $P = 0.19$). The qualitative and meta-analysis results showed that PRF increased the effect of implant stabilizers after implant surgery.
Conclusions: The results of the present systematic review and meta-analysis suggest that PRF can increase implant stability after implant surgery. PRF may also have a role in accelerating bone healing and tends to promote new bone formation at the implant site.

1. Introduction

Implant surgery is a common surgery performed by oral and maxillofacial surgeons. Dental implants are used to support fixed prostheses or removable overdentures for missing teeth. A successful implant is characterized by osseointegration, which is observed as close contact between the bone and the implant [1]. However, there is usually a loss of alveolar ridge height or width at the missing tooth sites, which influences implant osseointegration. Moreover, the quality of bone formation plays a key role in implant stability [2]. Studies have been conducted to enhance implant osseointegration by exploring implant designs, preservation of the host site, modification of surgical techniques or implant surface, loading time, and addition of bioactive materials into the prepared osteotomy site immediately before dental implant fixture insertion [3–6]. In various studies, the use of materials for guiding and promoting bone formation has been suggested as an effective means to enhance the bone quality and volume of implant sites. [7].

A lack of bone in the edentulous alveolar ridge mainly results in increased challenges during dental implant treatments [8,9]. Various bone graft materials are used for ridge preservation and bone graft augmentation to maintain the bone volume of the

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edentulous alveolar ridge at the dental implant insertion site [10]. The most popular materials are xenografts and autografts [11]. Xenografts are subject to cellular rejection, which is similar to that observed with allografts that also possess the risk of disease transmission. Synthetic graft substitutes (e.g., β-calcium phosphate tribasic, deproteinized bovine bone mineral [DBBM], and bone morphogenetic proteins) differ in their osteoinductive or osteogenic properties and are associated with a range of bone formation rates [12]. Moreover, some disadvantages, mainly related to a prolonged healing time and impact on immune responses, can occur when using these materials [12]. The gold standard approach for bone grafting is harvesting autologous cortical and cancellous bones from the iliac crest [13]. However, autografts also present some disadvantages, such as limited sources, additional surgical trauma, postoperative pain, and complications, which limit the clinical applications of autologous bone [14,15].

To overcome these shortcomings, new materials with osteoinductive properties, such as bone morphogenetic proteins, concentrated growth factors (CGF), and platelet-rich fibrin (PRF), have garnered great interest in the field of tissue engineering [16–18]. PRF has been introduced as an additional or replacement material in bone augmentation procedures for guiding bone formation. PRF represents a novel strategy for concentrating platelets (preparation without thrombin), as described by Choukroun et al. [19] In vitro studies have shown that PRF enhances cell proliferation, migration, adhesion, and osteogenic differentiation in a variety of cell types, along with cell signalling activation [20]. Furthermore, PRF reduces inflammation, suppresses osteoclastogenesis, and increases the expression of various growth factors in mesenchymal cells [21,22]. In the field of otolaryngology, a study conducted by Huseyin et al. showed that better results were obtained with the effects of PRF on wound healing in terms of adhesion, infection, bleeding, granulation, and frontal ostium stenosis after endoscopic sinus surgery [23]. In addition, Cieslik-Bielecka et al. introduced the potential application of PRF in esthetic plastic surgery and regenerative medicine for the skin, although PRF is widely used in bone graft surgery, the effectiveness of PRF in increasing implant site or postoperative bone mass and improving implant stability remains controversial [24].

We performed a meta-analysis of clinical standard randomized controlled trials (RCTs) using PRF in bone volume augmentation and dental implant surgeries to evaluate the application value of PRF with respect to bone mass increase, implant stability, and alveolar bone growth.

2. Materials and methods

This study was performed in strict accordance with the Cochrane Handbook for Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [25,26]. In addition, the review methodology was registered with PROSPERO (CRD42021230308).

2.1. Search strategy and information sources

An electronic search of five databases (PubMed, Embase, Web of Science, Wiley, and China National Knowledge Infrastructure [CNKI]) was performed. Articles published up to November 20, 2022, were considered. No time restrictions were applied during the search. The electronic search strategy included terms related to the intervention, and we used the following combination of keywords: "Platelet-rich fibrin (PRF)" AND "dental implants, single-tooth" OR "dental implants" OR "tooth implant" OR "stability" OR "implant stability quotient" OR "alveolar bone regeneration" OR "alveolar ridge augmentation" OR "alveolar bone loss" OR "bone resorption." Cochrane search filters for RCTs were implemented; cohort trials were also included. We reviewed reference lists of included studies to identify additional relevant publications. All search results are imported into the endnote software and duplicates are deleted.

2.2. Eligibility criteria

The inclusion criteria were listed as follows: (a) the article was published in English or Chinese; (b) the article had reported the association between the PRF and dental implants; (c) RCTs, including parallel RCTs and split-mouth RCTs, with at least 10 patients/sites were considered for inclusion. Only approved RCTs that followed an ethics committee guideline were included; d) Only human studies were included; (e) the report was not a review, comment or letter; and (f) full-text articles were available, with no limit to study type.

2.3. Exclusion criteria

In vitro and preclinical studies, cohort studies, case series, case studies, retrospective studies, RCTs involving less than 10 patients/sites, and studies that did not meet all inclusion criteria were excluded.

2.4. Study selection

The publication records and titles retrieved following electronic or manual searches were independently screened by two reviewers (GS and ZXK) based on the inclusion criteria. Discrepancies were resolved by consulting with a third reviewer (NCL). Cohen's kappa coefficient was used as a measure of agreement between readers. Thereafter, full texts of the selected abstracts were obtained. If the full text was not available, then the author and journal editor were contacted to obtain the full text. Two reviewers independently performed the entire screening process. Articles that met the inclusion criteria were processed for data extraction.

2.5. Data extraction and quality assessment

Studies were classified according to study design and type of intervention. The outcomes were then compiled in tables. All extracted data were double-checked, and any questions that arose during the screening and data extraction were discussed between this study's authors to reach a consensus. Two reviewers (GS and ZXK) independently evaluated the methodological quality of all the included studies using the Cochrane Collaboration tool for assessing the risk of bias in randomized trials. All included studies were checked for the following criteria: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcomes, incomplete outcome data, selective reporting, and other biases. Each study was classified into the following groups: low risk of bias if all quality criteria were judged to be met; moderate risk of bias if aspects of one or more of the key criteria mentioned above were unclear; and high risk of bias if one or more key criteria aspects were not met [26].

2.6. Statistical analysis

Statistical analysis was performed using Stata, version 16.0 (StataCorp LLC, College Station, TX, US). Split-mouth and parallel group studies were combined using the generic inverse variance option in the statistical software program. Heterogeneity was assessed using the I^2 statistic (a test for heterogeneity) at the level of $p \geq 0.10$. If there was considerable or substantial heterogeneity ($I^2 > 50\%$), then a random-effects model was adopted; otherwise, a fixed-effects model was used [27]. Treatment effect results are presented as mean differences (MDs) with 95% confidence intervals (CIs). Statistical significance was calculated at $p = 0.05$ (two-tailed z tests). The relative influence of each study on the pooled estimate was assessed by sequentially excluding each study for sensitivity analysis. Publication bias was evaluated based on the visual inspection of the symmetry of the funnel plot and the results of Begg's and Egger's tests ($P < 0.05$ was considered to indicate statistical significance) [28].

3. Results

3.1. Literature search

The literature search identified 390 potential references in PubMed, 376 in Embase, 186 in Web of Science, 486 in Wiley and 71 in CNKI, of which 22 were eligible after screening the title and abstract. Of the 22 full-text articles, 12 studies did not meet the inclusion criteria and were excluded (Table 1). Following selection according to our pre-established protocol, ten RCTs were included in the quantitative meta-analysis [29–38]. The details of the search procedure are presented in Fig. 1.

3.2. Characteristics of the included studies

All ten included RCTs contained a total of 246 patientswith 219 sits in the PRF group and 218 in the control group. Survival rates of implants were available in only 2 of the included studies [31,33] during the follow-up period, and the implant survival rates were 100% for both the PRF and non-PRF groups. One articles reported there was slight postoperative pain and swelling in a few patients [33]. No article reported complications, postoperative bleeding, and Schneiderian membrane perforation, which developed in augmented sinuses during the surgical and healing period. All ten included article analyzed the stability of implants after surgery, and reached different conclusions [29–38].

3.3. Radiographic observation

Tree studies evaluated the postoperative radiography with residual gratf, graft volume and bone volume density [29–31]. One article compared the newly formed bone height of the two groups 6 months after operation, and the results showed that the PRF group was higher than the control group [29]. Pichotano et al. Results showed that there was no differences related to graft volume changes

Table 1
List of excluded full-text papers and reasons for exclusion following full-text screening.

Author and year	Reasons for exclusion
Warisara Ouyyamwongs(2019)	No control group
Temmerman, A(2018)	Not appropriate PRF protocol
Zia Arshad Khan(2017)	Not appropriate PRF protocol
Nejat Nizam(2017)	No control group
Julia Hehn(2016)	No control group
Andy Temmerman(2016)	Not appropriate ISQ
Mahmoud Moussa(2016)	Not appropriate ISQ
Boora, Priyanka(2015)	Not appropriate ISQ
Elton Carlos Pichotano(2018)	CASE Report
Nilüfer Bölükbaşı(2015)	Not appropriate ISQ
Volker Gassling(2013)	Not appropriate ISQ
Kanokporn Areewong DDS(2019)	Not appropriate ISQ

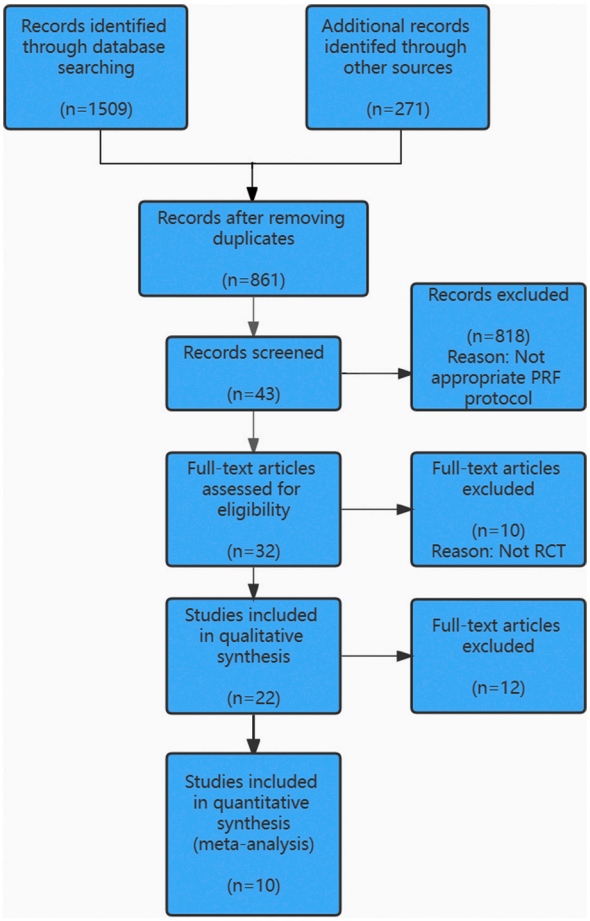

Fig. 1. Flowchart of the study selection process for the meta-analysis
From: Moher D, Liberati A, Tetzlaf J, Altman DG, The PRISMA Group (2009).

between groups immediately after graft placement and after the healing period of 4 and 8 months for the test and control group, respectively [30]. In another article, In another article, bone volume density was compared between PRF group and allograft group after surgery, it was concluded that the bone volume density of allograft group was significantly higher than that of PRF group [31].

3.4. Histological results

Three of 10 included studies reported histological results [30,31,33]. New bone formation was measured in all three articles. One article compared the residual graft material, the percentage of bone graft and fibrous tissue between groups and indicated that the use of PRF reduced the healing period, supporting optimal bone regeneration [31]. The other two study compared the newly formed bone between groups and indicated that there was no significant difference in histomorphology between PRF group and other collagen membrane groups [30,33].

3.5. Analysis of implant stability quotient heterogeneity and model analysis

The implant stability quotient (ISQ) was selected as an important parameter to evaluate the stability of implants in the ten studies (Table 2). We selected the ISQ data of the final experimental and control groups. The results of the heterogeneity test were $I^2 = 27.2\%$ (<50%) and $p = 0.19$ (>0.1), which suggested low heterogeneity among the selected studies. Therefore, a fixed-effects model was used for the meta-analysis. The variables of the studies were continuity variables; therefore, MDs were analyzed using the common-effect inverse-variance model. The MD of the ten studies was 1.96, and the 95% CI was 1.077–2.840($z = 4.355$, $p < 0.05$) (Fig. 2). The results suggested that PRF had increased implant stability after implant surgery. To measure if the heterogeneity of the biomaterials used or the location of implant sites would affect the overall effect, we performed subgroup analyses according to different biomaterials and implant sites.

Table 2
Included studies: implant stability quotient (ISQ).

Study(year), Funding	Studydesign, duration	No.of patients (implants)	PRF preparation	Group T: test C:control	Outcome
R.Tabrizi(2018) International Journal of Oral and Maxillofacial Surgery	RCT, split-mouth 6 weeks	20 (40implants)	2800 rpm for 12 min Hardware	T:PRF n = 20 No PRF n = 20	At 2 weeks after insertion, the mean ISQ was 60.60 ± 3.42 in group 1 and 58.25 ± 3.64 in group 2. There was a statistically signifiificant difference between the two groups (P = 0.04). At 4 weeks after insertion, the mean ISQ was 70.30 ± 3.36 in group 1 and 67.15 ± 4.33 in group 2. Analysis of the data demonstrated a signifiificant difference between the two groups at this time point (P = 0.014). The mean ISQ was 78.45 ± 3.36 in group 1 and 76.15 ± 2.94 in group 2 at 6 weeks afterinsertion. Assessment of the data showed a signifiificant difference between group 1 and group 2 at this time point (P = 0.027)
Elif Öncü(2017) Periodontics Restorative Dentistry	RCT, split-mouth 1 year	26 (60implants)	2700 rpm for 12 min Hardware PRF membranes	T:PRF n = 30 C:No PRF n = 30	T: t0:26.10 ± 12.83 t1:54.39 ± 15.88 t2:69.99 ± 11.87 t3:71.19 ± 10.31; C: t0:24.61 ± 11.97 t1:48.67 ± 13.61 t2:61.03 ± 12.02 t3:70.08 ± 11.2
Elton Carlo Pichotano(2018) Journal of Oral Implantology	RCT, split-mouth 8 months	12 (38implants)	10 min at 300 g (3000 rpm)	T:PRF n = 19 C:No PRF n = 19	3.group showed statistically higher ISQ values compared to the test group (75.13 ± 5.69; and 60.90 ± 9.35 for the control and test group, respectively). This outcome might be attributed to the difference in the healing time between both groups. According to a previous study,31 ISQ values after sinus augmentation utilizing L-PRF progressively increase over time, meaning that the time for implant healing play a crucial role for increased secondary implant stability. This was confirmed in our studies because the ISQ values at loading demonstrated a significant increase in the test group compared to the initial value immediately at implant placement (60.90 ± 9.35 and 76.08 ± 5.86).T:P = 0.0014 C:P = 0.9927
Elif Öncü(2015) The International journal of oral & maxillofacial implants	RCT, 1 months	20 (64implants)	2700 rpm for 12 min	T:PRF n = 31 C:No PRF n = 33	T: t0:59.39 ± 15.88 t1:69.29 ± 10.51 t2:77.19 ± 6.06 C: t0:62.67 ± 13.61 t1:60.03 ± 12.2 t2:70.49 ± 7.74 P1 = 0.002 P2 = 0.001
XIE Hui(2018) Shanghai Journal of Stomatology	RCT, 1 year	46(46 implants)	700 rpm for 3min	NR	T: t0 = 50.68 ± 5.17 t1 = 72.31 ± 5.06 C: t0 = 72.31 ± 5.06 t1 = 73.98 ± 5.38 t0 = 4 months t1 = 6 months P1=(P < 0.05) , P2=(P > 0.05)(4 months/6months)
C. Diana, S.Mohanty(2018) International Journal of Oral and Maxillofacial Surgery	RCT, 1 year	29 (41 implant)	2700 rpm for 12min	T:PRF n = 21 C:No PRF n = 20	T: t0 = 56.58 ± 18.81 t1:60.61 ± 11.49 C: t0 = 71.32 ± 7.82 t1:70.06 ± 8.69
Ebru Olgun(2018) Journal of Investigative and Clinical Dentistry	RCT, 6 months	18 (37 implants)	2800 rpm for 12min	T:PRF n = 10 C:No PRF n = 8	T:68.50 ± 8.87 C:66.37 ± 8.31 P = 0.611
Ali H. Abbas Alhussaini (2019) The Journal of Craniofacial Surgery	RCT, 12 weeks	32(102 implants)	3000 rpm for 12 min	T:PRF n = 27 C:No PRF n = 51	No significant statistical difference existed in primary implant stability between the groups (P = 0.054). An improvement in implant stability was observed in the PRF group(ISQ = 71.0 ± 7.3) compared with control group(ISQ = 67.2 ± 8.2) 6 weeks after implant insertion. After 12 weeks, implant stability was further enhanced in the PRF group (ISQ = 74.5 ± 8.1) compared with control group(ISQ = 70.8 ± 8.3).
Romesh Soni(2020) National Journal of Maxillofacial Surgery	RCT, 4 months	16(16 implants)	1300 rpm for 8 min	T:PRF n = 8 C: No PRF n = 8	PRF membrane group's average ISQ ranged from 38.5 to 61 (mean = 43.06,SD = 7.41) at baseline and ranged 66.5–71.5(mean = 69.12,SD = 1.78) at second-stage surgery. Collagen membrane group's average ISQ ranged from 34.5 to 40.5 (mean = 41.68, SD = 7.2) at baseline and ranged 65.5–71.5(mean = 68.56,SD = 1.52) at second-stage surgery.
		21(60implants)			

(*continued on next page*)

Table 2 (*continued*)

Study(year), Funding	Studydesign, duration	No.of patients (implants)	PRF preparation	Group T: test C:control	Outcome
Kapoor A(2022) Journal of Indian Society of Periodontology	RCT, 1 months		3000 rpm for 10 min	T:PRF n = 30 C:No PRF n = 30	There was a statistically significant difference seen for values between two groups ($P < 0.05$) with higher ISQ values in Group 1, 59.56 ± 4.51, than Group 2, 57.12 ± 3.82 at 1 month.

Note. RCT, randomized controlled clinical trial; SD, standard deviation; NR, not reported; w/wo, with or without; wo, without; SS, statistical significant difference; NS, no statistical difference; ISQ, Implant stability quotient.

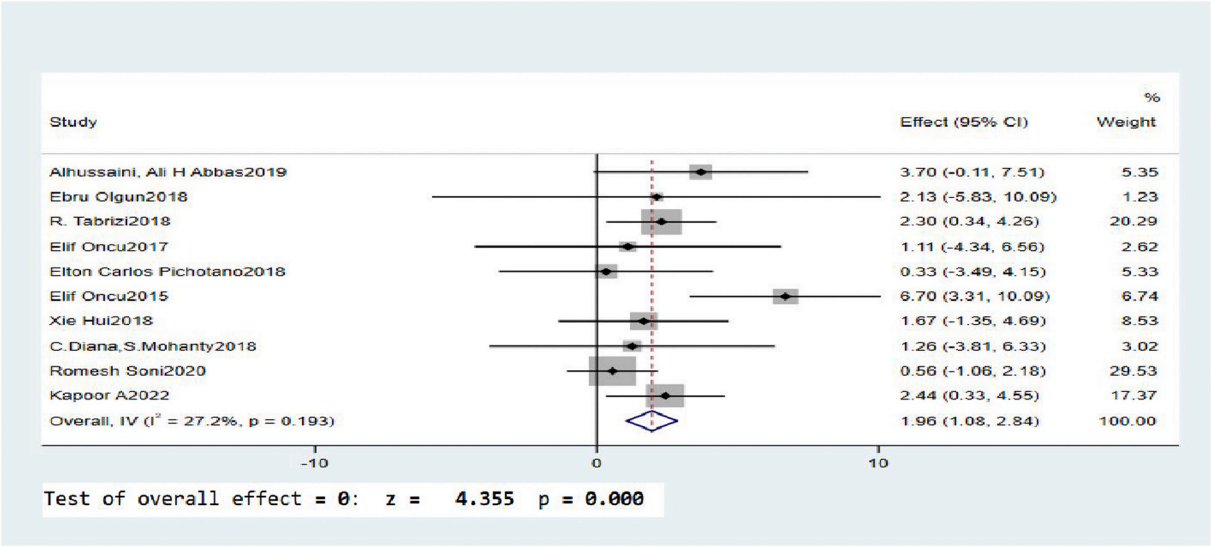

Fig. 2. Forest plot of studies on implant stability quotient (ISQ) of each group.
This was statistically analyzed in 10 articles and included in the study for heterogeneity analysis.

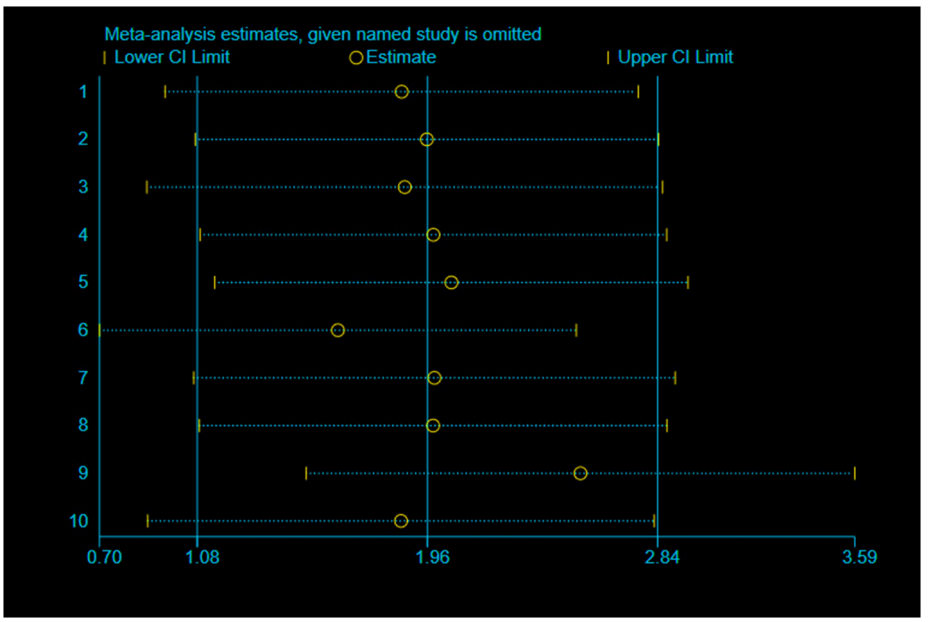

Fig. 3. Sensitivity analysis in the included studies: implant stability quotient (ISQ).

3.6. Migration analysis

We constructed funnel graphs to investigate whether there was a publication offset in this study. The symmetry test of the abovementioned image was carried out. We obtained $p > 0.05$, indicating that the funnel diagram was symmetrical and that there was no publication offset in this study.indicating that funnel plot was symmetric and unbiased.

3.7. Sensitivity analysis

None of the ten articles significantly interfered with the structure of the sensitivity meta-analysis. This indicates that our study has good stability (Fig. 3).

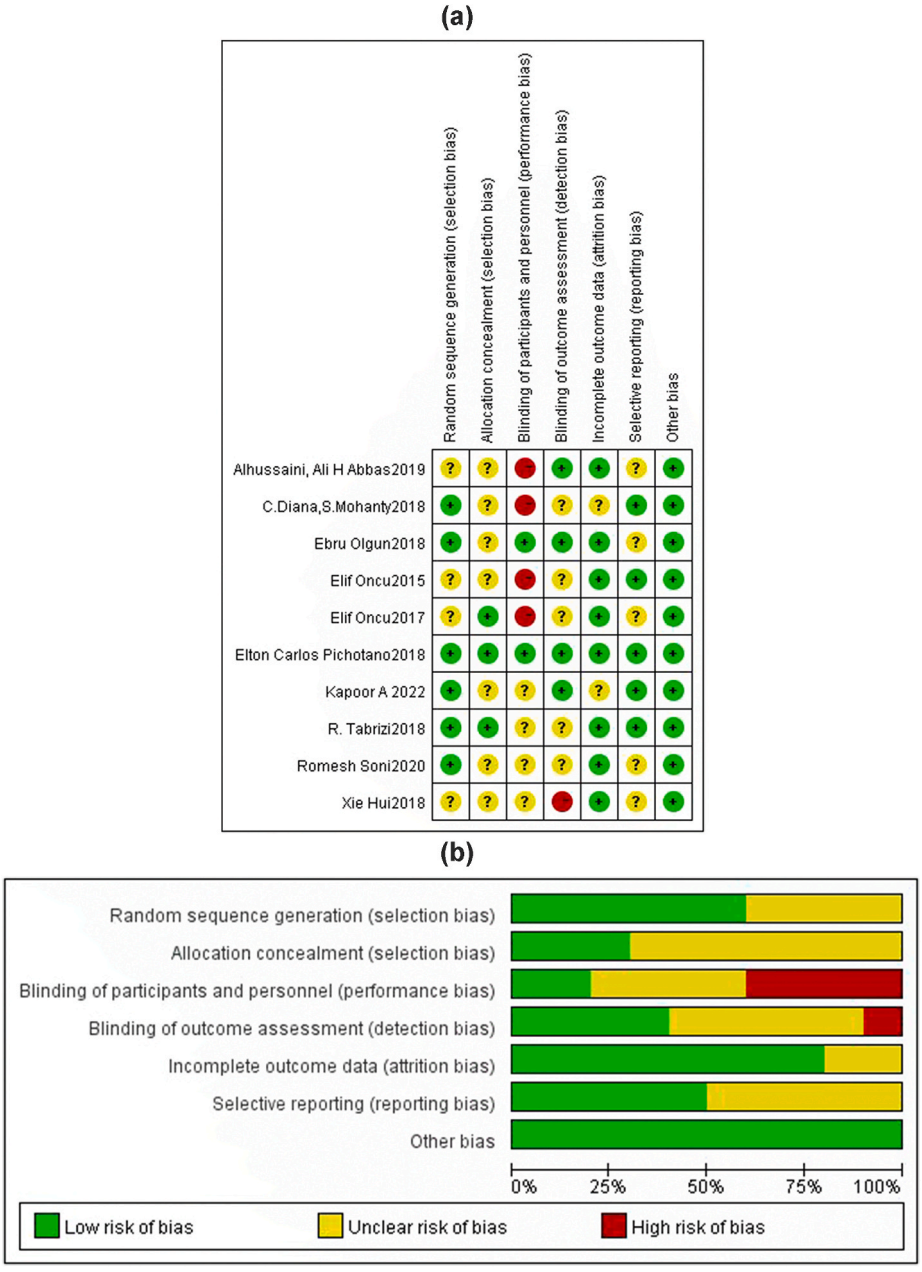

Fig. 4. Risk of bias assessment in the randomized trials included in the meta-analysis. a: Risk of bias summary; b: Risk of bias graph. Symbols. (+): low risk of bias; (?): unclear risk of bias; (−): high risk of bias.

3.8. Bias assessment

The ten studies were also assessed qualitatively using the tools recommended by the Cochrane Collaboration for the risk of bias. A graph and summary of the selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases identified in each study are presented in Fig. 4a and b. With fewer than 10 studies, publication bias was not formally assessed because the power to detect publication bias was limited.

4. Discussion

The present systematic review analyzed RCTs using PRF in implant dentistry, focusing on aspects including ISQ, implant sites, sinus floor augmentation, and biomaterial implants. The present study aimed to evaluate the current literature with regard to the clinical indications for PRF in increasing the stability of dental implants [39].

PRF has gained tremendous attention in recent years because of its capacity to successfully regenerate both soft and hard tissues, enhancing new blood vessels (angiogenesis) and tissue formation during healing [40]. In clinical applications, PRF has been used in the treatment of periodontal defects, sinus floor elevation, and preservation of the alveolar ridge after tooth extraction [30–32,41,42]. Clinical studies have shown that PRF enhances osseointegration in the early phase [43] and increases the width of the keratinized mucosa around implants [44]. However, the clinical value of PRF placement at implant sites to improve the survival rate of dental implants remains unclear, especially when compared to the other types of implanted biomaterials. The objective of this systematic review and meta-analysis was to evaluate which indications of PRF have been shown to be effective in dental implant procedures. Mechanistically, previous studies have revealed the roles of PRF in providing biocompatible scaffolds, continuously releasing cytokines and growth factors, and containing beneficial cell populations for tissue formation and osteogenesis [45,46]. PRF is a fibrin network containing nanoscale fibres that can act as a scaffold for cell proliferation, migration, and differentiation [47]. PRF also acts as a drug delivery system for growth factors, leading to the promotion of neoangiogenesis [47]. This may facilitate early bone-healing processes.

Our results show that PRF is effective in improving the stability of dental implants [29–38]. Resonance frequency analysis (RFA) was used as the standard to measure implant stability in eight of the ten articles [31–38]. Meredith et al. first proposed RFA for measuring implant stability [48,49]. RFA assesses implant stability as a function of the stiffness of the implant–bone interface and is affected by several factors [50]. In their study, Öncü et al. used RFA to evaluate implant stability. The average ISQ was calculated by measuring the resonance frequency measurements twice at the mesiodistal position and buccolingual position [36]. Pichotano et al.'s results showed that the application of PRF at 3–4 months after implant placement significantly improved ISQ values compared to the control group [29,31,35]. Öncü et al. and Tabrizi et al. found a significant increase in ISQ values in the PRF group 1 month after implantation [32,36]. Four of the studies used different postoperative observation time points but ultimately reached a similar conclusion [29,31,32,35]. Our meta-analysis showed that PRF could promote stability and accelerate bone healing after implant surgery. The finding that, compared with no intervention, the application of PRF alone led to increased stability of implants was proved by the meta-analysis of the five articles included [30,32,34–36]. A previous study suggests that the stability of implants increases with healing time [32]. In addition, PRF can be used for alveolar bone healing and the creation of an optimal epithelial wound healing microenvironment. It has a role similar to that of other biological materials in the promotion of bone healing. Several studies have shown that PRF can promote bone regeneration without complications [46]. The results of the present study, which relied on the evaluation of ISQ, showed higher implant stability in the PRF group, which demonstrated that PRF is beneficial for enhancing implant osseointegration.

PRF has been shown to promote osteogenic differentiation in bone marrow mesenchymal stem cells, human adipose-derived stem cells, and periodontal ligament stem cells [51–53]. Some cell signal channels are involved in the mechanisms of osteogenic differentiation [54–56]. Kargarpour et al. have found that PRF membranes can inhibit the formation of osteoclasts from hematopoietic progenitors in bone marrow cultures, suggesting that PRF suppresses osteoclastogenesis *in vitro*. [22] Dental implant osseointegration results from functional coupling and equilibrium between osteoblasts and osteoclasts, as well as between bone tissue and the immune system [57]. Implant osseointegration is a dynamic process closely related to peri-implant osteoclasts and peri-implant osteoblasts [58]. Therefore, local application of PRF in implant sites probably enhances implant osseointegration by playing a role in the functions of osteoblasts and osteoclasts through the cell signal channels involved in the osteogenic mechanism. By contrast, Pichotano et al. suggest that PRF has no effect on implant stability after implant surgery [30,31]. Both studies compared biomaterials, such as DBBM or allografts, with a combination of PRF and DBBM or PRF alone. All studies could be divided into two groups, namely, studies based on biomaterials and those on biomaterials combined with PRF, biomaterials and PRF, or PRF and blank, which may have resulted in a lack of significant differences.

After platelet-rich plasma (PRP), PRF became a popular material for clinical application in bone-preserving and augmentation surgeries [18]. Various bone graft materials, such as β-calcium phosphate tribasic and DBBM, have also been commonly used to promote bone mass [12,59]. As mentioned above, placing PRF at implant sites can significantly increase the ISQ after implant surgery compared with that in routine implant procedures. With the development and application of PRP, PRF, and CGFs, some researchers have explored the methods and mechanisms of bone healing acceleration and new bone formation by adding a combination of PRF and biomaterials [29–31,33]. In the present study, four of the ten articles focused on whether PRF could promote bone formation or improve the efficiency of bone healing compared to biomaterials alone [29–31,33]. To analyze the potential effect of PRF on implant sites and that of other biomaterials, we extended our research further.

Four articles included analysis evaluating the stability of implants when a combination of PRF/PRF and biomaterials (e.g., Bio-oss and DBBM) was applied to implant sites, and the group that received biomaterials alone was used as the control [29–31,33]. We failed

to observe that the application of a combination of PRF and biomaterials can promote the ISQ when compared with the application of biomaterials alone. Considering the inconsistency in the variables of the experimental and control groups and the differences in the measurement times of some articles, the results were considered unreliable.

Previous studies drew different conclusions regarding the use of biomaterials for implant site preservation, sinus augmentation, and accelerated bone healing. Kasabah et al. showed that Bio-Oss increased the survival rate of maxillary implants and was a suitable material for sinus augmentation [60]. Zhao et al. showed that on-site preservation using DBBM provided no additional benefit in terms of post-extraction new bone formation in comparison with natural healing [61]. Pichotano et al. showed that the addition of leukocyte and platelet-rich fibrin (L-PRF) to DBBM into the maxillary sinus allowed earlier implant placement (4 months) with increased new bone formation compared to DBBM alone after 8 months of healing [31]. Xie et al. showed that injectable-platelet-rich fibrin is a safe and reliable material for sinus lifts and can effectively shorten the healing time and enhance osteogenesis [29]. The effect of PRF on bone healing and bone formation requires further study.

Altogether, these results show that PRF alone may have a similar effect as that of other biomaterials. Although the statistical methods applied were insufficient and the sample size was small, the results suggest that the use of PRF alone could be a suitable clinical option in a range of implant surgeries in the future.

The results of most studies showed a poorer clinical outcome of dental implants in the maxilla than in the mandible [62]. Schwartz-Arad et al. showed that the total 10-year cumulative oral implant survival rate was 95.4% (maxilla, 83.5%; mandible, 99.5%) [63,64]. To study whether PRF plays a role in improving the clinical outcomes of dental implants in the maxilla, subgroup analysis was carried out to compare the ISQ between the maxilla and the mandible according to the implant site. Five of the ten studies reported the maxilla alone as the implant site [29–33]. The remaining four articles studied the maxilla and the mandible as the implant sites [34–37]. Öncü et al. and Tabrizi et al. measured the mean ISQ of the “PRF alone” group at the end of 4 weeks and found that PRF application increased implant stability during the early healing period [30,34,35]. This leads us to conclude that the application of PRF might is beneficial for early bone integration, One limitation of the present study was the lack of long-term postoperative evaluation (evaluation after 1 year postoperatively). Further research on long-term implant retention is required.

Based on the histological evaluation, the application of PRF showed a tendency to promote new bone formation at the implant site, which warrants confirmation in further studies correcting the design of the clinical experiments and increasing the sample size.

5. Conclusions

Altogether, the results of this systematic review and meta-analysis suggest that PRF may be able to improve the stability of implants after implant surgery. Compared with other biomaterials, the application of PRF may accelerate the bone healing process. More research is needed to further determine the role of PRF in increasing the rate of new bone formation.

CRediT author statement

Xiangjun Li Conceived and designed the experiments.
Shuai Guan and Tiepeng Xiao Performed the experiments; Wrote the paper.
Jiuping Bai and Chunliu Ning Analyzed and interpreted the data.
Lei Yang and Xingkui Zhang Contributed reagents, materials, analysis tools or data.

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Data availability statement

The authors are unable or have chosen not to specify which data has been used

Declaration of interest’s statement

The authors declare no competing interests.

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