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Efficacy of platelet-rich fibrin on bone formation, part 2: Guided bone regeneration, sinus elevation and implant therapy

KEY WORDS
biomaterials, bone graft, growth factors, platelet-rich fibrin, platelet concentrates

ABSTRACT

Purpose: To investigate the effect of platelet-rich fibrin on bone formation by investigating its use in guided bone regeneration, sinus elevation and implant therapy.

Materials and methods: This systematic review and meta-analysis were conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The eligibility criteria comprised human controlled clinical trials comparing the clinical outcomes of platelet-rich fibrin with those of other treatment modalities. The outcomes measured included percentage of new bone formation, percentage of residual bone graft, implant survival rate, change in bone dimension (horizontal and vertical), and implant stability quotient values.

Results: From 320 articles identified, 18 studies were included. Owing to the heterogeneity of the investigated parameters, a meta-analysis was only possible for sinus elevation. There is a general lack of data from comparative randomised clinical trials evaluating platelet-rich fibrin for guided bone regeneration procedures (only two studies), with no quantifiable advantages in terms of new bone formation or dimensional bone gain found in the platelet-rich fibrin group. For sinus elevation, the meta-analysis demonstrated no advantage in terms of histological new bone formation in the control group (bone graft alone) compared with the test group (bone graft and platelet-rich fibrin). Two studies demonstrated that platelet-rich fibrin may shorten healing periods prior to implant placement. Platelet-rich fibrin was also shown to slightly enhance primary implant stability (implant stability quotient value < 5) as assessed using implant stability quotients and resonance frequency analysis parameters, with no histological data evaluating bone–implant contact yet available on this topic. In one study, platelet-rich fibrin was shown to improve the clinical parameters when utilised as an adjunct for the treatment of peri-implantitis.

Conclusions: In the majority of studies, platelet-rich fibrin offered little or no clear advantage in terms of new bone formation as evaluated in various studies on guided bone regeneration and sinus elevation, nor in implant stability and treatment of peri-implantitis. Various authors and systematic reviews on the topic have now expressed criticism of the various study designs and protocols, and the lack of appropriate controls and available information regarding patient selection. Well-controlled human studies on these specific topics are required.

Conflict-of-interest statement: *Richard J Miron holds intellectual property on platelet-rich fibrin. All other authors declare no conflicts of interest.*

Introduction

Bone regeneration is a growing and often challenging clinical topic in implant dentistry, and a number of surgical techniques, biomaterials and growth factors have been brought to market in an attempt to further stimulate tissue/bone regeneration[1]. While a first generation of passive biomaterials including barrier membranes was introduced to prevent the faster growing soft tissues from infiltrating the slower growing bony tissue, advancements made in terms of bone graft (BG) materials, growth factors and stem cell technologies have been investigated more recently, and varying degrees of success have been reported[2,3]. Ambitious attempts, especially with regenerative bioactive growth factors such as bone morphogenetic proteins (BMPs), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF) and enamel matrix derivative (EMD), have all been explored for the regeneration of various tissues in the oral cavity[1]. Several decades have now passed since it was first proposed that the use of supraphysiological concentrations of platelets collected directly from a patient's peripheral vein could be utilised as a regenerative strategy for various clinical indications in medicine and dentistry[4-6].

Both platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have been utilised for over two decades owing to their ability to promote tissue regeneration by favouring angiogenesis and tissue healing using 100% naturally-derived autogenous growth factors[7,8]. Initial studies on PRP were developed to concentrate platelets effectively, but PRF has since been more frequently utilised due to its lack of chemical additives and the formation of a fibrin clot with entrapped regenerative cells, leucocytes and growth factors, promoting the slow and gradual release of growth factors[9]. PRF has therefore been used much like PRP during bone grafting procedures, though full-sized fibrin clots have typically been cut into smaller PRF fragments and mixed with various biomaterials such as BG, or subsequently flattened and utilised as a barrier over collagen membrane in guided bone regeneration (GBR) procedures to promote soft tissue healing[10,11].

While the effects of PRF on soft tissue healing, gingival recession coverage and periodontal regeneration are well documented in the literature[6,12,13], its effects on bone formation around implants remain less studied[6,12,14,15]. Thus, this systematic review (SR) aimed to address the impact of PRF on bone formation by evaluating human controlled clinical trials investigating the use of PRF for GBR and sinus elevation procedures, and as an adjunct to enhance implant stability and therapy.

Materials and methods

Protocol

This SR followed the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[16]. The protocol was based on the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) as outlined below[17]. A protocol including all aspects of an SR methodology was developed prior to initiation of the SR. This included defining the focused question, patient, intervention, comparison, outcome (PICO) question, search strategy, study inclusion criteria, outcome measures, and the methods for screening, data extraction, analysis and synthesis. There were no deviations from the initial protocol. The focused question was as follows: 'Is there an advantage to using PRF for bone regeneration in GBR and sinus elevation, and as an adjunct to enhance implant stability or therapy?'

Eligibility criteria and study selection process

The eligibility criteria were based on a population, intervention, comparison, outcomes and study design (PICOS) strategy[18]. The search and screening process was conducted by two independent reviewers (RJM and MFK), commencing with analysis of titles and abstracts. Full texts were then selected for close reading and matched with the eligibility criteria for future data extraction. Any disagreements between the reviewers were

resolved through careful discussion. The eligibility criteria were as follows:

- Population: Systemically healthy humans in need of GBR in the oral cavity;
- Intervention: Use of PRF either alone or in combination with a biomaterial during bone augmentation in GBR procedures or sinus elevation, or as an adjunct to implant stability or therapy;
- Comparison: PRF vs natural wound healing or in combination with other biomaterials;
- Outcomes: Percentage of new bone formation, percentage of residual bone graft, implant survival rate, change in bone dimensions (horizontal and vertical) and ISQ values;
- Study design: Human controlled clinical trials with a minimum of 10 patients.

Search strategy

MEDLINE (via PubMed), Central (Cochrane Library), Scopus, Embase and LILACS were used to search for articles published before June 2020. A search of the grey literature using the Grey Literature Report and OpenGrey databases was also conducted. Finally, the reference lists of potential articles were examined (cross-referenced) to identify other potential studies for inclusion. A combination of several search terms and search strategies were applied to identify appropriate studies.

The search strategies were as follows:

- For studies on use of PRF in GBR: (platelet rich fibrin OR PRF OR platelet-rich fibrin OR leukocyte platelet rich fibrin OR leukocyte platelet-rich fibrin OR LPRF OR L-PRF OR advanced platelet rich fibrin OR advanced PRF OR A-PRF OR APRF) AND (guided bone regeneration OR GBR or horizontal augmentation OR vertical augmentation OR ridge augmentation);
- For studies on use of PRF in sinus elevation: (platelet rich fibrin OR PRF OR platelet-rich fibrin OR leukocyte platelet rich fibrin OR leukocyte platelet-rich fibrin OR LPRF OR L-PRF OR advanced platelet rich fibrin OR advanced PRF OR A-PRF OR APRF) AND (sinus grafting OR sinus lift OR sinus elevation OR sinus floor elevation OR sinus augmentation);
- For studies on the use of PRF in implant dentistry: (platelet rich fibrin OR PRF OR platelet-rich fibrin OR leukocyte platelet rich fibrin OR leukocyte platelet-rich fibrin OR LPRF OR L-PRF OR advanced platelet rich fibrin OR advanced PRF OR A-PRF OR APRF) AND (implant dentistry OR implantology OR peri-implant OR peri-implantitis).

The reference lists of all articles identified were screened. Finally, hand searching of the Journal of Clinical Periodontology, Journal of Dental Research, Journal of Periodontal Research, Journal of Periodontology, Clinical Oral Implants Research, Clinical Implant Dentistry and Related Research, Clinical Oral Investigations and the International Journal of Periodontics and Restorative Dentistry was performed to identify articles published from January 2000 until June 2020.

Criteria for study selection and inclusion

Only articles published in English and describing the human clinical evaluation of PRF for the aforementioned procedures were included. Of these, only human studies evaluating the comparative effects of PRF compared to those of an appropriate control in human studies were included, whereas human studies evaluating PRF in a case report or case series that did not include a control were excluded. All animal and in vitro studies were also excluded.

Risk of bias assessment

Two reviewers (VM and RJM) analysed the risk of bias in RCTs using the Cochrane risk-of-bias tool for randomised trials (RoB-2)[19]. For each study, the randomisation method, deviations from intended interventions, missing outcome data, outcome measurement and selection of the reported research were classified as low risk, some concerns or high risk of bias. Studies that were classified as low risk in all five areas were judged as low risk; as some concerns when they raised some concerns in at least one area; and high risk when they were judged as high risk in at least one domain or when

Table 1 Assessment of the risk of bias of randomised clinical trials

Study	Domain					
	Bias arising from the randomisation process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall risk of bias judgement
Choukroun et al[23]	High	Some concerns	Low	Low	Low	Some concerns
Tatullo et al[29]	High	Some concerns	Low	Low	Low	Some concerns
Zhang et al[30]	Low	Low	Low	Low	Low	Low
Gassling et al[25]	Low	Low	Low	Low	Low	Low
Bosshardt et al[31]	Low	Low	Low	Low	Low	Low
Bolukbasi et al[22]	Low	Low	Low	Low	Low	Low
Boora et al[32]	High	Some concerns	Low	Low	Low	Some concerns
Hamzacebi et al[37]	Low	Low	Low	Low	Low	Low
Öncü and Alaaddinoğlu[33]	Low	Low	Low	Low	Low	Low
Gurler and Delilbasi[26]	Low	Low	Low	Low	Low	Low
Hehn et al[36]	High	Some concerns	Low	Low	Low	Some concerns
Moussa et al[20]	Low	Low	Low	Low	Low	Low
Cömert Kılıç et al[24]	Low	Low	Low	Low	Low	Low
Diana et al[35]	Low	Low	Low	Low	Low	Low
Nizam et al[27]	Low	Low	Low	Low	Low	Low
Tabrizi et al[34]	Low	Low	Low	Low	Low	Low
Hartlev et al[21]	Low	Low	Low	Low	Low	Low
Pichotano et al[28]	Low	Low	Low	Low	Low	Low

they were judged to raise some concerns in multiple domains in such a way as to substantially lower confidence in the result (Table 1).

Data synthesis

The following study data were extracted, where available, from the included studies by MFK and RJM: author, study design, follow-up, number of treated cases, number of subjects, age range, sex, number of smokers, surgical technique, percentage of new bone formation, percentage of residual bone graft, implant survival rate, horizontal and vertical dimensional bone gain, posttreatment change in bone dimensions, ISQ values, centrifugation system, volume of blood drawn, centrifugation parameters and conclusions. Due to the heterogeneity of the parameters investigated in the studies, no meta-analysis could be performed for GBR and implant therapy. Instead, the data were reported in a systematic fashion, with an overview of all studies fitting the search descriptions. Thereafter, data were extracted from the articles and discussed accordingly.

Statistical analysis

The continuous variables, such as percentage of new bone formation, of the included studies were categorised into groups and subgroups and evaluated in a meta-analysis using Review Manager software (version 5.2.8, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

The estimates of the intervention effects, such as the mean difference (MD), were expressed as percentages or millimetres with 95% confidence intervals (CIs). The inverse variance method was used for random effects or fixed effects models, depending on the heterogeneity between the studies. A chi-squared test was used to evaluate heterogeneity, which was considered low for

values ≤ 25%, moderate for values > 25% and ≤ 50%, and high for values > 50%[22]. For cases of low or medium heterogeneity, the random effects model evaluated the variance components in the presence of heterogeneity ($P < 0.10$) rather than the fixed effects model. A funnel plot was drawn for the primary outcome variable (clinical attachment level [CAL]) to assess publication bias across studies. Studies outside the confidence interval area may indicate possible publication bias. The level of statistical significance of the meta-analysis effect was set at $P < 0.05$.

Results

Literature search

The search process, including the selection and reasons for excluding studies, is shown in Fig 1. From the 320 articles originally screened, 18 RCTs[20-37] that met the inclusion criteria were included. Two RCTs examined GBR[20,21], ten investigated sinus elevation[22-31] and six studied implant therapy[32-37]. There was large variability in the protocols and centrifugation systems used. The most common protocol was 3000 revolutions per minute (rpm) for 10 minutes (four studies), followed by 2700 rpm for 12 minutes (three studies).

PRF for GBR

Although PRF has been used in clinical practice for over two decades, only two RCTs have been conducted into GBR procedures with PRF (Table 2), both of which investigated the impact of PRF in GBR procedures as a replacement for collagen[20,21]. As yet, no studies have compared the addition of PRF to a BG material in a comparative study (BG and PRF vs BG alone); it therefore remains impossible to determine whether PRF influences new bone formation during GBR procedures.

In a study by Moussa et al[20], lateral augmentation was performed with bone blocks either covered with PRF or left uncovered. There was a statistically significant increase in buccopalatal bone width in both groups, measured by CBCT and a manual caliper, with no differences reported between the groups; however, the PRF group showed statistically significantly lower mean graft resorption when compared to the control group (PRF, 0.8 ± 0.6 mm; control, 1.6 ± 0.9 mm; $P = 0.006$)[20]. Hartvel et al[21] performed staged lateral ridge augmentation with an autogenous bone block covered with either PRF or a resorbable collagen membrane. A total of 27 partially edentulous patients (test, n = 14; control, n = 13) were included. A CBCT assessment was performed prior to grafting and 2 weeks and 6 months after grafting, and no difference in mean volumetric bone loss was reported between the PRF group (14.7 ± 8.9%) and the collagen membrane group (17.8 ± 13.3%) at 6 months[21].

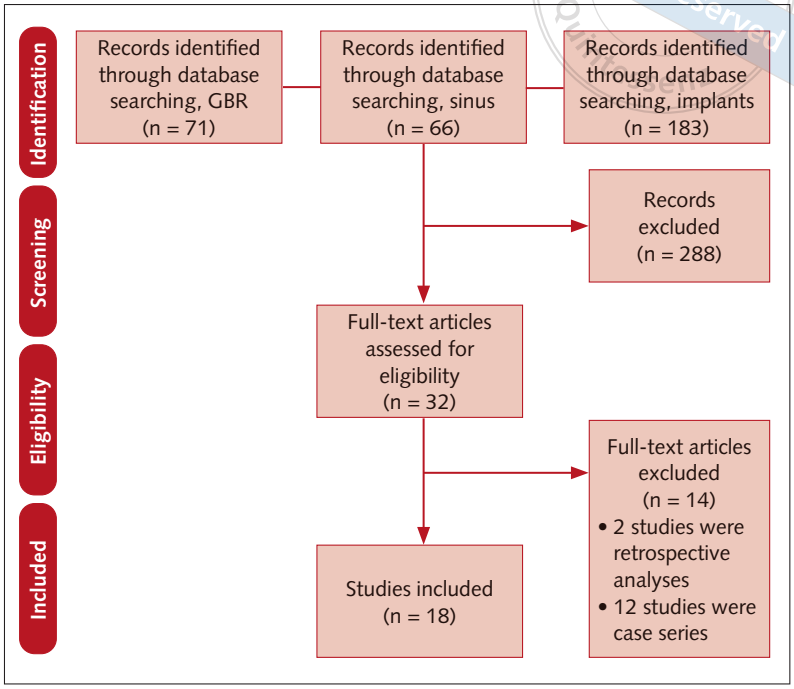

Fig 1 Flow diagram illustrating the screening and selection process.

PRF for sinus elevation procedures

PRF has been more frequently investigated with a BG material for sinus elevation procedures (Table 3)[22-31]. In total, 10 clinical trials have investigated the use of PRF for sinus elevation procedures: seven investigated the use of BG with/without PRF[22-24,27-30], two examined the use of PRF as a membrane for lateral wall closure[25,31], and one

Table 2 Main characteristics of the included studies investigating the use of PRF for GBR

Study	Study design and participants	Follow-up	Groups	Bone width gain	Augmented bone gain	
Moussa et al[20]	Controlled study, autogenous bone blocks covered with PRF vs alone. 12 patients (14 sites; 5 men and 7 women; mean age 26.2 y). Patients' smoking status was not reported	4 mo	C: 7, bone block T: 7, bone block + PRF	C: 3.8 ± 1.1 mm T: 3.4 ± 0.6 mm NS	C: 2.2 ± 0.8 mm T: 2.7 ± 0.9 mm NS	
Hartlev et al[21]	RCT, autogenous bone blocks covered with either CM or PRF. 27 patients (27 sites; 15 men and 12 women; mean age 50.0 y). Patients' smoking status was not reported	6 mo	C: 13, bone block + CM T: 14, bone block + PRF	NR	C: 465 ± 232 mm^3 T: 426 ± 144 mm^3 NS	

C, control group; CM, collagen barrier membrane (Bio-Gide; Geistlich, Wolhusen, Switzerland); NR, not reported; NS, no statistical difference between control group and test group; T, test group.

*Statistical difference between control and test group ($P < 0.05$).

Table 3 Main characteristics of the included studies investigating the use of PRF for sinus elevation

Study	Study design and participants	Purpose of PRF	Follow-up	Groups	New bone formation (%)	
Chouk-roun et al[23]	Parallel, lateral approach. Number of patients, sex, mean age and smoking status were not reported	Sinus elevation procedure	4 and 8 mo	C: 3, freeze-dried allogeneic bone (Phoenix, TBF, Mions, France) T: 6, freeze-dried allogeneic bone + PRF	C: 20.31 T: 20.95	
Zhang et al[30]	RCT, lateral approach. 10 patients (8 men and 2 women; mean age 43.5 y). Patients' smoking status was not reported	Sinus elevation procedure	6 mo	C: 5, DBBM T: 6, DBBM + PRF	C: 12.95 ± 5.33 T: 18.35 ± 5.62 NS	
Tatullo et al[29]	RCT, crestal approach. 60 patients (12 men and 48 women; age range 43–62 y); non-smokers	Sinus elevation procedure	106–150 d	C: 36, DBBM T: 36, DBBM + PRF	C: 38.97 T: 37.06 NS	
Bolukbasi et al[22]	Parallel, lateral approach. 25 patients (10 men and 15 women; mean age 50.1 y); non-smokers	Sinus elevation procedure	6 mo	C: 15, DBBM T: 17, DBBM + PRF	C: 32.97 ± 9.71 T: 35.0 ± 8.60 NS	
Cömert Kılıç et al[24]	RCT, lateral approach. 26 patients (17 men and 9 women; mean age 33.6 y). Patients' smoking status was not reported	Sinus elevation procedure	6 mo	C: 9, β-TCP T1: 9, β-TCP + PRP T2: 8, β-TCP + PRF	C: 33.40 ± 10.43 T1: 34.83 ± 10.12 T2: 32.03 ± 6.34 NS	
Nizam et al[27]	Split-mouth RCT, lateral approach. 13 patients (9 men and 4 women; mean age 49.9 y); non-smokers	Sinus elevation procedure	6 mo	C: 13, DBBM T: 13, DBBM + PRF	C: 21.25 ± 5.59 T: 21.38 ± 8.78 NS	
Pichotano et al[28]	Split-mouth RCT, lateral approach. 12 patients (6 men and 6 women; mean age 54.2 y); non-smokers	Sinus elevation procedure	4 and 8 mo	C: 12, DBBM T: 12, DBBM + PRF	C: 30.02 ± 8.42 T: 44.58 ± 13.90 ($P = 0.0087$*)	
Gassling et al[25]	Split-mouth RCT, lateral approach. 6 patients (sex and smoking status not reported; mean age 61.0 y)	Use of PRF to cover lateral window	5 mo	C: 6, CM T: 6, PRF	C: 17.2 (8.5–24.2) T: 17.0 (7.8–27.8)	
Bosshardt et al[31]	Parallel, lateral approach. 8 patients (1 man and 7 women; age range 41–64 y); non-smokers	Use of PRF to cover lateral window	7–11 mo (one case 24 mo)	C: 3, CM (4 biopsy specimens) T: 5, PRF (8 biopsy specimens)	C: 28.74 ± 5.44 T: 28.59 ± 6.90 NS	
Gurler and Delilbasi[26]	Parallel, lateral approach. 24 patients (14 men and 10 women; mean age 47.8 y); smokers (< cigarettes/day)	Use of PRF for early pain and wound healing	7 d	C: 12, allogeneic bone T: 12, allogeneic bone + PRF	Pain (7 d): C: 0.50 ± 0.85 T: 0.10 ± 0.32 NS	

β-TCP, beta-tricalcium phosphate (SupraBone, BMT Calsis Health Technologies, Ankara, Turkey); DBBM, deproteinised bovine bone mineral (Bio-Oss, Geistlich); NA, not applicable.

*Statistically significant difference ($P < 0.05$).

	Volumetric bone loss	Centrifugation system	Volume of tubes for blood drawn	Centrifugation parameters	Conclusions
	C: 1.6 ± 0.9 mm T: 0.8 ± 0.6 mm (P = 0.006*)	800D centrifuge (Makaad, Shanghai, China)	10–20 ml	3500 rpm for 12–15 min	No statistically significant differences between the two groups before and after treatment; however, autogenous bone block surface resorption was significantly decreased in the test group
	C: 17.8 ± 13.3% T: 14.7 ± 8.9% NS	A-PRF 12 (Process for PRF, Nice, France)	10-ml glass-coated plastic tubes (total 80 ml)	200 g for 14 min	No difference in volumetric changes of the augmented bone at 6-mo follow-up

	Residual bone graft (%)	Implant survival rate (%)	Centrifugation system	Volume of tubes for blood drawn	Centrifugation parameters	Conclusions
	C: 10.93 T: 9.41	NR	Lab Centrifuge (Process for PRF)	NR	2500 rpm for 10 min	PRF reduces healing time prior to implant placement
	C: 28.54 ± 12.01 T: 19.16 ± 6.89 NS	NR	Labofuge 300 (Kendro Laboratory Products, Hanau, Germany)	NR	300 g for 10 min	PRF in combination with DBBM has no effect on sinus elevation
	NR	C: 100 T: 100	NR	10-ml glass tubes	3000 rpm for 10 min	Histologically, no differences were noted between the control and test group at all investigated time points
	C: 33.79 ± 8.57 T: 33.05 ± 6.29 NS	C: 100 T: 100	Process for PRF (exact product not stated)	10-ml tubes (total 60 ml)	400 g for 12 min	No statistically significant differences in new bone formation and biomaterial remnants
	C: 30.39 ± 10.29 T1: 28.98 ± 7.94 T2: 32.66 ± 7.46 NS	NR	NR	5-ml tubes (total 10 ml)	3000 rpm for 10 min	No beneficial effect on new bone formation and regeneration when adding PRP or PRF to β-TCP graft substitute
	C: 32.79 ± 5.89 T: 25.95 ± 9.54 NS	C: 100 T: 100	NF 200 (Nüve Laboratory & Sterilisation Technology, Ankara, Turkey)	NR	400 g for 12 min	L-PRF + DBBM did not improve the amount of regenerated bone or the amount of graft integrated into the newly formed bone under histological and histomorphometric evaluation
	C: 13.75 ± 9.99 T: 3.59 ± 4.22 (P = 0.0111*)	C: 100 T: 100	K14-0815 (Kasvi, Curitiba, Brazil)	NR	3000 rpm for 10 min	Addition of PRF to DBBM allowed early implant placement (4 mo) with increased new bone formation compared to DBBM alone after 8 mo healing
	C: 17.3 (0.7–33.5) T: 15.9 (0.9–33.4)	C: 100 T: 100	NR	10 ml (total 40 ml)	400 g for 12 min	No difference between CM and PRF
	C: 25.50 ± 7.64 T: 25.67 ± 8.75 NS	NR	NR	NR	NR	No additional beneficial effect of PRF membrane over the non-crosslinked collagen membrane
	Swelling (7 d): C: 0.20 ± 0.42 T: 0.20 ± 0.42 NS	NA	IntraSpin (Intra-Lock, Boca Raton, FL, USA)	10-ml glass coated plastic tubes (total 40 ml)	2700 rpm for 12 min	Use of L-PRF and allogeneic bone in combination with L-PRF membrane does not significantly improve postoperative complications following direct sinus elevation

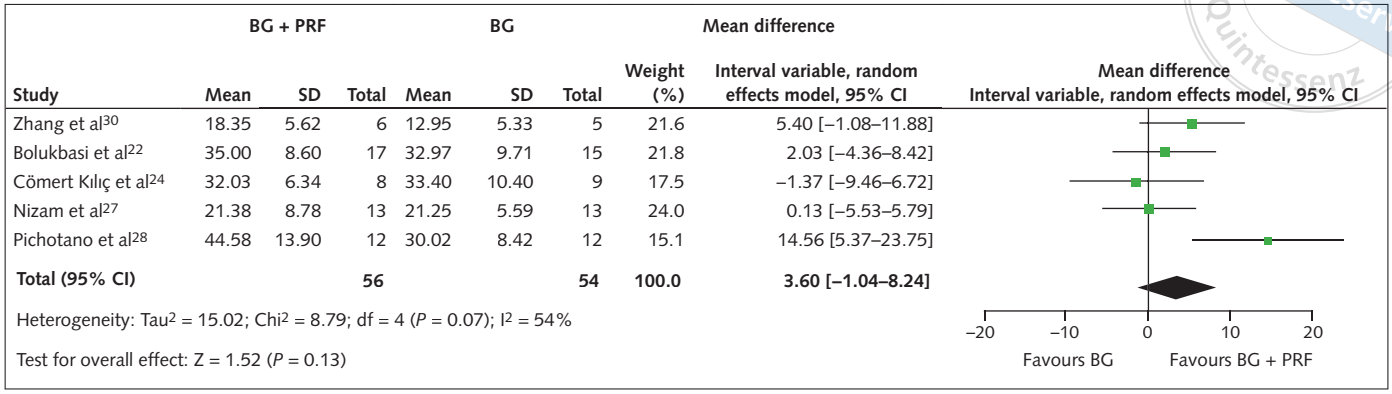

Fig 2 Results from the meta-analysis investigating the use of PRF for sinus elevation procedures (% new bone formation).

evaluated the effect of use of PRF on early pain management and postoperative swelling[26].

Of the seven studies evaluating bone formation, five demonstrated no significant histological improvement when PRF was added to a BG material[22,24,27,29,30], whereas two reported favourable results with respect to being able to place implants earlier in sites in which sinus elevation had been performed using PRF and BG[23,28]. The two studies that investigated the use of PRF compared to a collagen membrane to close lateral windows recorded similar outcomes[25,31].

Five studies were evaluated using a pairwise meta-analysis[22,24,27,28,30]. A random effects model was used due to the high heterogeneity between the studies ($P = 0.07$, $I^2 = 54\%$). There was no statistically significant difference when BG was compared with BG plus PRF ($P = 0.13$), with an MD of 3.60 (95% CI: –1.04 to 8.24) (Fig 2).

It can therefore be concluded that there is weak evidence demonstrating any long-term beneficial effect of adding PRF to BG. Some studies have suggested that it may be possible for implants to be placed earlier when grafted using a combination of BG and PRF[23,28]; however, further well-conducted studies are needed to confirm these outcomes.

PRF and dental implant therapy

The use of PRF has been investigated in six controlled studies of implant therapy (Table 4)[32-37]. The majority assessed either ISQ values or bone level changes after implant placement when PRF was used[32-35]. One study assessed soft tissue healing and mucosal thickness changes when PRF was used during implant therapy[36], and another investigated use of PRF for the management of peri-implantitis[38].

A prospective study by Boora et al[32] investigated the effect of PRF on peri-implant tissue response following single-stage implant placement with nonfunctional immediate provisionalisation in the maxillary anterior region with 20 patients. The mean marginal bone changes were observed from baseline to 3 months, with slightly lesser changes observed in the PRF group (0.5 to 0.6 mm bone change in the control group vs 0.2 mm in the PRF group)[32]. No significant differences in probing depth (PD) and bleeding on probing (BoP) were noted during follow-up[32].

Öncü and Alaaddinoğlu[33] investigated mean ISQ values 1 week and 1 month postoperatively. The PRF group demonstrated ISQ values of 69.3 ± 10.5, whereas the control group values were 64.5 ± 12.2 after 1 week. The mean ISQ values at 1 month were 77.1 ± 7.1 for the PRF group and 70.5 ± 7.7 for the control group[33].

Tabrizi et al[34] evaluated the stability of implants placed in the posterior maxilla with and without PRF in a split-mouth RCT involving 20 patients. At 2 weeks, the mean ISQ was 60.60 ± 3.42 in the PRF group and 58.25 ± 3.64 in the control group; at 4 weeks it was 70.30 ± 3.36 and 67.15 ± 4.33, respectively; and at 6 weeks it was 78.45 ± 3.36 and 76.15 ± 2.94, respectively. Although significant

differences in resonance frequency analysis (RFA) were found between the groups at 2 ($P = 0.040$), 4 ($P = 0.014$) and 6 weeks ($P = 0.027$) after placement, the increase in ISQ value was minimal when PRF was utilised, thus questioning the clinical relevance[34].

Diana et al[35] evaluated ISQ values and examined immediate implants grafted with and without PRF. PRF was placed in the peri-implant region of the test group (n = 21), whereas no elevation was performed in the control group (n = 20). A significant increase in ISQ value was noted in both groups over time (test group 56.58 ± 18.81 to 71.32 ± 7.82; control group 60.61 ± 11.49 to 70.06 ± 8.96; $P = 0.01$), but no significant difference was observed between the groups[35].

The effects of PRF on soft tissue thickness and initial marginal bone loss around implants were evaluated in an RCT using a split-flap technique[36]. Tissue thickness was measured at the point of implant insertion (baseline) and at the time of re-entry after 3 months, and standardised digital radiographs were obtained for evaluation at baseline, 3 months and 6 months[36]. PRF was not shown to demonstrate any advantage, and use of a split-flap technique with PRF was not recommended for thickening thin mucosa[36].

Hamzacebi et al[37] investigated the effect of PRF on peri-implantitis. During the surgical phase, full-thickness mucoperiosteal flaps were raised to gain access to the implant surface, and the inflammatory tissue was removed using handpieces[16,37]. Following implant decontamination using a Tigran PeriBrush (Panadent, Colton, CA, USA) and 4% pH 1 citric acid for 3 minutes or tetracycline hydrochloride (HCl) solution (1 g), the test group was filled with PRF membranes and a PRF plug was placed over the suprabony component of the defect[37]. At 3 and 6 months after surgery, the PRF group demonstrated a greater mean reduction in PD (2.41 ± 1.06 and 2.82 ± 1.03 mm vs 1.65 ± 1.02 and 2.05 ± 0.77 mm) and increased CAL (2.89 ± 1.01 and 3.31 ± 1.08 mm vs 1.43 ± 1.08 and 1.84 ± 0.81 mm), respectively, compared to the control group[37]. The increase in the amount of keratinised mucosa from baseline to 6 months postoperatively was statistically significantly greater in the PRF group ($P < 0.001$)[37]. The additional use of PRF for treatment of peri-implantitis may therefore provide better clinical outcomes than conventional flap surgery alone[37].

In summary, of the six controlled studies investigating the impact of PRF on implants, two noted slight improvements in ISQ values (± < 5) and one demonstrated some advantages when PRF was used as an adjunct for the management of peri-implantitis.

Risk of bias assessment

Four studies were classified as 'some concerns' because they showed a possibility of bias in the randomisation process or due to deviations from intended interventions[22,25,31,34]. All other studies were classified as 'low risk'. The RoB-2 analysis is presented in Table 1.

Discussion

The present SR aimed to investigate the use of PRF as an adjunctive regenerative agent in GBR procedures, sinus elevation and implant therapy. As such, all human clinical trials published on these topics to date were gathered. The general lack of well-conducted RCTs specifically examining these clinical indications was noted. For instance, although PRF has frequently been used (with sticky bone) to improve BG material handling[38], only two RCTs to date have investigated its ability to accelerate healing and promote bone formation, with few or no reported advantages[20,21]. Both studies also assessed the use of PRF as a barrier membrane rather than its ability to impact new bone formation[20,21].

Only one case series has utilised PRF cut into small fragments and mixed with BG particles[39]. In this pivotal proof-of-concept study, fragmented PRF membranes mixed with BG in a 50:50 ratio demonstrated improvements in linear horizontal bone gain of 4.6 ± 2.3 mm, 5.3 ± 1.2 mm and 4.4 ± 2.3 mm when measured at 2, 6 and 10 mm from the alveolar crest, respectively, with a mean resorption rate of 15.6 ± 6.7% at 5 to 8 months

Table 4 Main characteristics of the included studies investigating the use of PRF for implant dentistry

Study	Study design and participants	Purpose of PRF	Follow-up	Groups	ISQ values	
Boora et al[32]	RCT, one-stage, non-functional immediate implant coated with/without PRF. 20 patients (20 implants; 15 men and 5 women; mean age 24.6 y). Patients' smoking status was not reported	Implant placement (osseointegration)	3 mo	C: 10, implant alone T: 10, implant + PRF	NR	
Öncü and Alaaddinoğlu[33]	RCT, implants coated with/without PRF and investigated for ISQ. 20 patients (64 implants; 14 men, 6 women; mean age 44.2 y); smokers (≤ 10 cigarettes/ day)	Implant placement (osseointegration)	1 mo	C: 33 implants alone T: 31 implants + PRF	1 mo: C: 70.49 ± 7.74 T: 77.19 ± 6.06 (P = 0.002*)	
Tabrizi et al[34]	Split-mouth RCT, bilateral implant placement with/without PRF. 20 patients (40 implants; 9 men and 11 women; mean age 39.6 y). Patients' smoking status was not reported	Implant placement (osseointegration)	6 wk	C: 20 implants alone T: 20 implants + PRF	6 wk: C: 76.15 ± 2.94 T: 78.45 ± 3.36 (P = 0.027*)	
Diana et al[35]	RCT, implants coated with/without PRF and investigated for ISQ. 31 patients (41 implants; 18 men and 13 women; mean age 28.5 y); smokers	Implant placement (osseointegration)	1 y	C: 20 implants alone T: 21 implants + PRF	3 mo, NS C: 70.06 ± 8.96 T: 71.32 ± 7.82	
Hehn et al[36]	RCT, implant placement with/without soft tissue augmentation with PRF. 31 patients (31 implants; 16 men and 15 women; mean age 53.8 y); non-smokers	Implant placement (soft tissue management)	6 mo	C: 21 implants alone T: 10 implants + PRF	Mucosal thickness changes (mm), 3 mo: At crest: C: 2.64 ± 0.48 to 2.62 ± 0.61 T: 2.20 ± 0.48 to 0.90 ± 1.02 B and L: NS changes	
Hamzacebi et al[37]	RCT, conventional flap surgery for treatment of peri-implant bone loss with/without PRF. 19 patients (38 implants; 11 men and 8 women, mean age 61.0 y). Patients' smoking status was not reported	Management of peri-implantitis	6 mo	C: 19 OFD T: 19 OFD + PRF	PD reduction (mm), 6 mo: C: 2.05 ± 0.77 T: 2.82 ± 1.03 (P < 0.001*)	

B, buccal; D, distal; L, lingual; M, mesial; NR, not reported; OFD, open flap debridement.
*Statistically significant difference (P < 0.05).

postoperatively[39]. While the authors reported general improvements in BG material handling[39], it remains difficult to assess the actual additional benefit of incorporating PRF mixed with BG without a proper control. Future well-conducted RCTs on this topic are needed.

Following a systematic search, it was observed that five out of seven studies examinining the use of PRF in sinus elevation procedures found that combining PRF with a BG material showed no advantages in terms of increasing new bone formation, with the meta-analysis demonstrating no advantages (Fig 2). However, two studies reported that PRF could potentially reduce the postoperative healing time required prior to implant placement[32,37].The five studies that qualified for meta-analysis in this study showed that there was no statistically significant difference

	Bone level changes (mm)	Other changes	Centrifugation system	Volume of tubes for blood drawn	Centrifugation parameters	Conclusions
	C: M, 0.57 ± 0.22 T: M, 0.25 ± 0.06 (P = 0.0004*) C: D, 0.65 ± 0.28 T: D. 0.27 ± 0.07 (P = 0.0006*)	Probing depth (PD), NS C: 3.45 ± 1.17 mm T: 3.30 ± 1.39 mm Bleeding on probing (BoP), NS C: 30% T: 20%	NR	10-ml tubes	3000 rpm for 10–12 min	The mean marginal bone changes were observed from baseline to 3 mo in both groups, with lesser changes observed in the test group. No significant differences in PD and BoP were noted during follow-up
	NR	NR	PC-02 (Process for France; today IntraSpin, USA)	9-ml glass-coated plastic tubes	2700 rpm for 12 min	No difference in ISQ values was observed in either group
	NR	NR	IntraSpin	10-ml tubes (total 20 ml)	28,000 rpm for 12 min	No difference in ISQ values was observed in either group
	1 y, NS C: M, 0.85 ± 0.76 T: M, 1.17 ± 1.14 C: D, 0.92 ± 0.34 T: D, 1.15 ± 0.96	PD at 1 y, NS C: 2.60 ± 0.68 mm T: 2.01 ± 0.62 mm	NR	NR	NR	No difference in ISQ values was observed in either group
	Bone loss (defect depth/defect width) (mm) C: M, 0.72 ± 0.61/0.51 ± 0.48 T: M, 0.77 ± 0.42/0.57 ± 0.44 C: D, 0.82 ± –0.77/0.57 ± 0.58 T: D, 0.82 ± 0.42/0.62 ± 0.36	NR	IntraSpin	NR	NR	Soft tissue augmentation with PRF performed with a split-flap technique cannot be recommended for thickening thin mucosa
	CAL gain (mm), 6 mo: C: 1.84 ± 0.81 T: 3.31 ± 1.08 (P < 0.01*)	Change in keratinised mucosa, 6 mo, NS C: 0.05 ± 0.15 mm T: –0.62 ± 0.58 mm	NR	NR	NR	At 3 and 6 mo post-surgery, the test group demonstrated higher mean PD reductions and CAL gains compared with the control group. PRF statistically significantly increased keratinised mucosa from baseline to 6 mo post-operatively

between the BG and BG and PRF groups, although the outcomes were slightly in favour of the latter group[22,24,27,28,30]. This is in agreement with an SR and meta-analysis that assessed the role of PRF as an adjunctive material to BG in maxillary sinus elevation[40]. In this study, the authors also reported no statistical differences in survival rate, new bone formation, contact between newly formed bone and bone substitute, percentage of residual BG, or soft tissue area between the non-PRF and PRF groups, and also commented that the current evidence supporting the advantages of adding PRF to BG in sinus elevation is limited[40].

Several case series have investigated the use of PRF for sinus elevation procedures (Table 5). Of the 12 case series evaluating PRF[41-52], eight used it as a sole grafting material. Five of these eight studies utilised a crestal osteotome approach,

Table 5 Case series investigating use of PRF for sinus elevation

Study	Study design and participants	Follow-up	Residual bone height gain (mm)	Centrifugation system	
Diss et al[42]	Case series; PRF added as a sole grafting material during OMSFE with simultaneous implant placement. 20 patients (6 men and 14 women; mean age 54.8 y); smokers (< 20 cigarettes/day)	1 y	3.5 ± 1.4	NR	
Meyer et al[47]	Case series; PRF combined with β-TCP followed by delayed implant placement at 6 mo. 20 patients (33 sinuses; men–women ratio 2:1; mean age 52.0 y). Patients' smoking status was not reported	4 y	16.9 (10–22)	NR	
Mazor et al[46]	Case series; PRF added as a sole grafting material during OMSFE with simultaneous implant placement. 20 patients (6 men and 14 women; mean age 54.1 y); smokers (< 5 cigarettes/day)	6 mo	10.1 ± 0.9	Process for PRF (exact product not mentioned)	
Inchingolo et al[43]	Case series; PRF combined with DBBM followed by delayed implant placement at 6 to 9 mo. 23 patients (31 sinuses; 10 men and 13 women; age range 31–59 y); smokers	6–9 mo	NR	NR	
Toffler et al[51]	Case series; PRF added as a sole grafting material during OMSFE with simultaneous implant placement. 110 patients (138 sinuses; 40 men and 70 women; mean age 58.4 y). Patients' smoking habits were not reported	1–11 mo	3.4 (2.5–5.0)	Process for PRF (exact product not mentioned)	
Simonpieri et al[49]	Case series; PRF added as a sole grafting material during OMSFE with simultaneous implant placement. 20 patients (23 sinuses; 8 men and 12 women; mean age 59.8 y). Patients' smoking habits were not reported	2–6 y	10.4 ± 1.2	PC-02 (Intra-Lock)	
Tajima et al[50]	Case series; PRF added as a sole grafting material during lateral SFE with simultaneous implant placement. 6 patients (9 sinuses; 0 men and 6 women; mean age 67.8 y). Patients' smoking habits were not reported	6 mo	7.50 ± 1.51	Medifuge MF200, Silfradent	
Kanayama et al[44]	Case series; PRF added as a sole grafting material during OMSFE with simultaneous implant placement. 27 patients (39 implants; 12 men and 15 women; mean age 54.2 y). Patients' smoking habits were not reported	1y	4.19 ± 1.60	NR	
Barbu et al[52]	Case series; PRF added with DBBM during lateral SFE with simultaneous implant placement. 14 patients (14 sinuses; 10 men and 4 women; mean age 49.5 y). Patients' smoking habits were not reported	Mean 43.79 mo	10.12 ± 1.81	NR	
Aoki et al[41]	Case series; PRF added as a sole grafting material during crestal and lateral SFE with simultaneous implant placement. 34 patients (34 sinuses; 17 men and 17 women; mean age 57.6 y); smokers	1–7 y	4.26 ± 2.11	NR	
Kumar et al[45]	Case series; PRF added to DBBM during lateral SFE with simultaneous implant placement. 14 participants (14 sinuses; 10 men and 4 women; age range 18-65 y); non-smokers	1 y	6.87 ± 1.48	NR	
Molemans et al[48]	Case series; PRF added as a sole grafting material during crestal and lateral SFE with simultaneous implant placement. 26 patients (28 sinuses; 14 men and 12 women; mean age 55.0 y); non-smokers	6 mo	3.4 ± 1.2 crestal 5.4 ± 1.5 lateral	IntraSpin	

OMSFE, osteotome-mediated sinus floor elevation; SFE, sinus floor elevation.

	Volume of tubes for blood drawn	Centrifugation parameters	Conclusions
	10-ml glass-coated plastic tubes (total 80 ml)	3000 rpm for 10 min	The mean endosinus bone gain was 3.2 ± 1.5 mm 1meany after surgery
	NR	NR	After a mean follow-up of 4.5 y, the mean resorption rate of the grafted site was 20.3% and the mean residual bone height gain was 16.9 mm
	9-ml glass-coated plastic tubes (total 72 ml)	400 g for 12 min	Use of PRF as the sole filling material during simultaneous sinus elevation and implant placement resulted in a high volume of natural regenerated bone in the subsinus cavity up to the tip of the implants (10.1 ± 0.9 mm)
	10-ml tubes	3000 rpm for 10 min	In all cases included in this study, the authors observed successful implant-prosthetic rehabilitation using PRF combined with DBBM. Bone height was not reported
	9-ml glass-coated plastic tubes (total 18–54 ml)	2700 rpm for 12 min	The mean increase in the height of implant sites with OMSFE/PRF was 3.4 mm (range 2.5–5.0 mm)
	9-ml glass-coated plastic tubes (total 72 ml)	400 g for 12 min	No implants were lost and vertical bone gain was always substantial, between 8.5 and 12 mm (10.4 ± 1.2 mm)
	9-ml glass tubes (total 20–40 ml)	30 sec acceleration, 2 min at 2700 rpm, 4 min at 2400 rpm, 4 min at 2700 rpm, 3 min at 3000 rpm and 36 sec to decelerate and stop	Use of PRF for lateral sinus elevation with simultaneous implant placement led to an average 7.5-mm gain in bone height. All implants were clinically stable at the time of abutment insertion, 6 mo after sinus elevation
	10-ml glass tubes (total 20 ml)	400 g for 10 min	The mean bone height gain was 4.19 ± 1.60 when two different implant systems were used
	NR	NR	The mean vertical bone height gain was 10.12 mm 6 mo after surgery
	NR	NR	The mean residual bone height gain was 4.26 mm. SFE with PRF alone could be applied in cases of lower residual bone height; however, it should be carefully performed in cases of residual bone height < 4 mm before surgery
	NR	NR	12 mo after surgery, the endosinus bone gain noted was 7 mm, which indicated use of PRF with bovine BG as a reliable filling material during simultaneous sinus elevation and implantation
	9-ml glass-coated plastic tubes (total 72 ml)	408 g for 12 min	The mean vertical bone gain was 3.4 ± 1.2 mm and 5.4 ± 1.5 mm for transalveolar SFE and lateral SFE, respectively

Table 6 General clinical guidelines when using PRF for bone regeneration for various clinical indications

Indication	General guidelines
GBR procedures	Limited data in general exist from comparative RCTs evaluating PRF for GBR procedures. It is therefore not currently possible to substantiate the claims that PRF improves new bone formation, owing to a lack of well conducted studies. PRF was shown to increase the early vascularisation of bone tissues, important for new bone formation, but the amount of horizontal/vertical bone gain and dimensional stability was inconclusive
Sinus elevation	Data from RCTs demonstrate that PRF has more commonly been utilised in combination with a BG material. In the majority of studies (5/7), no additional gain in new bone formation was observed. Two studies demonstrated that PRF may favour slightly shorter healing periods prior to implant placement when compared to BG alone. PRF may be used to cover the lateral window. In both controlled studies, ISQ values were equivalent between sites grafted with either PRF or a collagen barrier membrane. PRF has been used as a sole grafting material in nearly a dozen case series. While favourable results have been observed, it is generally recommended to favour this approach for narrow sinuses and/or those requiring small (3–4 mm) sinus bumps. PRF has also been demonstrated in one clinical study to favour a significant reduction in patient-reported postoperative pain and swelling. This is likely due to improvements in soft tissue wound healing/closure following grafting procedures when placed in contact with soft tissues. PRF promotes better BG material handling in such cases, and less BG material may be needed when a combination approach is used
Implant therapy	PRF may enhance primary implant stability, though inconclusive/minimal data were found following assessment using ISQ and RFA parameters. To date, no histological data evaluating BIC exist on the topic. The data recommend avoiding soft tissue augmentation with PRF using a split-flap technique. Full-thickness flaps are therefore recommended. While only one study investigated use of PRF for the management of peri-implantitis, it was generally found that its application led to significant improvements in PD reduction, CAL gain and the amount of keratinised mucosa from baseline to 6 months. Further research is needed

three used a lateral approach, and two used either a crestal or lateral approach depending on the clinical situation. Although sinus elevation procedures are generally conducted using BG materials, a growing number of clinicians have proposed various platelet concentrates as a means to accelerate revascularisation to the sinus. One SR showed that the mean implant survival rate was 97.9% in a total of 864 implants placed simultaneously during a graftless sinus elevation procedure in a mean residual bone height of 5.7 ± 1.7 mm[53]. This suggested that implants can be successfully placed in the sinus cavity with a blood clot instead of BG materials when proper inclusion criteria are applied[53]. PRF may therefore be utilised in a similar approach acting as a space creator to allow for bone ingrowth.

Several studies evaluating PRF in implant therapy showed that PRF led to significant improvements in ISQ values, but these clinical findings should also be placed into context. For example, a study by Tabrizi et al[34] found that PRF improved ISQ values significantly at 2, 4 and 6 weeks when compared to a non-PRF treated control group. While significant advantages were reported in the PRF group at all time points in this study, it must also be questioned whether an ISQ value of 2 to 3 has any clinical relevance.

Various authors of SRs examining PRF and bone formation have criticised the various study designs and protocols and lack of appropriate controls and available information regarding patient selection in comparison to other sinus elevation studies[6,40]. Furthermore, it has previously been reported that the effectiveness of the different platelet concentrates/preparations is difficult to establish due to the great variability in study design, materials used (graft, membrane or a combination) and surgical techniques[54]. Improved clinical studies on this topic are therefore still needed. Based on the current knowledge available, Table 6 summarises conservative clinical guidelines for each of the three investigated clinical indications.

Table 7 Centrifugation devices and protocols utilised in the human clinical trials included in the present study and its preceding part

Clinical indication	Number of studies	Centrifugation device					Protocol utilised			
		IntraSpin	Duo Quattro	Remi	Other	NR	2700 rpm for 12 min	3000 rpm for 10 min	Other	NR
Gingival	17	5	0	2	4	6	7	7	2	1
Intrabony	27	1	0	15	3	8	2	20	5	0
Furcation	12	0	0	8	1	3	0	9	2	1
Extraction	16	9	1	1	1	4	8	5	2	1
Third molars	18	2	1	1	7	7	5	10	3	0
GBR/sinus	18	5	1	0	5	7	3	4	7	4
Total	108	22	3	27	21	35	25	55	21	7
% of all studies		20.4	2.8	25.0	19.4	32.4	23.1	50.9	19.4	6.5

The present study and its preceding part, regarding the use of PRF for gingival grafting procedures, comprehensively highlight the current state of research on PRF. One notable observation has been the variability in the protocols used to produce PRF and the centrifugation devices employed. Table 7 summarises these findings from 108 human clinical trials from this series of SRs. The most commonly used protocol was 3000 rpm for 10 minutes (51% of studies) followed by 2700 rpm for 12 minutes (23% of studies). With respect to centrifugation devices used, the Remi horizontal centrifugation system (Mumbai, India) was the most commonly utilised, in 25% of RCTs, followed by the IntraSpin (Intra-Lock, Boca Raton, FL, USA)/EBA 20 (Hettich, Tuttlingen, Germany) in 20% of studies. A large proportion of studies failed to report the device and/or centrifugation parameters used, and recent attempts have been made to report parameters more adequately in order to deepen knowledge in the field[55].

As understanding of relative centrifugal force (RCF) values versus rpm has improved[56], better attempts to standardise protocols based on RCF values as opposed to rpm have been brought to the attention of researchers in the field[57]. Within this context, it is interesting to note that the most utilised protocol from all the included RCTs was 3000 rpm for 10 minutes, and the majority were performed using the Remi system. Thus, although recent studies have clearly demonstrated the better ability for cell layer separation and distribution to occur when utilising horizontal centrifugation when compared to fixed angle[58,59], this coincides with the finding that the most used centrifugation system in the RCTs conducted to date also employs horizontal centrifugation. While extremely common in certain parts of the world, this relatively standard concept remains completely unfamiliar to many clinicians in other countries, mainly owing to the varying commercial entities and marketing efforts in different geographic regions of the world. Future research that aims to optimise PRF using standardised scientific approaches without commercial interest and with both RCF and centrifugation time applied to blood samples as opposed to the commonly reported commercial entities and tradenames is crucial to advance knowledge in this field. This will facilitate the sharing of data between researchers and clinicians and enable these data to be transmitted internationally to improve patient care.

Conclusion

In conclusion, these two SRs aimed to provide a commentary on and highlight the body of work that exists to date on the topic of PRF and its use in bone regenerative procedures. It is hoped that future investigators will update these reviews as new research becomes available, and better address some of the uncertainties that remain today.

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Literature abstract

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Al-Sawaf O, Tuna T, Rittich A, Kern T, Wolfart S. Randomized clinical trial evaluating the effect of splinting crowns on short implants in the mandible 3 years after loading.

Objective: To compare the radiographic marginal bone loss and clinical parameters of splinted and non-splinted fixed dental prostheses on short implants in the posterior region of the lower jaw 3 years after loading. **Material and methods:** Twenty patients, 15 female and five males, with uni- or bilateral free-end situations in the mandible participated in the study. Two short implants (7 mm) in the posterior mandible were placed and patients were randomized to receive splinted (n = 11) or non-splinted (n = 13) cemented crowns. Marginal bone loss (MBL) was assessed on radiographs taken with customized positioning jigs at baseline, 1 and 3 years after loading. Plaque index (PI), gingival index (GI), probing depth (PD), and bleeding on probing (BOP) were measured. (ClinicalTrials.gov; identifier: NCT03558347). **Results:** After 3-year survival rate of altogether 48 implants was 100% for both groups. Success rate (according to Papaspyridakos, Chen, Singh, Weber, & Gallucci, 2012) was 84.6% for non-splinted and 86.4% for splinted implants. At restoration level survival rate was 100% for both groups. Marginal bone level changes showed mean gain of 0.3 ± 0.8 mm for non-splinted and 0.1 ± 0.5 mm for splinted implants 3 years after loading. Statistical analysis showed no significant difference in PI, GI, PD, BOP, and marginal bone loss between both groups ($P > .05$). **Conclusion:** Within the limitations of this study it can be concluded that splinting crowns on short implants neither seems to affect the amount of marginal bone loss nor peri-implant health 3 years after loading. **Correspondence to:** omaralsawaf@gmail.com; swolfart@ukaachen.de. © 2020 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.