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# Socket Preservation Using Platelet-Rich Fibrin and Free Gingival Grafts

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ABSTRACT

*Objective:* The present randomised controlled trial is based on the null hypothesis that there is no difference in crestal bone levels (CBLs) following socket preservation (SP) using platelet-rich fibrin (PRF) and free gingival graft (FGG). The aim was to evaluate CBLs following SP using PRF and FGG.
*Methods:* This study is a parallel-arm randomised controlled trial. Patients in the test and control groups underwent SP using PRF and FGG, respectively. Intraoral visual examination was performed to clinically assess signs of swelling, pus/abscess, and stability of sutures and graft. Self-rated postoperative pain was assessed after 1 week and 6 months using the visual analogue scale (VAS). At the 6-month follow-up, cone-beam computed tomography was performed to evaluate CBL in mesiodistal and buccolingual dimensions. The preoperative cone-beam computed tomographic images were superimposed with those taken at the 6-month follow-up to compare CBLs. Statistical comparisons were performed and level of significance was set at $P < .05$.
*Results:* The test and control groups each comprised 13 individuals with comparable ages. All teeth included in the test and control groups were located in the maxillary aesthetic zone. At the 1-week follow-up, VAS scores were higher in the control than in the test group ($P < .01$). At the 6-month follow-up, none of the participants reported self-rated pain. The change in buccolingual dimension was greater in the control group than in the test group ($P < .05$).
*Conclusions:* Both FGG and PRF are effective techniques for SP; however, the latter technique is more effcacious in maintaining buccolingual dimensions of the extraction socket.



## Introduction

Tooth extraction (TE) is associated with osseous remodelling and a slight increase in soft tissue thickness both in the lingual and buccal aspects.[1,2] Socket preservation (SP) is essential in implant dentistry and related research, as it helps maintain the dimensions and contour of the alveolar ridge (AR) following tooth extraction.[3,4] The primary objective of SP is to minimise the loss of AR volume for successful implant placement and achievement of aesthetic outcomes.[5] Traditionally, a free gingival graft (FGG) is used to cover the extraction socket (ES), which in turn facilitates SP,[6] and has been considered the "gold standard" in soft tissue grafting procedures. The FGG involves harvesting a thin section of epithelial and connective tissue from the palate and transplanting it to the recipient site.[7,8] This technique provides an adequate supply of keratinised gingiva, which is essential for maintaining stable and healthy soft tissue around dental implants.[9,10] However, other techniques that have been employed to

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preserve the socket encompass the use of guided bone regeneration and use of growth factors (GFs) such as platelet-rich fibrin (PRF).[11]

The PRF is an autologous blood-derived product that has gained significant attention in recent years due to its potential regenerative properties.[12-14] It contains a concentrated mixture of platelets, GFs, cytokines, and leukocytes, which promote wound healing and tissue regeneration.[15-17] It has also been reported that PRF possesses antimicrobial properties against pathogens including *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Staphylococcus aureus*, and *Escherichia coli*.[18-20] The use of PRF in SP procedures has shown promising results in preserving the AR dimensions and improving bone formation.[21] According to results from a randomised controlled trial (RCT), PRF is a useful agent for SP after TE.[22] However, controversial results have also been reported. Results from a split-mouth RCT showed that PRF is ineffective in reducing AR alterations following extraction of multiple teeth.[23]

The aim of the present RCT is to evaluate and compare the effects of PRF and FGG on the crestal bone level (CBL) following SP. The present RCT is based on the null hypothesis that there is no difference in CBL following SP using PRF and FGG.

## Materials and methods

### *Ethical approval and trial registration*

Ethical approval was obtained from the Institutional Review Board at the College of Dentistry, Cario University, Cairo, Egypt. It was mandatory for all individuals to have read and signed a consent form. All participants were informed of their right to withdraw from the present investigation at any point without facing any penalty and/or consequences. All volunteering individuals were invited to ask questions. This RCT is registered with www.ClinicalTrials.gov, a comprehensive database of clinical trials. The trial was assigned the unique identification number NCT03628170 (First Posted 14/08/2018).

### *Trial design location and dates*

This parallel-arm RCT was conducted at the Department of Periodontology Clinic, College of Dentistry, Cairo University, Cairo, Egypt, between June 2018 and September 2019.

### *Eligibility criteria*

The inclusion criteria were as follows: (a) adults aged at least 18 years; (b) individuals with nonrestorable single-rooted teeth in the maxillary esthetic zone (canine to canine); (c) individuals with a satisfactory oral hygiene status; (d) cone beam computed tomography (CBCT)–based absence of preoperative osseous defects such as dehiscence and/or fenestrations (ProMax Classic, Planmeca). Participants who self-reported using combustible or non-combustible nicotinic products, individuals with a history of oral diseases such as periodontitis and cancer, and those with self-reported systemic conditions including diabetes mellitus (DM), cardiovascular disease (CVD), bone and joint disorders like arthritis and osteoporosis, viral diseases such as HIV/AIDS, as well as oral and/or systemic cancers were excluded from the study. Moreover, pregnant and/or nursing individuals and individuals diagnosed with periapical and periodontal infections, including periapical abscess/granuloma, were not sought.

### *Preoperative protocol*

Digital health care records of consenting participants were assessed to determine systemic health status and presence of any drug allergies. Supra- and subgingival mechanical debridement was done amongst all patients using sterile curettes (Gracey Curettes, HuFriedyGroup), and brushing and flossing techniques were explained verbally and in written format. Participants were also instructed to rinse twice daily with 15 mL of 0.12% chlorhexidine gluconate for 14 days. After 4 weeks, participants' compliance with routine oral hygiene maintenance (OHM) was reassessed. Individuals with plaque and gingival indices of 0.3 or less were considered compliant with routine OHM.[24-26] Preoperatively (immediately before extraction), a CBCT scan (ProMax Classic, Planmeca) was also done.

### *Surgical protocol*

All tooth extractions were performed atraumatically by an experienced investigator under local anaesthesia (4% articaine with 1/200,000 adrenaline) using the local infiltration technique. Following flapless tooth luxation, sterile forceps were used for tooth delivery without jeopardising socket walls. The ES was debrided with sterile hand curettes and irrigated with 0.9% sodium chloride. The test sockets were closed primarily with crisscross sutures without tension to support stability of the PRF. Postoperative antibiotics (amoxicillin tablet 500 mg p.o. every 8 hours for 7 days) and analgesics (ibuprofen tablet 600 mg p.o. every 12 hours for 2 days and then as needed) were prescribed.

### *Study groups, randomisation, and allocation concealment*

Participants were randomly divided into test and control groups. In the test and control groups, SP was performed using PRF and FGG, respectively. A simple randomisation was done using a computerised random number generator (https://www.random.org/). The process of allocation concealment was done by one investigator (HHALA) and involved associating even numbers with the test group and odd numbers with the control group. To ensure concealment, cards containing these numbers were enclosed in opaque envelopes and the treatment allocation was carried out at the time of participant enrolment.

In the test group, skin over the median cubital vein of the left arm was wiped with sterile gauze soaked in an alcoholic antiseptic (0.5% chlorhexidine, 70% ethanol). Venous blood (5 mL) was aseptically collected and placed into 10-mL sterile glass tubes without any anticoagulant. Subsequently, the tubes were immediately centrifuged at 2700 to 3000 rpm for 10 to 12 minutes to separate the

blood components. Following centrifugation, the middle fraction (PRF layer) was carefully separated from the other blood components by gently compressing the clot on a sterile metal plate using a sterile instrument. The PRF was inserted into the ES and primary closure was achieved using 5-0 silk sutures. In the control group, local anesthesia (LA) was administered at the donor (palate) site using 4% articaine with 1/200,000 adrenaline. Rectangular partial-thickness incisions extending from the mesial margin of the first premolar to the mesial margin of first molar were placed to dissect the palatal mucosa. The graft was harvested, placed over the ES, and immediately sutured using 5-0 silk sutures. These procedures were performed by a trained investigator.

### *Assessment of baseline ridge dimensions*

The buccolingual dimensions and CBLs (in axial, coronal, and sagittal dimensions) (primary outcome variables) were measured by maintaining the cementoenamel junction of the neighbouring teeth as reference points for standardisation of the measurements. The images were acquired on a computer screen connected to the CBCT machine via image acquisition, and these images were termed "basis images." The basis images were then transferred to the secondary workstation to a software (Planmeca Romexis) through a network where image reconstructios were carried out using the OnDemand3D software programme (v.1.0.9, Cybermed). The CBCT measurements spanned from the cementoenamel junction of the tooth adjacent to the mesial and distal aspects of the socket to the bone crest. Subsequently, the average dimensions were calculated. Regarding the buccolingual dimensions, measurements were taken from the labial plate of bone to the lingual plate of bone at 3 defined points (coronal third, middle third, and apical third). These measurements were then averaged to obtain the overall dimension (Figure 1A–1D).

### *Assessment of dimensional changes between pre- and postoperative CBCT measurements*

The images (preoperative and at 6-month follow-up) were superimposed in axial, coronal, and sagittal dimensions. One image was designated as the primary, whilst the other served as the secondary image. To distinguish between the primary and secondary images during the fusion process, each image was assigned a distinct colour. Additionally, one image was made more transparent than the other to enhance visibility when the images were fused together. The fusion process commenced by aligning the same plane in both primary and secondary images, approximately in the axial plane. Utilising fixed reference points such as the cusp tips of molars or the incisal edge of anterior teeth (point registration), the images were superimposed in the coronal view. Subsequently, the axial level was meticulously adjusted to ensure that both primary and secondary images aligned precisely on the same axial plane.

### *Assessment of postoperative self-rated pain and CBL at follow-up*

At the 1-week and 6-month follow-up, the visual analogue scale (VAS)[27] was used to assess self-rated postoperative pain (secondary outcome variable) in all patients. Intraoral visual examination of the treated sites was also performed to clinically assess signs of swelling, pus/abscess, and stability of sutures and graft. At the 6-month follow-up, CBCT (ProMax Classic, Planmeca) assessment of the treated sites was performed to evaluate crestal bone in the mesiodistal and buccolingual dimensions. The CBCT scans taken preoperatively and at the 6-month follow-up were superimposed in axial, coronal, and sagittal dimensions. These evaluations were performed by a calibrated and blinded investigator ($\kappa$ = 0.88).

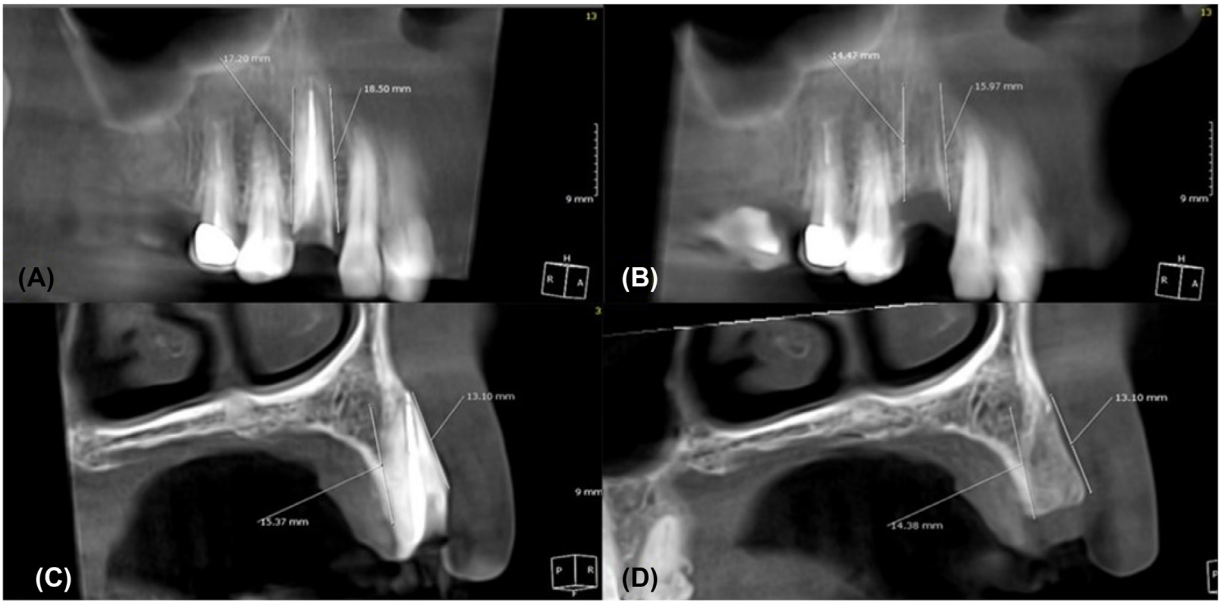


**Fig. 1 – Three-dimensional socket measurements on mesiodistal (A and B) and buccolingual (C and D) dimensions.**

### *Intraexaminer reliability (calibration)*

One trained investigator assessed 10 CBCT images at 2 different time points (baseline and after 2 weeks). In comparison of the 2 sets of measurements, the examiner's consistency towards evaluations of CBL was quantified and helped determine how often the examiner's assessments agreed between the 2 time points.<AQ: Please clarify "In comparison of the 2 sets of measurements, the examiner's consistency towards evaluations of CBL was quantified and helped determine how often the examiner's assessments agreed between the 2 time points."> Cohen's $\kappa$ was calculated to quantify the level of agreement beyond what would be expected by chance.

### *Power analysis*

Power analysis was done based on data from a previous study,[6] which showed that the mean (SD) difference in CBL change between test and control groups was 1.0 (0.8) mm. To achieve a statistical power of 80% with an alpha of 5%, a sample size of 11 participants was required in each group. However, to account for potential losses during the follow-up period, the sample size was increased to 13 participants per group, which represents a 20% increase over the initially calculated number. The power analysis was performed using a software programme (G*Power software version 3.1.9.2 (Axel Buchner - University of Dusseldorf, Edgar Erdfelder - University of Mannheim, Franz Faul - University of Kiel, and Albert-Georg Lang - University of Dusseldorf)).

### *Statistical analyses*

Statistical analyses were performed by a blinded statistician using SPSS Statistics for Windows (Version 26.0, IBM Corp.). Data were presented as means and standard deviations. Data normality was determined using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Statistical comparisons between test and cotnrol groups were performed using the Mann–Whitney *U* and independent *t* tests. A statistical significance level of $P < .05$ was used to determine the presence of statistically significant results.

## Results

### *Recruitment of participants*

The patient recruitment process is summarised in accordance with the Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 2). Initially, 63 potential participants were screened for eligibility. Amongst them, 37

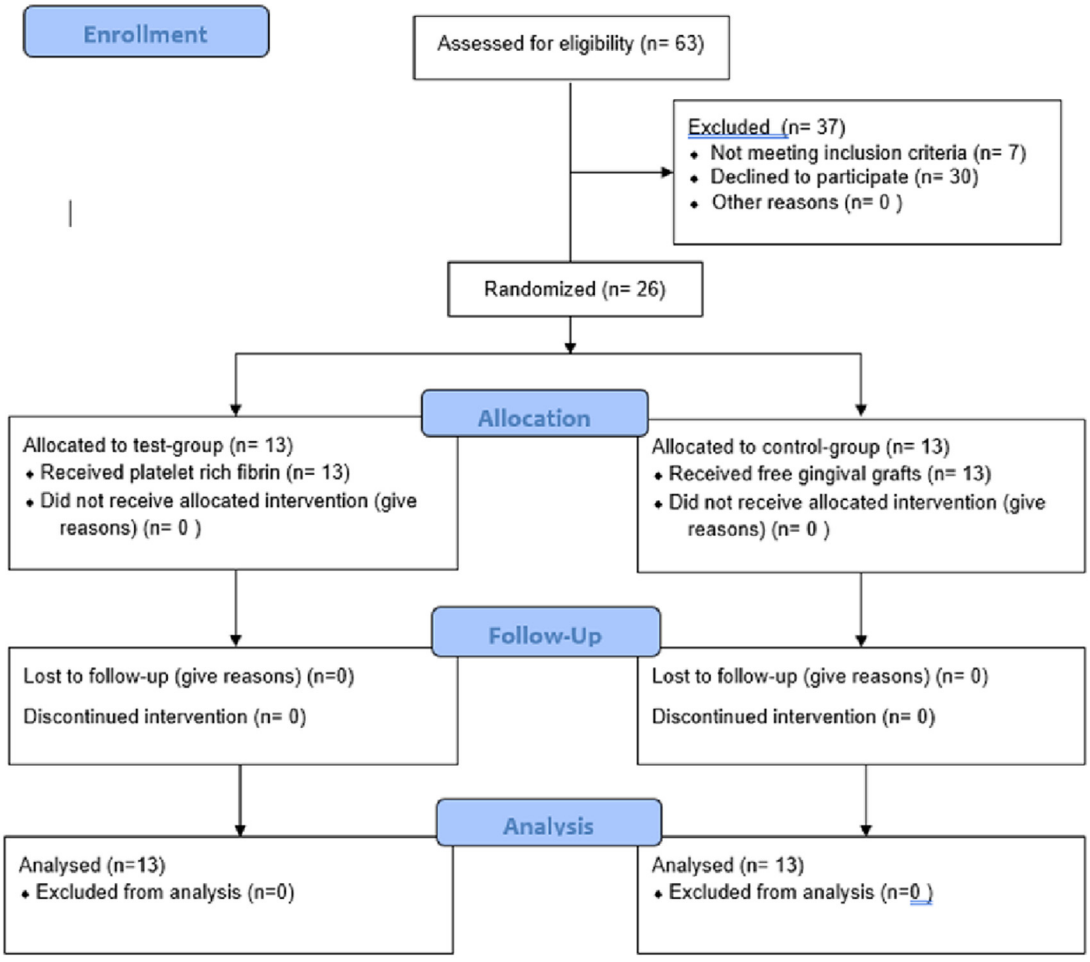


**Fig. 2 – CONSORT flow diagram.**

**Table 1 – Demographics of the study cohort.**

| Variables | All individuals | Test group | Control group |
|---|---|---|---|
| Participants, No. | 26 | 13 | 13 |
| Gender (male:female) | 10:16 | 6:8 | 4:8 |
| Mean (SD) age, y | 37.6 (3.5) | 40.3 (4.9) | 36.4 (6.2) |
| Teeth extracted | | | |
| Maxillary central incisor, No. % | 9 (34.6) | 5 (38.5) | 4 (30.8) |
| Maxillary lateral incisor, No. % | 7 (26.9) | 3 (23) | 4 (30.8) |
| Maxillary canine, No. % | 10 (38.5) | 5 (38.5) | 5 (38.4) |

were excluded due to not meeting the eligibility criteria. The most common reason for exclusion was refusal to participate in the present study (30 individuals). Four breastfeeding individuals and 3 individuals with type 2 DM were also excluded. In total, 26 individuals (10 male and 16 female) were included in the present RCT.

### *Demographics*

The test and control groups each comprised 13 individuals. In the test and control groups, 6 and 4 participants were male, respectively. The average age of the study population was 37.6 ± 3.5 years. The mean (SD) ages of individuals in the test and control groups were 40.3 (4.9) and 36.4 (6.2) years, respectively. All teeth included in the test and control groups were located in the maxillary aesthetic zone (Table 1). None of the participants had a self-reported penicillin allergy.

### *VAS*

At baseline, none of the participants reported self-rated pain. At the 1-week follow-up, the VAS scores were significantly higher amongst patients in the control group (7.8 ± 0.8) compared with the test group (2.4 ± 0.8) ($P < .01$), respectively. At the 6-month follow-up, none of the participants reported self-rated pain.

### *Comparison of total surfaces (ridge dimensions)*

No statistically significant differences were observed between the test and control groups in terms of total surfaces (mesial, distal, buccal, and lingual surfaces) during baseline assessments and at 6-month postsurgery evaluations (Table 2).

### *Comparison of the change in buccolingual and mesiodistal dimensions*

Overall, there was no statistically significant difference in the change in AR dimensions in the test (1.1 ± 0.5 mm) and control (0.8 ± 0.6 mm) groups. The change in buccolingual dimension was significantly higher in the control (1.6 ± 0.7 mm) than the test group (0.8 ± 0.4 mm) ($P < .05$). There was no significant difference in the mesiodistal dimensions in the test and control groups (0.3 ± 0.6 and 1.4 ± 1.2 mm, respectively) (Table 3).

**Table 2 – Comparison of total surfaces (mesiodistal and buccolingual) during baseline assessments and at 6-month postsurgical evaluation.**

| Ridge dimensions, mean (SD), mm | Test group (n = 13) | Control group (n = 13) |
|---|---|---|
| Baseline | 9.9 (3.3) | 8.6 (2.1) |
| Postoperative | 8.8 (2.9) | 7.9 (2.0) |

**Table 3 – Comparison of the change in buccolingual and mesiodistal dimensions.**

| Alveolar dimensions, mean (SD), mm | Test group (n = 13) | Control group (n = 13) |
|---|---|---|
| Mesiodistal | 0.3 (0.6) | 1.4 (1.2) |
| Buccolingual | 0.8 (0.4)* | 1.6 (0.7) |
| Overall | 1.1 (0.5) | 0.8 (0.6) |

* Compared with the control group ($P < .05$).

## Discussion

The FGG has traditionally been utilised as the "gold standard technique" for soft tissue augmentation. However, the limitations associated with FGG, including donor site morbidity and limited donor tissue availability, have prompted the search for alternative approaches. The PRF is an autologous platelet concentrate that has emerged as a promising option due to its ability to release GFs (such as vascular endothelial growth factor [VEGF], transforming growth factor $\beta$–1 [TGF$\beta$–1], fibroblast growth factor, and platelet-derived growth factor [PDGF]) and facilitate tissue regeneration.[11,15,21] Results from an in vitro investigation reported that the PRF, when used in combination with xenograft, enhances the proliferation of human periodontal ligament stem cells, thereby accelerating wound healing.[28] Likewise, results by Esfahrood et al[29] showed that the PRF acts as a physical support for cell migration and proliferation, creating a conducive environment for human gingival fibroblasts to facilitate wound closure and healing. Moreover, according to Ferrara,[30] VEGF (an endothelial cell–specific mitogen) facilitates healing via its unique role in the regulation of physiologic angiogenesis. Furthermore, PRF retards the proinflammatory response of primary macrophages, thereby facilitating osteogenic activity and wound repair.[31,32] From a clinical standpoint, implant dentistry and related research aim at maintaining the AR dimensions and optimising soft tissue healing following tooth TE.[33] The authors support the results of a recent CBCT-based comparative study with 9 months of follow-up evaluated the soft tissue changes around dental implants placed with and without PRF, which reflects the changes in CBL.[34] It was therefore

anticipated that SP using PRF is more effective in maintaining alveolar dimensions than FGG after TE.

Results of the present RCT are in accordance with the null hypothesis, since PRF and FGG were equally effective in preserving the CBL following SP. Moreover, there were no significant differences in bleeding index or plaque index score during the follow-up period. Here, it is worth mentioning that the principal objective underlying the assessment of the sockets was to specifically examine the prospective enduring impact of initial PRF therapy on SP over a 6-month follow-up period. A remarkable observation in the present RCT was that self-rated postoperative pain was markedly less amongst patients in the test group compared with the control group. The regenerative properties of PRF and its ability to modulate the release of inflammatory mediators may help reduce nerve sensitisation, resulting in decreased pain perception.[35] It could be contended that assessing self-rated pain after 6 months of treatment was rather irrelevant. However, a rationale for this assessment is that the CBL, the primary outcome variable, was evaluated both at baseline and at the 6-month follow-up. This provided no reasonable basis to exclude the evaluation of the secondary outcome variable, self-rated pain, at the 180-day follow-up. Nevertheless, caution should be exercised when interpreting these results, as several factors may have influenced the reported outcomes. Given the stringent control of these factors, it is conceivable that the complete extent of PRF's influence on enhancing healing and preserving osseous integrity may not have been fully apparent. As reflected in Table 3, the only significant difference between the test and control groups was noted when the change in buccolingual width of alveolar bone was compared. This parameter was significantly higher in the control than the test group. This outcome is in accordance with results from a split-mouth RCT,[36] which concluded that PRF is an autologous biomaterial that facilitates postextraction bone defect filling and faster bone regeneration. It is important to clarify that the primary objective of using PRF in the current investigation was to chiefly help preserve the alveolar dimensions, rather than actively regenerate the latter. Strict eligibility criteria were applied, which excluded individuals with a history of using nicotine products, those with systemic diseases such as CVD and DM, as well as patients with a history of periodontal disease. Furthermore, all surgical procedures were carried out using a flapless technique by a skilled and trained operator, reducing the likelihood of complications such as soft tissue damage and fracture of the alveolar walls. The detrimental effects of habitual use of nicotine products and persistent hyperglycaemia on osseous tissues are widely recognised.[37-39] These factors can impair the healing process and increase the risk of alveolar bone resorption.[37-39] Nevertheless, the clinical significance of such a minimal yet statistically significant change as observed in the present RCT remains open to debate. In summary, results of the present RCT suggest that local administration of PRF during implant placement has the potential to positively enhance osseous tissue regeneration and could therefore be utilised as a beneficial therapeutic adjunct in clinical scenarios involving implant placement. Considering the findings of the current RCT, the authors hypothesise that if postextraction complications, such as soft tissue trauma or osseous defects, had been present, PRF would have shown superior capabilities in ST healing and bone regeneration compared to FGG. However, additional power-adjusted and well-designed randomised clinical trials are necessary to validate this hypothesis.

## Conclusion

FGG and PRF are effective techniques for SP; however, the latter technique is advantageous in terms of maintaining buccolingual dimensions of the ES.

## Conflict of interest

None disclosed.

## Author contributions

All authors contributed equally to the present study. Conceptualisation: HHALA, MS, and SSN. Methodology: HHALA, MS, and SSN. Software: HH, MS, SSA, and SSN. Validation: HHALA, MSB, and MS. Formal analysis: MSB and SSA. Investigation: HHALA, MS, and SSN. Resources: HHALA, MS, and SSN. Data curation: HHALA and SSN. Writing–original draft preparation: HHALA, MSB, and SSA. Writing–review and editing: MSB and SSA. Visualisation: HHALA and MS. Supervision: SSN and MS. Project administration: HHALA and SSN. All authors have read and agreed to the published version of the manuscript.

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