Comparative Evaluation of Clinical Efficacy of Leukocyte-Rich Platelet-Rich Fibrin with Advanced Platelet-Rich Fibrin in Management of Gingival Recession Defects: A Randomized Controlled Trial

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Highlights of the Study
- In vitro studies have shown that advanced PRF (A-PRF) has a higher growth factor content, suggesting that it has a greater therapeutic potential than leucocyte-rich PRF (L-PRF).
- There have been no documented clinical trials comparing both treatment techniques in root coverage procedures in conjunction with coronally advanced flaps (CAFs).
- There were no statistically significant differences in therapeutic outcomes between the two groups (CAF + A-PRF and CAF + L-PRF).
- Both treatment modalities are equally effective in managing Miller’s class I and II maxillary recession defects.

Keywords
Gingival recession · Maxilla · Platelet-rich fibrin · Blood platelets

Abstract
Background: The aim of this research was to determine and compare the clinical efficacy of leukocyte platelet-rich fibrin (L-PRF) and advanced platelet-rich fibrin (A-PRF) in combination with coronally advanced flap (CAF) in the treatment of gingival recession defects. Methods: Systemically healthy subjects presenting with 30 Miller’s class I or II gingival recession defects in maxillary anteriors and premolars, were treated with either CAF + L-PRF or CAF + A-PRF. Clinical parameters such as recession height (RH), width, probing pocket depth, clinical attachment level (CAL), keratinized tissue height (KTH), and width of attached gingiva (WAG) were measured at baseline, 3, and 6 months. Gingival biotype was evaluated at baseline and 6 months post-surgery. Mean root coverage percentage (MRC%) was evaluated at 3 and 6 months. Results: Statistically significant reduction in mean RH was observed from baseline (2.53 ± 0.74 mm, 2.63 ± 0.82 mm) to 6 months (0.87 ± 0.83 mm, 0.53 ± 0.91 mm) in CAF + L-PRF and CAF + A-PRF groups, respectively. The MRC% achieved at 6 months was 67.20 ± 32.81 in the CAF + L-PRF group and 81.66 ± 28.21 in the CAF + A-PRF group. Statistically significant gain in CAL, WAG, and KTH was observed in both therapeutic groups (p < 0.05). Intergroup analysis re-
vealed no statistically significant differences among study parameters between groups at any time point (p > 0.05).

**Conclusion:** Based on the findings of this study, both L-PRF and A-PRF may be suggested as viable treatment options for the management of gingival recession in maxilla.

**Introduction**

Gingival recession is described as apical migration of the free gingival margin relative to the cemento-enamel junction resulting in root exposure [1]. The prevalence of mid-buccal recession defects was 91.6% as indicated in a recent epidemiological study conducted by NHANES 2020 [2]. Research in the South Indian population found approximately 40–68% of the subjects had at least one or more gingival recession defects [3, 4]. Gingival recession is often associated with dentinal hypersensitivity, aesthetic issues, and also root caries. Periodontal plastic procedures aim to achieve complete root coverage while enhancing aesthetics by integrating mucosa and keratinized gingiva with adjacent tissues.

Periodontal wound healing is a complex biological process consisting of multiple concurrent cellular events leading to repair or regeneration [5]. Platelets are the initial cells involved in the wound healing process. Upon activation, they release various bioactive molecules, cytokines, and adhesive proteins stimulating inflammatory cells to populate in the surgical area thereby setting the pace for the wound healing process. The second-generation platelet concentrates are formed by natural polymerization during centrifugation, resulting in a three-dimensional fibrin architecture with equilateral junctions mimicking the extracellular matrix structure, offering flexibility and elasticity. These linked junctions facilitate the migration of cells, entrapment of cytokines, and their continuous release over a period of time provides an atmosphere for cells to function optimally [6, 7]. Leukocyte platelet-rich fibrin (L-PRF) is being extensively used in various aspects of the medical field including dentistry. However, due to high centrifugation force (3,000 rpm for 10 min at 708 G) in L-PRF, cell populations shift to the bottom of the tubes, resulting in fewer desired cells in the procured PRF clot. The low-speed centrifugation concept led to the development of advanced platelet-rich fibrins (A-PRF, A-PRF+) [8]. A-PRF obtained by centrifugation protocol of 1,500 rpm for 14 min at 200 G yielded a porous fibrin structure with larger interfibrinous space incorporating higher numbers of platelets and inflammatory cells, evenly distributed all through the matrix releasing significantly increased levels of certain growth factors such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), insulin-like growth factor (IGF), and epidermal growth factor (EGF). A-PRF was found to contain increased levels of VEGF, responsible for angiogenesis, monocytes as a source for bone morphogenetic proteins (BMPs), and fibronectin for extracellular matrix formation [9–11]. Various in vitro and in vivo studies have shown the positive outcomes with A-PRF in hard and soft tissue regeneration [12–16]. However, the potential benefit of A-PRF in management of gingival recession has not yet been established. The aim of this clinical study was to evaluate and compare the clinical efficacies of L-PRF and A-PRF in the treatment of gingival recession defects.

**Materials and Methods**

This study was conducted in the Department of Periodontology, SRM Dental College, Chennai, from June 2021 to December 2021. The sample size was calculated based on the results obtained by Koseoglu et al. [17]. Twenty-four recession defects were needed in order to obtain 80% power, with 5% alpha error. A total of 30 recession sites were initially recruited to account for 20% drop out of subjects.

Systemically healthy individuals between the age of 18 and 65 years who had isolated Miller’s class I and II recession defects with a minimum recession depth of 2 mm in the maxillary anteriors and premolars were included in this intervention. Individuals with a known history of platelet disorders, systemic conditions/diseases influencing the course of periodontal disease and therapy, such as diabetes mellitus, past history of periodontal therapy, and current smokers were exempted from the study. Written informed consent was obtained from all the willing participants. Figure 1 depicts the study design.

Clinical parameters such as recession height (RH), recession width (RW), width of attached gingiva (WAG), keratinized tissue height (KTH), and relative vestibular depth (RVD) were documented using a university of North Carolina-15 (UNC-15) periodontal probe (Hu-Friedy) guided by a reference groove on a customized composite stent. Scaling and root surface debridement were performed using ultrasonic scalers (Satelec P5 Newton) and area-specific curettes (Hu-Friedy 1–2, 3–4, 5–6) and coronoplasty was done if needed. Recession sites with a minimum recession depth of 1–2 mm (Fig. 2a, 3a) were restored with glass ionomer restorative cement (GC Fuji IX GP Extra) (Fig. 2b, 3b). Patients were called back after 4 weeks to determine compliance with oral hygiene practices and tissue response after completing case-related care. On the day of the surgical intervention, recession sites were randomly allocated into either one of the two study groups CAF+L-PRF or CAF+A-PRF using a labelled slip method.

Under local anaesthesia (2% lignocaine, 1:80,000 adrenaline), horizontal butt incisions were given at the mesial and distal aspects of the free gingival margin relative to the cemento-enamel junction resulting in root exposure [1]. The prevalence of mid-buccal recession defects was 91.6% as indicated in a recent epidemiological study conducted by NHANES 2020 [2]. Research in the South Indian population found approximately 40–68% of the subjects had at least one or more gingival recession defects [3, 4]. Gingival recession is often associated with dentinal hypersensitivity, aesthetic issues, and also root caries. Periodontal plastic procedures aim to achieve complete root coverage while enhancing aesthetics by integrating mucosa and keratinized gingiva with adjacent tissues.

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Fig. 1. Flowchart showing the recruitment and therapeutic intervention. CAF, coronally advanced flap; L-PRF, leukocyte platelet-rich fibrin; A-PRF, advanced platelet-rich fibrin; RH, recession height; RW, recession width; PPD, probing pocket depth; CAL, clinical attachment level; WAG, width of attached gingiva; KTH, keratinized tissue height; RC%, root coverage percentage; GTH, gingival thickness; VAS-E, visual analogue scale-aesthetics; RES, recession aesthetic score.
of the defect site at the base of interdental papillae near the CEJ, as previously recommended [18]. Two oblique vertical divergent incisions were given at the end of these horizontal incisions extending up to the alveolar mucosa. The resultant trapezoidal flap was carefully elevated with a split-full-split approach. Muscle attachments were detached with a blunt dissection. The interdental papillae coronal to the horizontal incisions were de-epithelialized (Fig. 2c, 3c). Thorough root surface debridement was done using area-specific curette (Hu-Friedy 1–2, 3–4, 5–6) and the flap was checked for coronal advancement.

Ten millilitres of intravenous blood was collected from the antecubital vein of each subject. The PRF vacutainer tubes (Servident) were transferred to the centrifuge without delay and centrifuged at 1,500 rpm for 14 min (200 G) for A-PRF (LABTECH-Dentifuge) and 2,700 rpm for 12 min (708 G) for L-PRF (REMI R-8C Centrifuge), respectively [8, 10]. Centrifugation resulted in the formation of three layers, acellular platelet poor plasma at the top, a fibrin clot in the middle, and RBC at the bottom part. The clear supernatant fluid was discarded; PRF clots (Fig. 2d, 3d) were retrieved carefully and gently compressed to form membranes (Fig. 2d, 3d). The PRF membranes were adapted to the debrided root surface (Fig. 2e, 3e). Flaps were advanced coronally, secured with 4-0 vicryl sutures (Ethicon) (Fig. 2f, 3f), and the sites were protected with periodontal dressing (Coe-Pak).

The patients were prescribed amoxicillin 500 mg and paracetamol 500 mg every 8 h for 5 days. Patients were advised to refrain from brushing at the surgical sites for 4 weeks and to use 0.12% chlorhexidine mouth rinse twice daily for 1 month. Patients were recalled after 2 weeks for suture removal. Healing was uneventful without any post-operative complications. Patients were further reviewed at the end of 1, 3, and 6 months. Figures 2a–g and 3a–g depict the images of recession defects and the surgical intervention with A-PRF and L-PRF, respectively. Figures 2h and 3h show the post-operative view of the surgically treated sites with CAF + A-PRF and CAF + L-PRF at 6 months, respectively.

**Statistical Analysis**

Statistical analysis was performed using Statistical Package for Social Science software (SPSS, version 17). Descriptive statistics of demographic and clinical parameters were expressed as mean and standard deviation except for gender, tissue biotype, and Miller’s class of recession. The Kolmogorov Smirnov test was used to determine the normality of the data. Age, probing pocket depth (PPD), KTH, and RVD had a parametric distribution, while RD, RW, root coverage percentage, clinical attachment level (CAL), WAG, plaque index, gingival index, recession aesthetic score, and visual analogue scale-aesthetics (VAS-E) had a non-parametric distribution. Pearson $\chi^2$ analysis was used to identify significant differences in categorical parameters. For parametric and non-parametric data, statistically significant differences in clinical parameters between and within study groups at different time points were investigated using the $t$ test and Wilcoxon signed-ranks test, respectively. $p \leq 0.05$ was considered statistically significant by these statistical tools.
Results

Table 1 depicts demographic information of recruited participants, clinical characteristics of the recession sites at baseline. There were no significant differences in the mean clinical parameters (RH, PPD, CAL, KTH, WAG, and RVD) between the study groups at baseline except for the mean RW ($p = 0.033$). The mean descriptive values of clinical parameters at 3 and 6 months and their significant variation from baseline within the study groups are shown in Tables 2 and 3, respectively. At 3 months, there were no significant differences in the clinical parameters (RH, RW, PPD, CAL, WAG, and RVD) between the groups except for the mean KTH ($p = 0.016$). The mean clinical parameters did not differ significantly between the treatment groups at 6 months. When compared to the mean baseline values, the CAF + L-PRF and CAF + A-PRF sites showed statistically significant improvement in all clinical parameters at 6 months (Table 3).

Discussion

The primary objective of this investigation was to assess and compare the changes in RH. The secondary objectives included the comparison of changes in root coverage percentage, RW, PPD, CAL, recession aesthetic score, and VAS scores between the study groups.

Thirty systemically healthy subjects presenting with isolated gingival recession defects were randomly treated with either CAF + L-PRF or CAF + A-PRF. From baseline to 6 months, a mean reduction in RH of $1.66 \pm 0.09$ mm and $2.1 \pm 0.09$ mm was observed in the CAF + L-PRF and CAF + A-PRF groups, respectively.

Numerous studies have been published on the efficacy of L-PRF in combination with CAF in management of gingival recession; we compared our treatment outcomes with results described in recent meta-analyses on the intervention of multiple or isolated recession defects. An analysis of 3 randomized controlled trials (RCTs) concluded that the average reduction in RH in the CAF + L-PRF group ranged from $1.30 \pm 0.5$ mm to $2.53 \pm 0.64$ mm [19]. Another analysis of 4 RCTs reported a mean reduc-

![Fig. 3. Surgical intervention with L-PRF. a Class I gingival recession in relation to 23. b After restoration. c Flap elevation. d L-PRF clot and membrane preparation. e L-PRF adaptation. f Flap advancement and suturing. g Suture removal at 2 weeks. h Post-operative view at 6 months.](image-url)
tion of RH in the range of 1.30 ± 0.5 mm–3.44 ± 1.09 mm [20]. Similarly, a most recent meta-analysis by Rodas et al. [21] of 7 RCTs concluded that there is a mean reduction in RH within the limits of 1.07 ± 0.17 mm–3.56 ± 0.1 mm in the CAF + L-PRF group [21]. The mean recession reduction obtained in the present study is in accordance with the results of above-mentioned studies. As there was only one case series reported studying outcomes of the CAF + A-PRF combination [22], we are unable to correlate our findings with other literature.

At 6 months, the mean root coverage percentage (MRC%) achieved in our study was 67.20 ± 32.81%.
81.66 ± 28.21% in CAF + L-PRF and CAF + A-PRF groups, respectively. In their respective meta-analysis, the MRC% obtained in our study is within the range stated by published meta-analyses of RCTs [20, 23, 24] on intervention with CAF + LPRF and reported MRC% ranging from 72.7 to 100%. Though CAF + A-PRF treated sites had a greater MRC% at the end of 6 months in our study, no statistically significant difference was noted in comparison with the CAF + L-PRF group (p = 0.19). A total of 6 sites in L-PRF (40%) and 10 in the A-PRF group (66.66%) attained complete root coverage at the end of 6 months, which is in agreement with a previous study [25].

Among the 15 enrolled sites in each group, 14 recession sites belonged to thin biotype at baseline. Twelve sites in the CAF + L-PRF and 9 sites in the CAF + A-PRF group had transformed into a thick biotype by the end of 6 months. Significant reduction in mean PPD and gain in mean CAL values were noted from baseline to 6 months in both the study groups, respectively; this is consistent with observations of Rodas et al. [21].

An adequate zone of keratinized tissue was believed to be desirable as it acts as a resistant barrier to the inflammation induced by plaque, dissipates masticatory and functional stresses, and enhances aesthetics and patient comfort [26]. There was a statistically significant gain in the KTH from baseline to 6 months with mean values of 0.47 ± 0.19 mm and 0.54 ± 0.09 mm in CAF + L-PRF and CAF + A-PRF groups, respectively. Rodas et al. [21] reported a mean gain in KTH with a range of 0.38 ± 0.64 mm to 1.18 ± 0.19 mm among the RCTs on intervention with CAF + L-PRF.

### Conclusion

Within the limitations of the current study, we observed significant improvement in all the clinical parameters in both interventions suggesting the equivalent therapeutic benefits of both CAF + L-PRF and CAF + A-PRF application in managing Miller’s class I and II maxillary recession defects. Though literature on in vitro studies on A-PRF shows greater growth factor content and even cellular distribution than L-PRF, the clinical outcomes of the present study do not show any significant differences between the study groups. Outcomes of the current study could be strengthened by examining larger samples with a longer-term follow-up.

### Statement of Ethics

This randomized, controlled clinical trial was conducted in accordance with the Helsinki Declaration and was approved by the Institutional Ethics Committee and the Scientific Review Board (SRMU/M&HS/SRMDC/2021/S/007). The study was registered in the Clinical Trial Registry, India (CTRI/2021/05/033564). The essence of the research, possible risks, and benefits were explained to all eligible participants. Written informed consent was obtained from all willing participants.
Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conception and design, data interpretation and analysis, manuscript drafting, and final approval: Dr. Harinath Parthasarathy and Dr. Anupama Tadepalli. Data acquisition, interpretation, analysis, manuscript preparation, and drafting: Dr. Swapna Chekurthi and Dr. Swarupa Kavassery Balasubramanian. Data revision, statistical interpretation, technical assistance, and manuscript drafting: Dr. Deepa Ponnaiyan.

Data Availability Statement

Data will be provided upon reasonable request to the corresponding author.

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