Journal of Current Research in Oral Surgery
2025, Volume 5, Issue 2, Page No: 72-89

ISSN: 3062-3480

Original Article

Comparative Clinical and Radiographic Evaluation of Open Flap Debridement, Leukocyte-Rich PRF, and Titanium PRF in the Management of Three-Walled Intrabony Defects: A Randomized Controlled Trial

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Received: 12 April 2025; **Revised:** 11 August 2025; **Accepted:** 16 August 2025

ABSTRACT

Periodontal regeneration involves the complex, multi-step rebuilding of the tooth-supporting apparatus to re-establish clinical health. Complete restoration via currently available regenerative approaches remains achievable only to a limited degree. Platelet Rich Fibrin can be described as a polymerized fibrin construct created through a straightforward method aimed at potentiating the inherent wound-healing properties of a natural blood coagulum by enriching it with bioactive growth factors. This specialized framework doubles as a delivery platform for growth factor molecules while also shuttling cells critical for new tissue formation. Recognized shortcomings of PRF encompass possible silica-mediated cross-contamination, insufficient structural stiffness, and rapid breakdown in situ. Seeking to address these constraints, the third iteration of platelet concentrates—Titanium PRF—was fabricated using the body-friendly metal titanium. Within this formulation, the fibrin scaffold is characterized by a more prolonged resorption period, heightened osseointegrative properties, improved compatibility with blood components, superior cell-supporting architecture, and an enhanced capacity to stimulate periodontal regeneration. What this controlled clinical trial sets out to accomplish is a comparative evaluation of the clinical and radiographic performance of Leukocyte Rich Platelet Rich Fibrin [L-PRF] alongside open flap debridement versus Titanium-Platelet Rich Fibrin [T-PRF], as well as Open Flap Debridement [OFD] administered independently, when treating three-walled intrabony periodontal lesions. The present Randomized controlled clinical investigation took place at the Department of Periodontics, Rural Dental College, Loni. Twenty-five subjects, each presenting three-walled intrabony defects distributed across three distinct locations, underwent treatment allocation to one of three arms: OFD combined with L-PRF (experimental), OFD combined with T-PRF (experimental), and OFD as a standalone procedure (control). Shifts in probing pocket depth and improvements in clinical attachment level were documented at the 9-Month mark, whereas the extent of defect fill and crestal alveolar bone loss were quantified at both 6 and 9 Months following the surgical intervention; statistical evaluation was performed via Analysis of Variance (ANOVA) supplemented by Post hoc Tukey's test. Probing Pocket depth values were determined by measuring from the free gingival margin down to the pocket floor, and Clinical attachment Level values were obtained by gauging the span from each tooth's cementoenamel junction down to the soft tissue floor of the pocket with the aid of a customized stent. Before any surgical manipulation, a uniform digital periapical radiograph was obtained using a tailored bite plate and a paralleling angle technique. Radiographic assessments comprised (1) the measurement extending from the Cemento Enamel Junction [CEJ] to the most apical point of the vertical osseous lesion (BD), and (2) the measurement extending from the CEJ to the alveolar crest (AC). All values were recorded employing a calibrated millimeter grid. The discrepancy between the 6-month and 9-month readings and the initial CEJ-BD value indicated the volume of bone fill achieved. The discrepancy in CEJ-AC values was interpreted as the magnitude of crestal bone resorption, respectively. The evolution in Plaque Scores, tracked from Baseline to 9 Months across multiple assessment intervals, revealed that the alteration in average PI Scores observed between Baseline and 1 Month, Baseline and 3 Months, Baseline and 6 Months, and Baseline and 9 Months reached statistical significance across the entire study sample. Turning to the clinical indices, the head-to-head assessment of PPD reduction and CAL gain spanning Baseline to 9 Months across the three arms—OFD, L-PRF, and T-PRF—highlighted that the most substantial mean improvement was registered for T-PRF, followed sequentially by L-PRF and then OFD. Regarding the radiographic endpoint of defect fill, the data demonstrated that at both the 6- and 9-Month time points, osseous regeneration was most pronounced in the T-PRF cohort, followed by the L-PRF cohort, with the OFD cohort exhibiting the least bone formation. When the parameter of crestal bone resorption was scrutinized between baseline and 9 Months, the average CEJ-to-AC span in the OFD Group was found to have expanded; in the L-PRF group, no measurable shift was detected; and within the T-PRF group, the average CEJ-to-AC span was noted to have contracted (a finding indicative of bone apposition occurring solely within the T-PRF Group). While acknowledging the inherent limitations of this investigation, it may be deduced that the deployment of Titanium Platelet-Rich Fibrin unlocks novel avenues for amplified healing and functional reclamation in the context of intrabony defect management, delivering a more pronounced decrease in pocket depth, superior clinical attachment gain, and the capability of yielding a greater quantity of new bone over a condensed timeframe when contrasted with both L-PRF and OFD.

Keywords: Intra-bony defects, Leukocyte rich platelet rich fibrin, Open flap debridement, Randomized controlled clinical trial, Regeneration, Titanium platelet rich fibrin

How to Cite This Article: Hassan A, Siddiqui N, Khan B, Malik S. Comparative Clinical and Radiographic Evaluation of Open Flap Debridement, Leukocyte-Rich PRF, and Titanium PRF in the Management of Three-Walled Intrabony Defects: A Randomized Controlled Trial. J Curr Res Oral Surg. 2025;5(2):72-89. https://doi.org/10.51847/7JRZtV0cZ3

Introduction

Periodontitis, an inflammatory condition driven by immune responses and arising from a combination of etiological factors, is established as a cause of deterioration within the periodontal attachment apparatus [1]. Alveolar bone resorption remains a prominent hallmark of advancing periodontal pathology [2].

Deep intraosseous defects constitute a substantial clinical hurdle given their anatomical intricacy and have been linked to an elevated likelihood of ongoing disease progression. Management of these lesions routinely calls for an access flap, performed either in isolation or alongside osseous resection protocols or tissue regeneration strategies [3].

Contemporary ambitions in periodontal care extend beyond the mere control of inflammation and elimination of infection, aiming additionally to reconstruct lost anatomical components to restore physiological function and health [4]. The contributions of Prichard [5] furnish "proof of principle" confirmation that, under favorable clinical conditions, attaining periodontal regeneration through surgical debridement without the addition of adjunct techniques is feasible. In clinical investigations of regenerative interventions, open-flap debridement (OFD) has customarily served as the benchmark control treatment. Even when functioning solely in this control capacity, OFD has been associated with noteworthy clinical gains [6, 7].

Drawing upon a recent synthesis of the literature [8], the mean increment in clinical attachment level (CAL) yielded by OFD on its own reached 1.65 mm, the mean diminution in probing pocket depth (PPD) equalled 2.80 mm, the mean elevation in recession (REC) amounted to 1.26 mm, and osseous augmentation documented at 12 months corresponded to 1.04 mm when evaluated clinically and 0.95 mm through radiographic assessment. While the recorded soft-tissue responses following OFD point to measurable improvements, the corresponding effects on hard tissues have yielded a range of outcomes. Consequently, a variety of alternative strategies have been pursued to accelerate tissue repair, modulate inflammatory activity, and enhance the quality of regeneration.

Investigations at the molecular scale have illuminated the biology underpinning regeneration by cataloging locally derived mediators that become upregulated during the reparative phase. Such mediators, collectively termed growth factors (GF's), are capable of orchestrating an extensive array of cellular behaviors, among them chemotaxis, mitogenesis, phenotypic specialization, and the deposition of extracellular matrix constituents [9]. A persistent difficulty surrounding the therapeutic deployment of GF's has been the lack of a truly optimal carrier matrix [10].

A relatively recent advance adopted by the dental profession involves the preparation of autologous platelet-rich fibrin. Preparations derived from platelets, often referred to as platelet concentrates, have been proposed as biological response modifiers that support the healing process. Leukocyte platelet-rich fibrin (L-PRF), a second-generation platelet concentrate pioneered by Choukroun *et al*. [11] and Dohan *et al*. [12], permits the procurement of fibrin membranes densely populated with platelets and GFs, starting with a blood draw performed without anticoagulant additives and entirely free of synthetic chemical manipulation.

L-PRF, which functions concurrently as an immune-cell and platelet concentrate, assumes the form of a fibrin mesh concentrate exhibiting notable tensile robustness, durability, and structural firmness [13], properties that facilitate more proficient cellular migration and multiplication, thus fostering cicatrization that is conducive to both repair and immunological competence [14]. This singular configuration serves as a conduit for GF release while simultaneously transporting cells vital to tissue renewal. The cohesive interplay among fibrin, platelets, circulating stem cells, leukocytes, GFs, and cytokines establishes L-PRF as a restorative biomaterial with substantial promise for expediting regeneration in both osseous and soft-tissue compartments [15].

While encouraging clinical outcomes have been associated with the application of L-PRF [2, 16-21], this formulation is not without inherent shortcomings, including the hazard of silica cross-contamination, a deficiency in structural stiffness, and a relatively brief resorption profile [2]. A critical appraisal by Miron *et al*. [22] highlighted the deleterious effects of blood collection tubes containing silica and silicone. The data presented in that same review indicated that silica originating from tube surfaces provoked a perceptible decrease in the dimensions of the resulting PRF clot.

Prompted by the silica contamination concern inherent to L-PRF, O'Connell [23] and Tunalı *et al*. [24] set out to examine a next-generation biomaterial that eliminated the need for glass or glass-lined vacutainer systems. They succeeded in formulating a novel biomaterial within a titanium conduit, exploiting the metal's recognized osseointegrative quality, superior tissue compatibility, and inherent capacity to trigger platelet activation.

A third-generation platelet concentrate designated as titanium-prepared platelet-rich fibrin (T-PRF) yields a thicker fibrin stratum, a prolonged resorption timeline, enhanced osseointegration potential, improved compatibility with blood constituents, more robust cellular scaffolding, and the stimulation of genuine periodontal regeneration [24]. Beyond these features, T-PRF persists longer at the implantation site before undergoing resorption than L-PRF, thereby enabling an extended release profile for assorted GFs [23-25].

When weighing the observations summarized above together with the sustained liberation of numerous GFs, a plausible expectation emerges that subjecting an intra-bony defect (IBD) to T-PRF treatment could foster more robust wound repair and more complete periodontal regeneration relative to sites managed through standard open flap debridement and L-PRF. To formally examine this premise, the study reported herein was conducted as a single-site controlled clinical investigation aimed at probing the clinical and radiographic (bone fill) performance of autologous T-PRF when delivered into IBDs of individuals diagnosed with chronic periodontitis.

Aims

The central aim of this interventional, controlled clinical study was to assess, using both clinical measurements and radiographic visualization, the efficacy of L-PRF and T-PRF when deployed alongside OFD for the management of 3-walled IBDs, and to benchmark this against OFD alone.

Objectives

- To quantify the decrement in PPD, the increment in CAL, and the extent of radiographic bone fill (RBF) realized through periodontal treatment of 3-walled IBD's employing OFD
- To quantify the decrement in PPD, the increment in CAL, and the extent of RBF realized through periodontal treatment of 3-walled IBD's employing L-PRF in conjunction with OFD
- To quantify the decrement in PPD, the increment in CAL, and the extent of RBF realized through periodontal treatment of 3-walled IBD's employing T-PRF in conjunction with OFD
- To contrast the decrement in PPD, the increment in CAL, and the extent of RBF accomplished via L-PRF combined with OFD against T-PRF combined with OFD in the context of 3-wall IBD therapy
- To ascertain whether the supplementary incorporation of L-PRF and T-PRF into periodontal treatment protocols could potentially deliver a meaningfully larger gain in CAL and RBF, along with a more substantial reduction in PPD, when measured against the results obtained with OFD exclusively.

Materials and Methods

Study design

This controlled clinical investigation was conducted in the Department of Periodontics at Rural Dental College, Loni, from 2019 through 2023. Approval for the study was obtained following review and acceptance by the Institutional Ethics Committee, Pravara Institute of Medical Sciences, Loni, with clearance granted by the Institutional Ethics Committee, PIMS (Deemed to be University), Loni (PMT/PIMS/IEC/2019/14). The study design conformed to the CONSORT 2010 statement **(Figure 1).**

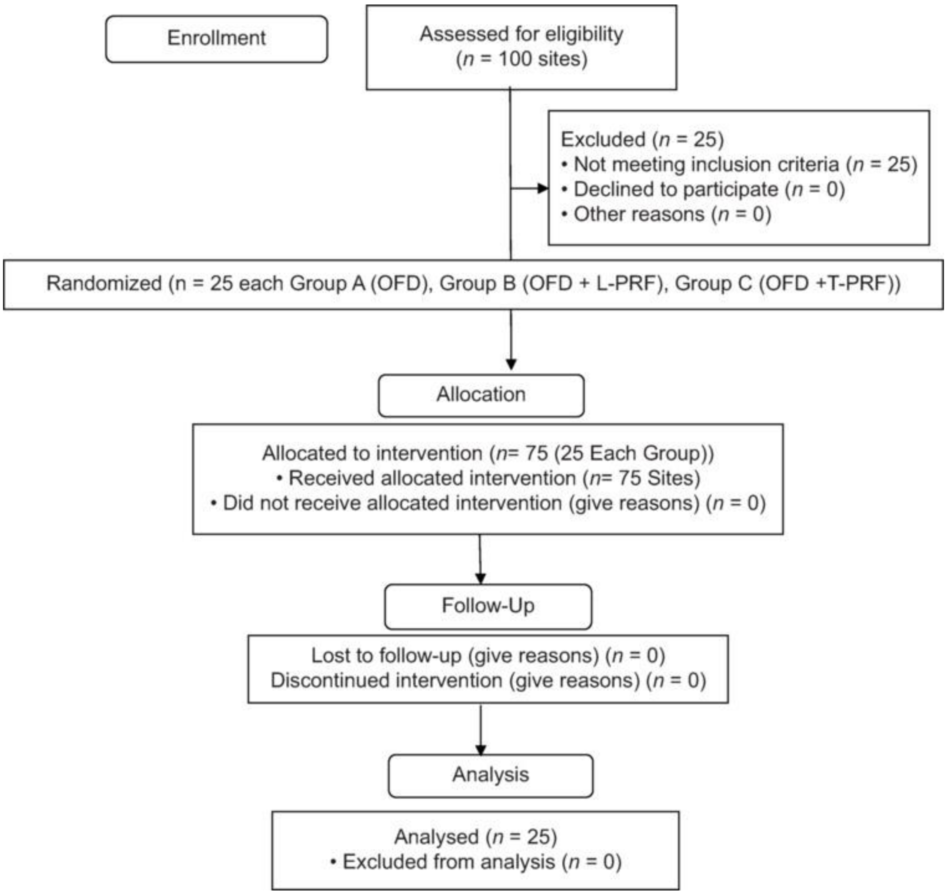


Figure 1. CONSORT 2010 flow diagram.

Study registration

Registration of the present clinical trial's protocol was completed within the Clinical Trials Registry of India, which operates under ICMR's National Institute of Medical Statistics, where it received the identification code CTRI/2021/03/031964.

A comprehensive questionnaire was administered to collect demographic particulars, together with clinical and radiographic measurements. Every facet of the investigation and its related procedures was elaborated upon in detail, and before study commencement, written informed consent was procured from all participants. Recruitment yielded 25 patients, identified according to the specifications enumerated below.

Inclusion criteria

Recruited subjects were required to be systemically healthy, aged between 25 and 40 years, possessing no fewer than 20 permanent teeth, among which a minimum of 3 teeth presented three-wall IBD's surpassing 4 mm in depth (measured as the interval from the alveolar crest (AC) down to the defect floor as identified on intraoral periapical radiographs), along with interproximal probing depth (PD) equalling or exceeding 5 mm and CAL reaching at least 3 mm upon examination 8 weeks post-completion of phase I therapy (scaling and root planning [(SRP]), and additionally presenting a minimum of 2 mm of keratinized gingiva on both facial and lingual aspects of the tooth designated for inclusion.

Exclusion criteria

Individuals were excluded from participation if they presented with blood-related or immune-mediated conditions, were pregnant or nursing, consumed tobacco via smoking or other means, were receiving pharmaceutical agents with established interference in wound repair pathways, disclosed a history of antibiotic consumption or periodontal treatment within the 6 months preceding enrolment, demonstrated platelet concentrations falling below the required threshold ($< 200{,}000/mm^3$), showed furcation involvement coexisting with the IBD, harboured restorations extending beyond the cementoenamel junction (CEJ) at the defect location, possessed a CEJ that could not be reliably discerned either through clinical inspection or radiographic evaluation, exhibited periapical pathology, untreated caries, compromised restorations, root resorption, or vertical root fracture, displayed tooth mobility graded as Miller class 2 or greater, maintained unsatisfactory oral hygiene standards (plaque index [PI > 1.5]) upon reassessment subsequent to phase I therapy, or expressed unwillingness to furnish signed informed consent.

Sample size

Estimation of the necessary sample size was performed utilizing G Power Software Version 3.1.9.4. (Heinrich-Heine-Universität (HHU), Düsseldorf, Germany). Maintaining a 95% confidence interval yielded an estimated requirement of 22 participants per study arm; however, to account for anticipated 10% attrition, this figure was rounded to 25 per arm. Hence, the overall sample comprised 75 sites.

Randomization procedure

Subjects meeting both inclusion and exclusion criteria underwent periodontal status evaluation and radiographic assessment. The quadrant containing the 3-walled IBD's was documented for each subject. Three individually marked slips—designated A, B, and C—were prepared and combined within a transparent vessel. Every participant was directed to randomly assign slips A, B, and C to three of the four quadrants; this process determined which sites received each intervention.

Grouping

Recruitment for the investigation comprised 25 systemically healthy volunteers, who were subsequently distributed across three groups: two experimental groups (each containing 25 sites) and one control group (25 sites). Experimental groups underwent treatment with either T-PRF or L-PRF following OFD (OFD + T-PRF and OFD + L-PRF, respectively), whereas the control group received OFD alone.

- Group A: Intra-bony defects receiving OFD treatment
- Group B: Intra-bony defects receiving OFD + L-PRF treatment
- Group C: Intra-bony defects receiving OFD + T-PRF treatment.

Blinding

Throughout this investigation, both the statistician performing analyses and the examiner conducting assessments remained masked. Achieving participant blinding regarding which therapeutic modality was administered proved impracticable given the distinctive blood collection procedures and the fabrication steps for platelet-rich fibrin inherent to the experimental sites.

Pre-surgical therapy

Initial sequence

Each participant underwent referral for a full-mouth periodontal assessment, following which the initial therapeutic phase—consisting of SRP—was performed. A period of 6–8 weeks after this preliminary periodontal therapy elapsed before re-evaluation of the participant's response to the initial treatment, aimed at gauging both the extent of tissue repair and the standard of oral hygiene. A subsequent full periodontal charting session was conducted, during which PPD, CAL, and PI values were recorded for each tooth.

Calibration of the study examiner

A single highly proficient clinician performed all surgical procedures, while a separate evaluator, someone other than the surgeon, carried out all clinical recordings, unaware of which treatment arm each site belonged to. To establish intra-examiner reliability, preoperative measurements were taken on three individuals receiving periodontal care on two distinct occasions, separated by a 48-hour interval, before the trial commenced. The calibration threshold was met when readings obtained at the initial session and at the 48-hour follow-up matched to the nearest whole millimeter at least 90% of the time.

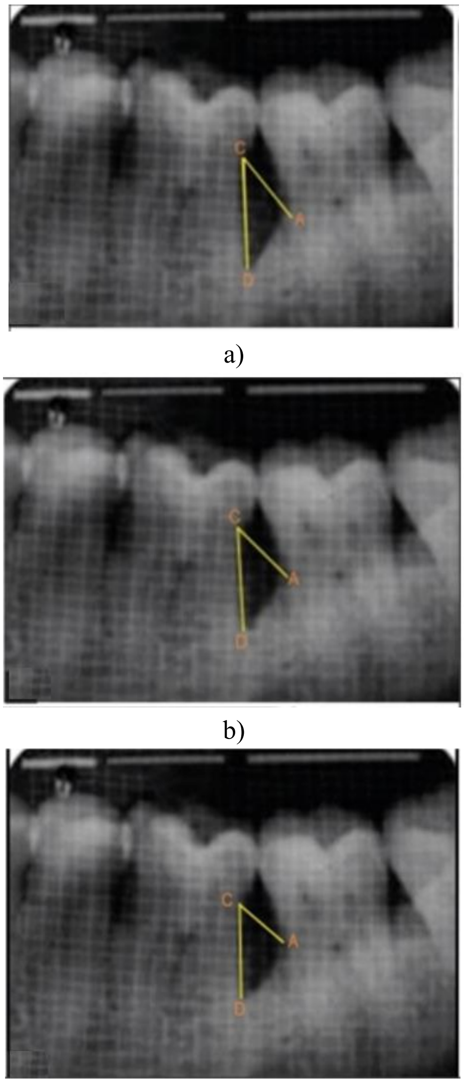
Before the operative phase, PI values and clinical parameters were captured with the prefabricated acrylic stent seated in position and a UNC-15 periodontal probe. Using the groove as a directional guide, both PPD and CAL were registered. A masked investigator performed every clinical recording. PPD and CAL were captured at the initial visit and again at 9 months, whereas plaque scores were documented at baseline, 1 month, 3 months, 6 months, and 9 months.

1. Probing pocket depth: expressed in millimeters, traversing from the free gingival margin down to the pocket's deepest point
2. Clinical attachment level: Quantified, extending from each tooth's CEJ down to the soft tissue floor of the sulcus
3. Plaque score: Plaque accumulation at the defect location was noted on the data capture form according to the Loe and Sillness Index criteria.

Ahead of the surgical intervention, a uniform digital periapical radiograph was obtained using a customized bite plate and the paralleling technique. Radiographs bore labels indicating the patient's full name, outpatient record number, and the date of image acquisition.

Radiographic quantification entailed (1) the interval from the CEJ to the most apical extent of the vertical osseous lesion (BD), and (2) the interval from the CEJ to the AC. All values were derived employing a millimeter grid.

The variance observed between the 6-month and 9-month readings relative to the baseline CEJ BD measurement denoted the volume of bone fill accomplished. Analogously, the variance within the CEJ AC span was taken to signify the magnitude of crestal bone resorption **(Figures 2-4).**



a)

b)

c)

Figure 2. Intraoral periapi cal radiographs at baseline, 6 months, and 9 months: (a) at baseline, (b) at 6 months, and (c) at 9 months

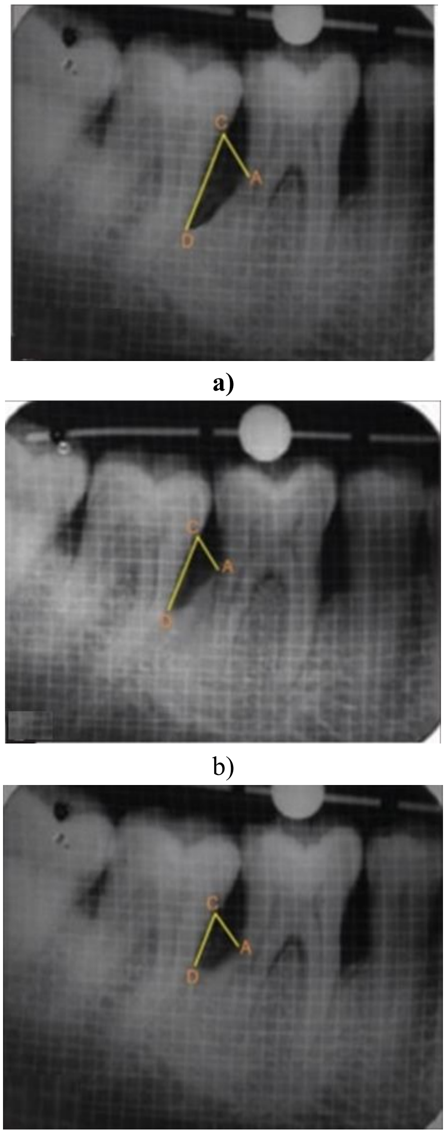


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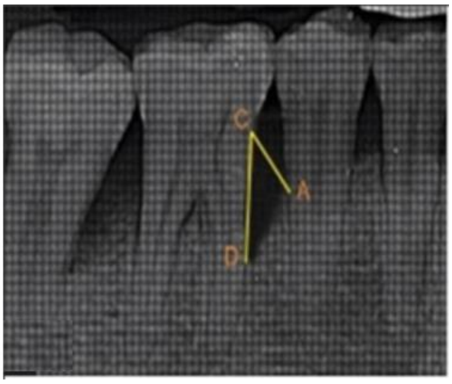
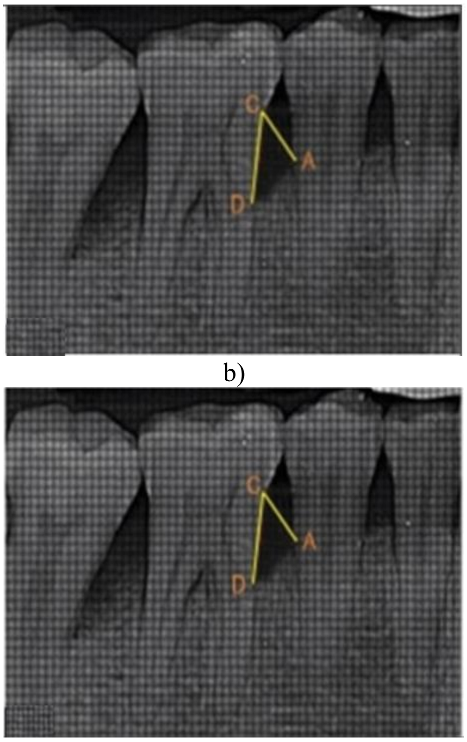
Figure 3. Intraoral periapical radiograph (test site leukocyte platelet-rich fibrin) at baseline, 6 months, and 9 months: (a) at baseline, (b) at 6 months, and (c) at 9 months



a)



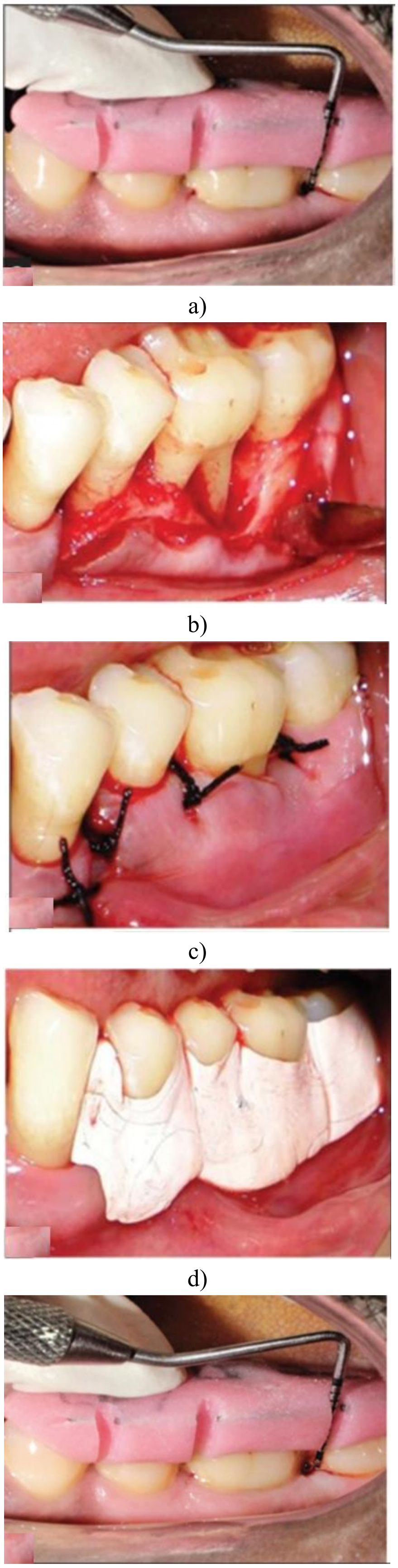
b)

c)

Figure 4. periapical radiographic images of the test location treated with a titanium-prepared platelet-rich fibrin were captured at the initial visit, at the 6-month recall, and at the 9-month follow-up: (a) Initial presentation, (b) Six-month reassessment, and (c) Nine-month evaluation.

Surgical procedure

Routine surgical steps were uniformly applied to both experimental and control locations, as outlined subsequently. Once local anesthesia took effect, crevicular incisions were executed, and mucoperiosteal flaps of full thickness were lifted. The operative area/defect was cleansed to eliminate subgingival biofilm, mineralized deposits, hyperplastic granulation tissue, and pocket lining epithelium, using a combination of manual instrumentation and a cavitron ultrasonic scaler **(Figures 5b, 6b, and 7b).** Every control site was handled identically to the experimental ones, except that neither L PRF nor T PRF was inserted into the defect spaces **(Figures 6c and 7c).** The regenerative substances (L-PRF and T-PRF) were produced in strict accordance with the guidelines issued by the manufacturers:



a)

b)

c)

d)

e)

Figure 5. Control location: (a) Pre-surgical measurement of probing pocket depth and clinical attachment level (control site), (b) Elevation of a

full-thickness mucoperiosteal flap, (c) Placement of sutures and periodontal pack, (d) Periodontal dressing in situ, and (e) Post-surgical evaluation of probing pocket depth and clinical attachment level.

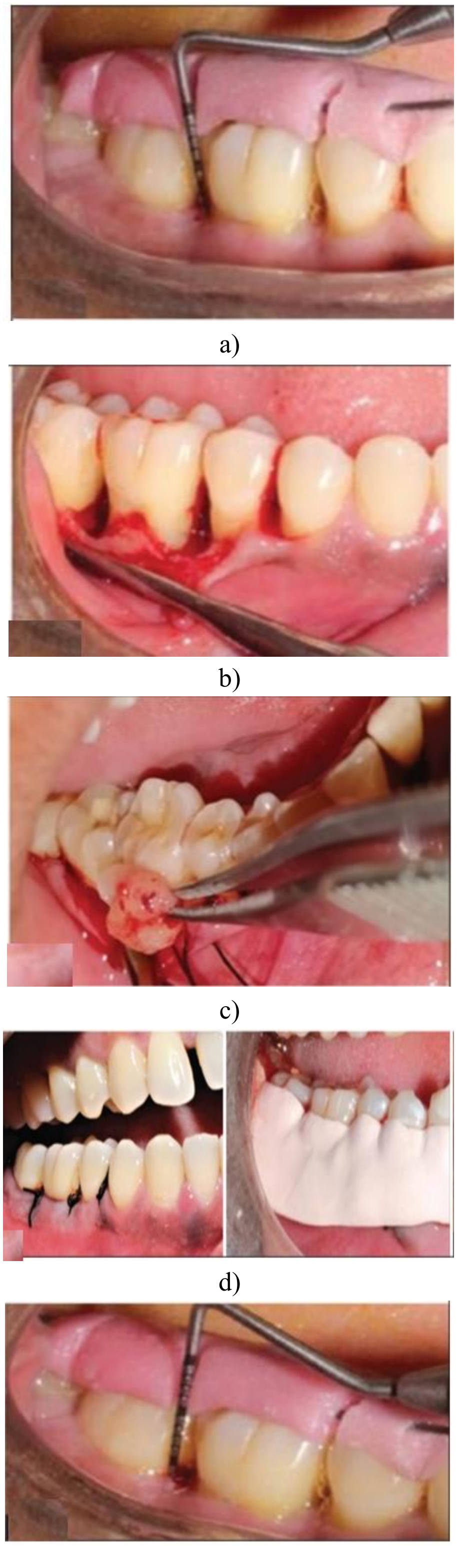

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Figure 6. Experimental location treated with leukocyte platelet-rich fibrin (L-PRF): (a) Preoperative measurement of probing pocket depth and clinical attachment level, (b) Reflection of a full-thickness mucoperiosteal flap, (c) Insertion of L-PRF into the intrabony defect, (d) Suturing and application of periodontal dressing, and (e) Postoperative assessment of probing pocket depth and clinical attachment level.

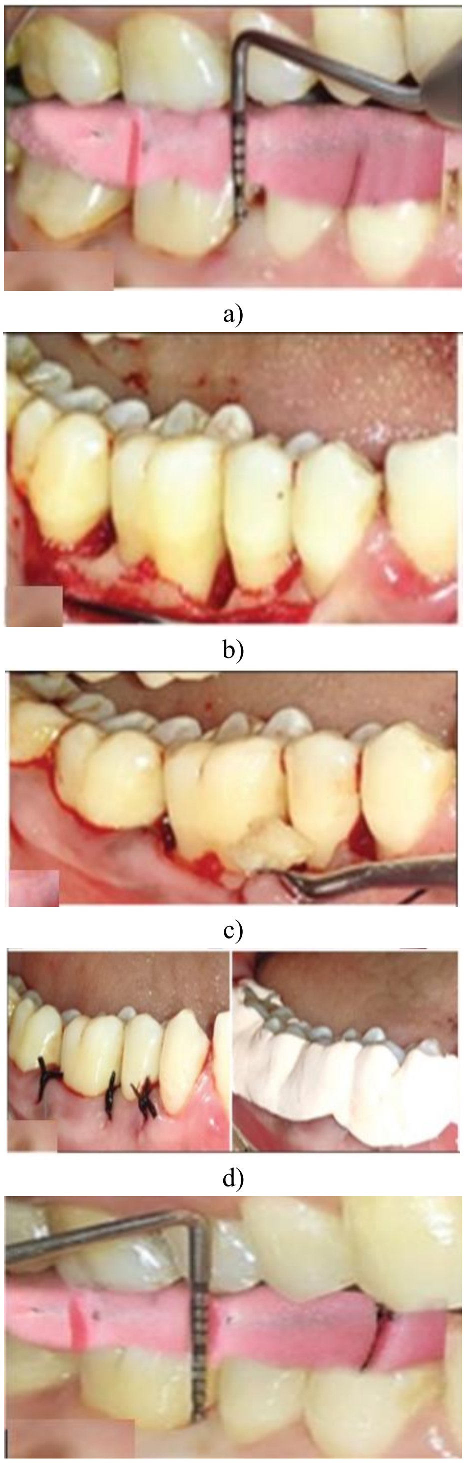
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Figure 7. Experimental location managed with titanium-prepared p latelet-rich fibrin (T-PRF): (a) Pre-surgical recording of probing pocket depth and clinical attachment level, (b) Elevation of a full-thickness mucoperiosteal flap, (c) Pre-placement

suturing followed by insertion of a titanium-prepared platelet-rich fibrin into the intrabony defect, (d) Final suturing and periodontal dressing application, and (e) Post-surgical measurement of probing pocket depth and clinical attachment level.

Method of preparation of leukocyte platelet-rich fibrin and titanium prepared platelet-rich fibrin

Leukocyte-rich platelet-rich fibrin preparation protocol [11]

The L-PRF was generated in accordance with the methodology set forth by Choukroun *et al*. [11]. In advance of the surgical appointment, 10 ml of intravenous blood was procured by puncturing the antecubital vein and collecting into sterile glass vessels (17 mm × 120 mm long) that contained no anticoagulant agent, then promptly transferred to a centrifugation machine# set at 2800 revolutions (approx × 400 g) per minute and spun for a total of 12 min inside a centrifuge unit (R-8C, REMI, Mumbai, INDIA). The disparity in constituent densities led to stratification into three principal tiers: erythrocytes settling as a basal layer, acellular plasma forming the uppermost stratum, and the L-PRF clot sandwiched between them. The supernatant fraction was drawn off with a sterile pipette; the intermediate fraction (L-PRF) was then grasped with sterile forceps and severed with scissors immediately after the platelet-poor plasma (PPP) was discarded. It was subsequently placed onto sterile gauze and pressed. A mechanically stable fibrin membrane was created by wringing serum out of the L-PRF clot.

Titanium platelet-rich fibrin preparation protocol [24]

T-PRF generation followed the protocol described by Tunalı *et al*. [24]. Via puncture of the antecubital vein, intravenous blood was collected into 10 ml sterile titanium test vessels (15 mm × 120 mm long) without any anticoagulant additive. These vessels were immediately placed in an R-8C centrifuge (REMI, Mumbai, India) and run at 3000 rpm for 10 min.

Spinning the blood specimen immediately upon harvest allows a structured fibrin clot to organize in the central zone of the vessel, lodged precisely between the erythrocyte mass at the bottom and the acellular plasma PPP supernatant. The T-PRF clot generated in this manner was then detached using sterile forceps and scissors and placed on sterile gauze for compression; a resilient fibrin membrane was obtained by expressing serum from within the T-PRF clot.

For group I (OFD only), after exhaustive cleansing of the defect, primary soft-tissue closure was achieved using 3-0 nonabsorbable black silk surgical suture (Ethicon, Johnson and Johnson, Somerville, NJ) in an interrupted fashion **(Figure 5c).** In the case of groups II and III, once thorough debridement was complete, the defect site received presuturing with 3-0 nonabsorbable silk suture **(Figures 6c and 7c),** and deliberate attention was directed toward positioning the basal aspect of the L-PRF and T-PRF clots so that they made direct contact with the floor of the IBD site. A periodontal pack was then applied to each treated location in Groups I, II, and III **(Figures 5d, 6d and 7d).**

Postoperative care

The regimen prescribed following surgery incorporated systemic antibiotic coverage. Specifically, Amoxicillin 500 mg was taken every 8 hours for 5 days; ibuprofen 800 mg was administered every 8 hours for 3 days; and 0.2% chlorhexidine digluconate solution (Rexidine) was used for rinsing twice daily for 14 days. The sutures were taken out at the 1-week postoperative mark.

Maintenance phase

After suture removal, participants were called back for weekly appointments during the initial month and thereafter once monthly through the 9-month postoperative endpoint to strengthen oral hygiene habits and provide professional prophylaxis. A blinded study assessor performed each clinical recording. PPD and CAL values were registered at the commencement of the trial **(Figures 5a, 6a and 7a)** and then again upon reaching the 9-month time point **(Figures 5e, 6e and 7e).**

Primary and secondary outcome measures

Defect fill was the primary endpoint of this investigation. In contrast, the secondary endpoints comprised the extent of diminution in probing depth, the magnitude of clinical attachment level improvement, and plaque index readings.

Statistical methodology

The gathered dataset was input into Microsoft Excel Version 13. Statistical analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) version 21 (IBM Corporation, Armonk, New York, USA). A combination of descriptive and inferential statistical techniques was utilized. Arithmetic means for the measured parameters were calculated using descriptive statistics.

To assess continuous data across the baseline, 6-month, and 9-month time points, analysis of variance (ANOVA) with post hoc Tukey's test was employed. To draw contrasts among the three arms, mean change values spanning baseline to 6 months, baseline to 9 months, and 6 months to 9 months were derived and subsequently analyzed across the study arms using ANOVA with post hoc Tukey's.

Every statistical procedure was executed with the confidence interval fixed at 95%, and probability values falling below 0.05 ($P < 0.05$) were regarded as denoting statistical significance.

Results and Discussion

The study cohort comprised 25 individuals with a mean age of 45.52 ± 5.36 years **(Table 1).**

Table 1. Mean age distribution of study participants.

Variable	N	Minimum	Maximum	Mean ± SD
Age	25	37.00	56.00	45.5200 ± 5.36284

SD = Standard Deviation

Table 2. Gender-wise distribution of participants.

Sex	Frequency (%)	P
Male	14 (56.0)	0.690
Female	11 (44.0)	
Total	25 (100.0)	

Breaking down the cohort by gender revealed that 14 (56.0%) were men and 11 (44%) were women ($P > 0.05$) **(Table 2).**

Tracing the evolution of plaque scores from the initial assessment through to 9 months across the sequential evaluation intervals showed that the shift in average PI scores attained statistical significance for the comparisons of baseline versus 1 month, baseline versus 3 months, baseline versus 6 months, and baseline versus 9 months. Sustained and adequate oral hygiene was consistently maintained throughout the maintenance period **(Table 3).**

Table 3. Alterations in plaque indices recorded between the initial visit and the 9-month follow-up across various assessment time points.

Plaque index scores	Mean	N	SD	SEM	Mean difference	*t*	P
Baseline	1.93	25.00	0.42	0.08	0.768	8.820	0.00
1 month	1.17	25.00	0.27	0.05			
Baseline	1.93	25.00	0.42	0.08	1.105	10.025	0.00
3 months	0.83	25.00	0.42	0.08			
Baseline	1.93	25.00	0.42	0.08	1.191	11.066	0.00
6 months	0.74	25.00	0.39	0.08			
Baseline	1.93	25.00	0.42	0.08	1.406	14.866	0.00
9 months	0.53	25.00	0.23	0.05			

SD denotes Standard Deviation, SEM signifies Standard Error of the Mean. At the initial assessment, the three treatment groups demonstrated comparable baseline characteristics for PD, CAL, the distance from CEJ to the base of the intrabony defect (CEJ-BD), and the distance from CEJ to the alveolar crest (CEJ-AC). Analysis of the changes in CEJ-BD measurements across the OFD, L-PRF, and T-PRF groups over the intervals from baseline to 6 months, baseline to 9 months, and 6 months to 9 months revealed that the greatest mean gain in bony fill was observed in the T-PRF group (0.81 ± 0.84), with the L-PRF group showing an intermediate response (0.49 ± 0.77), and the OFD group exhibiting the smallest change (0.12 ± 0.56). The pattern of mean differences indicated that new bone formation was most pronounced within the T-PRF arm, moderately evident in the L-PRF arm, and least substantial in the OFD arm **(Table 4).**

Table 4. Comparative evaluation of the shift in the cementoenamel junction to defect-based measurement across the open flap debridement, leukocyte platelet-rich fibrin, and titanium platelet-rich fibrin groups over the intervals spanning baseline to 6 months, baseline to 9 months, and 6 to 9 months.

Groups	CEJ-BD baseline		
	For 6 months	**To 9 months**	**6 –9 months**
OFD			
n	25.00	25.00	25.00
Minimum	−1.00	−0.80	−0.80
Maximum	1.00	1.30	1.50
Mean±SD	0.12±0.56	0.44±0.60	0.32±0.72
L-PRF			
n	25.00	25.00	25.00

Minimum	−1.00	−0.20	−1.30
Maximum	2.00	2.70	2.20
Mean±SD **T-PRF**	0.49±0.77	1.02±0.80	0.53±0.63
n	25.00	25.00	25.00
Minimum	−1.00	0.00	−1.00
Maximum	2.00	3.50	2.50
Mean±SD	0.81±0.84	1.47±0.85	0.66±0.87
P	0.005	0.010	0.283

CEJ-BD refers to the Cementoenamel Junction to Bone Defect distance, OFD stands for Open Flap Debridement, L-PRF designates Leukocyte Platelet-Rich Fibrin, T-PRF indicates Titanium Platelet-Rich Fibrin, and SD represents Standard Deviation.

Concerning the pairwise comparison of alterations in the cementoenamel junction to alveolar crest measurement conducted among the treatment arms from baseline to 6 months, the T-PRF group exhibited the smallest degree of crestal bone resorption (P < 0.05). In contrast, the OFD group demonstrated the most pronounced bone loss. When the evaluation was carried forward from baseline to 9 months, and similarly from 6 months to 9 months, a consistent statistical pattern was observed, with genuine bone gain being evident in the T-PRF arm **(Table 5).**

Table 5. Pairwise analysis of shifts in the cementoenamel junction to alveolar crest measurement among the open flap debridement, leukocyte platelet-rich fibrin, and titanium platelet-rich fibrin groups across the intervals of baseline to 6 months, baseline to 9 months, and 6 to 9 months.

Dependent variable	Mean	SE	P-value	CI 95%	
				Lower bound	Upper bound
CEJ-AC baseline to 6 months **OFD**					
L-PRF	−0.08800	0.07492	0.472	−0.2673	0.0913
T-PRF **L-PRF**	−0.21600	0.07492	0.014	−0.3953	−0.0367
T-PRF **CEJ-AC baseline to 9 months** **OFD**	−0.12800	0.07492	0.209	−0.3073	0.0513
L-PRF	−0.29600	0.14341	0.105	−0.6392	0.0472
T-PRF **L-PRF**	−0.44000	0.14341	0.008	−0.7832	−0.0968
T-PRF **CEJ-AC 6–9 months** **OFD**	−0.14400	0.14341	0.577	−0.4872	0.1992
L-PRF	−0.20800	0.13474	0.277	−0.5304	0.1144
T-PRF **L-PRF**	−0.22400	0.13474	0.227	−0.5464	0.0984
T-PRF	−0.01600	0.13474	0.992	−0.3384	0.3064

CI denotes Confidence Interval, OFD signifies Open Flap Debridement, L-PRF represents Leukocyte Platelet-Rich Fibrin, T-PRF indicates Titanium Platelet-Rich Fibrin, SD stands for Standard Deviation, SE refers to Standard Error, and CEJ-AC designates the Cementoenamel Junction to Alveolar Crest distance.

When a pairwise evaluation of PPD recorded at baseline and at 9 months across the OFD, L-PRF, and T-PRF groups was undertaken, the results revealed that the greatest mean PPD reduction was achieved in the T-PRF arm (4.22), followed by a lesser decrease in the L-PRF arm (3.26), and the smallest reduction in the OFD arm (2.54). This intergroup disparity in means attained statistical significance when baseline values were compared with 9-month outcomes across all treatment arms (P < 0.05), indicating that the T-PRF group elicited the most favorable soft-tissue healing response **(Table 6).**

Table 6. Pairwise comparison of probing pocket depth measurements recorded at baseline and at the 9-month follow-up across the open flap debridement, leukocyte platelet-rich fibrin, and titanium platelet-rich fibrin treatment groups.

	Mean	SD	SEM	Mean difference	*t*	P
PPD OFD						
Baseline	7.84	1.03	0.21	2.54	15.57	0.00
9 months PPD L-PRF	5.30	0.87	0.17			
Baseline	7.84	1.03	0.21	3.62	21.42	0.00
9 months PPD T-PRF	4.22	0.69	0.14			
Baseline	7.84	1.03	0.21	4.22	21.08	0.00
9 months	3.62	0.53	0.11			

PPD stands for Probing Pocket Depth, SD denotes Standard Deviation, SEM signifies Standard Error of the Mean, OFD represents Open Flap Debridement, L-PRF indicates Leukocyte Platelet-Rich Fibrin, and T-PRF refers to Titanium Platelet-Rich Fibrin.

Pairwise examination of CAL measurements taken at baseline and at the 9-month assessment within the OFD, L-PRF, and T-PRF groups revealed that the gain in CAL was most pronounced in the T-PRF arm (3.68), followed by the L-PRF arm (3.36), and was least substantial in the OFD arm (2.50). The difference in means was statistically significant ($P < 0.05$) **(Table 7).**

Table 7. Pairwise comparison of clinical attachment level values obtained at baseline and at the 9-month time point among the open flap debridement, leukocyte platelet-rich fibrin, and titanium platelet-rich fibrin treatment arms.

	Mean	*n*	SD	SEM	Mean difference	*t*	*P*
CAL OFD							
Baseline	6.80	25.00	1.04	0.21	2.50	14.43	0.00
9 months CAL L-PRF	4.30	25.00	0.87	0.17			
Baseline	6.80	25.00	1.04	0.21	3.36	20.10	0.00
9 months CAL T-PRF	3.44	25.00	0.65	0.13			
Baseline	6.80	25.00	1.04	0.21	3.68	19.70	0.00
9 months	3.12	25.00	0.30	0.06			

Abbreviations: SD = Standard deviation, SEM = Standard error of mean, OFD = Open flap debridement, L-PRF = Leukocyte platelet-rich fibrin, T-PRF = Titanium platelet-rich fibrin, CAL = Clinical attachment level.

The process of wound repair involves the liberation of assorted GFs and cytokines during the phases of coagulation and tissue renewal by endothelial cells, thrombocytes, and leukocytes. These GFs modulate chemotaxis, cellular differentiation, and matrix component deposition, thereby orchestrating the cellular events underpinning tissue regeneration. It is on this basis that platelet concentrates were developed to amplify this innate biological mechanism and have consequently found utility in both clinical and operative settings to augment healing [26]. What began as a surgical adjunct has seen PRF emerge as the primary regenerative agent for IBD's [27].

The central objective driving the present investigation was to determine whether supplementing three-walled IB defects with L-PRF and T-PRF yields measurable advantages in clinical outcomes. The research was conducted as a single-center randomized clinical trial.

This work assesses and contrasts the clinical performance of OFD, L-PRF, and T-PRF at the 9-month mark following intervention on three-walled IBD's. The investigation drew upon 75 intra-bony sites distributed across 25 individuals, a figure that aligns with comparable clinical studies documented in the periodontal literature. This sample size was sufficient to provide the study with 80% statistical power.

The full cohort of 25 patients remained in the study through to study completion. All measurements taken at the initial assessment showed nonsignificant variation across the three arms, thereby confirming a uniform starting point for each procedure and guarding against selection bias [28].

Periodontal defects most frequently occur in combined configurations, and their regenerative capacity depends on defect morphology. The current trial restricted inclusion to 3-walled defects alone, given that a greater number of residual bony walls surrounding a defect translates into more effective stabilization of biomaterials and blood clots, as well as more robust angiogenesis between the periodontal ligament and osseous walls—factors that collectively potentiate the regenerative capacity of grafted sites [29].

The outcomes of any surgical procedure aimed at periodontal regeneration are closely tied to the level of infection control and the rigor of maintenance protocols required to achieve meaningful clinical gains and long-term durability. Accordingly, in the present work, enrolment was limited to individuals capable of maintaining satisfactory oral hygiene and whose PI readings were below the acceptable cutoff (PI > 1.5) following phase I therapy [30, 31]. The EFP S3-Level Clinical Practice Guideline explicitly advises against performing periodontal surgical procedures in subjects who fail to demonstrate adequate oral hygiene [32]. Hence, to safeguard the stability and favorable outcome of treated sites, we scrupulously confirmed each participant's home care competence. We furnished a personalized maintenance regimen, as a result of which the shift in plaque scores from baseline to 1 month, baseline to 3 months, baseline to 6 months, and baseline to 9 months (0.768, 1.10, 1.191, and 1.406) rose progressively, and this shift in mean values attained statistical significance.

The literature contains contradictory findings concerning the deployment of platelet concentrates alongside other regenerative substances. Some reports assert superior clinical efficacy when PRF is applied in combination, whereas others document no supplementary benefit [33, 34]. For this reason, in the current study, PRF alone was used at the experimental sites, as concurrent application of additional regenerative materials could potentially obscure the genuine clinical effectiveness attributable to PRF alone.

The fabrication of L-PRF calls for nothing more than a simple glass receptacle to trigger the intrinsic coagulation cascade, culminating in fibrin clot formation. The requirement for glass vessels—and the interchangeable employment of silica-lined tubes—is accounted for by the activation of coagulation factor XII through interaction with the negatively charged silanol moieties present on glass surfaces [35]. Silica, constituting a principal component of glass, likewise carries a negative surface charge, permitting its glass substitution. An added advantage is that the silica microparticles, applied as an inner coating, readily detach during blood withdrawal and disperse, thereby initiating the coagulation cascade [36].

More recently, however, a growing body of evidence using spectrophotometric and microscopic analytical methods has shown that silica microparticles dislodged from the inner tube wall are immediately embedded within the PRF matrix. These particles elicit cytotoxic effects on cells [37-39] and pose localized hazards within the body. The postulated mechanism underlying this cytotoxicity involves disruption of the plasma membrane mediated by silica-driven generation of reactive oxygen species. To circumvent the detrimental consequences associated with silica-coated tubes, plain glass tubes were therefore adopted in our trial.

The findings from the present clinical experimental investigation revealed a noteworthy decrease in PPD and a gain in CAL across all three arms when baseline and 9-month data were compared. Nonetheless, the scale of these improvements reached its zenith in the T-PRF group relative to both the L-PRF and OFD groups.

The defined aims of regenerative surgical procedures include reducing PPD, improving CAL, and stimulating osseous gain to reinforce dental support.

For the treating clinician, a reduction in PPD is a parameter of considerable importance in ongoing patient care, as it directly affects the feasibility of instrumenting a treated area during recall maintenance visits. In the current investigation, when the three groups—OFD, L-PRF plus OFD, and T-PRF plus OFD—were compared at the 9-month postoperative interval, the residual PPD measured greatest in the OFD group (5.30 ± 0.87), followed by L-PRF (4.22 ± 0.69), and was lowest for T-PRF (3.62 ± 0.53), indicating that the most substantial persisting PPD was found in the OFD Group. Examining the shift in PPD spanning from the initial visit to the 9-month follow-up, the most pronounced alteration was observed in the T-PRF Group (4.22), succeeded by L-PRF (3.26), with OFD (2.54) trailing, implying a meaningful improvement within every arm, with the degree of PPD change being most prominent in the T-PRF cohort.

These outcomes align with the work of Sharma and Pradeep [40], Thorat *et al.* [41], Pradeep *et al.* [42], Rosamma *et al.* [43], Bajaj *et al.* [44], Kumar *et al.* [45], and Chatterjee *et al.* [46], each of whom arrived at the conclusion that the supplementary application of L-PRF or T-PRF reliably produced a significantly superior reduction in PD for IBDs in chronic periodontitis individuals postoperatively when measured against OFD applied in isolation. In contrast, the investigation by Ajwani *et al.* [47] found no meaningful difference in PPD reduction between the OFD and L-PRF cohorts.

CAL, widely regarded as a benchmark metric for gauging clinical responsiveness in periodontitis treatment, provides an estimate of the degree of connective tissue detachment from the radicular surface and is exceedingly valuable for tracking site-specific shifts in attachment levels.

In the present study, baseline CAL measurements were uniformly comparable across all arms. By the 9-month evaluation, the divergence in CAL values peaked in the T-PRF group (3.68), followed by the L-PRF group (3.36), and was lowest in OFD (2.50), a pattern indicating that the increase in CAL was most pronounced in the T-PRF cohort.

The intergroup findings comparing OFD and L-PRF, which showed the smallest CAL improvement in the OFD arm relative to L-PRF and T-PRF in our trial, are consistent with Thorat *et al*. [41] Chatterjee *et al*. [48] Rosamma *et al*. [43] whose analyses concluded that post-treatment CAL gains were greater in subjects managed with L-PRF plus OFD than in those receiving OFD alone, and diverge from the outcomes documented by Ozkal Eminoglu *et al*. [49] Ajwani *et al*. [47] Sharma and Pradeep [40] and Pradeep *et al*. [42] who detected no statistically meaningful difference between the L-PRF and isolated OFD arms concerning CAL gain for IBDs post-surgery.

Comparisons between the L-PRF and T-PRF groups within our study established that T-PRF delivered the most pronounced PPD decrease and CAL gain relative to L-PRF. These observations contrast with the work of Chatterjee *et al*. [46], Mitra *et al*. [50], and Gummaluri *et al*. [51], who found no appreciable difference in PPD and CAL gain results between L-PRF and T-PRF.

The CAL improvement likely stemmed from new attachment formation in the L-PRF or T-PRF cohorts, rather than repair-mediated healing, marked by a long junctional epithelium between the freshly regenerated tissues and the root face in the OFD cohort.

The more favorable results achieved with platelet-rich fibrin over OFD can be ascribed to L-PRF's capacity to polymerize and to the elements contained within the platelet-rich fibrin coagulum—namely fibrin, platelets, leukocytes, GFs, and cytokines. Polymerization gives rise to interconnected trimolecular or equilateral junction points within L-PRF, permitting the formation of a delicate yet pliable fibrin lattice that can support cytokine entrapment and the trafficking of endothelial cells, fibroblasts, inflammatory cells, and platelets. This process promotes swift angiogenesis, superior wound healing, regeneration, and periodontal tissue remodeling. Accordingly, the fibrin scaffold serves an essential role across four distinct healing dimensions: angiogenesis, immune modulation, recruitment of circulating stem cells, and wound protection through epithelial coverage [52]. GFs residing in the PRF coagulum—such as platelet-derived GFs, insulin-like GFs, and transforming GF-b—are fundamental to soft and hard periodontal tissue renewal. They trigger periodontal ligament cell chemotaxis, mitogenesis, and matrix production, while simultaneously lowering matrix metalloproteinase-8 and interleukin-1β concentrations and elevating tissue inhibitor of matrix metalloproteinase-1 levels, thereby fostering periodontal soft-tissue recovery. In addition, PRF inhibits epithelial cell movement [53].

Addressing IBDs represents a central therapeutic priority, with data supporting periodontal regeneration as an effective and foreseeable procedure [54]. In the current study, meaningful bone fill (defect depth reduction [DDR]) was observed across the experimental arms at baseline to 6 months, baseline to 9 months, and 6 to 9 months. At the 9-month mark, the greatest decrease in mean CEJ-to-BD distance was observed in the T-PRF arm, followed by the L-PRF arm and then the OFD arm. Notably, significant bone gain was confined to the T-PRF arm, whereas both the OFD and L-PRF arms exhibited nonsignificant bone increases when comparing baseline to 6 months.

Periodontal surgical interventions that aim to expose osseous structures and root surfaces inherently involve trauma to the supportive periodontium. Histological evidence from both human and animal investigations has revealed an early resorptive phase, potentially superseded later by new bone deposition, since lifting a flap to uncover alveolar bone stimulates osteoclastic action [55, 56].

Evaluating alveolar crestal bone loss using the CEJ-to-AC measurement, our study demonstrated that the greatest average distance was observed in the OFD arm, followed by the L-PRF arm and then the T-PRF arm, indicating that bone resorption between baseline and 6 months was most extensive in the OFD group. When comparing baseline to 9 months, crestal bone loss was evident in the OFD arm; no distance change was observed in the L-PRF arm, and a reduction in distance was observed in the T-PRF arm, indicating crestal bone apposition.

The superior defect-fill metrics—more rapid and sustained bone deposition alongside diminished crestal resorption—linked to T-PRF compared to OFD and L-PRF point to enhanced defect resolution, underscoring T-PRF's value in regenerative periodontal procedures. Thorat *et al*. [41] explored the clinical impact of L-PRF on IBD management and reported greater improvement in IBD fill at L-PRF sites compared with OFD controls. Findings related to DDR for IBDs at 9 months post-treatment indicate that combining L-PRF or T-PRF with OFD yields statistically significant and clinically superior defect-depth resolution compared to OFD alone [27, 57, 58].

The general benefits conferred by L-PRF may be linked to increased phosphorylation of extracellular signal-regulated protein kinase and to inhibition of osteoclast activity via OPG secretion induced by osteoblastic cells. Furthermore, the dense fibrin framework facilitates the release of transforming growth factor-β1 and platelet-derived growth factor-AB, which, in turn, drive ALP expression and the onset of mineralization, accompanied by endothelial cell migration that fosters vascularization and neoangiogenesis [59].

Investigations comparing L-PRF and T-PRF for bone healing have yielded conflicting findings.

In the present trial, intergroup analyses strongly favored the T-PRF cohort, demonstrating that defect resolution surpassed that observed in the L-PRF cohort. These outcomes contrast with the published work of Chatterjee *et al.* [46] and Gummaluri *et al.* [51], who reported no statistically significant difference between the L-PRF and T-PRF arms. In contrast, Mitra *et al.* [50] observed poorer depth reduction in the T-PRF arm, a finding potentially explained by an insufficient sample size or differences in defect architecture that shape healing responses.

The data gathered from this research showed greater improvement across both clinical and radiographic measures in sites managed with T-PRF compared with L-PRF and OFD. This trial, therefore, underscores the value of using titanium to enhance the quality of the fibrin network characteristic of L-PRF, thereby nurturing a stronger regenerative potential. The most plausible account for these enhanced T-PRF results rests on the superior hemocompatibility of titanium relative to glass, which yields a fibrin structure more thoroughly polymerized (woven with greater tightness and thickness) than L-PRF, given that the silica component in L-PRF hinders polymerization. As a result, T-PRF persists longer, with a delayed resorption timeline, allowing sustained release of GFs that facilitate superior wound repair [60].

The elaborate configuration of the fibrin matrix, together with its compactness, stands as a pivotal property of any platelet concentrate. A suitable biological vehicle, such as a fibrin matrix, can mediate the delivery of GFs and cytokines by enabling their discharge into the wound milieu. Heightened fibrin clot density translates into a more powerful biological healing platform by bolstering cellular migration and GF output [60].

Within research evaluating the mechanical characteristics of L-PRF membranes, Ravi and Santhanakrishnan [59] reported that T-PRF achieved the peak tensile strength (404.61 ± 5.92 MPa) and modulus of elasticity (151.9 ± 6.92 MPa), with advanced PRF (A-PRF) ranking next (362.565 ± 5.15 MPa, 122.51 ± 7.15 MPa), while L-PRF registered the lowest figures (290.076 ± 5.68 MPa, 98.01 ± 7.43 MPa).

Using ELISA to assess platelet-derived growth factor-AA secretion, Ravi and Santhanakrishnan [59] determined that T-PRF yielded markedly elevated initial concentrations (6060.4 pg/ml) relative to both L-PRF (5721.3 pg/ml) and A-PRF (5935.3 pg/ml). Platelet-derived growth factor-AA levels in T-PRF declined after the first day, whereas A-PRF maintained release for 10 days. No statistically meaningful differences were detected across groups at the multiple time intervals examined. However, the patterns suggested a more robust early-stage release for T-PRF and a more enduring secretion for A-PRF.

The same research team further assessed the chemical breakdown patterns of the three PRF membrane categories. After placing the three membrane types in an orbital shaker, all experienced degradation, reaching up to 82%. L-PRF underwent the most extensive breakdown (85.75%), followed by A-PRF (84.18%), with T-PRF undergoing the least (82.27%). T-PRF accordingly offered the optimal mechanical profile coupled with the lowest decomposition rate, whereas L-PRF combined the highest decomposition rate with the poorest mechanical performance [59].

Conclusion

The evidence from this study establishes that T-PRF provides meaningful clinical benefit in the management of IBDs, delivering superior PPD diminution, more substantial CAL improvement, and the ability to generate greater new bone volume over a shorter duration when applied independently compared with OFD and L-PRF. It may therefore find more routine application as a dependable alternative to grafting materials for IBD therapy. The deployment of autologous platelet-rich fibrin opens new avenues for enhanced healing and the restoration of functional integrity.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Iviglia G, Kargozar S, Baino F. Biomaterials, current strategies, and novel nano-technological approaches for periodontal regeneration. J Funct Biomater. 2019;10:3.
2. Li A, Yang H, Zhang J, Chen S, Wang H, Gao Y. Additive effectiveness of autologous platelet-rich fibrin in the treatment of intrabony defects: a PRISMA-compliant meta-analysis. Medicine (Baltimore). 2019;98:e14759.
3. Papapanou PN, Wennström JL. The angular bony defect as indicator of further alveolar bone loss. J Clin Periodontol. 1991;18:317-22.
4. Trombelli L, Heitz-Mayfield LJ, Needleman I, Moles D, Scabbia A. A systematic review of graft materials and biological agents for periodontal intraosseous defects. J Clin Periodontol. 2002;29 Suppl 3:117-35.
5. Prichard J. Regeneration of bone following periodontal therapy: report of cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1957;10:247-52.
6. Tonetti MS, Prato GP, Cortellini P. Factors affecting the healing response of intrabony defects following guided tissue regeneration and access flap surgery. J Clin Periodontol. 1996;23:548-56.
7. Caffesse RG, Sweeney PL, Smith BA. Scaling and root planing with and without periodontal flap surgery. J Clin Periodontol. 1986;13:205-10.
8. Graziani F, Gennai S, Cei S, Cairo F, Baggiani A, Miccoli M, et al. Clinical performance of access flap surgery in the treatment of the intrabony defect. A systematic review and meta-analysis of randomized clinical trials. J Clin Periodontol. 2012;39:145-56.
9. Graves DT, Cochran DL. Periodontal regeneration with polypeptide growth factors. Curr Opin Periodontol. 1994;2:178-86.
10. Vo TN, Kasper FK, Mikos AG. Strategies for controlled delivery of growth factors and cells for bone regeneration. Adv Drug Deliv Rev. 2012;64:1292-309.
11. Choukroun J, Adda F, Schoeffler C, Vervelle A. An opportunity in perio-implantology: the PRF. Implantodontie. 2001;42:55-62.
12. Dohan DM, Choukroun J, Diss A, Steve LD, Anthony D, Jaafar M, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:45-50.
13. Khorshidi H, Raoofi S, Bagheri R, Banihashemi H. Comparison of the mechanical properties of early leukocyte- and platelet-rich fibrin versus PRGF/Endoret membranes. Int J Dent. 2016;2016:17.
14. Dohan Ehrenfest DM, Del Corso M, Diss A, Mouhyi J, Charrier JB. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. J Periodontol. 2010;81:546-55.
15. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:e56-60.
16. Aroca S, Keglevich T, Barbieri B, Gera I, Etienne D. Clinical evaluation of a modified coronally advanced flap alone or in combination with a platelet-rich fibrin membrane for the treatment of adjacent multiple gingival recessions: a 6-month study. J Periodontol. 2009;80:244-52.
17. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:299-303.
18. Baeyens W, Glineur R, Evrard L. The use of platelet concentrates: platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in bone reconstruction prior to dental implant surgery. Rev Med Brux. 2010;31:521-7.
19. Inchingolo F, Tatullo M, Marrelli M, Inchingolo AM, Scacco S, Inchingolo AD, et al. Trial with platelet-rich fibrin and Bio-Oss used as grafting materials in the treatment of the severe maxillar bone atrophy: clinical and radiological evaluations. Eur Rev Med Pharmacol Sci. 2010;14:1075-84.
20. Toffler M, Toscano N, Holtzclaw D. Osteotome-mediated sinus floor elevation using only platelet-rich fibrin: an early report on 110 patients. Implant Dent. 2010;19:447-56.
21. Gürbüzer B, Pikdöken L, Tunali M, Urhan M, Küçükodaci Z, Ercan F. Scintigraphic evaluation of osteoblastic activity in extraction sockets treated with platelet-rich fibrin. J Oral Maxillofac Surg. 2010;68:980-9.
22. Miron RJ, Kawase T, Dham A, Zhang Y, Fujioka-Kobayashi M, Sculean A. A technical note on

contamination from PRF tubes containing silica and silicone. BMC Oral Health. 2021;21:135.

23. O'Connell SM. Safety issues associated with platelet-rich fibrin method. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103:587-93.
24. Tunalı M, Özdemir H, Küçükodacı Z, Akman S, Fıratlı E. In vivo evaluation of titanium-prepared platelet-rich fibrin (T-PRF): a new platelet concentrate. Br J Oral Maxillofac Surg. 2013;51:438-43.
25. Haripriya N, Mohan Kumar P, Penmetsa GS, Nvs Sruthima G, Ramesh KS, Keerthi V. Comparison of the effectiveness of DFDBA and T-PRF in the regeneration of intra-bony defects- a randomized split-mouth study. J Stomatol Oral Maxillofac Surg. 2024;125:101668.
26. Pirebas HG, Hendek MK, Kisa U, Yalim M, Erdemir EO. Effect of titanium-prepared platelet-rich fibrin treatment on the angiogenic biomarkers in gingival crevicular fluid in infrabony defects of patients with chronic periodontitis: a randomized controlled clinical trial. Niger J Clin Pract. 2018;21:69-75.
27. Bielecki T, Dohan Ehrenfest DM. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF): surgical adjuvants, preparations for in situ regenerative medicine and tools for tissue engineering. Curr Pharm Biotechnol. 2012;13:1121-30.
28. Ogihara S, Tarnow DP. Efficacy of enamel matrix derivative with freeze-dried bone allograft or demineralized freeze-dried bone allograft in intrabony defects: a randomized trial. J Periodontol. 2014;85:1351-60.
29. Selvig KA, Kersten BG, Wikesjö UM. Surgical treatment of intrabony periodontal defects using expanded polytetrafluoroethylene barrier membranes: influence of defect configuration on healing response. J Periodontol. 1993;64:730-3.
30. Cortellini P, Pini-Prato G, Tonetti M. Periodontal regeneration of human infrabony defects (v). Effect of oral hygiene on long-term stability. J Clin Periodontol. 1994;21:606-10.
31. Cortellini P, Paolo G, Prato P, Tonetti MS. Long-term stability of clinical attachment following guided tissue regeneration and conventional therapy. J Clin Periodontol. 1996;23:106-11.
32. Sanz M, Herrera D, Kebschull M, Chapple I, Jepsen S, Beglundh T, et al. Treatment of stage I-III periodontitis —The EFP S3 level clinical practice guideline. J Clin Periodontol. 2020;47 Suppl 22:4-60.
33. Ilgenli T, Dündar N, Kal BI. Demineralized freeze-dried bone allograft and platelet-rich plasma versus platelet-rich plasma alone in infrabony defects: a clinical and radiographic evaluation. Clin Oral Investig. 2007;11:51-9.
34. Markou N, Pepelassi E, Vavouraki H, Stamatakis HC, Nikolopoulos G, Vrotsos I, et al. Treatment of periodontal endosseous defects with platelet-rich plasma alone or in combination with demineralized freeze-dried bone allograft: a comparative clinical trial. J Periodontol. 2009;80:1911-9.
35. Margolis J. Glass surface and blood coagulation. Nature. 1956;178:805-6.
36. Takahashi A, Tsujino T, Yamaguchi S, Isobe K, Watanabe T, Kitamura Y, et al. Distribution of platelets, transforming growth factor-β1, platelet-derived growth factor-BB, vascular endothelial growth factor and matrix metalloprotease-9 in advanced platelet-rich fibrin and concentrated growth factor matrices. J Investig Clin Dent. 2019;10:e12458.
37. Fontana C, Kirsch A, Seidel C, Marpeaux L, Darne C, Gaté L, et al. In vitro cell transformation induced by synthetic amorphous silica nanoparticles. Mutat Res Genet Toxicol Environ Mutagen. 2017;823:22-7.
38. Kim IY, Joachim E, Choi H, Kim K. Toxicity of silica nanoparticles depends on size, dose, and cell type. Nanomed Nanotechnol Biol Med. 2015;11:1407-16.
39. Vicente S, Moia C, Zhu H, Vigé X. In vitro evaluation of the internalization and toxicological profile of silica nanoparticles and submicroparticles for the design of dermal drug delivery strategies. J Appl Toxicol. 2017;37:1396-407.
40. Sharma A, Pradeep AR. Autologous platelet-rich fibrin in the treatment of mandibular degree II furcation defects: a randomized clinical trial. J Periodontol. 2011;82:1396-403.
41. Thorat M, Pradeep AR, Pallavi B. Clinical effect of autologous platelet-rich fibrin in the treatment of intra-bony defects: a controlled clinical trial. J Clin Periodontol. 2011;38:925-32.
42. Pradeep AR, Nagpal K, Karvekar S, Patnaik K, Naik SB, Guruprasad CN. Platelet-rich fibrin with 1% metformin for the treatment of intrabony defects in chronic periodontitis: a randomized controlled clinical trial. J Periodontol. 2015;86:729-37.
43. Rosamma Joseph V, Raghunath A, Sharma N. Clinical effectiveness of autologous platelet rich

fibrin in the management of infrabony periodontal defects. Singapore Dent J. 2012;33:5-12.

44. Bajaj P, Pradeep AR, Agarwal E, Rao NS, Naik SB, Priyanka N, et al. Comparative evaluation of autologous platelet-rich fibrin and platelet-rich plasma in the treatment of mandibular degree II furcation defects: a randomized controlled clinical trial. J Periodontal Res. 2013;48:573-81.
45. Kumar HA, Raj R, Kaur S, Sunda S. Clinical and histological evaluation of Lprf and T-prf – A comparative review. Int J Curr Res. 2018;10:74275-9.
46. Chatterjee A, Debnath K, Ali MM, Babu C, Gowda PL. Comparative histologic evaluation of titanium platelet-rich fibrin and platelet-rich fibrin in hypertensive and smoker participants: a cell cytology study. J Indian Soc Periodontol. 2017;21:195-200.
47. Ajwani H, Shetty S, Gopalakrishnan D, Kathariya R, Kulloli A, Dolas RS, et al. Comparative evaluation of platelet-rich fibrin biomaterial and open flap debridement in the treatment of two and three wall intrabony defects. J Int Oral Health. 2015;7:32-7.
48. Chatterjee A, Pradeep AR, Garg V, Yajamanya S, Ali MM, Priya VS. Treatment of periodontal intrabony defects using autologous platelet-rich fibrin and titanium platelet-rich fibrin: a randomized, clinical, comparative study. J Investig Clin Dent. 2017;8:1-6.
49. Ozkal Eminoglu D, Arabaci T, Oztas Sahiner GA. The effect of titanium-platelet rich fibrin on periodontal intrabony defects: a randomized controlled split-mouth clinical study. PLoS ONE. 2024;19:1-15.1.
50. Mitra DK, Potdar PN, Prithyani SS, Rodrigues SV, Shetty GP, Talati MA. Comparative study using autologous platelet-rich fibrin and titanium prepared platelet-rich fibrin in the treatment of infrabony defects: an in vitro and in vivo study. J Indian Soc Periodontol. 2019;23:554-61.
51. Gummaluri SS, Bhattacharya HS, Astekar M, Cheruvu S. Evaluation of titanium-prepared platelet-rich fibrin and leucocyte platelet-rich fibrin in the treatment of intra-bony defects: a randomized clinical trial. J Dent Res Dent Clin Dent Prospects. 2020;14:83-91.
52. Patel GK, Gaekwad SS, Gujjari SK, Veerendra Kumar SC. Platelet-rich fibrin in regeneration of intrabony defects: a randomized controlled trial. J Periodontol. 2017;88:1192-9.
53. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:e45-50.
54. Dohan Ehrenfest DM, Diss A, Odin G, Doglioli P, Hippolyte MP, Charrier JB. In vitro effects of Choukroun's PRF (platelet-rich fibrin) on human gingival fibroblasts, dermal prekeratinocytes, preadipocytes, and maxillofacial osteoblasts in primary cultures. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108:341-52.
55. Reynolds MA, Kao RT, Nares S, Camargo PM, Caton JG, Clem DS, et al. Periodontal regeneration – Intrabony defects: practical applications from the AAP regeneration workshop. Clin Adv Periodontics. 2015;5:21-9.
56. Wilderman M. Repair after a periosteal retention procedure. J Periodontol. 1963;34:487-503.
57. Pradeep AR, Garg V, Kanoriya D, Singhal S. Platelet-rich fibrin with 1.2% rosuvastatin for treatment of intrabony defects in chronic periodontitis: a randomized controlled clinical trial. J Periodontol. 2016;87:1468-73.
58. Arabaci T, Albayrak M. Titanium-prepared platelet-rich fibrin provides advantages on periodontal healing: a randomized split-mouth clinical study. J Periodontol. 2018;89:255-64.
59. Ravi S, Santhanakrishnan M. Mechanical, chemical, structural analysis and comparative release of PDGF-AA from L-PRF, A-PRF and T-PRF – An in vitro study. Biomater Res. 2020;24:16.
60. Tunalı M, Özdemir H, Küçükodacı Z, Akman S, Yaprak E, Toker H, et al. A novel platelet concentrate: titanium-prepared platelet-rich fibrin. Biomed Res Int. 2014;2014:1-7.