

Laser Doppler evaluation of gingival and pulpal microcirculation after impacted mandibular third molar surgery: A retrospective comparison of L-PRF and T-PRF

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Abstract

Objective: The aim of this study was to compare the effects of leukocyte- and platelet-rich fibrin (L-PRF) and titanium-prepared platelet-rich fibrin (T-PRF), placed into extraction sockets after impacted mandibular third molar surgery, on the gingival and pulpal microcirculation of the adjacent mandibular second molar.

Methods: This retrospective comparative clinical study included 60 patients aged 20–30 years with fully impacted mesioangular mandibular third molars. Patients were divided into two groups according to the platelet concentrate used during surgery: L-PRF (n=30) and T-PRF (n=30). Gingival blood flow in the mucoperiosteal flap and pulpal blood flow in the adjacent mandibular second molar were measured with laser Doppler flowmetry, a well-established noninvasive method. Measurements were performed preoperatively and on postoperative day 7. Perfusion values were recorded as perfusion units (PU) and analyzed using non-parametric statistical methods with Bonferroni correction applied for multiple comparisons.

Results: Both the L-PRF and T-PRF groups demonstrated significant increases in pulpal and gingival perfusion values on postoperative day 7 compared with baseline measurements (all Bonferroni-adjusted $p < 0.001$). In the T-PRF group, pulpal perfusion increased by 8.10 PU and gingival perfusion increased by 11.09 PU, whereas the corresponding increases in the L-PRF group were 6.52 PU and 6.81 PU, respectively. Direct intergroup comparison of change scores (postoperative – preoperative) revealed that the increase in both pulpal blood flow ($U = 759.0$; $Z = 4.568$; $p < 0.001$; $r = 0.590$) and gingival blood flow ($U = 814.0$; $Z = 5.382$; $p < 0.001$; $r = 0.695$) was significantly greater in the T-PRF group. Intergroup comparisons further demonstrated higher postoperative perfusion values in the T-PRF group. The largest between-group difference was observed for gingival perfusion ($U = 900.0$; $Z = 6.653$; $p < 0.001$; $r = 0.859$), representing a very large effect size. A moderate effect size was observed for postoperative pulpal perfusion ($r = 0.332$).

Conclusion: Both platelet-rich fibrin protocols were associated with increased gingival and pulpal perfusion during the early postoperative healing period. T-PRF was associated with higher postoperative perfusion measurements,

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particularly in gingival tissues; this finding may indicate a more pronounced early microcirculatory response. However, because clinical healing outcomes were not directly evaluated and no untreated control group was included, the clinical significance of the observed perfusion differences remains uncertain and should be confirmed by prospective randomized controlled studies.

Keywords: impacted third molar, laser doppler flowmetry, platelet-rich fibrin

INTRODUCTION

The extraction of impacted mandibular third molars remains one of the most frequently performed surgical procedures in oral and maxillofacial surgery. Despite standardized surgical techniques, postoperative complications such as pain, swelling, trismus, bleeding, alveolar osteitis, and delayed soft and hard tissue healing are still commonly encountered (1–3). These outcomes are closely related to the severity of surgical trauma and the inflammatory and vascular responses that develop at the extraction site (2,3). Therefore, strategies aimed at enhancing local microcirculation and promoting wound healing have attracted increasing clinical interest (4–6).

Platelet concentrates have been extensively investigated as autologous biomaterials capable of enhancing tissue regeneration by delivering growth factors and cytokines directly to the surgical site (7–9). Among these, platelet-rich fibrin (PRF) is a second-generation platelet concentrate characterized by a fibrin matrix rich in platelets and leukocytes and obtained without the use of anticoagulants (7,10). Leukocyte- and platelet-rich fibrin (L-PRF) has been shown to promote the sustained release of angiogenic and regenerative mediators, including platelet-derived growth factor, vascular endothelial growth factor (VEGF), and transforming growth factor- β , thereby promoting angiogenesis, modulation of inflammation, and early wound healing (5,6,8).

Titanium-prepared platelet-rich fibrin (T-PRF) was subsequently developed as a modification of conventional PRF protocols in which titanium tubes are used instead of glass tubes for platelet activation (11,12). Experimental and clinical studies have demonstrated that T-PRF forms a denser and more organized fibrin network and exhibits a longer resorption time, which may allow a more prolonged and controlled release of growth factors (11,13,14).

These structural characteristics suggest that T-PRF may provide a more sustained biological environment for tissue repair than conventional L-PRF (13,15,16).

Microcirculation plays a critical role in wound healing because adequate blood flow is essential for oxygen delivery, nutrient transport, immune cell migration, and angiogenesis (17–19). Laser Doppler flowmetry (LDF) is an established and non-invasive method for the objective assessment of tissue microcirculation and has been used to evaluate microvascular blood flow in oral tissues, including the dental pulp and gingiva (20–22). Because LDF enables quantitative assessment of perfusion changes over time, it has become a valuable tool for monitoring healing dynamics following oral surgical procedures (21,23).

However, evidence comparing the effects of L-PRF and T-PRF on gingival and pulpal microcirculation following impacted mandibular third molar surgery remains limited. This retrospective comparative clinical study aimed to compare the effects of L-PRF and T-PRF, placed into extraction sockets after the surgical removal of impacted mandibular third molars, on gingival blood flow of the mucoperiosteal flap and pulpal blood flow of the adjacent mandibular second molar, using LDF. It was hypothesized that both platelet concentrates would be associated with increased local microcirculation during early wound healing, with a potentially greater response in the T-PRF group (6,13).

MATERIALS AND METHODS

Study design and review of records

In this retrospective comparative clinical study, the records of patients who underwent extraction of impacted mandibular third molars with placement of PRF into the extraction socket and who underwent routine LDF measurements preoperatively and on postoperative day 7 were reviewed.

Patients were grouped according to the PRF protocol routinely used during the respective treatment period. During the early phase of the study, L-PRF served as the standard clinical protocol. Following the introduction and routine availability of titanium tubes in our clinic, T-PRF became the preferred protocol. Therefore, allocation of patients to the L-PRF and T-PRF groups was based on chronological treatment periods rather than on patient-related clinical characteristics, surgeon preference, or patient selection. No patient-related clinical criteria were used to determine which platelet concentrate to apply.

Of the eligible records, 60 patients aged 20–30 years with fully impacted mesioangular mandibular third molars who received either L-PRF or T-PRF were included in the study. The baseline demographic and clinical characteristics of the study groups are presented in Table 1. All included teeth were classified as mesioangular impactions and exhibited a similar level of surgical difficulty, according to the Pell and Gregory and the Winter classification systems (24). To minimize operator-related variability, all surgical procedures were performed by the same experienced oral and maxillofacial surgeon using a standardized surgical protocol. Changes in gingival and pulpal blood flow were analyzed retrospectively.

Ethical approval and informed consent

Ethical approval was obtained from the institutional Clinical Research Ethics Committee before the study (date: 27.04.2021; decision no: 2021/62). Patient records containing signed informed consent forms were evaluated. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria

Patients meeting the following criteria were included in the study:

- Being between 20 and 30 years of age,
- Having a fully impacted mesioangular mandibular third molar,
- Having been treated with L-PRF or T-PRF,
- Having complete baseline and postoperative day 7 LDF recordings.

Exclusion criteria

Patients were excluded if any of the following conditions were present:

- Presence of a systemic disease,
- Use of systemic medications,

Table 1. Baseline characteristics of the study groups.

Variable	L-PRF (n=30)	T-PRF (n=30)	Exact p value	Bonferroni-adjusted p value
Age (years), mean $\pm$ SD	22.97 $\pm$ 2.47	22.33 $\pm$ 2.67	0.160	—
Age (years), median (min–max)	22.0 (20–30)	22 (20–30)	—	—
Female, n (%)	18 (60.0)	22 (73.3)	0.273	—
Male, n (%)	12 (40.0)	8 (26.7)	0.273	—
Left side (tooth #38), n (%)	11 (36.7)	18 (60.0)	0.071	—
Right side (tooth #48), n (%)	19 (63.3)	12 (40.0)	0.071	—
Tooth impaction status	Fully impacted	Fully impacted	—	—
Pell-Gregory Classification	Class II-B	Class II-B	1.000	—
Winter Classification	Mesioangular	Mesioangular	1.000	—
Baseline pulpal perfusion (PU), mean $\pm$ SD	15.10 $\pm$ 3.47	14.17 $\pm$ 2.99	0.021	0.086
Baseline gingival perfusion (PU), mean $\pm$ SD	14.97 $\pm$ 2.86	15.77 $\pm$ 3.28	0.017	0.071

Data are presented as mean $\pm$ SD, median (min–max), or n (%), where applicable. All included teeth were fully impacted mesioangular mandibular third molars. Patients were selected from cases with comparable surgical difficulty according to the Pell and Gregory and Winter classification systems. L-PRF: leukocyte- and platelet-rich fibrin; T-PRF: titanium-prepared platelet-rich fibrin; SD: standard deviation; min–max: minimum–maximum; n: number of patients; #38 and #48: mandibular left and right third molars (FDI notation); PU: perfusion unit.

- Use of local or topical oral medications,
- Smoking,
- Pregnancy,
- History of radiotherapy or chemotherapy to the head and neck region,
- Bisphosphonate use by any route of administration (oral, intravenous, or subcutaneous),
- Acute infection,
- Pain or swelling associated with the impacted tooth,
- Presence of a lesion within the flap design,
- Previous surgical intervention in the same region.

In addition, patients were excluded if any of the following conditions were present in the adjacent mandibular second molar:

- Missing tooth,
- Presence of dental caries,
- Extensive restoration or prosthetic restoration,
- Periapical radiolucency,
- Previous root canal treatment,
- Deep periodontal pocket,
- Periodontal destruction.

Study groups

Group 1 (L-PRF group) comprised patients in whom L-PRF was placed in the extraction socket (n=30).

Group 2(T-PRF group) consisted of patients in whom T-PRF was placed into the extraction socket (n=30).

Blinding of LDF measurements

Preoperative and postoperative LDF measurements were performed by a clinician blinded to the platelet concentrate used in each socket. The measurement procedure was non-invasive and did not affect the postoperative healing process. This blinded assessment strategy reduced observer-related bias, thereby enhancing the internal validity of the perfusion assessment.

Laser Doppler flowmetry protocol

The LDF device (Perimed Periflux 5000, Perimed, Sweden) was calibrated according to the manufacturer's instructions. The same dental unit

was used for all measurements and was fixed at a 90° angle to the ground. Patients were seated in an upright position, with the Frankfurt horizontal plane positioned parallel to the floor, and were instructed to remain motionless during recording.

All LDF measurements were performed under standardized clinical conditions using the same measurement setup and probe stabilization protocol. Patients were instructed to avoid caffeine-containing beverages, vigorous physical activity, and analgesic intake for at least 2 hours before the measurements. All recordings were obtained in the same clinical examination room under standardized environmental conditions (25). To avoid potential alterations in local perfusion, measurements on postoperative day 7 were performed before suture removal.

To standardize probe placement, alginate impressions were taken before surgery and plaster models were prepared. A 2-mm-thick transparent acrylic splint(Essix-type) was fabricated for each patient and was extended distally to include the flap boundaries. In accordance with previous studies emphasizing the importance of probe stabilization and position standardization in LDF measurements (26,27), guide slots were created to ensure that the probe could be positioned at the same location during each measurement.

The pulpal measurement point (A) was defined as the midpoint of the mesiodistal and occlusocervical axes of the adjacent second molar. Gingival measurements were obtained from three points located within the flap boundaries:

Point B: The intersection of a point 5 mm apical to the incision line and a point 5 mm distal to the distal surface of the adjacent second molar,

Point C: A point 5 mm distal to the cervical corner of the adjacent second molar,

Point D: A point 5 mm apical to the distocervical corner of the adjacent second molar.

Measurements were recorded for 30 seconds at each point using PeriSoft for Windows®(Perimed) software.

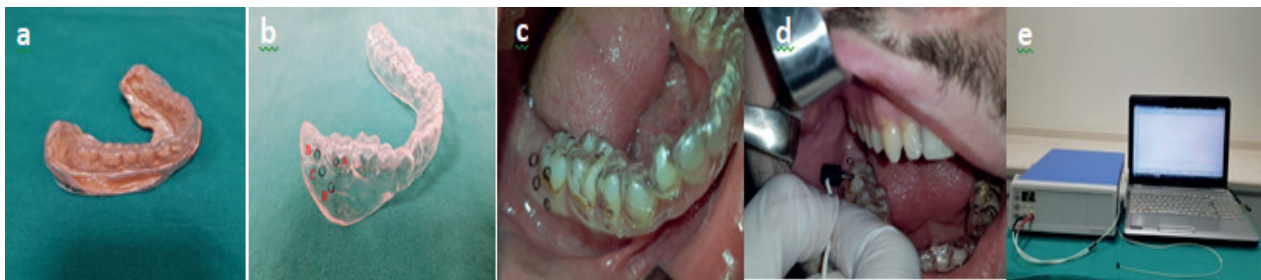


Figure 1. Standardization of laser Doppler flowmetry measurements.

- (a) Acrylic splint prepared on the plaster model.
- (b) Measurement points for pulpal (A) and gingival blood flow (B–D).
- (c) Intraoral placement of the acrylic splint.
- (d) Positioning of the laser Doppler flowmetry probe during measurement.
- (e) Laser Doppler flowmetry system (PeriFlux 5000, Perimed, Sweden) connected to a computer for real-time monitoring and recording of tissue perfusion measurements.

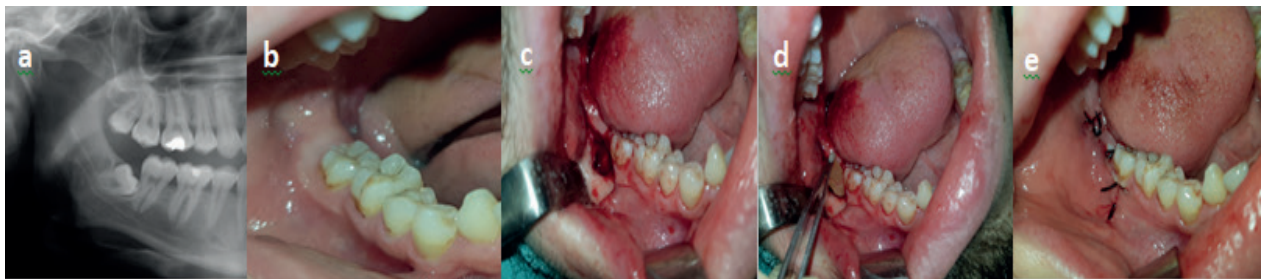


Figure 2. Surgical procedure and application of platelet-rich fibrin.

- (a, b) Impacted mandibular third molar teeth included in the study.
- (c) Extraction socket after tooth removal.
- (d) Placement of L-PRF or T-PRF into the extraction socket.
- (e) Primary wound closure with sutures.

The use of individualized acrylic splints, predefined reference points, and a standardized measurement environment was preferred to reduce variability and improve the reproducibility of LDF recordings (26,27) (Figure 1).

Surgical procedure

Following the preoperative LDF measurements, a local anesthetic solution containing articaine hydrochloride and epinephrine (Maxicaine Fort®, Vem Medicine, Türkiye) was administered for inferior alveolar, lingual, and buccal nerve blocks. A full-thickness triangular mucoperiosteal flap was elevated. Bone removal was performed using a round bur under sterile saline irrigation. Tooth sectioning was performed with a tungsten-carbide fissure bur, and the tooth fragments were removed. The socket was curetted, the sharp bony edges were smoothed, and the area was irrigated

with 20 mL of saline solution. Hemostasis was achieved before PRF application (Figure 2).

Preparation and application of L-PRF

Twenty milliliters of venous blood were drawn into two sterile glass tubes (10 mL each) without anticoagulant and were immediately centrifuged using the same centrifugation system (IntraSpin®, Intra-Lock, USA) throughout the study period. Centrifugation was performed for 12 minutes at 2700 rpm according to the standard Choukroun protocol; this corresponds to an approximate relative centrifugal force (RCF) of $400 \times g$. The fibrin clot was obtained and separated from the erythrocyte layer and was placed into the extraction socket in two layers before wound closure (7,10). All PRF preparation procedures were performed by the same clinician according to a standardized protocol (Figure 3).

Preparation and application of T-PRF

Twenty milliliters of venous blood were transferred into two sterile Grade IV titanium tubes (10 mL each) and immediately centrifuged for 12 minutes at 2700 rpm using the centrifugation system (IntraSpin®, Intra-Lock, USA), according to the standard T-PRF preparation protocol. This procedure corresponded to an approximate RCF of $400 \times g$. The fibrin clot was obtained and separated from the erythrocyte fraction and was placed into the extraction socket in two layers before wound closure (11,12) (Figure 4).

Postoperative period and postoperative measurements

The flaps were primarily closed using 3/0 silk sutures. In accordance with the routine protocol, patients were prescribed postoperative antibiotic therapy (amoxicillin/clavulanic acid), a nonsteroidal anti-inflammatory drug (naproxen sodium), and a 0.12% chlorhexidine mouthwash. Sutures were removed on postoperative day 7, and LDF measurements were repeated using the same acrylic splints and measurement points.



Figure 3. Preparation of leukocyte- and platelet-rich fibrin (L-PRF).

- (a, b) Blood collection into glass-coated plastic tubes.
- (c) Centrifugation procedure.
- (d, e) Separation of the fibrin clot.
- (f) Final L-PRF membranes ready for application.



Figure 4. Preparation of titanium-prepared platelet-rich fibrin (T-PRF).

- (a, b) Blood collection into titanium tubes.
- (c) Centrifugation procedure.
- (d) Separation of the fibrin clot.
- (e) Final T-PRF membranes ready for application.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows (version 30.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test, Kolmogorov–Smirnov test, and evaluation of skewness and kurtosis coefficients. Since the assumptions of normality were not satisfied for most variables, non-parametric statistical methods were used. Descriptive data were presented as mean $\pm$ standard deviation (SD) and median (minimum–maximum).

Intergroup comparisons were performed using the Mann–Whitney U test, whereas within-group preoperative–postoperative comparisons were analyzed using the Wilcoxon signed-rank test. Two-tailed exact p values, standardized Z statistics, rank-biserial correlation effect sizes (r), and their corresponding 95% confidence intervals (CIs) were calculated and reported. Effect sizes were interpreted according to Cohen’s criteria as small ($r=0.10$), medium ($r=0.30$), and large ($r=0.50$).

Bonferroni correction was applied to control the risk of Type I error arising from multiple comparisons. Because four primary comparisons were considered, the adjusted significance level was set at $p<0.0125$. Both unadjusted (exact) p values and Bonferroni-adjusted p values were reported.

To evaluate the adequacy of the sample size, an a priori power analysis was performed using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany), assuming a significance level of $\alpha=0.05$ and 80% statistical power. The planned sample size of 30 participants per group exceeded the calculated minimum sample size required to detect a large effect size (Cohen’s $d\geq 0.80$) in independent-group comparisons. The post hoc power value based on the observed effect size was calculated for descriptive purposes only. Unless otherwise specified, for analyses with Bonferroni correction, the level of statistical significance was accepted as $p<0.05$.

RESULTS

The baseline demographic and clinical characteristics of the study groups are summarized in Table 1.

Pulpal blood flow of the adjacent mandibular second molar and gingival blood flow of the mucoperiosteal flap were expressed in perfusion units (PU). Gingival perfusion was calculated as the mean of the measurements at the three predefined measurement sites.

Assessment of normality, performed using the Shapiro–Wilk and Kolmogorov–Smirnov tests (Table 2), revealed that most variables were not normally distributed. Therefore, non-parametric statistical methods were used for all analyses. Bonferroni correction was applied to reduce the risk of error arising from multiple comparisons.

Within-Group Comparisons

In both groups, pulpal perfusion values on postoperative day 7 were significantly increased compared with baseline values. In the T-PRF group, pulpal perfusion increased from 14.17 ± 2.99 PU to 22.28 ± 4.81 PU ($\Delta = +8.10$ PU; $Z = 4.535$; Bonferroni-adjusted $p < 0.001$; $r = 0.586$, 95% CI: 0.389–0.731). In the L-PRF group, pulpal perfusion increased from 15.10 ± 3.47 PU to 21.63 ± 3.49 PU ($\Delta = +6.52$ PU; $Z = 4.782$; Bonferroni-adjusted $p < 0.001$; $r = 0.617$, 95% CI: 0.431–0.753). Large effect sizes were observed for both comparisons. Within-group comparisons are presented in Table 3.

Similarly, gingival perfusion values increased significantly in both groups. In the T-PRF group, gingival perfusion increased from 15.77 ± 3.28 PU to 26.87 ± 1.03 PU ($\Delta = +11.09$ PU; $Z = 4.782$; Bonferroni-adjusted $p < 0.001$; $r = 0.617$, 95% CI: 0.431–0.753). In the L-PRF group, gingival perfusion increased from 14.97 ± 2.86 PU to 21.79 ± 0.91 PU ($\Delta = +6.81$ PU; $Z = 4.782$; Bonferroni-adjusted $p < 0.001$; $r = 0.617$, 95% CI: 0.431–0.753). Comparable effect sizes were obtained for gingival perfusion. The mean postoperative increases in pulpal and gingival perfusion values are shown in Figure 5.

Table 2. Normal distribution tests of measurement variables (Shapiro–Wilk, Kolmogorov–Smirnov, and Skewness–Kurtosis Coefficients).

Variable	Group	K-S Statistic	K-S p	S-W Statistic	S-W p	Skewness	Kurtosis	Decision
Pulpal Blood Flow (Preoperative)	T-PRF	0.330	0.002	0.716	<0.001	-1.966	3.012	Non-Normal
	L-PRF	0.230	0.071	0.739	<0.001	-1.920	2.881	Non-Normal
Pulpal Blood Flow (Postoperative)	T-PRF	0.372	<0.001	0.590	<0.001	-2.291	3.955	Non-Normal
	L-PRF	0.207	0.132	0.753	<0.001	-2.058	4.168	Non-Normal
Gingival Blood Flow (Preoperative)	T-PRF	0.267	0.022	0.742	<0.001	-1.740	2.029	Non-Normal
	L-PRF	0.264	0.025	0.694	<0.001	-2.128	3.663	Non-Normal
Gingival Blood Flow (Postoperative)	T-PRF	0.121	0.729	0.961	0.322	0.129	-0.659	Normal
	L-PRF	0.083	0.976	0.976	0.715	0.133	-0.612	Normal

L-PRF, leukocyte- and platelet-rich fibrin; T-PRF, titanium-prepared platelet-rich fibrin; K-S, Kolmogorov–Smirnov test; S-W, Shapiro–Wilk test. Normality was assessed using the Shapiro–Wilk test (n = 30 per group). Because normality assumptions were not consistently satisfied, non-parametric tests were used for all analyses.

Table 3. Preoperative–postoperative comparison of measurements within each PRF group separately.

Group	Measurement	Time	Mean ± SD	Postop-Preop Difference	T	Z	p (Bonf.)	r (95% CI)
T-PRF	Pulpal Blood Flow	Preop	14.17 ± 2.99	+8.10	12.0	+4.535	<0.001	0.586 (0.389–0.731)
		Postop	22.28 ± 4.81					
	Gingival Blood Flow	Preop	15.77 ± 3.28	+11.09	0.0	+4.782	<0.001	0.617 (0.431–0.753)
		Postop	26.87 ± 1.03					
L-PRF	Pulpal Blood Flow	Preop	15.10 ± 3.47	+6.52	0.0	+4.782	<0.001	0.617 (0.431–0.753)
		Postop	21.63 ± 3.49					
	Gingival Blood Flow	Preop	14.97 ± 2.86	+6.81	0.0	+4.782	<0.001	0.617 (0.431–0.753)
		Postop	21.79 ± 0.91					

PRF, platelet-rich fibrin; L-PRF, leukocyte- and platelet-rich fibrin; T-PRF, titanium-prepared platelet-rich fibrin; SD, standard deviation; Preop, preoperative; Postop, postoperative; T, Wilcoxon signed-rank test statistic; Z, standardized test statistic; p (Bonf.), Bonferroni-adjusted p value; r, effect size (rank-biserial correlation); 95% CI, 95% confidence interval. Postop – Preop differences were calculated as postoperative minus preoperative values; positive values indicate an increase. Significant p values are shown in bold italics.

Intergroup comparisons

Although preoperative pulpal and gingival perfusion values differed in the unadjusted analyses, these differences were not statistically significant after Bonferroni correction (adjusted p = 0.086 and 0.071, respectively). Therefore, after correction for multiple comparisons, no statistically significant baseline imbalance was detected between the groups. Intergroup comparisons are summarized in Table 4.

Postoperative pulpal perfusion was higher in the T-PRF group than in the L-PRF group (U = 624.0; Z = 2.572;

exact p = 0.010; r = 0.332; 95% CI: 0.085–0.540); however, the difference did not remain significant after Bonferroni correction. However, a direct comparison of change scores demonstrated a greater increase in the T-PRF group (U = 759.00; Z = 4.568; p < 0.001; r = 0.590). This result corresponds to a moderate effect size. Similarly, postoperative gingival perfusion was higher in the T-PRF group (U = 900.0; Z = 6.653; exact p < 0.001; r = 0.859; 95% CI: 0.774–0.914). This finding represents a very large effect size. Effect size estimates and their corresponding 95% CIs are presented in Figure 6.

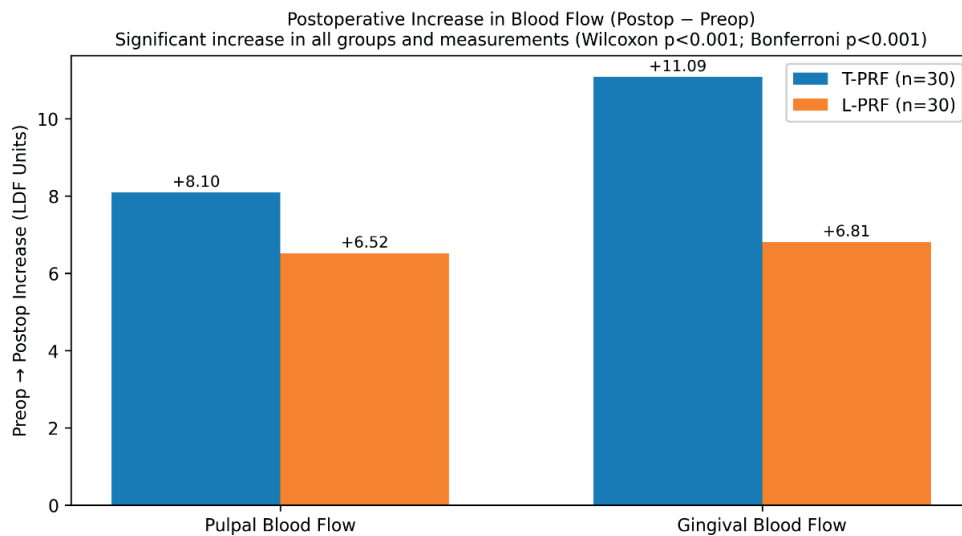


Figure 5. Mean postoperative increases in pulpal and gingival blood flow (postoperative minus preoperative values) in the T-PRF and L-PRF groups. Both platelet concentrates were associated with significant within-group increases in blood flow following surgery (Wilcoxon signed-rank test, $p < 0.001$ for all comparisons). Direct comparison of change scores (postoperative – preoperative) showed larger increases in the T-PRF group for both pulpal and gingival blood flow measurements, with the most pronounced difference observed for gingival perfusion.

L-PRF, leukocyte- and platelet-rich fibrin; T-PRF, titanium-prepared platelet-rich fibrin; LDF, laser Doppler flowmetry.

Table 4. Comparison of measurement values according to PRF groups.

Variable	Group	Mean $\pm$ SD	Median (Min–Max)	U	Z	P (Exact)	P (Bonf.)	r (95% CI)
Pulpal Blood Flow (Preoperative)	T-PRF	14.17 $\pm$ 2.99	14.92 (5.15–17.45)	294.00	–2.306	0.021	0.086	0.298 (0.047–0.513)
	L-PRF	15.10 $\pm$ 3.47	16.20 (4.67–18.41)					
Pulpal Blood Flow (Postoperative)	T-PRF	22.28 $\pm$ 4.81	23.81 (6.45–25.67)	624.00	+2.572	0.010	0.041	0.332 (0.085–0.540)
	L-PRF	21.63 $\pm$ 3.49	22.54 (9.18–24.91)					
Gingival Blood Flow (Preoperative)	T-PRF	15.77 $\pm$ 3.28	16.52 (6.34–19.80)	611.00	+2.380	0.017	0.071	0.307 (0.058–0.521)
	L-PRF	14.97 $\pm$ 2.86	15.85 (6.23–17.70)					
Gingival Blood Flow (Postoperative)	T-PRF	26.87 $\pm$ 1.03	26.63 (25.19–29.23)	900.00	+6.653	<0.001	<0.001	0.859 (0.774–0.914)
	L-PRF	21.79 $\pm$ 0.91	21.87 (20.23–23.70)					

PRF, platelet-rich fibrin; L-PRF, leukocyte- and platelet-rich fibrin; T-PRF, titanium-prepared platelet-rich fibrin; SD, standard deviation; Min–Max, minimum–maximum; U, Mann–Whitney U statistic; Z, standardized test statistic; p(Exact), exact two-tailed p value; p (Bonf.), Bonferroni-adjusted p value; r, effect size (rank-biserial correlation); 95% CI, 95% confidence interval. Significant p values are shown in bold italics. Significant between-group differences were observed for postoperative pulpal and gingival blood flow, with higher values in the T-PRF group.

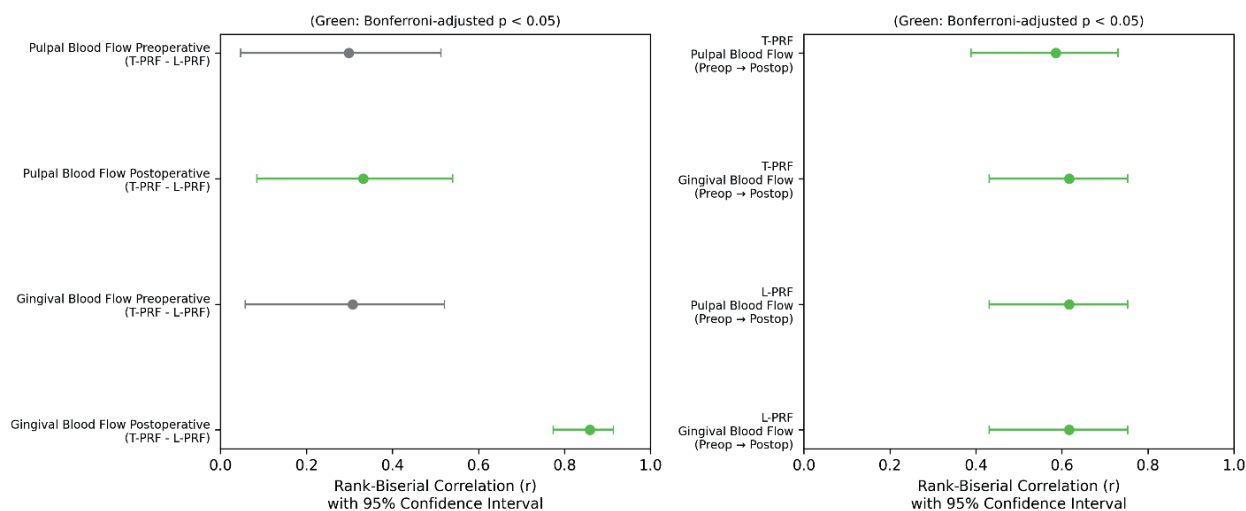


Figure 6. Effect Sizes (Rank-Biserial Correlation) and 95% Confidence Intervals for Intergroup (Left Panel) and Within-Group (Right Panel) Comparisons. Green markers indicate statistically significant comparisons after Bonferroni correction. Error bars represent 95% confidence intervals.

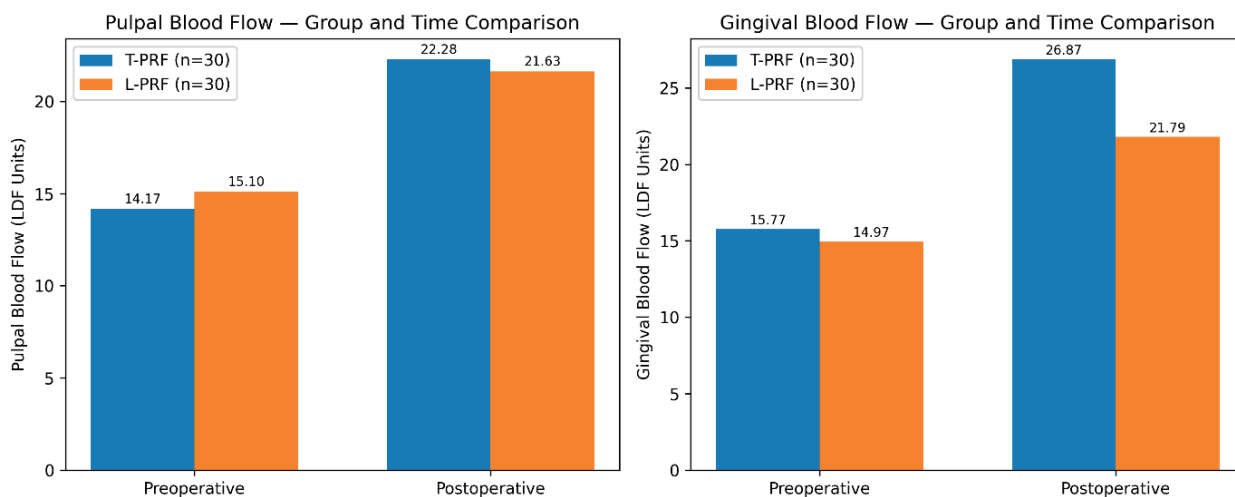


Figure 7. Comparison of mean preoperative and postoperative pulpal and gingival blood flow values between the T-PRF and L-PRF groups. Bars represent mean perfusion values measured by laser Doppler flowmetry (LDF). Higher postoperative perfusion values were observed in the T-PRF group; however, because of the retrospective design, these findings should be interpreted as an association rather than evidence of a causal effect.

Overall, both PRF preparations were associated with significant increases in pulpal and gingival perfusion following surgery. However, postoperative perfusion values were higher in the T-PRF group (Figure 7). To further account for potential baseline differences, change scores (postoperative – preoperative) were directly compared between the two groups using the Mann–Whitney U test. The magnitude of change

was greater in the T-PRF group for both pulpal blood flow (T-PRF: +8.10 PU vs. L-PRF: +6.52 PU; $U = 759.00$; $Z = 4.568$; $p < 0.001$; $r = 0.590$ [95% CI: 0.378–0.768]) and gingival blood flow (T-PRF: +11.09 PU vs. L-PRF: +6.81 PU; $U = 814.00$; $Z = 5.382$; $p < 0.001$; $r = 0.695$ [95% CI: 0.512–0.842]), with the largest difference observed in gingival perfusion (Table 5).

Table 5. Between-group comparison of change scores (Δ = postoperative – preoperative) in pulpal and gingival blood flow (Mann–Whitney U test; n = 30 per group).

Variable	Group	Mean $\pm$ SD	Median (Min–Max)	U	Z	p (Exact)	p (Bonf.)	r (95% CI)
Pulpal Blood Flow Change (Δ)	T-PRF	8.10 $\pm$ 4.88	9.04 (–8.10–16.61)	759.00	+4.568	<0.001	<0.001	0.590 (0.378–0.768)
	L-PRF	6.52 $\pm$ 1.09	6.27 (3.93–8.74)					
Gingival Blood Flow Change (Δ)	T-PRF	11.09 $\pm$ 3.47	10.21 (7.36–20.09)	814.00	+5.382	<0.001	<0.001	0.695 (0.512–0.842)
	L-PRF	6.81 $\pm$ 2.87	5.98 (3.61–17.22)					

L-PRF, leukocyte- and platelet-rich fibrin; T-PRF, titanium-prepared platelet-rich fibrin; SD, standard deviation; Min–Max, minimum–maximum; U, Mann–Whitney U test statistic; Z, standardized test statistic; p (Bonf.), Bonferroni-adjusted p value; r, effect size (rank-biserial correlation); CI, confidence interval; Δ , postoperative – preoperative change; PU, perfusion unit.

The T-PRF group demonstrated significantly greater increases in pulpal and gingival blood flow than the L-PRF group, with the largest effect observed for gingival perfusion.

DISCUSSION

This study demonstrated that both L-PRF and T-PRF were associated with significant increases in gingival and pulpal perfusion on postoperative day 7 compared with baseline values. Intergroup comparisons revealed higher postoperative perfusion values in the T-PRF group; the most pronounced difference was observed in gingival perfusion ($r=0.859$), whereas a moderate effect size was observed for postoperative pulpal perfusion ($r=0.332$).

Wound healing is a complex and multistage process consisting of the inflammatory, proliferative, and remodeling phases (17,18). The proliferative phase, which begins within the first few days after injury and generally continues until the second or third postoperative week, is characterized by angiogenesis, granulation tissue formation, and collagen deposition (17,18). Angiogenesis is a key event during this period because the formation of new capillary vessels supports tissue regeneration by increasing local blood flow (18,19). Therefore, evaluation on postoperative day 7 is particularly important for assessing the biological activities of platelet concentrates during the early healing period (8,17).

PRF-based biomaterials are known to provide the sustained release of angiogenic growth factors, particularly VEGF, during the early healing period

(5,6,8). Previous studies have shown that L-PRF releases VEGF and other cytokines predominantly within the first 7 days, corresponding to the period of peak angiogenic activity (8). The significant increase in gingival and pulpal perfusion observed in the L-PRF group in the present study is consistent with these findings and supports a potential role for L-PRF in enhancing early vascular responses (4,5).

One of the most important findings of this study is the magnitude of the observed effect sizes. Although both PRF protocols were associated with significant increases in perfusion values, the difference between the groups was particularly pronounced for gingival perfusion, showing a very large effect size ($r=0.859$). In contrast, the effect size for postoperative pulpal perfusion was moderate ($r=0.332$). These findings suggest that the effect of T-PRF on early postoperative microcirculation may be more pronounced in gingival tissues than in pulpal tissues. However, the biological mechanisms underlying this difference remain speculative and require further investigation.

The significantly greater increase in perfusion observed in the T-PRF group may be related to the unique fibrin architecture of this material. Experimental studies have revealed that T-PRF forms a thicker and more compact fibrin network than L-PRF, which may be resorbed more slowly and therefore maintain its scaffold function for a longer period (11,13,14). Its prolonged persistence

within the tissues may allow the sustained release of growth factors and cytokines, thereby contributing to angiogenic signaling and enhanced microvascular perfusion (13,15). The present findings are consistent with previous histological and biochemical studies reporting greater cellular entrapment and more prolonged growth factor activity in T-PRF compared with conventional PRF formulations (13,14). However, fibrin architecture, growth factor release, cytokine profiles, angiogenesis, and histological healing were not directly evaluated in the present study. Therefore, these mechanisms should be regarded as possible biological explanations rather than confirmed causes of the observed perfusion differences.

LDF was selected as the assessment method because tissue perfusion is a sensitive indicator of wound-healing quality (20,21,26). Increased PU values reflect enhanced microcirculation and oxygenation, which are essential for effective healing and resistance to infection (17,18). In the present study, standardized acrylic splints were used to ensure stabilization of the LDF probe, thereby improving measurement reproducibility and minimizing artifacts related to probe movement or positioning (26,27). This methodological approach strengthens the reliability of the observed perfusion changes.

Another clinically noteworthy finding was a significant increase in pulpal blood flow in the adjacent mandibular second molar, particularly in the T-PRF group. Increased pulpal perfusion may reflect changes in the vascular response of the pulp tissue during the early postoperative period. However, pulpal vitality, sensibility responses, clinical symptoms, and long-term pulp status were not evaluated in this study. Therefore, the increase observed in LDF values should not be interpreted as evidence of pulp preservation or maintenance of vitality, but rather as an indicator of changes in pulpal microcirculation. Furthermore, the increased perfusion values may reflect transient postoperative vascular or inflammatory responses. Prospective studies incorporating vitality tests, sensibility assessments, and long-term clinical follow-up are required to clarify the biological and clinical significance of these findings and to determine whether the observed perfusion changes translate into clinically meaningful pulpal benefits.

This study has several limitations. First, its retrospective, non-randomized design carries an inherent risk of selection bias. In addition, allocation to the treatment groups was not randomized; L-PRF was used during the early phase of the study, whereas T-PRF was used after titanium tubes were introduced into routine clinical practice. This assignment of groups according to chronological treatment periods (L-PRF applied during the earlier period and T-PRF during the later) may represent an important source of bias, as surgical experience, clinical routines, patient selection, measurement practices, and postoperative care protocols may have changed over time and thereby intergroup differences. Therefore, despite the use of standardized surgical and measurement protocols and the similar surgical characteristics of the groups, residual confounding effects related to time-dependent factors and unmeasured variables cannot be completely excluded.

After applying Bonferroni correction for multiple comparisons, no statistically significant difference was detected in baseline pulpal or gingival perfusion values. Although the unadjusted analyses suggested possible differences between the groups, these findings did not retain statistical significance after correction. Therefore, the available data do not demonstrate a statistically significant imbalance in baseline perfusion measurements. Nevertheless, because the study is retrospective and non-randomized, residual confounding from unmeasured factors cannot be completely excluded, and the findings should be interpreted with caution.

Another important limitation is the absence of a control group that did not receive PRF. Although increases in gingival and pulpal perfusion compared with baseline values were observed in both the L-PRF and T-PRF groups, the current study design does not allow the determination of whether these changes were directly attributable to the platelet concentrates or merely reflected the normal physiological healing response following third molar surgery. Therefore, the findings should primarily be interpreted as a comparison between two PRF protocols and should not be considered definitive evidence that either material alone enhances postoperative healing or microcirculation.

A strength of the present study is the inclusion of normality testing, effect size calculations, CIs, and Bonferroni-adjusted analyses, which improve the robustness of the statistical evaluation. Nevertheless, the relatively limited sample size and the retrospective design remain important factors that should be considered when interpreting the findings.

In addition, the follow-up period was limited to the early healing phase. Long-term clinical outcomes, such as bone regeneration, periodontal status of the adjacent tooth, postoperative complications, and patient-reported outcome measures, were not evaluated. However, the primary aim of the present study was to assess early microcirculatory changes occurring during the proliferative phase of wound healing, and postoperative day 7 represents a biologically meaningful and widely accepted time point for this purpose (8,17). Therefore, the present findings should be regarded as indicators of early microcirculatory responses rather than evidence of long-term clinical superiority.

Prospective randomized controlled studies including an untreated control group, larger sample sizes, formal corrections for multiple comparisons, and longer follow-up periods are needed to determine whether the observed perfusion differences translate into meaningful long-term clinical benefits.

Accordingly, these findings should be interpreted as physiological observations rather than evidence of superior clinical effectiveness. However, the clinical significance of these perfusion differences, and whether they translate into improved long-term healing outcomes, have not yet been clearly established.

CONCLUSIONS

Within the limitations of this retrospective study, both L-PRF and T-PRF were associated with significant increases in gingival and pulpal perfusion on postoperative day 7, and T-PRF was associated with greater increases, most notably in gingival perfusion. However, because no non-PRF control

group was included and the design was retrospective, these differences cannot be causally attributed to the platelet concentrates and may partly reflect the normal postoperative healing response. Prospective randomized controlled studies with a non-PRF control group, larger samples, and longer follow-up are needed to determine whether these microcirculatory differences translate into clinically meaningful healing outcomes.

Ethical approval

Approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (27.04.2021; No. 2021/62). Written informed consent was obtained from all participants prior to inclusion in the study.

Author contribution

Concept and design: NA; Data acquisition: NA, BM; Data analysis and interpretation: NA; Drafting of the manuscript: NA, BM; Critical revision of the manuscript: NA; Final approval of the version to be published: NA, BM. All authors meet the ICMJE authorship criteria and approve the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

Use of artificial intelligence

During the preparation of this manuscript, the authors used ChatGPT (GPT5.5, OpenAI, San Francisco, CA, USA) exclusively for language editing and grammatical refinement. The authors have critically reviewed, revised, and approved all generated content and take full responsibility for the final manuscript.

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