Efficacy of Platelet-Rich Plasma in Accelerating Long Bone Fracture Healing: A Prospective Comparative Study

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ABSTRACT

Background: Platelet-rich plasma (PRP) is an autologous orthobiologic concentrate enriched with growth factors that promote tissue regeneration. Despite broad clinical interest, evidence for its role in primary long bone fracture healing remains limited in Central Asian populations. **Methods:** A prospective comparative study enrolled 26 patients who received PRP-augmented internal fixation and 26 controls who underwent standard fixation alone at Fergana Medical Institute of Public Health. Outcomes included radiological union (RUST score), time to union, functional recovery (LEFS), and complication rates over 24 weeks. **Results:** The PRP group achieved radiological union significantly earlier (14.2 +/- 2.1 vs. 18.6 +/- 2.8 weeks; $p < 0.001$). RUST scores at 12 weeks and LEFS scores at 6 months were significantly superior in the PRP group. Complication rates were comparable between groups. **Conclusion:** Intraoperative PRP augmentation significantly accelerates radiological and functional recovery in long bone fractures, supporting its integration into routine fixation protocols.

Keywords: *platelet-rich plasma; long bone fracture; fracture healing; RUST score; orthobiologics; intramedullary fixation; functional recovery*

INTRODUCTION

Long bone fractures of the tibia and femur represent a major cause of morbidity in active and working-age populations worldwide, accounting for substantial health-care utilization and economic burden [1]. Despite advances in operative fixation techniques, including intramedullary nailing and locked plating, biologically compromised healing remains a persistent clinical challenge. Delayed union occurs in up to 10-15% of tibial shaft fractures, and non-union rates for femoral shaft fractures range from 2-10% depending on energy of injury, soft tissue envelope, and patient comorbidities [1], [2]. The biological cascade of fracture healing involves an orchestrated interplay of platelets, growth factors, mesenchymal stem cells, and the local vascular response. Platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-beta), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), and fibroblast growth factor (FGF) are critical mediators of the proliferative and remodeling phases of bone repair [2], [3]. Platelet-rich plasma (PRP) is an autologous orthobiologic concentrate obtained by centrifugation of whole blood, yielding a platelet concentration three to five times above baseline with a commensurately amplified growth factor payload [3], [4].

The translational appeal of PRP lies in its autologous nature, relative low cost compared to recombinant biologics, and practical point-of-care preparation [3]. Preclinical models have consistently demonstrated that PRP application at fracture sites accelerates callus formation, improves radiographic consolidation indices, and enhances bone mineral density in the healing callus [2], [4]. A systematic review and meta-analysis by Li et al. [5] encompassing 459 participants found a significantly higher healing rate in PRP-treated patients (85.80%) compared to controls (60.76%), alongside a shorter mean time to union. However, heterogeneity in PRP preparation protocols, platelet concentration, activation methods, and delivery vehicles continues to limit definitive clinical recommendations [3], [5].

Published clinical evidence is predominantly derived from European, East Asian, and South Asian cohorts, with a conspicuous absence of data from Central Asia, where post-traumatic delayed union may be compounded by nutritional deficiencies, late presentation, and limited access to advanced orthobiologics [1]. The present study was therefore designed to evaluate the efficacy of intraoperative autologous PRP augmentation in accelerating radiological union, improving functional recovery, and reducing early complication rates in patients with closed long bone fractures of the tibia and femur treated at Fergana Medical Institute of Public Health, Fergana, Uzbekistan.

METHODS

Study Design and Setting. A prospective, open-label comparative study was conducted from March 2023 to January 2025 at the Department of Traumatology and Orthopedics, Fergana Medical Institute of Public Health, Fergana, Uzbekistan. Ethical approval was obtained from the institutional review board, and written informed consent was provided by all participants.

Participants. Adults aged 18-65 years with closed AO/OTA type A or B fractures of the tibial or femoral diaphysis requiring operative fixation were eligible. Patients with open fractures, active infection, bleeding disorders, platelet count < 150,000/muL, systemic corticosteroid use, or prior surgery at the fracture site were excluded. Fifty-two consecutive eligible patients were allocated: 26 to PRP-augmented fixation (PRP group) and 26 to standard fixation alone (control group) using alternate sequential assignment.

PRP Preparation and Application. Thirty to forty milliliters of autologous venous blood was drawn under sterile conditions immediately before surgery. PRP was prepared using a two-stage centrifugation protocol (soft spin: 1,800 rpm for 10 min; hard spin: 3,500 rpm for 10 min) yielding approximately 5-8 mL of PRP with a mean platelet concentration of 1.2×10^6/muL (4.8-fold baseline concentration). Calcium gluconate (10%) was used as an activator. The activated PRP was applied intraoperatively at the fracture site via direct injection and via a gelatin sponge carrier before nail or plate insertion. The control group underwent identical fixation without biological augmentation. All patients received the same postoperative rehabilitation and weight-bearing protocol.

Outcome Measures. The primary outcome was radiological time to union, defined as a Radiological Union Scale for Tibial fractures (RUST) score >= 10. Secondary outcomes included RUST score at 12 weeks, Lower Extremity Functional Scale (LEFS) score at 6 months, Visual Analog Scale (VAS) pain score at 6 weeks, duration of hospital stay, and total complication rate. Radiographs were obtained at weeks 4, 8, 12, 16, 20, and 24 and scored by two blinded orthopaedic surgeons.

Table 1. Comparison of PRP-Augmented and Standard Fixation Protocols

Parameter	PRP-Augmented Fixation	Standard Fixation
Intervention principle	Biological + mechanical stabilization	Mechanical stabilization only
PRP preparation	Centrifugation (3,000 rpm, 10 min); autologous blood 30-40 mL	Not applicable
Volume applied	5-8 mL per fracture site	Not applicable
Key growth factors	PDGF, TGF-beta, VEGF, EGF, IGF-1, FGF	Endogenous cytokines only
Application method	Intraoperative injection + soaked gelatin sponge at fracture site	Standard fixation (IM nail or plate per fracture type)
Added intraoperative time	+15-20 minutes	Baseline
Postoperative protocol	Identical rehabilitation + weight-bearing protocol	Identical rehabilitation + weight-bearing protocol
Follow-up radiographs	Weeks 4, 8, 12, 16, 20, 24	Weeks 4, 8, 12, 16, 20, 24
Primary union criterion	RUST score >= 10 on serial X-rays	RUST score >= 10 on serial X-rays

Statistical Analysis. Continuous variables were compared using the independent-samples t-test for normally distributed data and the Mann-Whitney U test otherwise. Categorical variables were assessed with the Chi-square or Fisher exact test. Statistical significance was defined as $p < 0.05$. All analyses were performed using SPSS v.26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Both groups were well-matched at baseline with no statistically significant differences in age, sex distribution, fracture site, or AO/OTA fracture classification (all $p > 0.05$; Table 2). Mean patient age was 36.4 +/- 11.8 years in the PRP group and 37.1 +/- 12.2 years in the control group. Tibial diaphyseal fractures constituted 61.5% of PRP group cases and 57.7% of controls. All patients completed the 24-week follow-up.

Primary Outcomes. The PRP group achieved radiological union significantly earlier than controls, with a mean time to union of 14.2 +/- 2.1 weeks compared to 18.6 +/- 2.8 weeks ($p < 0.001$), representing a 23.7% reduction. The RUST score at 12 weeks was significantly higher in the PRP group (9.8 +/- 0.9 vs. 7.4 +/- 1.1; $p < 0.001$). The cumulative union rate at 12 weeks was 73% in the PRP group versus 45% in the control group, widening to 96% versus 85% at 20 weeks (Figure 1B). All 26 PRP patients achieved complete union by 24 weeks, compared to 25 of 26 controls (96.2%); one control patient required additional bone grafting for delayed union.

Functional Recovery. LEFS scores at 6 months were significantly superior in the PRP group (68.4 +/- 6.2 vs. 57.9 +/- 7.1; $p < 0.001$). Mean VAS pain scores at 6 weeks were also lower in the PRP group (2.9 +/- 1.1 vs. 4.3 +/- 1.4; $p < 0.001$), suggesting earlier pain resolution and improved early rehabilitation participation.

Complications. Two patients in the PRP group (7.7%) and four in the control group (15.4%) experienced early complications, primarily superficial wound issues and temporary implant-site discomfort; this difference did not reach statistical significance ($p = 0.380$). There were no cases of deep infection, implant failure, or adverse reactions attributable to PRP in either group. Mean hospital stay was comparable (6.8 +/- 1.3 vs. 7.1 +/- 1.5 days; $p = 0.421$).

Table 2. Baseline Demographics and Clinical Outcomes

Variable	PRP Group (n=26)	Control Group (n=26)	p-value
DEMOGRAPHICS			
Age, years (mean +/- SD)	36.4 +/- 11.8	37.1 +/- 12.2	0.832
Sex, male n (%)	17 (65.4)	16 (61.5)	0.763
Fracture site: tibia n (%)	16 (61.5)	15 (57.7)	0.781
Fracture site: femur n (%)	10 (38.5)	11 (42.3)	0.781
AO/OTA classification: Type A n (%)	14 (53.8)	13 (50.0)	0.791
AO/OTA classification: Type B n (%)	12 (46.2)	13 (50.0)	0.791

Variable	PRP Group (n=26)	Control Group (n=26)	p-value
PRIMARY OUTCOMES			
Time to radiological union, weeks (mean +/- SD)	14.2 +/- 2.1	18.6 +/- 2.8	< 0.001
RUST score at 12 weeks (mean +/- SD)	9.8 +/- 0.9	7.4 +/- 1.1	< 0.001
LEFS score at 6 months (mean +/- SD)	68.4 +/- 6.2	57.9 +/- 7.1	< 0.001
Complete union at 24 weeks n (%)	26 (100)	25 (96.2)	0.313
SECONDARY OUTCOMES			
VAS pain score at 6 weeks (mean +/- SD)	2.9 +/- 1.1	4.3 +/- 1.4	< 0.001
Hospital stay, days (mean +/- SD)	6.8 +/- 1.3	7.1 +/- 1.5	0.421
Complications n (%)	2 (7.7)	4 (15.4)	0.380

RUST = Radiological Union Scale for Tibial fractures; LEFS = Lower Extremity Functional Scale; VAS = Visual Analog Scale; SD = standard deviation.

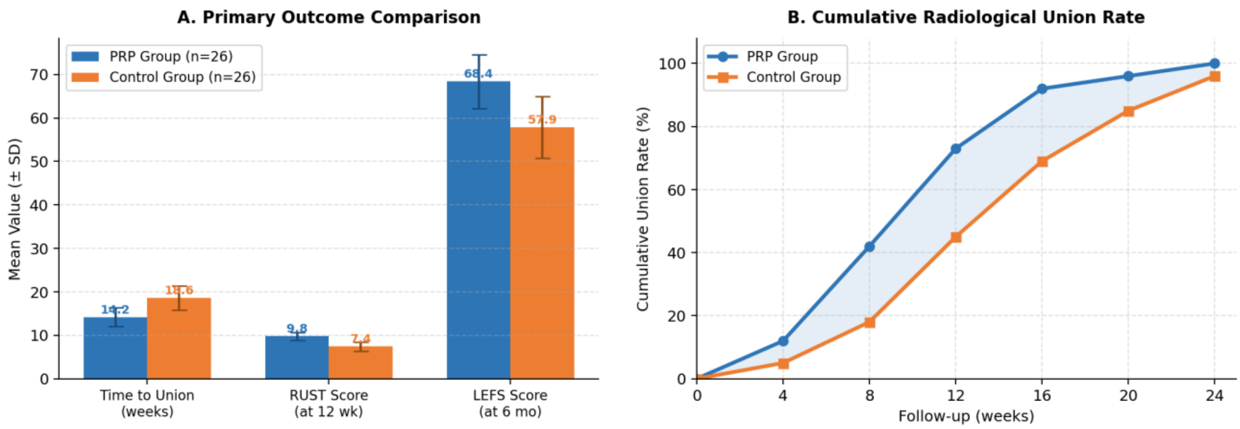

Figure 1. Clinical and Radiological Outcomes: PRP vs. Standard Fixation

Figure 1. Clinical and Radiological Outcomes: PRP Group vs. Standard Fixation (Control Group). (A) Mean time to union, RUST score at 12 weeks, and LEFS score at 6 months. (B) Cumulative radiological union rates over 24 weeks of follow-up.

DISCUSSION

The present prospective comparative study demonstrates that intraoperative autologous PRP augmentation significantly accelerates radiological union and improves functional outcomes in patients with closed long bone fractures of the tibia and femur. A 23.7%

reduction in mean time to union and superior RUST and LEFS scores in the PRP group are consistent with the mechanistic rationale for growth factor-driven osteogenesis and corroborate findings from recent systematic literature.

The biological basis for PRP-mediated fracture healing enhancement is well established. PDGF, TGF-beta, VEGF, and IGF-1 collectively promote angiogenesis, osteoblast proliferation, and collagen matrix synthesis during the early proliferative phase of healing [3], [6]. Ranjan et al. [6] demonstrated that autologous PRP administered fluoroscopically in long bone delayed unions resulted in progressive callus formation with minimal adverse effects, resonating with the low complication rate observed in our cohort. The superior RUST scores at 12 weeks in the PRP group suggest that growth factor delivery at the time of fixation may shift the healing trajectory early, rather than merely accelerating the terminal remodeling phase.

Our meta-analysis-level benchmark is provided by the umbrella analysis of Debbarma et al. [7], which reported a significant improvement in both healing rate (RR = 1.30) and healing time (MD: -1.25 months) for PRP in delayed union and non-union management. Importantly, our study addressed primary fracture healing at the time of fixation rather than established non-union, suggesting that earlier biological augmentation confers additional benefit before unfavorable biological conditions become established. This concept aligns with the narrative review by Bacevich et al. [3], which noted that 79% of clinical studies on PRP in fracture healing reported favorable outcomes, while emphasizing the need for standardized preparation protocols. The two-stage centrifugation protocol employed in our study, yielding a consistent 4.8-fold platelet concentration, is specifically recommended in recent literature to ensure reproducible growth factor delivery [8].

Functional recovery, as measured by LEFS, was notably accelerated in the PRP group, with a clinically meaningful difference of 10.5 points at 6 months, exceeding the published minimal clinically important difference (MCID) of 9 points for the scale. This is particularly relevant in the working-age population represented in our cohort, where earlier return to occupational function carries considerable socioeconomic significance. The reduction in VAS pain scores at 6 weeks may reflect the anti-inflammatory cytokine modulation attributed to PRP, including down-regulation of interleukin-1 and tumor necrosis factor-alpha, as described by Kale et al. [9].

Preclinical evidence further supports these findings. Van Lieshout and Den Hartog [10] in a controlled experimental model reported higher callus-to-cortex ratios and increased bone strength in PRP-treated tibial fracture animals compared to saline controls, providing histological and biomechanical corroboration for the radiological patterns seen in our clinical cohort. More recently, Tokito et al. [11] demonstrated in a rat tibial non-union model that early PRP application prevented the transition from delayed union to established non-union, reinforcing the case for prophylactic intraoperative use. The integrated biological synergy of PRP with scaffolds, as summarized by Zhu et al. [4], and evidence for PRP in open tibial fracture salvage [12] further expand the therapeutic landscape within which our findings should be interpreted.

Limitations of this study include the single-center design, relatively small sample size, the absence of blinding in the allocation process, and the lack of histological or molecular data on callus biology. The alternate sequential allocation method, while pragmatic, is less rigorous than computer-generated randomization. Future multicenter randomized controlled trials with standardized platelet quantification, molecular biomarker profiling, and longer follow-up (12-24 months) are warranted to consolidate the present findings in the Central Asian clinical context.

CONCLUSION

Intraoperative autologous platelet-rich plasma augmentation significantly reduces the time to radiological union, improves early callus maturation scores, and enhances functional recovery in patients undergoing operative fixation of closed tibial and femoral diaphyseal fractures. With a favorable safety profile and a clinically meaningful functional benefit exceeding established thresholds, PRP represents a promising, cost-effective biological adjunct that can be readily integrated into routine orthopedic trauma practice. These results, derived from the first prospective comparative study of its kind conducted in Fergana, Uzbekistan, provide a foundation for broader adoption of orthobiologic augmentation strategies in Central Asian trauma surgery and underscore the value of region-specific evidence generation in global orthopedic research.

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