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The Effect of Combined Platelet-Rich Plasma and Bone Graft for Bone Regeneration: A Systematic Review

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ABSTRACT

Introduction: Bone regeneration is a critical focus in orthopedic surgery, especially for challenging cases such as non-union fractures and large bone defects. Emerging treatments that combine platelet-rich plasma (PRP) with bone grafts (BG) have shown potential to enhance bone regeneration, reduce pain, and improve functional outcomes. This systematic review aims to evaluate the effect of PRP combined with BG on bone healing outcomes compared to standard treatments.

Methods: This review was conducted following the PRISMA guidelines, we explored published articles that experimented on the use of PRP combined with BG in treating any kind of bone injury from several databases encompassing PubMed, ScienceDirect, and grey literature (Google Scholar) for the last ten years. The authors name, year of publication, origin country, study design, sample size, PICO (population, intervention, control, and outcome) criteria and studies outcome will be extracted from the selected studies.

Result: Our systematic review identified seven studies encompassing a total of 455 samples from various countries. Functional scores, including the Harris Hip Score (HHS) in five studies, were consistently higher in PRP groups. Furthermore, VAS scores were significantly lower in the PRP groups compared to the control at the final follow up duration. Additionally, healing and union rates were notably higher in three studies compared to the control group. PRP groups also demonstrated shorter healing durations compared to the control group in three studies. Finally, the complication rates were notably higher in control group than PRP group.

Conclusion: PRP combined with BG enhances bone healing outcomes, reducing pain and recovery time and promoting functional improvement, thereby offering a promising approach for treating complex bone injuries.

Keywords: bone graft, bone regeneration, necrosis of the femoral head, non-union, platelet-rich plasma.

INTRODUCTION

Bone regeneration is a complex physiological process that presents a significant challenge in orthopedic surgery, especially in the management of critical-sized defects, delayed unions, and non-union fractures. Conventional treatments such as autologous and allogeneic bone grafting are widely employed to restore skeletal integrity and promote osteogenesis. However, these

approaches are constrained by issues including limited graft availability, donor site morbidity, immune rejection, and suboptimal biological integration.

Recently, biologically enhanced strategies have gained attention as potential adjuncts to improve bone healing. Among these, platelet-rich plasma (PRP) has garnered interest due to its autologous nature and elevated concentrations of bioactive molecules such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which play crucial roles in inflammation modulation, angiogenesis, and osteoblast proliferation[1]. When combined with bone graft materials, PRP is hypothesized to exert synergistic effects, enhancing both osteoinductive and osteoconductive properties of the grafts, thus supporting a more efficient regenerative process.

Despite numerous clinical and experimental studies evaluating PRP in conjunction with bone grafts, findings remain inconsistent due to heterogeneity in study design, PRP preparation methods, outcome assessment, and follow-up periods. Therefore, the clinical utility of this combination remains to be fully clarified.

This systematic review aims to critically appraise the existing literature on the combined use of PRP and bone grafts in bone regeneration. It evaluates the effects on union rates, pain reduction, healing duration, functional outcomes, and complication incidence, compared to standard treatment modalities.

METHODS

Aim

This systematic review aimed to critically evaluate the clinical efficacy of combining platelet-rich plasma (PRP) with bone graft (BG) in the context of bone regeneration. Primary outcomes included radiological union rates, time to union, pain scores, functional recovery, and complication rates, in comparison to standard therapeutic approaches.

Study Design

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A protocol was formulated a priori to define the inclusion criteria, data extraction process, and risk of bias assessment.

Search Strategy

A systematic search was undertaken across three major databases: PubMed, EMBASE, and Google Scholar, covering the period from January 2014 to March 2024. The search strategy employed Medical Subject Headings (MeSH) and free-text terms, using combinations of keywords such as “platelet-rich plasma,” “PRP,” “bone graft,” “bone regeneration,” “fracture healing,” “non-union,” and “orthopaedic.” Boolean operators (AND/OR) were utilized to optimize the search. Additional records were identified through manual screening of reference lists and grey literature.

Study Selection

Eligibility for inclusion in this systematic review was determined based on predefined PICO criteria. The population comprised human subjects presenting with bone defects, delayed unions, non-unions, or bone healing following fracture. The intervention involved the application of autologous PRP in combination with any form of bone graft material, including autografts, allografts, or synthetic substitutes. The comparison group consisted of patients receiving standard treatment modalities, such as bone grafting alone or no additional biological therapy. The outcomes of interest included quantitative measures of bone healing (e.g., union rate), time to radiographic or clinical union, functional outcomes (e.g., Harris Hip Score), pain assessment (e.g., Visual Analog Scale), and the incidence of postoperative complications.

Inclusion criteria for the study are study designs which included randomized controlled trials (RCTs), prospective and retrospective cohort studies, and case-control

studies. Exclusion criteria encompassed in vitro or animal studies, narrative reviews, case reports, and studies lacking comparative control groups.

Data Extraction

Data were extracted independently by two reviewers using a standardized data extraction form. Extracted variables included: first author, year of publication, study design, country of origin, sample size, patient demographics, details of the intervention and comparator groups, and, outcome measures. Discrepancies between reviewers were resolved through consensus or consultation with a third reviewer.

Quality Assessment

Methodological quality and risk of bias were assessed using validated tools appropriate for the respective study designs. For randomized controlled trials, the Cochrane Risk of Bias 2.0 (RoB 2) tool was applied, while non-randomized studies were evaluated with the ROBINS-1 tool.

Search Criteria

A comprehensive search of electronic databases yielded a total of 243 records. Following the removal of 172 duplicate entries, 71 unique records remained for initial title and abstract screening. Of these, 59 records were excluded based on irrelevance to the predefined eligibility criteria. The remaining 12 full-text articles were retrieved and assessed for eligibility.

During the full-text review, five studies were excluded: four due to unavailability of the full text in English and one due to complete inaccessibility of the full-text document. Consequently, a total of seven studies met all inclusion criteria and were incorporated into the final qualitative synthesis. No additional eligible studies were identified through other sources or reference list screening.

Figure 1. PRISMA Diagram

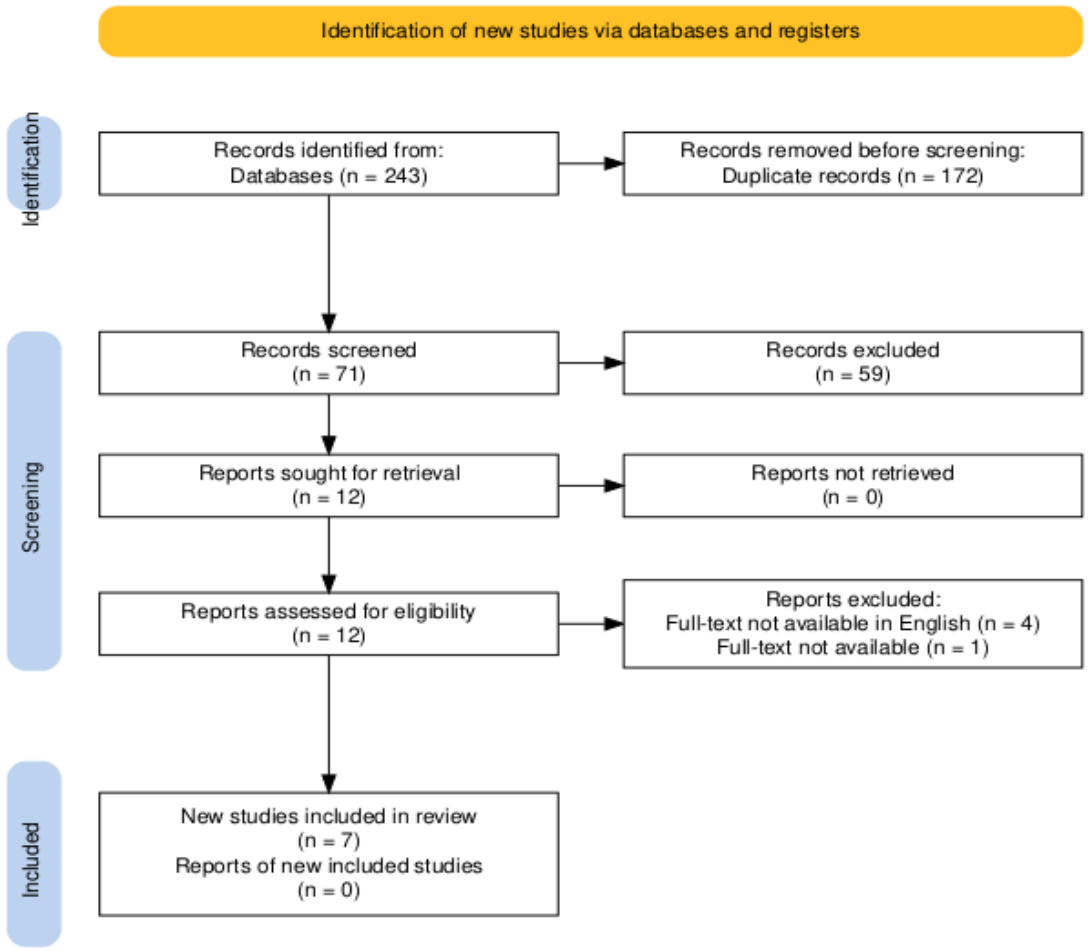


Table 1. Studies characteristics

Study	Country	Design	Sample Size	Population	Intervention	Control	Outcome
Ghaffarpasand et al 2016	Iran	RCT	75	Long bone non-union fractures	PRP + IM nailing/ORIF	Normal saline+IM nailing/ORIF	VAS, healing rate, healing duration, complication
Chen et al 2021	China	Case Control	184	Humeral condylar bone defect	PRP + Autogenous BG	Traditional surgery	VAS, MEPS, ADL, QOL, complication
Xu et al 2024	China	Retrospective	84	Avascular necrosis of femoral head Ficat-Arlet Classification Stage I-II	PRP + BG + CD	Symptomatic treatment BG + CD	VAS, HHS, THA incidence
Xian et al 2019	China	RCT	46	Post-Traumatic ONFH	PRP + CD + Autologous BG	CD + Autologous BG	VAS, HHS
Acosta-Olivo et al 2017	Mexico	RCT	16	Delayed union diaphyseal humeral fracture	PRP + Iliac Crest Bone Graft	Iliac Crest Bone Graft	Quick DASH, Consolidation Radiographs
Majeed et al 2020	Iraq	Cohort Prospective	32	Non-union distal tibia	PRP + Iliac Crest Bone Graft	Iliac Crest Bone Graft	VAS, healing duration, callus formation, union rate
Piacentini et al 2019	Italy	Retrospective	18	Critically sized post-traumatic long bone defects	PRP + BMCA + Autologous Iliac Crest + Cancelous Allograft	N/A	VAS, ROM, clinical union rate, radiological union rate

Table 2. Studies outcome results

Study	Level of Evidence	Postoperative VAS		Healing/Union Rate		Healing Duration		HHS		Other		Complication
		PRP	Control	PRP	Control	PRP	Control	PRP	Control	PRP	Control	
Ghaffarpasand et al 2016	I	1.1±0.3	1.1±0.3	81.1 %	55.3%	Upper: 7.9±0.6 Lower: 8.4±1.3 (months)	Upper: 8.4±1.3 Lower: 8.8±2.1 (months)	N/A	N/A	N/A	N/A	Infection is higher in PRP group compared to control
Chen et al 2021	III	3.57±0.36	4.26±0.48	N/A	N/A	N/A	N/A	N/A	N/A	MEPS: 79.68±5.46	MEPS: 68.32±5.34	Total complication is higher in control group

												compared to PRP
Xu et al 2024	III	1.74±0.73	3.38±1.36	N/A	N/A	N/A	N/A	89.47±8.72	80.14±11.47	N/A	N/A	Total complication is higher in control group (41.67%) compared to PRP group (22.73%)
Xian et al 2019	I	0.9±0.2	2.0±0.4	87.5 %	59.1%	N/A	N/A	86.5±1.6	79.3±2.4	N/A	N/A	N/A
Acosta-Olivo et al 2017	I	N/A	N/A	N/A	N/A	19.9±2.25 (weeks)	25.44±2.06 (weeks)	N/A	N/A	QDASH: 81.50±9.04	QDASH: 76.41±19.60	N/A
Majeed et al 2020	III	0.25±0.09	0.65±0.45	81%	69%	5.12 (Months)	6.1 (Months)	N/A	N/A	N/A	N/A	N/A
Piacentini et al 2019	III	38% free from pain 54% occasional pain 7% managed pain with daily NSAID		72%		N/A	N/A	N/A	N/A	Knee ROM: 108° (90-125) Ankle ROM: 10^{O} (0-20°) dorsifleion 32° (10-55°) plantar flexion 12 patients satisfied 4 patients not satisfied		N/A

Studies Characteristics

A summary of the studies included in this systematic review is presented in Table 1. This review comprises seven studies from diverse geographic regions, reflecting a global interest in the application of PRP in combination with BG or other interventions to enhance bone regeneration. The majority of studies originated from China[2,3,4], followed by Iran5, Iraq[6], Mexico[7], and Italy[8]. Collectively, these studies included a total of 455 participants with various bone-related conditions, such as non-union fractures, avascular necrosis of the femoral head, and critically sized bone defects.

Sample sizes varied widely across the studies, ranging from 16 participants in the study by Acosta-Olivo et al.[7] to 184 in the study by Chen et al.[2], highlighting differences in study design and target populations. Four studies employed RCT designs[4,5,7], offering a high level of evidence for assessing treatment efficacy. Two studies were retrospective cohort studies[3,8], while one study (6) utilized a prospective cohort design, enabling real-time tracking of clinical outcomes.

Control groups across the studies typically involved standard treatments without PRP. These included saline injections with surgical fixation for fractures, autologous bone grafting without PRP, and conservative symptomatic management in cases of avascular necrosis. The variation in control protocols underscores the comparative intent of these investigations and highlights the potential utility of PRP across a range of orthopedic pathologies. Together, the included studies provide a comprehensive overview of the clinical application of PRP in enhancing bone healing outcomes.

Quality Assessment

Risk of bias was assessed using the Cochrane RoB 2.0 tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies. Among the RCTs, Ghaffarpasand et al.[5] was judged as low risk across all domains. Xian et al.[4] and Acosta-Olivo et al.[7] were rated as having some concerns due to lack of blinding and absence of pre-registered protocols.

For non-randomized studies, Chen et al.[2], Xu et al.[3], and Majeed et al.[6] showed moderate risk of bias, primarily due to confounding, unblinded outcome assessment, and absence of prospective registration. In contrast, Piacentini et al.[8] demonstrated low risk across all ROBINS-I domains.

Overall, the included studies exhibited low to moderate risk of bias, with the primary limitations related to potential confounding, lack of blinding, and unclear reporting of outcome measurement. These factors were considered when interpreting the strength of the evidence.

Figure 2. Risk of Bias for Randomized Studies

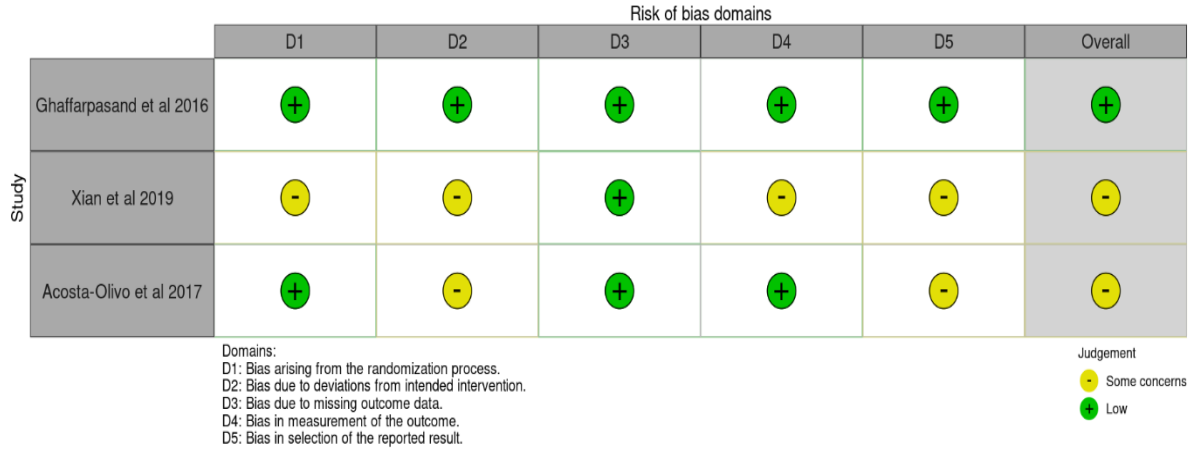
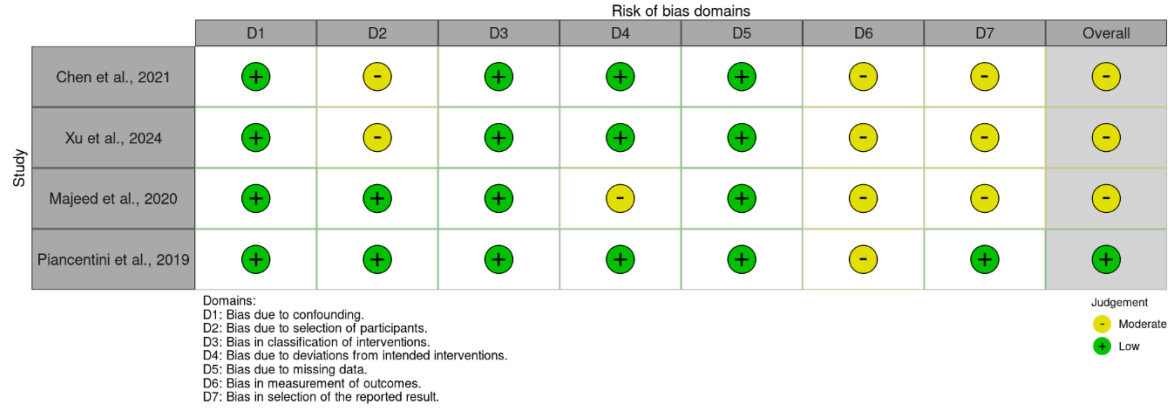


Figure 3. Risk of Bias for Non-Randomized Studies



Studies Outcome

Pain (VAS Score)

Most studies reported lower postoperative VAS scores in the PRP groups compared to controls. For example, Xian et al.[4] observed significantly lower VAS scores (0.9 ± 0.2) in the PRP group versus the control (2.0 ± 0.4). Chen et al.[2] similarly reported reduced VAS scores in the PRP group (3.57 ± 0.36) compared to the control (4.26 ± 0.48).

Healing/Union Rates

The use of PRP often resulted in higher union or healing rates. For instance, Ghaffarpasand et al.[5] demonstrated a healing rate of 81.1% with PRP versus 55.3% in the control. Similarly, Xian et al.[4] reported 87.5% union in PRP-treated post-traumatic ONFH patients compared to 59.1% in controls.

Healing Duration

PRP treatment showed a tendency toward shorter healing times. Acosta-Olivo et al.[7] reported a healing duration of 19.9 ± 2.25 weeks for the PRP group, contrasting with 25.44 ± 2.06 weeks for controls. Majeed et al.[6] also indicated shorter healing durations in the PRP group (5.12 months) compared to the control (6.1 months).

Other Outcomes

Functional outcomes were generally favorable for PRP-treated groups. For example, Chen et al.[2] reported a higher Mean Elbow Performance Score (MEPS) in PRP-treated patients (79.68 ± 5.46) compared to controls (68.32 ± 5.34). Xu et al.[3] observed higher Harris Hip Scores (HHS) in PRP-treated ANFH patients (89.47 ± 8.72) relative to the control group (80.14 ± 11.47).

Complications

Complication rates varied between studies. Some showed a higher incidence in the PRP group (e.g., Ghaffarpasand et al.[5], with increased infection rates), while others reported lower complication rates with PRP. Xu et al.[3] found complications to be more common in the control group (41.67%) than in the PRP group (22.73%).

DISCUSSION

This systematic review highlights the growing body of evidence supporting the use of platelet-rich plasma (PRP) combined with bone grafts (BG) in enhancing bone regeneration. Across various orthopedic indications—such as non-union fractures, avascular necrosis of the femoral head (ANFH), and critical-sized bone defects—PRP consistently demonstrated favorable outcomes in pain reduction, accelerated healing, and improved function.

Several studies in this review reported significantly lower postoperative pain scores in PRP groups[2,4], consistent with PRP's known anti-inflammatory properties attributed to bioactive molecules like TGF-β and PDGF1. Similarly, union rates were notably higher with PRP [4,5], supporting its osteoinductive effects, as previously

observed in both clinical and preclinical models[11].

Shorter healing durations in the PRP groups[6,7] align with findings from Malhotra et al.[10], who reported a 20% reduction in healing time for long bone non-unions treated with PRP. Functional outcomes, including HHS and MEPS, were also improved in PRP-treated patients[2,3], suggesting faster recovery and better rehabilitation trajectories[9].

Complication rates varied, with some studies noting higher infection risks in PRP-treated groups[5]. while others showed lower overall complications[3]. These discrepancies may stem from variability in PRP preparation, particularly in leukocyte content, which has been shown to influence inflammatory responses[12].

Despite promising results, heterogeneity in study designs, PRP protocols, and outcome measures limits definitive conclusions. Standardized classification and preparation methods, as advocated by Mautner et al.[13], are essential for optimizing clinical use and comparability.

CONCLUSION

This systematic review suggests that combining platelet-rich plasma (PRP) with bone grafts may improve bone healing outcomes by reducing pain, enhancing union rates, and shortening recovery time. While the results are encouraging, variability in study designs and PRP protocols limits definitive conclusions. Standardized methodologies and larger, high-quality trials are needed to confirm these findings and guide clinical application.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Anitua E, Sánchez M, Orive G, Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. Biomaterials. 2007;28(31):4551–6.
2. Chen J, Li L, Zhang X, Wang Y, Huang Z. Efficacy of bone graft combined with platelet-rich plasma on humeral condylar bone defect. Int J Clin Exp Med. 2021;14(1):521–9.
3. Xu RD, Duan SY, Liang HR, Sun M, Wen H, Zhou XT, et al. Efficacy of core decompression combined with platelet-rich plasma and bone grafting in early-stage avascular necrosis of the femoral head: a retrospective study. BMC Musculoskelet Disord. 2024; 25:796.
4. Xian H, Luo D, Wang L, Cheng W, Zhai W, Lian K, et al. Platelet-rich plasma-incorporated autologous granular bone grafts improve outcomes of post-traumatic osteonecrosis of the femoral head. J Arthroplasty. 2020;35(2):325–30.
5. Ghaffarpasand F, Shahrezaei M, Dehghankhalili M. Effects of platelet-rich plasma on healing rate of long bone non-union fractures: a randomized double-blind placebo controlled clinical trial. Bull Emerg Trauma. 2016;4(3):134–40.
6. Majeed GH, Al-Edanni MS, Hatem MW, Al-Mukhtar SA. Surgical fixation and grafting of traumatic distal tibia atrophic non-union with or without platelet-rich plasma: A comparative study. Rawal Med J. 2020;45(3):629–32.
7. Acosta-Olivo C, Garza-Borjon A, Simental-Mendia M, Vilchez-Cavazos F, Tamez-Mata Y, Peña-Martinez V. Delayed union of humeral shaft fractures: comparison of autograft with and without platelet-rich plasma treatment—a randomized, single-blinded clinical trial. Arch Orthop Trauma Surg. 2017;137(8):1247–52.
8. Piacentini F, Ceglia MJ, Bettini L, Campanacci DA, et al. Reconstruction of critical-sized post-traumatic long bone defects using an induced membrane technique enhanced with autograft, cancellous allograft, bone marrow concentrates, and platelet-rich plasma: a retrospective case series. J Orthop Traumatol. 2019; 20:23.
9. Volkmer DL. Editorial Commentary: Biologic augmentation of rotator cuff repair: Platelet-rich plasma may be of significant benefit, whereas atelocollagen cannot be recommended. Arthroscopy. 2024;40(11): 2678–80.
10. Malhotra R, Kumar V, Garg B, Singh R, Jain V, Coshic P, et al. Role of autologous

platelet-rich plasma in treatment of long-bone nonunions: a prospective study. Musculoskelet Surg. 2015;99(3):243–8.
11. Zhang Y, Xing F, Luo R, Duan X. Platelet-rich plasma for bone fracture treatment: a systematic review of current evidence in preclinical and clinical studies. Front Med (Lausanne). 2021; 8:676033.
12. Fitzpatrick J, Bulsara M, Zheng MH. The effectiveness of platelet-rich plasma in the treatment of tendinopathy: A meta-analysis of randomized controlled clinical trials. Am J Sports Med. 2017;45(1):226–33.
13. Mautner K, Malanga GA, Smith J, Shiple B, Ibrahim V, Sampson S, et al. A call for a standard classification system for future biologic research: The rationale for new PRP nomenclature. PM R. 2015;7(4 Suppl): S53–9.

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