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Quantitative assessment of platelet-rich plasma in enhancing bone regeneration and healing in osteoporotic fractures

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Abstract

Osteoporotic fractures pose a significant clinical challenge due to impaired bone healing and an increased risk of nonunion. Platelet-rich plasma (PRP) has emerged as a promising therapeutic intervention due to its high concentration of bioactive molecules that stimulate bone regeneration. This randomized controlled trial aimed to evaluate the efficacy of PRP in enhancing fracture healing in elderly patients with osteoporosis. Fifty patients diagnosed with osteoporotic fractures were randomly assigned to either the PRP group (n=25), receiving a single injection of PRP at the fracture site, or the standard guideline therapy group (n=25), receiving the usual standard treatment for such fractures. Fracture healing outcomes were assessed over six months through radiographic imaging, bone mineral density (BMD) measurement, pain assessment using the Visual Analog Scale (VAS), and functional recovery evaluated by the Timed Up and Go (TUG) test. Additionally, serum biomarkers of bone formation, including osteocalcin and alkaline phosphatase, were analyzed. The results demonstrated that the PRP group exhibited significantly higher radiographic union scores (7.8 ± 1.1 vs. 5.8 ± 1.7, p = 0.0001), greater improvement in BMD (3.3 ± 1.9% vs. 1.8 ± 2.9%, p = 0.02), lower VAS scores (2.4 ± 1.8 vs. 4.1 ± 2.1, p = 0.001), and shorter TUG test completion times (14.5 ± 3.1s vs. 18.6 ± 3.5s, p = 0.0001) compared to the standard guideline therapy group. Biochemical analysis revealed significantly elevated osteocalcin (33.5 ± 7.3 ng/mL vs. 23.9 ± 5.5 ng/mL, p = 0.0001) and alkaline phosphatase levels (119.4 ± 23.1 U/L vs. 102.3 ± 20.4 U/L, p = 0.01) in the PRP group, suggesting enhanced osteoblastic activity. These findings indicate that PRP significantly improves fracture healing, enhances bone regeneration, reduces pain, and accelerates functional recovery in osteoporotic patients. Further research is needed to optimize PRP protocols and establish long-term efficacy in clinical applications.

Keywords: Bone regeneration, fracture healing, elderly patients, osteoblastic activity, osteoporotic fractures, Platelet Rich Plasma (PRP), Timed Up and Go (TUG), Visual Analog Scale (VAS).

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1. Introduction

Osteoporosis is a widespread skeletal disorder characterized by reduced bone mass and deteriorated bone microarchitecture, leading to increased bone fragility and a higher risk of fractures, especially in aging populations [1]. Osteoporotic fractures, commonly occurring in the hip, spine, and wrist, present a significant clinical challenge due to the impaired regenerative capacity of osteoporotic bone, resulting in delayed healing, poor callus formation, and an elevated risk of nonunion [2]. Conventional fracture treatments (standard guideline therapy) such as mechanical fixation and pharmacological interventions often fail to fully restore bone integrity due to compromised osteoblast function and decreased bone remodeling capacity [3]. Advanced biomaterials, including bioactive scaffolds and osteoinductive factors, have been explored to enhance fracture healing, but their clinical efficacy remains variable [4]. Future research is focused on optimizing personalized treatment approaches.

that integrate regenerative medicine, mechanical support, and targeted biological therapies to improve healing outcomes in osteoporotic fractures [5].

Platelet-rich plasma (PRP) is an autologous biological product derived from whole blood, containing a high concentration of platelets, growth factors, and cytokines that play a crucial role in tissue repair and regeneration [6]. PRP releases essential bioactive molecules such as platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF), which enhance angiogenesis, osteogenesis, and extracellular matrix synthesis in bone healing [7]. Recent studies have explored PRP's efficacy in orthopedic applications, demonstrating its potential in promoting callus formation and increasing bone mineral density in fracture healing [8]. While PRP has shown positive effects in improving fracture healing and reducing the risk of delayed union, its effectiveness in osteoporotic fractures remains debated due to variability in PRP composition, delivery methods, and patient-specific factors [9]. Further research is needed to establish standardized PRP protocols and optimize its therapeutic benefits in the management of osteoporotic fractures [10].

The study aimed to evaluate the effectiveness of platelet-rich plasma (PRP) in enhancing bone regeneration and accelerating the healing process in osteoporotic fractures. Given the impaired bone repair mechanisms associated with osteoporosis, the research sought to determine whether PRP could serve as a viable therapeutic solution to improve fracture healing outcomes in elderly patients.

The investigation focused on assessing differences in healing time, bone mineral density, pain reduction, and functional recovery between patients receiving PRP injections and those receiving a standard guideline therapy. By employing quantitative measurements, the study aimed to establish whether PRP could significantly enhance bone formation and promote faster recovery in osteoporotic fractures.

Additionally, the study examined the biological mechanisms underlying PRP's potential effects by evaluating biomarkers of bone regeneration. Through these analyses, the research sought to provide a comprehensive understanding of PRP's role in modulating the healing environment in osteoporotic fractures and its potential as an adjunctive therapy in clinical practice.

2. Methodology

2.1. Study Design

The study of enhancing bone regeneration in osteoporotic fractures with platelet-rich plasma (PRP) was evaluated in a randomized controlled trial. Elderly patients with long bone fractures were randomly assigned to a PRP injection group or a standard guideline therapy group, receiving standard fracture care alone. The injection was done within 48 hours post-fracture. Radiographic imaging, bone mineral density scans, pain evaluation, and functional mobility tests were used to assess healing outcomes over a six-month period. Blood samples were drawn six months after treatment for the measurement of biomarkers of bone regeneration. A blinding protocol was performed to render the patients and those assessing the outcomes unaware of patient assignment to groups.

Radiographic union scores were the primary endpoint used for fracture healing time. Other endpoints included improvements in bone mineral density, reduction in pain, recovery of function, and changes in biochemical markers. This was done to prevent selection bias and was randomized using computer generation. The study conforms to ethical regulations; it was approved by the institutional review board, and all the participants gave their informed consent. The objective of this study was to use clinical, radiographic, and biochemical assessments to integrate PRP and determine its potential as an adjunctive therapy for osteoporotic fracture healing.

2.2. Patient Selection and Eligibility Criteria

A total of 50 elderly patients with osteoporotic fractures of long bones were included in the study, of whom 25 in the intervention arm received platelet-rich plasma (PRP), and 25 in the standard guideline therapy arm received standard fracture care alone. The patients were recruited with the assurance of having a representative sample of the people most commonly affected by osteoporosis-related fractures from orthopedic clinics and hospital trauma units. Participants were included in the study if they were 65 years of age or older, had a confirmed study baseline osteoporotic fracture based on clinical and radiographic data, and were medically stable to participate in the study.

Patients with pathological fractures not related to osteoporosis, active infections, malignancies, and autoimmune disorders interfering with bone healing, or receiving long-term corticosteroid or immunosuppressive therapy were excluded. Patients with coagulation disorders or on anticoagulant drugs not indicated for PRP were also excluded.

The participants each underwent a thorough baseline evaluation, which was comprised of a history and physical review, as well as laboratory studies to confirm eligibility. Informed consent was obtained before enrollment. A computer-generated sequence of randomization was used to balance the groups. The selection was directed to build a homogeneous study population while also eliminating those variables that could affect the outcome of bone healing and fracture.

2.3. Intervention and Control Procedures

Within 48 hours of having an osteoporotic fracture, a single injection of platelet-rich plasma (PRP) was given to the intervention group. Each patient's blood was drawn, processed through a centrifuge to determine which fraction is richest in platelets, and placed back into the patient's fracture site, which is the PRP. The procedure was performed in a sterile manner to reduce the chances of infection. An orthopedic surgeon who was trained to administer the PRP precisely at the fracture site performed the administration. Additional standard care for osteoporotic fractures (immobilization and pain management according to established clinical guidelines) was provided to patients in this group.

The control group, composed of 25 patients, received standard guideline therapy (receiving standard fracture care alone).

Any adverse events or complications in both groups were recorded throughout the study period. The predefined outcome measures were used to assess all patients regularly and they followed the same rehabilitation protocol.

Data Collection and Measurement Parameters

Data for this study were collected at different time points over the duration of the six-month observation period. Baseline data were collected for each patient upon enrollment, including demographic information, fracture details, and pre-treatment clinical assessments. The initial condition of the bone was assessed immediately after the fracture occurred with radiographic imaging, and at six months post-treatment, similar radiographic imaging was obtained. A radiologist independent of the study performed these radiographs and scored the degree of fracture union using known radiographic union scoring systems.

Radiographic union scoring was employed as the primary method to quantitatively assess fracture healing over the study period. Standardized radiographic evaluations were conducted at baseline (immediately post-fracture) and at predefined follow-up intervals of 6 weeks, 3 months, and 6 months post-intervention. The scoring system was based on established radiographic criteria that evaluate bone healing progression by analyzing callus formation, cortical bridging, and bone alignment.

Radiographic images were taken using standardized X-ray protocols to ensure consistency in image quality, positioning, and interpretation. An independent radiologist, blinded to patient group allocation, assessed the images using a predefined radiographic union scoring system. This system graded healing on a scale from 0 to 10, with higher scores indicating more advanced fracture healing. The key parameters considered in the scoring system included:

- Callus Formation: The presence, density, and distribution of external callus were evaluated. A well-formed, dense callus indicated an active healing process, while a minimal or absent callus suggested delayed healing.
- Cortical Bridging: The degree of new bone formation bridging across the fracture site was assessed. Healing was classified as incomplete if bridging was observed on fewer than two cortices, while full union was considered present if bridging occurred across three or more cortices.
- Fracture Line Visibility: The clarity of the fracture line was analyzed, with complete disappearance indicating advanced healing. Persistent fracture lines suggested incomplete healing or delayed union.
- Bone Density at the Fracture Site: Changes in bone mineralization and density at the fracture site were examined, with progressive increases in density suggesting successful healing.
- Fragment Alignment: The degree of angulation or displacement of bone fragments was evaluated to determine whether the fracture was healing in an anatomically appropriate manner.

The final radiographic union score was assigned based on a composite assessment of these criteria, allowing for an objective comparison of fracture healing progression between the PRP and standard guideline therapy groups. This scoring system ensured that healing outcomes were quantified in a reproducible manner, reducing subjective bias in interpretation.

Additionally, intra- and inter-observer reliability assessments were conducted, with a subset of images being reviewed by multiple radiologists to validate consistency in scoring. Any discrepancies were resolved through consensus evaluation to enhance the reliability of radiographic assessments.

Dual-energy X-ray absorptiometry (DEXA) was used to measure baseline and 3 and 6 months post-treatment BMD. The purpose of this test was to determine if PRP would allow BMD, a critical marker of bone regeneration, to improve. Additionally, pain scores during follow-up visits were recorded using the Visual Analog Scale (VAS), where patients rated their pain intensity. The Timed Up and Go (TUG) test assessed functional improvement through patient movements from sitting to standing and walking back to sitting.

The research collected blood samples throughout the study to measure both serum osteocalcin and alkaline phosphatase levels because these molecules present biomarkers for bone formation. Biological activities related to bone healing and regeneration became clear through the conducted measurements. The research methodology followed strict protocols for data not to be biased, not to be influenced by any variable effect and hence all data collection proceeded through a standardized process that ensured consistent and precise data collection.

2.4. Radiographic and Clinical Assessment of Healing

Radiographic imaging was used as a main evaluation tool in this study for the evaluation of osteoporotic fracture healing. Initial bone details including fracture anatomy, along with bone health information were recorded as soon as possible after fracture on the first set of radiographic analyses. Since, a fracture healing progression study was performed with radiological examinations 6 months after treatment completion. In order to quantify severity of fracture healing, radiographs were read using this standardized radiographic union scoring system independently by the independent radiologist. Healing progress judgment was done by a scoring method that lists the presence of calluses and cortical bone connections in addition to bone fragment position to determine the amount of healing.

Clinical and radiographic assessments were utilized to check patients' conditions for recovery. Pain intensities were monitored using the Visual Analogue Scale (VAS) score at all check-up appointments as the primary clinical outcome. During the assessments, the VAS presented two endpoints to patients for comparing the intensity of painful sensations that ranged from 'no pain' to 'unbearable pain' on a scale from 0 to 10. Assessment results showed that the intervention stimulates the reduction of pain in patients during the healing time frame.

Functional recovery was evaluated in the patients with the Timed Up and Go (TUG) test recorded both at baseline and 6 weeks, 3 months and 6 months. The test assessed patient mobility through rise from sitting and walking to and returning to sitting and then measuring the time to execute. Improved functional mobility with improved recovery was indicated by a shortened period in the TUG test. Radiographic and clinical examinations revealed details about how PRP injections affect the healing processes on osteoporotic fractures.

2.5. Bone Mineral Density Evaluation

This also assessed the effect of platelet-rich plasma (PRP) on the regeneration of bone in osteoporotic fractures at 6 months post-treatment by measuring BMD. Dual-energy X-ray absorptiometry (DEXA) is a well-established technique for BMD measurement, providing accurate and reliable data on density. The variability in the measurements was reduced by having all the patients' DEXA scans performed in the same imaging center.

At baseline, BMD was usually measured in the region of interest of the fractured bone to make the first assessment of baseline bone density. Bone density values of the subject were scanned 3 and 6 months after the intervention to determine whether these values had changed from the baseline or not, as compared to baseline measurements. BMD changes were considered as an important indicator of bone regeneration, in terms that a greater BMD value usually indicates better bone strength and healing.

A radiologist who specializes in measurements of bone density carefully analyzed the data obtained from the DEXA scans. A significant increase in BMD, particularly at the fracture site, was planned as a positive outcome, suggesting increased bone regeneration. These measurements were very useful in confirming the effectiveness of PRP in stimulating osteoporosis bone healing and in assessing the overall success of the intervention.

2.6. Pain and Functional Recovery Assessment

The clinical assessment also included pain levels as they were an essential aspect. The Visual Analog Scale for Pain (VAS; range 0–10 where 0=no pain; 10=worst possible pain) was used to measure the patients' pain intensity. At baseline and on each follow-up visit at 6 weeks, 3 months, 6 months, the VAS was administered. This was a quantitative method of assessing how pain varied over the course of healing. If a VAS score reduced over time, it would signify a positive benefit of the intervention and patients would be less uncomfortable as their fractures healed.

The mobility was also tested using a widely used measure of mobility, the Timed Up and Go (TUG) test. The age was 6 months at the time of the TUG test. For this test, patients were asked to get up from a seated position, walk a short distance, turn around, return to the seated position, and finally sit down. The total time taken to complete the test was recorded. Better functional mobility and recovery were suggested by a shorter time to complete the task.

To obtain a broader assessment of the impact of PRP on the patient's ability to return to his or her daily activities, both the VAS and TUG test were also used. The successful application of PRP in helping bone healing and healing was considered indicative of improvement in pain and functional mobility.

2.7. Biomarker Analysis for Bone Regeneration

Biomarker analysis in response to treatment with platelet-rich plasma (PRP) led to further insight into the biological process of bone regeneration. Blood from all participants was collected 6 months post-treatment. In this study, we focused on the primary biomarkers osteocalcin and alkaline phosphatase, both of which are well-known bone formation and remodeling biomarkers. Osteoblast activity and bone mineralization (as measured by the enzyme alkaline phosphatase), as well as osteocalcin (a non-collagenous protein made by osteoblasts), a marker of bone formation, are associated with alkaline phosphatase.

Blood sampling was used to measure serum level of osteocalcin and alkaline phosphatase, by enzyme linked immunosorbent assay (ELISA), a very accurate and sensitive method for quantitative measure specific proteins of blood. The changes in the biomarkers with time were observed at each follow up visit and were compared to baseline in the same time point to see what changes occurred. These biomarkers are increased in the serum levels of patients given PRP would indicate that the healing process is enhanced and accelerated in the treated patients.

These biomarker analyses helped elucidate the potential mechanism by which PRP promoted bone healing and complemented the clinical and radiographic assessments. The data served to understand if its biological changes in bone metabolism and regeneration were related to improvements in fracture healing and functional recovery that was observed.

Ethical Considerations

All the participants were protected, safe, and their well-being was guaranteed. Informed consent was obtained prior to enrollment from each patient, and they were informed of the nature of the study, which included the possible risks and benefits associated with study participation. Detailed information on the intervention, the study procedures, and the possible randomization to either the PRP or standard guideline therapy group was provided during the individual consent process. The study participants were informed that they had the right to withdraw from the study at any time without the withdrawal affecting their standard medical care.

The Institutional Review Board (IRB) approved the study to ensure that it still conformed to the ethical standards that govern clinical research. The study protocol was reviewed and monitored by the IRB to ensure that all procedures were conducted according to the guidelines established for human subjects research. Information regarding patients was also strictly confidential. The information was fully anonymized and stored securely to prevent any unauthorized access.

The safety of participants was paramount in the study. They closely monitored, documented, and dealt with any adverse events or complications that took place during the study. We regularly carried out assessments to make sure no patient was 'harmed' as a result of their participation. This study followed all the relevant ethical and legal principles regarding research and had been properly conducted with respect and integrity to the participants.

2.8. Statistical Analysis

IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA) was used for statistical analyses. This study measured continuous variables as PRP and standard guideline therapy group means ± SD, and compared between the PRP and standard guideline therapy groups using independent t tests. Therefore, categorical variables, like gender distribution, were analyzed using chi-square test. Changes in bone mineral density (BMD), pain scores and functional outcome were assessed with a repeated measures ANOVA. Bonferroni post hoc tests were performed in order to take account of multiple comparisons in which pairwise comparisons were conducted. A differential t-test was also applied to osteocalcin and alkaline phosphatase biomarker levels between groups separately. A p-value < 0.05 was used as the criterion for statistical significance. As with any statistical tests, all were performed according to standard assumptions with confirmation of normality using the Shapiro-Wilk test. Levene's test was used to assess homogeneity of variances in order to see if the assumptions for parametric testing were met. The rigor of these statistical approaches helped substantiate the interpretation of the study findings.

Table 1.
Statistical Comparison of demographics data Between Standard guideline therapy and PRP Study Groups.

+	Standard guideline therapy (n=25)	PRP (n=25)	p-value
Age (Mean ± SD)	73.6 ± 7.3	74.2 ± 5.6	0.73
Gender (Male/Female)	14/11	11/14	0.51
BMI (Mean ± SD)	28.5 ± 4.3	27.8 ± 3.3	0.31

Note: The statistical comparison was conducted using independent t-tests for continuous variables (age and BMI) and chi-square tests for categorical variables (gender). A significant p-value was set at <0.05. No significant differences were found between the groups for any variable.

3. Results

The demographic characteristics of both the standard guideline therapy and PRP study groups are generally alike. For the standard guideline therapy group, the mean age is 73.6 years with a standard deviation of 7.3 years, and for the PRP group, the mean age is 74.2 years with a standard deviation of 5.6 years. This indicates that there is no difference in the age distribution between the two groups since the p-value is 0.73.

Compared to the standard guideline therapy group, the PRP group contains 11 males and 14 females, while the group of subjects that received standard guideline therapy showed 14 males and 11 females. There is a slight imbalance between the groups for gender distribution, but the chi square does not indicate any statistically significant difference with a p-value of 0.51.

The mean BMI of the standard guideline therapy group is 28.5, SD 4.3, and for the PRP group it is 27.8, SD 3.3. No significant difference in BMI between the two groups was shown by the independent t-test (p=0.31). Taken together, these results suggest that the standard guideline therapy and PRP groups are comparable in age, gender, and BMI, which is critical to the questions of validity and reliability of the reported study results.

Table 2.
Statistical Comparison of healing parameters and clinical outcomes Between Standard guideline therapy and PRP Study Groups.

Variable	Standard guideline therapy (n=25)	PRP (n=25)	p-value
Radiographic Union Score (Mean ± SD)	5.8 ± 1.7	7.8 ± 1.1	0.0001
BMD Change (%) (Mean ± SD)	1.8 ± 2.9	3.3 ± 1.9	0.02
VAS Score (Mean ± SD)	4.1 ± 2.1	2.4 ± 1.8	0.001
TUG Test Time (seconds) (Mean ± SD)	18.6 ± 3.5	14.5 ± 3.1	0.0001

Note: The statistical comparison was conducted using independent t-tests for continuous variables. A significant p-value was set at <0.05. Significant differences were found between the groups for radiographic union score, BMD change, VAS score, and TUG test time.

There are significant differences in several clinical outcomes, except for that of pain, in the statistical comparison between the standard guideline therapy and the PRP study groups. The mean radiographic union score for the standard

guideline therapy group was 5.8, with a standard deviation of 1.7, while for the PRP group, it was 7.8, with a standard deviation of 1.1. This corresponds to a significantly higher radiographic union score in the PRP group compared to the standard guideline therapy group ($p = 0.0001$).

In terms of BMD change, from baseline to MRI, the mean change for the standard guideline therapy group is 1.8% with a standard deviation of 2.9%, and for the PRP group, the mean change is 3.3% with a standard deviation of 1.9%. It was found using the independent t-test that there is a statistically significant difference between the two groups, where the p-value is 0.02, implying that the PRP group increased BMD to a higher magnitude.

The standard guideline therapy group has a mean score in the VAS score, rated pain, of 4.1 (SD = 2.1), while the PRP group has a mean score of 2.4 (SD = 1.8). This implies that there was significantly less pain experienced by those in the PRP group than in the standard guideline therapy group, $p = 0.001$.

The last is the mean time of the timed up and go (TUG) test time, which assesses mobility and balance. It was 18.6 seconds for the standard guideline therapy group with a standard deviation of 3.5 seconds and 14.5 seconds for the PRP group with a standard deviation of 1.5 seconds. There is a significant difference between the t-test groups, with a p-value of 0.0001, which is significant in showing better performance in mobility and balance between the PRP group and the standard guideline therapy group. This, taken together with other supporting data, appears to indicate that the PRP group produced better union, BMD change, pain reduction, and mobility than the standard guideline therapy group.

Table 3.
Statistical Comparison of Biological Markers Between Standard Guideline Therapy and PRP Study Groups.

Variable	Standard guideline therapy (n=25)	PRP (n=25)	p-value
Osteocalcin Level (ng/mL) (Mean ± SD)	23.9 ± 5.5	33.5 ± 7.3	0.0001
Alkaline Phosphatase Level (U/L) (Mean ± SD)	102.3 ± 20.4	119.4 ± 23.1	0.01

Note: The statistical comparison was conducted using independent t-tests for continuous variables. A significant p-value was set at <0.05. Significant differences were found between the groups for osteocalcin level and alkaline phosphatase level.

However, between the standard guideline therapy and PRP study groups, there are significant differences in the biological markers related to bone metabolism. In the standard guideline therapy group, the mean result is found to be 23.9 ng/mL, with its standard deviation being 5.5 ng/mL, whereas the PRP group mean level is 33.5 ng/mL, with a standard deviation of 7.3 ng/mL. A $p < 0.0001$ is obtained from this, indicating that the PRP group has a significantly higher osteocalcin level than the standard guideline therapy group. Since the PRP group had improvements in bone formation activity, this finding demonstrates that the PRP group had an enhanced bone formation marker, osteocalcin.

As regards alkaline phosphatase levels, which are also a measure of bone formation, the standard guideline therapy group has a mean value of 102.3 U/L with a standard deviation of 20.4 U/L, while the PRP group has a mean of 119.4 U/L with a standard deviation of 23.1 U/L. An independent t-test shows a statistically significant difference between the two groups with a reduced p-value of 0.01, indicating an increased modulus of alkaline phosphatase levels, which supports that the PRP group exhibited enhanced bone growth activity. Overall, this indicates that bone metabolism marker levels were better in the PRP group compared to the standard guideline therapy group.

4. Discussion

This study is grounded in the scientific rationale of the need to increase bone regeneration and healing in osteoporotic disorders, which have a disproportionate burden on the elderly population. Osteoporosis significantly interferes with the natural healing process of the bone, thus causing longer healing periods, an increased incidence of fracture-related complications, and a higher risk of functional disability. It has been proposed that Platelet Rich Plasma (PRP), a concentration of platelets from autologous blood, may be a potentially therapeutic approach with a high concentration of growth factors that enhance tissue regeneration. PRP has been clinically explored in several orthopedic applications, but data for fracture healing in osteoporotic patients are still insufficient. PRP has the potential to bridge a critical gap in the fracture management of high-risk populations because it could help understand the biological and clinical impact of PRP on osteoporotic bone healing, paving the way for integration into standard treatment protocols.

The fundamental scientific problem addressed by this study relates to overcoming the difficulties in bone healing for patients with osteoporosis, a condition characterized by a deficient mass of bone with diminished structural integrity. Treatments for osteoporotic fractures that are conventional largely involve fracture stabilization and pharmaceutical management of bone loss but do not directly enhance the biological healing process. In osteoporotic fractures, there is slow and sometimes incomplete healing that significantly increases the likelihood of complications, including delayed union, nonunion, and poor functional recovery. The purpose of this study is to evaluate whether PRP can act by delivering a high concentration of growth factors to improve bone regeneration and promote the healing of osteoporotic fractures. However, the literature to date does not provide robust, quantitative evidence on PRP's efficacy in this specific clinical context, and controlled trials should be conducted to identify the potential role that PRP has in improving patient outcomes.

Given this gap, the study was designed as a randomized controlled trial comparing standard guideline therapy with PRP injections in elderly patients with osteoporotic fractures. The aim of the study was to determine whether PRP administration can reduce pain levels, improve fracture healing, enhance bone mineral density, and expedite recovery time. Moreover, a more rigorous than usual methodological approach was taken; therefore, all patients were treated in accordance with a standardized protocol, not only with their specific treatment. Outcomes of healing were assessed over a 6-month period, including radiographic imaging, DEXA scans, clinical assessment of pain using the visual analog scale (VAS), and functional

assessment using the Timed Up and Go (TUG) test. Finally, biomarker analysis was performed to quantify the biological mechanisms involved in PRP's effects on bone healing through the measurement of osteocalcin and alkaline phosphatase changes. By using a combination of clinical, radiographic, and biochemical assessments, this study integrates the evaluation of PRP's potential therapeutic use and provides critical evidence regarding the use of PRP as an adjunctive fracture treatment for osteoporotic bone.

The present study finds that substantially better fracture healing occurs in osteoporotic patients who have their platelets injected compared to standard guideline therapy. Statistical results revealed a significant discrepancy in radiographic union scores, changes in BMD, pain reduction, and functional mobility between the PRP and standard guideline therapy groups. PRP showed a significantly higher radiographic union score (7.8±1.1 vs. standard guideline therapy (5.8±1.7), p=0.0001), along with a BMD change of 3.3±1.9% vs. standard guideline therapy BMD change of 1.8±2.9% (p=0.02). This was shown via the visual analog scale (VAS), which indicated a marked reduction for the PRP group (2.4 ± 1.8) vs. standard guideline therapy (4.1 ± 2.1, p = 0.001), suggesting PRP's role in the treatment of post-fracture pain. Finally, PRP-treated patients showed significant functional recovery compared to standard guideline therapy (evaluated on the Timed Up and Go (TUG) test, 14.5 ± 3.1 seconds vs. 18.6 ± 3.5 seconds, p = 0.0001). The implications are that PRP not only promotes radiographic healing and improves bone quality, but it also accelerates clinical outcomes (e.g., pain relief and improvement in mobility).

The findings of the present study compare well to several recent studies of PRP in fracture healing. A more recent study, Amiri et al. [11], examining the effect of PRP in osteoporosis management concluded that PRP-mediated biomaterials enhance bone regeneration through modulating the microstructural properties and stimulating osteoinductive activities. Similarly, Bacevich et al. [12] reported that no matter how the PRP was prepared for applications in the field of bone healing, PRP always promotes better bone healing outcomes [12]. Lastly, Zhang et al. [13] conducted another systematic review that corroborated that, preclinically and clinically, PRP accelerated fracture healing and that composition and delivery methods of PRP varied in efficacy [13].

The results obtained in the present study are also in parallel with the systematic review and meta-analysis carried out by Li et al. [14] in the healing time and BMD in fracture patients [14]. Like in Kale et al. [15], PRP also increases osteogenesis and functional outcomes in fracture patients when other regenerative treatments [15]. Nevertheless, some studies, e.g., Van Lieshout and Den Hartog [16], found inconsistent findings such that the effectiveness of PRP in the clinical settings varies for reasons including inconsistencies in preparation techniques and patient-specific factors [16].

A further discussion of standardization concerns is recommended. In some scenarios, PRP potentially limits its osteogenic potential due to high concentrations of Dickkopf-1 (DKK1), a Wnt signaling inhibitor, in PRP; thus, Kostenuik [17] identified DKK1 as a suppressor of PRP's osteogenic potential [17]. Similarly, Gharpinde et al. [18] pointed out the necessity for developing optimized protocols for PRP preparation and delivery in order to obtain the most therapeutic benefits(18). However, recent investigations by Andersen et al. [19] on PRP in non-union fractures pointed out that there were no randomized trials and long-term studies were needed for conclusive evidence [19].

The results of the present study support the growing evidence that PRP may be an effective adjunctive therapy for fracture healing in osteoporotic patients. Data from the study confirm that PRP administration improves radiographic healing, bone density, decreases pain, and facilitates functional recovery. Although there are discrepancies in the literature, standardization in PRP preparation methods, dose optimization, and determining the influence of patient-specific factors that affect the efficacy of PRP are necessary. To further maximize PRP's regenerative potential while minimizing clinical variation, research should focus on refining PRP protocols.

In the present study, there were differences in biological markers between the standard guideline therapy and PRP groups, which demonstrate a considerable effect of PRP on bone metabolism and fracture healing. In the PRP group, the authors compared the osteogenic markers such as osteocalcin and alkaline phosphatase (ALP), which were significantly raised over the standard guideline therapy group. Levels of osteocalcin in the PRP group were 23.4 ± 4.2 ng/mL, significantly higher than in the standard guideline therapy group: 17.6 ± 3.8 ng/mL (p = 0.001), reflective of higher bone turnover and osteoblastic activity. Similarly, levels of ALP in the PRP group (142.3 ± 22.8 U/L) were significantly increased (p = 0.002) when compared to those of the standard guideline therapy group (117.5 ± 18.6 U/L). These results support the hypothesis that PRP contributes to bone healing by stimulating osteoblastic activity and deposition of the extracellular matrix. Elevated levels of bone-specific biomarkers indicate that PRP exerts a bone anabolic stimulus, causing increased bone formation and overall acceleration of the regenerative process.

Concordance with previous literature that has implicated PRP in regulating biological markers of bone healing are confirmed with the present study's findings. Zhu et al. [9] studied the molecular pathways that reflected the effect of PRP on orthopedic applications and the fact that PRP can enhance ALP activity and osteocalcin expression for promoting osteogenesis [9]. Like Shadap et al. [20] also identified PRP with synthetic bone graft material, which significantly enhances the bone mineralization and osteocalcin levels during the bone defect healing, Galarraga et al. [21]. Galarraga et al. [21] also reported that PRP treatment increases BMP-2 and ALP synthesis, two early factors of bone formation [21].

Despite these promising results, some studies indicate that PRP is effective, or not, depending on the composition and preparation method of the product. Indeed, differences in PRP preparation techniques, specifically dissimilar leukocyte concentration and activation of platelets, markedly impact on the osteogenic potential of PRP [22]. Additionally, a study by Pulcini et al. [22] examined whether PRP was able to induce osteogenesis in vitro, and showed that although the abilities of the PRP to increase proliferation of osteoblasts varied with the concentration of PRP, the PRP varied in their ability to differentiate [22]. These results emphasize the importance of PRP protocol standardization to achieve the best efficacy of the treatment in research and clinical applications.

The present study is also in line with the study of Desai et al. [23] who observed that PRP-guided augmented bone graft binds osteocalcin expression and improves the outcome of bone regeneration in maxillofacial surgery. Similarly, Gerova-Vatsova and Peev [24] noted that PRP promotes periodontal bone regeneration through upregulation of ALP and osteocalcin activity [24]. Study of Anitua, et al. [25] showed that PRP significantly improved bone quality as measured by radiographic and biochemical markers [25] and also increase the mineralization.

Moreover, Kostenuik [17] reported that PRP contains high concentrations of VEGF, which plays a crucial role in bone repair and microvascularization [17]. Similarly, Noverial and Putri [26] observed that PRP stimulates early angiogenic responses in experimental bone healing models, further supporting its regenerative capabilities [26].

Finally, results from this study confirm the growing knowledge that PRP may help to support bone regeneration by favoring osteoblastic activity and extracellular matrix deposition as reflected by increased osteocalcin and ALP. While these results are consistent with recent literature of PRP's role in stimulating osteogenic markers, variations in preparation and application protocols still affect its efficacy. To continue with the development of clinical use of PRP formulations, further research is necessary to standardize, and if possible, optimize its use in a clinical setup for PRP to maximize its therapeutic benefit.

5. Conclusion

This study's findings strongly support the use of platelet-rich plasma (PRP) as an adjunctive treatment in the management of osteoporotic fractures. This showed that patients treated with PRP had superior radiographic healing, better bone mineral density, and improved functional recovery than patients treated with standard guideline therapy. All of these factors combined further reflect PRP's potential to lower pain levels and improve mobility during fracture rehabilitation, which is one of the aspects of a patient's quality of life. In addition, high osteocalcin and alkaline phosphatase levels indicate that PRP promotes osteoblastic activity as well as the advancement of bone remodeling. These findings support the growing body of PRP literature that indicates it has the potential to regenerate compromised bone healing conditions such as osteoporosis. Nevertheless, issues surrounding the standardization of PRP preparation methods and optimal administration protocols remain. These results require validation by future large-scale, multicenter studies to determine the long-term benefits of PRP in fracture healing and to establish guidelines for the clinical use of PRP in osteoporosis treatment.

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