Journal of Orthopaedic Surgery and Research

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# Efficacy of multiple autologous apheresis platelet-rich plasma injections for treating knee osteoarthritis and its influencing factors: a retrospective cohort study

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## Abstract

**Background** The lack of standardized Platelet-Rich Plasma (PRP) protocols for Knee Osteoarthritis (KOA), combined with significant patient variability, leads to inconsistent PRP effectiveness across studies. This study aims to assess the influence of PRP injection frequencies on KOA treatment and explore the role of patient characteristics and PRP properties in the treatment's effectiveness.

**Methods** A retrospective cohort study was conducted with KOA patients who received three PRP injections (4-week intervals) at a hospital in Chongqing. The Wilcoxon signed-rank test was used to analyze differences in self-reported recovery rates across different treatment time points, with Bonferroni correction applied for significance level adjustment (α). The Mann-Whitney U test, Kruskal–Wallis H test, Spearman correlation analysis, and restricted cubic spline models were used to assess the associations between sex, baseline Kellgren–Lawrence grade, age, PRP red blood cell (RBC) concentration, PRP white blood cell (WBC) concentration, PRP platelet concentration, the multiple of PRP platelet concentration relative to the baseline autologous level (Enrichment-PLT), and self-reported recovery rates.

**Results** The study included 28 KOA patients. Significant improvement in self-reported recovery rate was observed 4 weeks after the first treatment (median: 30.0%, $P < 0.008$) and after the second treatment (median: 45.0%, $P < 0.008$). However, no significant change was noted 4 weeks after the third treatment (median: 55.0%, $P = 0.058$), and recovery rates at 8, 12, and 24 weeks post-third treatment showed no significant differences compared to 4 weeks (all $P > 0.008$). Additionally, no correlations were found between sex, baseline Kellgren–Lawrence grade, age, PRP RBC concentration, PRP WBC concentration, PRP platelet concentration, or Enrichment-PLT and self-reported recovery rates.

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**Conclusion** At least two PRP injections are recommended, with effects lasting for at least 24 weeks. Factors such as sex, age, baseline Kellgren–Lawrence grade, and PRP properties (prepared by apheresis) do not significantly affect treatment outcomes.

**Keywords** Knee osteoarthritis, Platelet-rich plasma, Injection frequencies, Efficacy, Influencing factors

## Introduction

Knee osteoarthritis (KOA) is a degenerative joint disease characterized primarily by joint pain, swelling, and impaired mobility, significantly affecting patients' daily quality of life [1]. According to global epidemiological data from 2019, the age-standardized prevalence of KOA is 4.3% (95% CI: 3.8-4.9%) [2]. Age is a major risk factor for KOA [3], with the prevalence significantly increasing after the age of 35, and the prevalence among those over 40 is approximately 22.9% (95% CI: 19.8-26.1%) [4].

Currently, there is no cure for KOA, and existing treatment options primarily focus on symptom relief and slowing disease progression [5]. Treatment strategies for KOA can be divided into non-pharmacological and pharmacological approaches [6]. Non-pharmacological treatments mainly include exercise, weight loss, physical therapy, and the use of orthotics, while pharmacological treatments include local anti-inflammatory drugs, oral nonsteroidal anti-inflammatory drugs (NSAIDs), and hyaluronic acid injections [7–9]. For severe KOA, knee arthroplasty is a widely used final treatment option; however, it is associated with limitations such as a finite lifespan of artificial joints and surgical risks [10]. Therefore, finding more effective non-surgical treatments has become a key focus of current clinical research.

Platelet-rich plasma (PRP) is a concentrated form of platelet plasma derived from blood through centrifugation. It is rich in growth factors, which contribute to its role in enhancing tissue repair, promoting regeneration, and providing anti-inflammatory effects [11, 12]. Recently, PRP has seen increased usage in treating KOA [13]. Several studies have demonstrated that PRP can effectively reduce pain and improve knee function in KOA patients, yielding better results than hyaluronic acid or NSAIDs [14–17]. However, other research has found no significant difference between PRP treatment and placebo [18], indicating that the effectiveness of PRP in KOA may vary widely across different cases.

The variability in PRP efficacy may be attributed to several factors, notably the lack of standardized treatment protocols, which limits its widespread clinical application [19, 20]. Specifically, the observed differences in PRP efficacy are likely influenced by: (1) the preparation process, including the method of preparation (e.g., manual vs. apheresis), the number of centrifugation cycles, and whether leukocytes are removed—these factors can significantly alter the concentrations of PLTs, leukocytes, and other components in PRP, thus affecting its therapeutic outcomes [21–26]; (2) treatment protocols, such as the number of injections, injection intervals, and dosage [23]; (3) patient-specific factors, including age, gender, disease severity, and the properties of the patient's own blood [23, 27].

Traditional PRP preparation methods typically rely on manual techniques, which present challenges in standardization. With advancements in technology, automated apheresis systems have been developed. Compared to traditional methods, apheresis reduces the risk of bacterial contamination, decreases the presence of RBCs and WBCs in PRP, and improves the stability and quality of the PRP product [28, 29].

Given these considerations, the aim of this study is to evaluate the effectiveness of different PRP (prepared by apheresis) injection protocols in the treatment of KOA, and to investigate whether patient characteristics and PRP properties influence treatment outcomes, thereby providing a reference for the standardization of PRP treatment for KOA.

## Patients and methods

### Study design and data collection

This study was a single-center, retrospective cohort study conducted at a hospital in Chongqing, China. Patients diagnosed with KOA and treated with PRP at the hospital's orthopedic department between April 2022 and March 2023 were included in this study.Recovery data were collected via telephone interviews and in-person visits. The inclusion criteria were as follows: (1) patients were diagnosed with KOA on the basis of clinical symptoms, signs, and imaging examinations, (2) patients who received PRP treatment, and (3) patients aged 20–70 years. Exclusion criteria were (1) patients who did not receive 3 PRP injections, and (2) patients without follow-up data.

## Study variables

The primary outcome variable of this study was the self-reported recovery rate. Patients were asked to rate their recovery on a scale from 0 to 10 (0 indicating no recovery and 10 indicating complete recovery). Follow-up visits were scheduled for the 4th week after each treatment, with additional visits at the 8th, 12th, and 24th weeks following the third treatment. The self-reported recovery rate was calculated by dividing the patient's score by 10 (ranging from 0 to 100%). The average self-reported recovery rate was determined by summing the recovery

rates at the 4th, 8th, 12th, and 24th weeks after the third treatment and dividing by 4.

In addition, the study also included the following potential variables that could influence PRP efficacy: the patient's sex, age, Kellgren–Lawrence grading of KOA (based on radiographic assessment) before treatment; the concentrations of PLTs, WBCs, RBCs in the PRP used, and the multiple of PRP PLT concentration relative to the baseline autologous level (Enrichment-PLT) [23, 27, 30–32].

Furthermore, the Magnetic Resonance Imaging (MRI) cartilage injury grading system, as established by the International Cartilage Repair Society (ICRS), was used to objectively assess the severity of KOA before and after treatment [33].

## PRP Preparation

PRP was prepared via an automated blood component separator (NGL-XCF-3000) with single-use consumables (P-2000 IE; Nigale, China). The technical settings were adjusted on the basis of the patient's height, weight, sex, and preoperative hematocrit and PLT concentrations. The pre-apheresis settings were as follows: apheresis speed: 50–80 mL/min; input speed: 50–80 mL/min; anticoagulant-to-whole blood ratio: 1:10–12 mL; PLT apheresis coefficient: 75–85 on the basis of the preoperative PLT concentrations. All PRP and whole blood samples were analyzed with an automated cell counter (XS-900i; Sysmex, Japan).

## Treatment procedure

Before injection, patients were placed in a supine position with the knee fully extended. PRP was injected into the suprapatellar bursa through a suprapatellar lateral approach, and no local anesthesia was applied. After the procedure, patients were advised to keep the knee immobile for 10 min. Each patient received three PRP injections with a 4-week interval between treatments.

**Table 1** Participant characteristics and PRP properties ($n=28$)

| Characteristics | Groups | All |
|---|---|---|
| Sex, n(%) | Male | 13 (46.4%) |
| | Female | 15 (53.6%) |
| Side, n(%) | Left only | 12 (42.9%) |
| | Right only | 8 (28.6%) |
| | Bilateral | 8 (28.6%) |
| Age, Mean ± SD | | 49.8 ± 9.9 |
| Pre- WBC ($10^9$/L), Median(Q1,Q3) | | 5.9(5.5,6.6) |
| PRP- WBC ($10^9$/L), Median(Q1,Q3) | | 0.5(0.3,1.2) |
| Pre- RBC ($10^{12}$/L), Median(Q1,Q3) | | 4.8(4.4,5.0) |
| PRP- RBC ($10^{12}$/L), Median(Q1,Q3) | | 0.1(0.1,0.1) |
| Pre- PLT ($10^9$/L), Mean ± SD | | 231.9 ± 72.8 |
| PRP- PLT ($10^9$/L), Median(Q1,Q3) | | 1542.0(1162.3,1883.8) |
| Enrichment- PLT, Mean ± SD | | 7.0 ± 1.1 |

Note: Pre, The patient's hematological parameters before Platelet-rich plasma collection; PRP, Platelet-rich plasma product's hematological parameters. RBC, Red Blood Cell; WBC, White Blood Cell; PLT, Platelet; Enrichment-PLT, The multiple of PRP platelet concentration relative to the baseline autologous level; SD, standard deviation

## Statistical analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were presented as mean ± standard deviation (SD), while non-normally distributed data were reported as median and interquartile range (Q1, Q3). Categorical variables were expressed as frequency (n) and percentage (%). To compare self-reported recovery rates at different time points, the Wilcoxon signed-rank test was applied, with Bonferroni correction used to adjust the significance level (α). The Wilcoxon signed-rank test was also used to analyze differences in ICRS scores before and after treatment. The Mann-Whitney U test was employed to access the influence of sex on self-reported recovery rates. The Kruskal–Wallis H test was employed to analyze differences in self-reported recovery rates across different Kellgren-Lawrence grades and age groups. Relationships between age, PRP RBC concentration, PRP WBC concentration, PRP PLT concentration, Enrichment-PLT, and self-reported recovery rates were examined using Spearman's rank correlation and restricted cubic spline models. Data were analyzed using SPSS 27.0 and R 4.3.1 software. All tests were two-tailed, and the significance level (α) was set at 0.05.

## Results

### Participant characteristics and PRP properties

A total of 28 patients were included in the study, comprising 13 males (46.4%) and 15 females (53.6%), with a mean age of 49.8 ± 9.9 years. Among the patients, 12 (42.9%) had unilateral left KOA, 8 (28.6%) had unilateral right KOA, and 8 (28.6%) had bilateral KOA. The mean Enrichment-PLT was 7.0 ± 1.1. Detailed information on the properties of both the PRP product and baseline blood samples was provided in Table 1.Additionally, pre-treatment Kellgren–Lawrence grades were available for 26 patients, among whom 2 (7.7%) were classified as grade 1, 21 patients (80.8%) as grade 2, and 3 patients (11.5%) as grade 3.

### Effectiveness of PRP

At four weeks after the first PRP injection, the median self-reported recovery rate reached 30.0% (5.0%, 67.5%). Following the second injection, this value increased to 45.0% (20.0%, 80.0%). After the third injection, the median self-reported recovery rates at 4, 8, 12, and 24 weeks were recorded as 55.0% (30.0%, 80.00%), 55.0% (7.5%, 80.0%), 55.0% (7.5%, 77.5%), and 50.0% (0.0%, 80.0%), respectively.

The Wilcoxon signed-rank test was used to access differences in self-reported recovery rates at different time points, with Bonferroni correction applied for adjusting significance (α). Statistically significant differences were observed between pretreatment and 4 weeks after the first PRP injection ($P < 0.001$, adjusted $\alpha = 0.008$) and between 4 weeks after the first and second injections ($P = 0.007$, adjusted $\alpha = 0.008$). No significant differences were found in the recovery rates at 8, 12, and 24 weeks after the third injection compared with those at 4 weeks after the third injection (all $P > 0.008$). Further details are presented in Fig. 1.

Additionally, MRI scans were of five patients were obtained before and after treatment. The median and interquartile range of the ICRS scores before treatment were 3.0 (2.5, 3.0), while after treatment, they were 2.0 (2.0, 3.0). The Wilcoxon signed-rank test showed no statistically significant difference in ICRS scores before and after treatment ($P = 0.317$).

### Univariate analysis of sex, age, Kellgren–Lawrence grade, and PRP properties in relation to self-reported recovery rates

The relationship between the average self-reported recovery rate (calculated by adding the self-reported recovery rates at 4 weeks, 8 weeks, 12 weeks, and 24 weeks after the third PRP injection and dividing by 4) and sex, age, Kellgren–Lawrence grade, and PRP-related hematological parameters was assessed. The Mann–Whitney U test was used to compare self-reported recovery rates between male and female patients. The median self-reported recovery rate for male patients was 50.0%(12.5%,87.5%), while for female patients it was 57.5%(15.0%,77.5%). Mann-Whitney U tests showed that there were no significant differences in self-reported recovery rates between sexes ($P = 0.964$). The Kruskal–Wallis H test was performed to analyze differences in self-reported recovery rates among patients with different Kellgren–Lawrence grades. The median recovery rates were 88.8% (87.5%, 90.0%) for patients with Kellgren–Lawrence grade 1, 50.0% (8.8%, 77.5%) for those with Kellgren–Lawrence grade 2, and 50.0% (42.5%, 77.5%) for those with Kellgren–Lawrence grade 3. The results showed no statistically significant differences in self-reported recovery rates among patients with different Kellgren–Lawrence grades ($P = 0.149$).

Spearman's correlation test was used to explore the association between age, PRP RBC concentrations, PRP WBC concentrations, PRP PLT concentrations, and Enrichment- PLTs and the average self-reported recovery rate. The results showed that none of these variables showed a significant monotonic relationship with the average self-reported recovery rate (all $P > 0.05$), as shown in Table 2.

Additionally, a restricted cubic spline model was employed to examine potential nonlinear associations between the aforementioned factors and the average

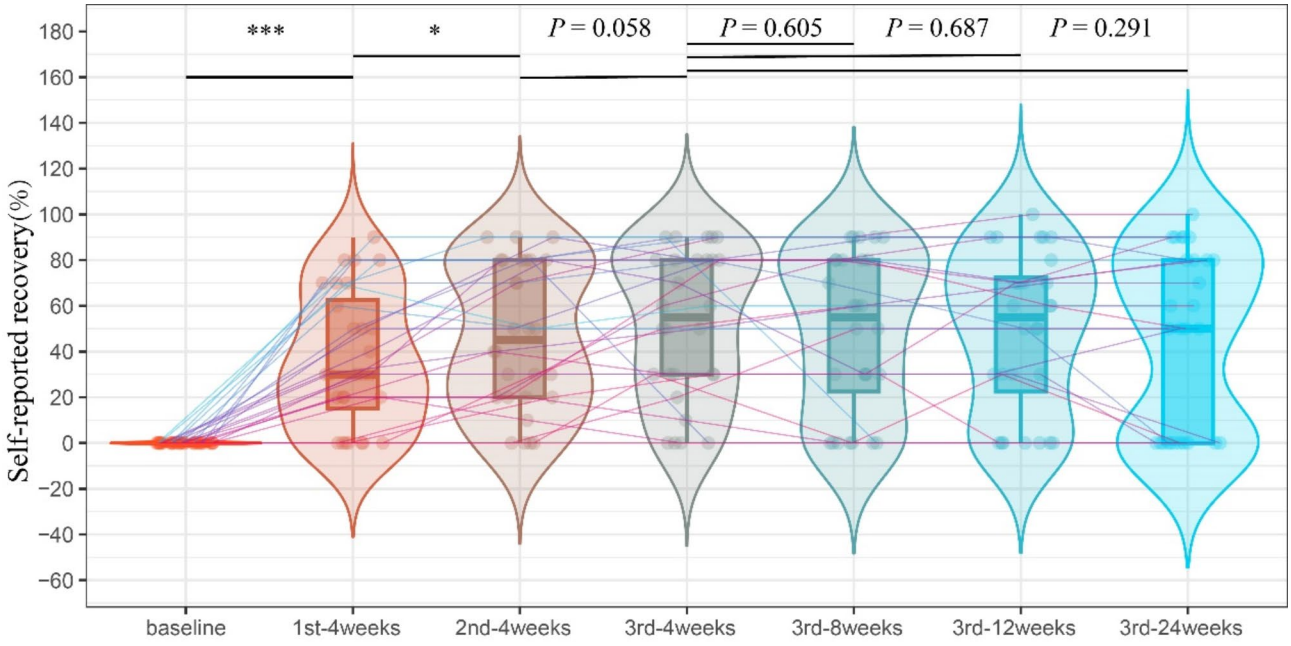


**Fig. 1** Changes in patient self-reported recovery rates before and after treatment (Violin Plot) ($n = 28$). The points in the figure represent the self-reported recovery rates of individual patients at each time point. The lines connect the recovery rates at different time points for each patient. The Wilcoxon signed-rank test was used to compare the differences in recovery rates between time points, with Bonferroni adjustment for significance level (α). * $P < 0.0083$, ** $P < 0.0017$, *** $P < 0.0002$

**Table 2** Spearman's correlation analysis of patient characteristics, PRP properties with the average self-reported recovery rate($n=28$)

| Variable | Average self-reported recovery | |
|---|---|---|
| | r | *P* Value |
| Age | 0.091 | 0.644 |
| PRP- RBC | -0.300 | 0.121 |
| PRP- WBC | 0.075 | 0.705 |
| PRP- PLT | 0.009 | 0.962 |
| Enrichment- PLT | -0.009 | 0.964 |

Note: PRP, Platelet-rich plasma product's hematological parameters. RBC, Red Blood Cell; WBC, White Blood Cell; PLT, Platelet; Enrichment-PLT, The multiple of Platelet-rich plasma platelet concentration relative to the baseline autologous level

self-reported recovery rate. The model fitting results are illustrated in Fig. 2.

Based on the results in Fig. 2a, age was categorized into three groups: <40 years, 40–60 years, and >60 years. The Kruskal–Wallis H test was employed to assess differences among these age groups. The results indicated no statistically significant difference in self-reported recovery rates among the three age groups (H = 4.086, $P=0.130$). The median self-reported recovery rates and interquartile ranges for the <40 years, 40–60 years, and >60 years groups were 90.0% (15.0%, 90.0%), 50.0% (8.8%, 71.3%), and 72.5% (48.8%, 92.5%), respectively.

## Discussion

Currently, PRP treatment for KOA typically involves PRP prepared using either the manual or apheresis methods, with 1 to 3 injections, and intervals ranging from 2 days to 4 weeks between each injection [17, 23, 34]. This study retrospectively analyzed a treatment protocol using PRP prepared by apheresis, with 3 injections (each spaced 4 weeks apart). The aim was to evaluate the effectiveness of different PRP injection frequencies for KOA patients and explore whether individual characteristics and PRP properties influence treatment outcomes, providing a reference for the standardization of PRP therapy in KOA.

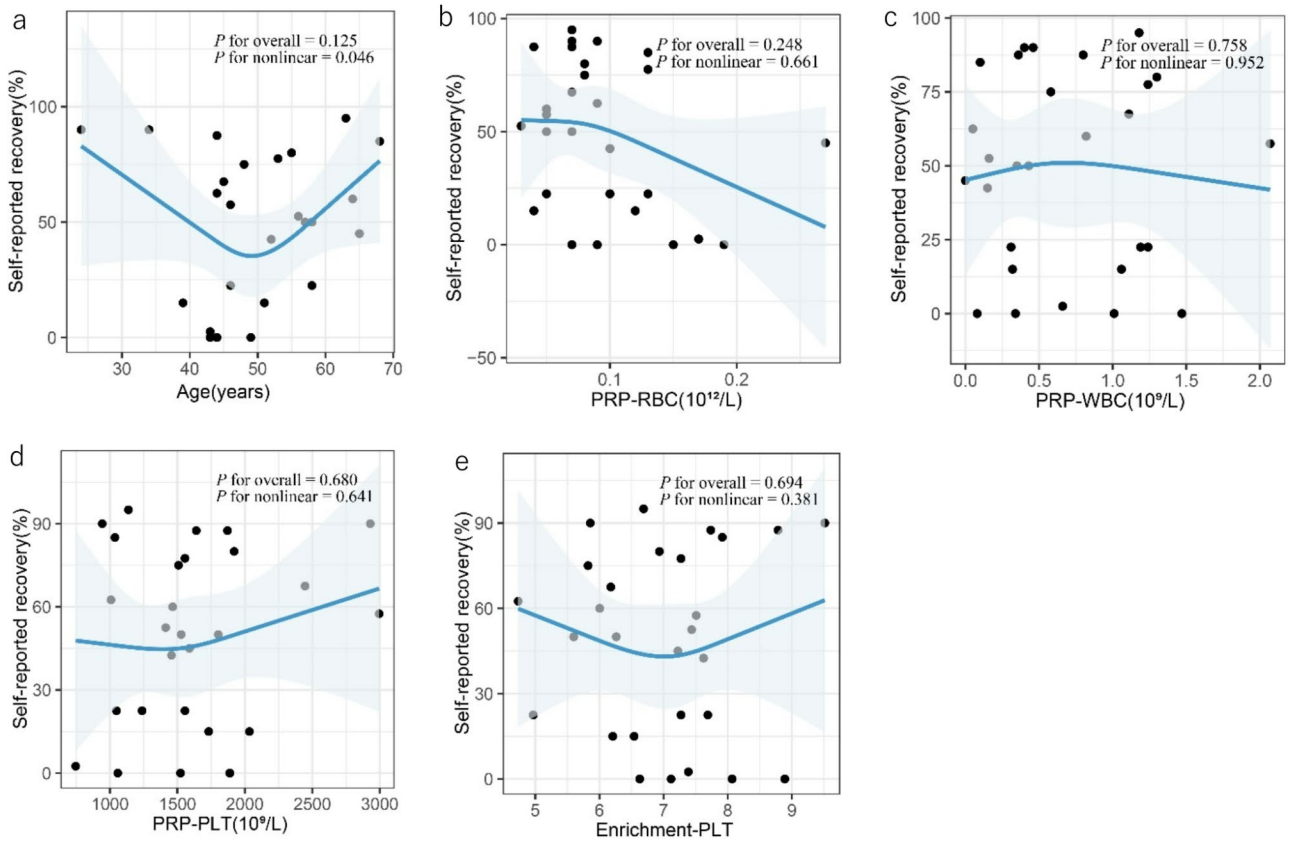


**Fig. 2** Restricted Cubic Spline Plots Illustrating the Relationships between patient characteristics, PRP properties and Average self-reported recovery rate($n=28$) **(a)** Age and self-reported recovery; **(b)** PRP product RBC concentration and self-reported recovery; **(c)** PRP product WBC concentration and self-reported recovery; **(d)** PRP product PLT concentration and self-reported recovery; **(e)** Enrichment of PLTs and self-reported recovery. The black dots represent individual samples used in the restricted cubic spline model. The blue lines indicate the dose–response relationships between the independent variables and self-reported recovery, with the shaded blue areas representing the 95% confidence intervals. PRP, Platelet-rich plasma product's hematological parameters. RBC, Red Blood Cell; WBC, White Blood Cell; PLT, Platelet; Enrichment-PLT, The multiple of Platelet-rich plasma platelet concentration relative to the baseline autologous level

Regarding effectiveness, the results of this study show that, 4 weeks after the first PRP injection, the median self-reported recovery rate was 30.0% (5.0%, 67.5%), which indicate a significant improvement compared to pre-treatment ($P < 0.008$). After the second injection, the recovery rate at 4 weeks increased to 45.0% (20.0%, 80.0%), with further improvement compared to the results after the first treatment ($P < 0.008$). However, no significant change was observed at 4 weeks after the third injection ($P = 0.058$). At 8, 12, and 24 weeks after the third injection, the self-reported recovery rates showed no significant difference compared to the results at 4 weeks after the third injection (all $P > 0.008$). These results suggest that, under this treatment protocol, at least two injections are required for KOA patients, with effects sustained up to 24 weeks. Our findings align with previous studies [35–37], although some studies [38] suggest that three injections may offer additional long-term benefits. this heterogeneity may stem from the relatively small sample size in our study, which may not have sufficiently captured subtle differences, and may also be related to differences in study designs. A possible explanation for the need for at least two PRP injections and the sustained effect for 24 weeks is as follows. Firstly, PRP's mechanism: PRP is rich in growth factors and cytokines. By injecting PRP, tissue repair, cartilage regeneration, and inflammation reduction can be promoted [39–41]. In chronic KOA, tissue repair is a gradual process. The second PRP injection continues the repair. After the third treatment, the repair effect levels off, indicating that the treatment effect begins to slow down. Secondly, sustained effect for 24 weeks: The stability of the effect for 24 weeks suggests that, as cartilage metabolism and structural adjustments gradually complete, the tissue repair and regeneration brought about by the treatment enter a stable state [37]. With respect to potential influencing factors, similar to Amit Saraf et al. [42, 43], our study revealed no statistically significant correlation between sex and recovery rates. However, a nonlinear relationship was observed between age and recovery rates. Notably, there is considerable heterogeneity in the literature regarding the effects of sex and age on treatment outcomes, with some studies reporting contradictory results [27, 44–46]. These discrepancies may stem from differences in PRP preparation, treatment protocols, and patient characteristics. Notably, the limited availability of radiographs in this study (n=26), along with the predominance of Kellgren–Lawrence grade 2 patients, may have contributed to the lack of significant differences in self-reported recovery rates among different Kellgren–Lawrence grades.

Regarding the ICRS scores before and after treatment, no statistically significant difference was found ($P = 0.317$). This result may be subject to bias. In routine clinical practice, post-treatment MRI assessments are not commonly performed unless patients are dissatisfied with their treatment outcomes and seek further medical intervention. Consequently, the subset of patients who underwent MRI evaluation after treatment may not be representative of the broader cohort. Additionally, the small sample size ($n = 5$) limits statistical power, increasing the likelihood of a Type II error in statistical inference.

Regarding PRP properties, no significant correlation was found between RBC, WBC, PLT concentrations, Enrichment-PLT, and recovery rates. As expected, there was no noticeable correlation between RBC and WBC concentrations and recovery rates at very low concentrations. Notably, some studies suggest that PRP with WBC depletion tends to have better therapeutic outcomes than PRP with a high WBC content [47]. Previous studies have shown that higher PLT concentration might lead to better results [30, 31]. Although our Spearman correlation analysis did not reveal a significant relationship, the restricted cubic spline plots suggest that higher PLT concentrations may be linked to improved recovery (Fig. 2d). With respect to the degree of Enrichment-PLT, some research recommends that therapeutic PRP should have Enrichment-PLT levels 4 to 6 times higher than those in whole blood, with concentrations outside this range possibly being ineffective or inhibiting the healing process [48]. However, our correlation analysis and the results from Fig. 2e did not fully support this conclusion. The observed heterogeneity might be due to factors such as the short observation period, limited intergroup differences, and small sample size, which may have prevented us from capturing subtle differences.

#### Strengths and limitations

This study boasts several strengths and practical implications. Firstly, it evaluated the impact of individual characteristics and PRP properties (prepared by apheresis) on treatment outcomes, contributing valuable insights toward the standardization of PRP therapy for KOA. Secondly, the use of a restricted cubic spline model allowed for an in-depth analysis of the relationships between patient age, PRP properties, and self-reported recovery rates, offering a more comprehensive understanding of these associations.

However, this study also has certain limitations. firstly, the primary outcome relied on patient self-reports, introducing a degree of subjectivity. Future studies should incorporate imaging assessments to enhance objectivity. Secondly, this was a small-sample retrospective cohort study without a standard control group, which may limit the external validity and generalizability of the findings. More importantly, the sample size was only 28, resulting in low statistical power and an increased risk of Type II error in statistical inference. Finally, the study considered

a limited set of variables, including only patient sex, age, and PRP properties. Factors such as physical activity level, body mass index, and additional treatments undertaken by patients may influence recovery outcomes and could serve as potential confounding variables in the analysis.

## Conclusion

In conclusion, the results support the recommendation for at least two times PRP injections, with effects lasting up to 24 weeks. PRP (prepared by apheresis) efficacy was not significantly correlated with factors such as sex, age,baseline Kellgren–Lawrence grade, residual WBC content in leukocyte-depleted PRP, RBC content, WBC concentration, or PLT concentration enrichment. Future research should explore other factors influencing PRP efficacy and validate these findings through large-scale, multicenter, prospective studies.

### Abbreviations

| | |
|---|---|
| KOA | Knee osteoarthritis |
| PRP | Platelet-Rich Plasma |
| CI | Confidence interval |
| NSAIDs | Nonsteroidal anti-inflammatory drugs |
| RBC | Red Blood Cell |
| WBC | White Blood Cell |
| PLT | Platelet |
| ICRS | The International Cartilage Repair Society |
| MRI | Magnetic Resonance Imaging |
| Enrichment-PLT | The multiple of PRP platelet concentration relative to the baseline autologous level |
| SD | Standard deviation |
| n | Number |

### Acknowledgements

Not applicable.

### Author contributions

All authors contributed to the study conception and design. CXW, NLS, and BZ conducted the investigation. GD, QL, CXW, NLS, and BZ developed the methodology. JY performed the formal analysis and created the visualizations. QL administered the project. JY and QL wrote the first draft of the manuscript. CYC and LY reviewed, edited, and critically revised the manuscript. All authors read and approved the final manuscript.

### Funding

The research was supported by the National Natural Science Foundation of China, grant number 82470235.

### Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval

The study was approved by the Ethics Committee of the First Affiliated Hospital (ethical approval number: (B)KY2024047). Informed consent was waived because of the retrospective nature of the study.

### Competing interests

The authors declare no competing interests.

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Received: 7 February 2025 / Accepted: 24 March 2025
Published online: 04 April 2025

### References

1. Yang B, Ma J. Meta-analysis of the efficacy and safety of arthroscopic surgery associated with platelet-rich plasma infusion when treating knee osteoarthritis. Int J Rheum Dis. 2023;26(11):2248–57. https://doi.org/10.1111/1756-185X.14921.
2. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. Lancet. 2020;396(10258):1204–22. https://doi.org/10.1016/S0140-6736(20)30925-9.
3. Gelber AC. Knee osteoarthritis. Ann Intern Med. 2024;177(9):ITC129–44. https://doi.org/10.7326/ANNALS-24-01249.
4. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. Eclinicalmedicine. 2020. https://doi.org/10.1016/j.eclinm.2020.100587. 29–30:100587.
5. Sahin N, Yesil H. Regenerative methods in osteoarthritis. Best Pract Res Clin Rheumatol. 2023;37(2):101824. https://doi.org/10.1016/j.berh.2023.101824.
6. Nowaczyk A, Szwedowski D, Dallo I, Nowaczyk J. Overview of first-line and second-line pharmacotherapies for osteoarthritis with special focus on intra-articular treatment. Int J Mol Sci. 2022;23(3):1566. https://doi.org/10.3390/ijms23031566.
7. Cook CS, Smith PA. Clinical update: why Prp should be your first choice for injection therapy in treating osteoarthritis of the knee. Curr Rev Musculoskelet Med. 2018;11(4):583–92. https://doi.org/10.1007/s12178-018-9524-x.
8. Hunter DJ, Bierma-Zeinstra S. Osteoarthr Lancet. 2019;393(10182):1745–59. https://doi.org/10.1016/S0140-6736(19)30417-9.
9. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. Oarsi recommendations for the management of hip and knee osteoarthritis: part Iii: changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010;18(4):476–99. https://doi.org/10.1016/j.joca.2010.01.013.
10. Price AJ, Alvand A, Troelsen A, Katz JN, Hooper G, Gray A, et al. Knee replacement. Lancet. 2018;392(10158):1672–82. https://doi.org/10.1016/S0140-6736(18)32344-4.
11. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-rich plasma: new performance Understandings and therapeutic considerations in 2020. Int J Mol Sci. 2020;21(20):7794. https://doi.org/10.3390/ijms21207794.
12. Rodríguez-Merchán EC. Intra-articular platelet-rich plasma injections in knee osteoarthritis: a review of their current molecular mechanisms of action and their degree of efficacy. Int J Mol Sci. 2022;23(3):1301. https://doi.org/10.3390/ijms23031301.
13. Ren B, Lv X, Tu C, Li ZH. Research trends of platelet-rich plasma application in orthopaedics from 2002 to 2020: a bibliometric analysis. Int Orthop 2021;45(11):2773-90 https://doi.org/10.1007/s00264-021-05163-6
14. Belk JW, Lim JJ, Keeter C, Mcculloch PC, Houck DA, Mccarty EC, et al. Patients with knee osteoarthritis who receive platelet-rich plasma or bone marrow aspirate concentrate injections have better outcomes than patients who receive hyaluronic acid: systematic review and meta-analysis. Arthroscopy. 2023;39(7):1714–34. https://doi.org/10.1016/j.arthro.2023.03.001.
15. Buendía-López D, Medina-Quirós M, Fernández-Villacañas MM. Clinical and radiographic comparison of a single lp-prp injection, a single hyaluronic acid injection and daily Nsaid administration with a 52-week follow-up: a randomized controlled trial. J Orthop Traumatol. 2018;19(1):3. https://doi.org/10.1186/s10195-018-0501-3.
16. Costa L, Lenza M, Irrgang JJ, Fu FH, Ferretti M. How does platelet-rich plasma compare clinically to other therapies in the treatment of knee osteoarthritis? A systematic review and meta-analysis. Am J Sports Med. 2023;51(4):1074–86. https://doi.org/10.1177/03635465211062243.

17. Tang JZ, Nie MJ, Zhao JZ, Zhang GC, Zhang Q, Wang B. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. J Orthop Surg Res. 2020;15(1):403. https://doi.org/10.1186/s13018-020-01919-9.
18. Bennell KL, Paterson KL, Metcalf BR, Duong V, Eyles J, Kasza J, et al. Effect of intra-articular platelet-rich plasma vs placebo injection on pain and medial tibial cartilage volume in patients with knee osteoarthritis: the restore randomized clinical trial. JAMA. 2021;326(20):2021–30. https://doi.org/10.1001/jama.2021.19415.
19. Chahla J, Cinque ME, Piuzzi NS, Mannava S, Geeslin AG, Murray IR, et al. A call for standardization in platelet-rich plasma Preparation protocols and composition reporting: a systematic review of the clinical orthopaedic literature. J Bone Joint Surg Am. 2017;99(20):1769–79. https://doi.org/10.2106/JBJS.16.01374.
20. Everts PA, van Erp A, Desimone A, Cohen DS, Gardner RD. Platelet rich plasma in orthopedic surgical medicine. Platelets. 2021;32(2):163–74. https://doi.org/10.1080/09537104.2020.1869717.
21. Belk JW, Kraeutler MJ, Houck DA, Goodrich JA, Dragoo JL, Mccarty EC. Platelet-rich plasma versus hyaluronic acid for knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Am J Sports Med. 2021;49(1):249–60. https://doi.org/10.1177/0363546520909397.
22. Dernek B, Kesiktas FN, Duymus TM, Aydin T, Isiksacan N, Diracoglu D, et al. Effect of platelet concentration on clinical improvement in treatment of early stage-knee osteoarthritis with platelet-rich plasma concentrations. J Phys Therapy Sci. 2017;29(5):896–901. https://doi.org/10.1589/jpts.29.896.
23. Eymard F, Ornetti P, Maillet J, Noel É, Adam P, Legré-Boyer V, et al. Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: a consensus statement from french-speaking experts. Knee Surg Sports Traumatol Arthrosc. 2021;29(10):3195–210. https://doi.org/10.1007/s00167-020-06102-5.
24. Magalon J, Bausset O, Serratrice N, Giraudo L, Aboudou H, Veran J, et al. Characterization and comparison of 5 platelet-rich plasma preparations in a single-donor model. Arthroscopy. 2014;30(5):629–38. https://doi.org/10.1016/j.arthro.2014.02.020.
25. Mazzocca AD, Mccarthy MB, Chowaniec DM, Cote MP, Romeo AA, Bradley JP, et al. Platelet-rich plasma differs according to Preparation method and human variability. J Bone Joint Surg Am. 2012;94(4):308–16. https://doi.org/10.2106/JBJS.K.00430.
26. Taniguchi Y, Yoshioka T, Sugaya H, Gosho M, Aoto K, Kanamori A, et al. Growth factor levels in leukocyte-poor platelet-rich plasma and correlations with donor age, gender, and platelets in the Japanese population. J Exp Orthop. 2019;6(1):4. https://doi.org/10.1186/s40634-019-0175-7.
27. Sánchez M, Jorquera C, López DDL, Martínez N, Espregueira-Mendes J, Vergés J, et al. Women show a positive response to platelet-rich plasma despite presenting more painful knee osteoarthritis than men. Knee Surg Sports Traumatol Arthrosc. 2024;32(10):2516–25. https://doi.org/10.1002/ksa.12080.
28. Al-Hamed FS, Abu-Nada L, Rodan R, Sarrigiannidis S, Ramirez-Garcialuna JL, Moussa H, et al. Differences in platelet-rich plasma composition influence bone healing. J Clin Periodontol. 2021;48(12):1613–23. https://doi.org/10.1111/jcpe.13546.
29. Piuzzi NS, Chughtai M, Khlopas A, Harwin SF, Miniaci A, Mont MA, et al. Platelet-rich plasma for the treatment of knee osteoarthritis: a review. J Knee Surg. 2017;30(7):627–33. https://doi.org/10.1055/s-0037-1603795.
30. Berrigan WA, Bailowitz Z, Park A, Reddy A, Liu R, Lansdown D. A greater platelet dose May yield better clinical outcomes for platelet-rich plasma in the treatment of knee osteoarthritis: a systematic review. Arthroscopy. 2024;3(41):807–17. https://doi.org/10.1016/j.arthro.2024.03.018.
31. Boffa A, De Marziani L, Andriolo L, Di Martino A, Romandini I, Zaffagnini S, et al. Influence of platelet concentration on the clinical outcome of platelet-rich plasma injections in knee osteoarthritis. Am J Sports Med. 2024;52(13):3223–31. https://doi.org/10.1177/03635465241283463.
32. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: kellgren-lawrence classification of osteoarthritis. Clin Orthop Relat Res. 2016;474(8):1886–93. https://doi.org/10.1007/s11999-016-4732-4.
33. Kleemann RU, Krocker D, Cedraro A, Tuischer J, Duda GN. Altered cartilage mechanics and histology in knee osteoarthritis: relation to clinical assessment (icrs grade). Osteoarthritis Cartilage. 2005;13(11):958–63. https://doi.org/10.1016/j.joca.2005.06.008.
34. Hohmann E, Tetsworth K, Glatt V. Is platelet-rich plasma effective for the treatment of knee osteoarthritis? A systematic review and meta-analysis of level 1 and 2 randomized controlled trials. Eur J Orthop Surg Traumatol. 2020;30(6):955–67. https://doi.org/10.1007/s00590-020-02623-4.
35. Kavadar G, Demircioglu DT, Celik MY, Emre TY. Effectiveness of platelet-rich plasma in the treatment of moderate knee osteoarthritis: a randomized prospective study. J Phys Therapy Sci. 2015;27(12):3863–7. https://doi.org/10.1589/jpts.27.3863.
36. Simental-Mendía M, Acosta-Olivo CA, Hernández-Rodríguez AN, Santos-Santos OR, de la Garza-Castro S, Peña-Martínez VM, et al. Intraarticular injection of platelet-rich plasma in knee osteoarthritis: single versus triple application approach. Pilot study. Acta Reumatol Port. 2019;44(2):138–44.
37. Tavassoli M, Janmohammadi N, Hosseini A, Khafri S, Esmaeilnejad-Ganji SM. Single- and double-dose of platelet-rich plasmaversus hyaluronic acid for treatment of knee osteoarthritis: a randomized controlled trial. World J Orthop. 2019;10(9):310–26. https://doi.org/10.5312/wjo.v10.i9.310.
38. Subramanyam K, Alguvelly R, Mundargi A, Khanchandani P. Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: a single-blind, randomized, superiority trial. Arch Rheumatol. 2021;36(3):326–34. https://doi.org/10.46497/ArchRheumatol.2021.8408.
39. Cheng L, Chang S, Tan Y, He B. Platelet-rich plasma combined with isometric quadriceps contraction regulates autophagy in chondrocytes via the pi3k/akt/mtor pathway to promote cartilage repair in knee osteoarthritis. Regen Ther. 2025;28:81–9. https://doi.org/10.1016/j.reth.2024.11.013.
40. O'Donnell C, Migliore E, Grandi FC, Koltsov J, Lingampalli N, Cisar C, et al. Platelet-rich plasma (prp) from older males with knee osteoarthritis depresses chondrocyte metabolism and upregulates inflammation. J Orthop Res. 2019;37(8):1760–70. https://doi.org/10.1002/jor.24322.
41. Szwedowski D, Szczepanek J, Paczesny Ł, Zabrzyński J, Gagat M, Mobasheri A, et al. The effect of platelet-rich plasma on the intra-articular microenvironment in knee osteoarthritis. Int J Mol Sci. 2021;22(11):5492. https://doi.org/10.3390/ijms22115492.
42. Raeissadat SA, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babaee M, et al. Knee osteoarthritis injection choices: platelet- rich plasma (prp) versus hyaluronic acid (a one-year randomized clinical trial). Clin Med Insights: Arthritis Musculoskelet Disorders. 2015;8. https://doi.org/10.4137/CMAMD.S17894. CMAMD.S17894.
43. Saraf A, Hussain A, Singhal A, Arora V, Bishnoi S. Do age, gender, Bmi and disease duration influence the clinical outcomes in patients of knee osteoarthritis treated with serial injections of autologous platelet rich plasma? J Clin Orthop Trauma. 2023;43:102226. https://doi.org/10.1016/j.jcot.2023.102226.
44. Filardo G, Kon E, Buda R, Timoncini A, Di Martino A, Cenacchi A, et al. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2011;19(4):528–35. https://doi.org/10.1007/s00167-010-1238-6.
45. Kon E, Buda R, Filardo G, Di Martino A, Timoncini A, Cenacchi A, et al. Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions. Knee Surg Sports Traumatol Arthrosc. 2010;18(4):472–9. https://doi.org/10.1007/s00167-009-0940-8.
46. Korpershoek JV, Vonk LA, Filardo G, Kester EC, van Egmond N, Saris D, et al. Effect of autologous conditioned plasma injections in patients with knee osteoarthritis. Orthop J Sports Med. 2023;11(7):961789904. https://doi.org/10.1177/23259671231184848.
47. Yin WJ, Xu HT, Sheng JG, An ZQ, Guo SC, Xie XT, et al. Advantages of pure platelet-rich plasma compared with leukocyte- and platelet-rich plasma in treating rabbit knee osteoarthritis. Med Sci Monit. 2016;22:1280–90. https://doi.org/10.12659/msm.898218.
48. Raeissadat SA, Sedighipour L, Rayegani SM, Bahrami MH, Bayat M, Rahimi R. Effect of platelet-rich plasma (prp) versus autologous whole blood on pain and function improvement in tennis elbow: a randomized clinical trial. Pain Res Treat. 2014;2014:1–8. https://doi.org/10.1155/2014/191525.


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