Am J Transl Res 2026;18(6):5368-5378
www.ajtr.org /ISSN:1943-8141/AJTR0172665

Original Article

Effects of platelet-rich plasma-assisted arthroscopic debridement plus microfracture surgery on visual analogue scale scores and cartilage repair indicators in early-stage knee osteoarthritis

Haolin Zhou, Qiongmei Zhang, Daoxiong Li, Qingchun Liu

Department of Orthopedics, Liqun Hospital, Putuo District, Shanghai 200333, China

Received March 16, 2026; Accepted April 24, 2026; Epub June 15, 2026; Published June 30, 2026

Abstract: Objective: To retrospectively analyze the clinical effects of platelet-rich plasma (PRP)-assisted knee-preserving surgery in early-stage knee osteoarthritis (KOA). Methods: Sixty-nine patients with early-stage KOA were enrolled and assigned to either a PRP-assisted surgery group or a surgery-only group. The following parameters were collected: visual analogue scale (VAS) scores; serum cartilage repair markers [transforming growth factor-β1 (TGF-β1), insulin-like growth factor-1 (IGF-1), matrix metalloproteinase-13 (MMP-13)]; synovial fluid inflammation and oxidative stress markers [superoxide dismutase (SOD), nitric oxide (NO)]; knee society score (KSS score); knee joint range of motion (ROM); and adverse reactions (ARs). Results: Compared with the surgery-only group, postoperative VAS scores, MMP-13, synovial fluid inflammatory markers, NO, and extension in the PRP-assisted surgery group were notably lower, and postoperative TGF-β1, IGF-1, SOD, KSS, flexion, internal rotation, and external rotation were notably higher. There were no significant differences in the rates of excellent/good response or overall ARs between the two groups. Conclusion: PRP-assisted knee-preserving surgery significantly alleviates pain symptoms in patients with early-stage KOA, promotes cartilage repair, suppresses synovial inflammation and oxidative stress, improves knee function and knee ROM, and demonstrates good safety.

Keywords: Platelet-rich plasma, knee-preserving surgery, knee osteoarthritis, visual analog scale, cartilage repair

Introduction

Knee osteoarthritis (KOA) is a chronic joint disease characterized by articular cartilage degeneration and bone proliferation. It is the most common form of osteoarthritis (OA) and a major cause of disability in middle-aged and elderly individuals [1]. With the acceleration of global aging and the increasing prevalence of obesity, the incidence of KOA is on the rise [2]. According to the 2024 Global Burden of Disease, Injury, and Risk Factors Study, 60-85% of the global burden of OA stems from KOA [3]. In China, approximately 50% of individuals aged ≥60 exhibit radiographic evidence of OA on X-rays, with 30-50% presenting clinical symptoms, and OA is projected to become the fourth leading cause of disability [4].

The primary symptoms of KOA include knee pain, tenderness, stiffness, swelling, limited mobility, and deformity, significantly impairing patients' quality of life and potentially increasing the incidence of cardiovascular events [5]. Currently, KOA treatment options are diverse. Early-stage management often involves non-surgical approaches such as physical therapy, exercise therapy, weight control, and medication (including nonsteroidal anti-inflammatory drugs, corticosteroids, antidepressants, and drugs that inhibit cartilage degradation). However, these methods primarily alleviate pain and improve function without fundamentally repairing damaged articular cartilage [6]. For early- to early-mid-stage KOA patients with limited local cartilage or meniscus injury who fail to respond to standard conservative treatment and are classified as Kellgren Lawrence grade I-II (or some grade III cases without significant alignment deformity), arthroscopic debridement combined with microfracture is commonly

https://doi.org/10.62347/UTXF3684

selected as a knee-preserving treatment option [7]. Advanced-stage patients often require total knee arthroplasty. However, this surgery presents challenges like difficulty in prosthesis positioning, high technical complexity, significant trauma, and postoperative complications [8].

Platelet-rich plasma (PRP) has received widespread attention in orthopedics in recent years as an emerging treatment method. PRP is a platelet-concentrated solution extracted from autologous whole blood via centrifugation, containing platelets, leukocytes, and fibrin at high concentration [9]. Platelets are rich in growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), and insulin-like growth factor-1 (IGF-1), which play crucial roles in self-healing and repair processes within the body [10]. In KOA treatment, PRP stimulates synovial cells to secrete endogenous hyaluronic acid to alleviate joint pain, acts on meniscus cells to enhance their survival capacity to promote meniscus repair, and facilitates the proliferation of knee joint chondrocytes and the secretion of extracellular matrix to repair damaged articular cartilage [11]. Simultaneously, it exerts anti-inflammatory and analgesic effects by regulating inflammatory mediators within the joint cavity. Multiple studies have shown that PRP has a positive effect in promoting fracture healing and soft tissue repair [12, 13].

Clinical studies on PRP combined with knee-preserving surgery for early KOA have been reported, but most of them focus on clinical efficacy observation. This study innovatively measured serum levels of TGF-β1, IGF-1, and matrix metalloproteinase-13 (MMP-13) to explore the potential molecular mechanisms by which PRP-assisted surgery promotes cartilage repair and inhibits degradation. This provides biological evidence for its "repair - anti-inflammatory - analgesic" multifunctional effects, further optimizes treatment regimens for early KOA, and deeply explores the impacts of PRP-assisted knee-preserving surgery on pain relief and cartilage repair in early KOA patients, which holds great significance for enhancing patient quality of life. The findings are reported as follows.

Materials and methods

Study subjects

This is a retrospective study. From January 2024 to March 2025, 69 patients with early-stage KOA admitted to the Orthopedic Department of Liqun Hospital, Putuo District were enrolled. They were divided into a PRP-assisted surgery group (n = 35) and a surgery-only group (n = 34). Baseline data (age, gender, Body Mass Index (BMI), Kellgren-Lawrence grading, etc.) were collected, as well as preoperative Visual Analogue Scale (VAS) scores, serum cartilage repair markers, and KSS scores, to ensure intergroup balance. This study was approved by the Ethics Committee of Liqun Hospital, Putuo District.

Sample size was calculated based on core outcome measures: taking improvement in VAS scores at 6 months postoperatively as the primary endpoint, with an expected difference between the PRP group and the surgery-only group of approximately 1.5 points, a standard deviation of 1.2 points, Cohen's d of 1.25 (moderate effect), $\alpha = 0.05$ (two-tailed), and $\beta = 0.10$ (90% power), the calculated sample size using the two-sample t-test formula yielded a theoretical value of 27 cases. Accounting for a 20% dropout rate and Bonferroni correction for multiple comparisons (α adjusted to 0.01), the corrected sample size required approximately 50 cases. To account for patient heterogeneity and ensure robust results, the sample size was expanded to 69 cases to ensure ≥90% test power and enhance the reliability of conclusions.

Individuals who met the following inclusion criteria were eligible for the study: aged 45-75 years; meeting the diagnostic criteria for KOA established by the American College of Rheumatology (ACR); Kellgren-Lawrence grade I-III; knee joint pain lasting ≥3 months; voluntarily signing the informed consent form.

Individuals who met any of the following exclusion criteria were excluded from the study: complicated with severe dysfunction of heart, liver, kidney, or other organs; with knee joint infection, tumor, trauma, or other conditions; with abnormal coagulation function or under anticoagulant treatment; allergic to PRP; receiv-

ing knee joint injection treatment or surgery within the past 6 months.

Specific criteria for Kellgren-Lawrence Grades I-III [14]. Grade I: Doubtful joint space narrowing; minimal/doubtful osteophytic lipping. Grade II: Definite osteophytes; normal or possible joint space narrowing; no obvious sclerosis. Grade III: Multiple osteophytes, definite joint space narrowing, sclerosis, and possible deformity of bone ends.

Treatment method

The surgery-only group underwent knee-preserving surgery. For arthroscopic debridement combined with microfracture surgery, the patient was positioned supine. Following continuous epidural anesthesia, routine sterilization and draping were performed. Anteromedial and anterolateral approaches to the knee joint were established. Arthroscopic exploration of the knee joint was conducted to remove loose bodies, proliferative synovium, and degenerative cartilage fragments. Microfracture was performed on areas of cartilage defect using a microfracture cone to create subchondral bone drill holes with 3-4 mm spacing and a depth of approximately 3-4 mm until blood exudation occurred.

The PRP-assisted surgery group received additional knee-preserving surgery with PRP therapy, as follows:

(1) PRP preparation: 40 mL of venous blood was drawn from the patient into a sodium citrate anticoagulant tube (Shanghai Kindly; specification: 10 mL × 50 tubes; batch No.: 20240301). PRP was prepared using the two-step centrifugation method (centrifuge: Xiangyi H1850; centrifuge radius: 12 cm): First centrifugation was performed at 1200 g × 10 min (centrifuge radius: 12 cm) to separate the plasma layer from the red blood cell layer, and the plasma was transferred to a new centrifuge tube. Second centrifugation was performed at 3000 g × 10 min (centrifuge radius: 12 cm). The upper platelet-poor plasma (PPP) layer was discarded and the lower sediment layer was retained as PRP. Platelet concentration was determined using the Sysmex XN-9000 fully automated hematology analyzer (Sysmex Corporation, Japan), which was required to be 3-5 times the baseline value (baseline platelet concentration: approximately 150-350 × 10^9/L; PRP platelet count: 450-1750 × 10^9/L). No calcium or thrombin activators were added to preserve the natural release process of platelet-derived growth factors.

(2) Injection regimen: At the conclusion of surgery, 2 mL of PRP was injected into the knee joint cavity via intra-articular puncture. Injections were repeated at 1 month and 2 months postoperatively, totaling 3 injections. This regimen references the *Consensus on Platelet-Rich Plasma Therapy for KNEE OSTEOARTHRITIS in China (2023)*, as multiple injections enable sustained release of growth factors to promote cartilage repair. The control group received an equivalent volume of 0.9% sodium chloride injection (Huaren Pharmaceutical; specification: 10 mL:90 mg; batch No.: 20240215) to exclude placebo effects.

(3) Follow-up design: Follow-up was conducted at 6 months postoperatively (primary endpoint), with an extension to 12 months postoperatively to evaluate long-term efficacy.

Outcome measures

(1) Pain assessment: The VAS was employed to assess knee pain severity preoperatively and at 3 months and 6 months postoperatively. Scores range from 0 (no pain) to 10 (severe pain).

(2) Serum cartilage repair marker measurement: 5 mL of fasting venous blood was drawn from patients preoperatively and at 6 months postoperatively. The blood was placed in procoagulation tubes containing separation gel (BD; batch No.: 20240508) and then separated by centrifugation at 3000 g for 10 minutes (centrifuge: Xiangyi H1850; No.: 20230612) to obtain serum. The levels of TGF-β1, IGF-1, and MMP-13 were measured by enzyme-linked immunosorbent assay (ELISA). All kits were purchased from Cusabio Technology LLC., with batch Nos. of HMY00724, HMY01124, and HMY02324, respectively. Procedures were performed in strict accordance with kit instructions. To further validate cartilage structural repair, some patients (10 patients selected from each group) underwent knee joint Magnetic Resonance Imaging (MRI) examination (Siemens 3.0T MRI; model: MAGNETOM Skyra) at 6 postoperatively. The T2 mapping sequence was

used to evaluate the cartilage defect area and signal intensity changes. Two senior radiologists (each with over 10 years of experience in musculoskeletal diagnosis) independently reviewed the images and averaged their assessments.

(3) Comparison of synovial fluid inflammation markers. Synovial fluid was collected from each group preoperatively and at 6 months postoperatively. After centrifugation at 4000 r/min for 10 minutes at a radius of 10 cm, the supernatant was obtained and stored at -70°C for subsequent analysis. ELISA was used to determine the levels of interleukin (IL)-1β and tumor necrosis factor (TNF)-α in the synovial fluid.

(4) Measurement of synovial fluid oxidative stress markers. Superoxide dismutase (SOD) and nitric oxide (NO) levels were measured preoperatively and at 6 months postoperatively using colorimetric and nitrate reductase assays, respectively.

(5) Knee function assessment: Knee function was evaluated using the Knee Society Score (KSS) by uniformly trained orthopedic surgeons (training included KSS scoring criteria, operational procedures, and consistency verification) preoperatively and at 6 months postoperatively. This scale was established by the American Knee Society in 1989 (Insall JN, et al. J Bone Joint Surg Am. 1989; 71(5): 778-783). It comprises a knee joint score (scored from 0 to 100, assessing pain, range of motion (ROM), and stability) and a function score (scored from 0 to 100, assessing walking distance, stair climbing ability, etc.). Scoring criteria: Excellent (scores ≥90), Good (scores 80-89), Fair (scores 70-79), Poor (scores <70). Scale reliability: Cronbach's α = 0.85. Validity was validated via structural equation modeling (Goodness-of-Fit Index (GFI) = 0.92, Adjusted Goodness-of-Fit Index (AGFI) = 0.88). To minimize subjective bias, walking distance in the function score was measured using a stopwatch during a 50-meter walk test. Stair climbing ability was assessed by timing the ascent of five standardized steps (15 cm height, 30 cm width) and the need for handrail assistance. Data were recorded simultaneously and cross-checked by two research assistants.

(6) Knee ROM. ROM was measured preoperatively and at 6 months postoperatively using a goniometer, including flexion, extension, internal rotation, and external rotation.

(7) Safety assessment: Postoperative adverse reactions (ARs) in both groups were recorded, including local redness and swelling, pain aggravated, infection, and allergy.

Statistical methods

Data analysis was performed using SPSS 26.0 statistical software. The measurement data were verified for normality by the Shapiro-Wilk test (P>0.05, conforming to normal distribution), and expressed as mean ± standard deviation (x ± sd). For measurement data at multiple time points, repeated measures analysis of variance (RM-ANOVA) was conducted first. In case of significant time effects or intergroup interaction effects, the Bonferroni correction was adopted for post hoc multiple comparisons. The independent sample t-test was applied for intergroup comparison at the same time point, and the paired t-test for intragroup comparison at different time points. Counting data were expressed as number of cases or percentage, with intergroup comparisons made using the χ^2 test or Fisher's exact test (if the theoretical frequency was <5). P<0.05 was considered statistically significant.

Results

Baseline data analysis

For baseline characteristics including age, gender, BMI, Kellgren-Lawrence grading, preoperative VAS score, serum cartilage repair markers, and knee function KSS score, no substantial differences were seen between the PRP-assisted surgery group and the surgery-only group (all P>0.05), indicating a favorable intergroup balance (**Table 1**).

Pain score

The PRP-assisted surgery group exhibited notably lower VAS scores at both 3 and 6 months postoperatively than the surgery-only group (P<0.001), demonstrating a marked advantage of PRP-assisted therapy in pain relief (**Table 2**).

Cartilage repair markers

At 1, 3, and 6 months postoperatively, serum levels of pro-cartilage repair factors (TGF-β1, IGF-1) were notably higher in the PRP-assisted surgery group relative to the surgery-only group, while levels of the cartilage degradation factor

Table 1. Comparison of baseline data

Item	PRP-assisted surgery group (n = 35)	Surgery-only group (n = 34)	t/χ^2	*P*
Age (years)	62.3 ± 5.8	61.7 ± 6.2	0.415	0.679
Gender (male/female)	12/23	10/24	0.189	0.664
BMI (kg/m^2)	25.8 ± 3.1	26.1 ± 2.9	0.415	0.680
Kellgren-Lawrence grading			0.337	1.000
Grade I	15 (42.9)	14 (41.2)		
Grade II	18 (51.4)	17 (50.0)		
Grade III	2 (5.7)	3 (8.8)		
Preoperative VAS score	6.8 ± 1.2	6.6 ± 1.3	0.664	0.509
Preoperative TGF-β1 (ng/mL)	21.2 ± 3.5	20.8 ± 3.8	0.455	0.651
Preoperative IGF-1 (ng/mL)	32.7 ± 5.1	33.1 ± 4.9	0.332	0.741
Preoperative MMP-13 (ng/mL)	26.5 ± 4.2	25.9 ± 4.5	0.573	0.569
Preoperative KSS score	65.2 ± 7.3	64.8 ± 6.9	0.234	0.816

Note: PRP, platelet-rich plasma; BMI, Body Mass Index; VAS, Visual Analogue Scale; TGF-β1, transforming growth factor-β1; IGF-1, insulin-like growth factor-1; MMP-13, matrix metalloproteinase-13; KSS, knee society score.

Table 2. RM-ANOVA for postoperative VAS scores

Time point	Group	Number of subjects	Mean ± SD (points)	F value	*P* value	Intergroup comparison (LSD test)
3 months postoperatively	PRP-assisted surgery group	35	4.1 ± 1.2	15.032	<0.001	PRP-assisted surgery group < surgery-only group
	Surgery-only group	34	5.3 ± 1.5			(P<0.001)
6 months postoperatively	PRP-assisted surgery group	35	3.2 ± 1.0	26.287	<0.001	PRP-assisted surgery group < surgery-only group
	Surgery-only group	34	4.6 ± 1.3			(P<0.001)
Time effects	-	-	-	48.519	<0.001	6 months postoperatively <3 months postoperatively
Interaction effects	-	-	-	3.147	0.079	No significant interaction between groups and time

Note: PRP, platelet-rich plasma; RM-ANOVA, Repeated Measures Analysis of Variance; LSD, Least Significant Difference.

Table 3. Comparison of serum cartilage repair markers at different postoperative time points

Item	Group	Number of subjects	1 month postoperatively	3 months postoperatively	6 months postoperatively	F value	*P* value
TGF-β1 (ng/mL)	PRP-assisted surgery group	35	24.1 ± 3.8	26.8 ± 4.0$^{\#}$	28.5 ± 4.2$^{\#,}$	10.75	<0.001
	Surgery-only group	34	21.5 ± 3.3	22.3 ± 3.5	22.1 ± 3.7	0.47	0.625
IGF-1 (ng/mL)	PRP-assisted surgery group	35	38.9 ± 5.6	42.7 ± 6.1$^{\#}$	45.6 ± 6.8$^{\#,\Delta}$	10.33	<0.001
	Surgery-only group	34	34.5 ± 5.0	36.1 ± 5.3	38.2 ± 5.5	4.21	0.018
MMP-13 (ng/mL)	PRP-assisted surgery group	35	22.3 ± 3.6	20.5 ± 3.3$^{\#}$	18.7 ± 3.1$^{\#,\Delta}$	10.17	<0.001
	Surgery-only group	34	25.1 ± 4.1	24.3 ± 3.9	23.5 ± 3.9	1.38	0.256

Note: PRP, platelet-rich plasma; TGF-β1, transforming growth factor-β1; IGF-1, insulin-like growth factor-1; MMP-13, matrix metalloproteinase-13. $^{\#}$P < 0.05 vs. 1 month postoperatively; $^{\Delta}$P < 0.05 vs. surgery-only group.

(MMP-13) were notably lower (P<0.05), suggesting that PRP modulates the balance between cartilage repair and degradation (**Table 3**).

In comparison to the surgery-only group, the PRP-assisted surgery group exhibited considerably smaller cartilage defect area (P<0.001) and lower T2 signal intensity (P<0.001), indicating that PRP-assisted therapy effectively promotes cartilage structural repair and improves cartilage degeneration (**Table 4**).

Synovial fluid inflammation

Preoperatively, no considerable intergroup differences were observed in synovial fluid inflammation markers (IL-1β, TNF-α) (P>0.05). At 6

Table 4. Knee MRI cartilage repair assessment results at 6 months postoperatively

Item	Group	Number of subjects	Mean ± SD	t value	*P* value
Cartilage defect area	PRP-assisted surgery group	10	12.5 ± 3.8	3.44	0.003
	Surgery-only group	10	18.9 ± 4.5		
T2 signal intensity	PRP-assisted surgery group	10	45.2 ± 5.1	5.27	<0.001
	Surgery-only group	10	58.7 ± 6.3		

Note: MRI, Magnetic Resonance Imaging; PRP, platelet-rich plasma.

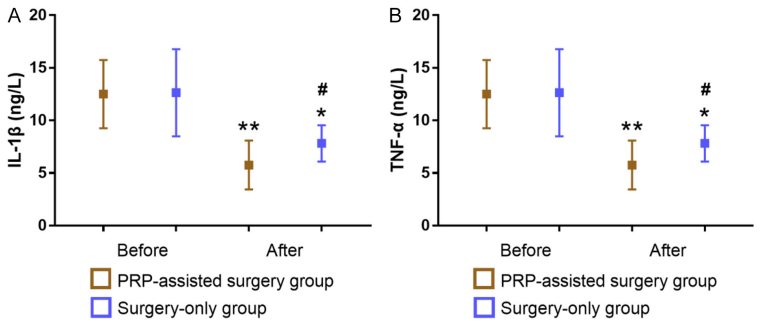

Figure 1. Comparison of synovial fluid inflammation preoperatively and at 6 months postoperatively. A. IL-1β preoperatively and at 6 months postoperatively. B. TNF-α preoperatively and at 6 months postoperatively. Note: **P<0.01, *P<0.05, compared with before surgery; #P<0.05, compared with the control group. IL, interleukin; TNF, tumor necrosis factor; PRP, platelet-rich plasma.

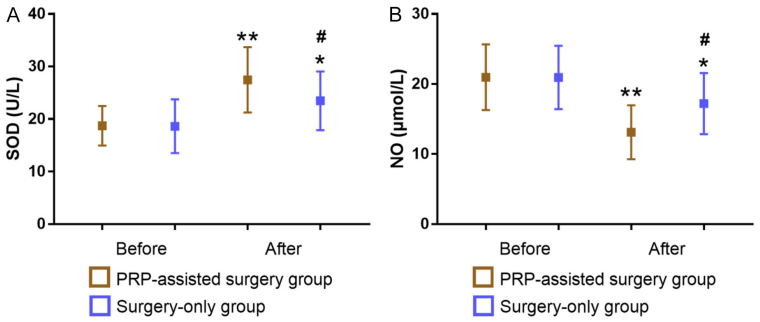

Figure 2. Comparison of synovial fluid oxidative stress preoperatively and at 6 months postoperatively. A. SOD preoperatively and at 6 months postoperatively. B. NO preoperatively and at 6 months postoperatively. Note: **P<0.01, *P<0.05, compared with before surgery; #P<0.05, compared with the control group. SOD, superoxide dismutase; NO, nitric oxide; PRP, platelet-rich plasma.

months postoperatively, all synovial fluid inflammation markers in the PRP-assisted surgery group were significantly reduced and lower than those in the surgery-only group, demonstrating the effects of PRP in suppressing synovial fluid inflammation (**Figure 1**).

Synovial fluid oxidative stress

Preoperatively, no remarkable intergroup differences were observed in oxidative stress markers (SOD, NO) (P>0.05). At 6 months postoperatively, SOD levels in the PRP-assisted surgery group were elevated and higher than those in the surgery-only group, while NO levels were reduced and lower than those in the surgery-only group. These findings indicate that PRP effectively suppresses oxidative stress in synovial fluid (**Figure 2**).

Knee function

At 6 months postoperatively, the KSS score of the PRP-assisted group was remarkably higher than that of surgery-only group (P<0.05), but there was no significant difference in good/excellent rate between the two groups (P>0.05), indicating that PRP-assisted therapy notably improves knee function (**Table 5**).

Knee ROM

There was no considerable intergroup difference in knee ROM (flexion, extension, internal rotation, and external rotation) preoperatively (P> 0.05). At 6 months postoperatively, the PRP-assisted surgery group demonstrated significantly increased ROM in flexion, internal rotation, and external rotation relative to the surgery-only group; the ROM in extension was notably reduced and lower than that in the surgery-only group. These data indicate that PRP effectively improves knee ROM (**Figure 3**).

Safety

No serious ARs occurred in either group. The number of infections, allergies, and minor reac-

Table 5. Comparison of knee function scores and excellent/good rate at 6 months postoperatively

Group	Number of subjects	KSS score	Excellent/good rate (%)
PRP-assisted surgery group	35	82.3 ± 6.5	85.7% (30/35)
Surgery-only group	34	75.1 ± 7.2	67.7% (23/34)
t/χ^2		4.363	3.161
P		<0.001	0.075

Note: KSS, knee society score; PRP, platelet-rich plasma.

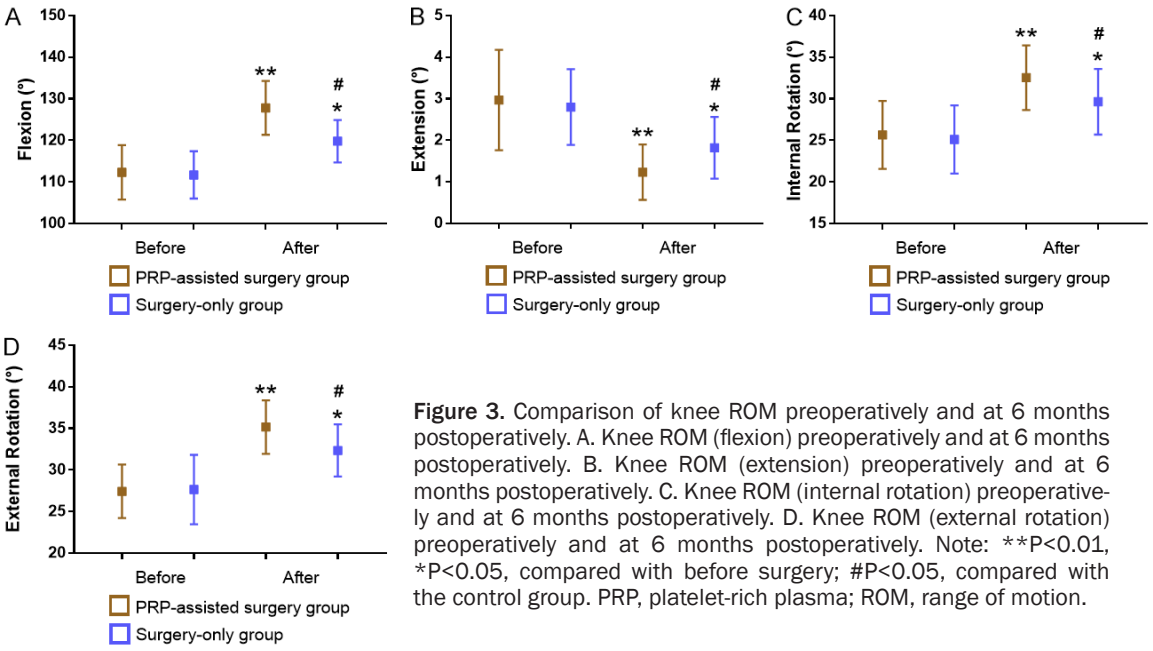

Figure 3. Comparison of knee ROM preoperatively and at 6 months postoperatively. A. Knee ROM (flexion) preoperatively and at 6 months postoperatively. B. Knee ROM (extension) preoperatively and at 6 months postoperatively. C. Knee ROM (internal rotation) preoperatively and at 6 months postoperatively. D. Knee ROM (external rotation) preoperatively and at 6 months postoperatively. Note: **P<0.01, *P<0.05, compared with before surgery; #P<0.05, compared with the control group. PRP, platelet-rich plasma; ROM, range of motion.

tions in the PRP-assisted surgery group was similar to that in the surgery-only group, with no remarkable difference in the overall AR rate (P = 0.782), indicating that PRP-assisted surgery did not increase additional safety risks (**Table 6**).

Discussion

Mechanism and effect of PRP-assisted knee-preserving surgery in pain relief for early-stage KOA patients

Pain is the core symptom in early-stage KOA patients, seriously impacting quality of life. This study demonstrated that the VAS scores at 3 and 6 months postoperatively were notably lower in the PRP-assisted surgery group than the surgery-only group (P<0.001), suggesting that PRP enhances the analgesic effect in knee-preserving surgery. This effect may be achieved through multiple mechanisms: on the one hand, TGF-β1 and IGF-1 enriched in PRP suppress intra-articular inflammatory responses, reducing the release of algogenic substances such as prostaglandin E_2 [15]; on the other hand, PRP promotes the synthesis of endogenous hyaluronic acid by synovial cells, improving joint lubrication and alleviating pain caused by cartilage wear [16]. Furthermore, PRP-induced cartilage repair may fundamentally alleviate pain sources (e.g., reducing neural stimulation caused by subchondral bone microfractures) [17]. At 6 months postoperatively, the VAS scores in the PRP group showed a further reduction compared to 3 months postoperatively, suggesting a sustained analgesic effect, which may be related to the time-dependence of cartilage repair. According to Srinivasan et al. [18], PRP-assisted knee-preserving surgery had a positive effect on both pain relief and knee function in patients with early-stage KOA, consistent with the findings of this study.

Table 6. Comparison of ARs

Group	Number of subjects	Infection (n)	Allergy (n)	Other minor reactions (n)	Overall AR rate
PRP-assisted surgery group	35	0	1 (2.9%)	3 (local swelling/itching, 8.6%)	11.4% (4/35)
Surgery-only group	34	1 (2.9%)	0	2 (pain aggravated/dizziness, 5.9%)	8.8% (3/34)
P value		0.493	1.000	1.000	1.000

Note: AR, adverse reactions; PRP, platelet-rich plasma.

Regulatory effects of PRP on cartilage repair markers

The core mechanism of cartilage degeneration is the imbalance between synthesis and degradation. This study found that at 6 months postoperatively, serum TGF-β1 and IGF-1 levels were notably higher in the PRP-assisted surgery group than the surgery-only group, while MMP-13 levels were notably reduced (P<0.001). TGF-β1 stimulates chondrocytes to synthesize collagen II and proteoglycans and inhibits MMP expression [19]; IGF-1 promotes chondrocyte proliferation and matrix synthesis by activating the PI3K/Akt pathway [20]; and reduced MMP-13 levels indicate suppressed cartilage degradation. This is consistent with the rat KOA study, which showed that PRP inhibits the PI3K/AKT/mTOR pathway and down-regulates the expression of MMP-13 in cartilage [21]. PDGF in PRP may promote cartilage defect repair by recruiting mesenchymal stem cells [22]. This study also directly validated the repair of cartilage structure by incorporating imaging evidence such as MRI re-exploration. In a rat experiment conducted by Zhang et al. [23], PRP up-regulated the protein expression of TGF-β1 in the KOA model; although this may aggravate synovial fibrosis, it was helpful in inhibiting cartilage degeneration and abnormal subchondral bone remodeling, which is similar to the results of this study.

Regulatory effects of PRP on synovial fluid inflammation markers

Inflammation is not only a key pathological mechanism in KOA but also a common cause of joint pain and disability in patients [24]. Our findings revealed significantly lower IL-1β and TNF-α in synovial fluid at 6 months postoperatively in patients receiving PRP intervention compared to those undergoing surgery alone. IL-1β and TNF-α are both inflammatory cytokines; their excessive secretion promotes cartilage matrix degradation and the development of KOA [25]. PRP promotes cartilage formation and alleviates joint pain by suppressing IL-1β and TNF-α levels while increasing fibroblast growth factor and TGF-β1 levels, consistent with the findings of this study [26].

Regulatory effects of PRP on synovial fluid oxidative stress markers

KOA progression involves oxidative stress damage to chondrocytes [27]. This study revealed significantly higher SOD and lower NO levels in synovial fluid at 6 months post-intervention with PRP compared to surgery alone, suggesting that PRP intervention is more effective in mitigating oxidative stress damage. SOD is an antioxidant enzyme that converts superoxide radicals into hydrogen peroxide and oxygen, protecting the body from oxidative stress [28]. NO induces free radical generation, leading to cellular exhaustion and hindering cellular repair; elevated NO levels exacerbate oxidative stress damage in the body [29]. Gato-Calvo et al. [30] also reported similar results that PRP exerts an antioxidant effect in KOA models by reducing NO production through downregulating the expression of inducible nitric oxide synthase (iNOS).

Improvement in knee function and ROM and relevant clinical significance

At 6 months postoperatively, the PRP-assisted surgery group demonstrated significantly superior KSS scores and joint ROM compared to the surgery-only group, indicating enhanced joint function and ROM. The mechanisms may include active movement promoted by pain relief, joint mechanical balance improved by cartilage repair, and exudation and adhesions reduced via synovial inflammation regulation [31]. Of note, greater improvements were observed in KSS function scores (walking distance, stair climbing ability), which may be related to PRP's potential role in regulating tendon repair and muscle metabolism. Although the excellent/

good rate was higher in the PRP-assisted surgery group than the surgery-only group, the difference was not statistically significant; this may be caused by the small sample size and short follow-up period in this study. However, the efficacy of PRP monotherapy versus PRP combined with other biological agents (e.g., sodium hyaluronate) was not compared, making it difficult to clearly define the relative advantages of PRP-assisted surgery. Further research is needed to validate these findings. In a report by Zhang et al. [32], PRP-assisted high tibial osteotomy was found to be more effective in improving knee function and ROM in KOA patients, consistent with the findings of this study.

Safety analysis and clinical applicability

No serious ARs occurred in either group. The incidence of minor reactions (local swelling) was low, without intergroup differences ($P > 0.05$), confirming the safety of PRP-assisted surgery. As an autologous biological product, PRP avoids the risk of immune rejection, but attention must be paid to the sterility control during preparation and precise injection technique. This study enrolled patients with early-stage KOA (Kellgren-Lawrence grades I-III). The efficacy may be limited for grade IV conditions, which may require treatment in combination with joint replacement. In a randomized clinical trial by Xu et al. [33], the combination of PRP and pulsed electromagnetic field therapy in patients with early-stage KOA did not result in increased incidence of ARs compared to either PRP alone or pulsed electromagnetic field therapy alone, which is consistent with the findings of this study.

Study limitations and future directions

This study has the following limitations: (1) It is a single-center, small-sample (69 cases) study conducted without blinding, which may have introduced bias; (2) Follow-up was limited to 6 months, resulting in a lack of long-term efficacy data; (3) The efficacy of PRP with other treatment regimens was not compared. In the future, multi-center, large-sample RCT with extended follow-up periods of 2-5 years are needed, while optimizing PRP preparation parameters (platelet concentration, activation method) to explore personalized treatment strategies.

In summary, this study confirmed through RCT that PRP-assisted knee-preserving surgery significantly relieved pain symptoms in early-stage KOA patients, regulated the balance between cartilage repair and degradation, suppressed synovial inflammation and oxidative stress, improved knee function and ROM, and exhibited favorable safety profiles. These findings provide a novel therapeutic approach for early-stage KOA: integrating the “repair - anti-inflammatory - analgesic” multifunctional effects of PRP with knee-preserving surgery to establish a stepwise treatment strategy. In clinical practice, PRP-assisted surgery may serve as a transitional solution between conservative management and joint replacement, particularly benefiting younger early-stage KOA patients with high activity demands.

Acknowledgements

This study was supported by Science and Technology Innovation Project of the Health System of Putuo District, Shanghai, Project No.: ptKwws202411.

Disclosure of conflict of interest

None.

Address correspondence to: Qingchun Liu, Department of Orthopedics, Liqun Hospital, Putuo District, No. 910 Taopu Road, Putuo District, Shanghai 200333, China. Tel: +86-021-52780030; E-mail: c550676724@163.com

References

[1] Diab AG, El-Kenawy EM, Areed NFF, Amer HM and El-Seddek M. A metaheuristic optimization-based approach for accurate prediction and classification of knee osteoarthritis. Sci Rep 2025; 15: 16815.

[2] Ishii Y, Noguchi H, Sato J, Takahashi I, Ishii H, Ishii R, Ishii K, Ishii K, Toyabe SI and Ogawara T. Pain relief improves key motor functions in refractory advanced knee osteoarthritis. Cureus 2025; 17: e83944.

[3] Langworthy M, Dasa V and Spitzer AI. Knee osteoarthritis: disease burden, available treatments, and emerging options. Ther Adv Musculoskelet Dis 2024; 16: 1759720X2412-73009.

[4] Zhu H, Yan XH, Chen S, Zhang GY, Zhang HB, Yang JS and Wang YY. Mechanism of electroacupuncture in improving cartilage tissue

injury in rats with knee osteoarthritis by regulating miR-335-5p expression. Zhen Ci Yan Jiu 2025; 50: 310-318.
[5] Yan J, Liu Q, Dai G, Wu C, Song N, Zhang B, Yang L and Yao C. Efficacy of multiple autologous apheresis platelet-rich plasma injections for treating knee osteoarthritis and its influencing factors: a retrospective cohort study. J Orthop Surg Res 2025; 20: 339.
[6] Patel S, Thami T, Gahlaut S, Chouhan D and Dhillon MS. Comparison of conventional dose versus superdose platelet-rich plasma for knee osteoarthritis: response. Orthop J Sports Med 2024; 12: 23259671241255962.
[7] Geng R, Li J, Yu C, Zhang C, Chen F, Chen J, Ni H, Wang J, Kang K, Wei Z, Xu Y and Jin T. Knee osteoarthritis: current status and research progress in treatment (review). Exp Ther Med 2023; 26: 481.
[8] Kon E, Anzillotti G, Conte P, Ruosi L, Cole B, Dragoo J, Zaslav K, Frank R, De Girolamo L, Mandelbaum B, Rodeo S, Marcacci M, Filardo G and Di Matteo B. The chimera of reaching a universal consensus on platelet-rich plasma treatment for knee osteoarthritis: a review of recent consensus statements and expert opinion. Expert Opin Biol Ther 2024; 24: 827-833.
[9] Klein J, Soni C, Ayotte B, Castro-Nunez C and Feketeova E. Are patients with knee osteoarthritis aware that platelet-rich plasma is a treatment option? Medicine (Baltimore) 2024; 103: e36712.
[10] Cheng L, Wang K, Chang S, Tan Y and He B. Effects of platelet-rich plasma combined with isometric quadriceps contraction on cartilage in a rat model of knee osteoarthritis. Regen Ther 2024; 26: 469-477.
[11] Zhang K, Xu T, Xie H, Li J and Fu W. Donor-matched peripheral blood-derived mesenchymal stem cells combined with platelet-rich plasma synergistically ameliorate surgery-induced osteoarthritis in rabbits: an in vitro and in vivo study. Am J Sports Med 2023; 51: 3008-3024.
[12] Kale P, Shrivastava S, Pundkar A and Balusani P. Harnessing healing power: a comprehensive review on platelet-rich plasma in compound fracture care. Cureus 2024; 16: e52722.
[13] Sivaramakrishnan G, Sridharan K and AlMuharraqi MA. Effectiveness of platelet-rich fibrin or platelet-rich plasma in mandibular fracture management: a systematic review and meta-analysis. J Stomatol Oral Maxillofac Surg 2026; 127: 102544.
[14] Kim KI, In Y, Choi HS, Lee JH, Sim JA, Lee HJ, Moon YW, Shon OJ, Seon JK, Kim YM, Song SJ, Chang CB and Han HS. A multicentre, double-blind, randomised, non-inferiority trial of a novel single-injection intra-articular HMDA-cross-linked hyaluronate gel for knee osteoarthritis. J Clin Med 2025; 14: 4384.
[15] Glinkowski WM, Gut G and Sladowski D. Platelet-rich plasma for knee osteoarthritis: a comprehensive narrative review of the mechanisms, preparation protocols, and clinical evidence. J Clin Med 2025; 14: 3983.
[16] Xie X, Zhang C and Tuan RS. Biology of platelet-rich plasma and its clinical application in cartilage repair. Arthritis Res Ther 2014; 16: 204.
[17] Cai L, Chen J, Yuan Q, Zhuang W, Wang G, Xu X, Yao Y and Hu WW. Recent advances in platelet-rich plasma therapy for osteoarthritis: mechanisms and clinical efficacy. J Mater Chem B 2025; 13: 9001-9022.
[18] Srinivasan V, Ethiraj P, Agarawal S, H S A and Parmanantham M. Comparison of various modalities in the treatment of early knee osteoarthritis: an unsolved controversy. Cureus 2023; 15: e33630.
[19] Zhu Y, Tao H, Jin C, Liu Y, Lu X, Hu X and Wang X. Transforming growth factor-beta1 induces type II collagen and aggrecan expression via activation of extracellular signal-regulated kinase 1/2 and Smad2/3 signaling pathways. Mol Med Rep 2015; 12: 5573-5579.
[20] Wen C, Xu L, Xu X, Wang D, Liang Y and Duan L. Insulin-like growth factor-1 in articular cartilage repair for osteoarthritis treatment. Arthritis Res Ther 2021; 23: 277.
[21] Cheng L, Chang S, Tan Y and 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: 81-89.
[22] Betsch M, Schneppendahl J, Thuns S, Herten M, Sager M, Jungbluth P, Hakimi M and Wild M. Bone marrow aspiration concentrate and platelet rich plasma for osteochondral repair in a porcine osteochondral defect model. PLoS One 2013; 8: e71602.
[23] Zhang JY, Xiang XN, Wang Q, Wang XX, Guan AJ, He CQ, Yu X and He HC. The effect of platelet-rich plasma on synovial fibrosis and cartilage degeneration in knee osteoarthritis. Am J Sports Med 2025; 53: 1428-1439.
[24] Du X, Liu ZY, Tao XX, Mei YL, Zhou DQ, Cheng K, Gao SL, Shi HY, Song C and Zhang XM. Research progress on the pathogenesis of knee osteoarthritis. Orthop Surg 2023; 15: 2213-2224.
[25] Tang H, Gong X, Dai J, Gu J, Dong Z, Xu Y, Hu Z, Zhao C, Deng J and Dong S. The IRF1/GBP5 axis promotes osteoarthritis progression by activating chondrocyte pyroptosis. J Orthop Translat 2024; 44: 47-59.
[26] Xu J, Chen X, Zhang H, Zhang X, Liu R, Li X, Wang J and Li T. Platelet-rich plasma relieves

inflammation and pain by regulating M1/M2 macrophage polarization in knee osteoarthritis rats. Sci Rep 2025; 15: 12805.
[27] He Q, Yang J, Pan Z, Zhang G, Chen B, Li S, Xiao J, Tan F, Wang Z, Chen P and Wang H. Biochanin a protects against iron overload associated knee osteoarthritis via regulating iron levels and NRF2/System xc-/GPX4 axis. Biomed Pharmacother 2023; 157: 113915.
[28] He R, Wei Y, Peng Z, Yang J, Zhou Z, Li A, Wu Y, Wang M, Li X, Zhao D, Liu Z, Dong H and Leng X. alpha-Ketoglutarate alleviates osteoarthritis by inhibiting ferroptosis via the ETV4/SLC7A11/GPX4 signaling pathway. Cell Mol Biol Lett 2024; 29: 88.
[29] Wang Z, Zheng X, Lin J, Zhou B, Zeng Z, Gao H, Chen H and Tang C. Electroacupuncture ameliorates cartilage damage in a rat model of knee osteoarthritis and regulates expression of miRNAs and the TLR4/NF-kappaB pathway. Acupunct Med 2025; 43: 164-173.
[30] Gato-Calvo L, Hermida-Gomez T, Romero CR, Burguera EF and Blanco FJ. Anti-inflammatory effects of novel standardized platelet rich plasma releasates on knee osteoarthritic chondrocytes and cartilage in vitro. Curr Pharm Biotechnol 2019; 20: 920-933.
[31] Wang C and Yao B. Efficacy and safety of platelet-rich plasma injections for the treatment of knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Eur J Med Res 2025; 30: 992.
[32] Zhang W, Ma Y, Lu F, Song H and Hu Y. Efficacy and safety of high tibial osteotomy combined with platelet-rich plasma for treating knee osteoarthritis: a systematic review and meta-analysis of the Chinese population. BMC Musculoskelet Disord 2024; 25: 876.
[33] Xu RD, Li JH, Zhang H, Liang HR, Duan SY, Sun M, Wen H, Zhou XT, Liu HF and Cai ZC. The combined application of pulsed electromagnetic fields and platelet-rich plasma in the treatment of early-stage knee osteoarthritis: a randomized clinical trial. Medicine (Baltimore) 2024; 103: e39369.