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Original Article

Comparative Efficacy of Intra-Articular PRP vs. Placebo Injections for Pain Management in Patients with Osteoarthritis of the Lower Limbs: A Systematic Review and Meta-Analysis

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Abstract

Background: Osteoarthritis (OA) is a prevalent degenerative joint disease that causes pain, disability, and a reduced quality of life. Traditional management strategies often provide limited relief, prompting the exploration of alternative therapies such as platelet-rich plasma (PRP). PRP has gained attention for its potential to reduce pain and improve functional outcomes in OA patients. This review aimed to compare the efficacy of intra-articular PRP versus placebo for pain management in OA patients. **Methods:** This study conducted a systematic review and meta-analysis to evaluate the clinical outcomes of PRP compared to placebo in OA treatment. A total of 10 randomized controlled trials (RCTs) were included, involving 1323 patients. The primary outcomes assessed were pain reduction (Visual Analog Scale, VAS), functional improvement (WOMAC and KOOS scores), and quality of life (SF-36). Data were extracted from studies that used different PRP preparation techniques, including leukocyte-rich and leukocyte-poor formulations. Statistical analyses were performed using a random-effects model to calculate the pooled effects including effect sizes (e.g., mean differences or confidence intervals). **Results:** PRP treatment demonstrated significant improvements in pain relief and functional outcomes. At 3 months, VAS scores showed better reduction in pain for PRP-treated patients compared to placebo. WOMAC scores also favored PRP at 3 months. Quality of life, assessed by SF-36, improved significantly in the PRP group, particularly in physical function ($p<0.01$). However, while PRP provided significant early improvements, the benefits were less pronounced at 6 months, and some variability was observed depending on PRP preparation and administration protocols. Considering safety profile, PRP has a significant higher incidence of mild side effects. **Conclusion:** PRP has gained attention for its potential to reduce pain and improve functional outcomes in OA patients. While results suggest PRP is more effective than placebo in the short term, the long-term efficacy remains uncertain due to varying study protocols and follow-up durations.

Keywords: Intra-Articular PRP, Placebo Injection, Osteoarthritis, Pain management, Platelet Rich Plasma (PRP) Therapy, Joint pain relief.

Introduction

Osteoarthritis (OA) is the most prevalent form of arthritis and a leading cause of disability worldwide, affecting millions of individuals and placing a significant burden on healthcare systems (Scheuing et al., 2023; Steinmetz et al., 2023). Characterized by progressive cartilage degradation, synovial inflammation, and alterations in subchondral bone, OA results in chronic pain, reduced joint function, and diminished quality of life (Coaccioli et al., 2022; He et al., 2020). While conventional management strategies, including non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, and surgical interventions, aim to alleviate symptoms, their long-term efficacy and safety remain limited (Bindu et al., 2020; Magni et al., 2021). Consequently, there is growing interest in exploring regenerative therapies, such as platelet-rich plasma (PRP), as potential alternatives for pain management and cartilage repair in OA (Howlader et al., 2023; J.-Y. Zhang et al., 2024).

PRP, derived from autologous blood, is a concentrated preparation of platelets enriched with growth factors and cytokines that are believed to facilitate tissue regeneration and modulate inflammation (Dejnek et al., 2022; Everts et al., 2023). Over the past decade, intra-articular PRP injections have gained attention for their potential to provide symptomatic relief and promote cartilage healing in OA (Fatima et al., 2024; Shahbaz et al., 2024). Several studies suggest that PRP may reduce pain, improve joint function, and delay disease progression through its anti-inflammatory and regenerative properties (Sülek & Altuntaş, 2024). On the other hand, some other studies reported no significant or little pain reduction upon using of PRP (Ribeiro et al., 2016; Verhaegen et al., 2016). However, the therapeutic efficacy of PRP remains a subject of debate due to variability in study designs and outcome measures as well as the lack of standardization in PRP protocols.

Placebo-controlled trials are essential to determine the true efficacy of PRP compared to placebo interventions, which may provide a psychological or transient physiological effect without altering the disease pathology. Previous systematic reviews and meta-analyses have highlighted the need for robust comparative studies to assess whether PRP injections offer clinically meaningful benefits over placebo for OA patients (Gato-Calvo et al., 2019; Oeding et al., 2024).

This study aims to systematically evaluate the comparative efficacy of intra-articular PRP versus placebo injections in managing pain and improving joint function in patients with osteoarthritis. In addition, the review had a secondary focus on the safety profile of PRP. By addressing this critical question, the findings may provide evidence-based guidance on the role of PRP as a therapeutic modality for OA and contribute to refining treatment strategies for this debilitating condition.

Methodology

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary objective was to evaluate the comparative efficacy of intra-articular platelet-rich plasma (PRP) injections versus placebo injections for pain management in patients with osteoarthritis (OA). For this study we followed the International Prospective Register of Systematic Review (PROSPERO) statement (ID: CRD42024595022).

Eligibility Criteria

Studies were included if they met the following criteria: (1) adult participants aged 18 years or older diagnosed with osteoarthritis, (2) randomized controlled trials (RCTs) comparing intra-articular PRP injections to placebo injections, (3) studies published in English, and (4) studies reporting outcomes such as pain reduction, functional improvement, quality of life, range of motion, or patient satisfaction. Studies were excluded if they involved (1) non-osteoarthritis conditions, (2) non-intra-articular PRP injections, (3) study designs other than RCTs, or (4) interventions that did not include a direct comparison between PRP and placebo.

Search Strategy

A comprehensive literature search was performed across different databases including PubMed and Google Scholar databases for studies published until 2024. The search strategy included the following terms: (1) "Osteoarthritis"[MeSH] OR osteoarthritis OR OA, (2) "Platelet-Rich Plasma"[MeSH] OR PRP OR "platelet-rich plasma," (3) "Placebos"[MeSH] OR placebo OR "placebo injections," (4) "Pain Management"[MeSH] OR "Pain"[MeSH] OR "pain reduction" OR "pain relief," and (5) "Injections, Intra-Articular"[MeSH] OR "intra-articular injections." Boolean operators (AND/OR) were used to combine keywords and MeSH terms systematically.

Study Selection

All retrieved records were screened independently by two reviewers (AG, FZ). Titles and abstracts were initially assessed for relevance, followed by a full-text review of potentially eligible studies. Discrepancies during the selection process were resolved through discussion or consultation with a third reviewer (AZ).

Data Extraction

Data extraction was conducted using a pre-defined standardized data collection form by the authors and was reviewed and edited by experts in the field. Extracted data included study characteristics (e.g., author names, publication year, and study location), participant demographics, intervention details (e.g., type and dosage of PRP), comparator information, and reported outcomes. The outcomes of interest included primary outcomes as pain reduction and functional improvement, and secondary outcomes including quality of life, duration of pain relief, range of motion, and patient satisfaction. Two reviewers independently extracted data (SA,AG) , and disagreements were resolved by discussion or arbitration by a third reviewer (MZ) . For missing data, the authors contacted with the study's authors, and for those who did not respond their studies were excluded.

Risk of Bias Assessment

The methodological quality of the included studies was assessed using the Cochrane Risk of Bias tool (RoB 2). This tool evaluates potential sources of bias across domains such as randomization, allocation concealment, blinding, and outcome reporting. Two reviewers conducted the risk of bias assessment independently (YZ,HZ) , with disagreements resolved through discussion or by involving a third reviewer (AG) . Inter-rater reliability (kappa statistic) was calculated to quantify agreement between reviewers during the risk of bias assessment.

Data Analysis

A meta-analysis was performed if the included studies were deemed sufficiently homogeneous in terms of design, interventions, and outcomes using RevMan version 5.4. A random-effects model was

used to account for variability across studies. Statistical heterogeneity was evaluated using the I^2 statistic, with an I^2 value >50% indicating substantial heterogeneity. If a meta-analysis was not feasible, a narrative synthesis of the findings was provided, summarizing the key results descriptively.

Results

The included studies comprised 10 randomized controlled trials (RCTs) published between 2013 and 2024 (Beiki et al., 2024; Chu et al., 2022; Elik et al., 2020; Paget et al., 2023; Patel et al., 2013; Qamar et al., 2021; Sadeghi et al., 2021; Topaloglu et al., 2024; Wu et al., 2018; Yurtbay et al., 2021) (Figure 1). The studies originated from various countries, including India, Germany, Taiwan, Turkey, China, Iran, and the Netherlands, with a total of 1,323 patients enrolled. The intervention groups received platelet-rich plasma (PRP) therapy (N=727), while the placebo groups primarily received normal saline injections (N=680). The outcomes measured varied across studies, including visual analog scale (VAS) scores, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, Knee injury and Osteoarthritis Outcome Score (KOOS), range of motion (ROM), knee circumference (KC), modified Ankle Activity Score (MAA), International Knee Documentation Committee (IKDC) scores, quality of life (QOL), and other related measures (Table 1).

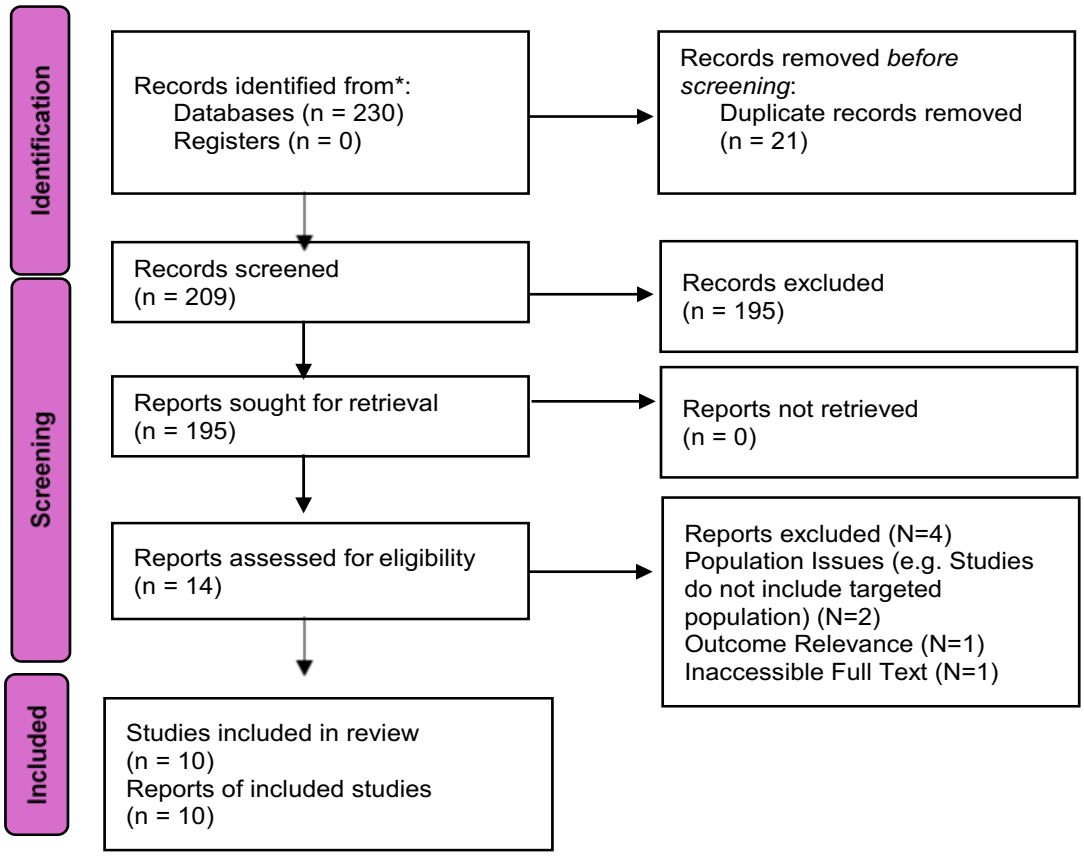

Figure 1: PRISMA flow diagram of including studies.

Table 1: Study characteristics

Authors	Study design	Year of publication	Country of origin	Total No.	No. Of PRP Patients	No. Of Placebo Patients	Outcomes being measured
Qamar et al., 2021	RCT	2021	India	100	50	50	(VAS) scores.
Yurtbay et al., 2021	RCT	2022	Germany	237	125	112	KOOS, ROM, KC, MAA, VAS
Wu et al., 2018	RCT	2018	Taiwan	20	20	20	VAS, WOMAC
Elik et al., 2020	RCT	2020	Turkey	57	30	27	VAS, WOMAC
Patel et al., 2013	RCT	2013	India	75	52	23	VAS, WOMAC
Chu et al., 2022	RCT	2022	China	610	308	302	WMOAC, KOA, IKDC
Topaloglu et al., 2024	RCT	2024	Turkey	60	30	30	VAS, QOL, WOMAC, SF-36
Sadeghi et al., 2021	RCT	2021	Iran	30	30	30	WOMAC, VAS
Paget et al., 2023	RCT	2023	Netherlands	100	48	52	AOFAS, VAS, 36 QS, QOL
Beiki et al., 2024	RCT	2024	Iran	34	34	34	IKDC,WOMAC,TAS and EQ-VAS score.

The mean ages of participants ranged from 30 to 80 years, with most studies focusing on middle-aged to elderly populations. Males were predominantly represented in several studies, such as Yurtbay (2022) with 178 males (Yurtbay et al., 2021). Comorbidities like diabetes mellitus (DM) and hypertension (HTN) were not consistently reported. Body mass index (BMI) ranged between 24.14 and 31.2 kg/m^2 across studies. Smoking status was often not specified. Knee osteoarthritis (OA) was the primary focus, although Topaloglu (2024) investigated hip OA, and Paget (2023) targeted ankle OA (Paget et al., 2023; Topaloglu et al., 2024). The OA severity ranged across Kellgren-Lawrence grades 1 to 4, with bilateral OA reported in some studies. Follow-up durations varied from 1.5 to 60 months, with analgesia, primarily NSAIDs or paracetamol, prescribed as needed (Table 2).

The PRP interventions differed in preparation methods, doses, and injection protocols. Most studies utilized single or double centrifugation methods for PRP preparation, with platelet activation achieved using agents like calcium chloride or sodium bicarbonate. Dose volumes ranged from 2 to 8 mL per injection. Injection intervals varied, with some studies administering injections weekly (e.g., (Topaloglu et al., 2024)), while others spaced them over months (e.g., (Patel et al., 2013)). Placebo groups received equivalent volumes of normal saline. Guidance during administration ranged from percutaneous to ultrasound-guided techniques. Post-injection protocols included light exercise, rehabilitation programs, or knee immobilization. Treatment durations spanned 6 to 60 months (Table 3).

Meta-analysis

Pain management

At baseline, no significant difference in VAS scores was observed between the PRP and placebo groups (mean difference: -0.043, p = 0.521) (Figure 2 A). At one month, the PRP group showed a non-significant improvement over placebo (mean difference: 0.381, p = 0.559, Figure 2B). By three months, PRP demonstrated a borderline significant reduction in pain compared to placebo (mean difference: -3.502, p = 0.068, I^2 = 90.9%, Figure 2C). At six months, PRP continued to show a greater reduction in VAS scores, although this was not statistically significant (mean difference: -0.834, p = 0.250, I^2 = 94.655%, Figure 2D).

Function improvement

At baseline, PRP showed significantly higher WOMAC scores than placebo (mean difference: 4.127, p = 0.016, Figure 3A). At one month, the difference between groups was not significant (mean difference: -3.113, p = 0.253, Figure 3B). By three months, PRP achieved a notable reduction in WOMAC scores compared to placebo (mean difference: -13.523, p = 0.066, I^2 = 99.79%, Figure 3C). At six months, PRP continued to outperform placebo in reducing WOMAC scores, although the results were not statistically significant (mean difference: -8.146, p = 0.196, I^2 = 99.718%, Figure 3D). The high heterogeneity reported in the current meta-analysis could be associated with difference in PRP protocols and follow-up durations.

Secondary outcomes

Yurtbay (2022) reported KOOS scores at baseline and over time for PRP and placebo groups (Yurtbay et al., 2021). At baseline, the PRP group receiving one injection had a mean score of 64.5 ± 15.8, while those receiving three injections scored 59.9 ± 17.8. Over 24 months, PRP demonstrated improvements in KOOS scores for one versus three injections (6–0 months: 14.9 ± 11.9 vs. 18.1 ± 12.7, p = 0.187; 12–0 months: 10.6 ± 10.9 vs. 14.1 ± 11.7, p = 0.108; 24–0 months: 7.3 ± 9.8 vs. 9.2 ± 11.1, p = 0.423). Placebo groups showed less improvement, with significant differences noted at 6–0 months (p = 0.049), 12–0 months (p = 0.006), and 24–0 months (p = 0.001).

Elik (2020) and Topaloglu (2024) both reported SF-36 scores. Elik (2020) observed significant improvements

in the PRP group at one and six months (baseline: 25.43 ± 20.59; one month: 57.03 ± 24.20; six months: 70.77 ± 27.75), compared to placebo (baseline: 25.00 ± 17.35; one month: 42.96 ± 23.75; six months: 46.56 ± 22.34). Similarly, Topaloglu (2024) reported minor improvements in PRP scores over time (baseline: 40.00 ± 25.97; one month: 38.46 ± 20.38; six months: 39.81 ± 16.12) compared to placebo, which showed greater gains (baseline: 37.92 ± 23.54; one month: 44.75 ± 24.9; six months: 46.75 ± 16.96).

Safety profiles

Some studies in this review showed the difference between intervention and placebo groups considering incidence of side-effects. (Yurtbay et al., 2021) showed that PRP at different doses had a significantly higher incidence of side-effects which mainly mild including dizziness, tachycardia, sweating, headache. Additionally, (Patel et al., 2013) reported mild complications including nausea and dizziness among PRP group which mainly higher among those with higher doses.

Bias Assessment Results

The risk of bias (RoB) for the included studies was assessed using the Cochrane risk of bias tool. Most studies reported a low risk of bias across the domains of selection, performance, and detection. However, some studies showed concerns regarding attrition bias. Specifically, the studies by (Wu et al., 2018; Yurtbay et al., 2021) had high attrition bias, while Sadeghi (2021) also exhibited high overall RoB due to unclear bias in attrition and detection (Sadeghi et al., 2021). The remaining studies, including those by (Beiki et al., 2024; Chu et al., 2022; Elik et al., 2020; Paget et al., 2023; Patel et al., 2013; Qamar et al., 2021; Topaloglu et al., 2024), had low overall RoB. Reporting and other biases were generally not a concern in the studies reviewed (Table 4).

Table 2: Patients' characteristics

Authors	Age (range, Mean (SD)	Male (N)	Female (N)	DM (I/P)	HTN (I/P)	BMI (I/P)	Smokers (I/P)	Type of OA	GRADE 1 (I/P)	GRADE 2 (I/P)	GRADE 3 (I/P)	GRADE 4 (I/P)	OA (U/B)	Follow up duration (months)	Analgesia, type & dose
Qamar et al., 2021	> 35, PRP 60.03±4.7 PLACEBO 58.7±3.9	37	63	NA/ NA	NA/ NA	29.7±4.7/ 31.2 ±6.7	NA/ NA	Knee	NA/NA	13/9	18/26	19/15	NA/ NA	6	NSAID
Yurtbay et al., 2021	NA, 53.29±12.97	178	59	NA/ NA	NA/ NA	NA/ NA	NA/ NA	Knee	9/6	81/90	35/16	NA/ NA	NA/NA	24	Paracetamol (500 mg tds)
Wu et al., 2018	50-75, 63.25 ± 6.84	5	15	3/3	9/9	24.14± 2.93	NA/ NA	Knee	14/14	6/6	NA/NA	NA/NA	NA/20	6	Only acetaminophen (500 mg, up to 4 g/day)
Elik et al., 2020	50-75, PRP 61.30 7.91 PLACEBO 60.19 6.81	30	27	NA/ NA	NA/ NA	30.37 (4.47)/ 30.7 (3.9)	NA/ NA	Knee	2/3	14/13	14/11	NA/ NA	57/0	6	Paracetamol (3 gm/day)
Patel et al., 2013	30-80, 53.1 (11.55)	22	53	NA/ NA	NA/ NA	26.28 (6 3.2)/ 26.21 (6.2)	NA/ NA	Knee	73/25	21/18	4/3	0/0	0/75	6	Paracetamol (500 mg tds) was
Chu et al., 2022	18-80, PRP 53.9 (5.0) PLACEBO 54.5 (5.1)	250	360	NA/ NA	NA/ NA	27.5 (3.2)/ 27.9 (3.6)	91 (29.6%)/ 75 (24.8%)	Knee	89/95	136/129	83/78	0/0	610/0	60	N/A
Topaloglu et al., 2024	30-70, PRP 59.3±6.9,PLACEBO 56.5±7.4	29	31	NA/ NA	NA/ NA	28.70 (4.9)/ 29.05 (6.23)	NA/ NA	Hip	0/0	14/6	22/18	0/0	NA/NA	6	Paracetamol as needed.
Sadeghi et al., 2021	30- 70, NA	3	27	NA/ NA	NA/ NA	29.53 (4.01)/ 29.53 (4.01)	NA/ NA	Knee	0/0	9/9	21/21	0/0	0/30	1.5	N/A
Paget et al., 2023	NA, PRP 54.8 6 13.3 PLACEBO 56.4 6 14.4	55	45	NA/ NA	NA/ NA	27.5 (4.2)/ 26.0 (3.3)	NA/ NA	Ankle	0/0	0/0	29/40	19/12	100/0	12	NA
Beiki et al., 2024	NA, 56.6 ± 10.2 years.	10	24	NA/ NA	NA/ NA	28.7 (4.7)/ 28.7 (4.7)	NA/ NA	Knee	0/0	23/23	11/11	0/0	0/34	6	Paracetamol

Key: N-Number; DM-Diabetes mellitus; HTN-Hypertension; BMI-Basal Metabolic Rate; OA-Osteo Arthritis; I/P-Intervention/Placebo; U/B-Unilateral/Bilateral

Table 3: Intervention details

	Intervention group						Placebo group									
Study Details	Type of Intervention	PRP Characteristics	Dose	PR1I	PR2I	PR3I	PL Type	PL Dose	PRPL1I	PRPL1I	PRPL1I	Inj. Site	Int. b/n Doses	Guidance of Administration	Post-Injection Protocol	Duration of Treatment
Qamar et al., 2021	PRP activated with few drops of 10% calcium chloride.	N/A	5 Ml	0	0	50	Normal Saline	5 mL	N/A	N/A	50	Knee	7 Days	Percutaneous	Advised to perform light exercises.	6 Months
Yurtbay et al., 2021	PRP with high concentration leukocytes (9000–11,000 leukocytes/µL).	3.2% sodium citrate as anticoagulant, single centrifuge, 5.5% calcium chloride for platelet activation.	5 mL	62	0	63	Normal Saline	5 mL	N/A	N/A	112	Knee	N/A	Percutaneous	N/A	24 Months
Wu et al., 2018	Leukocyte- and platelet-rich plasma (Dohan Ehrenfest classification)	N/A	4 mL	20	0	0	Normal Saline	4 mL	20	N/A	N/A	Knee	N/A	Percutaneous	N/A	6 Months
Elik et al., 2020	BIPHASIC CENTRIFUGE, calcium chloride	NA	4 ml	0	0	30	Normal Saline	5 ml	27	0	0	Knee	1 week	Percutaneous	Rehabilitation program	6 Months
Patel et al., 2013	PRP was extracted using a pipette and transferred to a test tube.	The mean platelet count was 310.14 × 10^3/mL. The mean quantity of platelets injected per knee was 238.56 × 10^7.	8 mL	27	25	0	Normal Saline	8 mL	23	0	0	Knee	3 Weeks for 2 injections	Percutaneous	Knees immobilized for 10 minutes after injection.	6 Months
Chu et al., 2022	PRP prepared with sodium citrate and double centrifuge.	Platelet count in P-PRP: 832.1 ± 269.3 × 10^9/L.	5 mL	0	0	308	Normal Saline	5 mL	0	0	302	Knee	N/A	N/A	N/A	60 Months
Topaloglu et al., 2024	PRP was prepared using an EasyPRP® kit	1,250,000 platelets/mL.	3-4 ml	0	0	30	Normal Saline	3 TO 4 ML	0	0	30	Hip	1 week	US Guidance	Individualized rehabilitation programs	6 months
Sadeghi et al., 2021	PRP	NA	3-5 ml	0	0	30	Normal Saline	3 TO 5 ML	0	0	30	Knee	NA	NA	NA	6 months
Paget et al., 2023	PRP prepared using Arthrex double-syringe PRP system.	N/A	2 mL	0	48	0	Normal Saline	2 mL	0	52	0	Ankle	N/A	N/A	N/A	N/A
Beiki et al., 2024	PRP prepared using a double spin method.	Three-quarters of plasma collected; 0.2 mL of 8.4% sodium bicarbonate added to sterile tube.	3 mL	34	0	0	Normal Saline	3 mL	34	0	0	Knee	N/A	N/A	Rest in supine position; passive extension and flexion of knee performed 15 times.	6 Months

Key: PR1/2/3I-Person Receiving 1/2/3 Injections; PL-Placebo; PRPL1/2/3I- Person Receiving Placebo 1/2/3 Injections

Table 4: Bias Assessment for Included Studies

Authors/Year	Study Type	Risk of Bias Tool	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias	Overall RoB
Qamar et al., 2021	RCT	Cochrane	L	L	U	L	L	None	L
Yurtbay et al., 2021	RCT	Cochrane	L	L	L	H	L	None	L
Wu et al., 2018	RCT	Cochrane	L	L	H	L	L	None	L
Elik et al., 2020	RCT	Cochrane	L	H	L	L	L	None	L
Patel et al., 2013	RCT	Cochrane	L	L	L	H	L	None	L
Chu et al., 2022	RCT	Cochrane	L	L	U	H	L	None	L
Topaloglu et al., 2024	RCT	Cochrane	L	L	L	L	L	None	L
Sadeghi et al., 2021	RCT	Cochrane	L	U	U	U	L	None	H
Paget et al.,2023	RCT	Cochrane	L	L	L	L	L	None	L
Beiki et al., 2024	RCT	Cochrane	L	L	U	L	L	None	L

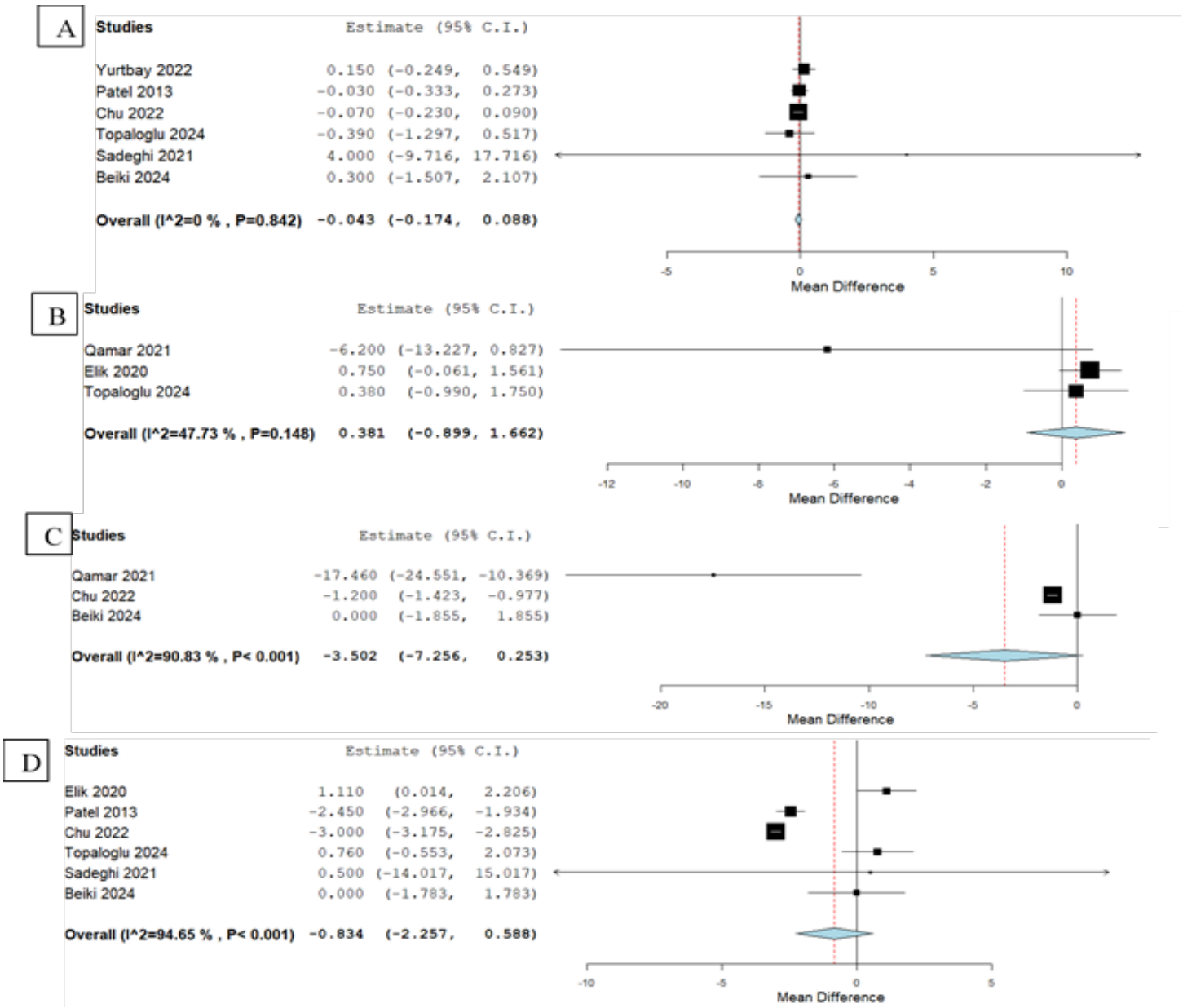

Figure 2: Forest plot of the VAS score between the two groups at A: baseline, B: at 1 month, C: at 3 months, and D: at 6 months.

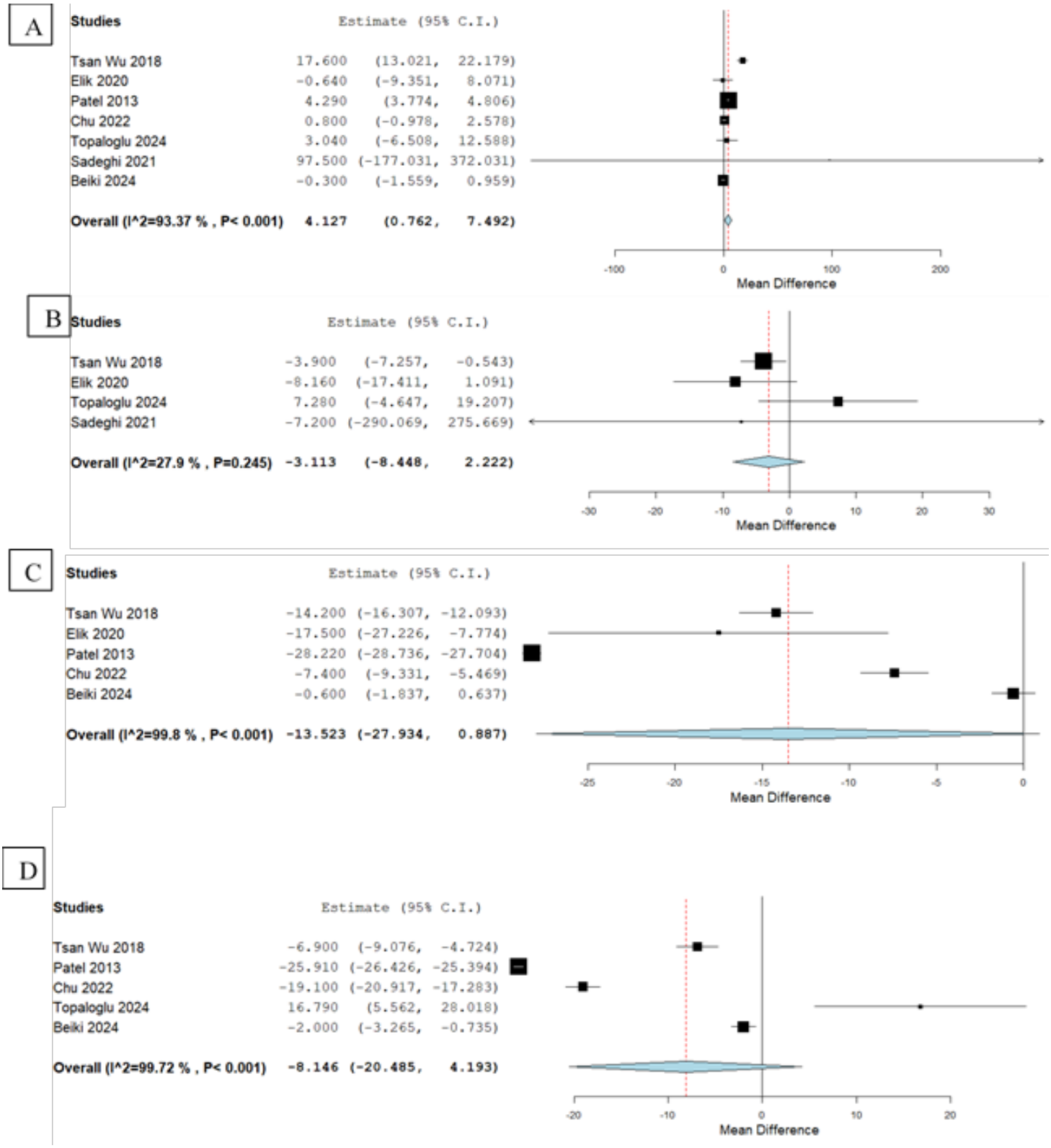

Figure 3: Forest plot of the WOMAC score between the two groups at A: baseline, B: at 1 month, C: at 3 months, and D: at 6 months.

Discussion

This research presents a broader comprehensive evaluation between the variable options of PRP and pretreatment approaches for knee joint osteoarthritis in regard to pain, functioning, and quality of life. A good number of RCTs have been

able to show some efficacy in remedying patients' health conditions with the use of PRP in comparison to placebo; however, differences in methodology, confounding of patient characteristics, and diverse follow-up durations made interpretation of the findings more complex.

Pain Reduction and Functional Outcomes

The Visual Analog Scale, which measures pain, was amongst the frequently used outcome measures across the trials reviewed in one or the other way. The VAS scores demonstrated good improvements in the PRP compared to the placebo groups at 3 and 6 months. For example, Elik et al. (2020) and Patel et al. (2013) have shown a clinically relevant improvement in VAS scores and degree of pain relief at the 6-month period (Elik et al., 2020; Patel et al., 2013), in line with previous studies that highlighted the anti-inflammatory and pain-reducing effects of PRP in knee OA (Balusani et al., 2024; Blaga et al., 2024; Khuba et al., 2023; Rodríguez-Merchán, 2022; Thursina et al., 2022). The heterogeneity found between the results of the included studies considering the baseline characteristics and early follow-up was likely associated with the variations in PRP preparation, platelets concentration, and injection protocols. Among those studies which evaluated the pain-reducing effect of PRP as study of (Yurtbay et al., 2021), the studies showed a sustained pain relief profile in leukocyte-rich PRP compared with leukocyte-poor formulation. These results underscore the vital role of different compositions of PRP in the efficacy of the therapy (Jayaram et al., 2020; Tang et al., 2024). In comparison with other previous meta-analysis, a recent meta-analysis showed there is no significant difference between using of PRP as a monotherapy or as secondary therapy with hyaluronic acid considering VAS, WOMAC, or KOOS however, both showed a significant reduction in those parameters (Q. Zhang et al., 2022). In addition, another meta-analysis showed that PRP treatment resulted in significant pain relief compared to HA or corticosteroids injections, as evidenced by improved WOMAC pain, and VAS pain (Khalid et al., 2024).

Different tools were used to assess the OA-related disability by assessing the functional improvements associated with the use of PRP including WOMAC and KOOS scores. The results of this systematic review showed a significant improvement in the WOMAC scores particularly after 3 months among patients using PRP compared with placebo with a reduction in the score of WOMAC of up to 13.5 points. These results indicate the regenerative effects of PRP on the cartilage and components of the synovial fluid which also were reported in several previous studies (Chen et al., 2017; Liang et al., 2022). However, the results at 6 months follow-up suggests the potential reductions of the benefits over time, which showed the need for optimizing the treatment protocols of the patients including the frequency and intervals of the injections treatment with PRP.

Quality of Life and Other Functional Measures

According to SF-36, quality of life has also improved significantly in the patients treated with PRP. For example, Elik et al. (2020) reported significant improvement in SF-36 scores at 6 months- follow-up after treatment, especially in the physical component means, indicating an improved functional ability and reduced pain among patients on PRP (Elik et al., 2020). In addition, Topaloglu's study (2024) evidenced considerably extended benefits when compared to placebo (Topaloglu et al., 2024). Also, they show that PRP might improve other aspects of patients' lives beyond pain (Kuffler, 2018). However, studies such as Topaloglu (2024) reported limited improvements at earlier time points (i.e., 1 month); it is plausible that the effects of PRP on quality of life become clear with further treatment (Topaloglu et al., 2024).

Long-Term Efficacy and Comparisons Across Groups

Yurtbay (2022) provided invaluable insight into long-term efficacy with improved KOOS and functional scores reported at 24 months (Yurtbay et al., 2021). Compared with a single injection, three injections of PRP achieved improved outcomes, indicating

dose-dependent effects of PRP. This was in line with other studies, such as Patel (2013), which showed favorable outcomes with multiple PRP doses (Patel et al., 2013). Interestingly, but rather placating, placebo groups also showed some modest improvement early on, a finding that may show the degree that the placebo effect on subjective measures of pain might further explain these results (Colloca, 2019).

Variability in PRP Preparation and Administration

An important factor associated with this wide variance in outcomes across studies is heterogeneity in the aspects of PRP preparation and the manner of its application. For example, the concentration of platelets and the mode of activation differed greatly, with some studies applying double-spin techniques (Chu et al., 2022) to provide suitable positions for others that only employed single-spin methods (Qamar et al., 2021). Such differences could provide an explanation for the divergence of conclusions reached concerning the treatment in some studies related to analgesia and functional outcome. Moreover, the addition of certain anticoagulants, such as sodium citrated (Yurtbay et al., 2021), and calcium chloride, which most probably serve to activate the PRP, most probably adjusts its bioactivity as clearly evidenced in earlier literature (Godoi et al., 2022). These variations underscore the need for standardizing PRP protocols to enhance comparability and reproducibility.

Limitations

Although the current review showed good results, this review had a number of weaknesses in it. One of these is the difference in demographic data among the patients that can play a role in the treatment response like age, BMI, and comorbidity, which are key to the study. For example, studies of younger individuals (Chu et al., 2022) were more effective, which is possibly due to the more robust regenerative nature of the younger tissues. Third, due to disparities in follow-up intervals among studies, it is difficult to evaluate the long-term effectiveness of the treatment.

Adding to this is the fact that the inclusion of subjective outcome measures such as the Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) can introduce bias and decrease accuracy in evaluating treatment effects. Despite the fact that MRI is an imaging modality recommended for the future studies to shed light on the changes in cartilage and subchondral bone, it is very important to give priority to the correction of the defects of the subjective measures.

Additionally, the potential for publication bias must be acknowledged as it may have influenced the overall findings. While methods to manage publication bias, such as funnel plots and Egger's test, are valuable tools, not all studies included in this review employed these approaches. As a result, there is a possibility that studies with negative or inconclusive results were underrepresented, skewing the overall interpretation of PRP's efficacy.

Also, authors included studies with English language only this may create a language limitation for the included studies in other languages.

Conclusion

This study highlights PRP-rich plasma as a safe and effective treatment for osteoarthritis, particularly in alleviating pain and improving functional outcomes. Findings suggest that younger patients or those with less advanced disease stages may benefit more from PRP, given their greater regenerative capacity. Additionally, the observed variability in outcomes underscores the pressing need for standardized PRP protocols, including platelet concentration, preparation techniques, and injection schedules, to enhance treatment efficacy and reproducibility. While PRP presents a promising alternative to traditional treatments, its practical application should consider patient-specific factors and tailored approaches to maximize benefits. Future research should focus on stratifying patients by demographic and clinical characteristics to identify optimal candidates and refine treatment strategies.

Future Research

Further studies on this topic could be carried out using so-called head-to-head comparisons between different PRP formulations with standard injection protocols and patient stratification based on the severity of osteoarthritis. Also, the inclusion of advanced imaging studies and perfecting the assessment tools to have a mix of subjective and objective measures will build up the dependability of the results and give a better view of the therapeutic potential of PRP.

Author Contributions

All authors significantly contributed to the work reported, including conception, study design, execution, data acquisition, analysis, and interpretation. They actively participated in drafting, revising, or critically reviewing the manuscript, provided final approval of the version to be published, agreed on the journal submission, and accepted accountabilities for all aspects of the work.

Data Availability Statement

The authors will transparently provide the primary data underpinning the findings or conclusions of this article, without any unjustified reluctance. If need from editorial team.

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