MEDICINE SOUTHEAST ASIA

SOPHISTICA
WHERE INNOVATION IN MEDICINE BEGINS

Review

The Effectiveness of Platelet-Rich Plasma in Alleviating Pain and Promoting Recovery in Knee Osteoarthritis: A Systematic Review and Meta-Analysis

Rifat Rasyid[1], Samuel Partogi Nababan[1], Debora Alim Riadi[1], Roy Novri Ramadhan[2], Jade Rampengan[3]*

[1] Faculty of Medicine, Universitas Sam Ratulangi - R. D. Kandou Central General Hospital, Manado, Indonesia
[2] Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[3] Faculty of Medicine, Universitas Atma Jaya, Jakarta, Indonesia
* Correspondence: Jade Rampengan (jadeaudreyc@gmail.com)

Abstract

Background: Knee osteoarthritis (OA) is a degenerative joint disease that causes chronic pain and functional limitation. Platelet-rich plasma (PRP) has been proposed to relieve symptoms and promote recovery, but trial results remain inconsistent. This systematic review and meta-analysis evaluated the effectiveness and safety of PRP for knee OA using validated pain and function outcomes.

Methods: This review followed the Cochrane Handbook and PRISMA. PubMed, Cochrane Library, EMBASE, Scopus, and ProQuest were searched for randomized controlled trials (restricted to 2018–2023) comparing intra-articular PRP with conventional therapy. Eligible studies enrolled adults/older adults with knee OA and reported VAS pain, WOMAC (function and/or pain), and/or IKDC. Risk of bias was assessed using RoB 2.0. Meta-analysis was performed in RevMan 5.4 using random-effects models; heterogeneity was assessed using I^2 and publication bias using funnel plots.

Results: Eleven RCTs (n=1884; mean age 65.2 years; predominantly female) were included. Controls were mainly hyaluronic acid, with some sham saline and other comparators; one trial combined PRP with bone marrow mesenchymal stem cells. PRP significantly reduced pain on VAS (SMD −0.75; 95% CI −1.48 to −0.02; p=0.04) and improved WOMAC global function (SMD −1.50; 95% CI −2.64 to −0.35; p=0.01) and WOMAC pain (SMD −1.02; 95% CI −1.98 to −0.06; p=0.04). IKDC improvement was not significant (SMD 0.86; 95% CI −0.87 to 2.60; p=0.33). Reported adverse events were generally mild, including injection-site pain/swelling and other transient symptoms.

Conclusion: PRP is associated with meaningful improvements in pain and WOMAC-measured outcomes in knee OA, but not IKDC, and results are limited by high heterogeneity. More standardized PRP protocols and longer follow-up trials—especially in resource-limited settings, are needed to clarify durability and generalizability.

Keywords: knee osteoarthritis; platelet-rich plasma; PRP; intra-articular injection; systematic review; meta-analysis; VAS; WOMAC; IKDC; randomized controlled trial

Academic Editor: Maulana A. Empitu

Received: 23 October 2025
Revised: 17 November 2025
Accepted: 25 December 2025
Published: date

Citation: To be added by editorial staff during production.

1. Introduction

Knee osteoarthritis (OA) is a degenerative joint disease characterized by the progressive loss of articular cartilage, leading to increased friction during mobility. Its etiology involves various factors, including chronic low-grade inflammation due to aging, pro-catabolic mediators, and mechanical stress, all of which contribute to structural joint degeneration, primarily through the loss of the extracellular matrix. As a result, individuals with knee OA often experience pain and reduced function, which worsen as the disease progresses.

Older adults are particularly susceptible to knee OA due to the chronic low-grade inflammation associated with aging. In Indonesia, the incidence of knee OA rises sharply between the ages of 50 and 75 before declining after 80, reflecting global trends. Given the substantial increase in the older adult population in Indonesia since 1994, it's logical to assume a corresponding rise in knee OA prevalence.

While patient education, exercise, and weight management are recommended as first-line treatments for knee OA, pharmacological interventions like NSAIDs pose risks, especially for older adults with comorbidities. Consequently, there's growing interest in alternative therapies. Intra-articular hyaluronic acid injections have shown promise in providing lubrication, shock absorption, and anti-inflammatory effects, but their cost remains a barrier to widespread use, leaving a gap in effective management strategies.

Platelet-rich plasma (PRP) therapy has garnered attention due to its potential to promote joint healing through growth factors present in platelets. However, PRP also contains inflammatory mediators that may exacerbate joint degradation. Despite increasing clinical trials, consensus on PRP's efficacy compared to other interventions remains elusive. Therefore, this meta-analysis and systematic review aim to assess PRP's effectiveness in alleviating pain and improving function in knee OA patients, as measured by the Visual Analogue Scale (VAS), International Knee Documentation Committee Subjective Knee Evaluation Form (IKDC), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Additionally, adverse effects of PRP will be examined to evaluate its feasibility in pain reduction and mobility improvement. Ultimately, this review aims to provide practical guidance for healthcare professionals considering PRP therapy for knee OA patients.

2. Results

2.1. Search Results and Study Characteristics

Quantitative analysis was conducted on eleven randomized controlled trials (RCTs), encompassing 1884 participants who received platelet-rich plasma (PRP) intervention compared to conventional therapy. All RCTs underwent qualitative analysis. The average participant age was 65.2 years, with females comprising the majority across all trials. Intra-articular PRP injection was the primary intervention in all studies, except Lamo-Espinosa et al. [1], which supplemented PRP with bone marrow mesenchymal stem cells. Although control groups varied, hyaluronic acid (HA), followed by sham saline and bone marrow cells, were the most frequently employed. Primary outcome measurement focused on Visual Analog Scale (VAS) pain reduction, while secondary outcomes included WOMAC global function and pain. Detailed study characteristics are provided in Appendix 4.

2.2. Study Outcome - Meta-analysis of the Efficacy of PRP in the Treatment of Knee OA

The meta-analysis encompassed eleven trials evaluating PRP efficacy for knee OA treatment. Results revealed a significant reduction in odds of knee OA occurrence post-PRP administration compared to baseline (OR = 0.48; 95% CI; 0.27 to 0.88, p-value = 0.02), with considerable heterogeneity (I^2 = 94%, $p < 0.00001$) (Appendix 5). Funnel plot analysis indicated no evidence of publication bias across trials (Appendix 6).

2.3. Study Outcome - VAS Pain Score

Analysis of VAS pain scores from five trials demonstrated a significant reduction post-PRP treatment (SMD = -0.75, 95% CI; -1.48, -0.02, p-value = 0.04), albeit with moderate heterogeneity (I^2 = 94%, p = 0.04) (Appendix 7). [Funnel plot VAS] (Appendix 8)

2.4. Study Outcome - IKDC Subjective Score

PRP treatment did not yield significant improvement in IKDC subjective scores for OA patients (SMD = 0.86, 95% CI; -0.87, 2.60, p-value = 0.33), with substantial heterogeneity (I^2 = 98%, p-value < 0.00001) (Appendix 9). Symmetrical funnel plot analysis suggested no publication bias (Appendix 10).

2.5. Study Outcome - WOMAC Global Function Score and WOMAC Pain Score

PRP intervention demonstrated superior improvement in WOMAC global function (SMD = -1.50, 95% CI; -2.64, -0.35, p-value = 0.01) and significant reduction in WOMAC pain (SMD = -1.02, 95% CI; -1.98, -0.06, p-value = 0.04) compared to control groups (Appendix 11).

3. Discussion

3.1. Mechanism of Platelet-Rich Plasma in Knee Osteoarthritis

Knee osteoarthritis stems from chronic proinflammatory mediators, pro-catabolic mediators, and mechanical stress, precipitating joint structural degeneration. Platelet-rich plasma (PRP) presents a potential therapeutic avenue due to its heightened platelet content compared to peripheral blood. Platelets harbor granules rich in growth factors such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF). These factors and other platelet-secreted substances exhibit diverse mechanisms including endothelial proliferation induction, angiogenesis initiation, lymphocyte and macrophage proliferation inhibition, and apoptotic inhibition, potentially fostering joint recovery. However, PRP also contains inflammatory mediators, matrix metalloproteins, and leukocytes, which, if unregulated, may contribute to joint degradation.

3.2. Efficacy of Platelet-Rich Plasma in Knee Osteoarthritis

This meta-analysis represents the first recent comprehensive investigation into PRP efficacy and clinical performance in knee osteoarthritis (OA). Results indicate PRP as a promising therapeutic modality for knee OA treatment, with improvements observed in VAS scores and WOMAC function and pain scores, though not in the IKDC score. These findings align with a previous meta-analysis comparing clinical outcomes of leukocyte-poor PRP and leukocyte-rich PRP. While WOMAC function score improvements showed insignificance, akin to our findings, a significant reduction in VAS scores was observed across trials.

3.3. Effectivity of Platelet-Rich Plasma in VAS Score Changes

Visual Analogue Scale (VAS) scores, measuring pain intensity, exhibited significant reductions post-PRP administration across multiple studies, indicating PRP's efficacy in alleviating knee OA-related pain.

3.4. Effectivity of Platelet-Rich Plasma in IKDC Score Changes

Despite PRP treatment, no significant improvement in International Knee Documentation Committee Subjective Knee Form (IKDC) scores was noted, with results

favoring control. Moreover, substantial heterogeneity was detected, indicating PRP's lack of efficacy in enhancing IKDC scores.

3.5. Improvement of WOMAC Function and Pain Reduction with Platelet-Rich Plasma

Meta-analysis revealed significant improvements in WOMAC function and pain scores following PRP treatment. While WOMAC pain score improvements were slightly less pronounced, PRP demonstrated efficacy in enhancing WOMAC function and pain scores.

3.6. Adverse Event of Platelet-Rich Plasma in Knee Osteoarthritis

Several adverse events were reported post-PRP treatment, including injection site pain, swelling, gastrointestinal disorders, and musculoskeletal pain. These findings underscore the importance of vigilant monitoring and management of potential complications associated with PRP therapy.

3.7. Strengths and Limitations

This study's strength lies in its exclusive focus on randomized controlled trials and the inclusion of various control group interventions, enabling comprehensive comparison. However, limitations include the restriction to studies from 2018 to 2023 and the high heterogeneity observed in follow-up periods and reported comorbidities.

4. Materials and Methods

4.1. Study Design

This meta-analysis and systematic review adhered to the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions 6.3 and followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.

4.2. Search Strategy

The meta-analysis utilized the PRISMA framework (Appendix 1). A comprehensive search was conducted across multiple databases including PubMed, Cochrane Library, EMBASE, Scopus, and ProQuest. The search strategy employed Boolean operators with keywords aligned with MeSH (Medical Subject Headings) terms, customized for each database's search manager.

4.3. Study Eligibility Criteria

Inclusion criteria were predefined according to the PICOS (Population, Intervention, Comparison, Outcome, Study design) framework (Appendix 2). Eligible studies included adult or elderly patients diagnosed with knee osteoarthritis, interventions involving platelet-rich plasma, comparisons against standard care, outcomes measured through WOMAC, VAS, and/or IKDC scores, and randomized controlled trials (RCTs). Exclusion criteria encompassed irretrievable full-text articles, non-English literature, and non-human clinical trials. Title and abstract screening was conducted independently by three reviewers (RRR, DRAS, SPN), with discrepancies resolved through discussion with a fourth reviewer (DDR) to reach consensus.

4.4. Data Extraction

A predetermined tabular format was used for data extraction, including author and publication year, study location, sample size, intervention details, adverse events, and outcome measures (VAS, WOMAC, IKDC, and KOOS). Three reviewers (RRR, DRAS,

SPN) performed qualitative evaluations, with data verification conducted by another author (DDR) during statistical analysis.

4.5. Quality Assessment and Publication Bias

Risk of bias in the included studies was assessed using the Revised Tool for Risk of Bias in Randomized Trials (RoB 2.0). Five domain areas were evaluated to assess bias potential. Assessment was conducted independently by three reviewers, and results were recorded in a bias domain file (.xlsx). Visualization of bias assessment was facilitated using the ROBVIS website. Discrepancies were resolved through consensus among reviewers. Evaluation of study quality is detailed in Appendix 3.

4.6. Quantitative Data Analysis

Statistical analysis was performed using RevMan version 5.4 software for systematic review and meta-analysis. Data extraction involved recording estimated means, standard deviations, and sample sizes for each study. A random-effects model was applied for continuous outcomes, while binary outcomes were analyzed using odds ratios. Heterogeneity was assessed using I^2, and publication bias was examined through funnel plots.

5. Conclusions

In conclusion, PRP emerges as a promising treatment option for knee OA, with significant improvements noted in VAS scores, WOMAC function, and pain scores. However, PRP failed to enhance IKDC scores, and substantial heterogeneity was observed across studies, highlighting the need for further research and standardization in PRP therapy for knee OA.

Further studies with longer follow-up time should be made to assess the long-term effect of PRP in Knee Osteoarthritis. Studies conducted in resource-limited settings are also still lacking, further review assessing the PRP conducted in resource-limited settings is required to determine its feasibility.

6. Patents

Acknowledgments: Authors appreciate the inter-institutional collaboration during the research and the making of this report.

Conflicts of Interest: There is no conflict of interest in the making of this review.

Abbreviations

The following abbreviations are used in this manuscript:

VAS	Visual Analogue Scale
WOMAC	Western Ontario and McMaster Universities Arthritis Index
IKDC	International Knee Documentation Committee
NR	Not Reported
RCT	Randomized Control Trial

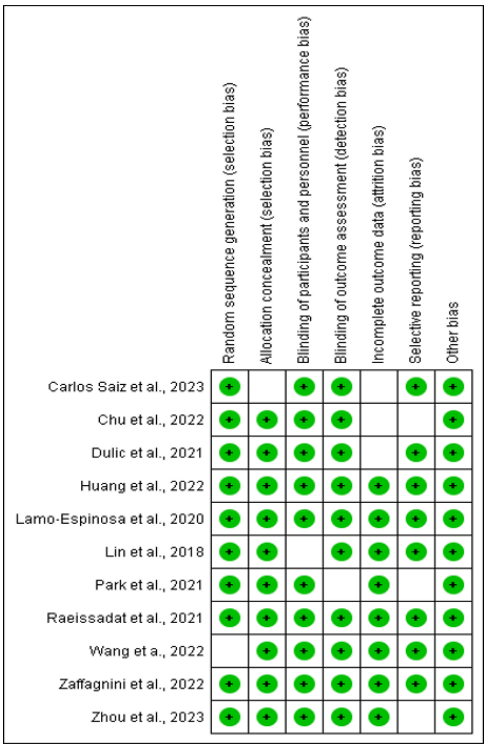
Appendix 1. Literature Search Strategy

Appendix 2. Literature Review PICOS Framework

Table 1. Literature Review PICOS Framework

Population	Intervention	Comparison	Outcome	Study Design
Geriatric aged 60 years old or older	Platelet-rich plasma (PRP)	Conventional therapy as control	VAS Pain Scale, IKDC Subjective Score and WOMAC global function and pain score.	Meta-analysis and Systematic Review from Randomized Controlled Trial

Appendix 3. Study Quality Assessment Based on Cochrane RoB 2.0*



(*Note: White = Unclear Risk)

Figure 1. Study Quality Assessment Based on Cochrane RoB 2.0*

Appendix 4. Characteristics of Included Studies

Table 2. Characteristics of Included Studies

Author First Name	Design	Intervention	Condition	Primary Outcome	Max Follow Up Time	Secondary Outcome	Patients	Mean Age (Yr)	Gender
Chu et al. [2]	Clinical Trial	Intra-Articula Injection of P-PRP	Knee osteoarthritis	WOMAC	60 months	IKDC, VAS, Intraarticular biochemical marker concentrations, cartilage volume, and adverse events	610	53.91	NR
Dulic et al. [3]	Prospective Clinical Trial	PRP	Knee osteoarthritis	VAS	12 months	WOMAC, KOOS (Knee injury and Osteoarthritis Outcome Score) and IKDC	195	58.8 (11.2)	Male = 85, Female = 90
Zhou et al. [4]	RCT	Intra-Articular Injection with P-PRP	Knee Cartilage Lesion	WOMAC scores	12 months	VAS Score	95	62.27 (5.27)	Male = 16, Female = 44
Raeissadat et al. [5]	RCT	Intra-Articular Injection of Platelet Rich Plasma	Knee osteoarthritis	WOMAC scores	2 months	VAS Score	238	56.9 (6.3)	Male = 61, Female = 139
Park et al. [6]	RCT	Platelet-Rich Plasma Injection	Mild to Moderate Knee Osteoarthritis	IKDC	6 months	VAS Pain and WOMAC	110	60.66 (8.2)	Male = 16, Female = 39

Zaffagnini et al. [7]	RCT	Platelet-Rich Plasma	Knee osteoarthritis	IKDC and KOOS	24 months	VAS Pain	118	NR	NR
Carlos Saiz et al. [8]	RCT	Plasma rich in growth factors (PRGF)	Knee osteoarthritis	VAS	25 months	WOMAC Score	176	60.5 (7.9)	Male = 54%, Female = 46%
Lamo-Espinosa et al., [1]	RCT	Intra-Articular Injection of Autologous BM with Platelet Rich Plasma	Knee osteoarthritis	VAS Score	12 months	WOMAC Score	50	54.6 (33.70)	Males = 62%
Wang et al. [9]	RCT	Intra-Articular Single Platelet-Rich	Early-Stage Knee Osteoarthritis	WOMAC Score	6-month	WOMAC Score	116	61.87 (5.46)	Male = 22.2%, Female = 77.8%
Huang et al. [10]	RCT	Intra-Articular Injection of Platelet Rich Plasma	Knee osteoarthritis	VAS Score	6-month	WOMAC Score	99	61.9 (8.8)	Female = 64.6%
Lin et al. [11]	RCT	Intra-Articular Injection of Platelet Rich Plasma	Knee osteoarthritis	WOMAC	12 months	IKDC Score	77	61.17 (13.08)	Male = 19, Female = 41

Appendix 5. Forest Plot showing the efficacy of PRP against the control group in Eleven Trials

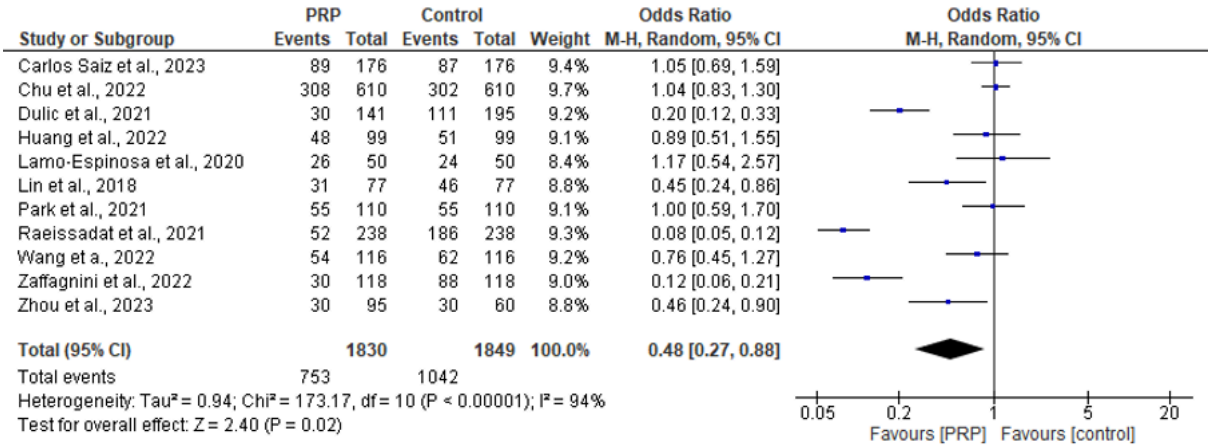


Figure 2. Forest Plot showing the efficacy of PRP against the control group in Eleven Trials

Appendix 6. Funnel plot: PRP vs Control

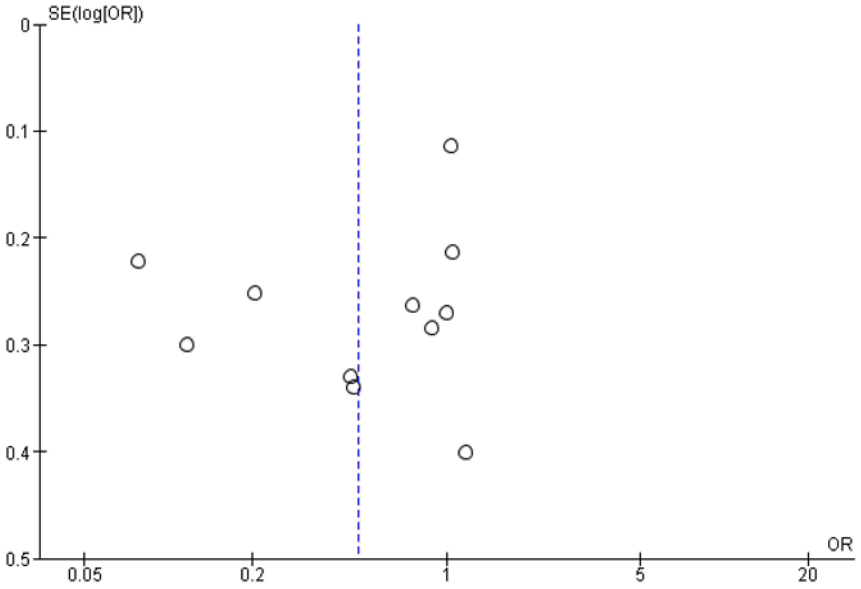


Figure 3. Forest Funnel plot: PRP vs Control

Appendix 7. VAS score Forest Plot

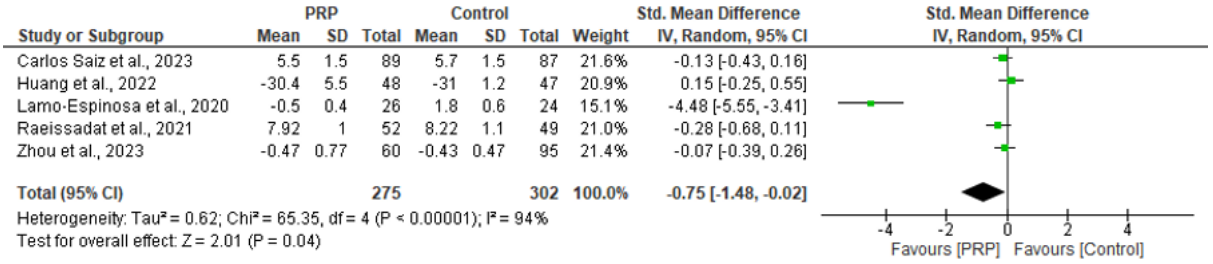


Figure 4. VAS score Forest Plot

Appendix 8. Funnel plot; VAS Pain

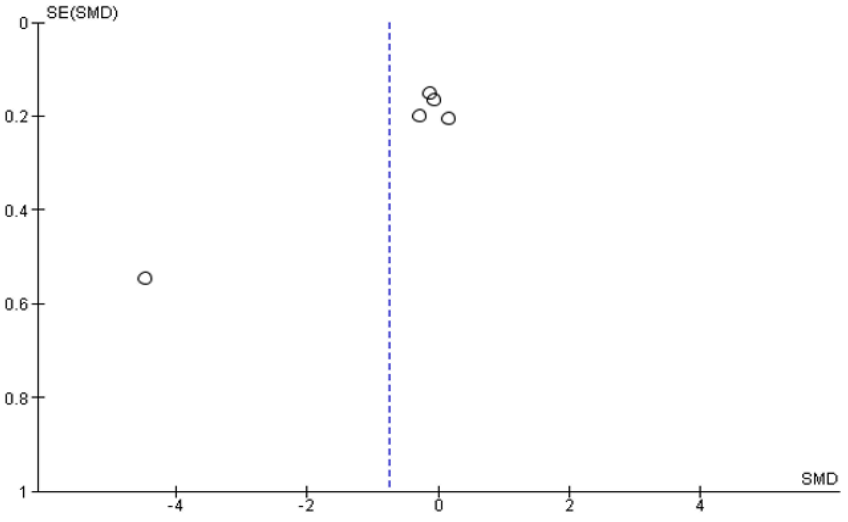


Figure 5. Funnel plot; VAS Pain

Appendix 9. IKDC Score Forest Plot

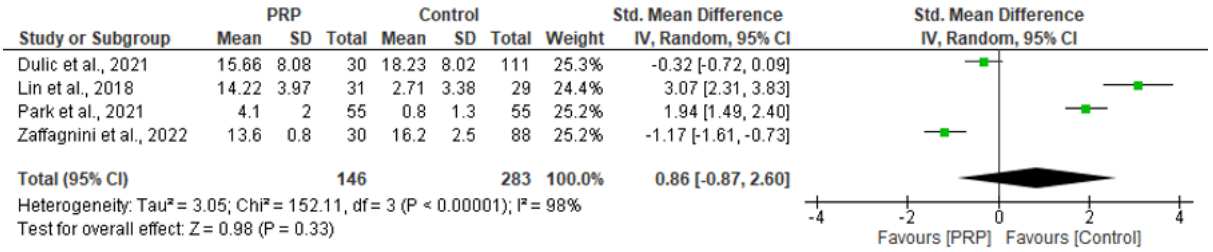


Figure 6. IKDC Score Forest Plot

Appendix 10. Funnel plot: IKDC score

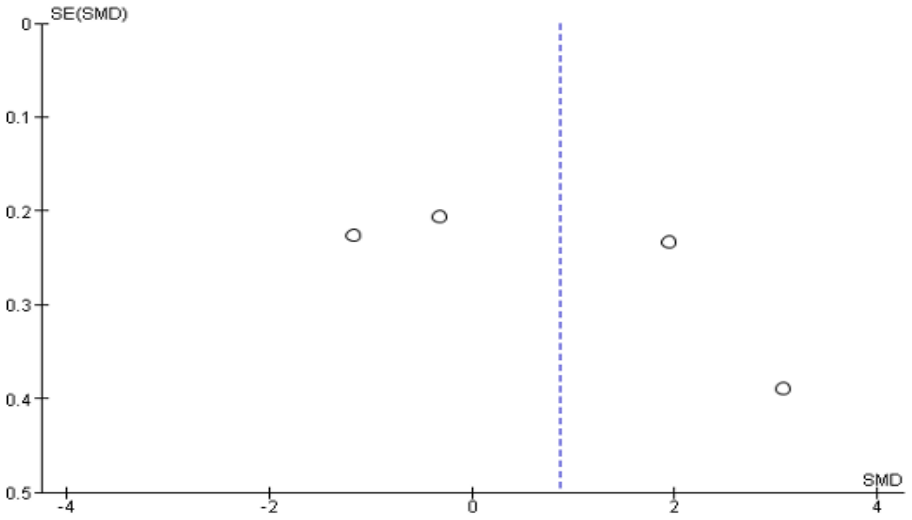


Figure 7. Funnel plot: IKDC score

Appendix 11. WOMAC Function (4.1.1), WOMAC pain (4.1.2)

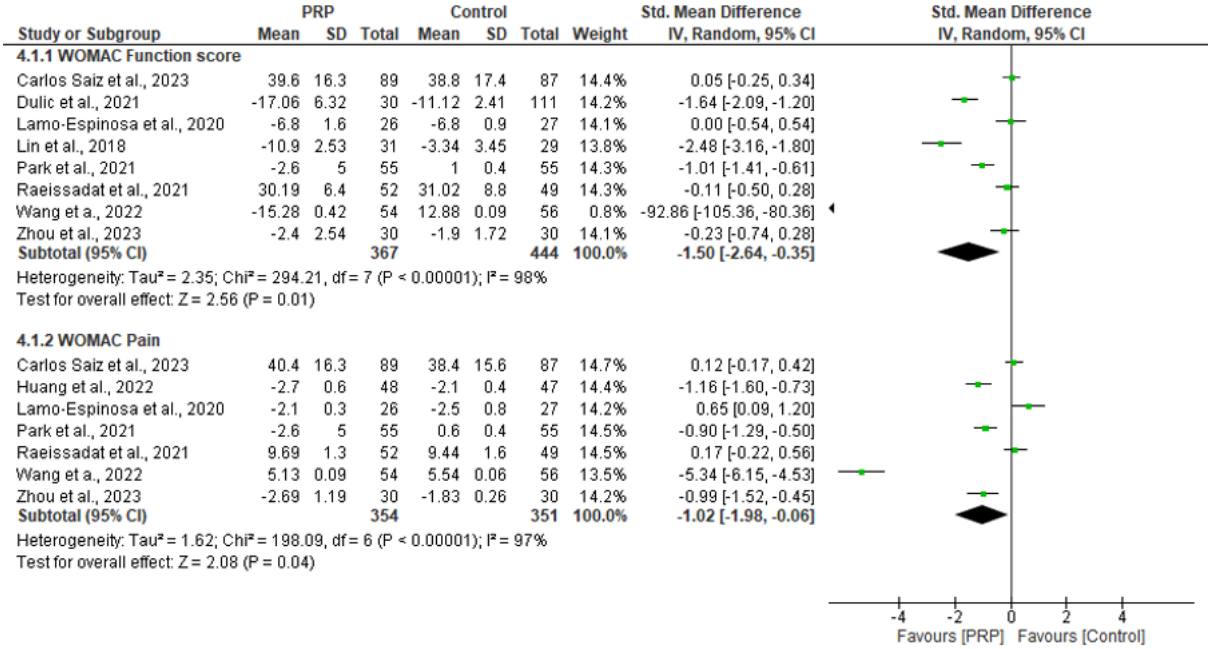


Figure 8. WOMAC Function (4.1.1), WOMAC pain (4.1.2)

Appendix 12. Visual Analogue Scale

Figure 9. Visual Analogue Scale

References

1. Lamo-Espinosa JM, Blanco JF, Sánchez M, Moreno V, Granero-Moltó F, Sánchez-Guijo F, et al. Phase II multicenter randomized controlled clinical trial on the efficacy of intra-articular injection of autologous bone marrow mesenchymal stem cells with platelet rich plasma for the treatment of knee osteoarthritis. J Transl Med. 2020;18(1):356. doi: 10.1186/s12967-020-02530-6.

2. Chu J, Duan W, Yu Z, Tao T, Xu J, Ma Q, et al. Intra-articular injections of platelet-rich plasma decrease pain and improve functional outcomes than sham saline in patients with knee osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2022;30(12):4063–71. doi: 10.1007/s00167-022-06887-7.

3. Dulic O, Rasovic P, Lalic I, Kecojevic V, Gavrilovic G, Abazovic D, et al. Bone marrow aspirate concentrate versus platelet rich plasma or hyaluronic acid for the treatment of knee osteoarthritis. Medicina (Mex). 2021;57(11):1193. doi: 10.3390/medicina57111193.

4. Zhou Y, Li H, Cao S, Han Y, Shao J, Fu Q, et al. Clinical Efficacy of Intra-Articular Injection With P-PRP Versus That of L-PRP in Treating Knee Cartilage Lesion: A Randomized Controlled Trial. Orthop Surg. 2023;15(3):740–9. doi: 10.1111/os.13643.

5. Raeissadat SA, Ghazi Hosseini P, Bahrami MH, Salman Roghani R, Fathi M, Gharooee Ahangar A, et al. The comparison effects of intra-articular injection of Platelet Rich Plasma (PRP), Plasma Rich in Growth Factor (PRGF), Hyaluronic Acid (HA), and ozone in knee osteoarthritis; a one year randomized clinical trial. BMC Musculoskelet Disord. 2021;22(1):134. doi: 10.1186/s12891-021-04017-x.

6. Park YB, Kim JH, Ha CW, Lee DH. Clinical efficacy of platelet-rich plasma injection and its association with growth factors in the treatment of mild to moderate knee osteoarthritis: a randomized double-blind controlled clinical trial as compared with hyaluronic acid. Am J Sports Med. 2021;49(2):487–96. doi: 10.1177/0363546520986867.

7. Zaffagnini S, Andriolo L, Boffa A, Poggi A, Cenacchi A, Busacca M, et al. Microfragmented adipose tissue versus platelet-rich plasma for the treatment of knee osteoarthritis: a prospective randomized controlled trial at 2-year follow-up. Am J Sports Med. 2022;50(11):2881–92. doi: 10.1177/03635465221115821.

8. Saiz LC, Erviti J, Leache L, Gutiérrez-Valencia M. Restoring Study PRGF: a randomized clinical trial on plasma rich in growth factors for knee osteoarthritis. Trials. 2023;24(1):37. doi: 10.1186/s13063-022-07049-3.

9. Wang YC, Lee CL, Chen YJ, Tien YC, Lin SY, Chen CH, et al. Comparing the efficacy of intra-articular single platelet-rich plasma (PRP) versus novel crosslinked hyaluronic acid for early-stage knee osteoarthritis: A prospective, double-blind, randomized controlled trial. Medicina (Mex). 2022;58(8):1028. doi: 10.3390/medicina58081028.

10. Huang HY, Hsu CW, Lin GC, Lin HS, Chou YJ, Liou IH, et al. Comparing efficacy of a single intraarticular injection of platelet-rich plasma (PRP) combined with different hyaluronans for knee osteoarthritis: a randomized-controlled clinical trial. BMC Musculoskelet Disord. 2022;23(1):954. doi: 10.1186/s12891-022-05906-5.

11. Lin KY, Yang CC, Hsu CJ, Yeh ML, Renn JH. Intra-articular injection of platelet-rich plasma is superior to hyaluronic acid or saline solution in the treatment of mild to moderate knee osteoarthritis: a randomized, double-blind, triple-parallel, placebo-controlled clinical trial. Arthrosc J Arthrosc Relat Surg. 2019;35(1):106–17. doi: 10.1016/j.arthro.2018.06.035.