



Systematic Review

Management of platelet-rich plasma and stem cells versus conventional treatments in musculoskeletal injury repair: A systematic review

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ABSTRACT

Musculoskeletal injuries are a prevalent cause of disability, often impairing daily function and overall well-being. Standard treatments – including physiotherapy, anti-inflammatory medications, and surgery – frequently fall short in achieving optimal outcomes. Regenerative strategies, particularly platelet-rich plasma (PRP) and stem cell (SC) therapies, have emerged as alternatives due to their biological capacity to promote tissue regeneration and repair. This systematic review synthesizes evidence from randomized controlled trials that compare PRP and SC interventions with conventional management of musculoskeletal injuries. Literature was systematically searched in PubMed, Embase, and LILACS for relevant studies published through a structured search strategy. A total of 23 studies met the eligibility criteria. Findings indicate that PRP facilitates early pain relief and functional gains, while SC therapies contribute to sustained regenerative effects. When used in combination, PRP and SC demonstrated enhanced clinical outcomes. Although no serious adverse events were consistently reported, marked heterogeneity in protocols and outcomes was observed. Risk of bias varied across studies, highlighting the need for methodological rigor. Overall, the evidence suggests that PRP and SC therapies hold potential for musculoskeletal repair. However, standardized protocols and further robust clinical trials are essential to confirm their safety, efficacy, and broader applicability.

Keywords: Clinical trials, Musculoskeletal injuries, Platelet-rich plasma, Regenerative medicine, Stem cells

INTRODUCTION

Musculoskeletal injuries constitute a leading cause of morbidity and functional impairment, exerting a substantial burden on quality of life. Conventional therapeutic approaches – such as physical rehabilitation, non-steroidal anti-inflammatory drugs (NSAIDs), and surgical procedures in severe cases – are widely used but often provide limited and inconsistent outcomes in terms of pain relief, recovery speed, and recurrence rates.^[1]

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In response to these limitations, biologically based interventions have garnered increasing attention. Platelet-rich plasma (PRP), derived from autologous blood and enriched with growth factors, has demonstrated potential to accelerate tissue healing. Likewise, stem cell (SC) therapy, particularly using mesenchymal stem cells (MSCs), is of interest due to its capacity for differentiating and regenerating damaged musculoskeletal structures.^[2]

These therapies have been prioritized in this review because conventional treatments often fail to promote tissue regeneration and tend to offer only symptomatic relief. In contrast, PRP and SCs hold biological potential to target the underlying pathophysiology of musculoskeletal damage.

Despite the expanding body of research on these therapies, findings remain inconclusive. Some clinical studies report significant improvements in pain, function, and tissue repair with PRP or SC, while others show marginal or no added benefit over traditional treatments. Further complicating interpretation, the protocols for preparing and applying these therapies vary widely, limiting comparability and clinical translation.^[3]

Recent studies, including those by Shanmugasundaram *et al.* (2021)^[4] and Tsubosaka *et al.* (2021),^[5] highlight the promise of these biologics but emphasize the need for standardized methods and rigorous clinical trials.

Given the regenerative capabilities of PRP and SC, it is hypothesized that these modalities may provide superior clinical outcomes compared to conventional treatments in musculoskeletal injury management. This systematic review addresses the question: How do PRP and SC therapies compare with conventional interventions in terms of efficacy, safety, and functional recovery in musculoskeletal injuries?^[6]

To answer this, a structured literature review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, focusing on randomized controlled trials (RCTs) that evaluated PRP and/or SC therapies in comparison to standard treatments. Primary outcomes included pain reduction, functional recovery, and time to return to activity. Secondary outcomes examined adverse events and quality-of-life indicators.^[7,8]

This review is expected to provide a clear and evidence-based synthesis of the usefulness of PRP and stem cells in managing musculoskeletal injuries, which could contribute to optimizing therapeutic strategies and supporting clinical decision-making.

MATERIALS AND METHODS

Type of study

A systematic review of the literature was conducted, following the PRISMA guidelines. RCTs evaluating the effectiveness,

efficacy, and safety of PRP and SCs compared to conventional treatments for the repair of musculoskeletal injuries were included.

Selection criteria

RCTs

Types of interventions/exposures

Intervention group

The use of PRP and/or mesenchymal SCs administered through injection, surgery, or any other method.

Comparator group

Conventional treatments include physical therapy, NSAIDs, corticosteroids, hyaluronic acid, or a placebo.

Types of outcomes

Primary outcomes

- Pain reduction (measured using validated scales such as the Visual Analog Scale (VAS) or Likert scale).
- Functional improvement (assessed with injury-specific scales such as International Knee Documentation Committee (IKDC) for the knee, Disabilities of the Arm, Shoulder, and Hand (DASH), for the upper limb, and Western Ontario and McMaster Universities (WOMAC) for osteoarthritis [OA]).
- Recovery time until return to prior activity.

Secondary outcomes

- Adverse events related to the intervention (infections, adverse reactions, post-injection pain, etc.).
- Additional procedures (revision surgeries, repeated injections).
- Quality of life (measured with Short Form-36 [SF-36] Health Survey or EuroQol 5-Dimension [EQ-5D] Questionnaire).

Search methods for study identification

Electronic searches

Systematic searches were performed in the following electronic databases:

MEDLINE (via PubMed), Embase, LILACS

These databases were selected due to their comprehensive coverage of biomedical literature, including clinical trials and Latin American publications relevant to musculoskeletal conditions. The study selection process is illustrated in Figure 1.

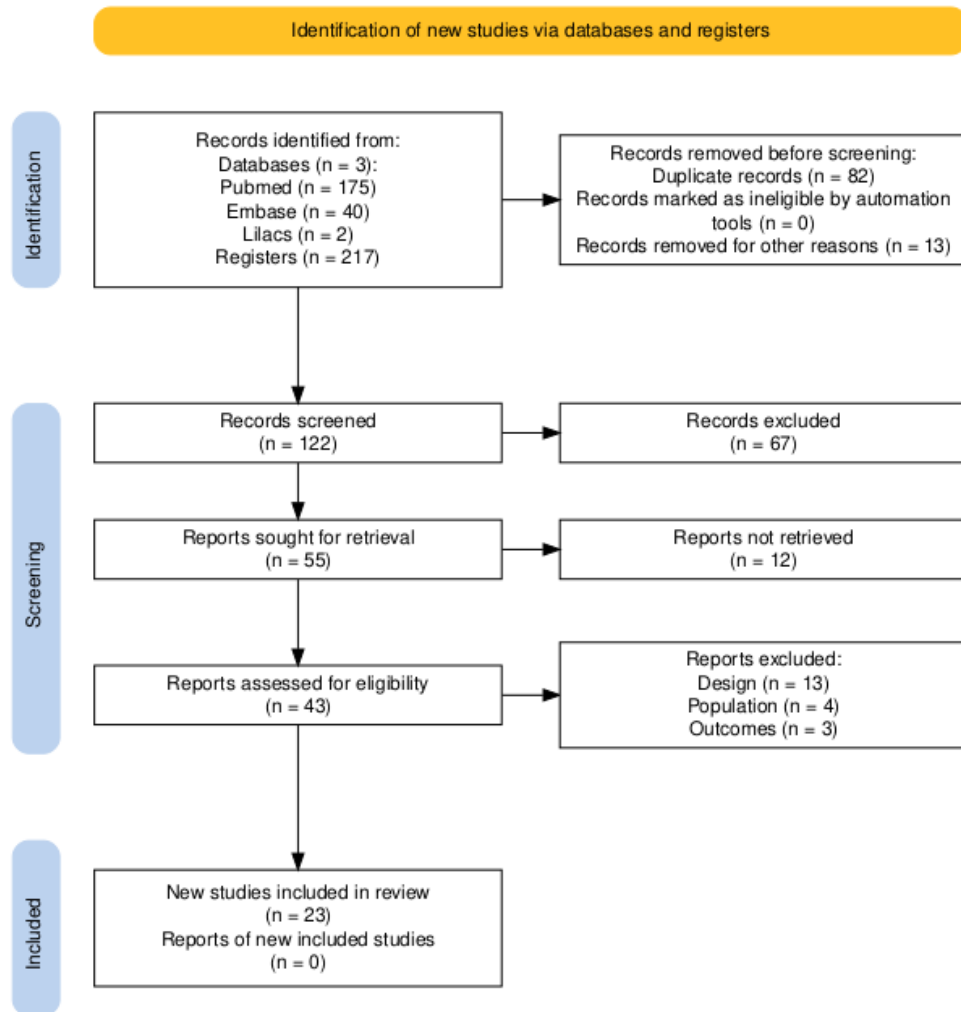


Figure 1: PRISMA 2020 flow diagram illustrating the process of study selection. A total of 437 records were identified, of which 122 were screened after removing duplicates and ineligible records. Ultimately, 23 studies met the inclusion criteria and were included in the systematic review.

Language restrictions were applied to include only studies published in English and Spanish, as these languages were accessible to the research team. Studies in other languages were excluded due to limitations in translation capacity.

Search strategy

("Platelet-Rich Plasma" [MeSH Terms] OR "platelet-rich plasma" [Title/Abstract] OR PRP [Title/Abstract]) AND ("Stem Cells" [MeSH Terms] OR "stem cells" [Title/Abstract] OR "mesenchymal stem cells" [Title/Abstract] OR MSCs [Title/Abstract]) AND ("Musculoskeletal Diseases" [MeSH Terms] OR "musculoskeletal injuries" [Title/Abstract] OR "musculoskeletal lesions" [Title/Abstract] OR "muscle injuries" [Title/Abstract] OR "tendon injuries" [Title/Abstract] OR "ligament injuries" [Title/Abstract] OR "bone injuries" [Title/Abstract]) AND ("Pain" [MeSH Terms] OR

pain [Title/Abstract] OR "pain reduction" [Title/Abstract]) AND ("Treatment Outcome" [MeSH Terms] OR "treatment outcome" [Title/Abstract] OR "functional improvement" [Title/Abstract] OR "recovery time" [Title/Abstract] OR "time to recovery" [Title/Abstract]).

Additional boolean strategy

([tw: ("Platelet-Rich Plasma" OR "PRP" OR "platelet-rich fibrin" OR "autologous platelet concentrate" OR "platelet-derived growth factors" OR "platelet concentrate" OR "platelet gel" OR "platelet lysate")]) OR [mh: "Plasma Rico en Plaquetas"]) AND ([tw: ("Stem Cells" OR "mesenchymal stem cells" OR MSC OR "progenitor cells" OR "bone marrow-derived cells" OR "adipose-derived stem cells" OR "hematopoietic stem cells" OR "stromal cells" OR "pluripotent stem cells" OR "multipotent stem cells" OR

“induced pluripotent stem cells” OR “iPSC”) OR [mh: “Células Madre”) AND ([tw: (“musculoskeletal injuries” OR “musculoskeletal disorders” OR “musculoskeletal trauma” OR “muscle injuries” OR “muscle tears” OR “tendon injuries” OR “tendon tears” OR “ligament injuries” OR “ligament tears” OR “cartilage injuries” OR “cartilage degeneration” OR “bone fractures” OR “joint injuries” OR “osteoarthritis” OR “sports injuries” OR “soft tissue injuries” OR “connective tissue injuries” OR “degenerative joint diseases”) OR [mh: “Lesiones Musculoesqueléticas”) OR [mh: “Enfermedades Musculoesqueléticas”) AND ([tw: (“pain relief” OR “pain reduction” OR “pain management” OR “analgesia” OR “functional recovery” OR “rehabilitation” OR “functional improvement” OR “healing time” OR “recovery time” OR “wound healing” OR “tissue repair” OR “regeneration” OR “mobility improvement”) OR [mh: “Dolor”) OR [mh: “Recuperación Funcional”) OR [mh: “Cicatrización”).

Search for other resources

The references of the included articles were reviewed to identify additional studies.

Data collection and analysis

Study selection

Two independent reviewers selected the studies based on inclusion and exclusion criteria. Discrepancies were resolved by consensus or consultation with a third reviewer.

Data extraction and management

Data were extracted with attention to participant characteristics, including knee osteoarthritis (OA) as well as chronic tendinopathy, and interventions such as intra-articular injections of PRP or SCs. Comparators included platelet-rich growth factors (PRGF), hyaluronic acid, and corticosteroids. The assessed outcomes were pain improvement, range of motion, functional improvement, and quality of life.

Study quality assessment

The Cochrane Risk of Bias 2.0 tool was used.

Bias management

Handling missing data

In cases of missing data, study authors were contacted for clarification. When no response was received, sensitivity analyses were conducted, excluding these studies to assess their impact on the overall findings.

RESULTS

The studies included in this systematic review evaluated the effectiveness, efficacy, and safety of PRP and SCs therapies compared to conventional treatments for the repair of musculoskeletal injuries. An overview of the main findings is summarized.

In patients with knee OA, the administration of mesenchymal stem cells (MSCs) with or without PRP showed significant improvements in both the global Knee Injury and Osteoarthritis Outcome Score (KOOS) and pain scores at 12 months compared to corticosteroids, with statistically significant differences in pain reduction ($\Delta 23.2$, $P < 0.001$) and functional improvement ($\Delta 24.0$, $P = 0.002$).^[9] Similarly, Prizov *et al.* reported that PRP significantly improved global KOOS scores ($\Delta + 40$ points, $P < 0.05$) and reduced VAS pain scores ($\Delta -5$ points, $P < 0.05$) in patients undergoing high tibial osteotomy, with better cartilage regeneration observed in those treated with stromal vascular fraction (SVF).^[10] In patients with lumbar disc degenerative disease, SVF injection with PRP resulted in a 35.7% reduction in VAS pain scores ($P = 0.01$) and a 19.1% increase in lumbar range of motion ($P = 0.02$) at 6 months.^[11] In contrast Nguyen *et al.* found that the combination of PRP and SVF in patients with knee OA significantly improved function (WOMAC: $\Delta -71\%$, $P < 0.05$; Lysholm: $\Delta + 58.5\%$, $P < 0.05$) and reduced VAS pain by 75% ($P < 0.05$) at 18 months, compared to arthroscopic microfracture alone, which showed no significant improvements.^[12]

Other studies on knee OA have shown that MSCs reduced WOMAC scores by 55% ($P < 0.001$) and VAS pain scores by 50% ($P < 0.001$), whereas the control group showed no significant changes.^[13]

Studies by Angoorani *et al.* and Raeissadat *et al.* analyzed PRP, PRGF, hyaluronic acid, and ozone therapy, demonstrating that PRP and PRGF achieved significant pain reduction (VAS: -41.1 – -52.3% , $P < 0.001$) and improvements in functionality (WOMAC: -36.2 – -55.3% , $P < 0.001$);^[14,15] with greater satisfaction reported in these groups compared to hyaluronic acid and ozone therapy. Finally, compared with Transcutaneous Electrical Nerve Stimulation (TENS) and exercise, PRP significantly increased the time to intolerable pain on a treadmill ($P < 0.001$) and improved KOOS symptom scores ($P = 0.010$) at 8 weeks.^[16,17]

These results suggest that PRP- and SC-based therapies may offer superior benefits in pain reduction and functional improvement across various musculoskeletal conditions compared to conventional treatments [Table 1].

To ensure consistency, effect sizes were expressed either as percentage reductions in western ontario and mcmaster universities osteoarthritis index SCORES (WOMAC)/VAS scores or as absolute change (Δ) values whenever possible.

Table 1: Summary of findings for the application of PRP and/or Stem Cells compared to conventional treatments for musculoskeletal injury repair.

Lead Author, Year	Population Characteristics	Intervention	Comparator	Outcomes
Bastos <i>et al.</i> , 2019 ^[9]	47 patients with knee OA, mean age 57.3 years, mean BMI 30.2 kg/m ² , KL grades I–IV	Cultured MSCs±PRP	Corticosteroid injection	KOOS global: MSCs+PRP Δ22.7. IL-10 reduction in MSCs+PRP: 3.33→0.52 ng/mL.
Prizov <i>et al.</i> , 2022 ^[10]	20 patients undergoing HTO, mean age 54.5 years, BMI 31.5 kg/m ²	PRP	SVF	KOOS: PRP Δ+40; VAS: PRP Δ-5. Cytokines: PRP increased PDGF .
Comella <i>et al.</i> , 2017 ^[11]	15 patients with lumbar DDD, mean age 51.5 years	SVF+PRP	No comparator	VAS: Δ-35.7%; ROM flexion: Δ+19.1%.
Nguyen <i>et al.</i> , 2016 ^[12]	30 patients with KL grade 2 or 3 knee OA	AM+SVF/PRP	AM only	WOMAC: SVF/PRP Δ-71% ; VAS: Δ-75%.
Dadgostar <i>et al.</i> , 2021 ^[23]	58 with rotator cuff tendinopathy	PRP	Corticosteroids	VAS: PRP Δ-53.7%; ROM increased.
Lee <i>et al.</i> , 2019 ^[13]	24 with KL grade 2–4 knee OA	AD-MSCs	Saline	WOMAC: Δ-55%; VAS: Δ-50%.
Angoorani <i>et al.</i> , 2015 ^[14]	54 with knee OA	PRP	TENS+exercise	KOOS: Δ+10. VAS: PRP Δ-53.7%.
Raeissadat <i>et al.</i> , 2020 ^[25]	102 with KL grade 2–3 OA	PRGF	HA	WOMAC: PRGF Δ-35.4%; VAS: Δ-42.3%.
Raeissadat <i>et al.</i> , 2021 ^[26]	200 with KL grade 2–3 OA	PRP, PRGF, HA, ozone	Cross comparisons	WOMAC: PRGF Δ-37.1%; PRP Δ-36.2%; Ozone Δ-14.9%.
Raeissadat <i>et al.</i> , 2015 ^[27]	160 with KL grade 1–4 OA	PRP	HA	WOMAC: PRP Δ-53.3%; VAS: Δ-52.3%.
Rayegani <i>et al.</i> , 2014 ^[28]	62 with KL grade 1–4 OA	PRP	Exercise only	WOMAC: PRP Δ-55.3%; VAS: Δ-53.9%.
Raeissadat <i>et al.</i> , 2017 ^[15]	69 with KL grade 2–3 OA	PRGF	HA	WOMAC: PRGF Δ-43.1%; VAS: Δ-41.0%.
Thanasas <i>et al.</i> , 2011 ^[16]	28 with epicondylitis	PRP	Autologous blood	VAS: PRP Δ-70.8%; function improved more in PRP.
Wong <i>et al.</i> , 2013 ^[29]	56 with varus OA knees	MSC+HA	HA	IKDC: MSC Δ+7.65; MOCART: Δ+19.6 .
Başar <i>et al.</i> , 2021 ^[30]	192 with degenerative meniscal tears	APM±HA, PT±HA	APM, PT	WOMAC, VAS improved in all groups; no differences.
Garza <i>et al.</i> , 2020 ^[17]	39 with KL grade 2–3 OA	SVF	Placebo	WOMAC at 12 mo: SVF high-dose Δ+89.5%, low-dose Δ+68.2%.
Montalvan <i>et al.</i> , 2016 ^[31]	50 with epicondylitis	PRP	Saline	VAS: both groups Δ~75%. No significant difference.

PRP: Platelet-rich plasma; MSC: Mesenchymal stem cell, SVF: Stromal vascular fraction, HA: Hyaluronic acid, OA: Osteoarthritis, KL: Kellgren-Lawrence, KOOS: Knee injury and osteoarthritis outcome score, WOMAC: Western ontario and McMaster universities osteoarthritis index, VAS: Visual analog scale, AM: Arthroscopic microfracture, DDD: Degenerative disc disease, ROM: Range of motion, TENS: Transcutaneous electrical nerve stimulation, PRGF: Plasma rich in growth factors, MRI: Magnetic resonance imaging, MOCART: Magnetic resonance observation of cartilage repair tissue, APM: Arthroscopic partial meniscectomy, PT: Physical therapy

In patients with knee OA, multiple studies reported significant reductions in pain, as measured by the VAS scale, in groups treated with bone marrow aspirate concentrate (BMAC), MSCs, and PRP.^[18] Dulic *et al.* found that treatment with BMAC resulted in greater short-term pain reduction ($P < 0.001$) and functional improvement as measured by WOMAC and KOOS, compared to PRP and hyaluronic acid.^[18] LamoEspinosa *et al.* reported greater pain reduction with Bone Marrow-derived Mesenchymal Stem Cells (BM-MSC) + PRGF compared to PRGF alone (−1.8 vs. −0.5 points on the VAS, $P = 0.01$).^[19] Similarly, Mormone *et al.* showed that

BMAC obtained from the iliac crest and proximal tibia had a greater impact on pain reduction and functional improvement compared to PRP ($P < 0.001$ for both VAS and WOMAC).^[20]

Conversely, Bąkowski *et al.* evaluated the use of fragmented autologous adipose tissue versus PRP, observing improvements in the KOOS, IKDC, and WOMAC scores over a 1-year period.^[21] Mormone *et al.* and Koh and Choi found that combining adipose-derived MSCs with PRP significantly improved joint function (as measured by the Lysholm and Tegner Activity Scale) and reduced pain compared to PRP alone ($P < 0.001$).^[20,22]

Table 2: Summary of findings from bone marrow aspirate stem cell therapies versus platelet-rich plasma for musculoskeletal injury repair

Lead Author, Year	Population Characteristics	Intervention	Comparator	Outcomes
Dulic <i>et al.</i> , 2021 ^[18]	175 with KL grade II–IV OA	BMAC	PRP, HA	VAS: greater reduction in BMAC days 3–21. KOOS: BMAC >PRP >HA. IKDC mostly superior.
Lamo-Espinosa <i>et al.</i> , 2020 ^[19]	60 with KL ≥2 OA, VAS ≥2.5, failed HA	BM-MSc+PRGF	PRGF	VAS: BM-MSc Δ-1.8; WOMAC: pain Δ-45.5%, stiffness Δ-50%.
Bąkowski <i>et al.</i> , 2020 ^[21]	45–65 years, KL I–III OA	Adipose tissue injection	PRP	KOOS, IKDC, WOMAC improved; no comparative results shown.
Mormone <i>et al.</i> , 2024 ^[20]	45 with KL I–IV OA, VAS 8–10	BMAC (iliac/tibia)	PRP	VAS: iliac Δ-5.0; WOMAC: tibia Δ-16. Iliac MSCs more abundant than tibia.
Usuelli <i>et al.</i> , 2018 ^[24]	44 with Achilles tendinopathy	SVF	PRP	VAS: SVF Δ-67.7%; VISA-A: SVF Δ+113%; AOFAS improved.
Koh and Choi, 2012 ^[22]	25 with knee OA	MSc+PRP	PRP	Lysholm: MSc Δ+26.9; VAS: MSc Δ-2.2.

PRP: Platelet-rich plasma, MSc: Mesenchymal stem cell, SVF: Stromal vascular fraction, BMAC: Bone marrow aspirate concentrate, HA: Hyaluronic acid, PRGF: Plasma rich in growth factors, OA: Osteoarthritis, KL: Kellgren-Lawrence, KOOS: Knee injury and osteoarthritis outcome score, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, VAS: Visual Analog Scale, IKDC: International Knee Documentation Committee, VISA-A: Victorian Institute of Sports Assessment-Achilles, AOFAS: American Orthopaedic Foot and Ankle Society

Another study on rotator cuff tendinopathy has demonstrated that PRP reduces VAS pain by 53.7% ($P = 0.023$) and improves range of motion at 3 months compared to corticosteroids.^[23] In the treatment of Achilles tendon tendinopathy, Usuelli *et al.* reported that injection of SVF derived from adipose tissue resulted in a greater reduction in pain (–67.7% vs. –58.7%) and improved function (VISA-A: +113.2% vs. +77%, $P < 0.001$) compared to PRP.^[24] These findings suggest that biological therapies, particularly those combining MSCs with PRP, may offer superior benefits in pain reduction and functional improvement compared to PRP alone or conventional treatments. However, the heterogeneity in intervention protocols and the lack of studies with low risk of bias highlight the need for more high-quality clinical trials to confirm these results [Table 2].

A high degree of heterogeneity was observed in intervention protocols (e.g., LR-PRP vs. LP-PRP, MSc sources, dosing, and delivery methods) and outcome measures (VAS, WOMAC, KOOS, etc.), which limits the interpretation of pooled data.

Risk of bias analysis in the 23 included studies revealed that a significant proportion had methodological limitations that could compromise the validity of their findings. In total, 10 studies (43.5%) were classified as having a high risk of bias, while the remaining 13 (56.5%) had “some concerns.”

This variability in study quality underscores the need for cautious interpretation of the observed effects [Table 3].^[25–31]

DISCUSSION

The findings of this systematic review highlight the potential of PRP and SC therapies as regenerative strategies for

Table 3: Risk of bias assessment.

Author	Overall risk of bias
Dulic <i>et al.</i> , 2021 ^[18]	Some concerns
Bastos <i>et al.</i> , 2019 ^[9]	Some concerns
Lamo-Espinosa <i>et al.</i> , 2020 ^[19]	High
Prizov <i>et al.</i> , 2022 ^[10]	High
Bąkowski <i>et al.</i> , 2020 ^[21]	High
Mormone <i>et al.</i> , 2024 ^[20]	High
Comella <i>et al.</i> , 2017 ^[11]	High
Nguyen <i>et al.</i> , 2016 ^[12]	High
Usuelli <i>et al.</i> , 2018 ^[24]	Some concerns
Koh and Choi, 2012 ^[22]	High
Dadgostar <i>et al.</i> , 2021 ^[23]	Some concerns
Lee <i>et al.</i> , 2019 ^[13]	Some concerns
Angoorani <i>et al.</i> , 2015 ^[14]	Some concerns
Raeissadat <i>et al.</i> , 2020 ^[25]	Some concerns
Raeissadat <i>et al.</i> , 2021 ^[26]	Some concerns
Raeissadat <i>et al.</i> , 2015 ^[27]	Some concerns
Rayegani <i>et al.</i> , 2014 ^[28]	High
Raeissadat <i>et al.</i> , 2017 ^[15]	High
Thanasas <i>et al.</i> , 2011 ^[16]	High
Garza <i>et al.</i> , 2020 ^[17]	Some concerns
Wong <i>et al.</i> , 2013 ^[29]	High
Başar <i>et al.</i> , 2021 ^[30]	Some concerns
Montalvan <i>et al.</i> , 2016 ^[31]	Some concerns

“High” indicates high overall risk of bias, “Some concerns” indicates risk of bias in one or more domains according to the Cochrane Risk of Bias 2 (RoB 2) tool

musculoskeletal injuries. Across a range of RCTs, these interventions consistently demonstrated clinically meaningful improvements in pain reduction, joint function, and patient-reported outcomes, particularly in conditions such as knee OA, rotator cuff tendinopathy, and degenerative disc disease (DDD).

These results align with prior meta-analyses and systematic reviews. For instance, Hurley *et al.* (2019)^[3] found that PRP significantly improved outcomes in arthroscopic rotator cuff repair compared to control groups, while Ding *et al.* (2021)^[2] showed superior efficacy of intra-articular cell-based therapies over HA or corticosteroids in OA management. Our findings reinforce these conclusions and further suggest that combining PRP with MSCs – particularly BM-MSCs or AD-MSCs – may offer synergistic benefits.

In comparison with conventional modalities, such as NSAIDs, corticosteroid injections, HA, and PT, biological therapies appear to produce more sustained improvements in function and symptom control. For example, several included studies reported greater and longer-lasting reductions in VAS and WOMAC scores with PRP or MSCs versus corticosteroids or HA alone. This suggests that regenerative approaches may address underlying pathology more effectively, rather than merely alleviating symptoms.

However, the significant heterogeneity across studies remains a challenge. Differences were observed in PRP preparation methods (e.g., leukocyte-rich vs. leukocyte-poor PRP, activated vs. non-activated), MSC sources (bone marrow, adipose tissue), cell doses, and delivery routes (injection vs. surgical implantation). These factors likely contribute to the variability in outcomes and complicate comparison across trials.

In addition, nearly half of the included studies were classified as having a high risk of bias. This raises concerns about the internal validity of their results and highlights the necessity for better-designed trials with blinding, larger sample sizes, and longer follow-up periods.

From a translational perspective, practical issues such as the high cost of biologic therapies, lack of standardized preparation protocols, and regulatory variability across regions pose barriers to clinical implementation. Differences in product formulation between centers also pose challenges to reproducibility.

In terms of clinical applicability, PRP and SC therapies may be considered particularly in patients who are refractory to conventional care or those seeking to delay or avoid surgery. Future clinical guidelines should clearly define their role within treatment algorithms for musculoskeletal conditions.

CONCLUSION

This systematic review suggests that both PRP and SC therapies hold promise for treating musculoskeletal

injuries. While the magnitude of effect varies, many studies demonstrate improved pain control and functional recovery when compared to conventional therapies. However, methodological limitations and protocol heterogeneity limit the ability to draw definitive conclusions. As such, these biologic treatments should be considered as emerging options with the potential to enhance musculoskeletal repair in selected clinical scenarios.

Recommendations

It is essential to develop and adopt standardized protocols for the preparation and administration of PRP and stem cells (SCs), conduct large-scale, high-quality RCTs with extended follow-up periods, and design direct comparative studies between biological and conventional treatments to clarify their relative efficacy. In addition, promoting transparent reporting standards is crucial to minimizing publication bias and enhancing the overall quality and reliability of the available evidence.

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Authors' contributions: FJG-B conceived and designed the study, conducted the systematic search, and collected and organized data. LNA-V participated in data extraction, critically reviewed selected studies, and contributed to data interpretation. JRB conducted additional research, supported analysis of results, and revised content to enhance intellectual depth. JAC-L synthesized findings and drafted significant portions of the results and discussion. DSJ-A contributed to methodological quality assessment, assisted in formatting and referencing, and reviewed statistical interpretations. JPA-G coordinated the research process, finalized the draft, and ensured compliance with reporting standards. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

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REFERENCES

- Chahla J, Cinque M, Piuze NS, Mannava S, Geeslin AG, Murray IR, *et al.* A call for standardization in platelet-rich plasma preparation protocols and composition reporting: A systematic review of the clinical orthopaedic literature. *J Bone Joint Surg Am* 2017;99:1769-79.
- Ding W, Xu YQ, Zhang Y, Li AX, Qiu X, Wen HJ, *et al.* Efficacy and safety of intra-articular cell-based therapy for osteoarthritis: Systematic review and network meta-analysis. *Cartilage* 2021;13(1 Suppl):104S-15.
- Hurley ET, Lim Fat D, Moran CJ, Mullett H. The efficacy of platelet-rich plasma and platelet-rich fibrin in arthroscopic rotator cuff repair: A meta-analysis of randomized controlled trials. *Am J Sports Med* 2019;47:753-61.
- Shanmugasundaram S, Vaish A, Chavada V, Murrell WD, Vaishya R. Assessment of safety and efficacy of intra-articular injection of stromal vascular fraction for the treatment of knee osteoarthritis-a systematic review. *Int Orthop* 2021;45:615-25.
- Tsubosaka M, Matsumoto T, Sobajima S, Matsushita T, Iwaguro H, Kuroda R. Comparison of clinical and imaging outcomes of different doses of adipose-derived stromal vascular fraction cell treatment for knee osteoarthritis. *Cell Transplant* 2021;30:9636897211067454.
- Migliorini F, Rath B, Colarossi G, Driessen A, Tingart M, Niewiera M, *et al.* Improved outcomes after mesenchymal stem cells injections for knee osteoarthritis: Results at 12-months follow-up: A systematic review of the literature. *Arch Orthop Trauma Surg* 2020;140:853-68.
- Sánchez M, Delgado D, Sánchez P, Muiños-López E, Paiva B, Granero-Moltó F, *et al.* Combination of intra-articular and intraosseous injections of platelet rich plasma for severe knee osteoarthritis: A pilot study. *Biomed Res Int* 2016;2016:4868613.
- Moraes VY, Lenza M, Tamaoki MJ, Faloppa F, Belloti JC. Platelet-rich therapies for musculoskeletal soft tissue injuries. *Cochrane Database Syst Rev* 2013;12:CD010071.
- Bastos R, Mathias M, Andrade R, Amaral RJ, Schott V, Balduino A, *et al.* Intra-articular injection of culture-expanded mesenchymal stem cells with or without addition of platelet-rich plasma is effective in decreasing pain and symptoms in knee osteoarthritis: A controlled, double-blind clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2019;28:1989-9.
- Prizov A, Tchetina E, Eremin I, Zagorodniy N, Pulin A, Belyak E, *et al.* Differences in synovial cytokine profile associated with long-term clinical outcomes in patients with knee osteoarthritis undergoing corrective osteotomy with platelet-rich plasma or stromal vascular fraction post-treatments. *Int J Mol Sci* 2022;23:12835.
- Comella K, Silbert R, Parlo M. Effects of the intradiscal implantation of stromal vascular fraction plus platelet rich plasma in patients with degenerative disc disease. *J Transl Med* 2017;15:12.
- Nguyen PD, Tran TD, Nguyen HT, Vu HT, Le PT, Phan NL, *et al.* Comparative clinical observation of arthroscopic microfracture in the presence and absence of a stromal vascular fraction injection for osteoarthritis. *Stem Cell Transl Med J* 2016;6:187-95.
- Lee W, Kim HJ, Kim KI, Kim GB, Jin W. Intra-articular injection of autologous adipose tissue-derived mesenchymal stem cells for the treatment of knee osteoarthritis: A phase IIB, randomized, placebo-controlled clinical trial. *Stem Cells Transl Med* 2019;8:504-11.
- Angoorani H, Mazaherinezhad A, Marjomaki O, Younespour S. Treatment of knee osteoarthritis with platelet-rich plasma in comparison with transcutaneous electrical nerve stimulation plus exercise: A randomized clinical trial. *Med J Islam Repub Iran* 2015;29:223.
- Raeissadat SA, Rayegani SM, Ahangar AG, Abadi PH, Mojgani P, Ahangar OG. Efficacy of intra-articular injection of a newly developed plasma rich in growth factor (PRGF) versus hyaluronic acid on pain and function of patients with knee osteoarthritis: A single-blinded randomized clinical trial. *Clin Med Insights Arthritis Musculoskelet Disord* 2017;10:1179544117733452.
- Thanasas C, Papadimitriou G, Charalambidis C, Paraskevopoulos I, Papanikolaou A. Platelet-rich plasma versus autologous whole blood for the treatment of chronic lateral elbow epicondylitis: A randomized controlled clinical trial. *Am J Sports Med* 2011;39:2130-4.
- Garza JR, Campbell RE, Tjoumakaris FP, Freedman KB, Miller LS, Santa Maria D, *et al.* Clinical efficacy of intra-articular mesenchymal stromal cells for the treatment of knee osteoarthritis: A double-blinded prospective randomized controlled clinical trial. *Am J Sports Med* 2020;48:588-98.
- 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 (Kaunas)* 2021;57:1193.
- 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;18:356.
- Mormone E, Savastano L, Rossi G, Maruccia F, Di Maggio G, Sinisi NP, *et al.* Posterior iliac crest vs. Proximal tibia: Distinct sources of anti-inflammatory and regenerative cells with comparable 6-month clinical outcomes in treatment of osteoarthritis. *J Transl Med* 2024;22:1101.
- Bąkowski P, Kaszyński J, Walecka J, Ciemniewska-Gorzela K, Bąkowska-Żywicka K, Piontek T. Autologous adipose tissue injection versus platelet-rich plasma (PRP) injection in the treatment of knee osteoarthritis: A randomized, controlled study - study protocol. *BMC Musculoskelet Disord* 2020;21:314.
- Koh YG, Choi YJ. Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis. *Knee* 2012;19:902-7.
- Dadgostar H, Fahimipour F, Pahlevan Sabagh A, Arasteh P, Razi M. Corticosteroids or platelet-rich plasma injections for rotator cuff tendinopathy: A randomized clinical trial study. *J Orthop Surg Res* 2021;16:333.
- Usuelli FG, Grassi M, Maccario C, Viganò M, Lanfranchi L, Alfieri Montrasio U, *et al.* Intratendinous adipose-derived stromal vascular fraction (SVF) injection provides a safe, efficacious treatment for Achilles tendinopathy: Results of a

- randomized controlled clinical trial at a 6-month follow-up. *Knee Surg Sports Traumatol Arthrosc* 2018;26:2000-10.
25. Raeissadat SA, Gharooee Ahangar A, Rayegani SM, Minator Sajjadi M, Ebrahimpour A, Yavari P. Platelet-rich plasma-derived growth factor vs hyaluronic acid injection in the individuals with knee osteoarthritis: A one year randomized clinical trial. *J Pain Res* 2020;13:1699-711.
 26. Raeissadat SA, Hosseini PG, Bahrami MH, Fathi M, Roghani RS, Ahangar AG, *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;22:134.
 27. Raeissadat SA, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babae M, *et al.* Knee osteoarthritis injection choices: Platelet- rich plasma (PRP) versus hyaluronic acid (a one-year randomized clinical trial). *Clin Med Insights Arthritis Musculoskelet Disord* 2015;8:1-8.
 28. Rayegani SM, Raeissadat SA, Taheri MS, Babae M, Bahrami MH, Eliaaspour D, *et al.* Does intra articular platelet rich plasma injection improve function, pain and quality of life in patients with osteoarthritis of the knee? A randomized clinical trial. *Orthop Rev (Pavia)* 2014;6:5405.
 29. Wong KL, Lee KB, Tai BC, Law P, Lee EH, Hui JH. Injectable cultured bone marrow-derived mesenchymal stem cells in varus knees with cartilage defects undergoing high tibial osteotomy: A prospective, randomized controlled clinical trial with 2 years' follow-up. *Arthroscopy* 2013;29:2020-8.
 30. Başar B, Başar G, Büyükkuşçu MÖ, Başar H. Comparison of physical therapy and arthroscopic partial meniscectomy treatments in degenerative meniscus tears and the effect of combined hyaluronic acid injection with these treatments: A randomized clinical trial. *J Back Musculoskelet Rehabil* 2021;34:767-74.
 31. Montalvan B, Le Goux P, Klouche S, Borgel D, Hardy P, Breban M. Inefficacy of ultrasound-guided local injections of autologous conditioned plasma for recent epicondylitis: Results of a double-blind placebo-controlled randomized clinical trial with one-year follow-up. *Rheumatology (Oxford)* 2016;55:279-85.