Platelet-Rich Plasma Does Not Improve Pain or Function in Patients With Lateral Epicondylitis as Compared With Placebo

A Meta-analysis of Randomized Clinical Trials

César Romero Antunes Júnior,*† Ramon Sampaio Souza Santos,‡ MD, Eduardo Silva Reis Barreto,† Guilherme Neves Azevedo,† Ewerton Borges de Souza Lima,‡ MD, MBA, Paulo Henrique Schmidt Lara,‡ MD, PhD, Alberto de Castro Pochini,‡ MD, PhD, Carlos Vicente Andreoli,‡ MD, PhD, Benno Ejnisman,‡ MD, PhD, and Paulo Santoro Belangero,‡ MD, PhD
Investigation performed at Federal University of São Paulo, São Paulo, Brazil, and Federal University of Bahia, Salvador, Brazil

Background: Lateral epicondylitis, commonly known as tennis elbow, is a prevalent musculoskeletal disorder characterized by pain and functional impairment. Platelet-rich plasma (PRP) has been proposed as a regenerative treatment, but its efficacy remains controversial.

Purpose: To assess the efficacy and safety of PRP in improving pain and function in patients with lateral epicondylitis as compared with placebo through a systematic review and meta-analysis of randomized clinical trials (RCTs).

Study Design: Systematic review and meta-analysis of RCTs; Level of evidence: 1.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Embase, and Cochrane CENTRAL for RCTs comparing PRP with placebo in lateral epicondylitis. Primary outcomes included pain relief and functional improvement assessed at multiple time points (4, 8-12, and 24-26 weeks). Secondary outcomes included adverse events and grip strength. Statistical analyses used standardized mean difference (SMD), mean difference (MD), and risk ratios with 95% confidence intervals (95% CIs).

Results: Six RCTs with 355 patients were included. PRP did not provide significant pain relief at 4 weeks (SMD, 0.08; 95% CI, –0.17 to 0.34; $P = .526$), 8 to 12 weeks (SMD, –0.36; 95% CI, –0.99 to 0.27; $P = .263$), or 24 to 26 weeks (MD, –1.58; 95% CI, –4.74 to 1.58; $P = .328$). Functional improvement was also not significantly different at 4 weeks (SMD, 0.09; 95% CI, –0.18 to 0.37; $P = .518$), 12 weeks (SMD, –0.09; 95% CI, –0.39 to 0.21; $P = .565$), or 24 to 26 weeks (SMD, 0.13; 95% CI, –0.18 to 0.43; $P = .413$). No significant difference was found in adverse events (risk ratio, 1.66; 95% CI, 0.65-4.19; $P = .287$).

Conclusion: PRP does not provide significant pain relief or functional improvement in patients with lateral epicondylitis in the current study of available RCTs as compared with placebo at all evaluated time points. These findings do not support PRP as a recommended treatment for this condition.

Keywords: lateral epicondylitis; tennis elbow; platelet-rich plasma; pain management.

Lateral epicondylitis, commonly known as tennis elbow, is a prevalent musculoskeletal condition characterized by pain and tenderness in the lateral epicondyle region of the humerus.[12] This disorder frequently affects individuals who perform repetitive wrist and forearm movements, leading to microinjuries and degeneration of the extensor carpi radialis brevis tendon.[12] Clinically, patients with lateral epicondylitis report pain that worsens with activities such as gripping or lifting objects, significantly impairing daily functioning and quality of life.[2]

Several noninvasive treatment options have been proposed, including physical therapy, nonsteroidal anti-inflammatory drugs, rest, orthoses, and extracorporeal shockwave therapy.[8,39,41] Alternatively, injectable therapies with agents such as autologous blood, dextrose, corticosteroids, and platelet-rich plasma (PRP) have been widely advocated.[8,39,41] Corticosteroids, considered safe and effective, have been the most widely accepted standard for injectable therapy for decades.[27] However, their use may lead to adverse effects such as subcutaneous atrophy,

The American Journal of Sports Medicine
1–11
DOI: 10.1177/03635465251383039

skin depigmentation, and damage to tendon structures.[6] Furthermore, corticosteroid injections can downregulate inflammatory cells and reduce type I collagen synthesis, potentially delaying the healing process.[36]

In this context, PRP emerges as a promising alternative, as it is derived from the patient's own blood and contains growth factors that can promote tissue regeneration and tendon healing.[18,28] Studies have explored its potential to provide sustained pain relief and functional improvement, particularly in chronic conditions such as lateral epicondylitis, where traditional treatments may have limitations.[10] However, it is important to note that, despite numerous studies being conducted, results are heterogeneous, and the quality of the evidence is often considered questionable.[5,34,35]

Therefore, this study aims to provide an updated and methodologically rigorous systematic review and meta-analysis of the efficacy and safety of PRP in the treatment of lateral epicondylitis. In contrast to previous reviews, our analysis exclusively includes randomized controlled trials comparing PRP with placebo, excludes studies with active comparators such as corticosteroids or autologous blood, incorporates recently published randomized clinical trials, and applies the updated Cochrane Risk of Bias 2.0 (RoB2) tool.[37] These methodological refinements are intended to enhance the reliability of the findings and reduce heterogeneity and bias, thus offering clearer guidance for clinical decision making.

METHODS

This is a systematic review guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses)[30] recommendations to assess the efficacy of PRP in treating pain and function in lateral epicondylitis. The PICOS strategy was applied as follows:

Population: Patients with tennis elbow
Intervention: PRP
Comparison: Placebo (normal saline or sham)
Outcomes: Primary—pain relief, function; secondary—quality of life, adverse effects, treatment tolerability, grip strength
Study type: Randomized controlled trial

This review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42024598709). The methodology was defined and registered before the database search began.

Eligibility Criteria

The eligibility criteria included full-text randomized clinical trials that were published by October 2024 and written in English; that were available in the PubMed, Scopus, Embase, and Cochrane CENTRAL databases; and that involved patients diagnosed with lateral epicondylitis. The studies had to compare PRP with placebo (considered normal saline or sham injection) and report outcomes on pain relief, function, quality of life, adverse effects, tolerability of treatment, and grip strength.

Exclusion criteria comprised articles not available in full text on digital platforms, studies addressing the use of PRP for conditions other than lateral epicondylitis, conference abstracts, preprints, letters to the editor, case reports and series, observational studies, nonrandomized trials, reviews, and studies with insufficient data on relevant outcomes. Duplicate publications of the same study were also excluded, with only the most comprehensive report included.

Search Strategy

We used keywords related to "platelet rich plasma" and "lateral epicondylitis" for the database search strategy. The descriptors were obtained from Medical Subject Headings. Boolean descriptors *AND* and *OR* were used for term searches on the mentioned platforms, adhering to the articles' inclusion and exclusion criteria. All descriptors and the complete search strategy for each database are available in the Appendix (available in the online version of this article).

Selection of Studies

Two reviewers (E.S.R.B. and C.R.A.J.), who had no access to each other's assessments, evaluated the titles and abstracts of the identified articles, selecting those that met the inclusion criteria. Articles that passed the initial screening were examined in their entirety to determine inclusion in the systematic review. In situations where discrepancies arose between the reviewers, a senior reviewer (P.H.S.L.), who had exclusive access to the conflicting articles, intervened to resolve differences. The studies were selected by using the Rayyan QCRI (Qatar Computing Research Institute).[29]

Data Summarization

Data extraction was performed independently and in duplicate (E.S.R.B. and C.R.A.J.) to ensure accuracy and reliability. Two reviewers extracted data from the studies using a predesigned data extraction form created in Microsoft Excel (Version 2205). The form captured comprehensive details on study characteristics, including population size, intervention

*Address correspondence to César Romero Antunes Júnior, Federal University of Bahia, Av Reitor Miguel Calmon, S/N–Vale do Canela, Salvador, Bahia State, Brazil, 40110-100 (email: cesarromeroaj@gmail.com; cesar.romero@ufba.br).
†Federal University of Bahia, Salvador, Brazil.
‡Federal University of São Paulo, São Paulo, Brazil.
Submitted February 24, 2025; accepted July 23, 2025.
The authors have declared that there are no conflicts of interest in the authorship and publication of this contribution. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

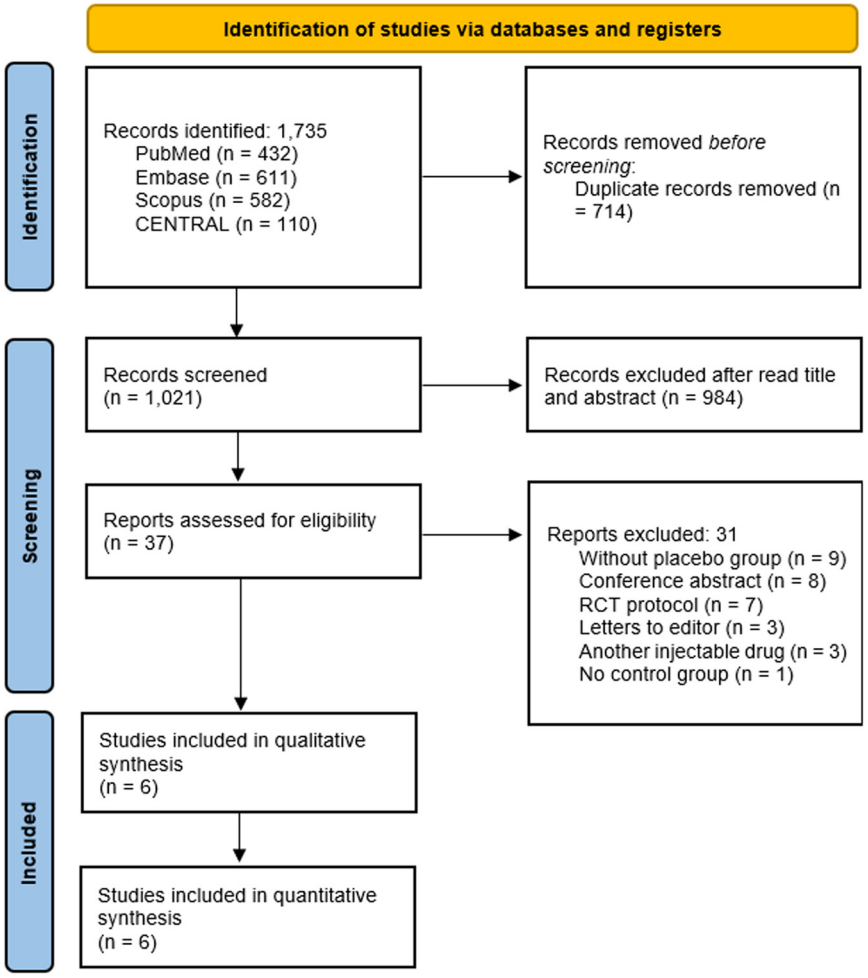

Figure 1. Flowchart of included studies. RCT, randomized clinical trial.

and control group specifics, methodological approaches, and the outcomes assessed. Any discrepancies between reviewers were resolved through discussion or consultation with a senior reviewer (E.B.S.L.) to achieve consensus.

Quality Assessment

The risk-of-bias assessment was conducted by using the Cochrane RoB2 tool for randomized trials,[37] as evaluated independently by 2 reviewers (E.S.R.B. and R.S.S.S.), with discrepancies resolved through a senior reviewer (P.H.S.L.). Publication bias was investigated by funnel plot analysis of point estimates about study weights.[31]

Statistical Analysis

Functional outcomes at 4, 12, and 24 to 26 weeks and pain at 4 and 8 to 12 weeks were evaluated by the standard mean difference (SMD) owing to the use of different scales. Pain outcomes at 24 to 26 weeks, as measured with the same scale, were assessed by the mean difference. Given the nature of event-based data, adverse effects were evaluated by risk ratio. All outcomes were presented with 95% confidence intervals (95% CIs). The Cochran Q test and I^2 statistic were used to assess heterogeneity, with $P < .10$ and $I^2 > 25\%$ considered significant for heterogeneity. Only a random-effects model employing the restricted maximum likelihood method was used to account for the between-study variance because of the methodological heterogeneity across studies, even in the absence of statistical heterogeneity.

A leave-one-out sensitivity analysis was conducted to evaluate the influence of individual studies on the overall meta-analysis results. An additional sensitivity analysis based on the 8-week results from Linnanmäki et al[22] was performed to assess their influence on the 8- to 12-week pain outcome. All statistical analyses were conducted in RStudio Version 764 via the *meta* and *metafor* packages.

RESULTS

After study selection, 6 articles were included in the meta-analysis.[18,22,26,32,33,42] The flowchart outlining the study

TABLE 1
Main Characteristics of Included Studies[a]

First Author (Year)	Type of Study	Test Group		Control		Injection Technique	Follow-up, wk
		No.	Intervention	No.	Intervention		
Linnanmäki (2020)[22]	Double blind	40	PRP, 4-6 mL	39	Normal saline	Intratendinous	52
Yerlikaya (2018)[42]	Double blind	LP-PRP, 30; LR-PRP, 30	LP- or LR-PRP, 1.5 mL	30	Normal saline	Intratendinous peppering	8
Seetharamaiah (2017)[33]	Open label	30	PRP, 1.5 mL	30	Normal saline	Peritendon	24
Schöffl (2017)[32]	Double blind	18	LP-PRP, 1 mL[b]	18	Normal saline	Peritendinous peppering	24
Montalvan (2015)[26]	Double blind	25	LP-PRP, 2 mL[c]	25	Normal saline	Intratendinous	54
Krogh (2013)[18]	Double blind	20	PRP, 3-3.5 mL	20	Normal saline	Peritendinous peppering	12

	Age, y, Mean ± SD		Gender: No. of Men/Women		Pain Baseline: VAS, Mean ± SD		Function Baseline, Mean ± SD	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Linnanmäki (2020)[22]	46.0 ± 5.0	49.0 ± 8.0	18/22	17/22	5.7 ± 1.7	5.9 ± 1.8	35.6 ± 15.5[d]	37.8 ± 14.8[d]
Yerlikaya (2018)[42]	LP-PRP, 45.0 ± 8.6 LR-PRP, 46.5 ± 8.7	47.6 ± 9.1	LP-PRP, 4/26 LR-PRP, 11/19	11/19	LP-PRP, 7.4 ± 2.1 LR-PRP, 6.5 ± 2.4	6.8 ± 1.8	—	—
Seetharamaiah (2017)[33]	20-40		12/18	13/17	6.5[e]	6.5[e]	—	—
Schöffl (2017)[32]	52.6 ± 11.5	52.6 ± 11.6	9/9	9/9	—	—	41.0 ± 18.0[d]	36.4 ± 17.7[d]
Montalvan (2015)[26]	47.0 ± 9.2	46.4 ± 8.6	17/8	17/8	6.8 ± 0.8	7.0 ± 1.0	3.3 ± 0.7[f]	3.4 ± 0.5[f]
Krogh (2013)[18]	47.6 ± 7.1	44.7 ± 7.9	9/11	9/11	27.5 ± 7.6[g]	25.0 ± 7.16[g]	51.5 ± 19.2[h]	47.1 ± 22.4[h]

[a]DASH, Disabilities of the Arm, Shoulder and Hand; LP, leukocyte poor; LR, leukocyte rich; PRP, platelet-rich plasma; PRTEE, Patient-Rated Tennis Elbow Evaluation; VAS, visual analog scale.
[b]The authors used 3 injections of PRP 7 to 10 days apart each.
[c]The authors used 2 injections of PRP 4 weeks apart each.
[d]The authors used the DASH score.
[e]The authors did not present the dispersion measures.
[f]The authors used the Role-Maudsley scale.
[g]The authors used the pain subscale of the PRTEE score.
[h]The authors used the PRTEE score.

selection process and reasons for exclusion is presented in Figure 1.

Characteristics of the Studies

Five articles were double-blind trials[18,22,26,32,42] and 1 was open label.[33] In total, 355 patients were assessed, with 193 receiving PRP applications. Among the participants, 156 were men, accounting for 43.94% of the population. Five studies focused on patients with chronic lateral epicondylitis and symptoms lasting at least 3 months[18,22,26,32,42]; however, Seetharamaiah et al[33] did not specify symptom duration for their participants. The mean ± SD age of patients was 47.22 ± 8.93 years. Yet, Seetharamaiah et al did not report the exact mean age or standard deviation, stating only that the population ranged from 20 to 40 years.

The studies administered PRP volumes ranging from 1 to 6 mL. Three studies used leukocyte-poor PRP,[26,32,42] while the other 3 did not specify PRP type.[18,22,33] Additionally, Yerlikaya et al[42] included a treatment arm with leukocyte-rich PRP. Peritendinous PRP was applied in 3 studies,[18,32,33] typically near the lateral epicondyle or the extensor tendons. Two studies used the peppering technique before peritendinous injection.[18,32] Two authors injected directly into the insertion of the extensor tendons at the lateral epicondyle.[22,26] Furthermore, Yerlikaya performed intratendinous peppering.

Two studies involved multiple PRP applications: Schöffl et al[32] applied 3 injections spaced 7 to 10 days apart, and Montalvan et al[26] administered 2 applications (baseline and at 4 weeks). All studies used normal saline as the control. Only 2 trials prescribed resistance exercises as post-treatment rehabilitation for both groups.[18,42] Follow-up periods varied across studies, ranging from 3 months to 1 year. Further details on the studies are provided in Table 1. Specific information regarding PRP preparation protocols, injection techniques, platelet concentrations, and activation methods can be found in Table 2.

Sample Size Calculations and Power Analyses in the Included Trials

Among the randomized controlled trials in this review, only 2 explicitly reported sample size calculations or power analyses. Krogh et al[18] performed an a priori sample size estimation to detect a minimum clinically important difference of 10 points on the pain subscale of the Patient-Rated Tennis Elbow Evaluation (PRTEE), assuming a standard deviation of 10 points, a 2-sided alpha of 0.05, and 86.9% power, resulting in the inclusion of 20 participants per group. Similarly, Montalvan et al[26] estimated a required sample size of 22 participants per group to detect a 10% difference in pain scores with 90% power and a 5% significance level, based on an assumed standard deviation of 0.10. In contrast, the remaining trials—conducted by Linnanmäki et al,[22] Yerlikaya,[42] Seetharamaiah et al,[33] and Schöffl et al[32]—did not report any justification for sample size or power estimation.

TABLE 2
PRP Preparation and Application Parameters in the Included Studies[a]

First Author (Year)	PRP Type	Dose	Injection Technique	Platelet Concentration	Preparation Method
Linnanmäki (2020)[22]	—	4-6 mL	Single injection into the insertion of the extensor tendons at the lateral epicondyle with a 22G × 1.5′′ needle	3613 × 10^3 platelets/μL	Blood drawn from the cephalic vein. Single centrifugation at 1500 rpm for 5 min
Yerlikaya (2018)[42]	LP-PRP, LR-PRP	1.5 mL	Peppering technique at the most sensitive point	2-8× platelet blood baseline	Manual method: 16 mL of blood drawn with 4 mL of citrate 1st centrifugation: 1075 rpm for 15 min 2nd centrifugation: 1495 rpm for 15 min
Seetharamaiah (2017)[33]	—	1 mL + 0.1 mL calcium chloride (activation method)	Injection into and around the extensor carpi radialis brevis tendon (5 mm distal to the lateral epicondyle). Local anesthetic (1 mL, mepivacaine 1%)	—	1st centrifugation: 1500 rpm for 15 min 2nd centrifugation: 2500 rpm for 10 min Anticoagulant: 0.9% sodium citrate
Schöffl (2017)[32]	LP-PRP	3 injections (7- to 10-d interval)	Dry needling of the tendon at the site of maximum tenderness. Injection into the site of tendinosis. Local anesthetic (2 mL, lidocaine 1%)	—	ACP system (Arthrex)
Montalvan (2015)[26]	—	2 injections of 2 mL (4 wk apart)	Ultrasound guided. Parallel to the tendon fibers of the extensor carpi radialis brevis/common tendons	1.6× platelet blood baseline	ACP system (Arthrex)
Krogh (2013)[18]	—	3-3.5 mL	Ultrasound guided. Antiseptic peppering technique. 1 skin portal, ~7 perforations into the common tendon origin (lateral epicondyle to humeroradial joint).	8× platelet blood baseline	27 mL of venous blood drawn by a 30-mL syringe with 3 mL of sodium citrate Centrifuge with Recover GPS II Platelet Concentrate Separation KIT (Biomet Biologics Inc) for 15 min Buffered with sodium bicarbonate to physiologic pH.

[a]ACP, autologous conditioned plasma; LP, leukocyte poor; LR, leukocyte rich; PRP, platelet-rich plasma.

Meta-analysis of Included Studies

Only 1 study assessed grip strength,[22] making it impossible to conduct a meta-analysis for this outcome. None of the studies evaluated quality-of-life outcomes, representing a relevant gap in the current evidence. However, meta-analyses were conducted for pain relief, function, and adverse effects.

Pain Relief. Four studies assessed pain relief using the visual analog scale,[22,26,33,42] while Krogh et al[18] utilized the pain subscale of the PRTEE. All studies measured pain at rest.

At the 4-week follow-up, pain relief was evaluated in 4 studies, encompassing a total of 259 patients. No significant difference was observed between the PRP and placebo groups (SMD, 0.08; 95% CI, –0.17 to 0.34; $P = .526$; $I^2 = 7\%$) (Figure 2A). A leave-one-out sensitivity analysis confirmed the robustness of this result (Appendix 2, Figure A1, available online). Additionally, no evidence of publication bias was identified in the funnel plot analysis (Appendix Figure A2, available online).

At 8 to 12 weeks, pain relief was evaluated in 5 studies with 319 patients. Similarly, no significant difference was found between the PRP and placebo groups (SMD, –0.36; 95% CI, –0.99 to 0.27; $P = .263$; $I^2 = 84\%$) (Figure 2B). A leave-one-out sensitivity analysis did not alter this finding (Appendix Figure A3, available online). An additional sensitivity analysis incorporating the 8-week data from Linnanmäki et al[22] yielded consistent results (SMD, –0.44; 95% CI, –1.05 to 0.17; $P = .162$; $I^2 = 83\%$) (Appendix Figure

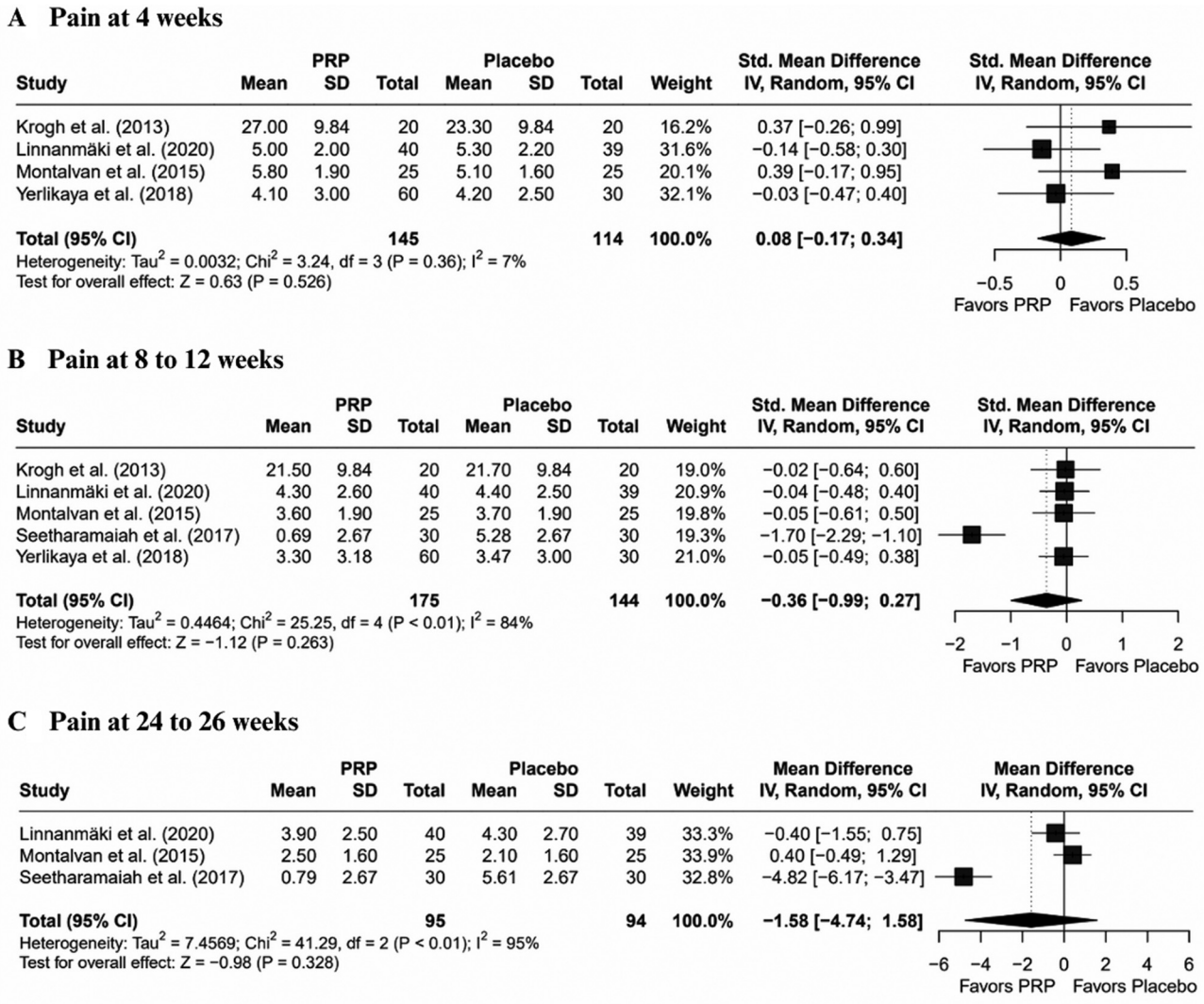

Figure 2. Forest plots depict pain relief in patients treated with platelet-rich plasma (PRP) as compared with placebo: standard mean difference in pain at (A) 4 weeks and (B) 8 to 12 weeks; (C) mean difference in pain at 24 to 26 weeks.

TABLE 3
Pooled Effect Sizes for Pain and Function by Follow-up Duration[a]

Time Point: Outcome	Effect Size: SMD	95% CI	*P* Value
4 wk			
Pain	0.08	–0.17 to 0.34	.526
Function	–0.36	–0.99 to 0.27	.263
12 wk			
Pain	–1.58	–4.74 to 1.58	.328
Function	0.09	–0.18 to 0.37	.518
24-26 wk			
Pain	–0.09	–0.39 to 0.21	.565
Function	0.13	–0.18 to 0.43	.413

[a]SMD, standardized mean difference.

A4, available online). However, asymmetry was detected in the funnel plot for this time point, suggesting potential publication bias or heterogeneity among studies (Appendix Figure A5, available online).

Three studies involving 189 patients assessed pain relief at 24 to 26 weeks. Once again, no significant difference was observed between the PRP and placebo groups (mean difference, –1.58; 95% CI, –4.74 to 1.58; P = .328; I^2 = 95%) (Figure 2C). This high level of heterogeneity indicates substantial variability among the studies at this time point. A leave-one-out sensitivity analysis confirmed the stability of this result (Appendix Figure A6, available online). Nevertheless, asymmetry in the funnel plot was noted, which may indicate publication bias or inconsistencies in the studies (Appendix Figure A7, available online).

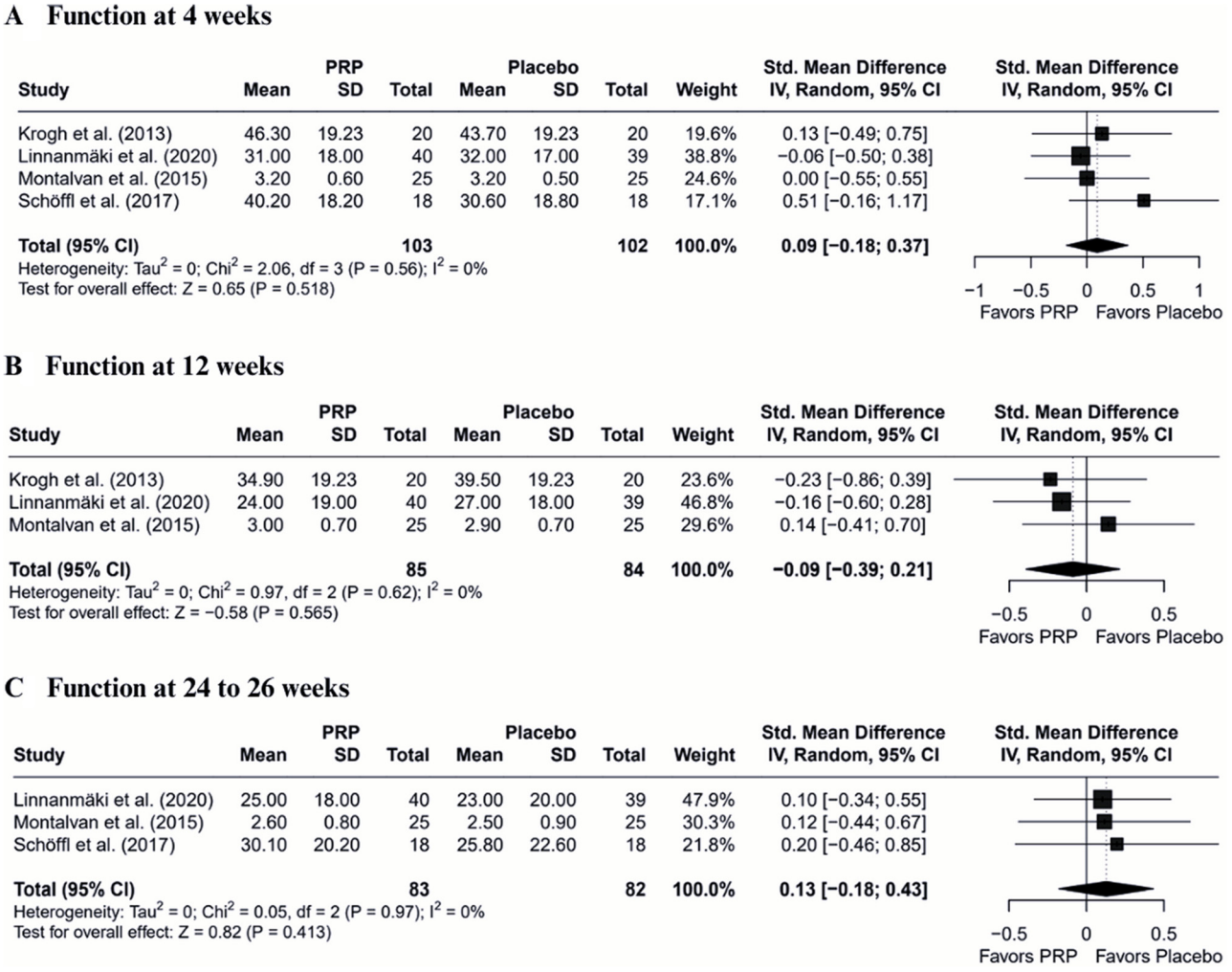

Figure 3. Forest plots depict function in patients treated with platelet-rich plasma (PRP) as compared with placebo: standard mean difference in function at (A) 4 weeks, (B) 12 weeks, and (C) 24 to 26 weeks.

The pooled effect sizes (SMDs), 95% CIs, and *P* values for pain and functional outcomes at each follow-up time point (4, 12, and 24-26 weeks) can be viewed in Table 3.

Function. Functional improvement was assessed by different scales across the studies. Two studies used the Disabilities of the Arm, Shoulder and Hand scale,[22,32] while Montalvan et al[26] utilized the Role-Maudsley scale and Krogh et al[18] used the PRTEE scale.

At the 4-week follow-up, 4 studies with a total of 205 patients evaluated functional improvement. The results showed no significant difference between the PRP and placebo groups (SMD, 0.09; 95% CI, –0.18 to 0.37; $P = .518$; $I^2 = 0\%$) (Figure 3A).

At 12 weeks, functional improvement was assessed in 3 studies involving 169 patients. As with the 4-week time point, no significant difference was observed between the PRP and placebo groups (SMD, –0.09; 95% CI, –0.39 to 0.21; $P = .565$; $I^2 = 0\%$) (Figure 3B).

At 24 to 26 weeks, 3 studies with 165 patients evaluated functional improvement. The findings remained consistent, showing no significant difference between the groups (SMD, 0.13; 95% CI, –0.18 to 0.43; $P = .413$; $I^2 = 0\%$) (Figure 3C). Sensitivity analysis confirmed the results, and no evidence of publication bias was found in the funnel plot analysis for all time points (Appendix Figures A8-A13, available online).

Adverse Events. Four studies were included in the combined analysis, which revealed no difference in adverse effects between the PRP and placebo groups (risk ratio, 1.66; 95% CI, 0.65-4.19; $P = .287$; $I^2 = 0\%$), indicating comparable safety profiles (Figure 4).[18,26,32,42] Two studies did not report adverse effects and were excluded from the analysis.[22,33] The most commonly reported adverse effects included pain during application, cutaneous allergic reactions, hematoma, and persistent pain lasting 3 to 4 days. All adverse effects were self-limiting and resolved within 3 to 4 days.

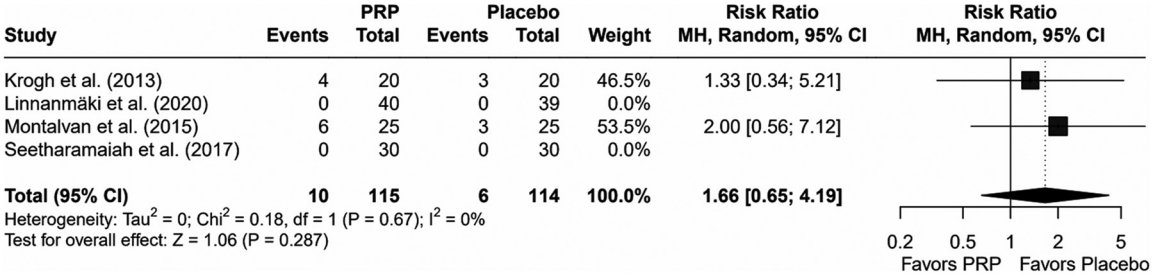

Figure 4. Forest plot depicts the risk ratio for adverse events in patients treated with platelet-rich plasma (PRP) as compared with placebo.

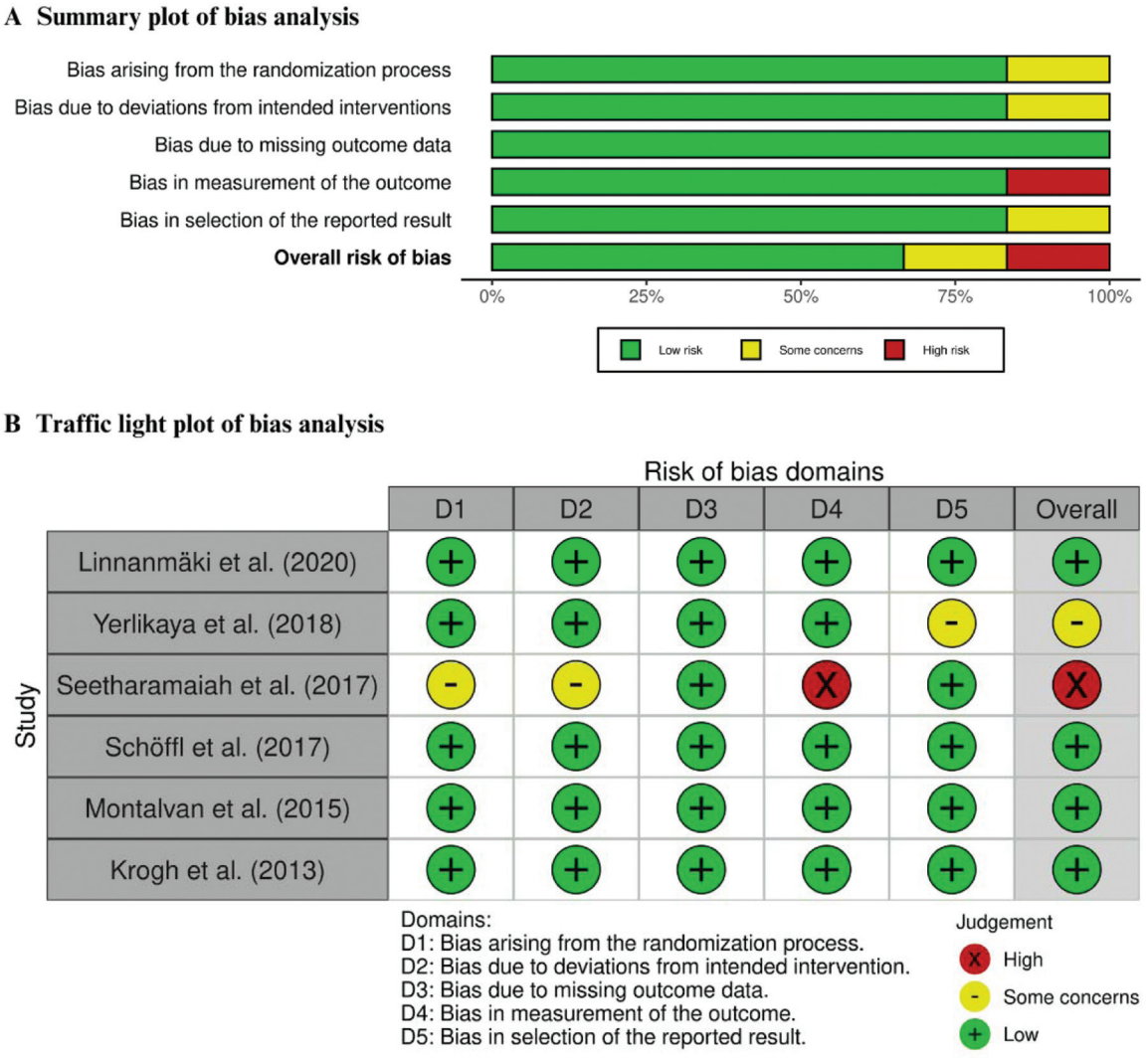

Figure 5. Risk of bias of included studies. (A) Summary plot of bias analysis. (B) Traffic light plot of bias analysis.

Risk of Bias of the Included Studies

The risk of bias of the studies is summarized in Figure 5.

Randomization Process. Five studies were classified as having a low risk of bias in the randomization process.[18,22,26,32,42] However, the Seetharamaiah et al[33] study was rated as "some concerns" because the randomization procedure was unclear.

Intervention. Five studies were classified as having a low risk of bias in the intervention process.[18,22,26,32,42]

In contrast, the Seetharamaiah et al[33] study was rated as having "some concerns" because it was an open-label trial. Knowledge of the interventions assigned by participants and assessors could influence the measurement and evaluation of outcomes.

Outcome. All studies were classified as having a low risk of bias in item 3 of the RoB2 tool, which evaluates missing outcome data.[18,22,26,32,33,42] For item 4, which assesses the measurement of outcomes, 5 studies were rated as having a low risk of bias.[18,22,26,32,42] However, the Seetharamaiah et al[33] study was rated as having a high risk of bias for being an open-label trial; the lack of blinding for participants and outcome assessors may have influenced outcome measurement.

Selective Reports. Five studies were classified as having a low risk of bias for selective outcome reporting.[18,22,26,32,33] In contrast, the Yerlikaya[42] study was rated as "some concerns" because, although the author indicated that grip strength was measured, specific results were not reported. Instead, all that was stated was that grip strength increased significantly as compared with baseline.

DISCUSSION

Our findings support the idea that PRP does not significantly improve pain or joint functionality. In addition, the interventions had similar safety profiles, with self-limiting adverse events reported. Previous meta-analyses evaluating PRP for lateral epicondylitis present important methodological limitations.[5,34,35] For instance, Averell et al[5] included randomized clinical trials and observational studies, increasing heterogeneity and introducing potential biases. Additionally, their use of a single-arm meta-analysis, without a control group, limits the strength of their conclusions. Similarly, Shim et al[34] combined studies with different comparators (placebo, corticosteroids, among others) without conducting subgroup analyses, which compromises internal validity. Although they reported benefits for PRP in pain relief, the lack of comparator balance calls these findings into question. Simental-Mendí et al[35] compared PRP with placebo and found no significant improvements in pain or function but used the outdated RoB1 tool to assess risk of bias, which is not aligned with current Cochrane recommendations. In contrast, our meta-analysis applied the RoB2 tool, ensuring greater methodological rigor. We also included the recent trial by Linnanmäki et al,[22] increasing the total sample size and improving the precision of the effect estimates.

The main findings of the present study did not reveal significant differences in pain reduction or functional improvement between PRP and placebo injections in patients with lateral epicondylitis. Additionally, the absence of reported minimal clinically important differences in the studies limits the interpretation of the results, hindering the ability to determine their true clinical significance. These findings contrast with those of Arirachakaran et al,[3] who observed the best short-term pain relief outcomes (after 2 months) with PRP application as compared with corticosteroid and autologous blood injections in a previous network meta-analysis. However, that study did not include any placebo-controlled trials. Mi et al[24] and Niemiec et al[28], similarly reported functional improvement between 3 months and 1 year following PRP treatment. Consequently, our findings do not support the recommendation of PRP for this condition, and its use remains inadvisable in light of the current evidence.

In this review, no significant differences were observed in the incidence of adverse events between PRP and placebo. The most common reactions were application-related pain, mild allergic responses, hematomas, and transient pain lasting 3 to 4 days, all of which resolved spontaneously. These findings are consistent with previous studies reporting transient postinjection pain as the most frequent adverse event associated with PRP.[24,28] In contrast, studies comparing PRP with steroids or autologous blood have noted potentially more severe adverse events, such as skin atrophy and pigmentation changes.[17,24] The wide variation in PRP preparation methods (leukocyte-rich or leukocyte-poor formulations)[20] and the absence of a standardization assessment protocol[19] may affect the incidence and severity of adverse events. Postinjection pain likely reflects physiologic responses to platelet and leukocyte activity and the release of bioactive proteins.[35] The lack of standardization in PRP protocols significantly hampers the comparability of studies and the reliability of their outcomes. Chahla et al[9] found that only 10% of clinical trials on PRP adequately reported preparation protocols and a mere 16% provided quantitative metrics on PRP composition, thus undermining reproducibility and interpretation of results. This methodological inconsistency contributes to the uncertainty surrounding PRP's efficacy, which, to date, has not demonstrated superiority over placebo in treating lateral epicondylitis.

PRP has been extensively investigated in the treatment of tendinopathies, but meta-analyses report conflicting results, largely attributed to methodological heterogeneity. Fitzpatrick et al[14] suggest that leukocyte-rich PRP may reduce pain in tendinopathies, emphasizing the importance of preparation methods. In contrast, Dai et al[13] found no significant difference between PRP and placebo in pain or function across various tendinopathies. In Achilles tendinopathy, Arthur Vithran et al[4] and Liu et al[23] found no robust evidence of clinical benefits from PRP as compared with placebo. Barreto et al[7] also reported no significant benefits in short-term outcomes. Regarding rotator cuff tendinopathies, Hamid et al[1] suggest that PRP may be effective for long-term pain management. Our findings are consistent with this broader literature, demonstrating no significant advantage of PRP over placebo for lateral epicondylitis. The effectiveness of PRP in tendinopathies appears limited and context dependent, as influenced by variability in preparation methods, application techniques, and outcome assessments.[9,16] Although the overall findings do not support a clear benefit, PRP may still be of value in specific subgroups, such as high-performance athletes or recalcitrant cases, which merits further investigation.

Available meta-analyses comparing PRP and corticosteroids for lateral epicondylitis report results that vary by

follow-up duration. In general, corticosteroids appear more effective for short-term pain relief and functional improvement (up to 8 weeks), while PRP shows potential benefits in longer-term outcomes, from 6 months onward.[21,38,40] This temporal difference reflects distinct pharmacologic profiles: corticosteroids provide immediate effects whereas PRP may act more gradually and persistently. However, beyond 8 weeks, the active effects of corticosteroids are no longer present, making comparisons with PRP less appropriate during this period.[11,25] The superior efficacy of PRP reported in some studies may thus be attributed to residual bias arising from uncontrolled confounding factors, such as the severity of patients' conditions, technical variations, or placebo effects.[15] This is particularly relevant in subjective outcomes such as pain, especially in small trials. In the present meta-analysis, no significant differences were found between PRP and placebo for any outcome assessed. These results suggest that, in the absence of superiority over placebo, the clinical efficacy of PRP remains uncertain and warrants further investigation. Placebo-controlled trials remain essential to reliably assess the therapeutic effect of PRP.

An analysis of the funnel plot to investigate the presence of publication bias revealed asymmetry in the distribution of the studies. However, this asymmetry does not appear to be directly attributable to publication bias but instead to the influence of the study conducted by Seetharamaiah et al,[33] which presented a high risk of bias and a substantially favorable effect for the intervention. This disproportionate contribution likely accounts for the observed distortion, suggesting that the asymmetry is more reflective of methodological heterogeneity than of selective publication. Future studies with greater methodological rigor and standardized bias assessments are essential to mitigate these discrepancies and provide more accurate estimates regarding possible publication biases in PRP research for lateral epicondylitis.

Study Limitations

This study has some limitations that should be taken into account. The small number of clinical trials and the methodological heterogeneity—particularly regarding PRP formulation, volume, application techniques, and follow-up protocols—limit the generalizability of the findings. To mitigate these factors, random-effects models were applied, along with leave-one-out sensitivity analyses to assess robustness and funnel plots to explore potential publication bias. The lack of blinding in one of the studies may also have introduced bias into the results. Accordingly, a leave-one-out sensitivity analysis was performed to verify the estimates' robustness, confirming the findings' overall consistency. The lack of standardization in evaluation instruments, as evidenced by the variation in methods used to measure pain and function, represents a relevant limitation. In addition, the absence of quality-of-life outcomes further restricts a comprehensive evaluation of the clinical impact of the interventions. Nonetheless, all analyses were based on the available data, prioritizing comparable outcomes to reinforce the reliability of the results. Funnel plot asymmetry suggested a potential publication bias, possibly related to the underreporting of small negative studies—an issue common in evaluations of emerging therapies. Nonetheless, even under these conditions, PRP did not demonstrate superiority over placebo, reinforcing the consistency and robustness of our findings.

CONCLUSION

Our results found no significant benefit of PRP over placebo in improving pain or function in patients with lateral epicondylitis. Given the lack of clinically meaningful effects and consistent results across time points, PRP should not be recommended for the treatment of this condition based on the current body of evidence. Furthermore, the lack of quality-of-life outcomes in the trials indicates the necessity for future research to integrate patient-centered measures, which will more effectively capture the clinical impact of PRP.

ORCID iDs

César Romero Antunes Júnior https://orcid.org/0000-0003-1701-5279
Ramon Sampaio Souza Santos https://orcid.org/0000-0003-4677-1874
Eduardo Silva Reis Barreto https://orcid.org/0009-0008-4688-8857
Guilherme Neves Azevedo https://orcid.org/0009-0007-4271-7543

REFERENCES

1. A Hamid MS, Sazlina SG. Platelet-rich plasma for rotator cuff tendinopathy: a systematic review and meta-analysis. *PLoS One*. 2021;16(5):e0251111.
2. Aben A, De Wilde L, Hollevoet N, et al. Tennis elbow: associated psychological factors. *J Shoulder Elbow Surg*. 2018;27(3):387-392.
3. Arirachakaran A, Sukthuayat A, Sisayanarane T, Laoratanavoraphong S, Kanchanatawan W, Kongtharvonskul J. Platelet-rich plasma versus autologous blood versus steroid injection in lateral epicondylitis: systematic review and network meta-analysis. *J Orthop Traumatol*. 2016;17(2):101-112.
4. Arthur Vithran DT, Xie W, Opoku M, Essien AE, He M, Li Y. The efficacy of platelet-rich plasma injection therapy in the treatment of patients with Achilles tendinopathy: a systematic review and meta-analysis. *J Clin Med*. 2023;12(3):995.
5. Averell N, Goodwin B, Park S, et al. The concentration of platelets in PRP does not affect pain outcomes in lateral epicondylitis: a systematic review and meta-analysis. *Pain Manag*. 2024;14(4):223-233.
6. Barnett J, Bernacki MN, Kainer JL, Smith HN, Zaharoff AM, Subramanian SK. The effects of regenerative injection therapy compared to corticosteroids for the treatment of lateral epicondylitis: a systematic review and meta-analysis. *Arch Physiother*. 2019;9(1):12.
7. Barreto ESR, Antunes Júnior CR, Cardoso IS, Alencar VB, Faleiro TB, Kraychete DC. Is platelet-rich plasma effective in treating achilles tendinopathy? A meta-analysis of randomized clinical trials. *Clin Orthop Relat Res*. 2024;483(5):779-790.
8. Calfee RP, Patel A, DaSilva MF, Akelman E. Management of lateral epicondylitis: current concepts. *J Am Acad Orthop Surg*. 2008;16(1):19-29.

9. Chahla J, Cinque ME, Piuzzi NS, et al. A call for standardization in platelet-rich plasma preparation protocols and composition reporting. *J Bone Joint Surg Am*. 2017;99(20):1769-1779.
10. Chen X, Jones IA, Park C, Vangsness CT. The efficacy of platelet-rich plasma on tendon and ligament healing: a systematic review and meta-analysis with bias assessment. *Am J Sports Med*. 2018; 46(8):2020-2032.
11. Coombes BK, Bisset L, Vicenzino B. Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: a systematic review of randomised controlled trials. *Lancet*. 2010;376(9754):1751-1767.
12. Cutts S, Gangoo S, Modi N, Pasapula C. Tennis elbow: a clinical review article. *J Orthop*. 2020;17:203-207.
13. Dai W, Yan W, Leng X, et al. Efficacy of platelet-rich plasma versus placebo in the treatment of tendinopathy: a meta-analysis of randomized controlled trials. *Clin J Sport Med*. 2023;33(1):69-77.
14. Fitzpatrick J, Bulsara M, Zheng MH. The effectiveness of platelet-rich plasma in the treatment of tendinopathy: a meta-analysis of randomized controlled clinical trials. *Am J Sports Med*. 2017;45(1):226-233.
15. Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? *N Engl J Med*. 2001;344(21):1594-1602.
16. Karjalainen TV, Silagy M, O'Bryan E, Johnston RV, Cyril S, Buchbinder R. Autologous blood and platelet-rich plasma injection therapy for lateral elbow pain. *Cochrane Database Syst Rev*. 2021;9(9): CD010951.
17. Kaux JF, Emonds-Alt T. The use of platelet-rich plasma to treat chronic tendinopathies: a technical analysis. *Platelets*. 2018;29(3): 213-227.
18. Krogh TP, Fredberg U, Stengaard-Pedersen K, Christensen R, Jensen P, Ellingsen T. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline. *Am J Sports Med*. 2013;41(3): 625-635.
19. Kwapisz A, Prabhakar S, Compagnoni R, Sibilska A, Randelli P. Platelet-rich plasma for elbow pathologies: a descriptive review of current literature. *Curr Rev Musculoskelet Med*. 2018;11(4):598-606.
20. Le ADK, Enweze L, DeBaun MR, Dragoo JL. Platelet-rich plasma. *Clin Sports Med*. 2019;38(1):17-44.
21. Li A, Wang H, Yu Z, et al. Platelet-rich plasma vs corticosteroids for elbow epicondylitis. *Medicine*. 2019;98(51):e18358.
22. Linnanmäki L, Kanto K, Karjalainen T, Leppänen OV, Lehtinen J. Platelet-rich plasma or autologous blood do not reduce pain or improve function in patients with lateral epicondylitis: a randomized controlled trial. *Clin Orthop Relat Res*. 2020;478(8):1892-1900.
23. Liu CJ, Yu KL, Bai JB, Tian DH, Liu GL. Platelet-rich plasma injection for the treatment of chronic Achilles tendinopathy. *Medicine*. 2019;98(16):e15278.
24. Mi B, Liu G, Zhou W, et al. Platelet rich plasma versus steroid on lateral epicondylitis: meta-analysis of randomized clinical trials. *Phys Sportsmed*. Published online February 21, 2017.
25. Mikolyzk DK, Wei AS, Tonino P, et al. Effect of corticosteroids on the biomechanical strength of rat rotator cuff tendon. *J Bone Joint Surg Am*. 2009;91(5):1172-1180.
26. 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*. 2016;55(2):279-285.
27. Newcomer KL, Laskowski ER, Idank DM, McLean TJ, Egan KS. Corticosteroid injection in early treatment of lateral epicondylitis. *Clin J Sport Med*. 2001;11(4):214-222.
28. Niemiec P, Szyluk K, Jarosz A, Iwanicki T, Balcerzyk A. Effectiveness of platelet-rich plasma for lateral epicondylitis: a systematic review and meta-analysis based on achievement of minimal clinically important difference. *Orthop J Sports Med*. 2022;10(4):23259671221 0869.
29. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210.
30. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. Published online March 29, 2021.
31. Peters JL. Comparison of two methods to detect publication bias in meta-analysis. *JAMA*. 2006;295(6):676.
32. Schöffl V, Willauschus W, Sauer F, et al. Autologous conditioned plasma versus placebo injection therapy in lateral epicondylitis of the elbow: a double blind, randomized study. *Sportverletz Sportschaden*. 2017;31(1):31-36.
33. Seetharamaiah VB, Gantaguru A, Basavarajanna S. A comparative study to evaluate the efficacy of platelet-rich plasma and triamcinolone to treat tennis elbow. *Indian J Orthop*. 2017;51(3):304-311.
34. Shim JW, Lee JS, Park YB, Cho HC, Jung HS. The effect of leucocyte concentration of platelet-rich plasma on outcomes in patients with lateral epicondylitis: a systematic review and meta-analysis. *J Shoulder Elbow Surg*. 2022;31(3):634-645.
35. Simental-Mendía M, Vilchez-Cavazos F, Álvarez-Villalobos N, et al. Clinical efficacy of platelet-rich plasma in the treatment of lateral epicondylitis: a systematic review and meta-analysis of randomized placebo-controlled clinical trials. *Clin Rheumatol*. 2020;39(8):2255-2265.
36. Sirico F, Ricca F, Di Meglio F, et al. Local corticosteroid versus autologous blood injections in lateral epicondylitis: meta-analysis of randomized controlled trials. *Eur J Phys Rehabil Med*. 2017;53(3): 483-491.
37. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
38. Tang S, Wang X, Wu P, et al. Platelet-rich plasma vs autologous blood vs corticosteroid injections in the treatment of lateral epicondylitis: a systematic review, pairwise and network meta-analysis of randomized controlled trials. *PM R*. 2020;12(4):397-409.
39. Taylor SA, Hannafin JA. Evaluation and management of elbow tendinopathy. *Sports Health*. 2012;4(5):384-393.
40. Xu Y, Li T, Wang L, Yao L, Li J, Tang X. Platelet-rich plasma has better results for long-term functional improvement and pain relief for lateral epicondylitis: a systematic review and meta-analysis of randomized controlled trials. *Am J Sports Med*. 2024;52(10):2646-2656.
41. Yao G, Chen J, Duan Y, Chen X. Efficacy of extracorporeal shock wave therapy for lateral epicondylitis: a systematic review and meta-analysis. *Biomed Res Int*. 2020;2020(1):2064781.
42. Yerlikaya M. Comparison of effects of leukocyte-rich and leukocyte-poor platelet-rich plasma on pain and functionality in patients with lateral epicondylitis. *Arch Rheumatol*. 2018;33(1):73-79.