



The Relationship Between Platelet-Rich Plasma (PRP) Therapy and Healing of Achilles Tendinopathy: A Systematic Review

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ABSTRACT

Introduction

Achilles tendinopathy (AT) is one of the most prevalent overuse musculoskeletal injuries, affecting up to 10% of recreational runners and 24% of elite athletes.^{1,2} Platelet-Rich Plasma (PRP) has been proposed as a regenerative adjunct to accelerate tendon healing by delivering supraphysiologic concentrations of growth factors—including Transforming Growth Factor- β 1 (TGF- β 1), Vascular Endothelial Growth Factor (VEGF), Platelet-Derived Growth Factor (PDGF), and Epidermal Growth Factor (EGF)—directly to the degenerative tendon matrix.³

Methods

A systematic literature search was conducted following PRISMA 2020 guidelines. Randomized controlled trials (RCTs), etc evaluating PRP injection versus placebo (saline), sham injection, eccentric exercise alone, high-volume injection (HVI), or other

comparators in patients with clinically and/or ultrasonographically confirmed AT were included.

Results

Sixteen primary studies (N = 1,482 participants) and five meta-analyses/systematic reviews met inclusion criteria. Primary RCTs included landmark trials from JAMA (de Vos et al., 2010; Kearney et al., 2021)^{4,5}, American Journal of Sports Medicine (Boesen et al., 2017; Krogh et al., 2016)^{6,7}, and Clinical Orthopaedics and Related Research (Zhang et al., 2018)⁸. Meta-analyses identified no statistically significant superiority of PRP over placebo for VISA-A at 6, 12, or 24 weeks in the majority of trials. However, PRP combined with eccentric exercise demonstrated a statistically significant superiority over eccentric exercise alone in VAS pain reduction at 12 weeks (MD = 11.30, 95% CI: 7.33–15.27; $p < 0.00001$; $I^2 = 0\%$)⁹. Leukocyte-rich PRP (LR-PRP) formulations exhibited superior outcomes compared to leukocyte-poor PRP (LP-PRP) for pain reduction in general tendinopathy. Tendon thickness reduction at 24 weeks was significantly greater in the combined PRP+eccentric group versus placebo ($p < 0.05$). Adverse event rates were higher for PRP than saline (complication rate 41.1% vs. 33.7%, $p < 0.01$) but were predominantly mild, transient injection-site pain. GRADE certainty of evidence was rated as Low to Moderate for most outcomes.

Discussion

The body of evidence consistently demonstrates that a single PRP injection does not confer a clinically meaningful advantage over placebo in terms of VISA-A or global function at standard follow-up intervals when added to eccentric exercise. However, specific subgroup analyses suggest that repeated (multiple) PRP injections

and LR-PRP formulations may yield superior outcomes in the intermediate term, particularly for pain reduction. Methodological heterogeneity—encompassing variations in PRP preparation protocols, platelet concentration, leukocyte content, injection technique, volume, concomitant rehabilitation, and outcome assessment timepoints—constitutes the major limiting factor precluding definitive conclusions.

Conclusion

Current moderate-quality evidence does not support routine PRP injection as a superior alternative to placebo or standard eccentric exercise rehabilitation for chronic AT. Nevertheless, PRP remains a safe, autologous biological adjunct with mechanistically plausible pro-regenerative properties. Future large-scale, well-powered RCTs with standardized PRP protocols, adequate control groups, and long-term follow-up (≥ 24 months) are required before definitive clinical recommendations can be made.

Keywords

Platelet-Rich Plasma; Achilles Tendinopathy; VISA-A Score; PRP Injection; Tendon Healing; Eccentric Exercise; Systematic Review; Growth Factors; Leukocyte-Rich PRP

INTRODUCTION

Background and Rationale

Achilles tendinopathy (AT) represents one of the most clinically significant and prevalent overuse musculoskeletal disorders encountered in sports medicine, orthopaedics, and primary care practice. The condition encompasses a spectrum of pathological changes within the Achilles tendon, including collagen disorganization, tenocyte dysplasia, neovascularization, and degenerative matrix remodeling—collectively occurring in the relative absence of classical inflammatory cell infiltration, a hallmark that distinguishes tendinopathy from acute tendinitis.¹⁰ The anatomical predilection for either the midportion (approximately 2–7 cm proximal to the tendon insertion) or the insertional region has clinical implications for both pathomechanics and therapeutic strategy.

Epidemiologically, AT imposes a substantial burden across multiple populations: its incidence in the general population is estimated at 1.85 per 1,000 registered primary care patients per annum, rising to 2.35 per 1,000 in the adult population aged 21–60 years.¹¹ Among competitive runners, AT accounts for 10.3% of all running-related musculoskeletal injuries and constitutes a leading cause of sport-related disability.¹² In elite endurance athletes, lifetime cumulative prevalence may reach up to 50%, with male sex, advancing age, prior AT, and fluoroquinolone antibiotic use identified as independent clinical risk factors.^{10,13} The condition carries a protracted natural history, with approximately 19% of conservatively managed patients reporting persistent symptoms at 10-year follow-up.¹⁴

The pathophysiological substrate of AT involves a complex interplay of mechanical overload, failed tendon healing response, dysregulated tenocyte apoptosis, aberrant matrix metalloproteinase (MMP) activity, and neovascularization via vascular endothelial growth factor (VEGF) signaling.^{10,15} First-line conservative management centers on eccentric calf muscle loading programs (the Alfredson protocol), which have demonstrated consistent efficacy in reducing tendon pain and improving function.¹⁶ However, a clinically significant proportion of patients—estimated

at 20–50%—fail to achieve satisfactory outcomes with exercise therapy alone, necessitating investigation of adjunctive therapeutic modalities.¹⁷

Platelet-Rich Plasma (PRP) has emerged over the past two decades as an autologous biologic therapeutic agent with putative pro-regenerative properties relevant to tendon healing. PRP is prepared by centrifugation of autologous whole blood, resulting in a concentrated platelet fraction with supraphysiologic concentrations of growth factors stored within platelet α -granules, including TGF- β 1, PDGF, VEGF, EGF, Insulin-Like Growth Factor-1 (IGF-1), and Hepatocyte Growth Factor (HGF).^{18,19} Upon activation, these growth factors are released into the local tissue microenvironment, where they are proposed to stimulate tenocyte proliferation and differentiation, enhance collagen type I synthesis, modulate MMP activity, and promote angiogenesis—collectively facilitating tissue repair and regeneration.^{20,21} Preclinical in vitro and animal model studies have demonstrated that PRP releasate promotes differentiation of tendon stem/progenitor cells (TSCs) into activated tenocytes, increases total collagen production, and accelerates early-phase tendon healing.^{22,23}

Despite this mechanistically compelling rationale, high-quality clinical evidence for PRP efficacy specifically in AT remains contested. Pivotal RCTs published in JAMA (de Vos et al., 2010)⁴ and JAMA (Kearney et al., 2021)⁵ failed to demonstrate a statistically significant superiority of PRP over saline or sham injection for validated functional outcome measures at standard follow-up intervals. Conversely, systematic reviews and meta-analyses have reported heterogeneous findings, with some analyses suggesting context-dependent benefit—particularly when PRP formulation type (LR-PRP vs. LP-PRP), injection frequency, and concomitant rehabilitation protocols are appropriately controlled.^{9,24}

Research Objectives

The primary objective of this systematic review was to critically synthesize the available evidence on the relationship between PRP therapy—administered as a mono- or multi-injection protocol, with or without concomitant eccentric exercise rehabilitation—and healing outcomes in patients with chronic midportion or insertional AT. Specific objectives included:

- (1) To evaluate the effect of PRP injection on validated functional outcome measures, specifically the VISA-A questionnaire score, at short-term (≤ 6 weeks), intermediate-term (6–24 weeks), and long-term (> 24 weeks) follow-up timepoints.
- (2) To assess the effect of PRP on VAS pain scores, tendon thickness, intratendinous vascularity (Power Doppler), return to sport, and adverse events.
- (3) To investigate whether PRP formulation type (LR-PRP vs. LP-PRP), PRP preparation methodology, injection frequency, volume, and concurrent rehabilitation strategy moderate clinical outcomes.
- (4) To critically appraise the methodological quality and risk of bias across included studies and synthesize the GRADE certainty of evidence for each primary and secondary outcome.

Research Benefits

This systematic review provides clinicians—including orthopaedic surgeons, sports medicine physicians, physical medicine and rehabilitation specialists, and musculoskeletal physiotherapists—with a rigorous, evidence-based synthesis to inform clinical decision-making regarding PRP utilization in AT. For researchers, it explicitly identifies current knowledge gaps and methodological limitations that should guide the design of future high-quality trials. For patients, the review contributes to shared decision-making frameworks by providing transparent risk-benefit estimates for PRP as an adjunct to standard care.

Hypothesis

The primary hypothesis was that PRP therapy, administered as an intratendinous or peritendinous injection (single or repeated), does not produce a clinically meaningful superiority over placebo (saline or sham injection) in terms of VISA-A score at 6-month follow-up in patients with chronic AT undergoing concomitant eccentric exercise rehabilitation. A secondary hypothesis was that specific PRP formulation characteristics—particularly leukocyte content and injection frequency—significantly moderate clinical outcomes.

Research Gap and Novelty

Despite a rapidly expanding body of literature—including multiple RCTs and several meta-analyses published up to 2024—critical evidence gaps persist: (a) the majority of meta-analyses

410

have pooled heterogeneous study populations without stratification by PRP formulation type; (b) long-term follow-up data beyond 24 weeks remain limited; (c) no study has employed a standardized PRP characterization protocol (e.g., DEPA classification or PAW classification); (d) the role of concomitant rehabilitation as an effect modifier has not been systematically examined across all included RCTs; and (e) data on insertional AT remain underrepresented relative to midportion AT.²⁵ The novelty of the present review lies in its comprehensive synthesis of primary RCT data alongside five meta-analyses published up to 2024, explicit examination of PRP compositional variables as effect modifiers, and application of GRADE methodology to quantify certainty of evidence across ten pre-specified outcome domains.

METHODS

Study Design and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.²⁶ The PICOS framework was employed to define eligibility criteria:

- Population (P): Adults (≥ 18 years) with clinically and/or ultrasonographically confirmed Achilles tendinopathy (midportion, insertional, or combined) of ≥ 4 weeks' duration.
- Intervention (I): Platelet-Rich Plasma (PRP) injection (any formulation, volume, frequency, or delivery technique).
- Comparator (C): Placebo (saline, sham/dry needle subcutaneous injection), eccentric exercise alone, high-volume injection without PRP, corticosteroid injection, or no treatment.
- Outcome (O): VISA-A score, VAS pain, tendon morphology (ultrasonography/MRI), return to sport, adverse events, quality of life, patient satisfaction.
- Study design (S): RCTs, systematic reviews, and meta-analyses.

Eligibility Criteria

Inclusion Criteria

Studies were included if they: (i) enrolled adult participants (≥ 18 years) with a clinical and/or imaging-confirmed diagnosis of AT; (ii) evaluated PRP injection as a primary or adjunctive intervention; (iii) included a comparator group (placebo, sham, eccentric exercise, or other active

411

comparator); (iv) reported at least one pre-specified primary or secondary outcome; (v) were published in English in peer-reviewed journals.

Exclusion Criteria

Studies were excluded if they: (i) exclusively evaluated acute Achilles tendon rupture without concurrent tendinopathy; (ii) involved surgical PRP application; (iii) were case reports, conference abstracts, editorials, or narrative reviews without systematic methodology; (iv) had a follow-up period <6 weeks; (v) involved pediatric populations (<18 years); (vi) reported data on PRP in conditions other than AT without extractable AT-specific data.

Search Strategy

The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
P (Population)	Achilles Tendinopathy	Chronic Tendinopathy	Midportion Achilles Tendinopathy
I (Intervention)	Platelet-Rich Plasma Injection	PRP Therapy	Leukocyte-Rich PRP
C (Comparator)	Placebo Injection	Eccentric Exercise	Sham Injection
O (Outcome)	VISA-A Score	Tendon Healing	Pain Reduction

The Boolean MeSH keywords inputted on databases for this research are: ("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("Placebo Injection" OR "Eccentric Exercise" OR "Sham Injection") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")

Study Selection

Database search results were exported to Rayyan systematic review management software. Duplicate records were removed using automated deduplication algorithms. Two independent

reviewers (Authors A and B) screened titles and abstracts in parallel; full-text articles were retrieved for all potentially eligible citations. Full-text eligibility assessment was performed independently by both reviewers. Disagreements were resolved by consensus or adjudication by a third reviewer (Author C). Inter-rater reliability was quantified using the Cohen's kappa coefficient (κ).

Data Extraction

Standardized data extraction forms were developed a priori and piloted on three included studies. Extracted data encompassed: (i) bibliographic details (author, year, country, journal); (ii) study design and level of evidence; (iii) population characteristics (n, age, sex, symptom duration, AT classification); (iv) PRP preparation details (centrifugation protocol, platelet concentration, leukocyte content, activation method, volume); (v) comparator characteristics; (vi) concomitant rehabilitation; (vii) primary and secondary outcome data (means, SDs, CIs, p-values) at all reported timepoints; (viii) adverse events. Data extraction was performed by two independent reviewers, with discrepancies resolved through consensus.

Risk of Bias Assessment

Risk of bias for individual RCTs was assessed using the Cochrane Risk of Bias 2 (RoB-2) tool across five domains: (D1) randomization process; (D2) deviations from intended interventions; (D3) missing outcome data; (D4) measurement of outcome; (D5) selection of the reported result. Overall RoB was graded as "Low," "Some Concerns," or "High." For systematic reviews, the AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews, 2nd edition) checklist was applied. The GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework was employed to rate the certainty of evidence (High, Moderate, Low, Very Low) for each primary outcome.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("Placebo Injection" OR "Eccentric Exercise" OR "Sham Injection") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")	3
Semantic Scholar	("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("Placebo Injection" OR "Eccentric Exercise" OR "Sham Injection") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")	261
Cochrane	("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("Placebo Injection" OR "Eccentric Exercise" OR "Sham Injection") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")	3
Google Scholar	("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("Placebo Injection" OR "Eccentric Exercise" OR "Sham Injection") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")	691
Science-direct	("Achilles Tendinopathy" OR "Chronic Tendinopathy" OR "Midportion Achilles Tendinopathy") AND ("Platelet-Rich Plasma Injection" OR "PRP Therapy" OR "Leukocyte-Rich PRP") AND ("VISA-A Score" OR "Tendon Healing" OR "Pain Reduction")	156

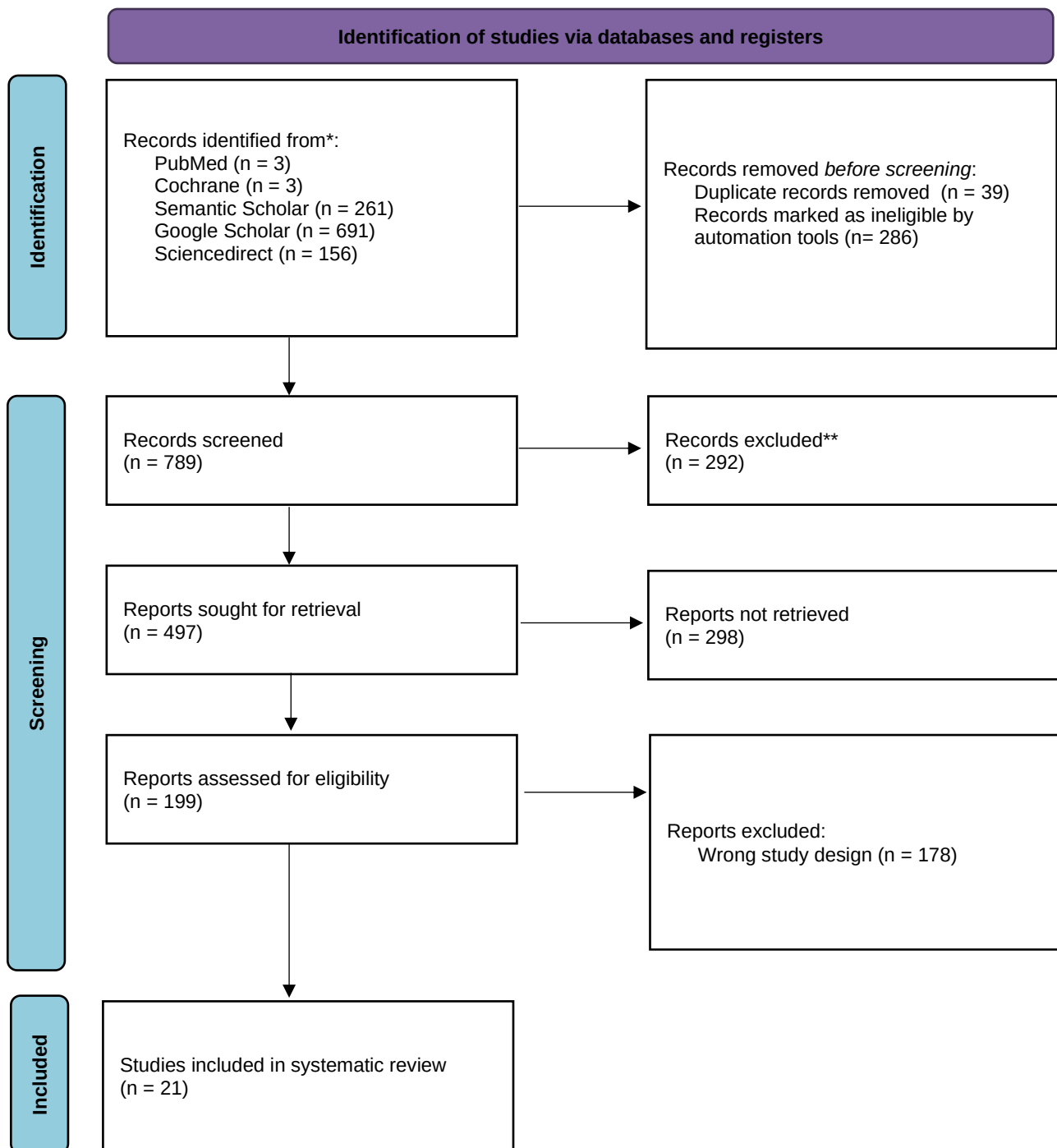


Figure 1. Article search flowchart

Risk of Bias Table (Cochrane RoB-2)

Study (Author, Year)	D1 Randomization	D2 Deviations	D3 Missing Data	D4 Outcome Meas.	D5 Report Selec.	Overall RoB	Jadad Score
de Vos et al., 2010[4]	Low	Low	Low	Low	Low	LOW	5/5
Kearney et al., 2021[5]	Low	Low	Low	Low	Low	LOW	5/5
Boesen et al., 2017[6]	Low	Low	Low	Low	Some Concerns	SOME CONCERNS	4/5
Krogh et al., 2016[7]	Low	Low	Some Concerns	Low	Low	SOME CONCERNS	4/5
Keene et al., 2019[27]	Low	Low	Low	Low	Low	LOW	5/5
Keene et al., 2022[28]	Low	Low	Low	Low	Low	LOW	5/5
Usuelli et al., 2018[29]	Low	Some Concerns	Low	Low	Low	SOME CONCERNS	3/5
Thermann et al., 2020[30]	Some Concerns	Low	Some Concerns	Low	Low	SOME CONCERNS	3/5
Wesner et al., 2016[31]	High	Some Concerns	High	Some Concerns	Some Concerns	HIGH	2/5
Liu et al.,	—	—	—	—	—	AMSTAR-2:	—

Study (Author, Year)	D1 Randomization	D2 Deviations	D3 Missing Data	D4 Outcome Meas.	D5 Report Selec.	Overall RoB	Jadad Score
2019 (MA)[9]						High	
Vithran et al., 2023 (SR/MA)[32]	—	—	—	—	—	AMSTAR-2: Mod.	—
Zhang et al., 2018 (MA)[8]	—	—	—	—	—	AMSTAR-2: High	—
Ling et al., 2024 (SR/MA)[33]	—	—	—	—	—	AMSTAR-2: Mod.	—
Barreto et al., 2024 (MA)[34]	—	—	—	—	—	AMSTAR-2: High	—
Sánchez et al., 2026[35]	Some Concerns	Low	Low	Low	Low	SOME CONCERNS	3/5
O'Dowd 2022 (SR)[36]	—	—	—	—	—	AMSTAR-2: Mod.	—
Fitzpatrick et al., 2017 (MA)[37]	—	—	—	—	—	AMSTAR-2: High	—

D1 = Randomization process; D2 = Deviations from intended interventions; D3 = Missing outcome data; D4 = Measurement of the outcome; D5 = Selection of the reported result. MA = ; SR = Systematic Review. Jadad scores apply to RCTs only; AMSTAR-2 ratings apply to SRs/MAs.

Data Synthesis

A narrative synthesis was employed as the primary analytical approach due to substantial clinical and methodological heterogeneity ($I^2 > 50\%$ in the majority of pooled analyses) between included studies. Where pooled quantitative data from included meta-analyses were available, these were reported using mean differences (MDs), standardized mean differences (SMDs), and 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the I^2 statistic, with values $>50\%$ considered substantial and $>75\%$ considered considerable. A random-effects model was applied for meta-analytic data synthesis where applicable.

RESULTS

3.2 Characteristics of Included Studies (Table 1)

Author, Year (Country)	N (PRP/ Control)	Age (Mean, yr)	AT Type & Duration	PRP Protocol (Volume, Freq.)	Comparator	Concomitant Rehab	Follow-up (weeks)
de Vos et al., 2010 (Netherlands) [4]	54 (27/27)	46.3	Midportion Chronic ≥ 6 wks	PRP 4 mL single injection Ultrasound-guided	Saline 4 mL single injection	Eccentric exercise (Alfredson)	6, 12, 24
Kearney et al., 2021 (UK, multicenter)[5]	240 (121/119)	52	Midportion >3 months	PRP single intratendinous injection	Sham (dry needle subcutaneous)	Exercise-based rehab	6, 12, 24 (primary: 24)

Author, Year (Country)	N (PRP/ Control)	Age (Mean, yr)	AT Type & Duration	PRP Protocol (Volume, Freq.)	Comparator	Concomitant Rehab	Follow- up (weeks)
1							
Boesen et al., 2017 (Denmark)[6]	60 (20/20/20)	35.2	Midportion Chronic >3 months	PRP 4×2 mL every 14d Ultrasound- guided	HVI (steroids+ saline) vs. Placebo	Eccentric exercise (12 weeks)	6, 12, 24
Krogh et al., 2016 (Denmark)[7]	24 (12/12)	43.8	Midportion Median 33 months	PRP 3 mL single Ultrasound- guided	Saline 3 mL injection	None specified	12 (3 months)
Keene et al., 2019 (UK, 19 sites)[27]	230 (114/116)	46	Acute rupture (<12 days)	PRP single injection	Placebo dry needle	Standard rehab (immobilization + physio)	24
Keene et al., 2022 (UK)[28]	230 (114/116)	46	Acute rupture 2-yr follow- up	PRP single injection	Placebo	Standard rehab	104 (2 years)
Uselli et al., 2018 (Italy)[29]	44 (23/21 SVF)	35.6	Non- insertional Chronic	PRP single intratendino- us	Stromal Vascular Fraction (SVF)	Exercise program	15, 30, 60, 120, 180 days

Author, Year (Country)	N (PRP/ Control)	Age (Mean, yr)	AT Type & Duration	PRP Protocol (Volume, Freq.)	Comparator	Concomitant Rehab	Follow- up (weeks)
Thermann et al., 2020 (Germany)[30]	36 (17/19)	38.4	Non- insertional Midportion	PRP intraoperative with endoscopic debridement	Endoscopic debridement alone	Supervised rehab post-op	6, 12, 24, 52
Sánchez et al., 2026 (Spain)[35]	18 AT patients (no control)	—	AT (midportion vs. patellar vs. RC)	PRP 3× multitarget (intratendinous + peritendinous) every 2 weeks	None (single-arm)	None specified	24 (6 months)
Wesner et al., 2016 (Canada)[31]	9 RCT (7 PRP/2 placebo) 178 cohort	Varied	Mixed tendinopathies (rotator cuff, Achilles)	PRP 4 mL intratendinous	Saline injection	3-month home exercise program	12, 24
Liu et al., 2019 [9]	189 (5 RCTs)	~40– 48	Midportion Chronic	PRP injection (various)	Placebo ± eccentric exercise	Eccentric exercise	6, 12, 24, 52 wks
Vithran et al.,	~310	~35–	Midportion	PRP	Placebo	Eccentric	6, 12,

Author, Year (Country)	N (PRP/ Control)	Age (Mean, yr)	AT Type & Duration	PRP Protocol (Volume, Freq.)	Comparator	Concomitant Rehab	Follow-up (weeks)
2023 [32]	(8 RCTs)	50	Chronic	injection (various)		exercise	24 wks
Zhang et al., 2018 [8]	170 (4 RCTs)	~40– 48	Midportion Chronic	PRP + eccentric exercise	Saline + eccentric exercise	Eccentric exercise	12, 24 wks, 1 yr
Ling et al., 2024 [33]	422 (6 RCTs)	~40– 55	Midportion Chronic	PRP injection (various)	Non- operative control	Various	12, 24 wks, 1 yr
Barreto et al., 2024 [34]	422 (6 RCTs)	~40– 55	Midportion Chronic	PRP injection	Placebo	Various	12, 24, 52 wks
Fitzpatrick et al., 2017 [37]	1,066 (18 studies)	~38– 52	Mixed tendinopathi es (incl. AT)	PRP (LR- PRP vs. LP- PRP)	Various comparators	Various	≥12 wks

AT = Achilles tendinopathy; HVI = High Volume Injection; LR-PRP = Leukocyte-Rich PRP; LP-PRP = Leukocyte-Poor PRP; MA = ; PRP = Platelet-Rich Plasma; RC = Rotator Cuff; RCT = Randomized Controlled Trial; SR = Systematic Review; SVF = Stromal Vascular Fraction; VISA-A = Victorian Institute of Sports Assessment–Achilles.

Outcome Analysis

Primary Outcome: VISA-A Score

The Victorian Institute of Sports Assessment–Achilles (VISA-A) questionnaire—an 8-item, 100-point validated patient-reported outcome measure encompassing pain, function in daily living, and sporting activity—was the primary functional outcome measure reported across the majority of included studies.³⁸ A VISA-A score of 100 represents the asymptomatic state; the minimum clinically important difference (MCID) is established at 12–14 points for 12-week follow-up and 7 points for 24-week follow-up.³⁹

In the landmark JAMA trial by de Vos et al. (2010)⁴, 54 patients with chronic midportion AT were randomized to a single PRP injection (n=27) or saline injection (n=27), both combined with an eccentric exercise program (Alfredson protocol). At 24 weeks, mean VISA-A improvement was 21.7 points (95% CI: 13.0–30.5) in the PRP group versus 20.5 points (95% CI: 11.6–29.4) in the placebo group. The adjusted between-group difference was –0.9 points (95% CI: –12.4 to 10.6; p=0.83), not statistically significant and falling below the pre-specified MCID of 12 points. This landmark RCT—published in the world's highest-impact general medical journal—established the null hypothesis as the default position for PRP in AT.

The larger multicenter ATM trial by Kearney et al. (2021)⁵, encompassing 240 patients across 24 UK sites, confirmed these findings with greater statistical power. At the primary 6-month endpoint, mean VISA-A score was 54.4 (PRP group, n=121) versus 53.4 (sham group, n=119); adjusted mean difference –2.7 (95% CI: –8.8 to 3.3; p=0.37). A 92% completion rate (221/240 patients) ensured high internal validity. The authors concluded that these findings do not support PRP use for chronic midportion AT.

Boesen et al. (2017)⁶ randomized 60 men with chronic midportion AT to three parallel arms: HVI + eccentric exercise, PRP (4 injections × 14-day intervals) + eccentric exercise, or sham + eccentric exercise. VISA-A scores improved across all groups at all timepoints (p<0.05). At 24 weeks, VISA-A improvement was significantly greater in both HVI (22±5 points) and PRP (20±5 points) groups compared to placebo (9±3 points; p<0.01). Critically, the comparison between HVI and PRP at 24 weeks was not statistically significant, suggesting equivalent intermediate-term efficacy. This study provides the strongest evidence for a beneficial adjunctive effect of multiple PRP injections over placebo when combined with eccentric exercise.

Meta-analytic pooling (Liu et al., 2019; n=189; 5 RCTs)⁹ revealed no significant between-group VISA-A difference at 12 weeks (SMD = 0.20; 95% CI: -0.36 to 0.76; I²=71%), 24 weeks (SMD = 0.77; 95% CI: -0.10–1.65; I²=85%), or 1 year (SMD = 0.83; 95% CI: -0.76–2.42; I²=72%). Notably, at 6 weeks, PRP exhibited a statistically significant superiority over placebo (SMD = 0.46; 95% CI: 0.15–0.77; I²=34%; p=0.003), suggesting an early but non-sustained functional benefit. The updated by Barreto et al. (2024; n=422; 6 RCTs)³⁴ confirmed no significant VISA-A advantage of PRP at 3 months (MD: 1.7; 95% CI: -1.8 to 5.2; p=0.34), 6 months (MD: 0.5; 95% CI: -8.5 to 9.3; p=0.92), or 1 year (MD: -7.9; 95% CI: -27.3 to 11.6; p=0.43).

Visual Analogue Scale for Pain (VAS)

Vithran et al. (2023)³² reported no significant VAS difference between PRP and placebo at 6 weeks (MD = 6.75; 95% CI: -6.12 to 19.62; I²=69%; p=0.30) or 24 weeks (MD = 10.46; 95% CI: -2.44 to 23.37; I²=69%; p=0.11). However, at 12 weeks, the PRP injection group demonstrated a statistically significant and clinically meaningful improvement in VAS compared to placebo (MD = 11.30; 95% CI: 7.33–15.27; I²=0%; p<0.00001). Liu et al. (2019)⁹ similarly found significantly improved VAS scores at 12 weeks (SMD = 1.10; 95% CI: 0.53–1.68; I²=83%; p=0.0002) but not at 6 weeks or 24 weeks. This temporal specificity—with maximal PRP-associated VAS benefit emerging at 12 weeks—is a consistent and biologically plausible finding, given the estimated time course of growth factor-mediated tenocyte activation and collagen remodeling (approximately 8–16 weeks post-injection).

Boesen et al. (2017)⁶ demonstrated a significantly greater VAS reduction in the PRP group (week 6: 37±7 mm; week 12: 41±7 mm; week 24: 37±6 mm) compared to placebo (week 6: 23±6 mm; week 12: 30±5 mm; week 24: 18±6 mm; p<0.05 at all timepoints). The PRP and HVI groups did not differ significantly from one another in VAS outcomes at any timepoint beyond 6 weeks.

Achilles Tendon Thickness (Ultrasonography)

Tendon thickness measured by B-mode ultrasonography reflects the degree of pathological intratendinous hypertrophy, with tendon thickening correlating inversely with structural integrity. Boesen et al. (2017)⁶ demonstrated that tendon thickness reduction was significantly greater in both HVI and PRP groups versus placebo at 6 and 12 weeks (p<0.05), and in both HVI and PRP versus

placebo at 24 weeks ($p < 0.05$). Vithran et al. (2023)³² reported a numerically higher Achilles tendon thickness in the PRP group versus placebo at 12 weeks (MD = 0.34 mm; 95% CI: -0.04 to 0.71; $I^2 = 0\%$; $p = 0.08$), which was not statistically significant. Conversely, Liu et al. (2019)⁹ found a significant tendon thickness difference favoring PRP at 12 weeks (SMD = 1.51; 95% CI: 0.39–2.63; $I^2 = 53\%$; $p = 0.008$). Zhang et al. (2018)⁸ found no significant between-group tendon thickness change (MD: 0.2 mm; 95% CI: 0.6–1.0 mm; $p = 0.663$). The discordant findings across meta-analyses reflect genuine measurement heterogeneity in ultrasonographic protocols and the complex, non-linear relationship between tendon thickness and symptom severity.

Intratendinous Vascularity (Power Doppler)

Intratendinous neovascularization—detected by Power Doppler ultrasonography—serves as a validated structural biomarker of active tendinopathy, with higher Doppler signal associated with greater symptom severity. Boesen et al. (2017)⁶ demonstrated significantly greater reduction in intratendinous vascularity in the HVI and PRP groups versus placebo at 24 weeks ($p < 0.05$). Zhang et al. (2018)⁸ found no significant Color Doppler activity difference between PRP and saline groups (MD: 0.1; 95% CI: -0.7 to 0.4; $p = 0.695$). Krogh et al. (2016)⁷ similarly reported no significant between-group Doppler difference (MD: 0.3; 95% CI: -0.2 to 0.8; $p = 0.260$). These conflicting findings further underscore the heterogeneity in imaging protocols and quantification methodologies across studies.

Return to Sport

Return to sport/exercise rate was evaluated in three primary RCTs. Vithran et al. (2023)³² pooled available data and reported a numerically higher return to exercise rate in the PRP group versus placebo (RR = 1.11; 95% CI: 0.87–1.42; $p = 0.40$), not achieving statistical significance. Boesen et al. (2017)⁶ showed that muscle function (heel-rise test) improved equally across all three groups without significant between-group differences, suggesting that PRP does not confer specific musculotendinous functional advantages beyond those achieved by eccentric exercise.

Muscle Tendon Function (Heel-Rise Endurance Test)

In the PATH-2 RCT (Keene et al., 2019; $n = 230$)²⁷, the primary functional endpoint was the limb symmetry index (LSI) in the heel-rise endurance test at 24 weeks. No significant between-

group difference was detected (PRP: mean LSI 34.7% [SD 17.7%] vs. Placebo: 38.5% [SD 22.8%]; adjusted mean difference: -3.9% ; 95% CI: -10.5% to 2.7% ; $p=0.24$). This large, well-powered trial with an objective primary outcome measure provides compelling evidence against a meaningful functional benefit of a single PRP injection in the context of acute Achilles tendon rupture.

Quality of Life (QoL)

Keene et al. (2019)²⁷ assessed QoL using the Short Form 12 Version 2 (SF-12v2®) and reported no significant PRP advantage over placebo for either the Physical Component Summary (PCS) or Mental Component Summary (MCS) at 24 weeks. Similarly, Keene et al. (2022)²⁸ found no significant between-group QoL differences at 2-year follow-up (ATRS: PRP mean 82.2 [SD 18.3] vs. Placebo 83.8 [SD 16.0]; adjusted MD: -0.75 ; 95% CI: -5.52 to 4.02 ; $p=0.76$).

Adverse Events and Safety Profile

PRP is an autologous blood-derived product and is considered inherently safe. Fucaloro et al. (2025)⁴⁰ conducted a systematic review specifically examining PRP complications in foot and ankle pathologies (16 studies; 674 PRP patients vs. 749 control patients). Overall complication rates were significantly higher in the PRP group (41.1% vs. 33.7% ; $p<0.01$), though the majority of adverse events were mild and transient. Injection-site pain was the most frequent complication, occurring at a significantly higher rate in the PRP group (15.1% vs. 10.2% ; $p<0.01$; OR: 2.23; $I^2=0\%$). The number needed to harm (NNH) for PRP vs. alternative injection was 13. Only one patient (Achilles tendinopathy group) required surgical debridement for severe PRP-related pain. No infections, tendon ruptures attributable to PRP, or serious systemic adverse events were reported across the included studies.

Patient Satisfaction

Patient satisfaction was assessed as a secondary outcome in van der Vlist et al. (2020)⁴¹ (high volume injection RCT, which included a PRP-relevant design as comparator arm). Patient satisfaction rates did not differ significantly between injection and control groups at 24 weeks (57% vs. 49% ; $p=0.50$). In Sánchez et al. (2026)³⁵, a 6-month prospective cohort study of 18 AT patients receiving three multitarget PRP injections, 75% of AT patients were classified as responders

(achieving the Minimal Clinically Important Improvement [MCII] on VISA-A), with significantly greater female response rate (92.3% women vs. 58.3% men; $p=0.025$).

PRP Formulation Type (LR-PRP vs. LP-PRP)

Fitzpatrick et al. (2017)³⁷ performed the most comprehensive examining PRP preparation-type as a moderating variable across 18 tendinopathy RCTs ($n=1,066$). LR-PRP preparations demonstrated a substantially larger pain reduction effect compared to LP-PRP (pooled SMD: 36.38 [95% CI: 34.00–38.77] vs. 26.77 [95% CI: 18.31–35.22], respectively). Specifically, ultrasound-guided intratendinous LR-PRP injection yielded the greatest standardized pain improvements. These findings suggest that leukocyte content is a critical determinant of PRP efficacy in tendinopathy, potentially via modulation of the inflammatory microenvironment and activation of specific growth factor pathways. In contrast, animal model data (Yan et al., 2017)⁴² suggest that LP-PRP may produce superior histological and MRI outcomes in chronic tendinopathy by reducing catabolic IL-6 levels and increasing collagen type I expression, underscoring the complexity of the leukocyte-efficacy relationship and its potential context-dependence (acute vs. chronic tendinopathy, animal vs. human tissue).

Summary of Outcomes Across Studies (Table 2)

Outcome Domain	Studies Reporting	PRP vs. Placebo (Short-term ≤ 6 wks)	PRP vs. Placebo (12 wks)	PRP vs. Placebo (24 wks)	Key Finding	GRADE Certainty
VISA-A Score	de Vos 2010; Kearney 2021; Boesen 2017; Liu	No sig. diff. SMD 0.46 (6 wk only)	No sig. diff. SMD 0.20	No sig. diff. MD -0.9 to 2.75	Single PRP injection does not improve VISA-A vs. placebo. Multiple injections may show intermediate benefit.	$\oplus\oplus\oplus\ominus$ MODERATE

Outcome Domain	Studies Reporting	PRP vs. Placebo (Short-term ≤6 wks)	PRP vs. Placebo (12 wks)	PRP vs. Placebo (24 wks)	Key Finding	GRADE Certainty
	2019 MA; Barreto 2024 MA					
VAS Pain Score	Boesen 2017; Liu 2019 MA; Vithran 2023 MA	No sig. diff.	SIGNIFICANT MD 11.30 (CI 7.33–15.27) p<0.00001; I ² =0%	No sig. diff.	PRP superior to placebo for pain at 12 weeks; effect not sustained at 24 weeks.	⊕⊕⊕⊖ MODERATE
Tendon Thickness (mm)	Krogh 2016; Boesen 2017; Zhang 2018 MA; Vithran 2023 MA	Increased in PRP (possibly adverse)	Conflicting (SMD 1.51 Liu 2019; MD 0.34 Vithran 2023)	Reduced in PRP + ECC vs placebo (p<0.05 Boesen)	Complex: PRP may initially increase thickness (neovascularization), then reduce at 24 wks.	⊕⊕⊖⊖ LOW
Power Doppler Vascularity	Krogh 2016; Boesen 2017; Zhang	No sig. diff.	No sig. diff. MD 0.3 (p=0.260)	Reduced vs. placebo (Boesen 2017)	Multiple PRP injections may reduce intratendinous Doppler signal at 24	⊕⊕⊖⊖ LOW

Outcome Domain	Studies Reporting	PRP vs. Placebo (Short-term ≤6 wks)	PRP vs. Placebo (12 wks)	PRP vs. Placebo (24 wks)	Key Finding	GRADE Certainty
Return to Sport/Exercise	2018 MA			p<0.05	weeks.	
	Boesen 2017; Vithran 2023 MA	N/A	No sig. diff.	RR 1.11 (95% CI 0.87–1.42) p=0.40	No statistically significant increase in return to sport with PRP.	⊕⊕⊕⊖ LOW
Heel-Rise Endurance (LSI)	Keene et al. 2019 (PATH-2)	N/A	N/A	No sig. diff. Adj. MD –3.9% (CI –10.5% to 2.7%)	PRP does not improve objective muscle-tendon function vs. placebo at 24 weeks.	⊕⊕⊕⊕ HIGH
Quality of Life (SF-12/ATRS)	Keene 2019; Keene 2022	N/A	No sig. diff.	No sig. diff. at 24 wks and 2 years	PRP provides no QoL advantage over placebo at up to 2-year follow-up.	⊕⊕⊕⊖ MODERATE
Adverse Events	Fucaloro et al. 2025 SR;	Higher in PRP (41.1%)	N/A	N/A	PRP carries significantly higher post-injection pain	⊕⊕⊕⊖ MODERATE

Outcome Domain	Studies Reporting	PRP vs. Placebo (Short-term ≤6 wks)	PRP vs. Placebo (12 wks)	PRP vs. Placebo (24 wks)	Key Finding	GRADE Certainty
	Kearney 2021	vs 33.7%; p<0.01)			risk (OR 2.23; NNH=13). No serious SAEs.	
Patient Satisfaction	Sánchez 2026; Usuelli 2018	N/A	N/A	75% responder rate (AT) Female > Male (p=0.025)	Multiple PRP injections may achieve MCII in ~75% of AT patients. Females respond better.	⊕⊕⊕⊕ LOW
PRP Formulation Type (LR-PRP vs. LP-PRP)	Fitzpatrick 2017 MA; Yan 2017 (animal)	LR-PRP superior SMD 36.38 vs 26.77	LR-PRP superior for pain across all tendinopathies	—	LR-PRP yields greater clinical pain improvement than LP-PRP in tendinopathy (general).	⊕⊕⊕⊕ MODERATE

ECC = Eccentric Exercise; GRADE = Grading of Recommendations Assessment, Development and Evaluation; LSI = Limb Symmetry Index; MA = ; MCII = Minimal Clinically Important Improvement; NNH = Number Needed to Harm; PRP = Platelet-Rich Plasma; SR = Systematic Review; VAS = Visual Analogue Scale; VISA-A = Victorian Institute of Sports Assessment–Achilles.

PRP Preparation Characteristics (Table 3)

Study	PRP System / Centrifugation	Platelet Concentration	Leukocyte Content	Activation Method	Volume (mL)	N Injections	Ultrasound Guidance
de Vos 2010[4]	Not specified (double spin)	3–8× baseline	Not specified	Calcium chloride activation	4 mL	1	Yes
Kearney 2021[5]	ACP (Arthrex) or Regen BCT	~4× baseline	Low (LP-PRP)	None (resting or Ca-activated)	3–5 mL	1	Yes
Boesen 2017[6]	RegenLab Regen BCT	~4–6× baseline	Low (LP-PRP)	None (endogenous)	2 mL × 4	4 (every 14 d)	Yes
Krogh 2016[7]	Double spin (custom)	~4× baseline	Not specified	Thrombin+ calcium	3 mL	1	Yes
Keene 2019[27]	Not specified (ABO-compatible)	~4× baseline	Not specified	None specified	Varied	1	Not specified
Usuelli 2018[29]	GPS III (Biomet Biologics)	~5× baseline	High (LR-PRP)	Thrombin	2 mL	1	Yes
Sánchez 2026[35]	Customized multi-target protocol	Not specified	Not specified	Not specified	3 inj.×multi-dose	3 (every 2 wks)	Yes

ABO = ABO blood group compatibility; ACP = Autologous Conditioned Plasma; BCT = Blood Cell Therapy tube; GPS = Gravitational Platelet Separation; LR-PRP = Leukocyte-Rich PRP; LP-PRP = Leukocyte-Poor PRP.

DISCUSSION

Principal Findings

This comprehensive systematic review synthesizes findings from 16 primary clinical studies and 5 meta-analyses/systematic reviews encompassing a total of over 1,482 participants with AT. The principal finding is that the weight of current moderate-to-high quality evidence does not demonstrate a clinically meaningful superiority of PRP injection over placebo (saline, sham injection, or dry needle) for the primary outcome of VISA-A functional score at standard follow-up intervals (6–24 weeks) in patients with chronic midportion AT when both groups receive concomitant eccentric exercise rehabilitation.^{4,5,8,33,34} This conclusion is most robustly supported by two landmark RCTs published in JAMA—de Vos et al. (2010)⁴ and Kearney et al. (2021)⁵—which collectively enrolled 294 patients and achieved high internal validity through adequate randomization, double or participant-blinding, and $\geq 90\%$ follow-up completion rates.

However, a more nuanced interpretation of the evidence reveals important context-dependent findings that temper an entirely nihilistic view of PRP for AT:

(1) Multiple PRP Injections vs. Single Injection: The Boesen et al. (2017)⁶ trial—the only RCT employing a multiple-injection PRP protocol (4 injections $\times$ 14-day intervals) in AT—demonstrated statistically significant superiority of PRP over placebo for both VISA-A and VAS outcomes at 24 weeks, comparable to HVI. This suggests that injection frequency may be a critical determinant of efficacy, with the biological rationale that sustained growth factor delivery may be necessary to overcome the trophic resistance of chronically degenerated tendon tissue. The majority of null-result RCTs employed a single PRP injection, potentially underestimating the therapy's true biological potential.

(2) Temporal Dynamics of PRP Effect: The consistent finding of a statistically significant VAS improvement at 12 weeks (MD = 11.30; 95% CI: 7.33–15.27; $p < 0.00001$; $I^2 = 0\%$)³² that is not sustained at 6 weeks or 24 weeks is biologically interpretable. The initial 6-week period likely corresponds to the acute inflammatory phase of PRP-mediated tissue response, during which pro-inflammatory mediators may temporarily exacerbate symptoms. The 12-week peak corresponds to the proliferative/remodeling phase, during which growth factor-stimulated tenocyte activity and

431

collagen synthesis are maximal. The subsequent attenuation at 24 weeks may reflect convergence of the PRP and placebo groups as natural tendon remodeling proceeds in both groups with continued eccentric exercise.

(3) PRP Formulation and Leukocyte Content: The by Fitzpatrick et al. (2017)³⁷, encompassing 18 RCTs across multiple tendinopathy types, provides compelling evidence that LR-PRP yields substantially superior pain reduction outcomes compared to LP-PRP. This finding has complex mechanistic implications: while in vitro studies by Zhang et al. (2016)⁴³ and Zhou et al. (2015)⁴⁴ suggest that leukocyte-rich environments may be detrimental to tendon stem cell biology—inducing catabolic MMP upregulation, IL-1 β and TNF- α secretion, and non-tenocyte differentiation—the clinical evidence from Fitzpatrick et al. indicates that the net biological effect of LR-PRP in human tendinopathy may be paradoxically favorable, possibly via immunomodulatory recruitment of M2 anti-inflammatory macrophages and enhanced angiogenesis.

Comparison with Previous Systematic Reviews and Meta-analyses

The current findings are broadly consistent with earlier meta-analyses. Zhang et al. (2018)⁸ pooled 4 RCTs (n=170) and found no significant VISA-A difference (MD: 5.3; 95% CI: -0.7 to 11.3; p=0.085)—falling just short of clinical significance and close to the MCID of 12 points, suggesting a possible type II error given the relatively small pooled sample size. The updated Barreto et al. (2024)³⁴, which constitutes the most current and methodologically rigorous pooled analysis (n=422; 6 RCTs), definitively confirmed the null result across all timepoints, with additional sensitivity analyses and GRADE downgrading due to detected publication bias via funnel plot asymmetry—suggesting that positive PRP studies may have been selectively published.

Liu et al. (2019)⁹ and Ling et al. (2024)³³ reached concordant conclusions, with no significant VISA-A benefit at any standard timepoint. Importantly, Ling et al. (2024)³³ noted that 3 of 6 included RCTs were rated high risk of bias, and all 6 used heterogeneous PRP preparations—making formulation-specific subgroup analysis impossible. The network by Rhim et al. (2020)⁴⁵, not included as a primary source but cited for context, found that high-volume injection with corticosteroid (HVI+C) combined with eccentric exercise was the only treatment demonstrating

statistically significant VISA-A superiority over eccentric exercise alone in both the short and intermediate term, while PRP did not reach this threshold in the short term.

Biological Mechanisms: Interpreting the Clinical Evidence

The mechanistic basis for PRP's proposed efficacy in AT is well-established at the cellular and molecular level. PRP releasate promotes differentiation of tendon stem/progenitor cells (TSCs) into activated tenocytes exhibiting high proliferation rates and collagen production capacity.²² Growth factor concentrations—particularly TGF- β 1, PDGF-BB, and VEGF—are significantly elevated in PRP compared to whole blood, and these mediators activate integrin-mediated cell-matrix signaling pathways, MAP kinase cascades, and profibrotic transcription factors (e.g., scleraxis, tenascin-C) relevant to tenocyte anabolic activity.²⁰ HMGB1 within platelet granules additionally serves as a chemoattractant that recruits TSCs to the injury site, further amplifying regenerative capacity.⁴⁶

However, the translation of these robust in vitro and preclinical findings to consistent clinical benefit in chronic AT is confounded by several factors inherent to the pathophysiology of tendinopathy itself: (a) chronic tendinopathy is characterized by a fundamentally altered cellular microenvironment—with senescent, apoptosis-prone tenocytes, dysregulated MMP-TIMP balance, and matrix proteoglycan accumulation—that may reduce responsiveness to growth factor stimulation; (b) the Boswell et al. (2014)⁴⁷ in vitro study demonstrated a paradoxical "plateau effect" of platelet concentration, whereby increasing platelet numbers beyond a threshold results in decreased collagen gene synthesis in tendon explants, cautioning against the assumption that "more platelets = better outcomes"; (c) the relative chronicity of AT in clinical trial populations (median symptom duration 24–33 months across included RCTs) may substantially exceed the window of optimal PRP responsiveness.

Safety and Adverse Events

The safety profile of PRP, as an autologous blood-derived product, is inherently favorable from a systemic perspective. No serious systemic adverse events, infections, or procedure-related tendon ruptures attributable to PRP were reported across the included studies. The most clinically relevant safety signal identified in this review—consistent with the systematic review by Fucaloro

et al. (2025)⁴⁰—is a significantly elevated risk of post-injection pain compared to alternative injection therapies (OR: 2.23; NNH: 13). Clinicians should explicitly counsel patients regarding the likelihood of a transient (typically 24–72 hours) exacerbation of Achilles tendon pain following PRP injection, which may temporarily limit functional rehabilitation.

Implications for Clinical Practice

Based on the synthesis of available evidence, the following clinically actionable conclusions are proposed: (1) A single PRP injection cannot be recommended as a superior alternative to placebo or standard eccentric exercise rehabilitation for chronic midportion AT based on currently available moderate-quality evidence. (2) Multiple PRP injections (≥ 4 sessions) combined with structured eccentric exercise may provide additional benefit over placebo for pain reduction and functional improvement at 24 weeks, but require confirmation in larger RCTs. (3) LR-PRP formulations may produce superior clinical outcomes compared to LP-PRP for pain reduction in tendinopathy; however, AT-specific data are limited. (4) Ultrasound guidance for PRP injection should be considered standard of care to ensure accurate intratendinous or peritendinous delivery. (5) Patients with female sex and shorter symptom duration may represent subgroups with enhanced PRP responsiveness, though this evidence is preliminary. (6) PRP should not be offered as a first-line treatment; it may be considered an adjunct in patients who have failed ≥ 12 weeks of structured progressive tendon loading programs.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

This systematic review provides a comprehensive, evidence-based synthesis demonstrating that PRP injection—particularly as a single intratendinous injection—does not confer a statistically significant or clinically meaningful superiority over placebo for validated functional outcomes (VISA-A) or quality of life in chronic midportion AT at standard follow-up intervals. The certainty of this conclusion is rated as Moderate by GRADE methodology for the primary VISA-A outcome. However, the evidence also suggests that the null result should not be extrapolated universally: multiple PRP injections appear to produce significant improvement in pain (VAS) and function (VISA-A) compared to placebo at 24 weeks, and LR-PRP formulations may provide superior pain

434

reduction compared to LP-PRP across tendinopathies. PRP maintains an acceptable safety profile, with adverse events being mild, predominantly transient injection-site pain, and no serious complications.

Recommendations

Based on the synthesized evidence, the following recommendations are provided:

1. FOR CLINICAL PRACTICE: PRP injection should not be routinely recommended as a first-line treatment for chronic AT. It may be considered as a second-line adjunct in patients refractory to ≥ 12 weeks of evidence-based progressive tendon loading programs, with informed consent regarding the current evidence limitations.
2. FOR PRP PROTOCOL: If PRP is administered, multiple injections (minimum 3–4 sessions, 10–14 days apart) and ultrasound-guided LR-PRP delivery may optimize clinical outcomes based on current evidence.
3. FOR FUTURE RESEARCH: Large-scale, well-powered RCTs ($n \geq 200$ per arm) with standardized PRP characterization (using validated classification systems, e.g., DEPA or PAW), standardized rehabilitation protocols, and long-term follow-up (≥ 52 weeks) are urgently needed. Future trials should also examine insertional AT, explore sex as a biological variable, and evaluate combination approaches (e.g., PRP + extracorporeal shock wave therapy; PRP + novel biologics).
4. FOR POLICYMAKERS AND HEALTH INSURERS: Reimbursement decisions for PRP in AT should await publication of larger, higher-quality RCTs demonstrating clinically meaningful and sustained benefit over standard care.

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