Update on the Use of Platelet-Rich Plasma Injections in the Management of Musculoskeletal Injuries

A Systematic Review of Studies From 2014 to 2021

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Background: There has been expanding use of platelet-rich plasma (PRP) in the management of musculoskeletal soft tissue injuries.

Purpose: To determine if there are any recent studies that show any clear benefits regarding the use of PRP in the management of soft tissue injuries.

Study Design: Systematic review.

Methods: This review was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The EMBASE, MEDLINE, PubMed, and Cochrane Bone, Joint and Muscle Group Specialised Register databases were queried for randomized controlled trials comparing PRP with a non-PRP/placebo in participants >18 years of age with musculoskeletal soft tissue injuries. Exclusion criteria were non–soft tissue injuries and research published in journals with an impact factor <3.5. The main outcome measure analyzed across all injury types was the effect of PRP injections on pain and function.

Results: Of the 853 studies initially screened, 32 were included in this review. There were 13 studies that investigated the effects of PRP on the management of rotator cuff injuries; 7 studies that investigated PRP in conjunction with arthroscopy found no significant difference between PRP groups and controls, while 5 of 6 studies that investigated nonsurgical management showed positive results for PRP. Eight studies investigated various tendinopathies; of these, 2 studies demonstrated positive results for PRP in Achilles and gluteal tendinopathy management. Six studies examined PRP in acute soft tissue injuries, with 2 of these reporting significant improvements in recovery time for hamstring injuries and 1 study showing positive results for ankle ligament injuries. Two studies looked at acute rupture of soft tissues and found no benefit to PRP use. Two studies investigated PRP injections for chronic plantar fasciitis, and both reported positive results in pain and function with PRP. Finally, 1 study evaluated the effects of PRP on meniscal injuries and reported significant improvement in the healing rate and a decreased need for surgical repair.

Conclusion: Currently, there is no research strongly advocating the use of PRP compared with traditional management strategies (rest, ice, corticosteroid injection, rehabilitation program). No long-term physiological benefits were reported to justify the invasive and costly technique of obtaining, producing, and implementing PRP.

Keywords: platelet-rich plasma; soft tissue injury; muscle injuries; tendinopathy; ligament injuries; musculoskeletal injuries

There has been expanding use of platelet-rich plasma (PRP) in the management of musculoskeletal soft tissue injuries in recent years. PRP is used to aid bone and soft tissue healing by injecting supraphysiological concentrations of autologous platelets in an area of tissue damage.[1] The use of PRP in the treatment of tendinopathy has been controversial.[30] Some tendons may respond differently to PRP treatment. Part of the reason for this is that PRP has a slow onset of action; it takes 3 to 6 months to see its effectiveness.[10]

Blood taken from an individual is centrifuged to produce platelet-rich concentrates, made from autogenous blood producing a high number of platelets in a small volume of plasma.[12] Platelets contain a host of physiologically active substances including locally active growth factors such as platelet-derived growth factor, transforming growth factor, platelet factor interleukin, platelet-derived angiogenesis factor, vascular endothelial growth factor, epidermal

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growth factor, insulin-like growth factor, and fibronectin.[27] These substances have protean anabolic properties, including the capacity to remodel bone and blood vessels and promote angiogenesis, chondrogenesis, and collagen synthesis.[20] In 2015, Andia et al[2] concluded that PRP injections in pathological and nearby tissue can help in recovering tendon homeostasis.

Based on the physiological properties of PRP, its application in musculoskeletal soft tissue injuries is hoped to stimulate an accelerated rate of soft tissue healing, improving outcomes for musculoskeletal injuries; however, this has not yet been proven. A systematic review (conducted in 2014 by Moraes et al[30]) concluded that there was insufficient evidence to support the use of PRP for treating musculoskeletal soft tissue injuries.

The purpose of this review was to update the work of Moraes et al[30] and determine if there are any recent studies that show any clear benefits regarding the use of PRP in the management of musculoskeletal soft tissue injuries. The hypothesis was that there would be a positive impact of PRP use in improving function and reducing pain in the management of musculoskeletal injuries.

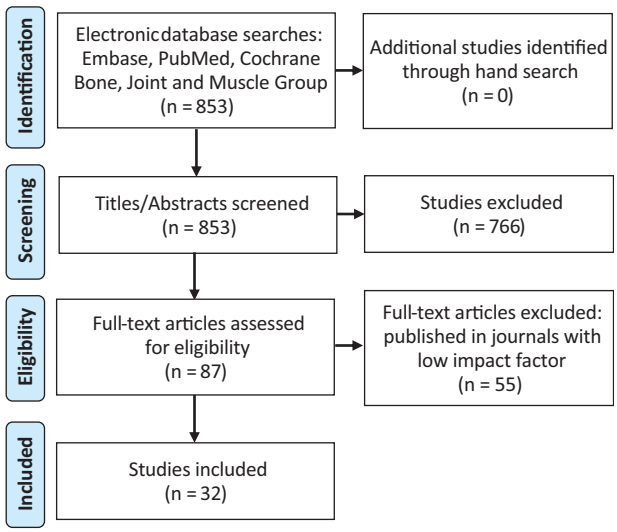

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of studies included in this review.

METHODS

This review was performed in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[32] The EMBASE, MEDLINE, PubMed, and Cochrane Bone, Joint and Muscle Group Specialised Register databases were searched for studies published between March 2014 and December 2021. The keywords searched included "platelet-rich plasma," "soft tissue injury," "muscle injuries," "tendinopathy," "ligament injuries," and "musculoskeletal injuries."

Inclusion and Exclusion Criteria

The scope of the review included randomized controlled trials (RCTs) comparing PRP with a non-PRP/placebo in participants >18 years of age. Included were studies in the English language that were published in journals with a minimum impact factor of 3.5. Exclusion criteria were studies published before March 2014 and research on PRP injections in the management of non–soft tissue musculoskeletal injuries, including osteoarthritis, bone fractures, and nerve injuries.

Data Extraction, Analysis, and Quality Appraisal

This research was carried out by a single reviewer. Studies meeting inclusion criteria were assessed and data pertaining to the study's aims, interventions used, outcome measures used, and results were extracted. Data findings from these studies were synthesized based on injury type, levels of PRP used, and comparison with corticosteroid injections. Quality appraisal of each RCT was performed using the Critical Appraisal Skills Programme tool (CASP, 2018).[8]

RESULTS

Electronic databases produced a total of 853 studies. Through screening titles and abstracts, a total of 766 studies were excluded. Eighty-seven full-text articles were screened for eligibility, producing a total of 32 studies that were included in this review (Figure 1).

Of the 32 RCTs included in this study, 13 were investigating the effects of PRP on the management of rotator cuff injuries (Appendix Table A1).[‡] Eight studies investigated tendinopathies (4 Achilles tendinopathy,[3,4,21,23] 2 lateral epicondylitis,[26,29] 1 patellar tendinopathy,[38] 1 gluteal tendinopathy[10]) (Appendix Table A2), 6 studies examined acute tissue injuries (Appendix Table A3),[14,15,25,34-36] 2 studies looked at acute rupture of soft tissues (Appendix Table A4),[22,40] 2 studies investigated PRP injections effect on chronic plantar fasciitis (Appendix Table A5),[13,33] and 1 study evaluated the effect of PRP on meniscal injury (Appendix Table A6).[18]

There were 32 RCTs included in this review; 17 of these were double blinded,[§] 3 were assessor blinded,[16,26,38]

[‡]References 4, 5, 7, 9, 11, 16, 17, 24, 28, 31, 37, 39, 41.
[§]References 3-5, 10, 15, 18, 22-24, 28, 29, 31, 33, 35, 37, 39, 40.

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1 study blinded participants,[21] and 11 were not blinded.‖ Participant follow-up ranged from 3 weeks to 42 months; 19 studies followed up participants for at least 1 year after intervention.¶

Analysis of Individual Injury Types

Rotator Cuff Injuries

Thirteen studies investigated the effects of PRP on the management of rotator cuff injuries. Seven of these studies examined the effects of PRP in conjunction with arthroscopic rotator cuff repair. All showed that there was no statistical difference between the PRP groups and control groups in clinical outcome measures ($P > .05$).[6,9,11,17,28,39,41] On imaging, all studies showed no significant differences in magnetic resonance imaging (MRI) except for Jo et al,[17] who showed retear rates to be significantly lower in the PRP group after 1 year ($P = .032$); however, this was in contrast to the study of Carr et al,[6] which found that the PRP groups included significantly reduced cellularity and vascularity and an increase in a marker for cell apoptosis ($P = .03$), which may increase the likelihood of retears. Both Carr et al[6] and Jo et al[17] satisfied all 11 criteria in the CASP appraisal tool.[8]

In nonsurgical rotator cuff tear management using PRP, 5 of the 6 studies included found positive results supporting the use of PRP.[5,7,16,24,31] Oedelaar et al,[31] Kwong et al,[24] and Jo et al[16] all showed statistically significant ($P < .05$) findings, suggesting that PRP is a superior treatment of rotator cuff injuries compared with corticosteroids at 6 months, but not show statistically significant long-term results. Cai et al[5] showed PRP alone and sodium hyaluronate (SH) combined with PRP both gave significantly higher Constant and American Shoulder and Elbow Surgeons scores at 6 and 12 months after treatment ($P < .01$) and that the tear size significantly decreased in both the PRP and the SH and PRP groups on MRI ($P < .01$). Centeno et al[7] showed similar results with significant differences seen at 3, 6, and 24 months ($P < .05$), and MRI review showed a size decrease of most tears posttreatment ($P < .05$). Schwitzguebel et al,[37] however, did not find any statistical difference between groups.

Tendinopathy Injuries

Eight studies investigated the nonsurgical management of tendinopathies using PRP.[3,4,10,21,23,26,29,38] Four studies examined the effect of PRP on chronic Achilles tendinopathy; 3 found no difference at any time in functional outcomes comparing PRP and placebo injections ($P > .05$).[3,21,23] Boesen et al[4] found that PRP in combination with eccentric training in chronic Achilles tendinopathy was more effective in reducing pain, improving activity level, and reducing tendon thickness and intratendinous vascularity than eccentric training alone ($P < .05$).

There were 2 studies that explored the use of PRP in the management of lateral epicondylitis. Both Linnanmäki et al[26] and Montalvan et al[29] concluded that there was no benefit to using PRP injections compared with a control.

Scott et al[38] examined the effect of leukocyte-rich PRP, leukocyte-poor PRP, and placebo on patellar tendinopathy. No significant outcome was found between the 3 groups on any of the outcome measures investigated ($P > .05$). Fitzpatrick et al[10] investigated the long-term effects of PRP in the treatment of chronic gluteal tendinopathy; the study found that PRP injections provided statistically important clinical improvements compared with corticosteroid injections at 12 weeks ($P = .048$). Furthermore, the improvement after PRP injection was sustained at 2 years, whereas the improvement from a corticosteroid injection was maximal at 6 weeks and not maintained beyond 24 weeks.

Acute Soft Tissue Injuries

Six studies were carried out on the effects of PRP on acute soft tissue injuries. Hamilton et al,[15] Hamid et al,[14] Reurink et al,[35] and Rossi et al[36] explored the effects of PRP on acute hamstring injuries in athletes, while Laver et al[25] examined the benefits of PRP injections in athletes with ankle ligament injuries. Hamilton et al[15] and Reurink et al[35] found no significant difference in return to play and reinjury rate between the PRP and control groups ($P = .05$). Elsewhere, Hamid et al[14] and Rossi et al[36] found that participants in the PRP group achieved full recovery significantly earlier than controls ($P = .02$ and $P = .001$). Hamid et al[14] showed that patients in the PRP group had significantly lower pain severity scores than controls at all time points ($P = .007$) and pain intensity did not show any statistical difference ($P = .157$). Punduk et al[34] found that PRP could improve inflammation after high-intensity exercise by reversing the increase in iron levels as a response. Laver et al[25] showed that athletes receiving PRP returned to play significantly sooner ($P = .006$) and had significantly less pain when compared with controls in the context of acute Anterior Talo-Fibular Ligament (ATFL) injury.

Acute Rupture of Soft Tissues

Two studies considered the use of PRP after acute ruptures of soft tissues. Keene et al[22] found no benefit to using PRP compared with placebo at 24 weeks after Achilles tendon ruptures ($P > .05$). Walters et al[40] showed that scores were not different between treatment groups at any time interval ($P = .8$-$.83$), and MRI indicated no healing differences between groups ($P = .90$) when the intraoperative inclusion of PRP injections during anterior cruciate ligament reconstruction was investigated.

Plantar Fasciitis

Two studies investigated the effects of PRP for the management of plantar fasciitis. Haddad et al[13] and Peerbooms et al[33] found statistically significant advantages when comparing PRP and other treatment measures commonly used

‖References 6, 7, 9, 11, 13, 14, 17, 25, 34, 36, 41.
¶References 3, 5-7, 10, 11, 17, 18, 24, 26, 28, 29, 31, 33, 36-40.

for chronic plantar fasciitis. Haddad et al[13] found that PRP showed significantly better outcomes for visual analog scale compared with extracorporeal shockwave therapy ($P = .001$). Peerbooms et al[33] showed a statistically significant increase in function and reduction in pain and disability compared with corticosteroids in the management of chronic plantar fasciitis ($P = .003$).

Meniscal Injuries

Kaminski et al[18] investigated the effects of percutaneous trephination with PRP intrameniscal injections for the repair of degenerative meniscal injuries. Interestingly, it showed significant improvement in the rate of meniscal healing compared with placebo (52% vs 30%, $P = .04$) and a decreased necessity for arthroscopy in the future (8% vs 28%, $P = .032$).

Analysis of the PRP Application

Quantities of PRP administered during each of the included studies ranged from a 1-mL injection to a 10-mL injection in the 32 studies examined. The results of these studies did not indicate any pattern for the optimal quantity of PRP needed to produce satisfactory outcomes. Varying results were produced using different quantities of PRP. There was no linear pattern indicating statistically significant results due to higher or lower quantities of being PRP used.

Nine studies examined the effects of multiple applications of PRP. Schwitzguebel et al,[37] Montalvan et al,[29] Ebert et al,[9] Boesen et al,[3] Reurink et al,[35] and Wang et al[41] all used between 2 and 4 injections of 2 to 4 mL PRP and did not produce any statistically significant results to show any improvements compared with the control groups. Three studies using multiple applications of PRP did produce significantly significant results. Cai et al[5] used 4 applications of PRP with 1-week intervals between applications. Their results showed that PRP alone and SH combined with PRP both gave significantly higher Constant and American Shoulder and Elbow Surgeons (ASES) scores at 6 and 12 months after treatment ($P < .01$) and that the tear size significantly decreased in both the PRP and the SH and PRP groups on MRI ($P < .01$). In a similar context, Boesen et al[4] used 4 applications of PRP 14 days apart and showed statistically significant results, recording a decrease in tendon thickness ($P < .05$). Laver et al[25] showed that players who received applications of PRP 1 and 7 days after acute ankle ligament injuries benefited with a return to play significantly sooner ($P = .006$), with considerable improvements in pain levels.

Comparison of PRP Against Corticosteroid Injections

Five studies compared the application of PRP and corticosteroid directly.[4,16,24,31,33] Oedelaar et al,[31] Jo et al,[16] and Kwong et al[24] showed positive statistically significant findings in favor of PRP compared with corticosteroid injections in the management of rotator cuff injuries. Interestingly, Oedelaar et al[31] found a significant difference in favor of needle aspiration of calcific deposits in rotator cuff calcific tendonitis combined with PRP (Constant-Murley score, $P < .001$; Disabilities of the Arm, Shoulder and Hand, $P = .002$; Oxford Shoulder Score, $P = .010$; EuroQol 5-Dimension, $P < .001$) at 6 months; however, at the 6-week follow-up, a clinically relevant difference in favor of needle aspiration of calcific deposits and corticosteroids was found for all clinical scores except for the numeric rating scale ($P < .05$).

Jo et al[16] found that the Constant score was not significantly different between the 2 groups at any time point after the injection. The Disabilities of the Arm, Shoulder and Hand score, overall function, and external rotation were statistically significantly better in the PRP group at 6 months ($P > .05$). Generally, PRP slowly but steadily reduced pain and improved function of the shoulder until 6 months, but there were no significant differences between the groups in any of the pain measurements at 6 months. Kwong et al[24] showed that at 3 months, there was a significant difference in pain reduction favoring PRP over corticosteroid injections ($P = .02$). After injection, the American Shoulder and Elbow Surgeons and Western Ontario Rotator Cuff scores showed statistically significant differences at 3 months favoring PRP over corticosteroid injection ($P < .05$).

Peerbooms et al[33] showed participants with chronic plantar fasciitis treated with PRP injections showed significantly lower foot function index disability scores ($P = .003$) compared with the corticosteroid injection group. Boesen et al[4] showed a significant decrease in tendon thickness in corticosteroid groups at 6 and 12 weeks ($P < .05$) and significant improvements at 6 and 12 weeks in Victorian Institute of Sport Assessment–Achilles scores and visual analog scale scores at 6 weeks compared with the PRP groups ($P < .05$).

DISCUSSION

The most significant findings of this review indicate promising results in favor of PRP use in the nonsurgical management of rotator cuff injuries, plantar fasciitis, and meniscal injuries. The results show that the general use of PRP as a main treatment or in conjunction with other conventional treatments is not yet fully justified for all musculoskeletal injuries. All the studies carried out on patients undergoing surgery (arthroscopic rotator cuff repair and anterior cruciate ligament reconstruction) did not show any valuable improvements and therefore should not be recommended as part of surgical intervention. There was some evidence suggesting that the use of PRP in the nonsurgical management of rotator cuff injuries was beneficial; however, further studies need to be carried out to clarify the exact application of PRP that will produce consistent positive results.[5,7,16,24,31]

Interestingly, there are multiple studies included that showed positive outcomes from the application of PRP in the context of sports medicine. Laver et al[25] produced statistically significant results for athletes' ability to return to

play quicker and with decreased pain with acute ankle ligament injuries. Hamid et al[14] and Rossi et al[36] showed positive results for PRP application for acute hamstring injuries; patients recovered from injury quicker and had a significantly lower pain severity. Punduk et al[34] showed positive results for the use of PRP 24 hours after exercise-induced muscle damage. This result suggests that the application of PRP may be used to improve inflammation in athletes by reversing the increase in iron levels postexercise. Further investigation is warranted into the use of PRP in this fashion, as it may prove to be beneficial in athletes to aid recovery and decrease muscle damage induced by high-intensity exercise and training regimes. It would also be beneficial to investigate the use of PRP in elite athletes training at high intensities over a long period of time to determine if fewer injuries are sustained or if performance levels improve because of augmented athlete recovery.

Through investigating the current evidence for the use of PRP, there are no data to suggest the optimal application of PRP. Standardized application methods are yet to be established. Currently, there is no clear indication of what levels of PRP should be used or that multiple applications are beneficial. Further investigation is required to determine standard practice for the use of PRP in musculoskeletal soft tissue injuries.

There was no obvious additional benefit to arthroscopically guided or ultrasound-guided application of PRP, which correlates with Kane et al,[19] who showed there was no advantage to ultrasound guidance over direct palpation of the most tender area for the application of PRP injections.

It was difficult to draw conclusions based on studies producing contrasting results as all the studies included in this review scored highly on the CASP appraisal tool, and therefore it was difficult to suggest one study was superior in nature in comparison with another.

Some studies showed negative ramifications for the use of PRP. Carr et al[6] showed findings that have not previously been reported, revealing the potentially detrimental effect of PRP on the long-term structural properties of tendons, which may increase the likelihood of tears. Krogh et al[23] also found there was a significant change in tendon thickness, indicating that PRP may increase thickness ($P = .03$). These suggested negative effects of PRP and the small amount of strong positive evidence do little to advocate the use of PRP for the management of musculoskeletal injuries.

Limitations

There are some limitations in this review. A large number of studies (n = 55) were excluded because they were published in journals with impact factors <3.5; including those studies may have allowed for a more comprehensive set of results. However, having to exclude so many studies indicates that the majority of research on the application of PRP for musculoskeletal injuries is substandard and therefore makes it difficult to get a clear consensus on the merits of PRP. Furthermore, we did not assess for heterogeneity in each of these studies, which can confound the interpretation of the data. Therefore, further work with high-quality randomized controlled studies with longer-term follow-up is needed.

CONCLUSION

The majority of the evidence in this review demonstrates no difference between conventional management of musculoskeletal injuries and the application of PRP. There is some evidence in favor of PRP interventions in the nonsurgical management of rotator cuff disease. Currently, there is no research strongly advocating the use of PRP compared with traditional management to produce a long-term physiological benefit or to suggest a benefit needed to justify the invasive and costly technique of obtaining, producing, and implementing PRP. Further research is necessary to evaluate the possible benefit of PRP in sports medicine as part of an athlete's recovery or in the management of acute injuries.

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APPENDIX

TABLE A1
Included Studies on PRP in Rotator Cuff Injuries (n = 13)[a]

Lead Author (Year)	Aims	Sample Size	Intervention	Outcome Measures	Results
Snow (2020)[39]	Effects of delayed application of PRP on arthroscopic RC repair	N = 87 (40 PRP, 47 control [saline])	6 mL PRP + saline at 10-14 d after arthroscopic RC repair; US guided	■ ASES, Constant score, WORC, DASH at 6 wk, then 3, 6, 9, and 12 mo postop ■ MRI after 12 mo	■ No difference between the treatment groups on any of the outcome measures at 1 y postop ■ No difference in the retear rate on postop MRI analysis
Ebert (2017)[9]	To investigate whether the clinical and radiographic outcomes of arthroscopic supraspinatus repair are enhanced after repeated postop PRP applications	N = 55 (27 PRP, 28 control)	2× 2-4 mL PRP at 7 and 14 d postop; US guided	■ Constant score, DASH, OSS, VAS, global rating of change scale, at 6, 12, and 16 wk ■ MRI 3.5 y postop	■ No differences between the groups on any of the outcome measures ■ MRI showed PRP delivered at 7 and 14 d postop provided no additional benefits to tendon integrity
Flury (2016)[11]	To investigate whether an intraoperative pure PRP injection, compared with ropivacaine, improves patient-reported outcomes at 3 and 6 mo after arthroscopic RC repair	N = 120 (60 PRP, 60 control)	4 mL PRP or 10 mL 1% ropivacaine; arthroscopic placement	■ OSS, ASES, DASH, EQ-5D at 3, 6, and 24 mo ■ MRI at 24 mo	Patients treated with pure PRP showed no significantly improved function at 3, 6, and 24 mo
Carr (2015)[6]	To investigate both the clinical and tissue effects of the co-application of PRP injection with arthroscopic acromioplasty in patients with chronic RC tendinopathy	N = 60 (30 PRP, 30 control)	5 mL PRP; arthroscopic guidance	■ OSS, VAS pain, overall quality of life at 0 and 6 wk, 3, 6, 12, and 24 mo ■ Tendon biopsy at 12 wk	■ No significant differences in outcome measures between groups ■ PRP included significantly reduced cellularity and vascularity and an increase in a marker of apoptosis ($P = .03$) ■ Revealed a potentially detrimental effect of PRP to the long-term structural properties of the tendon, which may increase the likelihood of tears
Jo (2015)[17]	To assess the efficacy of PRP augmentation on the speed and quality of healing in patients undergoing arthroscopic repair for medium to large RC tears	N = 74 (37 PRP, 37 control)	3× 3-mL PRP gels applied between tear and greater tuberosity during arthroscopy	■ Constant score, VAS, ROM, muscle strength, overall satisfaction and function at baseline, 3, 6, and 12 mo ■ MRI for retear at 9 mo	■ No significant difference in Constant score or any other outcome measure at any point ■ Retear rate for PRP was significantly lower after 1 y ($P = .032$)
Wang (2015)[41]	To evaluate the benefits of application of PRP after arthroscopic supraspinatus repair	N = 60 (30 PRP, 30 control)	US-guided PRP injection (2-4 mL) at 7 and 14 d postop	■ OSS, QuickDASH, VAS preop and at 6, 12, and 16 wk ■ MRI at 16 wk	PRP did not improve early functional recovery, ROM, strength or pain scores
Malavolta (2014)[28]	To investigate if PRP promotes better functional and structural results in arthroscopic RC repair	N = 75 (39 PRP, 36 control)	10 mL PRP or saline between portal sites; not US guided	■ UCLA, Constant score, VAS pain at 0, 3, 6, 12, and 24 mo ■ MRI at 12 mo	■ No statistically significant differences between PRP and control except 12-mo UCLA was higher in PRP ($P = .046$) ■ No clinical improvements at 24 mo
Oudelaar (2021)[31]	To compare the effects of adjuvant application of PRP after NACD with those of conventional NACD + CS on pain, shoulder function, and quality of life for treatment of RC calcific tendinitis	N = 80 (41 NACD + PRP, 39 NACD + CS)	Single PRP injection (2.9 mL) at the site of affected RC tendon	■ NRS pain, Constant score, DASH, OSS, EQ-5D ■ Calcific deposits and the integrity of RC tendons were assessed by using standard radiographs and US examination ■ Follow-up at 6 wk, then 3, 6, 12, and 24 mo	■ Significant difference in favor of NACD + PRP (Constant score, $P < .001$; DASH, $P = .002$; OSS, $P = .010$; EQ-5D, $P < .001$) ■ Clinically relevant differences in favor of NACD + PRP were only seen at 6 mo for NRS and CMS scores, whereas at the 6-wk follow-up a clinically relevant difference in favor of NACD + CS was found for all clinical scores except for the NRS
Kwong (2021)[24]	To compare PRP with CS injection in providing pain relief and improved function in patients with RC tendinopathy and partial-thickness RC tears	N = 104 (50 PRP, 54 CS injection)	US-guided injection of PRP (3-5 mL) or CS (3-5 mL)	Primary: VAS; secondary: ASES, WORC at 6 wk, 3 mo, and 12 mo	■ Significantly greater reduction in pain for PRP vs CS injections at 3 mo ($P = .02$) ■ Significantly higher ASES and WORC for PRP vs CS injection at 3 mo ($P < .05$)
Jo (2020)[16]	To investigate the safety and efficacy of PRP injection in comparison with CS injection into the subacromial space of patients with RC disease	N = 60 (30 PRP, 30 CS injection)	US-guided injection of PRP (4 mL) or 4-mL mixture of 1 mL 40 mg/mL triamcinolone acetonide and 3 mL 2% lidocaine	Primary: safety (treatment-related adverse event) and Constant score (primary); secondary: pain, ROM, muscle strength, shoulder function scores (SPADI, ASES, UCLA, SST, DASH), overall satisfaction and function at 1 wk, then 1, 3, and 6 mo	■ There was no treatment-related adverse events and no difference in Constant score at any time point after the injection ■ Significantly better DASH score, overall function, and external rotation in the PRP group at 6 mo ($P < .05$) ■ Generally, PRP slowly but steadily reduced pain and improved function of the shoulder until 6 mo; no significant group differences on any pain measurements at 6 mo

(continued)

Table A1 (continued)

Lead Author (Year)	Aims	Sample Size	Intervention	Outcome Measures	Results
Cai (2019)[5]	Compare subacromial injections of saline (control), SH, PRP, or SH + PRP in the management of partial-thickness RC tears	N = 200 (50 control, 50 SH, 50 PRP, 50 SH + PRP)	4 mL PRP alone or 4 mL SH alone or 2 mL + 2 mL SH + PRP given 1× per wk for 4 wk; US guided	■ Constant score, ASES, VAS pain at 0, 6, and 12 mo ■ MRI at 1 y	■ PRP alone and SH + PRP showed significantly higher Constant score and ASES after treatments ($P < .01$) ■ MRI showed that the tear size significantly decreased in both the PRP and SH + PRP groups ($P < .01$) ■ SH + PRP yielded better clinical outcome than SH or PRP alone
Centeno (2020)[7]	Comparing autologous BMC and platelet product indexes vs exercise therapy in partial- and full-thickness supraspinatus tears	N = 25 (11 control, 14 treatment)	1-2 mL 60% BMC, 20% PRP, and 20% platelet lysate; US guided	■ DASH, NRS pain scale, SANE ■ MRI at 3, 6, and 24 mo	■ Significant differences were seen in favor of autologous BMC and platelet product indexes vs exercise therapy at 3, 6, and 24 mo ($P < .05$) ■ MRI review showed size decrease of most tears after BMC treatment ($P < .05$)
Schwitzguebel (2019)[37]	To determine whether PRP is superior to saline (placebo) in the management of isolated interstitial supraspinatus tears	N = 84 (42 PRP, 42 control)	2× 2 mL PRP or saline with 1-mo interval; US guided	■ Lesion volume via MRA at 7 mo ■ Pain and SANE at 12 mo	PRP injections within interstitial supraspinatus tears did not improve tendon healing or clinical scores compared with saline injections

[a]ASES, American Shoulder and Elbow Surgeons score; BMC, bone mineral concentrate; CMS, Constant-Murley score; CS, corticosteroid; DASH, Disabilities of the Arm, Shoulder and Hand; EQ-5D, EuroQol 5-Dimension; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; NACD, needle aspiration of calcific deposits; NRS, numeric rating scale; OSS, Oxford Shoulder Score; postop, postoperative; preop, preoperative; PRP, platelet-rich plasma; QuickDASH, 11-Item Disabilities of the Arm, Shoulder and Hand; RC, rotator cuff; ROM, range of motion; SANE, Single Assessment Numeric Evaluation; SH, sodium hyaluronate; SPADI, Shoulder Pain and Disability Index; SST, Simple Shoulder Test; UCLA, University of California–Los Angeles score; US, ultrasound; VAS, visual analog scale; WORC, Western Ontario Rotator Cuff score.

TABLE A2
Included Studies on PRP in Tendinopathy Injuries (n = 8)[a]

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Kearney (2021)[21]	To assess the effect of single-dose PRP compared with sham for treatment of Achilles tendinopathy	N = 240 (121 PRP, 119 control)	Single PRP injection (3 mL)	VISA-A, VAS, EQ-5D-5L at 2 wk, 3 and 6-mo follow-ups	■ No significant difference in VISA-A between the PRP group and the sham group at 3 and 6 mo after treatment allocation ■ No significant differences in quality of life (EQ-5D-5L utility and VAS score) or pain (VAS) at 2-wk, 3-mo, or 6-mo time points
Boesen (2020)[3]	Comparing the use of PRP injections to placebo in the nonsurgical intervention for Achilles tendon ruptures	N = 40 (20 PRP, 20 control)	4 PRP (4 mL) or 4-mL saline injections 14 d apart; US guided	ATRS, heel-rise height, tendon elongation, calf circumference and ankle dorsiflexion ROM	No difference at any time between groups over 12 mo in functional outcomes
Krogh (2016)[23]	To examine whether PRP would improve outcomes more effectively than placebo (saline) after 3 mo in patients with Achilles tendinopathy	N = 24 (12 PRP, 12 placebo)	6 mL PRP or saline; US guided	VISA-A, pain NRS, US changes at 3 mo	■ No difference between the PRP and saline groups could be observed with regard to the primary outcome ($P = .868$) ■ Significant difference between the groups in change in tendon thickness ($P = .03$), indicating PRP may increase thickness
Boesen (2017)[4]	To determine whether eccentric training in combination with HVI of PRP improves outcomes in chronic midportion Achilles tendinopathy	N = 60 (20 PRP, 20 HVI CS, 20 placebo)	4 x 4 mL PRP or saline 14 d apart; 20 mg Depo-Medrol at baseline; US guided	VISA-A, VAS, tendon thickness and intratendinous vascularity (US imaging and Doppler signal); heel-rise test at 0, 6, 12, and 24 wk	■ Tendon thickness showed a significant decrease only in the HVI and PRP groups during the intervention, and this was greater in the HVI vs PRP and placebo groups at 6 and 12 wk ($P< .05$) ■ Treatment with HVI or PRP in combination with eccentric training in chronic Achilles tendinopathy seemed more effective in reducing pain, improving activity level, and reducing tendon thickness and intratendinous vascularity than eccentric training alone
Linnanmäki (2020)[26]	Comparing PRP, autologous blood, and placebo saline (1:1:1) for the treatment of lateral epicondylitis	N = 119 (40 PRP, 40 autologous blood, 39 saline)	4-6 mL PRP, single injection; autologous blood or saline; not US guided	VAS pain, DASH, grip strength at 4,8, 12, 26, and 52 wk	PRP or autologous blood injections did not improve pain or function at 1-y follow-up
Montalvan (2016)[29]	To assess the efficacy of 2 intratendinous injections of PRP on lateral epicondylitis of acute nature (<3 mo)	N = 50 (25 PRP, 25 control)	2 mL PRP or saline at 0 and 4 wk; US guided	VAS pain, Roles-Maudsley score, pain on isometric contraction of ECRB and EDC at 1, 3, 6, and 12 mo	No significant difference in outcome measures between groups at 6 and 12 mo

(continued)

Table A2 (continued)

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Scott (2019)[38]	To determine if a single US-guided PRP injection (either LR or LP) was superior to saline injection for the treatment of patellar tendinopathy	N = 61 (20 LR-PRP + exercise, 21 LP-PRP + exercise, 20 saline + exercise)	■ US-guided injection of LR-PRP (3.5 mL), LP-PRP (3.5 mL), or saline (3.5 mL) ■ All patients engaged in a supervised gym-based rehabilitation program 3 times/wk for 6 wk	VISA-P, NRS for pain; patients' perception of change was assessed with a 7-point scale; follow-up at 12 wk and 1 y	No significant difference in outcome scores between LR-PRP, LP-PRP, and saline at 12 wk or 1 y
Fitzpatrick (2019)[10]	To determine whether there is a sustained long-term difference in the mHHS at 2 y for LR-PRP in the treatment of chronic gluteal tendinopathy	N = 80 (40 PRP, 40 control CS)	6-7 mL PRP; US guided	mHHS at 0, 2, 6, and 12 wk, then 6, 12, and 24 mo	■ Greater clinical improvements at 12 wk when treated with single PRP injection or single CS injection ($P = .048$) ■ Improvement after LR-PRP injection sustained at 2 y, whereas the improvement from a CS injection was maximal at 6 wk and not maintained beyond 24 wk

[a]ATRS, Achilles tendon rupture score; CS, corticosteroid; DASH, Disabilities of the Arm, Shoulder and Hand; ECRB, extensor carpi radialis brevis; EDC, extensor digitorum communis; EQ-5D-5L, 5-Level Health-Related Quality of Life; gym, gymnasium; HVI, high-volume injection; LP, leukocyte poor; LR, leukocyte rich; mHHS, modified Harris Hip Score; NRS, numeric rating scale; PRP, platelet-rich plasma; ROM, range of motion; US, ultrasound; VAS, visual analog scale; VISA-A, Victorian Institute of Sport Assessment–Achilles score; VISA-P, Victorian Institute of Sport Assessment–Patellar score.

TABLE A3
Included Studies on PRP in Acute Soft Tissue Injuries (n = 6)[a]

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Hamilton (2015)[15]	To evaluate the efficacy of a single PRP injection in reducing the return-to-sport duration in male athletes after acute hamstring injury	N = 90 (30 PRP, 30 PPP, 30 control)	3 separate deposits of 1 mL PRP or PPP at different injection sites using MRI for reference with clinical palpation; standardized rehab for all participants	Days until return to sport; reinjury rate at 2 and 6 mo	■ No statistically significant difference on outcome measures between groups ■ No benefit of a single PRP injection over intensive rehab in athletes who sustained acute MRI-positive hamstring injury
Hamid (2014)[14]	To investigate the effect of a single PRP injection in the treatment of grade 2 hamstring muscle injuries	N = 28 (14 PRP, 14 control [exercise only])	3 mL PRP; US guided	Return to play, pain severity, pain interference	■ Patients in the PRP group achieved full recovery significantly earlier than controls ($P = .02$) ■ Patients in the PRP group had significantly lower pain severity scores than controls at all time points ($P = .007$) ■ No difference in pain intensity ($P = .157$)
Reurink (2014)[35]	To investigate the effects of PRP in acute sporting hamstring injuries	N = 80 (41 PRP, 39 control)	3 mL PRP in 2 injections: (1) within 5 d of acute injury, (2) 5-7 d after; US-guided technique	Time to return to play; reinjury rate at 2 mo assessed	No clinically relevant change was found between the PRP group and control group with regard to return to play ($P = .66$) or reinjury rate ($P = .81$)
Rossi (2017)[36]	To investigate the effects of autologous PRP injections on time to return to play and recurrence rate after acute grade 2 muscle injuries in recreational and competitive athletes	N = 75 (35 PRP, 40 control)	3 mL PRP; US guided	Return to play, pain, recurrence rates	■ The PRP group achieved full recovery significantly earlier than controls ($P = .001$) ■ Lower pain severity scores were observed in the PRP group ■ The difference in the recurrence rate after 2-y follow-up was not statistically significant between groups
Punduk (2016)[34]	To investigate the effects of intramuscular delivery of PRP on hematologic and biochemical responses and recovering strategy muscle damage induced by high-intensity muscle exercises	N = 12 (6 PRP, 6 control)	4 mL PRP 24 h after exercise-induced muscle damage; not US guided	Samples were collected before and 4 d after exercise, and analyzed for WBC, RBC, Hb, serum Fe, IBC, CK, LDH, AST, and ALT	■ PRP administration decreased plasma Fe levels compared with controls on day 2 after exercise ■ Plasma IBC increased in the PRP group from days 2 to 4 after exercise compared with controls ■ PRP administration had no effect on plasma ferritin, CK, AST, ALT, or LDH ■ PRP improved inflammation by reversing the increase in the Fe levels after exercise
Laver (2015)[25]	To investigate the effect of PRP injections into the injured anteroinferior tibiofibular ligaments in athletes	N = 16 (8 PRP, 8 control)	1.5 mL PRP at time of diagnosis and again at 7 d; US guided	Time needed to return to preinjury level of training; duration of residual pain; dynamic stability and scarring	Athletes receiving PRP returned to play significantly sooner ($P = .006$) and had significantly less pain when compared with controls

[a]ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; Fe, iron; Hb, hemoglobin; IBC, iron binding capacity; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PPP, platelet-poor plasma; PRP, platelet-rich plasma; RBC, red blood cell; rehab, rehabilitation; US, ultrasound; WBC, white blood cell.

TABLE A4
Included Studies on PRP in Acute Soft Tissue Rupture (n = 2)[a]

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Keene (2019)[22]	To determine the efficacy of autologous PRP for treatment of acute ATR	N = 230 (114 PRP; 116 placebo [deep dry needling])	8 mL PRP; not US guided	LSI, heel-rise endurance test, ATRS, SF-12, pain at 24 wk	At 24 wk, there was no difference between PRP and placebo groups on any outcome
Walters (2018)[40]	To examine the effect of the intraoperative administration of PRP on postoperative kneeling pain after anterior cruciate ligament repair	N = 59 (30 PRP, 29 sham	3-5 mL PRP; not US guided	IKDC, VAS at 12 wk and 6, 12, and 24 mo	■ No difference in outcome scores between treatment groups at any time interval (P = .8-.83) ■ MRI indicated healing not different between groups (P = .90)

[a]ATR, Achilles tendon rupture; ATRS, Achilles tendon rupture score; IKDC, International Knee Documentation Committee; LSI, limb symmetry index; MRI, magnetic resonance imaging; PRP, platelet-rich plasma; SF-12, 12-Item Short Form Survey; US, ultrasound; VAS, visual analog scale.

TABLE A5
Included Studies on PRP in Plantar Fascia Injuries (n = 2)[a]

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Haddad (2021)[13]	To evaluate PRP and ESWT in pain reduction in patients with chronic plantar fasciitis	N = 110 (55 PRP, 55 ESWT)	Single PRP injection (3 mL) into plantar fascia; ESWT applied vertically with a depth of 15 mm, pressure of 1500 bar, resistance of 4 Hz, and energy of 0.089 MJ/mL until pain threshold; this procedure was performed once a week for 3 wk	VAS pain at 2, 4, 8, 12, 16, and 24 wk	Pain in the PRP group decreased more than in the ESWT group at a statistically significant level (P = .001)
Peerbooms (2019)[33]	To determine the effectiveness of PRP compared with CS injections in the treatment of chronic planter fasciitis	N = 115 (63 PRP, 52 control [CS])	1 mL PRP; 40 mg/mL CS; not US guided	FFI pain score, FFI function, FFI disability, AOFAS, quality of life measured at 4, 12, 26, and 52 wk	■ Treatment of patients with chronic planter fasciitis with PRP shows significantly lower pain scores than patients in the control group (mean difference, 14.4; 95% CI) ■ The PRP group showed significantly lower FFI disability scores that the control group (P = .003)

[a]AOFAS, American Orthopaedic Foot and Ankle Society; CS, corticosteroid; ESWT, extracorporeal shockwave therapy; FFI, foot function index; PRP, platelet-rich plasma; US, ultrasound; VAS, visual analog scale.

TABLE A6
Included Studies on PRP in Meniscal Injuries (n = 1)[a]

Lead Author (Year)	Aims	Population	Intervention	Outcome Measures	Results
Kaminski (2019)[18]	To investigate the use of percutaneous trephination with PRP intrameniscal injections for repair of degenerative meniscal injuries	N = 72 (42 PRP, 30 placebo)	6-8 mL PRP; US guided; 6-8 mL sterile 0.9% normal saline	MRI; VAS, KOOS, WOMAC, and IKDC at 3, 6, 12, and 24 mo	■ The PRP group had significant improvement in the rate of meniscal healing (52% vs 30%, P = .04) ■ PRP decreased the necessity for arthroscopy in the future (8% vs 28%, P = .032)

[a]IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MRI, magnetic resonance imaging; PRP, platelet-rich plasma; US, ultrasound; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Arthritis Index.