Platelet-Rich Plasma in Sports Medicine – What Does Level I Evidence Support?

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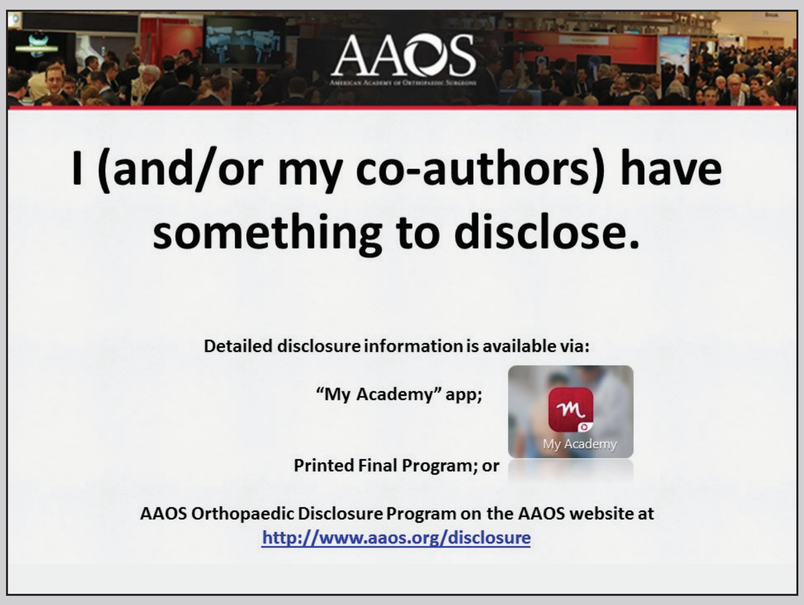
DISCLOSURE



INTRODUCTION

+ Platelet-rich plasma (PRP) is an autologous blood product containing an increased concentration of platelets, growth factors and bioactive molecules
+ PRP is increasingly being used in many areas of orthopaedic sports medicine
+ Inconsistent clinical results, as well as different preparation and treatment strategies, mean there is still considerable debate over the role of PRP
+ Significant controversies remain surrounding the contents of PRP, including leukocyte concentration, as well as delivery, timing, and injection frequency, which further confound our understanding

The purpose of this exhibit is to present the findings of a systematic review of Level 1 studies published on PRP in orthopaedics sports medicine.

METHODS

Literature Search

+ Literature search was perfomed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines
+ Level I randomized controlled trials assessing PRP were included

Statistics

+ Quantitative analysis (i.e. statistical pooling) was used to compare the outcomes of PRP to the controls where possible and appropriate
+ Qualitative analysis (i.e. description of the available studies) was used when there was a mix of controls used, or quantitative analysis was not appropriate
+ The Grade of Recommendation was evaluated based on the criteria by The Journal of Bone and Joint Surgery

GRADE OF RECOMMENDATION

A	Good evidence (Level-I studies with consistent findings) for or against recommending intervention
B	Fair evidence (Level-II or III studies with consistent findings) for or against recommending intervention
C	Poor-quality evidence (Level-IV or V studies with consistent findings) for or against recommending intervention
I	There is insufficient evidence to make a recommendation

KNEE OSTEOARTHRITIS

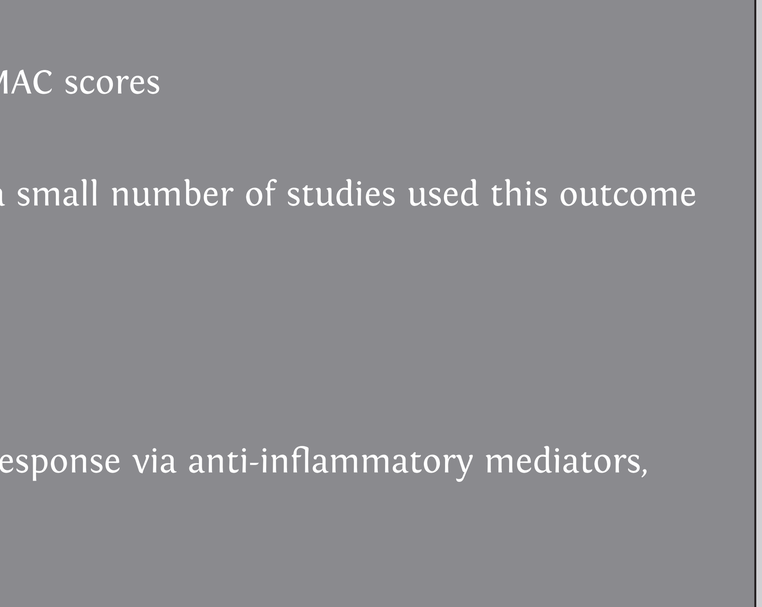
+ 10 RCTs (1,097 patients) compared the use of PRP to hyaluronic acid (HA) in knee osteoarthritis
  + Pooled analysis: statistically significant benefit with PRP at 3, 6, and 12 months in the WOMAC scores
  + There was a statistically significant benefit with PRP at 6 and 12 months in the VAS score
  + However, there was no significant difference at 6 or 12 months with IKDC score, but only a small number of studies used this outcome measure
+ 3 RCTs (241 patients) compared the use of PRP to a saline placebo in knee osteoarthritis
  + All 3 studies found improved pain and functional outcome scores with PRP
+ The improvement in clinical outcomes from PRP use is likely due to the immune-modulatory response via anti-inflammatory mediators, and not through cartilage regeneration

GRADE OF RECOMMENDATION: A
(Evidence supports the use of PRP)

Table 1. Knee Osteoarthritis Results

OUTCOME	N	RESULT	FAVOURS
Western Ontario & McMaster University Osteoarthritis Index			
3 Months	PRP: 202 HA: 204	MD; -10.73, 95% CI, -18.61 to -2.85, I^2 = 83%, p < 0.01	PRP
6 Months	PRP: 339 HA: 339	MD; -12.59, 95% CI, -22.32 to -2.76, I^2 = 95%, p = 0.01	PRP
12 Months	PRP: 205 HA: 188	MD; -13.72, 95% CI, -20.95 to -6.50, I^2 = 80%, p < 0.01	PRP
Visual Analogue Scale			
3 Months	PRP: 44 HA: 44	MD; -0.19, 95% CI, -0.57 to 0.20, I^2 = 0%, p = 0.34	None
6 Months	PRP: 82 HA: 84	MD; -0.62, 95% CI, -1.15 to -0.10, I^2 = 72%, p = 0.02	PRP
12 Months	PRP: 82 HA: 84	MD; -1.65, 95% CI, -2.06 to -1.23, I^2 = 0%, p < 0.01	PRP
International Knee Documentation Index			
6 Months	PRP: 182 HA: 178	MD; 7.75, 95% CI, -0.30 to 15.81, I^2 = 84%, p = 0.06	None
12 Months	PRP: 143 HA: 139	MD; 3.85, 95% CI, -0.64 to 8.34, I^2 = 60%, p = 0.09	None

HA; hyaluronic acid, PRP; platelet-rich plasma.



PRP Preparation Kit

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ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Graft-Tunnel Healing

+ 7 RCTs (355 patients) assesed the use of PRP vs no PRP on graft tunnel healing following anterior cruciate ligament (ACL) reconstruction with a hamstring-tendon autograft
+ No study found PRP resulted in improvement in any clinical outcome measures
+ However, 3 studies found PRP improved the rate of graft maturation on MRI

+ 2 RCTs (250 patients) assessed the use of PRP versus no PRP for graft tunnel healing following ACL reconstruction with an allograft
+ Both studies found that PRP did not result in any improvement over the control in clinical or radiographic outcomes

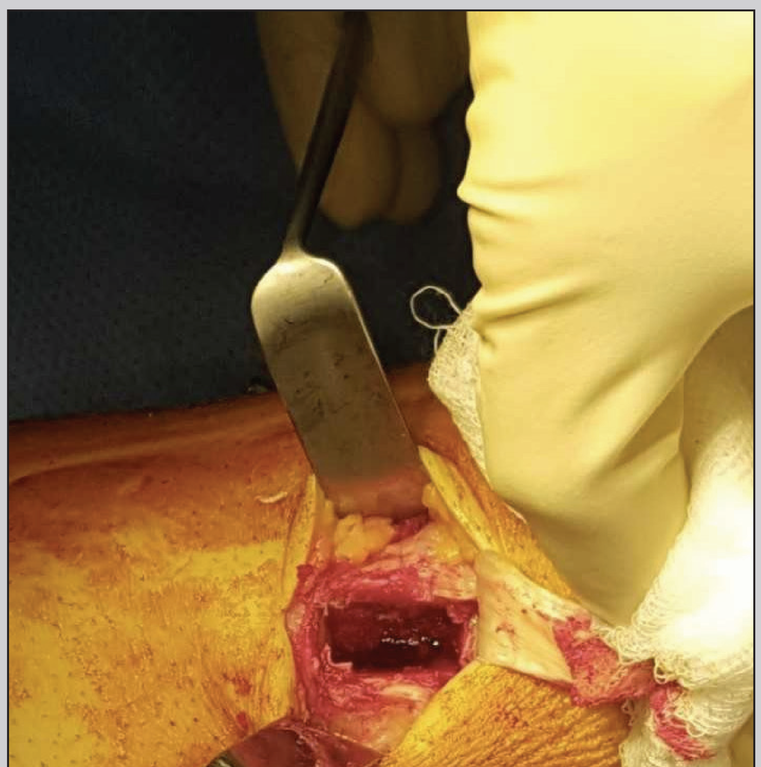
+ PRP does not appear improve clinical outcomes in ACL reconstruction
+ While several studies found PRP improved the rate of graft maturation, the clinical significance of this and its potential effects on return to sport are unclear

GRADE OF RECOMMENDATION: A
(Evidence does not support the use of PRP)

Bone-Patellar Tendon Donor Site

+ 3 RCTs (110 patients) assesed the use of PRP versus no PRP for bone-patellar tendon (BPT) donor site morbitiy following ACL reconstruction
+ All 3 studies utilized PRP in the form of platelet-rich fibrin matrix (PRFM)
+ No study found any difference in functional outcome measures
+ 1 study found PRP reduced the immediate post-operative pain levels, but at 1-year follow-up there was no difference
+ 2 studies assessing bone/tendon gap formation found PRP resulted in a smaller defect size
+ PRP may have the potential to reduce immediate pain from the BPT donor site in the immediate postoperative period but this does not appear to improve the functional outcomes

GRADE OF RECOMMENDATION: I
(Evidence is unclear in supporting the use of PRP)



Bone-patellar donor site

HAMSTRING INJURIES

+ 3 RCTs (184 patients) assessed the use of PRP in acute hamstring injuries
+ Only 1 study showed a beneficial effect of PRP over a control, achieving full recovery significantly earlier than physiotherapy alone
+ No other study found any significant difference between PRP and autologous blood, placebo injection or PPP
+ The evidence supporting the use of PRP for hamstring injuries is limited, without a clear consensus in the literature

GRADE OF RECOMMENDATION: I
(Evidence is unclear in supporting the use of PRP)

PATELLAR TENDINOPATHY

+ 2 RCTs (69 patients) assessed the use of PRP versus a control
+ Dragoo et al. found PRP injections accelerated recovery from patellar tendinopathy compared to dry-needling alone, but the relative benefit of PRP dissipates over time
+ Vetrano et al. found that PRP resulted in superior clinical outcomes at 6- and 12-month follow-up compared to shockwave therapy
+ While PRP appears to be beneficial in the treatment of patellar tendinopathy, there is still a paucity of clinical data and thus further randomized control trials are needed

GRADE OF RECOMMENDATION: I
(Evidence is unclear in supporting the use of PRP)

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OSTEOCHONDRAL LESIONS OF THE TALUS

+ 3 RCTs (92 patients) assessed the use of PRP for osteochondral lesions of the talus (OLT)
+ Pooling was not possible to perform due to a mix of controls and associated procedures
+ All 3 studies found PRP resulted in improved functional outcomes and pain scores, suggesting that PRP can have a beneficial effect in the treatment of OLT as a solo injection or alongside operative treatment
+ Additional well-designed randomized control trials with homogenous methods are needed to confirm this evidence
+ Further study is needed to clarify the best time to administer this intervention in the perioperative setting in order to yield the optimum results

GRADE OF RECOMMENDATION: B
(Evidence supports the use of PRP)

ACHILLES TENDINOPATHY

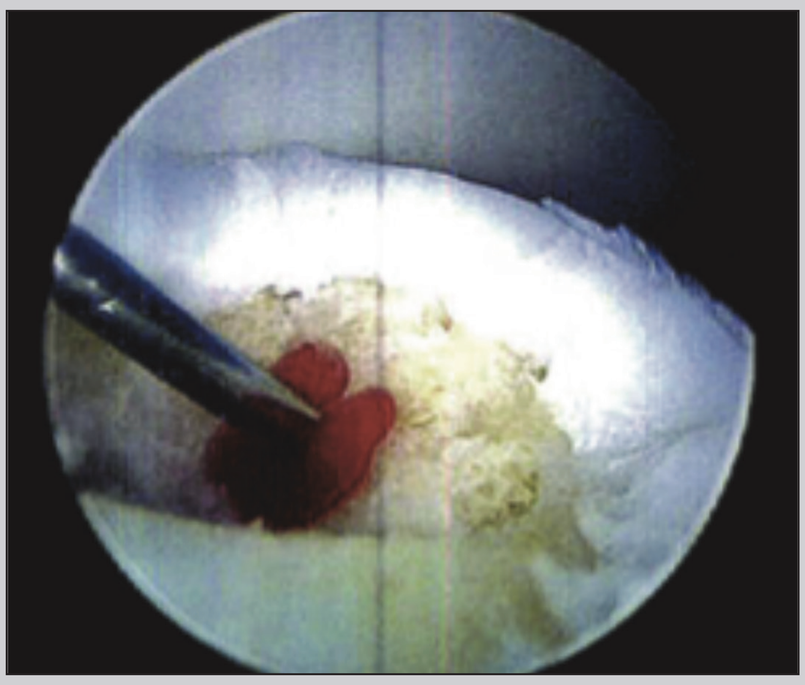
+ 4 RCTs (154 patients) compared the use of PRP in Achilles tendinopathy to a control
+ No study showed a significant benefit in favor of PRP with VISA-A scores
+ Meta-analysis and pooling of the data was not possible
+ The current clinical evidence does not support the use of PRP for Achilles tendinopathy

GRADE OF RECOMMENDATION: A
(Evidence does not support the use of PRP)

PLANTAR FASCIITIS

+ 7 RCTs (320 patients) assessed the use of PRP injections for plantar fasciitis
+ At all follow-up time points, including 1, 1.5, 3, 6 months, there were statistically significant differences in the VAS scores in favor of PRP
+ Pooled analysis: statistically significant benefit with PRP at 1.5, 3, and 6 months in the VAS scores
+ There was a statistically significant benefit with PRP at 12 months in the AOFAS score, but not at 3 and 6 month
+ The literature supports the use of PRP as it significantly reduces pain when compared to corticosteroids, at least up to 6 months following treatment, however, the long-term outcomes of PRP treatment for plantar fasciitis are still unknown

GRADE OF RECOMMENDATION: A
(Evidence supports the use of PRP)



Arthroscopic image of the intra-articular administration of PRP following microfracture for an osteochondral lesion of the talus.

PRP applied after Achilles tendoscopy

Table 2. Plantar Fasciitis Results

OUTCOME	N	RESULT	FAVOURS
Visual Analogue Scale			
1 Month	PRP: 45 CS: 45	MD; -0.49, 95% CI, -0.91 to -0.07, I^2 = 42%, p = 0.02	PRP
1.5 Month	PRP: 40 CS: 40	MD; -3.03, 95% CI, -4.07 to -1.99, I^2 = 39%, p < 0.01	PRP
3 Months	PRP: 125 CS: 125	MD; -0.65, 95% CI, -0.92 to -0.39, I^2 = 0%, p < 0.01	PRP
6 Months	PRP: 60 CS: 60	MD; -0.78, 95% CI, -1.09 to -0.47, I^2 = 0%, p < 0.01	PRP
American Orthopaedic Foot and Ankle Score			
3 Months	PRP: 90 CS: 90	MD; 1.00, 95% CI, -1.28 to 3.39, I^2 = 73 %, p = 0.39	None
6 Months	PRP: 50 CS: 50	MD; 12.75, 95% CI, -2.19 to 27.70, I^2 = 92%, p = 0.71	None
12 Months	PRP: 50 CS: 50	MD; 25.06, 95% CI, 2.96 to 47.17, I^2 = 95%, p = 0.03	PRP

CS; corticosteroids, PRP; platelet-rich plasma

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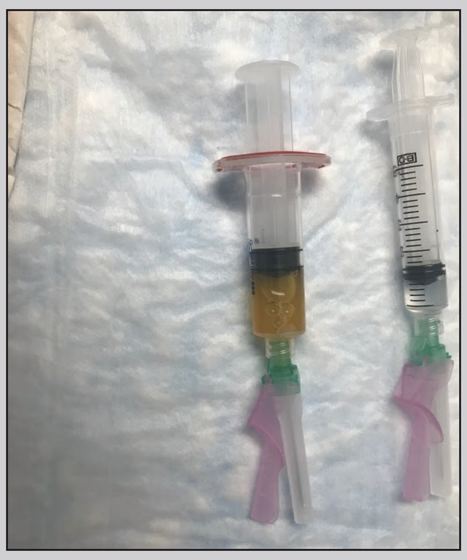
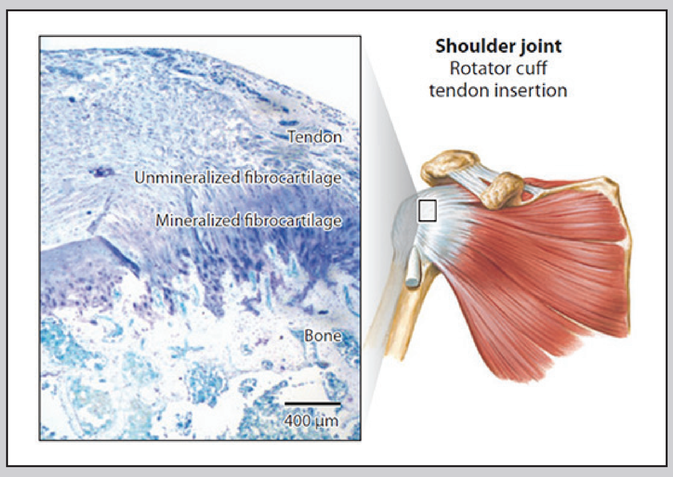


Leukocyte Poor Platelet-Rich Plasma



Bone-Tendon Interface

ARTHROSCOPIC ROTATOR CUFF REPAIR

+ 18 RCTs (1,147 patients) assessed the use of PRP as an adjunct to arthroscopic rotator cuff repair
  + Pooled analysis revealed that leukocyte-poor PRP resulted in a reduced rate of incomplete healing in tendon tears of all sizes
  + PRP resulted in improvement in clinical outcomes in the form of the Constant and UCLA scores
  + Additionally, PRP resulted in lower VAS scores at day 30 and final follow-up
  + However, using the leukocyte-rich PRP and platelet-rich fibrin matrix (PRFM) preparation method of PRP did not result in any significant difference in any outcome measure
+ Leukocyte poor platelet-rich plasma has been shown to improve tendon-healing rates in tears of all sizes (previously the literature only supported it's use in small-medium tears), as well as improved pain scores and improved functional outcomes
+ While it had been proposed that the PRFM method would be more beneficial than PRP due to the prolonged release of cytokines over days not hours, it was shown that PRFM had no benefit in in terms of tendon healing or functional outcomes

GRADE OF RECOMMENDATION: A
(Evidence supports the use of PRP)

Table 3. Clinical outcomes Following Leukocyte-Poor Platelet-Rich Plasma Application

OUTCOME	N	RESULT		FAVOURS
Tendon Healing Rate	PRP: 283 C: 278	PRP: 17.0% vs C: 30.9%	RR; 0.55, 95% CI, 0.42 to 0.73, I^2 = 4%, p < 0.05	LP-PRP
Tendon Healing Rate in Medium-Large Tears	PRP: 105 C: 98	PRP: 6.7% vs C: 26.5%	RR; 0.25, 95% CI, 0.12 to 0.53, I^2 = 0%, p < 0.05	LP-PRP
Visual Analogue Scale at Day 30	PRP: 64 C: 63	PRP: 3.3 vs C: 4.9	MD; -1.48, 95% CI, -1.77 to -1.14, I^2 = 8%, p < 0.05	LP-PRP
Visual Analogue Scale at Final Follow-Up	PRP: 113 C: 111	PRP: 0.6 vs C: 0.9	MD; -0.22, 95% CI, -0.37 to -0.06, I^2 = 0%, p < 0.05	LP-PRP
Constant Score	PRP: 225 C: 230	PRP: 87.1 vs C: 84.3	MD; 2.65, 95% CI, 0.90 to 4.41, I^2 = 0%, p < 0.05	LP-PRP
University of California Los Angeles Score	PRP: 172 C: 169	PRP: 30.8 vs C: 29.7	MD; 1.39, 95% CI, 0.61 to 2.17, I^2 = 0%, p < 0.05	LP-PRP
American Shoulder and Elbow Surgeons Score	PRP: 198 C: 203	PRP: 88.6 vs C: 87.0	MD; 1.22, 95% CI, -0.65 to 3.09, I^2 = 0%, p = 0.20	None

C; control, PRP; platelet-rich plasma

LATERAL EPICONDYLITIS

+ 9 RCTs (561 patients) compared the use of PRP to corticosteroid in lateral epicondylitis
  + Pooled analysis showed that there was no difference in VAS score at 1, 2, or 3 month follow-up
  + However, there a siginicantly lower VAS score at 6 and 12 months when using PRP
  + There was a statistically significant lower DASH score with CS at 1 month, but at all other follow-up time points there was no significant difference
+ 3 RCTs (126 patients) compared the use of PRP to a saline placebo in lateral epicondylitis
  + No study found a difference between the clinical outcomes of those treated with PRP and a placebo, although it was not possible to meta-analyze this
+ The results indicate a time dependent effect that while CS may have a slightly improved result in the short term, in the long-term PRP may result in reduced pain levels but no clinically significant difference
+ These results are limited by the significant heterogeneity in the reported outcome measures, and further study is still needed to elucidate whether PRP is the optimal treatment for lateral epicondyliitis

GRADE OF RECOMMENDATION: C
(Evidence is conflicted in supporting the use of PRP)

GRADE OF RECOMMENDATION

KNEE	GRADE	SUPPORTS THE USE OF PRP
ACL Graft Tunnel Healing	A	No
ACL BPT Donor Site	I	Unclear
Hamstring Injuries	I	Unclear
Knee Osteoarthritis	A	Yes
Patellar Tendinopathy	I	Unclear

UPPER LIMB	GRADE	SUPPORTS THE USE OF PRP
Arthroscopic Rotator Cuff Repair	A	Yes
Lateral Epicondylitis	C	Conflicted

FOOT & ANKLE	GRADE	SUPPORTS THE USE OF PRP
Achilles Tendinopathy	A	No
Osteochondral Lesions of the Talus	B	Yes
Plantar Fasciitis	A	Yes