Current Reviews in Musculoskeletal Medicine (2018) 11:593–597
https://doi.org/10.1007/s12178-018-9517-9

PROTEIN-RICH PLASMA: FROM BENCH TO TREATMENT OF ARTHRITIS (S CHOATE AND J TOKISH, SECTION EDITORS)

Platelet-rich plasma and the shoulder: clinical indications and outcomes

Andrew Schneider[1] · Rebecca Burr[1] · Nickolas Garbis[1] · Dane Salazar[1]

Published online: 8 September 2018
© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract

Purpose of Review The orthopedic community has seen a rapid rise in the clinical use of platelet-rich plasma (PRP) in the management of shoulder pathologies over the past decade. The purpose of this paper is to review the current literature regarding the indications and outcomes of PRP for the surgical and non-surgical management of common shoulder pathologies, including rotator cuff tears.

Recent Findings Multiple studies have been published recently regarding the use of PRP for the operative and non-operative treatment of rotator cuff tears. There has been less research published on the use of PRP in the management of other conditions of the shoulder. Despite attempts to standardize and classify PRP formulations, there remains great variation in the inter- and intra-subjection composition, preparation, and administration techniques of PRP, limiting the conclusions that can be drawn regarding the utility and effectiveness of this biologic treatment as reported by Mazzocca et al. (J Bone Joint Surg Am. 94(4):308–16, 2012).

Summary Recent literature has shown equivocal to minor benefit of PRP use for shoulder pain, function, and healing. While few complications have been reported and PRP administration appears to carry little risk to the patient, the body of literature is currently inconclusive regarding the clinical benefit and cost-effectiveness of PRP in the treatment of shoulder pathology. As for PRP use specifically as an adjunct to surgical rotator cuff repairs, there is no clear consensus on its effectiveness in either clinical or structural outcomes. To further delineate the efficacy of PRP for shoulder pathology, it is essential that more double-blinded, randomized controlled investigations with large sample sizes and standardized PRP preparations be performed.

Keywords Platelet-rich plasma · PRP · Shoulder · Rotator cuff tear · Biologic augmentation · Regenerative medicine

Introduction

The medical community as a whole, and in particular orthopedic surgery, has seen a rapid rise in the clinical use of platelet-rich plasma (PRP) over the past decade [1, 2]. As an autologous derivative of whole blood, PRP is rich with growth factors that are theorized to modulate the inflammatory pathway and to encourage healing of tendon, ligament, muscle, and bone [2–5]. The potential for biologic healing augmentation combined with low risk for adverse reaction makes PRP an attractive treatment option for many musculoskeletal pathologies [6•]. However, while the basic science is compelling, clinical outcome studies on the efficacy of PRP is conflicting and unclear, leaving the need for future large, prospective randomized controlled trials. The purpose of this paper is to review the current literature on common indications and outcomes for the use of PRP in the non-operative and operative management of common shoulder pathologies: rotator cuff tendinopathy, biceps tendinopathy, rotator cuff tears, and labral tears.

This article is part of the Topical Collection on *Protein-Rich Plasma: From Bench to Treatment of Arthritis*

✉ Dane Salazar
dsalazar@lumc.edu

[1] Division of Shoulder and Elbow Surgery, Department of Orthopaedic Surgery and Rehabilitation, Loyola University Hospital System, 2160 South 1St Ave., Maywood, IL 60153, USA

Basics of PRP

PRP prepared and administered for clinical purposes is the delivery of autologous human plasma-containing platelets and associated growth factors at supra-physiologic levels [2, 3]. Blood is drawn from a peripheral vein and centrifuged to separate the whole blood components into layers. A high

concentration of platelets can then be mixed with a small amount of plasma and injected at a site of injury [5]. Current theories suggest that the local release of growth factors contained in PRP such as transforming growth factor beta, basic fibroblast growth factor, platelet-derived growth factor, and connective tissue growth factor, combined with high concentrations of activated platelets, stimulate healing and promote growth of muscle and tendon [7, 8].

Significant variability exists in the methods used to prepare PRP, resulting in differences in blood component concentrations and biomolecular characteristics. Additionally, the final concentration of platelets, growth factors, and leukocytes has been shown to vary between and within patients as well [9]. The varying quality and preparations of PRP make comparison amongst clinical research studies challenging. Attempts to classify and standardize preparations have been made; however, no consensus has been reached by either basic scientists or clinicians on the optimal preparation [10]. Leukocyte-poor (LP)-PRP and pure (P)-PRP formulations are prepared using only the plasma layer of the centrifuged blood sample, while leukocyte-rich (LR)-PRP preparations also include part of the leukocyte-containing buffy coat layer [11]. The benefits of including leukocytes in the final concentration remain particularly controversial. While some studies suggest that LR-PRP has an immunity-regulating property, as well as pain relief benefits in the medium to long term, other researchers believe that the presence of leukocytes in PRP is a cause of inflammation, decreasing the likelihood of successful surgical repair [11].

Non-surgical indications and outcomes for PRP in the shoulder

PRP has shown potential for its use in the non-surgical management of various shoulder pathologies. A growing body of literature exists regarding the use of PRP in treating rotator cuff tears; however, there remains great variation in PRP preparations and methods of administration, limiting the collective conclusion of these studies [1, 12, 13]. For select patients with rotator cuff tears, non-surgical measures such as strengthening exercises, NSAIDs, and corticosteroid injections may effectively address clinical symptoms and functional deficits [14]. The proposed role of PRP in the non-operative treatment of rotator cuff tears is to decrease pain and inflammation and potentially to stimulate healing, providing a viable alternative to surgery. Specifically, PRP has been studied as an alternative to corticosteroid injection. Shams et al. conducted a prospective randomized controlled study to evaluate sub-acromial PRP injections versus corticosteroid injections in 40 patients with symptomatic partial rotator cuff tears at 6-weeks, 12-week, and 24-week time points [14]. Both injection groups showed a statistically significant improvement in clinical outcomes compared with before injection. At 12 weeks after injection, the PRP group demonstrated a statistically significant improvement in the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES), the Constant-Murley Score (CMS), the Simple Shoulder Test (SST), and a Visual Analog Scale (VAS) for pain. There was no difference in any of the outcome scores in the two injection groups at the 24-week time point. The study presented evidence for PRP injection as a good alternative to corticosteroid injection for patients with partial rotator cuff tears, especially in patients with a contraindication to corticosteroid administration.

Alternatively, other studies have shown no clear outcome benefit of PRP compared to a placebo control in the non-operative treatment of rotator cuff tears. Kesikburun et al. carried out a double-blinded randomized controlled trial of 40 patients with rotator cuff tendinopathy or partial tears [15•]. Patients either received PRP or a placebo injection (saline solution) followed by participation in a rehabilitation program. Twenty patients were randomized into each group, and outcome measures such as the Western Ontario Rotator Cuff Index (WORC), Shoulder Pain and Disability Index (SPADI), VAS of shoulder pain with the Neer test, and shoulder range of motion were assessed at baseline and at 3 weeks, 6 weeks, 12 weeks, 24 weeks, and 1 year after injection. They found no difference in pain or functional outcome scores at any time point up to 1 year.

At the time of this publication, very few studies have been published regarding the efficacy of PRP in treating calcific tendonitis and sub-acromial bursitis and no studies have been published regarding its use in treating biceps tendinopathy or labral tears. Therefore, the role of PRP in managing these conditions must be extrapolated from anecdotal experiences of shoulder and sports surgeons, and the existing data from its other uses. One randomized controlled trial by Say et al. compared the efficacy of a single sub-acromial PRP injection with a single sub-acromial corticosteroid injection in 50 patients with calcific tendonitis who had failed treatment with NSAIDs and exercise therapy for at least 3 months [16•]. Mean Constant-Murley scores improved from 40.9 to 43.8 at week 6 and to 52.5 at month 6 in the PRP group, compared to an improvement from 38.3 ($p = 0.182$) to 59.1 ($p < 0.001$) at week 6 and 65.5 ($p < 0.001$) at month 6 in the corticosteroid group. Similarly, mean VAS scores improved from 7.5 to 5.1 at week 6 and 5.3 at month 6 in the PRP group, compared to an improvement from 7.8 ($p = 0.508$) to 3.0 ($p < 0.001$) at week 6 and 2.1 ($p < 0.001$) at month 6. There was no significant difference in shoulder range of motion between the two groups. More recently, a randomized controlled trial by Nejati et al. compared targeted physical therapy for a 3-month period with a series of two sub-acromial PRP injections over a 3-month period for the treatment of sub-acromial impingement [17]. Both groups improved from their baseline; however, at months 1 and 3 following the completion of treatment, the physical therapy group was significantly superior in

pain improvement, shoulder flexion and abduction, and shoulder function. Mean DASH scores in the PRP group improved from 54.2 to 45.1 at month 1 and 30.7 at month 3, as compared to the physical therapy group where DASH scores improved from 50.5 ($p = 0.53$) to 35.0 ($p < 0.01$) at month 1 and 30.7 ($p < 0.01$) at month 3. These studies provide evidence that PRP alone can improve pain, range of motion, and function in patients with calcific tendonitis and sub-acromial bursitis, but remains inferior to the more established corticosteroid injections and physical therapy.

While some studies have shown therapeutic benefit for the use of PRP in non-operative treatment of rotator cuff tears, no consensus has been established in the literature, as other studies have shown no clear benefit of PRP over corticosteroid injection or physical therapy. There has been little published regarding negative outcomes from PRP use, so it may be a viable treatment method in specific populations, such as patient for whom corticosteroid use is a concern. Currently, there is little evidence to support PRP's use in treating rotator cuff tendinopathy, biceps tendinopathy, and labral tears. Research in this area should continue to expand.

Surgical indications and outcomes for PRP in the shoulder

There has been a significant increase in the adjunctive use of PRP in rotator cuff repairs, mirrored by a growth in the number of studies published regarding its efficacy in this context in reducing post-operative pain, improving healing of repairs, and reducing risk for re-tear [1, 18–20]. However, despite multiple level I studies on these topics, conclusions are limited by heterogeneity with regard to platelet concentration, method of administration, tear size, and cuff repair technique.

Several studies have examined clinical outcomes after the use of PRP in the surgical treatment of rotator cuff repairs. In a prospective, double-blinded randomized controlled trial, Randelli et al. tested the potential effect of PRP on pain and functional outcome scores in the setting arthroscopic repairs of full-thickness rotator cuff tears. The PRP group was compared to a control group (no PRP application), and both were evaluated using validated outcome scores. The pain score in the PRP group was lower than the control group at 3, 7, 14, and 30 days after surgery. The Simple Shoulder Test (SST), University of California (UCLA), and Constant scores were significantly higher in the treatment group, and strength in external rotation was greater at 3 months after surgery. However, there was no significant difference in all clinical outcome measures between the two groups after 6, 12, and 24 months post-surgery. Likewise, a recent meta-analysis by Hurley et al. examined the efficacy of PRP in arthroscopic rotator cuff repairs and included 18 randomized controlled trials with 1147 total patients [21•]. The analysis found that PRP use significantly decreased rates of incomplete tendon healing in small-medium tears, medium-large tears, and all tears combined compared to the control groups. There was a significant result in favor of PRP use for the Constant score and the visual analog scale (VAS) for pain at 30 days post-operatively and at final follow-up compared to the control groups (no PRP). A systematic review of meta-analyses by Saltzman et al. in 2015 assessed whether PRP administered at the time of rotator cuff repair surgery improved clinical outcomes compared to control cohorts with no PRP administered [22]. The seven meta-analyses included looked at a mean follow-up of 12–31 months in a total of 3193 overlapping patients. No consistent clinical difference was found in the clinical outcome measures assessed: Constant (no difference in 5 of 6 meta-analyses), UCLA (6 of 6), ASES (4 of 4), and SST (3 of 5). One of the meta-analyses included in that systematic review, by Warth et al., performed a subgroup analysis of the Constant scores across their included studies [23]. They found a lower gain in Constant score when liquid PRP was applied over the tendon surface compared to when it was applied at the tendon-bone interface (− 6.48 v + 0.78, $p = 0.046$); however, the gain was not enough to reach clinical significance.

There have also been multiple studies published examining structural outcomes following the use of PRP in the surgical treatment of rotator cuff tears. Jo et al., in a randomized controlled trial, showed improvement in structural outcomes in patients who received PRP and underwent arthroscopic rotator cuff repair of large to massive tears [24•]. Only 3.0% of the patients in the PRP group experienced a re-tear compared to 20.0% of patients in the control group (no PRP), a significant difference ($p < 0.05$). They also found that the 1-year post-operative cross-sectional area as assessed by MRI and immediately post-operative cross-sectional area of the supraspinatus tendon was significantly increased in the PRP group. They concluded that PRP use increases the quality of the tendon healing post-operatively. There was no difference in speed of healing and functional outcomes between the two groups. Two years later in 2015, the same group published a similar study looking at the effect of PRP on medium to large rotator cuff tears undergoing arthroscopic repairs [25]. The results were similar, showing a decrease in re-tear rates and an increase in surface area of tendon repair in the PRP group, with no difference in outcomes or speed of healing. In the subgroup meta-analysis by Warth et al., comparing the effectiveness of PRP-augmented arthroscopic rotator cuff repairs with control cases (no PRP), PRP had a large re-tear reduction effects when used after double-row rotator cuff repairs in patients with initial tear sizes > 3 cm (25.9% v 57.1%, $p = 0.046$) [23]. They also found larger re-tear reduction effects when platelet-rich fibrin matrix (PRFM) was used as opposed to liquid PRP (14.8% v 46.8%, $p = 0.054$). The meta-analysis by Vavken et al. also assessed re-tear rate as it related to

PRP with a focus on its cost-effectiveness in that context [26]. They similarly found that PRP decreased the relative risk of re-tear after arthroscopic repair of small to medium tears (< 3 cm) with a p value of 0.038. However, the gain of 0.0059 quality-adjusted years with PRP augmentation was only cost-effective when the preparation and administration of PRP cost less than $652.11. They concluded that PRP in this context was not cost-effective, with standard preparations of PRP ranging from $450 to $2500 on average at the time of publication.

Few studies have been published on the efficacy of PRP in the surgical treatment of other conditions of the shoulder. A randomized controlled trial by Carr et al. assessed the efficacy of arthroscopic acromioplasty alone versus arthroscopic acromioplasty with PRP injection for the treatment of rotator cuff tendinopathy. The study group was comprised of 60 randomized patients with clinical and radiographic-proven rotator cuff tendinopathy, and 2-year outcomes were based on patient-reported Oxford Shoulder Scores (OSS) and tissue biopsy Bonar scores [27]. Though OSS improved in the 2 years following intervention for both groups, there was no significant difference ($p < 0.001$) between the groups at any time point. On the other hand, shoulders cotreated with PRP showed reduced cellularity and vascularity and increased levels of apoptosis relative to the group that received arthroscopic acromioplasty alone. Similarly, a randomized controlled trial by Verhaegen et al. compared PRP-augmented arthroscopic needling with unaugmented arthroscopic needling in patients with chronic symptomatic calcific tendonitis [28]. Sub-acromial decompression was also performed in patients with evidence of impingement of the coracoacromial ligament (65% of patients in each group). Though patients in both groups improved significantly from their pre-operative state, there was no significant difference between the two groups at 6 weeks, 3 months, 6 months, and 1 year post-operatively in Constant, modified Constant, QuickDASH, or SST scores. Additionally, ultrasound at 3 and 6 months and MRI at 1 year showed no significant differences between the two groups. At the time of this publication, no articles were found in our literature review regarding the use of PRP for the surgical treatment of proximal biceps tendinopathy or labral tears.

Discussion and future directions

The use of PRP in orthopedic surgery is becoming more common, with increasing use in the shoulder in both operative and non-operative settings [1, 13, 25]. According to basic science and animal research, PRP is thought to promote healing and stimulate growth by the release of growth factors from a high concentration of activated platelets [23, 24•, 26, 27]. Yet despite this exciting promise, human subject research with PRP has not produced consistent results in favor of its use in either operative or non-operative conditions of the shoulder, and thus, no consensus exists regarding its therapeutic guidelines or application.

There are some limitations in the study of the efficacy of PRP for the treatment of shoulder pathology. One limitation includes the lack of standardized dosing, formulation, and concentration of the platelets and growth factors that comprise PRP. Additionally, the benefit of including leukocytes in PRP preparations remains a point of controversy. The application of PRP can also differ between administering clinicians, as there is no standardized technique. These variations make cross-study comparisons difficult to interpret.

Based on our review of the current literature, evidence in favor of PRP use for operative and non-operative management of shoulder conditions is inconsistent and cannot be absolutely supported or refuted. The potential benefits of PRP, perhaps not yet elucidated, could outweigh the risks, which are minimal. Additionally, cost-benefit analyses of PRP in rotator cuff repairs indicate that the benefits of its use do not compensate for current costs [26]. To further delineate the efficacy and cost-effectiveness of PRP for shoulder pathology, it is essential that more double-blinded, randomized controlled investigations with large sample sizes and optimized PRP preparations be performed.

Compliance with ethical standards

Conflict of interest Dr. Garbis reports non-financial support from Wright Medical, outside the submitted work. Other authors declare no conflicts of interest.

Human and animal rights and informed consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance

1. Hussain N, Johal H, Bhandari M. An evidence-based evaluation on the use of platelet rich plasma in orthopedics - a review of the literature. SICOT J. 2017;3(1):57. https://doi.org/10.1051/sicotj/2017036.
2. Charles MD, Christian DR, Cole BJ. The role of biologic therapy in rotator cuff tears and repairs. Curr Rev Musculoskelet Med. 2018;11(1):150–61. https://doi.org/10.1007/s12178-018-9469-0.
3. Andia I, Martin JI, Maffulli N. Advances with platelet rich plasma therapies for tendon regeneration. Expert Opin Biol Ther. 2018;4(8):1–10. https://doi.org/10.1080/14712598.2018.1424626.
4. Klatte-Schulz F, Schmidt T, Uckert M, Scheffler S, Kalus U, Rojewski M, et al. Comparative analysis of different platelet lysates and platelet rich preparations to stimulate tendon cell biology: an

in vitro study. Int J Mol Sci. 2018;19(1):212. https://doi.org/10.3390/ijms19010212.

5. Kim SJ, Kim EK, Kim SJ, Song DH. Effects of bone marrow aspirate concentrate and platelet-rich plasma on patients with partial tear of the rotator cuff tendon. J Orthop Surg Res. 2018;13(1):1. https://doi.org/10.1186/s13018-017-0693-x.

6.• Garbis N, Romeo AA, Van Thiel G, et al. Clinical indications and techniques for the use of platelet-rich plasma in the shoulder. 2011: 1–5. https://doi.org/10.1053/j.otsm.2011.03.002. **This paper is a review on the use of PRP in the non-operative and operative management of the shoulder based on current literature at the time of publication. The authors detail important clinical studies and their results and propose what future studies were needed to further clarify PRP's effectiveness in the shoulder.**

7. Sheth U, Dwyer T, Smith I, et al. Does platelet-rich plasma lead to earlier return to sport when compared with conservative treatment in acute muscle injuries? A systematic review and meta-analysis. Arthroscopy. 2018;34(1):281–288.e281. https://doi.org/10.1016/j.arthro.2017.06.039.

8. Ebert JR, Wang A, Smith A, Nairn R, Breidahl W, Zheng MH, et al. A midterm evaluation of postoperative platelet-rich plasma injections on arthroscopic supraspinatus repair: a randomized controlled trial. Am J Sports Med. 2017;45(13):2965–74. https://doi.org/10.1177/0363546517719048.

9. Mazzocca A, McCarthy M, Chowaniec D, et al. Platelet-rich plasma differs according to preparation method and human variability. J Bone Joint Surg Am. 2012;94(4):308–16. https://doi.org/10.2106/JBJS.K.00430.

10. DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: the PAW classification system. Arthroscopy. 2012;28(7):998–1009. https://doi.org/10.1016/j.arthro.2012.04.148.

11. Kobayashi Y, Saita Y, Nishio H, Ikeda H, Takazawa Y, Nagao M, et al. Leukocyte concentration and composition in platelet-rich plasma (PRP) influences the growth factor and protease concentrations. J Orthop Sci. 2016;21(5):683–9. https://doi.org/10.1016/j.jos.2016.07.009.

12. Miranda I, Sánchez-Alepuz E, Lucas FJ, Carratalá V, González-Jofre CA. Use of platelet-rich plasma in the treatment of rotator cuff pathology. What has been scientifically proven? Rev Esp Cir Ortop Traumatol. 2017;61(4):249–58. https://doi.org/10.1016/j.recot.2017.03.001.

13. Zhang JY, Fabricant PD, Ishmael CR, Wang JC, Petrigliano FA, Jones KJ. Utilization of platelet-rich plasma for musculoskeletal injuries: an analysis of current treatment trends in the United States. Orthop J Sports Med. 2016;4(12):2325967116676241. https://doi.org/10.1177/2325967116676241.

14. Shams A, El-Sayed M, Gamal O, Ewes W. Subacromial injection of autologous platelet-rich plasma versus corticosteroid for the treatment of symptomatic partial rotator cuff tears. Eur J Orthop Surg Traumatol. 2016;26(8):837–42. https://doi.org/10.1007/s00590-016-1826-3.

15.• Kesikburun S, Tan AK, Yilmaz B, Yaşar E, Yazicioğlu K. Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy: a randomized controlled trial with 1-year follow-up. Am J Sports Med. 2013;41(11):2609–16. https://doi.org/10.1177/0363546513496542. **This study found no difference in pain or functional outcome scores at any time point up to 1 year in patients who received PRP or a placebo injection (saline solution) followed by participation in a rehabilitation program.**

16.• Say F, Gurler D, Bulbul M. Platelet-rich plasma versus steroid injection for subacromial impingement syndrome. J Orthop Surg (Hong Kong). 2016;24(1):62–6. https://doi.org/10.1177/230949901602400115. **This study showed that improvements in pain in patients with calcific tendonitis were greater in patients who received corticosteroid injections compared to those who received PRP injections.**

17. Nejati P, Ghahremaninia A, Naderi F, Gharibzadeh S, Mazaherinezhad A. Treatment of subacromial impingement syndrome: platelet-rich plasma or exercise therapy? A randomized controlled trial. Orthop J Sports Med. 2017;5(5): 2325967117702366. https://doi.org/10.1177/2325967117702366.

18. Meadows MC, Levy DM, Ferry CM, Gardner TR, Teratani T, Ahmad CS. Effects of platelet-rich plasma and indomethacin on biomechanics of rotator cuff repair. Am J Orthop. 2017;46(5): E336–43.

19. Fu C-J, Sun J-B, Bi Z-G, Wang X-M, Yang C-L. Evaluation of platelet-rich plasma and fibrin matrix to assist in healing and repair of rotator cuff injuries: a systematic review and meta-analysis. Clin Rehabil. 2017;31(2):158–72. https://doi.org/10.1177/0269215516634815.

20. Beck J, Evans D, Tonino PM, Yong S, Callaci JJ. The biomechanical and histologic effects of platelet-rich plasma on rat rotator cuff repairs. Am J Sports Med. 2012;40(9):2037–44. https://doi.org/10.1177/0363546512453300.

21.• Hurley ET, Lim Fat D, Moran CJ, Mullett H. The efficacy of platelet-rich plasma and platelet-rich fibrin in arthroscopic rotator cuff repair: a meta-analysis of randomized controlled trials. Am J Sports Med. 2018;79(1):363546517751397. https://doi.org/10.1177/0363546517751397. **This meta-analysis found that PRP use significantly decreased rates of incomplete tendon healing in small-medium tears, medium-large tears, and all tears combined compared to control groups.**

22. Saltzman B, Jain A, Campbell K, et al. Does the use of platelet-rich plasma at the time of surgery improve clinical outcomes in arthroscopic rotator cuff repair when compared with control cohorts? A systematic review of meta-analyses. Arthrosc J Arthrosc Relat Surg. 2016;32(5):906–18. https://doi.org/10.1016/j.arthro.2015.10.007.

23. Warth RJ, Dornan GJ, James EW, Horan MP, Millett PJ. Clinical and structural outcomes after arthroscopic repair of full-thickness rotator cuff tears with and without platelet-rich product supplementation: a meta-analysis and metaregression. Arthroscopy. 2015;31(2):306–20.

24.• Jo CH, Shin JS, Lee YG, et al. Platelet-rich plasma for arthroscopic repair of large to massive rotator cuff tears: a randomized, single-blind, parallel-group trial. Am J Sports Med. 2013;41(10):2240–8. https://doi.org/10.1177/0363546513497925. **This study showed improvement in structural outcomes in patients who received PRP and underwent arthroscopic rotator cuff repair of large to massive tears.**

25. Jo CH, Shin JS, Shin WH, Lee SY, Yoon KS, Shin S. Platelet-rich plasma for arthroscopic repair of medium to large rotator cuff tears: a randomized controlled trial. Am J Sports Med. 2015;43(9):2102–10. https://doi.org/10.1177/0363546515587081.

26. Vavken P, Sadoghi P, Palmer M, Rosso C, Mueller AM, Szoelloesy G, et al. Platelet-rich plasma reduces retear rates after arthroscopic repair of small- and medium-sized rotator cuff tears but is not cost-effective. Am J Sports Med. 2015;43(12):3071–6. https://doi.org/10.1177/0363546515572777.

27. Carr A, Murphy R, Dakin S, et al. Platelet-rich plasma injection with arthroscopic acromioplasty for chronic rotator cuff tendinopathy. Am J Sports Med. 2015;43(12):2891–7. https://doi.org/10.1177/0363546515608485.

28. Verhaegen F, Brys P, Debeer P. Rotator cuff healing after needling of a calcific deposit using platelet-rich plasma augmentation: a randomized, prospective clinical trial. J Shoulder Elb Surg. 2016;25(2):169–73. https://doi.org/10.1016/j.jse.2015.10.009.