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# Does Platelet-Rich Plasma Therapy in Arthroscopic Rotator Cuff Repair Improve Patient Outcome?

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**Does platelet-rich plasma therapy in arthroscopic rotator cuff  
repair improve patient outcome?**

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
Philadelphia, Pennsylvania

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## Abstract

**Objective:** The objective of this selective EBM review is to determine whether or not platelet-rich plasma therapy (PRP) improves patient outcome in arthroscopic rotator cuff repair.

**Study Design:** Review of three primary research studies published in the English language in 2011.

**Data sources:** Three double blind, randomized, controlled trials analyzing the effect of augmentation of rotator cuff repair surgery with PRP therapy were found using PubMed.

**Outcomes Measured:** Each of the three studies measured the effectiveness of PRP therapy in arthroscopic rotator cuff repair, with specific regards to pain improvement after surgery, healing time and durability of the repair. Each patient was measured using the Constant score preoperatively and at varying intervals postoperatively from three months up to two years. The Constant score measures pain, limitations of activities of daily living, range of motion and strength.

**Results:** Three randomized controlled trials were included in this review. The study by Randelli found that there was a significant increase in Constant scores for the PRP group at 3 months postoperative, but no significant difference was found at 6, 12 and 24 months postoperative. The study by Sánchez Márquez found no significant difference between the Constant Scores of both groups at 12 months. The study by Castricini found that there was no significant difference in Constant score at an average of 20.2 months postoperative.

**Conclusions:** Based upon analysis of three RCT's, one study found significant improvement in pain and strength at various postoperative intervals, while two additional studies found no significant improvement. The mixed nature of these results identifies the need for further investigation into the effectiveness of this treatment method.

**Key Words:** Platelet rich plasma AND rotator cuff

Introduction:

Rotator cuff tears are a common reason for visits to medical practitioners in the United States. They can be caused by acute injuries related to falls on an outstretched arm or by pulling on the shoulder. It can also be a chronic injury due to long-term and frequent insults to the joint, including repetitive overhead movement and lifting. Tears are often the result of trauma and occur more commonly in the elderly.<sup>2</sup> Tendons of the supraspinatus, infraspinatus, teres minor and subscapularis muscles form the rotator cuff, which is the basis of stability of the shoulder joint. The most commonly torn tendon is the supraspinatus tendon. Patients typically present with weakness or pain with overhead movement. Additionally, there may be clinical evidence of impingement syndrome, where subacromial inflammation leads to decreased muscle strength, pain with overhead movement and nocturnal pain. This paper evaluates three randomized controlled trials (RCTs) investigating whether or not platelet-rich plasma (PRP) therapy improves patient outcome in arthroscopic rotator cuff repair.

The exact pathogenesis of rotator cuff tears is not clearly understood at this point. The causes may stem from degeneration, impingement or overload. It is thought to be a combination of intrinsic and extrinsic factors that cause joint injury.<sup>1</sup> Extrinsic factors include repetitive microtrauma and impingement. Intrinsic factors include hypovascularity of tendons, as well as age related changes including decreased cellular activity and changes in the composition of the matrix of the tendon.<sup>1</sup> Once injured, it is likely that there is difficulty healing due to poor blood supply at the humeral insertion point. Diagnosis is made based on clinical suspicion with supporting radiographic evidence. The preferred imaging method is magnetic resonance imaging (MRI), which can show partial or small rotator cuff tears. Initial work-up includes a radiograph, and if patients are unable to have an MRI performed, ultrasound may be used as an alternative.<sup>2</sup>

In many cases, particularly in partial-tears, the preferred method of treatment is conservative. This includes rest, ice, physical therapy, muscle strengthening and analgesia. In some instances, particularly full-thickness tears, the injury is unlikely to heal without proper surgical intervention. Surgical techniques vary, but may consist of arthroscopic repair with reanchoring of the tendons to the tubercle of the humerus. Surgical techniques have improved bone-to-tendon fixation, but the long term re-tear rates and overall tendon degradation are common.<sup>10</sup>

To improve outcomes, the relatively new technique of augmenting surgical repair with the addition of PRP intraoperatively is under investigation. This technique uses platelet-rich plasma, which is a whole blood fraction containing high platelet concentration. This provides the addition of various growth factors, including transforming growth factor beta (TGF- $\beta$ ), fibroblast growth factor (FGF), platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), connective tissue growth factors and epidermal growth factor (EGF).<sup>3</sup> The proposed benefit of including PRP in surgical rotator cuff repair is that it allows platelet-derived factors to be locally available to the tissue throughout the healing process.<sup>4</sup>

Rotator cuff tears are one of the most common pathologies affecting the shoulder. Estimates in prevalence of shoulder pain range from 16 to 34 percent in the general population.<sup>5,6</sup> In the United states there are greater than 4.5 million annual physician visits due to rotator cuff tears and greater than 250,000 rotator cuff repairs are performed each year.<sup>7</sup> A cadaveric study found the incidence of full-thickness rotator cuff tears in subjects older than 60 years to be 30 percent.<sup>3</sup> The cost of an individual surgery has been estimated at between \$10,605 and \$11,914 for the physician and hospital services.<sup>8</sup> This cost estimate does not include the cost of early re-

tears which lead to more frequent physician visits, longer rehabilitation time and costly repeat rotator cuff surgeries.

Objective:

The objective of this selective EBM review is to determine whether or not platelet-rich plasma therapy improves patient outcome in arthroscopic rotator cuff repair.

Methods:

The chosen studies were all randomized controlled trials. The populations included were patients with rotator cuff tears who had chosen to undergo arthroscopic rotator cuff repair. The intervention used in these studies was augmentation of arthroscopic rotator cuff repair with intraoperative platelet-rich plasma therapy. These groups were compared to control groups, which included patients receiving arthroscopic rotator cuff repair without PRP therapy. The outcomes measured in these studies were the effectiveness of PRP therapy in arthroscopic rotator cuff repair, with specific regards to pain improvement after surgery, healing time and durability of the repair.

A detailed search was completed utilizing the search engine Pubmed. The keywords “platelet rich plasma” and “rotator cuff” were used in combination to search for English-language articles. All of the resulting qualified articles were published in 2011 in peer-reviewed journals. The included studies must have been randomized, controlled, double blind studies and they must have included patient oriented outcomes (POEMs). The studies also must have included patients with complete rotator cuff tears who had failed conservative treatment. Studies were excluded if they had been included in previous systematic reviews or meta-analyses. Studies were excluded if patients had previous surgery to the affected shoulder. Each study had its own specific inclusion and exclusion criteria, which are included in table 1. The continuous

data in the studies included the use of p-values, 95% confidence intervals (CI), Student's *t*-test, the Mann-Whitney U test, unpaired *t* test and various probabilities. Because none of the studies presented dichotomous data, there were no reported RRR, ARR, and NNT values. Table 1 demonstrates the demographics included in the studies.

Table 1: Demographics and Characteristics of Included Studies

Study	Type	# pts	Age	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Randelli <sup>3</sup> , 2011	Double blind RCT	45	Mean (61.6; 59.5)	1) A complete rotator cuff tear 2) Brace 4 weeks postoperative 3) platelet count > than 150,000 4) Hgb $\geq$ 11.0g/dL 5) No infectious disease prior that inhibits follow up 6) Had a BMI $\leq$ 33	1) Previous rotator cuff repair 2) Active infection, osteomyelitis, sepsis 3) Bone disorders 4) Uncooperative pt 5) Disease of shoulder 6) Smoke cigarettes 7) Steroid injection in affected shoulder.	9	Applying intraoperative autologous platelet-rich plasma (PRP) to arthroscopic rotator cuff repair.
Castricini <sup>4</sup> , 2011	Double blind RCT	88	37-72	1) Supraspinatus tear 2) Failed 6 months nonoperative tx 3) No episodes of shoulder instability 4) No signs of fx of the glenoid, greater or lesser tuberosity 5) MRI showing tear 6) Repairable full-thickness tear 7) injury of long head of the biceps	1) Inflammatory joint disease 2) Irreparable tear 3) Symptomatic arthritis of AC joint 4) Rotator cuff arthropathy 5) Pathologic abnormalities of the subscapularis tendon 6) Workers' compensation claims 7) Prior surgery on the affected shoulder	N/A	Applying intraoperative autologous platelet-rich fibrin matrix (which can be sutured in place at the site of the tear) to arthroscopic rotator cuff repair.
Sanchez <sup>6</sup> , 2011	Double blind RCT	28	53-78	1) Massive rotator cuff tear (>5cm) 2) Supraspinatus and infraspinatus tendons involved 3) Conservative tx at least 3 months	1) Prev. shoulder sx 2) Small/subscapular tendon tear 3) Capsulitis 4) Degenerative change 5) Chronic infectious disease 6) Hgb <13g/dL 7) Hematological or coagulation disorder 8) h/o difficulty cannulating a peripheral vessel	N/A	Applying platelet-rich plasma (PRP) with high fibrin content in the repair area of massive rotator cuff tears treated using arthroscopic techniques.

### Outcomes Measured

Clinical outcome was measured using the “Constant score”. The Constant-Murley scoring system was used to measure shoulder pain, activities of daily living, range of movement and power. Each of these variables was measured separately and combined to form a total score to assess overall patient outcome. Pain and ADLs were subjectively measured, and range of movement and power were objectively measured. Pain, ADLs, range of movement and power were all measured based on the patient’s self-described pain level. Even while the range of movement and power were objectively measured, the measurements were gathered based upon the degree to which the patient was able to use their shoulder without experiencing subjective pain.

The Constant score is based on a point total out of a maximum of 100. Pain is measured using the Visual Analog score (VAS) and given a maximum of 15 points if there is a total absence of pain. Limitations of activities of daily living include disturbances in sleep, work and recreation, with a maximum of 20 points if there are no limitations. Range of motion is measured and given a maximum score of 40 points if full range of motion is achieved without significant pain. Strength is measured using a dynamometer and given a maximum score of 25 points. Strength is measured to the point at which patients experience pain.

### Results

The three randomized controlled trials in this review utilized continuous data and could not be converted to dichotomous data. The three studies looked at the use of PRP augmentation in arthroscopic rotator cuff repair. In all studies, the placebo used was arthroscopic rotator cuff repair without the use of PRP therapy augmentation. The type of PRP augmentation and the surgical technique varied slightly between studies. The Randelli et al study used 6ml of

injectable PRP in combination with autologous thrombin component and a surgical technique involving a single-row anchor technique with acromioplasty. The Sánchez Márquez et al study used 7ml of injectable fibrin-rich PRP and a surgical technique involving a single-row anchor technique. The Castricini et al study used a suturable membrane of autologous fibrin PRP and a surgical technique involving a double-row anchor technique. The Randelli et al study and the Castricini et al study included patients with any complete rotator cuff tears confirmed intraoperatively, while the Sánchez Márquez et al study included only patients with a massive rotator cuff tear. In all studies patients were evaluated preoperatively using the Constant-Murley score, and they were then evaluated postoperatively at varying time periods. Patients were also evaluated using the Visual Analog scale alone in the immediate postoperative period in the Randelli et al study.

In the Randelli et al study, there was no significant difference in Constant scores pre-operative, or at 6, 12 or 24 months. There was, however, significant difference in Constant scores at 3 months post-operative. The reported values for Constant scores found that pre-operatively, the PRP group reported a score of  $44 \pm 16.5$  and the control group reported a score of  $42.2 \pm 15.2$  ( $P = .6$ ). At 3 months post-op, the PRP group reported Constant scores of  $65 \pm 9$  and the Control group reported scores of  $57.8 \pm 11$  ( $P = .02$ ). At 6 months, the PRP group reported scores of  $73.1 \pm 8.7$  and the control group reported scores of  $72.3 \pm 12.6$  ( $P = .7$ ). At 12 months the PRP group reported scores of  $79.3 \pm 6.4$  and the control reported  $75.7 \pm 9.5$  ( $P = .3$ ). At 24 months the PRP group reported scores of  $82.4 \pm 6.3$  and the control group reported  $78.7 \pm 10$  ( $P = .1$ ). Table 2 shows the Constant scores at each of the reported time intervals. Table 3 reports the mean change of the Constant values from the pre-operative value to the last reported post-operative value.

In the Sánchez Márquez et al study, there was no significant difference in reported Constant scores at a pre-operative visit and at 12 months post-operative. The pre-operative values were reported as  $39.7 \pm 10.2$  in the PRP group and  $34.3 \pm 11.7$  in the control group ( $P = .79$ ). At 12 months, the PRP group reported  $65.6 \pm 13.1$  and the control group reported  $64.1 \pm 13.6$  ( $P = .79$ ). Table 2 shows the Constant scores at each of the reported intervals. Table 3 reports the mean change of the Constant values from the pre-operative value to the last reported post-operative value.

In the Castricini et al study, patients were evaluated pre-operatively and again post-operatively at an average of 20.2 months (range 16-30 months). There was no significant difference in total Constant score between the control and PRP groups. Pre-operative values were reported as a Constant score of  $42 \pm 6.65$  in the PRP group and  $42.9 \pm 7.92$  in the control group. Post-operative follow-up was reported as  $88.4 \pm 7.62$  in the PRP group and  $88.4 \pm 7.78$  in the control group ( $P = .44$ ). Table 2 shows the Constant scores at each of the reported intervals. Table 3 reports the mean change of the Constant values from the pre-operative value to the last reported post-operative value.

Table 2: Platelet-Rich Plasma therapy vs. Control mean values

Study	Pre-op Constant score (PRP; Control)	3-month Constant score (PRP; Control)	6-month Constant score (PRP; Control)	12-month Constant score (PRP; Control)	24-month Constant score (PRP; Control)
Randelli et al, 2011	$44 \pm 16.5$ ; $42.2 \pm 15.2$ ( $P = .6$ )	$65.0 \pm 9.0$ ; $57.8 \pm 11$ ( $P = .02$ )	$73.1 \pm 8.7$ ; $72.3 \pm 12.6$ ( $P = .7$ )	$79.3 \pm 6.4$ ; $75.7 \pm 9.5$ ( $P = .3$ )	$82.4 \pm 6.3$ ; $78.7 \pm 10$ ( $P = .1$ )
Sánchez Márquez et al, 2011	$39.7 \pm 10.2$ ; $34.3 \pm 11.7$ ( $P = .79$ )	NR*	NR*	$65.6 \pm 13.1$ ; $64.1 \pm 13.6$ ( $P = .79$ )	NR*
Castricini et al, 2011	$42 \pm 6.65$ ; $42.9 \pm 7.92$ ( $P = .44$ )	NR*	NR*	NR*	<i>(Average 20.2 months post-op)</i> $88.4 \pm 7.62$ ; $88.4 \pm 7.78$ ( $P = .44$ )
*NR = not reported					

Table 3: Mean change of Constant score from baseline to final reported value

	Randelli et al, 2011 (PRP; Control)	Sánchez Márquez et al, 2011 (PRP; Control)	Castricini et al, 2011 (PRP; Control)
Mean change from baseline to final Constant score	38.4; 36.5 (P = .01)	25.9; 29.8 (P < .005)	46.4; 45.5 (P < .001)

### Discussion

All three randomized, controlled studies found a high degree of patient satisfaction from rotator cuff repair, regardless of the addition of PRP to conventional repair. Patients' Constant scores significantly improved in all aspects in both arms of each study, the PRP group and the control group.

The study by Randelli et al was a randomized, controlled trial, which found that there was a lower pain score observed in the PRP group in the first month after surgery. A multivariate model was used to analyze the Constant scores, which concluded that pain and activity scores significantly improved at 3 months postoperative. Constant scores were higher in the PRP group throughout the study, but the difference was not significant at 6, 12 and 24 months. The study reports that a potential reason for the lower pain scores observed in immediate post-operative period may be due to the analgesic properties of platelets.

The study by Sánchez Márquez et al was a randomized, controlled trial, which found that, in massive rotator cuff tears, application of PRP during arthroscopic repair does not improve functional results and does not reduce the risk of re-tear. In this study, "the Student's t-test was used to compare the mean for each group. When the assumption of normality was not accepted, the non-parametric Mann-Whitney U test was used."<sup>9</sup> Results were presented with statistical significance being accepted when  $P < .05$ . This study only included patients with massive rotator cuff tears. Patients with massive rotator cuff tears are at very high risk of

re-tearing the tendons, which is why in theory applying PRP during surgery could help with patient outcomes. The results of this small study, however, found no such benefit.

In the randomized, controlled trial by Castricini et al, it was found that in small and medium rotator cuff tears, augmentation with PRP did not result in significant improvement in shoulder function (measured by the Constant score) and structural outcome (evaluated by MRI). The statistical analysis was done using the “intention-to-treat” principle. The distribution of both groups’ Constant scores was normal, therefore the study, “used the unpaired *t* test to compare the post-operative results between the 2 groups.”<sup>7</sup> 95% confidence intervals were then calculated and a P value less than .05 was considered significant. The study also concluded that the use of autologous platelet-derived growth factors result in longer surgical time and higher expense.

### Conclusion

Based on the studies reviewed, the addition of PRP therapy to conventional arthroscopic rotator cuff repair in patients with complete tears appears to be inconclusive. In all studies, patient outcome was significantly improved after having arthroscopic rotator cuff repair, regardless of whether or not there was the addition of PRP. There were no reported adverse events due specifically to the PRP therapy, but the cost and increased time in surgery are significant and need to be taken into consideration. Randelli et al found that there was improvement in pain scores in the first month after surgery as well as in the Constant scores at 3 months. This led to the conclusion that this therapy may be effective in the short term, allowing quicker return to activity and work. The other two studies, Sánchez Márquez et al and Castricini et al, did not find any statistically significant improvement in patient outcomes when PRP augmentation was used.

There were certain shortcomings in each of the trials that could have led to discrepancies in the observed outcomes. One of the most important weaknesses of these trials is their small sample size. There was also a lack of information about the exact numbers of platelets and the quantity of growth factors actually delivered to the patients.<sup>7</sup> There is currently a widespread heterogeneity of collection methods and application techniques of PRP. In order to improve accuracy of trials in the future, a more homogenous method of platelet collection and application should be established and studied. The mixed results of these trials highlights the need for further studies to be completed before a definitive conclusion can be reached on the use of PRP augmentation in the repair of rotator cuff tears.

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