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Efficacy of platelet-rich plasma in arthroscopic repair of full-thickness rotator cuff tears: a meta-analysis

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Background: The use of platelet-rich plasma (PRP) is an innovative clinical therapy, especially in arthroscopic rotator cuff repair. The purpose of this study was to compare the clinical improvement and tendon-to-bone healing with and without PRP therapy in arthroscopic rotator cuff repair.

Methods: A systematic search was done in the major medical databases to evaluate the studies using PRP therapy (PRP+) or with no PRP (PRP−) for the treatment of patients with rotator cuff tears. We reviewed clinical scores such as the Constant score, the American Shoulder and Elbow Surgeons score, the University of California at Los Angeles (UCLA) Shoulder Rating Scale, the Simple Shoulder Test, and the failure-to-heal rate by magnetic resonance imaging between PRP+ and PRP− groups.

Results: Five studies included in this review were used for a meta-analysis based on data availability. There were no statistically significant differences between PRP+ and PRP− groups for overall outcome scores ($P > .05$). However, the PRP+ group exhibited better healing rates postoperatively than the PRP− group ($P = .03$) in small/moderate full-thickness tears.

Conclusion: The use of PRP therapy in full-thickness rotator cuff repairs showed no statistically significant difference compared with no PRP therapy in clinical outcome scores, but the failure-to-heal rate was significantly decreased when PRP was used for treatment of small-to-moderately sized tears. PRP therapy may improve tendon-to-bone healing in patients with small or moderate rotator cuff tears.

Level of evidence: Level I, Meta-analysis.

Keywords: Rotator cuff repair; platelet-rich plasma; tendon-to-bone healing; meta-analysis; biological therapy

Rotator cuff tears have an adverse effect on daily activities in personal disability and functional restriction. Currently, patients with symptomatic full-thickness rotator cuff tears can be repaired arthroscopically, often with significant functional improvement.[8,26,31] However, after large or massive rotator cuff tears repaired arthroscopically, there is still a significant failure-to-heal rate, in 1 study as high as 94%[12] Furthermore, tear size influences rotator cuff healing, because a large tear often has a lower healing rate.[7,32] Some patients treated arthroscopically whose tendons fail to heal have good clinical outcomes due to pain relief, but some patients with tendon healing

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postoperatively may have better overhead function. Although transosseous suture-bridge techniques have been developed to improve the mechanical properties of the rotator cuff, the healing rate was still less than satisfactory,[4,35] possibly as a result of the abnormal regeneration of tissue at the tendon-to-bone interface that was replaced with fibrous scar tissue.[29] Some researchers have attempted to promote tendon-to-bone healing with the use of biological strategies, such as growth factors, stem cells, and biomaterials.[1,21]

Platelet-rich plasma (PRP) has been defined as "a sample of autologous blood with concentrations of platelets above baseline values"[15] and was first used in plastic surgery in the 1990s. Compared with mesenchymal stem cells (MSCs), it is simpler to isolate PRP from a wide variety of tissue sources. PRP is rich in several growth factors and cytokines, such as platelet-derived growth factors, transformation growth factor-β, and insulin-like growth factor, which play key roles in hemostasis, construction of new connective tissue, and revascularization, and might improve tendon-to-bone healing.[10,25] This is a retrospective meta-analysis of the use of PRP in arthroscopic rotator cuff repairs.

Materials and methods

A literature search was conducted from January 1990 to January 2015 in the electronic databases of PubMed, Web of Science (SCI-E/SSCI/A&HCI), and EMBASE with the following parameters: "platelet-rich plasma" *or* "platelet gel" *or* "platelet plasma" *or* "PRP" combined with the keywords "rotator cuff tear" *or* "shoulder" *or* "tendon."

The retrieved articles were initially screened for relevance by the title and abstract. Inclusion criteria were (1) Level I evidence studies of PRP use in repairs compared with repairs without PRP; (2) adequate statistical power to defect differences with 95% confidence intervals (CIs) and follow-up >80%; (3) full-thickness rotator cuff tears; and (4) arthroscopic rotator cuff repairs. Exclusion criteria were case control studies, case reports, and studies without abstracts, and patients with partial-thickness rotator cuff tears, a history of previous injury or surgery to the same shoulder, postoperative infection, arthrofibrosis, rheumatoid arthritis, inadequate follow-up, and thrombocytopenia.

The full text of the remaining articles was obtained and further reviewed for quality by 2 separate observers, based on the Cochrane Handbook for Systematic Reviews of Interventions.[18] To determine the possibility of bias, we examined selection bias, performance bias, incomplete attrition bias, detection bias, and publication bias. An additional quantification of the degree of possible bias was performed by the modified Coleman Methodology Score.[9] Level of evidence (LOE) was determined for all included studies (as given at http://handbook.cochrane.org/). After this evaluation, articles were selected on the basis of the risk of bias, modified Coleman score, and LOE to answer our clinical research question.

Data were collected from the remaining high-quality articles that were all Level I studies with a high modified Coleman score (>80), including authors, number of patients, mean age, method of preparation (focused on type of preparation, blood volume, final PRP concentration, activating agent, and site of application), and outcomes including the Constant score, the American Shoulder and Elbow Surgeons (ASES) score, the UCLA Shoulder Rating Scale, the Simple Shoulder Test (SST), and magnetic resonance imaging (MRI). The Constant, ASES, UCLA, SST, and MRI were compared approximately 12 months postoperatively. Rotator cuff integrity was classified as intact or retorn.

Statistical analysis was performed using Review Manager 5.3 (Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark). Continuous variables were analyzed using the weighted mean difference, and categoric variables were assessed using relative risks. $P < .05$ was considered to be statically significant, and 95% CIs were reported. Homogeneity was tested by the Q statistic (significance level at $P < .1$) and the I^2 statistic (significance level at $I^2 > 50\%$). A random-effects model was used if the Q or I^2 value was statistically significant; otherwise, a fixed-effects model was used.

Results

The literature search identified 207 relevant articles. The titles of these articles were carefully screened, and 167 were excluded for not investigating the topic. After application of inclusion and exclusion criteria, 35 articles were excluded (13 laboratory or animal studies, 8 reviews and meta-analyses, 2 case reports, and 12 with Level II, III, or IV evidence), leaving 5 selected articles[6,20,22,28,37] for analysis. The flow diagram is shown in Fig. 1. All studies involved patients with arthroscopic rotator cuff repairs, clinical outcome scores, and healing rates reported with at least 12 months of follow-up. The quality of included studies was determined on the risk of bias, including selection, performance, attrition, detection, and reporting bias, and Coleman score (Table I). The funnel plots demonstrated no visual evidence of publication bias (Fig. 2). All included studies were randomized controlled trials with a high level of methodologic quality in which 303 patients were enrolled (150 for PRP and 153 for control). The characteristics of the included studies are summarized in Table II.

There was no evidence indicating a difference in pooled clinical outcomes between the PRP group (PRP+) and the control group (PRP−) for the Constant score (0.70 [95% CI, −1.62 to 3.03], $P = .55$, $I^2 = 0\%$; Fig. 3), the UCLA score (0.36 [95% CI, −1.48 to 2.19], $P = .70$, $I^2 = 60\%$; Fig. 4), SST (0.49 [95% CI, −0.11 to 1.09], $P = .11$, $I^2 = 0\%$; Fig. 5), and the ASES score (0.91 [95% CI, −3.72 to 5.54], $P = .70$, $I^2 = 0\%$; Fig. 6) with no significant heterogeneity. However, the pooled outcome of overall rotator cuff failure-to-heal rate in PRP+ was significant lower, with no heterogeneity (0.05 [95% CI, 0.31-0.83], $P = .007$, $I^2 = 0$; Fig. 7), compared with PRP−. Furthermore, based on the initial tear size, subgroups of mild-to-moderate and severe-to-massive tear size were analyzed.