

# Application of Platelet-Rich Plasma in Arthroscopic Rotator Cuff Repair

## A Systematic Review and Meta-analysis

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**Background:** It is unclear how and which factors affect the clinical efficacy of platelet-rich plasma (PRP) applied during arthroscopic rotator cuff repair.

**Purpose:** To evaluate the clinical efficacy of PRP for arthroscopic repair of full-thickness rotator cuff tear and investigate the factors that affect its clinical efficacy.

**Study Design:** Systematic review; Level of evidence, 1.

**Methods:** We searched Cochrane Library, EMBASE, MEDLINE, and OVID to identify randomized controlled trials (RCTs) of patients who received PRP treatment and arthroscopic rotator cuff repair (PRP group) versus controls (no-PRP group). The primary outcomes included retear rate, Constant-Murley score, University of California Los Angeles (UCLA) score, short-term American Shoulder and Elbow Surgeons (ASES) score, visual analog scale (VAS) score for pain, and adverse events.

**Results:** A total of 14 RCTs were included in this systematic review. Significant improvement in Constant-Murley, UCLA, and VAS pain scores were found in the PRP group during short-term, midterm, and long-term follow-up. The PRP group had a significantly decreased retear rate (risk ratio [RR], 0.57 [95% CI, 0.42 to 0.78];  $P = .0003$ ), especially for long-term follow-up (RR, 0.38 [95% CI, 0.17 to 0.83];  $P = .02$ ), large to massive tears (RR, 0.58 [95% CI, 0.42 to 0.80];  $P = .0008$ ), use of leukocyte-poor PRP (RR, 0.50 [95% CI, 0.33 to 0.76];  $P = .001$ ), and intraoperative application of PRP (RR, 0.57 [95% CI, 0.42 to 0.79];  $P = .0007$ ). No significant difference between the 2 groups was found in the incidence of adverse events (RR, 1.34 [95% CI, 0.83 to 2.15];  $P = .23$ ) or in ASES scores at short-term follow-up (weighted mean difference, 1.04 [95% CI, -3.10 to 5.19];  $P = .62$ ).

**Conclusion:** The results of this review indicated that arthroscopic rotator cuff repair with PRP significantly reduced the long-term retear rate and shoulder pain and provided improved long-term shoulder function in patients. Intraoperative application of PRP, use of leukocyte-poor plasma, and large to massive tear size contributed to a significantly decreased retear rate for rotator cuff repair combined with PRP.

**Keywords:** rotator cuff; arthroscopic; platelet-rich plasma; retear rate

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Rotator cuff injury is one of the most common causes of shoulder pain, with a prevalence of 2.5% to 62%; the prevalence increases with older age.<sup>16,32,37</sup> Although arthroscopic rotator cuff repair can improve postoperative function and pain, the postoperative retear rate varies between 5% and 51%, with a higher retear rate in older patients.<sup>6,10,26</sup> Therefore, more studies are being performed on biological therapies to assist the healing of rotator cuff tendon, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF).<sup>4,13,14,17,22,29,30</sup>

PRP is an autologous plasma produced using centrifugation and separation of whole blood, which is enriched with a higher platelet concentration than normal blood.<sup>36</sup> Dohan Ehrenfest et al<sup>7</sup> classified different platelet concentrates into 4 categories according to the content of fibrin and leukocyte: pure platelet-rich plasma, leukocyte- and platelet-

rich plasma, pure PRF, and leukocyte and PRF. Each technique for deriving platelet concentrates results in different biological characteristics, clinical efficacy, and applications.

Numerous studies have been published on the clinical efficacy of PRP in patients who received arthroscopic rotator cuff repair,<sup>1,3,9,30</sup> but the conclusions have been inconsistent. Some studies found that PRP reduced the retear rate and improved shoulder function,<sup>5,18</sup> whereas other studies came to a different conclusion.<sup>1,9</sup> Controversies exist regarding the application time of PRP.<sup>8,30,34</sup> In addition, differences in the number of participants, the methods used, and factors such as tear size, type of injured rotator cuff, time of PRP application, PRP type, and type of surgical procedure might affect the final conclusions.<sup>8,12,19,22</sup> Sufficient knowledge is lacking about the role of these factors in patients who receive arthroscopic rotator cuff repair combined with PRP. In addition, research about the cost-effectiveness of PRP in the arthroscopic surgery of rotator cuff tear is limited.<sup>28,33</sup>

To evaluate the efficacy of PRP and investigate the role of related factors, we performed a systematic review and meta-analysis. We hypothesized that arthroscopic rotator cuff repair combined with PRP would reduce the postoperative retear rate but would not improve postoperative shoulder function.

## METHODS

### Search Strategy

The study was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.<sup>23</sup> Electronic databases including Cochrane Library, EMBASE, MEDLINE, and OVID were searched between inception and June 20, 2020, for randomized controlled clinical trials (RCTs) on patients treated using arthroscopic rotator cuff repair combined with PRP; there were no language restrictions. We used the following search string: ((((((random\*[Title/Abstract] OR prospect\*[Title/Abstract] OR RCT\*[Title/Abstract]))) OR "Random Allocation"[Medical Subject Headings (MeSH)])) AND (((PRP[Title/Abstract] OR "Platelet-Rich Plasma"[MeSH]) OR "platelet - rich plasma"[Title/Abstract]))) AND (((("Rotator Cuff Injuries"[MeSH] OR "Rotator Cuff Tear Arthropathy"[MeSH]) OR (((("Rotator Cuff"[MeSH] OR "Rotator Cuff Injuries"[MeSH] OR "Shoulder Impingement Syndrome"[MeSH]) OR subscapularis[Title/Abstract]) OR infraspinatus[Title/Abstract]) OR supraspinatus[Title/Abstract]) OR "rotator cuff"[Title/Abstract]))) to identify the relevant RCTs.

### Eligibility Criteria

Articles were assessed by both authors (W.X. and Q.X.) independently using predesigned eligibility criteria, and any disagreements between researchers were settled via consensus. We also evaluated the reference lists of related comparative studies and reviews for additional relevant studies.

Studies were selected based on the following inclusion criteria: (1) participants: patients with arthroscopic rotator cuff repair; (2) intervention: PRP; (3) comparison: placebo group (saline solution); (4) outcome measures: reported at least 1 of the following outcomes: retear rate, Constant-Murley score, University of California Los Angeles (UCLA) score, American Shoulder and Elbow Surgeons (ASES) score, visual analog scale (VAS) score for pain, and adverse events; and (5) study design: RCT. Exclusion criteria were studies in which (1) PRF matrix or platelet-leukocyte membrane was involved, (2) none of the above major outcomes were reported, and (3) no detailed data were provided and (4) related studies including the same patients.

### Data Extraction

Data that contained related information and major outcomes were independently extracted from the included studies by both authors. The recorded data included patient sex, tear size (small to massive), number of injured tendons, follow-up time (short term vs midterm vs long term), leukocyte concentration of PRP (leukocyte poor vs leukocyte rich), PRP volume, PRP type (gel vs liquid), time of PRP application (intraoperative vs postoperative), injection site, type of surgical procedure (single row vs double row), and postoperative rehabilitation. We considered retear rate to be the primary outcome measure, with patient-reported outcomes (Constant-Murley, UCLA, ASES, and VAS pain scores) and adverse events as secondary outcome measures.

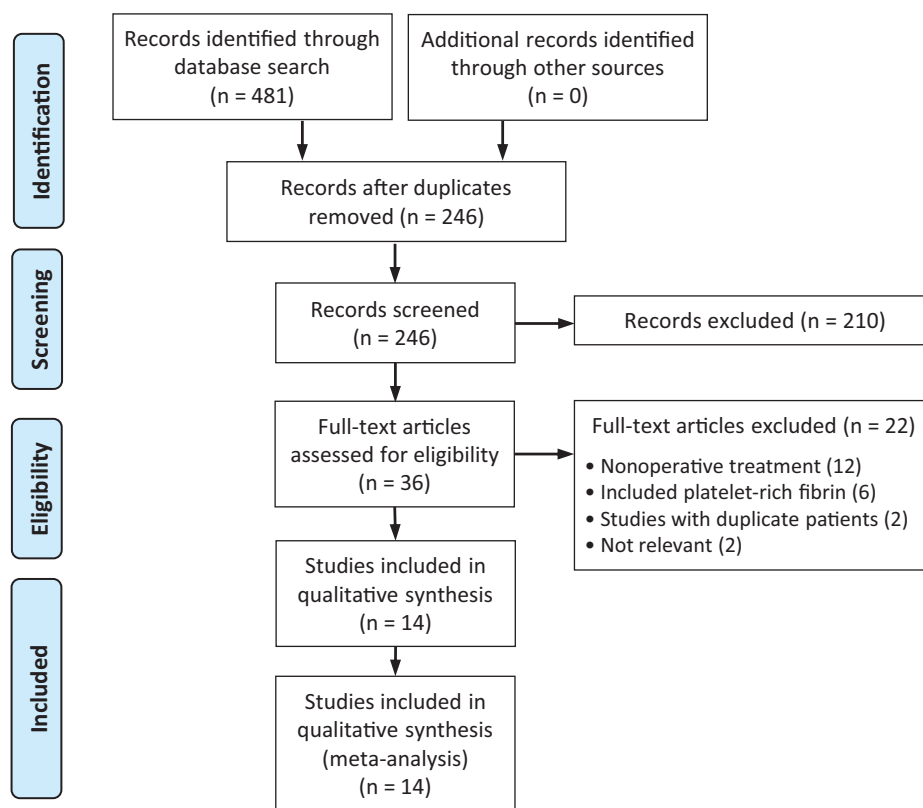
Considering that most of the studies provided multiple results at different follow-up points, we pooled the outcomes that were reported in  $\geq 4$  studies at 3 months, 6 months, 12 months, and 24 months. In addition, we categorized follow-up time as short term (up to 6 months), midterm ( $\geq 12$  months), and long term ( $\geq 24$  months). Sugaya grades 4 and 5 were considered retear events.<sup>31</sup> Adverse events included complications such as infection, excessive pain, local swelling, postoperative shoulder stiffness, and neurologic or vascular deficit.

### Quality Assessment of Methodology

The methodological quality assessment for the included studies was based on the Cochrane risk-of-bias criteria. The 7 items used to evaluate bias in each trial included randomization sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias; items were graded as *low risk*, *high risk*, or *unclear risk*. The included studies were independently assessed by both researchers, and any controversy was resolved by final consensus.

### Statistical Analysis

Data from the included studies were analyzed using Stata 15 software. Dichotomous variables (retear rate and adverse events) were expressed using risk ratio (RR) and 95% confidence interval (CI), whereas weighted mean difference (WMD) was calculated for continuous data



**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Meta-Analyses) flow diagram of study selection.

(Constant-Murley, UCLA, and VAS pain scores). The  $Q$  and  $I^2$  tests were used to estimate the heterogeneity among studies. The  $I^2$  test was used to assess heterogeneity based on the thresholds reported in the Cochrane Handbook for Systematic Reviews of Interventions<sup>15</sup>: 0%-40%, not significant, 30%-60%, moderate heterogeneity; 50%-90%, substantial heterogeneity; and 75%-100%, considerable heterogeneity. When  $I^2 < 50\%$  or  $P > .1$ , a fixed-effects model was applied for the meta-analysis; otherwise, a random-effects model was used.

Subgroup analysis of retear rate was conducted according to the following factors: follow-up time (short term vs midterm vs long term), tear size (small to medium vs large to massive), number of injured tendons (1 or 2 [supraspinatus and/or infraspinatus] vs 3 [supraspinatus, infraspinatus, and subscapularis]), leukocyte concentration of PRP (leukocyte poor vs leukocyte rich), PRP type (gel vs liquid), surgical procedure (single row vs double row), and time of PRP application (intraoperative vs postoperative). For all outcome measures, forest plots were used to present the results of the individual studies and the pooled estimates of effect size.

## RESULTS

### Study Selection

A total of 481 potentially relevant citations were extracted from the 4 electronic databases. After removing duplicates

and reading the abstract and title, we screened the full-text of 36 studies for relevance. Of these, 14 RCTs<sup>‡</sup> with 923 patients were considered to meet the eligibility criteria and were included in the systematic review. All studies were published between 2011 and 2020. The process of selecting appropriate studies is shown in Figure 1.

### Characteristics of Included Studies

Of the 923 patients with arthroscopic rotator cuff repair included in this systematic review and meta-analysis, 458 patients received PRP treatment (PRP group), and 465 patients did not receive PRP treatment (no-PRP group). All of the included studies reported patient sex, tear size, number of injured tendons, follow-up time, leukocyte concentration, PRP type, time of PRP application, injection site, surgical procedure, postoperative rehabilitation, and at least 1 major outcome. Detailed information of the studies is displayed in Table 1.

In all of the studies, the rotator cuff injuries were full-thickness tears, and the PRP group received saline solution injection as a placebo. The total number of participants ranged from 25 to 120, with 423 male patients and 500 female patients, and the age range was 54 to 63 years. The follow-up time ranged from 6 weeks to 51 months. We found that 9 studies<sup>§</sup> used leukocyte-poor PRP, whereas

<sup>‡</sup>References 5, 8, 9, 11, 12, 18, 19, 21, 24, 25, 27, 30, 34, 39.

<sup>§</sup>References 8, 9, 11, 18, 19, 21, 24, 27, 34.

TABLE 1  
Characteristics of the Included Studies<sup>a</sup>

Lead Author (Year)	Patients (PRP/no-PRP), n	Tear Size	Involved Tendons	Age, y, mean $\pm$ SD	Follow-up Time	LR vs LP PRP	PRP Type	Time of PRP Application	Surgical Procedure	Time Immobilized
Holtby (2016) <sup>12</sup>	82 (41/41)	Small to medium	Supraspinatus and/or infraspinatus	59.0 $\pm$ 8.0	6 mo	LR	Gel	Intraoperative	Single or double row	4 wk
Hak (2015) <sup>11</sup>	25 (12/13)	Small to medium	Supraspinatus and/or infraspinatus	55.0 $\pm$ 6.4	6 wk	LP	Liquid	Intraoperative and 4 wk postoperative	Single row	NR
Pandey (2016) <sup>24</sup>	102 (52/50)	Medium to large	Supraspinatus and/or infraspinatus	54.5 $\pm$ 8.4	24 mo	LP	Liquid	Intraoperative	Single row	4 wk
Randelli (2011) <sup>25</sup>	53 (26/27)	Small to massive	Supraspinatus, infraspinatus, subscapularis	60.5 $\pm$ 9.6	24 mo	LR	Gel	Intraoperative	Single row	4 wk
Snow (2020) <sup>30</sup>	87 (40/47)	Small to large	Supraspinatus and/or infraspinatus	61.3	12 mo	LR	Liquid	10-14 d postoperative	Single or double row	6 wk
Ebert (2017) <sup>8</sup>	55 (27/28)	Small to medium	Supraspinatus	59.6 $\pm$ 11.2	36-51 mo	LP	Liquid	7 and 14 d postoperative	Double row	6 wk
Flury (2016) <sup>9</sup>	120 (60/60)	Small to massive	Supraspinatus, infraspinatus, subscapularis	58.4 $\pm$ 8.1	24 mo	LP	Liquid	Intraoperative	Double row	6 wk
Jo (2013) <sup>18</sup>	48 (24/24)	Large to massive	Supraspinatus, infraspinatus, subscapularis	63.1 $\pm$ 7.3	16 mo	LP	Gel	Intraoperative	Double row	4-6 wk
Jo (2015) <sup>19</sup>	74 (37/37)	Medium to large	Supraspinatus, infraspinatus, subscapularis	60.5 $\pm$ 6.2	12 mo	LP	Gel	Intraoperative	Double row	4 wk
Malavolta (2014) <sup>21</sup>	54 (27/27)	Small to medium	Supraspinatus	54.7 $\pm$ 7.5	24 mo	LP	Liquid	Intraoperative	Single row	6 wk
Wang (2015) <sup>34</sup>	60 (30/30)	Medium	Supraspinatus	59.1	16 wk	LP	Liquid	7 and 14 d postoperative	Double row	6 wk
D'Ambrosi (2016) <sup>5</sup>	40 (20/20)	Medium	Supraspinatus	60.0 $\pm$ 9.6	6 mo	LR	Gel	Intraoperative	Single row	4 wk
Ruiz-Moneo (2013) <sup>27</sup>	63 (32/31)	Medium to massive	Supraspinatus, infraspinatus, subscapularis	55.5	12 mo	LP	Liquid	Intraoperative	Double row	NR
Zhang (2016) <sup>39</sup>	60 (30/30)	Medium to massive	Supraspinatus and/or infraspinatus	57.1 $\pm$ 6.7	12 mo	LR	Liquid	Intraoperative	Double row	NR

<sup>a</sup>LP, leukocyte poor; LR, leukocyte rich; NR, not reported; PRP, platelet-rich plasma.

5 studies<sup>5,12,25,30,39</sup> used leukocyte-rich PRP. Liquid PRP was used in 9 studies,<sup>11</sup> and 5 studies<sup>5,12,18,19,25</sup> used gel-type PRP. Except for 3 studies,<sup>8,30,34</sup> the studies used PRP intraoperatively. Single-row repair and double-row repair were adopted in 5 studies<sup>5,11,21,24,25</sup> and 7 studies,<sup>8,9,18,19,27,34,39</sup> respectively.

Studies conducted by Ruiz-Moneo et al<sup>27</sup> and Zhang et al<sup>39</sup> did not provide detailed information about the volume of PRP. Only 2 studies<sup>5,24</sup> used ultrasound to determine rotator cuff retear after surgery, whereas the rest used magnetic resonance imaging. A total of 8 studies<sup>5,9,18,21,24,27,30,34</sup> did not report the number of patients undergoing revision surgery for retears; in the remaining 6 studies,<sup>8,11,12,19,25,39</sup> the total revision rate was 18.1% (63/349). All but 2 studies<sup>5,39</sup> reported detailed information regarding the use of subacromial decompression and acromioplasty.

### Risk-of-Bias Assessment

Among the 14 included RCTs,<sup>¶</sup> 7 studies<sup>8,9,12,18,19,30,39</sup> had an unclear risk of bias in random sequence generation, and 2 studies<sup>8,39</sup> had a high risk of bias in the blinding of participants and personnel. All of the studies had a low risk of bias in allocation concealment, blinding of outcome assessment, incomplete outcome data, and selective reporting. The risk-of-bias summary is shown in Figure 2.

### Retear Rate

The overall retear rate was 15.7% (11.4% for the PRP group vs 20.0% for the no-PRP group). The retear rate was 5.2% in patients with small to medium tears and 21.6% in those

<sup>||</sup>References 8, 9, 11, 21, 24, 27, 30, 34, 39.

<sup>¶</sup>References 5, 8, 9, 11, 12, 18, 19, 21, 24, 25, 27, 30, 34, 39.



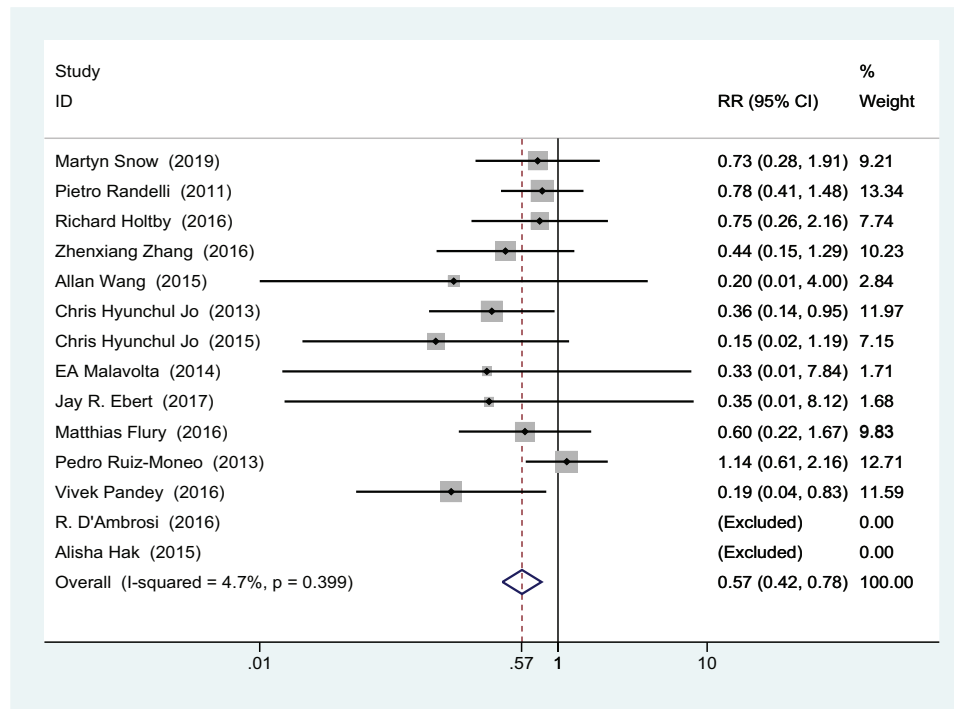


Figure 3. Forest plot of the overall effect of pooled outcomes in the retear rate. RR, risk ratio. ID, identification.

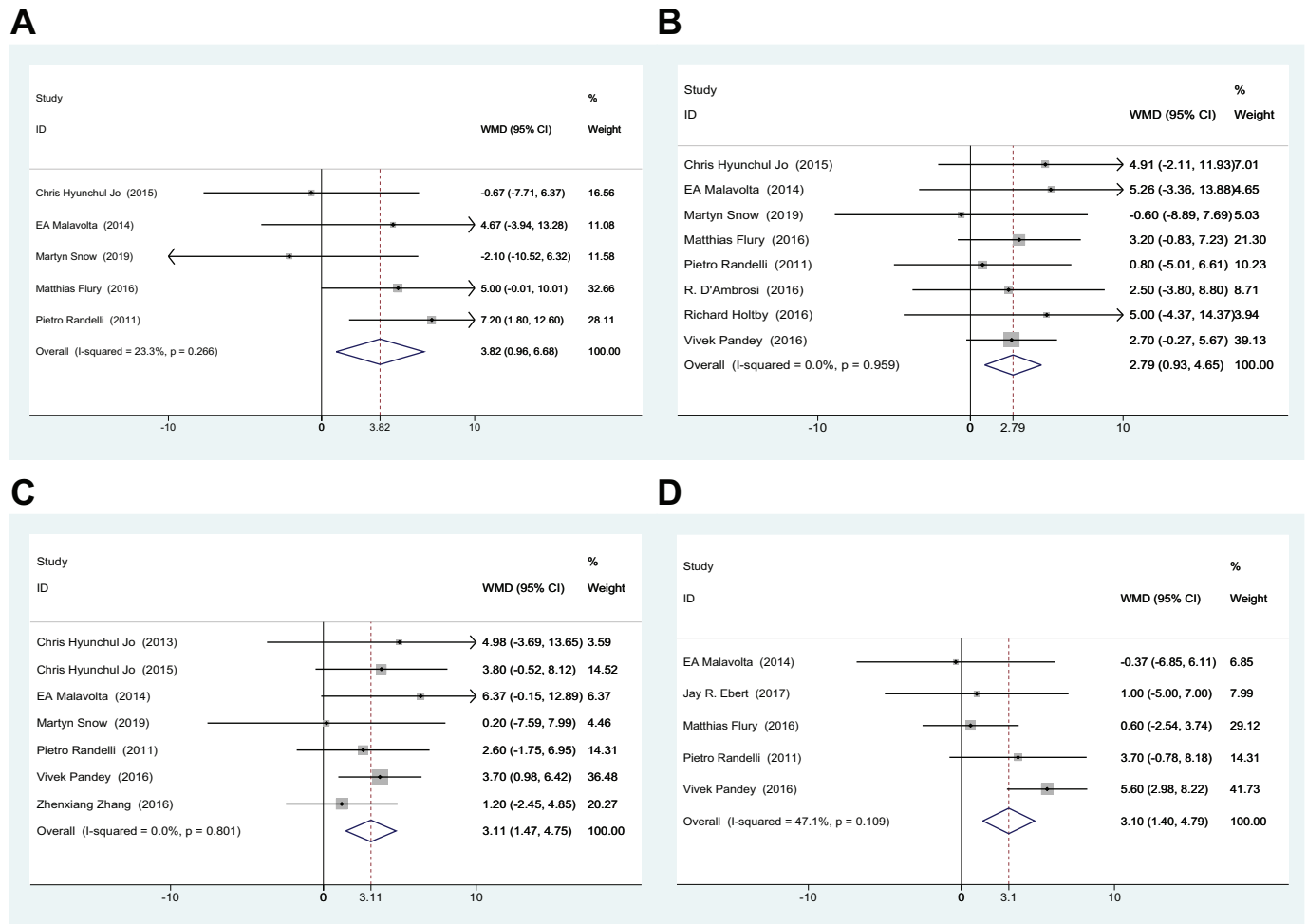
TABLE 2  
Subgroup Analysis of Retear Rates<sup>a</sup>

Variable	No. of Studies	No. of Patients	Risk Ratio (95% CI)	P Value
Follow-up time				
Short term (≤6 mo)	3	168	0.68 (0.25-1.83)	.44
Midterm (≥12 mo)	5	302	0.76 (0.51-1.12)	.17
Long term (≥24 mo)	3	259	0.38 (0.17-0.83)	<b>.02</b>
Tear size				
Small to medium	6	308	0.54 (0.22-1.32)	.18
Large to massive	8	550	0.58 (0.42-0.80)	<b>.0008</b>
No. of torn tendons				
1 or 2 (supraspinatus and/or infraspinatus)	9	547	0.47 (0.28-0.78)	<b>.004</b>
3 (supraspinatus, infraspinatus, and subscapularis)	5	311	0.66 (0.46-0.96)	<b>.03</b>
Leukocyte concentration of PRP				
Leukocyte poor	9	562	0.50 (0.33-0.76)	<b>.001</b>
Leukocyte rich	5	296	0.68 (0.44-1.06)	.09
PRP type				
Gel	5	260	0.54 (0.34-0.86)	<b>.009</b>
Liquid	9	598	0.60 (0.40-0.89)	<b>.01</b>
Surgical procedure				
Single row	5	266	0.50 (0.28-0.90)	<b>.02</b>
Double row	7	441	0.56 (0.37-0.84)	<b>.005</b>
Time of PRP application				
Intraoperative	10	641	0.57 (0.42-0.79)	<b>.0007</b>
Postoperative	3	192	0.57 (0.24-1.37)	.21

<sup>a</sup>Bolded P values indicate statistical significance (P < .05). PRP, platelet-rich plasma.

assessed at 3, 6, 12, and 24 months of follow-up. The results indicated statistically significant differences at 3 months (WMD, 3.82 [95% CI, 0.96-6.68]; P = .009; I<sup>2</sup> = 23%), 6 months (WMD, 2.79 [95% CI, 0.93-4.65]; P = .03;

I<sup>2</sup> = 0), 12 months (WMD, 3.11 [95% CI, 1.47-4.75]; P = .0002; I<sup>2</sup> = 0), and 24 months (WMD, 3.10 [95% CI, 1.40-4.79]; P = .0003; I<sup>2</sup> = 47%) (Figure 4). Patients in the PRP group had statistically better Constant-Murley scores



**Figure 4.** Forest plots of clinical outcomes according to Constant-Murley score at a follow-up of (A) 3 months, (B) 6 months, (C) 12 months, and (D) 24 months. ID, identification; WMD, weighted mean difference.

compared with patients in the no-PRP group in the short term, midterm, and long term.

### UCLA Score

Outcomes reported using the UCLA score were offered by 6 studies<sup>18,19,21,24,25,27</sup> with 394 patients. Participants were assessed at 3, 6, 12, and 24 months postoperatively. The results indicated statistical differences at 3 months (WMD, 2.43 [95% CI, 0.93-3.93];  $P = .002$ ;  $I^2 = 0$ ), 6 months (WMD, 1.74 [95% CI, 0.86-2.62];  $P = .0001$ ;  $I^2 = 0$ ), 12 months (WMD, 1.38 [95% CI, 0.62-2.14];  $P = .0004$ ;  $I^2 = 0$ ), and 24 months (WMD, 1.64 [95% CI, 0.13-3.15];  $P = .03$ ;  $I^2 = 63%$ ) (Figure 5). Patients in the PRP group had statistically better UCLA scores compared with those in the no-PRP group in the short term, midterm, and long term.

### ASES Score

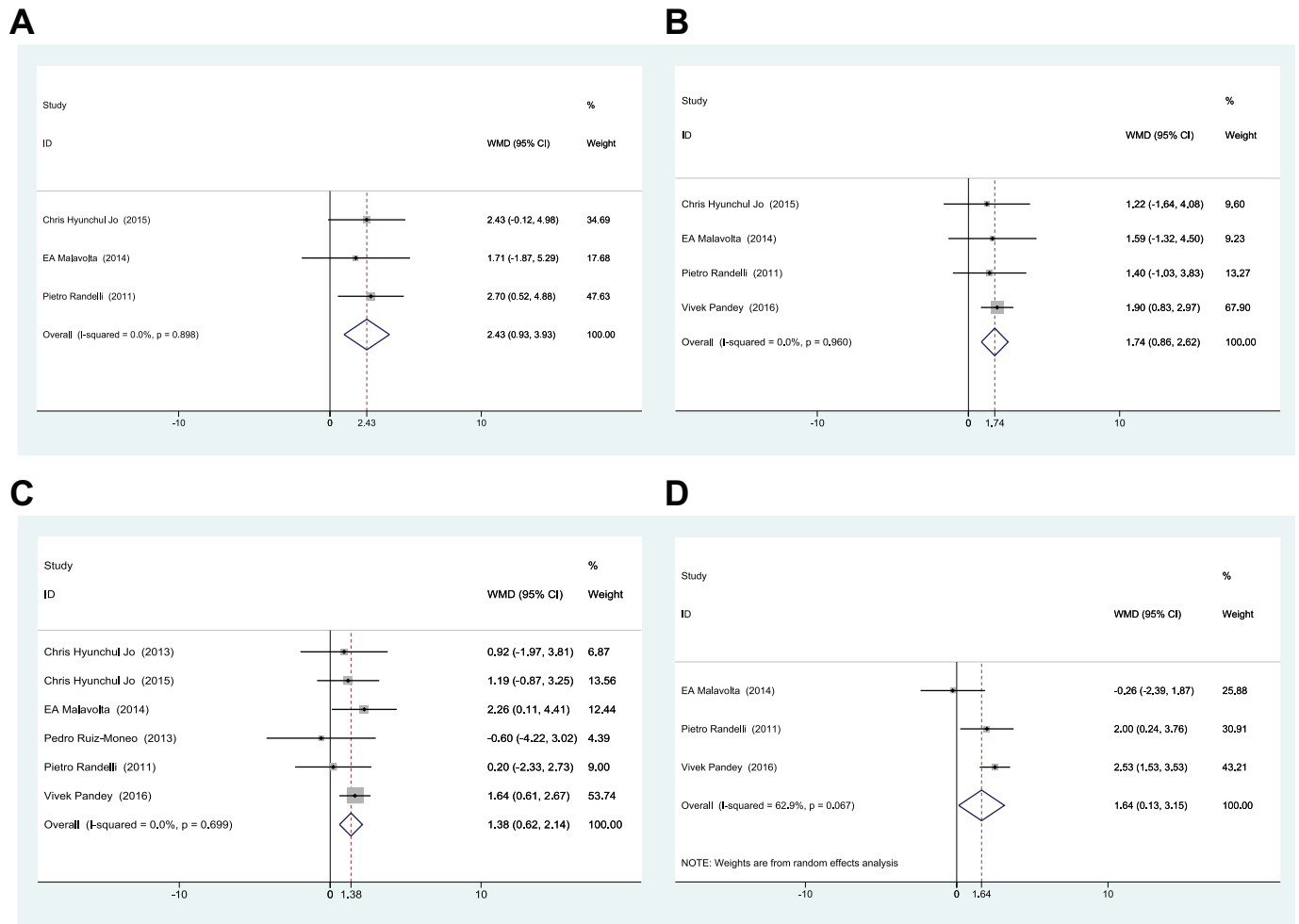
A total of 6 studies<sup>9,12,18,19,24,30</sup> including 513 patients reported outcomes using the ASES score. We assessed

participants only at 6 months postoperatively. There was no significant difference in short-term follow-up (WMD, 1.04 [95% CI, -3.10 to 5.19];  $P = .62$ ;  $I^2 = 52%$ ) between the 2 groups (Figure 6). Patients allocated to the PRP group did not have significantly better ASES scores than did those in the no-PRP group at 6-month follow-up.

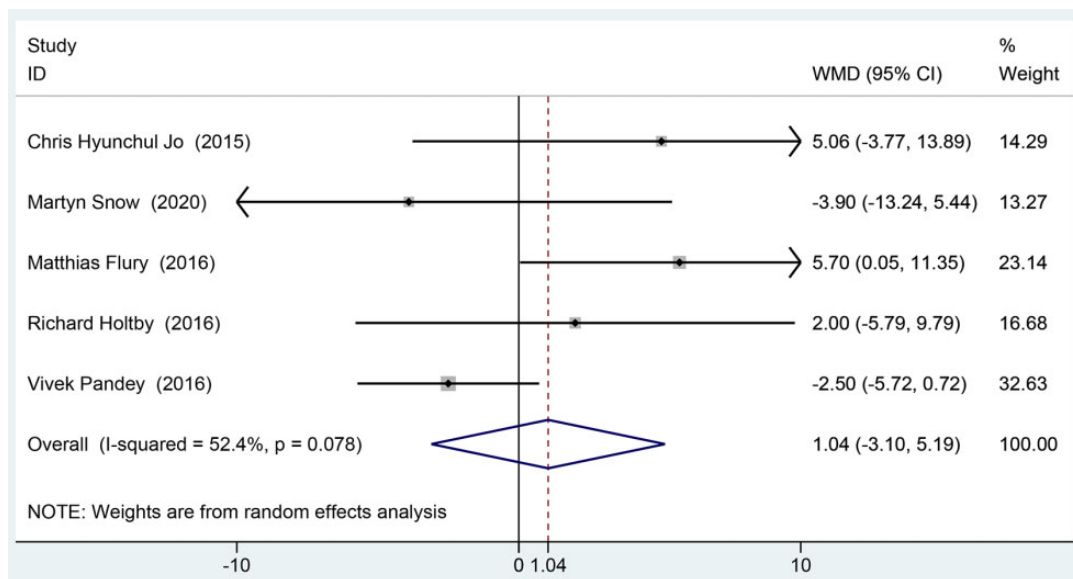
### VAS Pain Score

VAS pain scores were reported in 11 RCTs<sup>††</sup> with 653 patients, and participants were evaluated at 1, 6, and >12 months postoperatively. Statistically significant differences in scores were found at 1 month (WMD, -0.81 [95% CI, -1.41 to -0.22];  $P = .008$ ;  $I^2 = 88%$ ), 6 months (WMD, -0.61 [95% CI, -0.84 to -0.38];  $P < .00001$ ;  $I^2 = 0$ ), and  $\geq 12$  months (WMD, -0.13 [95% CI, -0.20 to -0.06];  $P = .0006$ ;  $I^2 = 4%$ ) (Figure 7), indicating that the PRP group had greater improvement in VAS pain scores compared with the no-PRP group up to 12 months postoperatively.

<sup>††</sup>References 5, 8, 11, 12, 18, 19, 21, 24, 25, 34, 39.

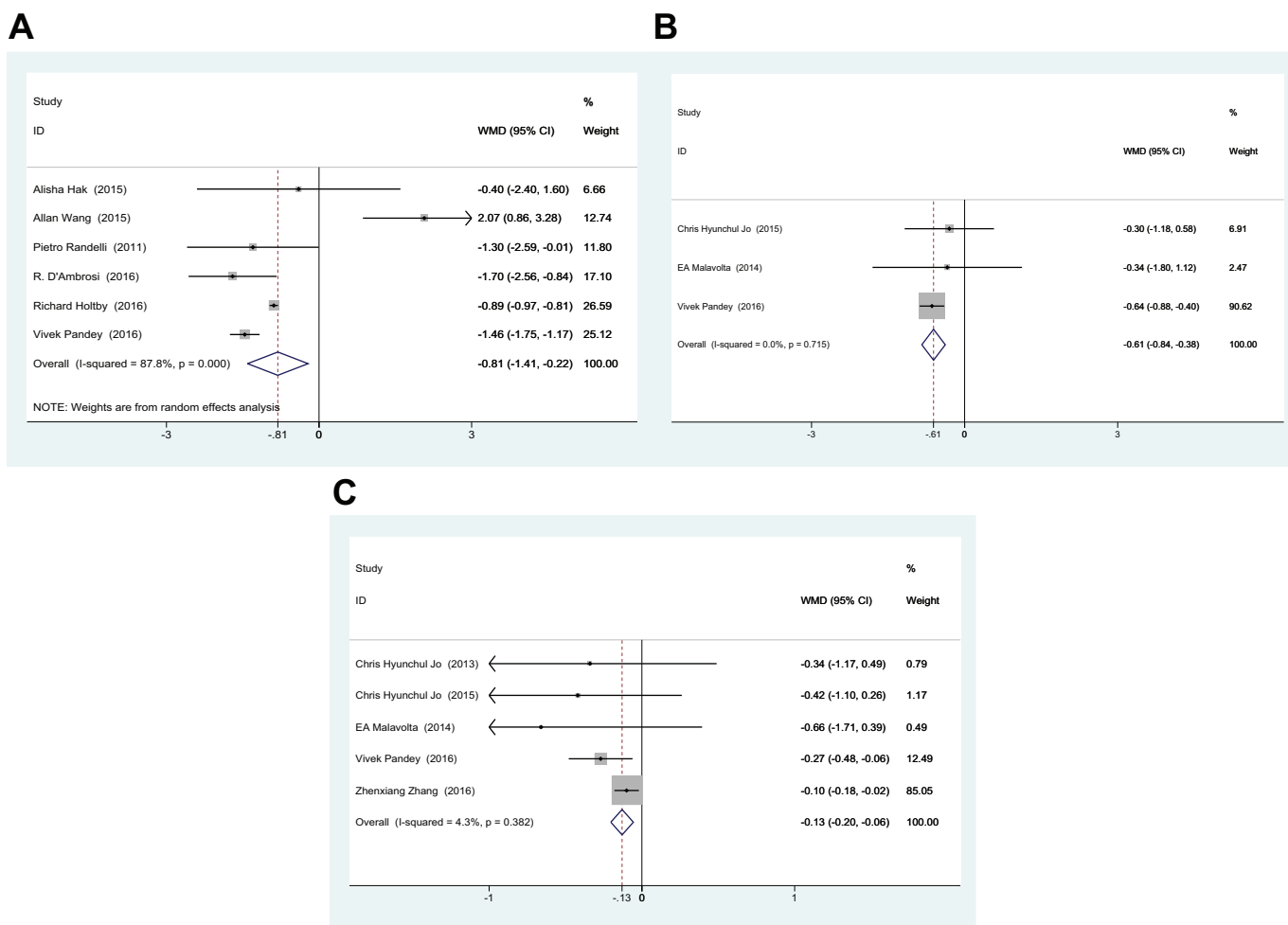


**Figure 5.** Forest plots of clinical outcomes according to the University of California Los Angeles score at a follow-up of (A) 3 months, (B) 6 months, (C) 12 months, and (D) 24 months. ID, identification; WMD, weighted mean difference.



**Figure 6.** Forest plot of clinical outcomes according to American Shoulder and Elbow Surgeons score at 6-month follow-up. ID, identification; WMD, weighted mean difference.





**Figure 7.** Forest plots of clinical outcomes according to visual analog scale pain scores at a follow-up of (A) 1 month, (B) 6 months, and (C)  $\geq 12$  months. ID, identification; WMD, weighted mean difference.

### Adverse Events

Considering that 10 studies<sup>‡‡</sup> with 659 patients reported adverse events, we performed a meta-analysis for adverse events using a fixed-effects model. We found no significant difference between the 2 groups in adverse events at the final follow-up (RR, 1.34 [95% CI, 0.83-2.15];  $P = .23$ ;  $I^2 = 0$ ) (Figure 8). Patients in the PRP group had an increased incidence of adverse events compared with those in the no-PRP group.

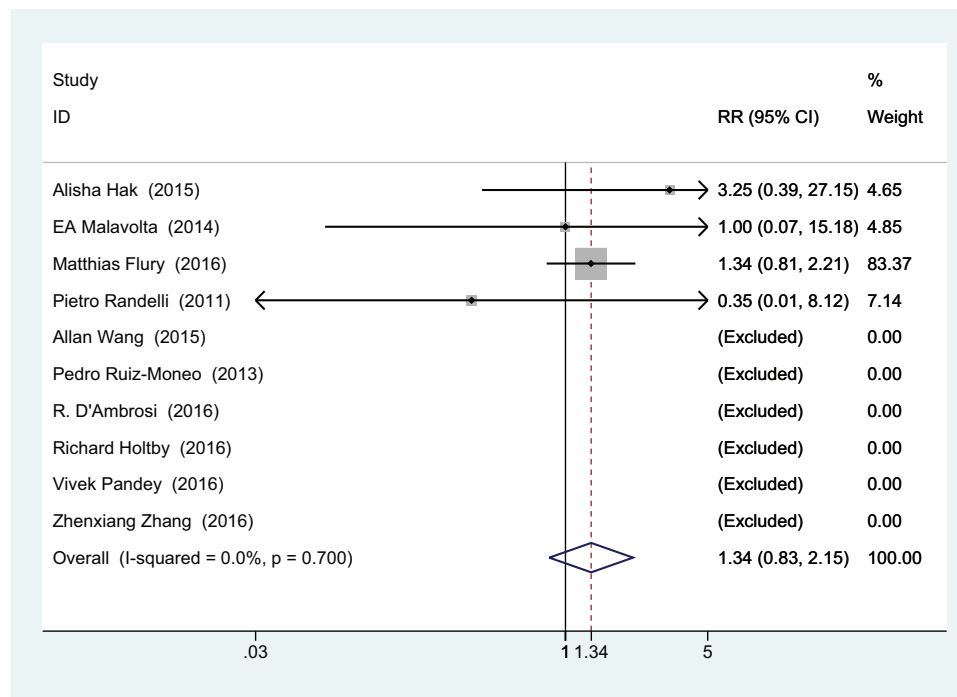
### DISCUSSION

In this study we evaluated the actual effect of PRP in patients who received arthroscopic rotator cuff repair, and we investigated the related factors that affected the utility of PRP in reducing the retear rate. Patients who underwent arthroscopic rotator cuff repair and received an intraoperative augmentation of PRP had significantly superior retear

rates and Constant-Murley, UCLA, and VAS pain scores without increased adverse events. Although some factors affected the efficacy of PRP in reducing the retear rate, significantly decreased retear rates were found in long-term follow-up, intraoperative use of PRP, application of leukocyte-poor PRP, and large to massive tear size. In addition, the PRP type (gel vs liquid), the surgical procedure (single row vs double row), and the number of torn tendons did not affect the efficacy of PRP in decreasing the retear rate. However, small to medium tear size, postoperative application of PRP, and application of leukocyte-rich plasma were not associated with decreased retear rate. Thus, this research did not support the adjuvant application of PRP in these 3 conditions during arthroscopic rotator cuff repair.

Chen et al<sup>3</sup> found that PRP decreased long-term retear rate with a minimal clinically importance difference. They defined *long-term* as follow-up  $>12$  months, which was equal to our midterm condition. However, their systematic review included patients who underwent arthroscopic rotator cuff repair and nonoperative treatment without subgroup analysis. Meanwhile, some studies about PRF were incorrectly taken for PRP studies and were included in

<sup>‡‡</sup>References 5, 9, 11, 12, 21, 24, 25, 27, 34, 39.



**Figure 8.** Forest plot of adverse events by study. ID, identification; RR, risk ratio.

their meta-analysis. Wang et al<sup>35</sup> evaluated the efficacy of PRP in arthroscopic repair of full-thickness rotator cuff tear. They suggested that PRP could effectively improve short-term outcomes and reduce the retear rate in arthroscopic rotator cuff repair. Moreover, Wang et al<sup>35</sup> recommended PRP injection as a supplementary therapy in single-row fixation in rotator cuff repair.

Although RCTs about PRP have been published, we found that the use of PRP differed among those studies. Some studies used liquid PRP,<sup>8,9,11,21,24,27,30,34</sup> and others used gel PRP.<sup>5,12,18,19,25</sup> Most studies used PRP intraoperatively, but in a few studies,<sup>8,30,34</sup> the investigators injected PRP after arthroscopic shoulder surgery. Animal studies found that different types of growth factors were active at specific time points; some investigators<sup>20</sup> reported that platelet-derived growth factor had mild expression between 7 and 14 days, whereas others<sup>2</sup> suggested that platelet-derived growth factors had a more obvious effect on tendon healing at day 7. However, our study found that postoperative application of PRP was not associated with a significantly decreased retear rate. Moreover, the concentration of leukocyte was an important factor. Our review found that treatment using leukocyte-poor PRP in arthroscopic rotator cuff repair could decrease the retear rate, but there was no significant benefit associated with leukocyte-rich PRP.

Some studies suggested that the size of the rotator cuff tear could affect the efficacy of PRP.<sup>18,19,38</sup> Our study indicated that PRP was not associated with a decreased retear rate in small to medium tears but had a potential benefit in large to massive tears. In addition, neither the single-row nor the double-row fixation technique affected the utility of PRP in reducing the retear rate in arthroscopic rotator cuff

repair. Vavken et al<sup>33</sup> found that PRP truly reduced the retear rate in arthroscopic rotator cuff repair, but this treatment was not cost-effective in small and medium-sized tears. Samuelson et al<sup>28</sup> indicated that if the cost of PRP were increased to \$1000, the retear rate would need to be decreased by at least 12.1% to achieve cost-effectiveness. All of these studies suggested that PRP cost-effectiveness needs to be taken into account as well as clinical outcomes.

Considering that the pooled outcomes of the meta-analysis might be affected by the above factors, we used strict eligibility criteria for the RCTs and performed subgroup analysis to assess the real utility of PRP. Although we have addressed the insufficiencies and confusion raised by previous studies, some limitations should be recognized. First, because different groups were separated according to the follow-up time, this may have resulted in insufficient studies or participants to analyze. Second, limited studies evaluated the cost-effectiveness of PRP during arthroscopic rotator cuff repair, and further related studies may be needed on this topic. Third, PRP technology and concentrations of PRP growth factors differed across studies, and we did not assess preoperative muscle quality on magnetic resonance imaging scans.

## CONCLUSION

Our study suggests that intraoperative augmentation using PRP in patients who receive arthroscopic rotator cuff repair could improve long-term shoulder function and pain and significantly decrease the retear rate. However, this research did not show a reduction of the retear rate in patients who had small to medium-sized tears, in patients who received postoperative PRP, and when leukocyte-rich

plasma was used in performing arthroscopic rotator cuff repair with PRP.

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