Research Article

Clinical Evaluations of Intraoperative Injection of Platelet-Rich Plasma in Arthroscopic Single-Row Rotator Cuff Repair at 2-Year Follow-Up

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Background. The clinical evidence is conflicted on whether platelet-rich plasma (PRP) therapies have a positive effect on tendon healing and improved functional outcomes. *Purpose.* To evaluate the potentials of intraoperative injection PRP on the speed and quality of healing in patients undergoing arthroscopic repair for small to medium rotator cuff tears. *Methods.* A total of 86 patients scheduled for arthroscopic single-row repair of small to medium rotator cuff tears were assigned to undergo either PRP injection (PRP group) or conventional repair (control group). The PRP group ($N = 43$) consisted of patients who received an intraoperative injection of liquid PRP. The control group ($N = 43$) consisted of patients who did not receive that treatment. The visual analogue scale (VAS) for pain before treatment and at 1, 14 days, 3, 6, and 24 months after surgery were recorded. The clinical outcomes were assessed by the University of California, Los Angeles (UCLA) and Constant scores before treatment and at 3, 6, and 24 months after surgery and magnetic resonance imaging or ultrasound examination at 24 months. Patient satisfaction and retear rate were also assessed. *Results.* No statistical differences in baseline characteristics such as age, gender, dominant arm, and tear size were observed between the two groups ($P > 0.05$). For the PRP group, the mean operation time was 40.22 minutes, and for the control group, the mean operation time was 36.3 minutes. There was a statistically significant difference ($P = 0.036$). After surgery, all VAS measurements significantly decreased over time until final follow-up in both groups. No significant difference between the 2 groups was found for any VAS pain measurement at any time point except for the VAS at 1 day postoperatively, which was significantly lower in the PRP group (2.39 ± 1.03) than that in the control group (3.21 ± 1.85) ($P = 0.014$). Analysis of the PRP and control groups demonstrated a statistically significant improvement in UCLA and Constant scores from baseline to the 3-, 6-, and 24-month follow-up assessments ($P < 0.05$). However, no significant intergroup differences were observed in the clinical scores between the three follow-up time points ($P > 0.05$). At the 24-month follow-up, patient satisfaction rates reached 95.65% and 93.48% for the PRP and control groups, respectively. The retear rate of the PRP group (2/43, 4.65%) was lower than that of the control group (6/43, 13.95%). *Conclusions.* Although the pain at 1 day after surgery and the retear rate in the PRP group were significantly lower than those in the control group, the liquid PRP injection did not promote better clinical outcomes at the 2-year follow-up.

1. Introduction

Rotator cuff tears are the most commonly encountered shoulder disorder affecting millions of people across all parts of the globe. They can be degenerative or traumatic. The purpose of rotator cuff tear treatment is to relieve pain and restore function. There are many treatments for rotator cuff tears, and the best treatment is different for different patients.

The patient's age, activity level, and tear size are all important factors that determine the treatment plan. When conservative treatment fails, surgical repair provides a reliable treatment alternative [1]. Single-row and double-row fixation techniques under shoulder arthroscopy have been verified in the repair of rotator cuff tears. Due to multiple surgical techniques to improve bone-to-tendon healing, the results after rotator cuff repair are usually good. However, rerupture

of the rotator cuff is still a significant postoperative issue and can be as high as 27% [2]. It is important to explore methods of biological augmentation to reduce the postsurgical rerupture rate and improve long-term shoulder function after rotator cuff repair. In the past few years, the biomechanical repair of rotator cuff tears has made significant progress, which has promoted research on bioassisted rotator cuff repair. Biological methods are aimed at optimizing tissue healing to improve clinical outcomes.

During the inflammation and repair phase of tendon healing, platelets accumulate at the tissue injury site and release a large number of growth factors (GFs), which promote cell migration and differentiation at the injury site. Platelet-rich plasma (PRP) is a fraction of the plasma containing platelets and GF concentrations above baseline that can be produced by centrifugal separation of whole blood [3, 4]. Basic scientific studies have shown the potential benefit of PRP for tendon healing. In vitro studies have shown that the GFs in PRP, including transforming growth factor beta (TGF-b), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), connective tissue growth factors, and epidermal growth factor (EGF), can influence healing and reduce inflammation [5].

PRP has been used to successfully treat chronic elbow tendinosis and refractory wounds [6–8], and a number of basic studies have demonstrated the favourable effectiveness of PRP in rotator cuff repair [9]. However, comparative clinical studies have reported conflicting results. The results of one systematic review indicated that the use of PRP in rotator cuff repair can improve healing rates, pain levels, and functional outcomes [10]. A randomized controlled trial used PRP as an augment to rotator cuff repair versus a conventional repair in patients undergoing arthroscopic repair for medium to large rotator cuff tears. They reported that PRP significantly improved the quality, as evidenced by a decreased retear rate, but not the speed of healing [11]. However, another meta-analysis described unfavourable results [12].

The objective of this study was to evaluate the potentials of intraoperative injection PRP on the speed and quality of healing in patients undergoing arthroscopic single-row repair for small to medium rotator cuff tears. The speed of healing was measured by clinical scores, and the quality of healing was evaluated by retear rate. Our hypothesis was that PRP injection would accelerate the speed of healing and improve the quality of healing in this population.

2. Materials and Methods

2.1. Patients.
The present study was a retrospective comparative study using conventional treatment as the control. This study was carried out in accordance with the ethical standards recognized by the Declaration of Helsinki rules and the principles of Good Clinical Practice guidelines. Additionally, the study was approved by the Hospital Ethics Committee prior to study commencement (No. 2015006). Enrolled patients were allocated to undergo either arthroscopic rotator cuff repair with PRP (PRP group) or conventional arthroscopic rotator cuff repair (control group). All patients with rotator cuff tears in the associated study period were screened for inclusion. The inclusion criteria were as follows: (i) age between 18 and 80 years old, (ii) symptoms or signs of rotator cuff tears, and (iii) MRI findings (Figure 1(a)) of minor to medium rotator cuff tears (anteroposterior size 0 mm and 30 mm). The exclusion criteria included the following: (i) a history of shoulder surgery, a chronic dislocation or pyogenic infection, or rotator cuff arthropathy with glenohumeral osteoarthritis; (ii) a large or massive tear (anteroposterior size > 30 mm) during surgery; (iii) pregnant or lactating women; (iv) rheumatoid arthritis; (v) gout; (vi) blood diseases; (vii) severe cardiovascular diseases; (viii) infections; (ix) immunodepression; (x) patients receiving anticoagulant therapy; and (xi) patients with haemoglobin values < 11 g/dl and platelet values < 150, 000/ mm^3. Patients who did not complete 24 months of follow-up were also excluded from the study.

2.2. PRP Preparation.
For each preparation, a 50 ml blood sample was collected from the median elbow vein using a 50-G needle, such that the ratio of blood to anticoagulant reached 9 : 1. PRP was prepared using a separation set (Weigao New Polymer Materials Co., Ltd.) and a standard collection programme during surgery as previously described [13]. A total of 4.5 ml of PRP was obtained, of which 3.5 ml was immediately transferred to a sterile syringe for injection (Figure 1(b)), and the remainder was sent to the laboratory for platelet concentration analysis. The PRP platelet and leukocyte counts were $802.26 \pm 171.56 \times 10^9$/l and $33.2 \pm 9.56 \times 10^{12}$/l, respectively, which were 6.35 ± 1.08 and 6.21 ± 0.97 times greater than those in the peripheral blood, respectively. All procedures were performed in 30 minutes in the same operating room.

2.3. Surgical Procedures.
All surgical procedures were performed by the same surgeon (ML) with patients in the lateral decubitus position under general anaesthesia. Systematic glenohumeral joint and subacromial exploration was performed, the rotator cuff tear was carefully evaluated (Figure 1(c)), and the anteroposterior size and the presence of subacromial impingement were documented. Tenotomy of the biceps tendon was performed in cases with severe tendinitis, partial tears, subluxations, and complete dislocations. Debridement of bursal tissue and acromioplasty was minimally performed. Rotator cuff repair was performed to cover the original footprint using a single-row technique whenever possible (Figure 1(d)). Absorbable anchors (Twinfix; Smith & Nephew, USA) of 5.5 mm in diameter were used to repair the rotator cuff tears.

At the end of the arthroscopic procedure of the PRP group, the portals were sutured except for the posterior portal, which was left for observation. The posterior portal was sutured after the positioning needle was placed at the tendon-to-bone interface through the lateral portal. Then, the fluid remaining in the subacromial space was aspirated, and 3.5 ml of PRP was injected at the position through the needle (Figure 1(e)). The injection site was covered with a
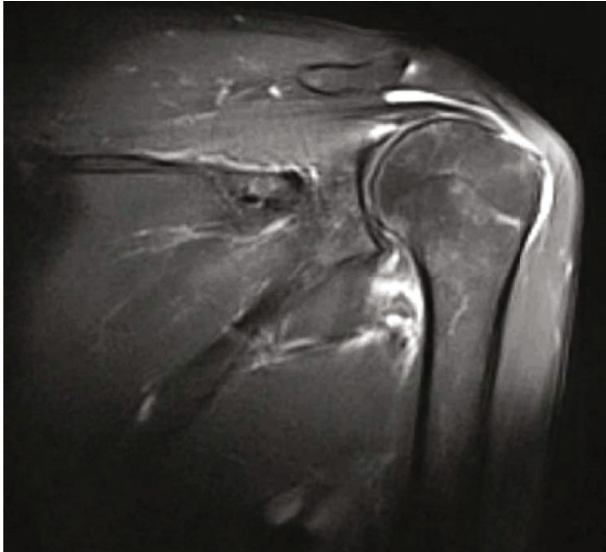
(a)

(b)

(c)

(d)

FIGURE 1: Continued.

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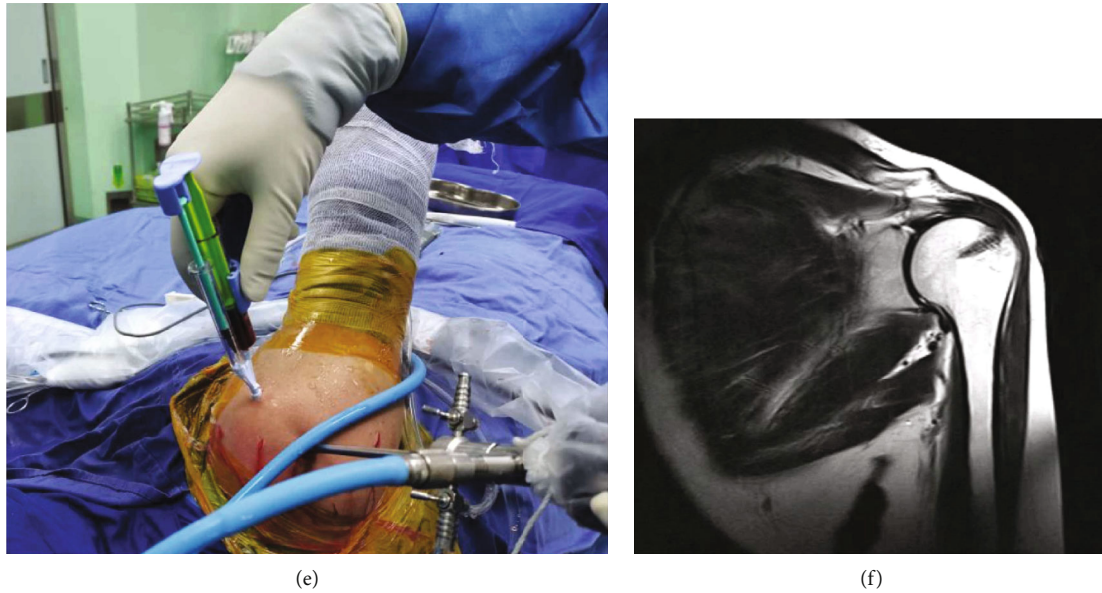<tr><td>(e)</td><td>(f)</td></tr>
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FIGURE 1: (a) MRI showed a torn rotator cuff. (b) PRP was transferred to a sterile syringe. (c) Arthroscopic exploration of a torn rotator cuff. (d) Single-row rotator cuff repair. (e) Intra-articular injection of PRP. (f) MRI showed an intact rotator cuff.

sterile dressing, and the assistant was asked to press the portals for two minutes to prevent PRP leakage.

2.4. Clinical Evaluation. Outcome assessments were performed by a clinician blinded to the treatment. Each patient was evaluated at a preoperative clinical evaluation, as well as at 3, 6, and 24 months postoperatively. Additionally, pain was assessed using the visual analogue scale (VAS) at 1 and 14 days postoperatively. The functional assessment included the University of California, Los Angeles (UCLA) and the Constant shoulder scale and pain as measured by the VAS. Patients with a tear size of less than 10 mm were classified as the small tear group, and patients with a tear size between 10 and 30 mm were classified as the medium tear group, so patients in the PRP or control groups were divided into two subgroups. The clinical outcomes of the patients in the two subgroups were compared.

To evaluate the structural integrity, ultrasound or magnetic resonance imaging (MRI) (Achieva 3.0-T; Philips Medical Systems) with a dedicated shoulder coil was performed at a minimum of 24 months after surgery. Criteria for retear were lack of continuity of the tendon in 1 slice of the coronal plane. We only differentiated between retear and intact tendons (Figure 1(f)). All images were interpreted by a single radiologist with extensive experience in the interpretation of shoulder ultrasound or MRI. The radiologist was blinded to the treatment group and was not involved in the clinical evaluation.

2.5. Statistical Analysis. Sample size calculation is performed with the VAS score as the outcome measure. Based on the previous study, the smallest change score for the VAS score to be considered clinically relevant is 2 points (on a 0-10 scale) between the PRP group and the control group. Power calculation is performed based on the VAS score difference

using a two-sided hypothesis test at an alpha level of 0.05 and a power of 80%, and a total of 42 participants is needed in each group. Taking into account the possibility of 20% violators or dropouts, we will include at least 52 patients in each group.

The data are expressed as the mean ± SD unless otherwise indicated. Two-way ANOVA was performed to assess the differences between groups at different follow-up times. Friedman's test followed by the Wilcoxon signed rank test with Bonferroni correction was used to evaluate the data at different time points within a single group. Statistical analyses were performed using SPSS version 23.0 (IBM Corp.), and $P < 0.05$ was considered statistically significant.

3. Results

Between October 2017 and September 2018, 123 patients with rotator cuff tears received arthroscopic repair in our department; due to incomplete treatment data, 37 of these patients were excluded from the present study. In total, 86 patients (86 shoulders) met the study criteria (43 patients and 43 shoulders in each group) and completed 24 months of follow-up examinations.

3.1. Baseline Data. No differences in baseline characteristics of age, gender, dominant arm, tear size, percentage of acromioplasty, and follow-up were observed between the two groups (Table 1). Tenotomy of the biceps tendon was performed in 5 cases in the PRP group and in 6 cases in the control group due to severe tendinitis, partial tears, subluxations, and complete dislocations. The number of anchors ranged from 1 to 2, with a mean of 1.78 ± 0.42 in the PRP group and 1.74 ± 0.45 in the control group, with no significant difference ($P = 0.37$). For the PRP group, the mean operation time was 40.22 minutes, and for the control group, the

TABLE 1: Basal characteristics of patients in the two groups.

Characteristic	PRP group	Control group	P value
No. of patients	43	43	
Age	57.35 ± 6.85	55.70 ± 7.30	0.21
Percentage of males, n (%)	22 (47.83%)	20 (43.48%)	
Percentage of right shoulder, n (%)	30 (65.22%)	28 (60.87%)	
Duration (mo)	7.61 ± 6.27	6.78 ± 4.19	0.30
Size (anteroposterior) (mm)	21.30 ± 8.29	23.57 ± 7.45	0.17
Percentage of acromioplasty, n (%)	40 (86.96%)	41 (89.13%)	
Biceps procedure (tenotomy), n (%)	5 (11.63%)	6 (13.95%)	
Number of anchor, n	1.74 ± 0.45	1.78 ± 0.42	0.37
Operation time (min)	40.22 ± 6.65	36.30 ± 7.72	0.03
Follow-up (mo)	24.87 ± 1.22	24.70 ± 1.06	0.25
MRI follow-up (mo)	24.63 ± 1.01	24.14 ± 0.87	0.30

PRP: platelet-rich plasma; MRI: magnetic resonance imaging.

mean operation time was 36.30 minutes. There was a statistically significant difference ($P = 0.036$).

3.2. Clinical Evaluations. No significant difference was found in VAS scores between the PRP and control groups at baseline ($P = 0.15$). After surgery, all VAS measurements significantly decreased over time until final follow-up in both groups (Figure 2). No significant difference between the 2 groups was found for any VAS pain measurement at any time point except for the VAS at 1 day postoperatively, which was significantly lower in the PRP group (2.39 ± 1.03) than that in the control group (3.21 ± 1.85) ($P = 0.014$).

No significant difference was found in the UCLA and Constant scores between the PRP and control groups at baseline ($P > 0.05$). Preliminary analysis of the PRP and control groups demonstrated a statistically significant improvement in UCLA and Constant scores from baseline to the 3-, 6-, and 24-month follow-up assessments ($P < 0.05$). However, no significant intergroup differences were observed in the clinical scores between the three follow-up time points ($P > 0.05$). For example, in the PRP group, the UCLA score increased from 10.52 ± 4.99 at the baseline evaluation to 24 ± 3.50 at 3 months, 29.3 ± 2.73 at 6 months, and 32.13 ± 1.79 at 24 months. In the control group, the UCLA score increased from 11.83 ± 4.33 at the baseline evaluation to 23.52 ± 3.28 at 3 months, 28 ± 2.97 at 6 months, and 32.08 ± 2.02 at 24 months (Figure 3). Similar results were documented for the Constant scores (Figure 4). There were 19 patients in the small tear subgroup: 10 patients in the PRP group and 9 patients in the control group. There were 67 patients in the medium tear subgroup: 33 patients in the PRP group and 34 patients in the control group. There was no significant difference in functional scores between the subgroups at baseline and at the 3-, 6-, 12-, and 24-month follow-up postoperatively (Table 2).

Complications such as infection, haematoma, or other major adverse events were not observed in either group. At
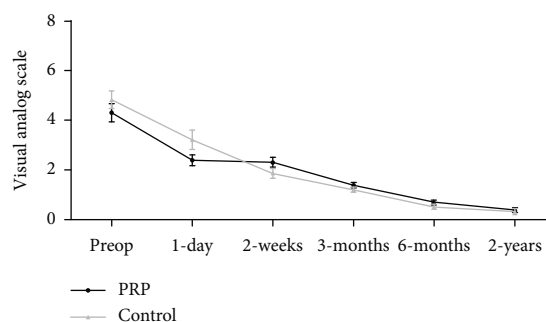

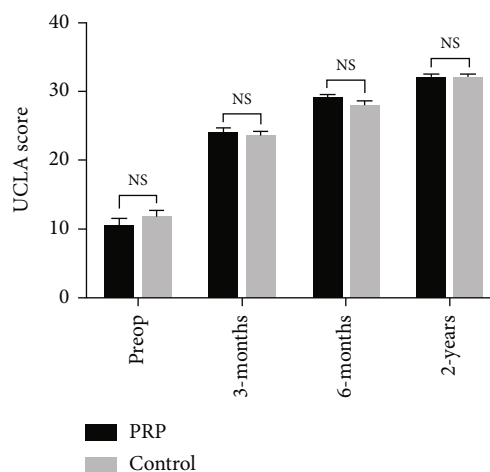FIGURE 2: Pain level assessment: visual analogue scale score. PRP: platelet-rich plasma.

FIGURE 3: UCLA score in the PRP and control groups. NS (not significant) indicated a $P > 0.05$ for the pairwise comparison between the two groups. UCLA: University of California, Los Angeles.
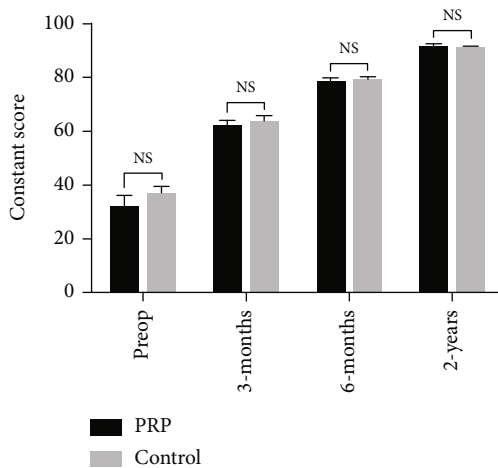
FIGURE 4: Constant score in the PRP and control groups. NS (not significant) indicated a $P > 0.05$ for the pairwise comparison between the two groups.

the 24-month follow-up, patient satisfaction rates reached 95.65% and 93.48% for the PRP and control groups, respectively, indicating no significant difference between the two treatment options. At 24 months, 16 patients underwent MRI, and 70 patients were examined by ultrasound. The control group exhibited 6 partial-thickness retears, while the PRP group had 2 partial-thickness retears. The retear rate of the PRP group (2/43, 4.65%) was lower than that of the control group (6/43, 13.95%).

4. Discussion

The most important findings of the study are that intraoperative injection PRP in patients undergoing arthroscopic single-row repair for small to medium rotator cuff tears did not accelerate the speed of healing but improved the quality of healing. Previous studies have demonstrated the positive effects of PRP on rotator cuff repair. A randomized controlled trial is aimed at assessing the efficacy of PRP augmentation on the speed and quality of healing in patients undergoing arthroscopic repair for medium to large rotator cuff tears. Compared with repairs without PRP augmentation, the PRP preparation and application methods significantly improved the quality of healing [11]. Randelli et al. [14] reported a prospective randomized controlled trial in which 26 patients received an intraoperative application of PRP in combination with an autologous thrombin component. The results of the study showed that autologous PRP reduced pain in the first postoperative months. These results are different from the results of our study. We found that the pain scores of patients in the PRP group were significantly lower than those in the control group at 1 day after surgery, which may be related to the potential role of PRP. Studies have concluded that the PRP effect is likely to last the first 24 postoperative hours but no longer than 48 hours [15]. Warth et al. [12] conducted a systematic review of all level I and level II studies, comparing the clinical and structural results of rotator cuff repair with or without PRP. There

was no significant difference in the overall gain of outcome scores or retears, but they noticed that when PRP was applied to the tendon-bone interface and PRP was applied to the top of the repaired tendon, the shoulder Constant score increased significantly [12]. Hurley et al. [10] performed a systematic review of 1147 patients in the literature to ascertain whether PRP improved patient outcomes in arthroscopic rotator cuff repair. PRP resulted in significantly decreased rates of incomplete tendon healing for all tears combined, incomplete tendon healing in small to medium tears, and incomplete tendon healing in medium to large tears compared to the control. They concluded that the use of PRP in rotator cuff repair results in improved healing rates, pain levels, and functional outcomes [10]. However, studies have also reported the negative aspects of rotator cuff repair. Malavolta et al. [16] published a prospective randomized study of 54 patients who underwent arthroscopic single-row repair of small to medium supraspinatus tears. The clinical evaluations were conducted using the UCLA and Constant scales and the VAS for pain at 6, 12, 24, and 60 months after surgery and MRI at 12 and 60 months. Statistical analysis revealed that PRP did not promote better clinical or structural results at the 60-month follow-up [16]. Our study did not demonstrate any difference between groups at any of the evaluation times in relation to the clinical scales, similar to the findings described by Malavolta et al. One meta-analysis including seven randomized controlled studies compared rotator cuff repair with and without PRP and suggested that PRP use at the time of arthroscopic rotator cuff repair does not universally improve retear rates or affect clinical outcome scores [17]. In addition, Moraes et al. [18] collected 19 studies, and a total of 1088 participants used PRP, including not only the rotator cuff but also 5 other tendinopathies. They found no significant improvement in functional outcomes and insufficient evidence to support the use of PRP in clinical practice [18]. Although the existing research results were conflicting, the potential of PRP to promote rotator cuff repair is worthy of further study. We found that some common limitations in the above studies may affect the results and conclusions, such as the lack of standardization in the operative technique, inconsistent use of double-row repair and single-row repair among studies, and a combination of all tear sizes.

PRP can be used as a liquid, gel, or matrix scaffold. The conventional and most commonly used method is the addition of calcium and thrombin to obtain PRP gel or matrix scaffolds [19–22]. Although the gel may produce a longer-lasting release effect, the fixation of the gel is not a simple procedure. The liquid form of PRP can also be activated by endogenous methods, such as by contacting type I collagen in the rotator cuff tendon to act as an activator. The advantage of liquid PRP injection is that the liquid form can be applied directly to the tendon-bone interface after the subacromial fluid is evacuated. Another reason we chose liquid PRP instead of gel PRP in our study is that the injection is relatively simple and time-saving.

PRP can be applied intraoperatively or postoperatively. Although it is not clear which method has the best effect on tendon-bone healing, most studies chose intraoperative

TABLE 2: The Clinical outcomes in the small and medium tear subgroups before surgery and at 3-, 6-, 12-, and 24-month follow-up postop.

	Preop	3 months	6 months	24 months
VAS of PRP group				
Small tear subgroup	4.8 ± 1.78	1.2 ± 0.44	0.6 ± 0.54	0.2 ± 0.44
Medium tear subgroup	4.17 ± 1.72	1.47 ± 0.51	0.72 ± 0.45	0.44 ± 0.51
P value	0.51	0.34	0.57	0.34
VAS of control group				
Small tear subgroup	4.4 ± 2.3	1 ± 0.71	0.4 ± 0.54	0.2 ± 0.44
Medium tear subgroup	6.53 ± 1.58	1.28 ± 0.46	0.55 ± 0.51	0.39 ± 0.50
P value	0.54	0.29	0.55	0.46
ULCA of PRP group				
Small tear subgroup	13.2 ± 7.79	24.8 ± 4.81	30 ± 4	32.6 ± 2.30
Medium tear subgroup	9.77 ± 3.91	23.78 ± 3.19	29.11 ± 2.39	32 ± 3.24
P value	0.18	0.57	0.53	0.52
ULCA of control group				
Small tear subgroup	11 ± 7.58	25.4 ± 3.21	28.8 ± 2.92	32.6 ± 2.30
Medium tear subgroup	12.05 ± 3.24	23 ± 3.19	27.78 ± 2.92	31.94 ± 1.98
P value	0.64	0.15	0.51	0.53
Constant of PRP group				
Small tear subgroup	42.8 ± 24.96	62.6 ± 10.89	81 ± 2.23	93.6 ± 3.51
Medium tear subgroup	58.89 ± 16.28	62.22 ± 8.01	78.22 ± 5.56	91.44 ± 2.77
P value	0.16	0.93	0.29	0.16
Constant of control group				
Small tear subgroup	33.2 ± 19.43	70 ± 9.06	79.2 ± 7.12	92.8 ± 2.58
Medium tear subgroup	38.06 ± 10.61	62.17 ± 8.59	83.43 ± 0.96	90.88 ± 2.24
P value	0.46	0.089	0.95	0.12

VAS: visual analog scale score for pain; PRP: platelet-rich plasma; UCLA: University of California, Los Angeles.

injection. Wang et al. [23] studied the effect of PRP injection after rotator cuff repair and found that it did not improve tendon-bone healing or functional recovery. Moraes et al. [18] found that PRP injection under arthroscopy did not affect the retear rate or affect the functional outcome. However, when it is applied to the tendon-bone interface, double-row repair, and small and medium-sized rotator cuff tears, there is a tendency to reduce the retear rate [20]. In addition, in a study by Randelli et al. [14], compared with the control group, the early functional results of intraoperative PRP treatment of rotator cuff repair were significantly improved.

Our study showed that the clinical outcomes of patients were not significantly different between the small tear group and the medium tear group at the 3-, 6-, 12-, and 24-month follow-up postoperatively. However, some data support PRP use in some patients. Two meta-analyses focusing on the potential of PRP application showed improvement in tendon healing of small and medium-sized tears but not large tears [24, 25]. The retear rate of patients who undergo treatment for small and medium rotator cuffs may be reduced. In a meta-analysis of 5 studies of 300 patients, Cai et al. [24] found significant differences in repair failures of small to medium rotator cuffs when PRP was not used. Bergeson

et al. [26] found that retear rates (56.2% vs. 38.1%) were significantly higher in the platelet-rich fibrin matrix group than the controls. The retear rate of the PRP group in our study (2/43, 4.65%) was lower than that of the control group (6/43, 13.95%). It seems that our results showed better retear rates, which may be related to the fact that the patients we enrolled all had small and medium tears, and other studies also included large and massive tears.

There was no indication that the use of PRP in our study was associated with the occurrence of more complications within 24 months compared with the non-PRP group. This is consistent with previous data. Clinical reports recording the occurrence of adverse events have shown that the PRP group does not have an increased incidence of adverse events compared with the control group [27, 28].

There are a number of limitations in the present study, including the nonrandomized double-blind design, the small sample size, and a lack of direct evidence of rotator cuff healing (such as arthroscopic findings). The results of our study indicated that intra-articular injection of liquid PRP for small to medium rotator cuff repair did not accelerate the speed of healing but improved the quality of healing compared with repairs without PRP application. In addition, the method of PRP injection neither increased the operation time nor

increased the occurrence of adverse events such as infection. Previous literature has shown that PRP presents a wide variation in the different preparation protocols and dosages, activation methods, white blood cell concentrations, and concentrations of platelets and GFs. These factors may bias research results. Further studies may be needed to investigate the effects of different characteristics of PRP on the speed and quality of rotator cuff repair healing.

Data Availability

The datasets used and/or analysed during the present study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no competing interests.

Acknowledgments

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