Platelet-Rich Plasma for Arthroscopic Repair of Large to Massive Rotator Cuff Tears: A Randomized, Single-Blind, Parallel-Group Trial

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Platelet-Rich Plasma for Arthroscopic Repair of Large to Massive Rotator Cuff Tears

A Randomized, Single-Blind, Parallel-Group Trial

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Background: Platelet-rich plasma (PRP) is expected to have a biological augmentation potential in the healing of various diseases and injuries, including rotator cuff tears. However, few evaluations have been performed specifically for large to massive tears.

Purpose: To assess the efficacy of PRP augmentation in patients undergoing arthroscopic repair for large to massive rotator cuff tears.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 48 patients scheduled for arthroscopic repair of large to massive rotator cuff tears were randomly assigned to receive either PRP-augmented (PRP group) or conventional treatment (conventional group). In the PRP group, 3 PRP gels (3×3 mL) were applied to each patient between the torn end and the greater tuberosity. The primary outcome measure was the retear rate assessed by magnetic resonance imaging (MRI) or computed tomographic arthrography (CTA) at a minimum of 9 months after surgery. Secondary outcome measures included pain, range of motion, muscle strength, overall satisfaction, functional scores, and the change in cross-sectional area (CSA) of the supraspinatus.

Results: The retear rate of the PRP group (20.0%) was significantly lower than that of the conventional group (55.6%) ($P = .023$). Clinical outcomes showed no statistical difference between the 2 groups (all $P > .05$) except for the overall function ($P = .043$). The change in 1-year postoperative and immediately postoperative CSA was significantly different between the 2 groups: -15.54 ± 94.34 mm^2 in the PRP group versus -85.62 ± 103.57 mm^2 in the conventional group ($P = .047$).

Conclusion: The application of PRP for large to massive rotator cuff repairs significantly improved structural outcomes, as evidenced by a decreased retear rate and increased CSA of the supraspinatus compared with repairs without PRP augmentation. While there was no significant difference in clinical outcomes except the overall shoulder function after 1-year follow-up, better structural outcomes in the PRP group might suggest improved clinical outcomes at longer term follow-up.

Keywords: platelet-rich plasma; large to massive rotator cuff tear; rotator cuff repair; biological augmentation; retear; integrity

There is still a significant retear rate after rotator cuff repair, especially for large to massive tears. While some studies have reported improved clinical outcomes after rotator cuff repair regardless of the occurrence of retears, several recent studies have paid more attention to repaired tendon integrity, as structurally intact tendons appear to produce better long-term outcomes.[1,29,35,37,45] With recent biomechanical advances in suture materials, anchors, and repair configurations, the retear rate has been reported to decrease to as low as 9% to 12%.[10,11,26,28,37] However, the high retear rate in large to massive cuff tears remains a challenge.[5,15,37,41] Failure to regenerate a normal tendon-to-bone interface consists of 4 continuous phases (ie, tendon, unmineralized fibrocartilage, mineralized fibrocartilage, and bone), and replacement with reactive fibrous scar tissue after repair is a well-known factor

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that can consequently lead to retears.[24,38] One of the attempts of researchers to overcome this effect is to use biological strategies with cells, appropriate signals including growth factors, and adequate scaffolds that could contain them.[25]

Platelet-rich plasma (PRP) is a platelet concentrate that typically contains more than 1000×10^3 platelets/mL, representing a 3- to 5-fold increase as compared with whole blood.[19] It is known to contain more than 1500 bioactive proteins, including important growth factors for tendon healing.[19,31] Recently, many authors have reported on the effect of PRP on rotator cuff repair[2,4,7,13,32,34,40]; however, the outcomes and mechanisms are still controversial. Furthermore, little has been investigated regarding the effect of PRP in large to massive rotator cuff repairs.[13,33] One of the most important reasons why we do not yet know much about the effect of PRP despite the large research effort is that different studies used different PRPs, which necessarily resulted in varying outcomes. Thus, while it is not possible to standardize the preparation and application of PRP in all studies by various researchers, a maximum effort to standardize the process within each study should be attempted, and minimum information that could characterize the PRP used should be provided. In this sense, consistent with our previous study,[18,19] we prepared PRP with a fully automated plateletpheresis system because it allowed better standardization in the preparation of PRP. Also, we described PRP used in this study using our own PRP characterization tool with respect to 3 crucial properties: PRP concentration, activation, and method of application.

The purpose of this study was to assess the efficacy of PRP in patients undergoing arthroscopic repair of large to massive rotator cuff tears. Our hypothesis was that PRP would improve the structural and clinical outcomes of this population.

MATERIALS AND METHODS

Patient Enrollment

This study was a randomized controlled trial in a university hospital enrolling patients with a large to massive rotator cuff tear undergoing arthroscopic rotator cuff repair. The study was approved by our hospital's institutional review board and registered at ClinicalTrials.gov (NCT01238302). Patients between 45 and 85 years of age were eligible if they had a large to massive rotator cuff tear (>30-mm anteroposterior size) as determined by clinical examination and magnetic resonance imaging (MRI) before surgery. We excluded patients if they had a history of shoulder surgery, had acute trauma, had a chronic dislocation or pyogenic infection, had rotator cuff arthropathy with glenohumeral osteoarthritis and superior migration of the humeral head, showed abnormal serological test results or thrombocytopenia (<15,000 platelets/μL), had been receiving antiplatelet medication, had psychiatric problems that precluded informed consent or inability to read or write, and had other serious issues that precluded participation in the study.

Enrolled patients were randomly allocated in a 1:1 ratio, with block sizes of 4 and 6 using the randomization sequence created using SAS 9.1 statistical software (SAS Institute Inc, Cary, North Carolina), to undergo either conventional arthroscopic rotator cuff repair (conventional group) or arthroscopic rotator cuff repair with PRP (PRP group). Platelet-rich plasma was prepared in patients in the PRP group 1 day before surgery.

As confirmative determination of tear size was performed during surgery, some patients could be identified to have a small to medium tear or would only be treated with partial repair because of irreparability. These patients were also excluded from the per-protocol analysis of the primary outcome measure of the occurrence of retears but were included in the intention-to-treat analysis of the other outcome measures.

Preparation of PRP

The PRP was prepared using a plateletpheresis system with a leukoreduction set (COBE Spectra LRS Turbo, Caridian BCT, Lakewood, Colorado) and a standard collection program.[18] The system was set and primed according to the manufacturer's instructions with saline solution used for priming and anticoagulant acid citrate dextrose solution (ACD-A) as the anticoagulant. Platelet-rich plasma collection was performed 1 day before surgery, as it has been shown that PRP components can be stored without significant growth factor loss for 1 day.[44] Platelet-rich plasma was stored at room temperature with agitation until used. An aliquot was used for determining complete blood counts using a fully automated analyzer (XE-2100, Sysmex Corp, Kobe, Japan) and the concentration of fibrinogen using an automated coagulation analyzer (CA-7000, Sysmex Corp). The activation status of platelets was determined using flow cytometry with CD61 and CD62P in 5 patients.[14] For the application to rotator cuff repair, platelet counts in PRP were adjusted with saline to 1000×10^3 platelets/μL. To produce a gel from prepared PRP, 0.3 mL of 10% calcium gluconate was added to 3 mL of PRP. The dilution and gelling procedure were performed within 1 hour of surgical application.

Surgical Procedures and PRP Application

All arthroscopic procedures were performed with patients in the lateral decubitus position under general anesthesia as previously described.[18,22] Briefly, systemic glenohumeral joint and subacromial exploration were performed, and lesions were managed as necessary. In each case, after removing the frayed and atrophied torn end, the rotator cuff tear was carefully evaluated, and anteroposterior size, mediolateral retraction, the numbers of involved tendons, visual tendon grade,[22] excursion, and presence of the subscapularis tear were documented.[30] If excursion of the torn end was inadequate, tendon mobilization procedures including superior capsulotomy, coracohumeral ligament release, and medialization of the supraspinatus insertion in the greater tuberosity were performed. Anterior or posterior interval slide was not performed in any patient. The footprint of the greater tuberosity was debrided, and only a minimal layer of cortical bone was removed.

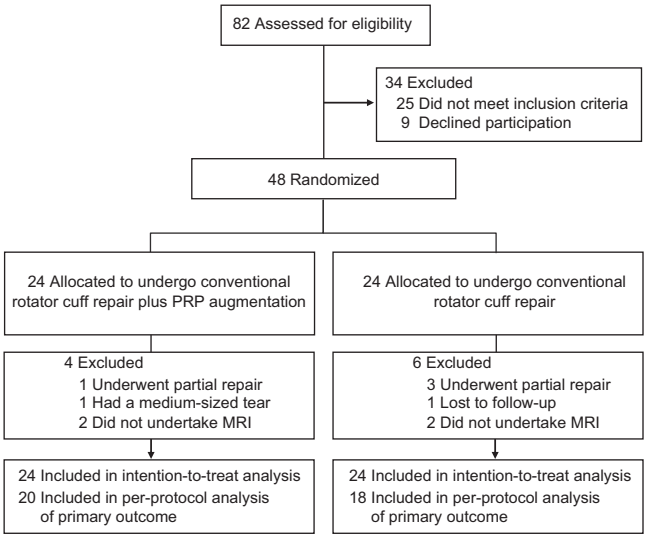

Figure 1. Study flow diagram.

Debridement of bursal tissue and subacromial and distal clavicle osteophytes was minimally performed. Extensive acromioplasty to flatten a hooked or curved acromion was rarely performed.

Rotator cuff repair was performed to cover the original footprint using a suture bridge technique whenever possible. Suture anchors were inserted through the accessory portal. Generally, 3 to 5 suture anchors were used: 1 or 2 anchors for the medial row, and 2 or 3 anchors for the lateral row. Medial row anchors were inserted first just lateral to the articular surface of the humeral head, and sutures were then threaded through the rotator cuff. After the medial row sutures were threaded, the PRP gel was applied as previously described.[16,18] Briefly, a No. 1 PDS II suture (Ethicon, Somerville, New Jersey) was threaded to the posterior portion of the tear near the footprint of the rotator cuff. One end of the suture was then retrieved through an 8.0-mm cannula in the lateral portal and then through a long 5.5-mm cannula without a diaphragm. Three PRP gels were threaded to the suture per patient and introduced into the long 5.5-mm cannula. With a knot pusher threaded to the suture to back up the PRP gels, the 5.5-mm cannula was introduced into the 8.0-mm cannula, which was aimed at the repair site. As the 5.5-mm cannula reached the repair site, the PRP gels were placed into the site by pulling the suture end in the posterior cannula and by pushing the knot pusher. After the PRP gels were out of the 5.5-mm cannula, the knot pusher was then quickly removed. While the surgeon blocked the outer opening of the 5.5-mm cannula with a finger, a suture retriever was introduced via the anterior portal. The suture was then seized and retrieved through the anterior portal, and the 5.5-mm cannula was removed. With the PRP gels in place, medial row sutures were tied using the slippage-proof knot if necessary.[23] The lateral row was then secured using suture anchors, and the PRP gels were interposed at the tendon-bone interface. After repair, greater tuberosity coverage of the repaired tendon was measured to evaluate the repair status as previously described.[22]

Postoperative Protocol

The shoulder was immobilized for 4 to 6 weeks using an abduction brace (4 weeks for large tears, 6 weeks for massive tears). Shrugging, protraction, and retraction of shoulder girdles; intermittent exercise of the elbow, wrist, and hand; and external rotation of the arm to neutral with the brace were encouraged as tolerated, usually immediately after surgery. Further passive range of motion (ROM) and active-assisted ROM exercises were allowed after gradual weaning off the abduction brace from 4 to 6 weeks after surgery. Patients began strengthening exercises after 3 months. Light sports activities, such as jogging, were allowed after 3 months, and full return to sports was allowed after 6 to 9 months according to individual recovery.

Outcome Assessments

The primary outcome measure was the retear rate, which was measured using MRI and computed tomographic arthrography (CTA). To evaluate the structural integrity, MRI (Achieva 3.0 T, Philips Medical System, Eindhoven, the Netherlands) with a dedicated shoulder coil or CTA (Ingenuity CT scanner, Philips, Cleveland, Ohio) was performed at a minimum of 9 months after surgery. Retears were evaluated using the classification by Sugaya et al[36] for patients with MRI or using a modified Boileau et al[5] grading system for patients with CTA.[22] According to the classification by Sugaya et al,[36] types I, II, and III are considered as healing, and types IV and V are considered as retears. In the modified Boileau et al[5] grading system, healing and incomplete healing are considered as "healing," while types of retears and new tears are classified as "retears."[22] All images were first reviewed blinded by a fellowship-trained musculoskeletal radiologist and then by an orthopaedic surgeon. When there was a discrepancy in reading, integrity was graded as the worse option.

The secondary outcome measure includes clinical outcomes and the change in cross-sectional area (CSA) of the supraspinatus.[20,21] For clinical evaluation, each patient completed a questionnaire that consisted of standardized outcome assessments at baseline and at a minimum of 12 months after surgery. Clinical outcomes were assessed according to (1) pain, (2) ROM, (3) muscle strength, (4) overall satisfaction, and (5) functional scores. A visual analog scale (VAS) was used to evaluate pain at rest, in motion, and at night. Patients were asked to use a 10-cm scale marked from "no pain" to "unbearable pain." Average pain scores were calculated and compared. Range of motion was measured with a goniometer in active forward flexion, abduction, external rotation with the arm at the side, and internal rotation. Internal rotation was measured using vertebral levels, and these were translated into numbers from 1 for the buttocks to 17 for T2. The strength of the supraspinatus, infraspinatus, and subscapularis muscle was measured using a handheld electronic scale (CHS, CAS, Yangju, Korea). To evaluate overall satisfaction, patients were asked to answer "yes" or "no" to questions concerning their willingness to undergo surgery again and whether they were

TABLE 1
Comparison of the Baseline Demographics Between the PRP and Conventional Groups[a]

Variable	PRP (n = 24)	Conventional (n = 24)	*P* Value
Age, y	64.21 ± 6.09	61.92 ± 8.36	.283
Sex (male:female), n	10:14	14:10	.248
Dominance (yes:no), n	22:2	20:4	.383
Duration, mo	27.42 ± 75.35	18.59 ± 37.83	.611
Aggravation	5.93 ± 11.11	2.42 ± 1.32	.219
AP size, mm	38.54 ± 8.31	42.50 ± 8.76	.115
ML size, mm	22.63 ± 8.94	26.83 ± 11.53	.164
Cofield type (S:M:L:MSV), n	0:1:20:3	0:0:20:4	.462
Boileau stage (I:II:III:IV), n	5:8:4:7	4:2:5:13	.085
Involved tendons	2.25 ± 0.61	2.38 ± 0.49	.439
Tendon grade (A:B:C),[b] n	8:10:6	2:18:4	.376
Excursion (A:B:C),[c] n	10:9:5	7:7:10	.161
SB grade (0:1:2:3),[d] n	2:10:6:6	2:11:5:6	.880
SB repair (none:debride:repair), n	1:15:8	2:15:7	.819
Partial repair:1 row:2 row,[e] n	1:0:23	3:1:20	.331
Acromioplasty (yes:no), n	9:15	10:14	.768
GT medialization (yes:no), n	6:18	9:15	.350
GT coverage (A:B:C:D),[f] n	14:3:5:2	8:7:5:4	.186
Goutallier grade (0:1:2:3:4), n			
Supraspinatus	0:3:10:3:8	0:0:8:9:7	.293
Infraspinatus	1:14:6:0:3	0:9:9:1:5	.121
Subscapularis	2:12:9:0:1	0:16:4:2:2	.521
Tangent sign (1:2:3),[g] n	8:9:7	4:16:4	.836
Occupation ratio (1:2:3),[h] n	5:9:10	2:11:11	.418
Follow-up, mo	15.88 ± 5.54	17.26 ± 7.18	.462
MRI follow-up, mo	13.38 ± 6.38	11.10 ± 3.02	.155

[a]Values are expressed as mean ± standard deviation unless otherwise specified. AP, anteroposterior; GT, greater tuberosity; ML, mediolateral; MRI, magnetic resonance imaging; PRP, platelet-rich plasma; S:M:L:MSV, small:medium:large:massive; SB, subscapularis.

[b]Tendon grade assesses rotator cuff quality using 3 gross tendon criteria[22]: (1) fraying over half of the tendon thickness, (2) delamination of the supraspinatus tendon, and (3) thinning of less than half of the normal thickness. A, none of these criteria were met; B, fraying or delamination was identified; C, both fraying and delamination or thinning regardless of the other criteria.

[c]Excursion evaluates the lateral displacement of the tear end by manual pulling: A, over the ridge of the greater tuberosity; B, within the original footprint in the greater tuberosity; C, cannot be reduced to the original footprint.

[d]Subscapularis tear was graded according to Pfirrmann et al.[30] Grade 0, normal tendon; grade 1, tear less than one quarter; grade 2, tear more than one quarter but not complete; grade 3, complete tear.

[e]Partial repair means that the majority of the rotator cuff tear was left unrepaired, and only partial repair in the anterior and/or posterior aspect of the tear was performed.

[f]GT coverage evaluates the repair quality. A, complete coverage of the original footprint; B, incomplete coverage more than half of the footprint; C, incomplete coverage less than half of the footprint; D, presence of the defect into the glenohumeral joint.

[g]Tangent sign assesses muscle atrophy of the supraspinatus. Grade 1, negative, which means that the superior border of the supraspinatus was superior to the line tangential to the coracoid and scapular spine; grade 2, borderline, which means that the superior border was located about the tangential line; grade 3, positive, which means that the superior border was inferior to the tangential line.

[h]Occupation ratio means the ratio of the cross-sectional area of the supraspinatus to the fossa. Grade 1, 0.6 to <1; grade 2, 0.4 to <0.6; grade 3, <0.4.

prepared to recommend surgery to others. We also evaluated overall function and satisfaction using a 10-cm scale marked from "I cannot use it" to "I feel normal" for function and from "never satisfied" to "very satisfied" for satisfaction. The functional scoring systems used were the American Shoulder and Elbow Surgeons (ASES) system, the Constant system, the University of California, Los Angeles (UCLA) system, the Disabilities of the Arm, Shoulder and Hand (DASH) system, the Simple Shoulder Test (SST), and the Shoulder Pain and Disability Index (SPADI). The change in CSA of the supraspinatus was calculated by subtracting measures of the 2 different time points.[20,21,42]

Statistical Analysis

To determine study sample size, an a priori power analysis was performed to provide a statistical power of 80% at an α level of .05. We believed that an expected decrease in the retear rate of the PRP group would be significant if it decreased to that of small to medium tears. Previous data of ours and other authors reported that the mean retear rate of small to medium and large to massive retears would be approximately 35% and 80%, respectively.[12,18] With these data, a sample size of 24 patients per group was determined assuming a 25% probability of data loss. Outcome

TABLE 2
Characterization of the PRP Used in the Study With Respect to Properties of Concentration, Activation, and Method of Application[a]

Concentration	
Platelets, $10^3/\mu L$	1096.48 ± 255.40
WBC, $10^3/\mu L$	0.04 ± 0.06
RBC, $10^3/\mu L$	0.18 ± 0.06
Fibrinogen, mg/dL	222.24 ± 55.21
Activation	
Status, %[b]	14.98 ± 4.55
Method	Calcium alone
Method	
State	Gel
Volume, mL	3 × 3
Number	1
Interval, d	0

[a]Values are expressed as mean ± standard deviation in concentration properties. PRP, platelet-rich plasma; RBC, red blood cell; WBC, white blood cell.

[b]Activation status was measured using flow cytometry with CD61 and CD62P in 5 patients. Values are expressed as the percentage of CD62P-positive counts over CD61-positive counts.

measures except for the retear rate were analyzed based on the intention-to-treat population. Missing data of the patients who dropped out of the study were imputed with last observation carried forward. Nominal and ordinal values were compared using the Pearson χ^2 test. The demographic values, overall satisfaction, and change in the CSA were compared using the independent t test. The values of the VAS, ROM, strength, functional scores, and overall function were analyzed using analysis of covariance and adjusted for preoperative values. Analysis was performed using SPSS version 13.0 (SPSS Inc, Chicago, Illinois), and the significance level was set at $P = .05$ throughout.

RESULTS

Patients

Between July 2009 and August 2011, 82 patients were screened for eligibility; 57 were eligible, and 48 patients were randomized and underwent either arthroscopic rotator cuff repair with or without PRP (Figure 1). Of these, 47 patients were followed up clinically, and 1 patient was lost to follow-up (97.9%). Postoperative MRI or CTA at a minimum of 9 months after surgery for assessing the retear was performed in 38 of 48 patients in the study (79.2%): 20 patients (83.3%) in the PRP group, and 18 patients (75.0%) in the conventional group. Meanwhile, preoperative, immediately postoperative, and 1-year postoperative MRI for assessing change in the CSA were performed in 19 patients (79.2%) in the PRP group and in 16 patients (66.7%) in the conventional group. There were no significant differences in baseline demographic characteristics, tear size, representative operative findings and procedures, the status of rotator cuff muscles, and follow-up between the 2 groups (Table 1).

Characteristics of PRP Application

The characteristics of PRP application are described with our own reporting tool with respect to properties of the concentration, activation, and method of application (CAM tool) (Table 2). The average platelet count increased from 238.67 ± 63.33 × 10^3 platelets/μL in whole blood to 1096.48 ± 255.40 × 10^3 platelets/μL in PRP, which is a 4.6-fold increase from baseline ($P < .001$). The average red and white blood cell counts changed from 4.49 ± 0.57 to 0.18 ± 0.06 (× 10^3 cells/μL) and from 6.19 ± 1.47 in whole blood to 0.04 ± 0.06, which is a 0.04- and 0.01-fold decrease from baseline, respectively (all $P < .001$). The average plasma fibrinogen concentration in PRP was 222.24 ± 55.21 mg/dL. The average percentage of activated platelets was 14.98% ± 4.55%.

Retear Rate

The retear rate of the PRP group (4/20, 20.0%) was significantly lower than that of the conventional group (10/18, 55.6%) ($P = .023$).

Pain

Pain before and after surgery was not significantly different between the 2 groups (Table 3). After surgery, average pain scores significantly decreased from 4.91 ± 2.22 to 0.84 ± 1.01 in the PRP group ($P < .001$) and from 4.31 ± 2.53 to 1.18 ± 1.81 in the conventional group ($P < .001$).

Range of Motion

No significant difference between the 2 groups was found for active forward flexion, abduction, external rotation with the arm at the side, and internal rotation before and after surgery (Table 3). After surgery, forward flexion, abduction, and internal rotation increased, whereas external rotation with the arm at the side did not in both groups.

Strength

Strength of the supraspinatus, infraspinatus, and subscapularis was not significantly different between the 2 groups before and after surgery (Table 3). Strength of the supraspinatus and subscapularis significantly increased after surgery in both groups, whereas that of the infraspinatus significantly increased in the PRP group only from 5.31 ± 3.71 lb to 7.16 ± 3.33 lb in the PRP group ($P = .037$) and from 5.40 ± 4.67 lb to 7.60 ± 3.33 lb in the conventional group ($P = .102$).

Overall Satisfaction

Patients in the 2 groups showed no significant difference in willingness to undergo surgery again and to recommend surgery to others after surgery (Table 3). Overall function was not significantly different between the 2 groups before surgery ($P = .468$), whereas it became significantly different after surgery ($P = .043$). However, it significantly

TABLE 3
Pain, ROM, Strength, and Overall Satisfaction of the PRP and Conventional Groups[a]

Variable	PRP (n = 24)	Conventional (n = 24)	*P* Value
Pain at rest			
Preoperative	3.92 ± 2.42	3.17 ± 2.30	.276
Final	0.71 ± 0.95	0.92 ± 1.56	.438
Pain in motion			
Preoperative	5.41 ± 2.55	5.47 ± 3.02	.939
Final	1.18 ± 1.75	1.42 ± 1.76	.635
Pain at night			
Preoperative	5.40 ± 2.81	4.29 ± 3.63	.245
Final	0.63 ± 0.88	1.21 ± 2.60	.104
Average pain			
Preoperative	4.91 ± 2.22	4.31 ± 2.53	.390
Final	0.84 ± 1.01	1.18 ± 1.81	.227
Worst pain			
Preoperative	8.52 ± 1.85	8.22 ± 2.32	.621
Final	2.10 ± 2.38	2.92 ± 2.55	.137
Forward flexion, deg			
Preoperative	121.67 ± 50.96	129.79 ± 54.96	.598
Final	165.63 ± 18.67	157.71 ± 29.74	.190
Abduction, deg			
Preoperative	126.67 ± 56.06	132.71 ± 57.31	.714
Final	165.00 ± 20.96	164.58 ± 26.62	.859
External rotation, deg			
Preoperative	41.04 ± 19.94	36.67 ± 20.36	.456
Final	44.79 ± 18.15	43.33 ± 20.20	.979
Internal rotation, vertebral level			
Preoperative	7.71 ± 4.34	7.21 ± 3.59	.666
Final	9.63 ± 2.22	9.96 ± 1.85	.440
Supraspinatus, lb			
Preoperative	5.50 ± 4.60	5.15 ± 5.41	.813
Final	8.61 ± 5.08	8.05 ± 4.76	.749
Infraspinatus, lb			
Preoperative	5.31 ± 3.71	5.40 ± 4.67	.937
Final	7.16 ± 3.33	7.60 ± 3.33	.703
Subscapularis, lb			
Preoperative	7.91 ± 5.14	8.05 ± 5.13	.928
Final	11.35 ± 5.01	11.54 ± 3.76	.952
Undergo surgery again, n (%)			
Final	22 (91.7)	19 (79.2)	.220
Recommend surgery, n (%)			
Final	24 (100.0)	21 (87.5)	.074
Overall function			
Preoperative	3.40 ± 2.32	3.92 ± 2.60	.468
Final	8.44 ± 1.31	7.21 ± 2.64	.043
Overall satisfaction			
Final	83.13 ± 19.88	83.33 ± 20.99	.972

[a]Values are expressed as mean ± standard deviation unless otherwise specified. PRP, platelet-rich plasma; ROM, range of motion.

improved after surgery in both groups (all $P < .001$). Overall satisfaction was not significantly different.

Functional Scores

The 2 groups showed similar shoulder function scores before and after surgery according to ASES, Constant, UCLA, DASH, SST, and SPADI scores (all $P > .05$) (Table 4). All functional scores significantly improved after surgery compared with those before surgery in both groups (all $P < .001$).

Change in CSA of the Supraspinatus

Preoperative, immediately postoperative, and 1-year postoperative CSAs of the supraspinatus were not different between the 2 groups (Table 5). The change between the immediately postoperative and preoperative CSA was not significantly different between the 2 groups ($P = .127$). The change between the 1-year postoperative and immediately postoperative CSA was significantly different between the 2 groups: –15.54 ± 94.34 mm^2 in the PRP group, and −85.62 ± 103.57 mm^2 in the conventional

TABLE 4
ASES, Constant, UCLA, DASH, SST, and SPADI Scores of the PRP and Conventional Groups[a]

Variable	PRP (n = 24)	Conventional (n = 24)	*P* Value
ASES			
Preoperative	43.45 ± 20.62	50.05 ± 22.61	.296
Final	88.94 ± 13.61	85.56 ± 17.26	.252
Constant			
Preoperative	43.04 ± 18.79	46.73 ± 21.67	.531
Final	74.82 ± 14.30	69.84 ± 16.29	.188
UCLA			
Preoperative	13.08 ± 4.53	15.42 ± 7.06	.180
Final	30.13 ± 3.98	29.21 ± 6.04	.284
DASH			
Preoperative	51.67 ± 22.89	45.49 ± 21.95	.345
Final	9.97 ± 11.38	13.58 ± 13.93	.259
SST			
Preoperative	3.79 ± 3.04	4.38 ± 2.98	.505
Final	10.33 ± 2.30	9.88 ± 2.79	.397
SPADI			
Preoperative	60.66 ± 20.59	51.21 ± 27.87	.188
Final	10.02 ± 13.46	14.36 ± 18.50	.162

[a]Values are expressed as mean ± standard deviation. ASES, American Shoulder and Elbow Surgeons; DASH, Disabilities of the Arm, Shoulder and Hand; PRP, platelet-rich plasma; SPADI, Shoulder Pain and Disability Index; SST, Simple Shoulder Test; UCLA, University of California, Los Angeles.

group ($P = .047$). The change between the 1-year postoperative and preoperative CSA was not significantly different between the 2 groups ($P = .278$).

TABLE 5
Change in CSA of the Supraspinatus at 1 Year After Rotator Cuff Repair in the PRP and Conventional Groups[a]

CSA, mm^2	PRP (n = 19)	Conventional (n = 16)	*P* Value
Preoperative	339.53 ± 144.84	313.11 ± 90.82	.535
Immediately postoperative	421.58 ± 134.66	430.92 ± 99.36	.821
1-year postoperative	406.04 ± 162.13	345.30 ± 116.35	.224
Δ(ImPO – Preop)	82.05 ± 53.95	117.81 ± 78.27	.127
Δ(PO1yr – ImPO)	–15.54 ± 94.34	–85.62 ± 103.57	.047
Δ(PO1yr – Preop)	66.51 ± 90.40	32.20 ± 90.41	.278

[a]Values are expressed as mean ± standard deviation. Δ(ImPO – Preop), the change in CSAs between the immediate postoperative measures and preoperative measures; Δ(PO1yr – ImPO), change between the 1-year postoperative measures and immediate postoperative measures; Δ(PO1yr – Preop), change between the 1-year postoperative measures and preoperative measures. CSA, cross-sectional area; PRP, platelet-rich plasma.

DISCUSSION

In our previous study, we showed that PRP application in large to massive tears might be effective for structural integrity, whereas it failed to provide statistically significant evidence.[18] We believe that one of the reasons may be that it was an underpowered study to detect a difference in the retear rate, which led us to initiate the present study. The findings of the current study showed that PRP application in large to massive rotator cuff repairs significantly improved the structural outcomes in terms of the retear rate and the change in CSA of the supraspinatus compared with those without PRP. Structural integrity, which means the absence of retears after surgery, has been recognized as one of the most important outcomes after rotator cuff repair, as most recent research demonstrated better outcomes in patients without retears.[37,39,45] The change in CSA of the supraspinatus is a new structural outcome measure that is specific to function of the repaired rotator cuff muscle.[21] Meanwhile, in contrast to improved structural outcomes, the clinical outcomes were not different between the 2 groups except the overall function of the shoulder. We believe that this divergence of the results comes from the difference in appropriate evaluation time points between the structural and clinical outcome measures. Considering that recent studies have demonstrated that most retears occur within the first 6 months after surgery,[3,27] and that the change in CSA of the supraspinatus would be assessed at 1 year after surgery,[21] the evaluation time for the structural outcomes used in this study at a minimum of 9 months after surgery seems to be appropriate. Meanwhile, 1 year is too short to properly evaluate clinical outcomes. We expect that better structural outcomes in the PRP group will bring better long-term clinical outcomes, which should be demonstrated in a further study.

We prepared PRP with a fully automated plateletpheresis system in this investigational clinical trial, as in our previous report,[18,19] in spite of the relative inconvenience and high expense in comparison with small commercial tabletop systems. We believe that one of the reasons why the exact effects and mechanisms of PRP are still unclear is the lack of standardization or inadequate characterization of the preparation and application process of PRP. Although it is impractical to measure all components of PRP, and to standardize or monitor the whole process of the preparation and application of PRP in each use, minimum information about the characteristics of PRP should be obtained and provided in each study. Here, we used our own tool for reporting characteristics of the PRP preparation and application process. It includes 4 concentration properties (platelets, red blood cells, white blood cells, and fibrinogen), 2 activation properties (status and method), and 4 methods of application (state, volume, number, and interval of application). As red blood cells, white blood cells, and fibrinogen are also known to have bioactive properties, we included their concentration in addition to that of platelets.[6,8,9] Activation status as well as activation method of PRP is also crucial. Premature activation caused by multiple transfers, centrifugation, and aggregation during or after PRP preparation, especially in some manual preparation systems, results in the application of ineffective material and therefore should be identified and avoided.[17,43] In addition, volume, number, and interval of application are also important characteristics and should be reported. As a reporting tool of PRP treatment, we hope

that the CAM tool could be used like a camera recording a scene of PRP usage in daily practice and research.

Despite a recent surge in studies of PRP with respect to rotator cuff repair, few studies focused on large to massive tears, even though they would be given priority in investigation. Sánchez Márquez et al[33] reported that the application of PRP did not decrease the retear rate in patients with massive tears: 42.9% in patients with PRP versus 62.3% in patients without PRP. Meanwhile, Gumina et al[13] reported that no retears occurred in patients treated with PRP (0%, 0/39), while 3 retears occurred in control patients (8.1%, 3/37) at a mean of 13 months of follow-up. The authors attributed such a low rate of retears to the short follow-up and the absence of patients with massive tears.[13] In a systematic review, Chahal et al[7] showed that the use of PRP significantly decreased the rate of retears in patients with small- to medium-sized tears. Interestingly, there was no significant difference in retear rates among patients who had large or at-risk tears regardless of PRP treatment.[7] We believe that these large discrepancies are caused by the difference in PRPs used in the studies: the difference in both the preparation and application. As various authors used different biological materials under the same term of "PRP," different results would be inevitable. Furthermore, the contradictory results in the systematic review by Chahal et al[7] would suggest that PRP application was not optimized rather than it having had no effect on the structural integrity. Therefore, we suggest that as further studies are necessary, they should provide not only the results of the structural and clinical outcomes but also the characteristics of PRP preparation and application. As it does not seem to be possible to standardize PRP preparation and application in each use just like chemical drugs, reporting of the characteristics of PRP should be a minimum prerequisite for better understanding and advancement of PRP usage.

Limitations of the study are that this (1) was a single blind study; (2) had a relatively small sample size determined by the authors' relatively old study,[12,22] suggesting that a larger sample size should be calculated with recent studies with lower retear rates[27,28,37]; (3) had a decreased number of patients in the analysis of the primary outcome measure; (4) had a still incomplete characterization of PRP with minimum information and no information about important components such as growth factors; (5) arbitrarily used PRP in rotator cuff repair (component concentrations, activation method, and application state, number, and method); (6) had different imaging modalities of MRI and CTA; and (7) had a short length of clinical follow-up, which should normally be a minimum of 2 years.

In conclusion, PRP used in this study significantly improved the structural outcomes of large to massive rotator cuff repairs compared with repairs without it. These results suggest that better long-term clinical outcomes are expected, whereas there was no significant difference in clinical outcomes except the overall shoulder function in the short length of clinical follow-up, which should normally be a minimum of 2 years.

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