Master's Thesis of Orthopedic Surgery

Efficacy of intraoperative platelet-rich plasma (PRP) augmentation and postoperative PRP booster injection for rotator cuff healing

- A randomized controlled clinical trial -

회전근개 치유를 위한
수술 중 혈소판 풍부 혈장(PRP)의 주입 및
수술 후 PRP 주사의 효과
– 무작위 대조 임상 시험 –

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회전근개 치유를 위한 수술 중 혈소판 풍부 혈장(PRP)의 주입 및 수술 후 PRP 주사의 효과

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Abstract

Background: Platelet-rich plasma (PRP) has been applied as an adjuvant treatment of arthroscopic rotator cuff repair (ARCR) to enhance rotator cuff healing. However, it remains debatable whether PRP enhances tendon-to-bone healing.

Purpose: To assess the efficacy of intraoperative augmentation and postoperative injection of PRP with double-spin preparation and calcium activation without thrombin in ARCR.

Methods: A total of 58 patients underwent ARCR with intraoperative PRP augmentation, and half were randomly assigned to receive an additional ultrasound-guided PRP injection to the repair site at 2 weeks postoperatively (booster injection group vs PRP-only group). A control group who did not receive any PRP treatment was retrospectively matched by propensity score matching. Structural integrity was assessed using magnetic resonance imaging (MRI) at 1 year postoperatively. Functional outcomes were assessed using the visual analog scale (VAS) for pain and satisfaction, shoulder range of motion, Constant score, American Shoulder and Elbow Surgeons Shoulder Score, and Simple Shoulder Test score at minimum 2-year follow-up.

Results: In patients with tears >2 cm, the healing failure rate at 1-year follow-up was significantly less in the overall PRP group than in the control group (12.9% vs 35.7%; p = 0.040), however, the booster injection group did not present a better healing rate than PRP-only group (6.7 % vs 18.8 %; p = 0.316). The PRP group had lower VAS pain scores (0.5 ± 1.1 vs 1.3 ± 1.8; P = 0.016) and higher VAS satisfaction scores (9.2 ± 1.2 vs 8.6 ± 1.7; P = 0.023) at the final follow-up, while there was no statistical difference between the PRP-only and PRP booster groups in functional outcomes.

Conclusion: Intraoperative PRP augmentation during ARCR demonstrated superior anatomic healing results in rotator cuff tears >2 cm, as well as reduced pain and increased subjective satisfaction. PRP booster injection provided no additional benefit to tendon integrity or functional recovery.

Keyword : Platelet-rich plasma, rotator cuff tear, healing of rotator cuff tear, clinical outcome of platelet-rich plasma
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Chapter 1. Introduction

1.1. Study Background

Healing failure after arthroscopic rotator cuff repair (ARCR) remains an unsolved problem. Despite the development of operative techniques and surgical devices, healing failure rates have been reported to be up to 20-94% [6,12,36]. Furthermore, healing failure tends to be higher as the tear size increases, and the postoperative functional outcome is generally worse in patients with healing failure [2,6,7,25]. Therefore, achieving anatomical healing of a torn rotator cuff is a crucial factor for better long-term outcomes [6,12,37]. Healing failure may be caused by abnormal fibrous regeneration of tissue at the tendon-to-bone interface [2,32]. To improve healing after rotator cuff repair, several biologic augmentations have been attempted, such as growth factors, stem cells, and platelet-rich plasma (PRP) [17,18,27,28,32]. Among the various options for biologic augmentations, PRP has been most widely used [10,38]. Several animal studies reported that PRP may help the regeneration of tendon tissue [1,23,24,34]; however, there have been mixed results regarding PRP use in the literature in terms of human rotator cuff healing [2,11,34]. The lack of standardization of PRP related issues would be the most important reason for these mixed results, as PRP application protocols vary from study to study. There is currently no accepted consensus on which growth factor in PRP is essential for rotator cuff healing, and whether specific preparation methods show different growth factors and cellular composition. Every researcher

has different application methods during the operation, and some surgeons spray the PRP over the repair site or make PRP-gel and interpose between tendon and bone. It is uncertain whether an additional secondary application of PRP after surgery would enhance rotator cuff healing. Furthermore, we do not have accepted clinical indications of intraoperative PRP application, and there are also mixed outcomes in the literature regarding whether a large tear is a proper indication that PRP should be applied

1.2. Purpose of Research

Therefore, the purpose of this study was to assess the clinical efficacy of intraoperative PRP augmentation and postoperative PRP booster injection at 2 weeks after surgery with double-spin preparation and calcium activation without thrombin in patients undergoing ARCR. We hypothesized that intraoperative PRP augmentation with an additional booster injection of PRP at postoperative 2 weeks, which was prepared by the double-spin method and activated by calcium [31,33], would enhance rotator cuff healing and improve functional outcomes after ARCR.

Chapter 2. Materials and methods

2.1. Study design

This study consisted of two parts: 1) a prospective randomized controlled trial to compare the efficacy of intraoperative PRP augmentation with additional ultrasound-guided PRP booster injection around the repair site at 2 weeks after surgery and 2) a comparative cohort study to assess the efficacy of PRP administration within the control group using propensity score matching. Both the clinical trial and cohort study were approved by the institutional review board of the senior author's affiliation (IRB number: E-1405/250/004).

A sample size calculation was performed to determine the required number of participants for the prospective randomized controlled trial. According to a previous study [19], the minimal clinically important difference (MCID) and the standard deviation of the Constant score in patients with rotator cuff tears is 10.4 points and 8 points, respectively. With a statistical power of 80% at a significance level of 5%, at least 48 participants (24 in each group) were required to detect an MCID between the PRP only group and additional booster injection group. Assuming a 20% dropout rate, the sample size was determined to be 58 participants.

Candidates of the clinical trial were recruited among those who were planning to undergo ARCR, and all patients enrolled in this study had a symptomatic chronic shoulder pain or other symptoms related to rotator cuff tendon for more than six

months and had full-thickness rotator cuff tear confirmed by MRI from October 2014 to January 2015. The actual tear size of rotator cuff tendon was eventually measured using a probe after debridement during the arthroscopic surgery. The patients who met one or more of the following criteria were excluded from the clinical trial: 1) the presence of previous surgical history on the ipsilateral shoulder, 2) an active infection and/or rheumatological / autoimmune disease, 3) rotator cuff tear arthropathy, or 4) a preoperative platelet count less than 150,000/μL. After screening for eligibility, candidate groups were informed about PRP and this clinical trial, and only patients who agreed to participate in the clinical trial by written informed consent were enrolled.

A total of 58 patients were enrolled, and were divided into two groups randomly through a computer-generated random table: 29 patients received only intraoperative PRP augmentation (PRP only group) and 29 patients received both intraoperative PRP augmentation and the additional PRP booster injections under ultrasound guidance at 2 weeks postoperative (Booster injection group). To compare the effect of PRP itself, patients who underwent ARCR without any application of PRP were retrospectively enrolled as the control group. Propensity score matching (1:1) was performed retrospectively using variables such as age [30], sex, osteoporosis, stiffness [29], and tear size [2].

Of the 58 randomized participants, 48 (24 patients each in the PRP-only and PRP booster injection groups) completed radiological follow-up at 1 year postoperatively and had a minimum of 2 years postoperative follow-up data on functional outcomes. The final propensity score-matched control group consisted of 48 patients (Figure 1).

Rotator cuff healing was evaluated using MRI at 1 year postoperative. At this moment, healing failure rate in the PRP-only and PRP Booster injection groups was evaluated according to the cut-off tear size for rotator cuff healing, which was determined by previous study as 2cm. A musculoskeletal radiologist with 15-years of experience who was unaware of the present study interpreted the MRIs and further evaluated rotator cuff healing to the greater tuberosity. According to the classification by Sugaya et al. [36] (Figure 2), types I, II, and III are considered as healing, and types IV and V are considered as healing failure. Clinical outcomes, which were evaluated using ROM, visual analog scale (VAS) for pain and satisfaction, Constant score, American Shoulder and Elbow Surgeons (ASES) score, and Simple Shoulder Test (SST) score, were assessed at minimum 2-year follow-up. Outcome evaluations were conducted preoperatively and at the annual follow-ups by a clinical researcher who was blinded to the current study.

2.2. Preparation of autologous PRP

After induction of general anesthesia, at least 30 mL of whole venous blood was sampled from the peripheral limbs of all patients, using a 1mL of Anticoagulant Citrate Dextrose Solution (ACD-A) preloaded syringe. The anti-coagulated blood was then transferred to a commercial kit (TriCell, RevMed, Seongnam-si, Gyeonggi-do, Republic of Korea) which was designed to be leukocyte rich PRP. PRP was prepared by double-spin centrifugation. The first separating centrifugation (first spin) to separate the plasma layer was 1889 g for 4 minutes.

The separated top plasma layer then underwent the second condensation centrifugation (second spin), which was 2009 g for 3 minutes. Finally, 3 ml of PRP was collected, and the extracted PRP with 0.3 ml of 10% calcium gluconate loaded 5 ml syringe was used to produce a PRP gel (Figure 3).

2.3. Surgical procedures with the application of PRP and rehabilitation

All surgeries were performed by the senior author (J.H.O), with patients in the lateral decubitus position under general anesthesia. After systemic glenohumeral joint and subacromial space exploration, subacromial decompression for the removal of inflamed bursal tissue and acromioplasty confined to the anterolateral aspect of the acromion were performed. The presence of SLAP lesions was recorded; however, no SLAP repairs were performed as none of the subjects had pre-operative SLAP related symptoms or physical examination. Distal clavicle resection was performed in patients who experienced symptomatic acromioclavicular arthritis, and biceps tenotomy or tenodesis was performed for symptomatic biceps tears involving more than 50% of the tendon according to the age and activity level of the patient. If the patient had a stiff shoulder, concomitant manipulation under anesthesia with an arthroscopic capsular release was performed. Rotator cuff repair was performed with the double-row suture bridge technique. 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. To enhance the tendon to bone healing, footprint

was prepared with ring curette and rasp in all groups. After the medial row sutures were tied, the PRP gel was applied to the tendon-to-bone interface in a water arthroscopic setting through percutaneous injection without cannula. Then the PRP gel was delivered by the surgeon with the help of a sterile surgical forceps and probe, which could ensure the PRP augmentation be administrated directly to the interface and stayed firmly between the bone and repaired rotator cuff. When the PRP gel was placed properly, the lateral row was secured using suture anchors. Finally, the PRP gel was interposed securely at the tendon-to-bone interface. We did not observe any dilution or washout effect that occur with arthroscopic fluid lavage (Figure 4).

Patients in the PRP booster injection group received an additional ultrasound-guided PRP injection around the repair site at 2 weeks postoperatively. PRP preparation was carried out in the same manner as in the operation, but calcium gluconate activation was not added, as it is not needed to make the gel. 3 ml of PRP was sprayed on and around the repair site under visualization using ultrasound by the same shoulder fellowship-trained orthopedic surgeon. Needle placement was guided by the identification of the echogenic suture material at the tendon repair site.

Immobilization after the surgical repair was maintained with an abduction brace for 5 to 6 weeks according to the tear size [29]. Shrugging of both shoulders, active elbow flexion/extension, active forearm supination/pronation, and active hand and wrist motion were encouraged immediately after surgery. Active assisted ROM exercises were allowed after patients were weaned off the brace. Muscle-strengthening exercises were started at about 12 weeks, and sports activities were

usually permitted at 6 months after surgery. All rehabilitation was supervised by the Department of Rehabilitation at the senior author's institution.

2.4. Statistical analysis

All surgeries statistical analyses were conducted using the SPSS statistics software package, ver. 19 (SPSS Inc, Chicago, Illinois), except propensity score matching (PSM). Propensity score matching was performed by the statistician in the senior author's affiliation. The Kolmogorov-Smirnov normality test was conducted for continuous variables. Subsequently, an independent T-test or Mann-Whitney U test was conducted according to the characteristics of the data distribution. The chi-squared test or Fisher's exact test was used for nominal variables. All statistical tests were two-sided, with a significance level of 0.05.

Chapter 3. Results

3.1. Demographics

The mean final follow-up period of study participants was 51.9 ± 21.7 months (range 24-100). No differences were observed for preoperative demographics and intraoperative findings, (including tear size, biceps lesion, SLAP lesion and glenohumeral osteoarthritis) which indicated that the randomization was well-balanced (all $p > 0.05$, Table 1).

3.2. Healing failure rate

A total of 96 participants (24 PRP only group, 24 PRP booster injection group, 48 control group) were available for radiological examination at 1 year postoperative. The healing failure rate had no significant difference between the PRP only group and Booster injection group (8.3% vs. 16.7 %, $p = 0.383$). However, the healing failure rate in the overall PRP group was significantly lower than in the control group (12.5% vs. 29.2%, $p = 0.038$). In patients whose tear size was > 2 cm, the healing failure rate in overall PRP group was also significantly lower than in the control group (12.9% vs. 35.7%, $p = 0.040$); however, this was

not observed in patients whose tear size was ≤ 2 cm (11.8% vs. 20.0%, respectively, p = 0.498) (Table 2).

3.3. Functional outcomes

The functional outcomes showed no statistical difference (p > 0.05) between the PRP only group and PRP booster injection group for functional recovery. There were no significant differences in the ranges of motions and all functional measurements between the PRP group and control group. A significant difference in pain VAS was found between the PRP group and the control group at the final follow-up (0.5 ± 1.1 vs. 1.3 ± 1.8, p = 0.016). Subjective satisfaction VAS improved significantly in PRP group (9.2 ± 1.2 vs. 8.6 ± 1.7, p = 0.023) (Table 3).

A subgroup analysis of functional outcomes according to healing failure was also conducted, and pain VAS (p = 0.004), forward flexion (p = 0.041), Constant score (p = 0.002), ASES score (p = 0.013), and satisfaction VAS (p = 0.001) were significantly better in the healed group than the healing failure group (Table 4).

Chapter 4. Discussion

The purpose of this study was to evaluate the efficacy of intraoperative PRP gel interposition between the tendon and bone during arthroscopic rotator cuff repair and an additional ultrasound-guided PRP booster injection around the repair site at 2 weeks after surgery, which was prepared by the double-spin method activated by calcium without thrombin [31,33]. According to the current data, we found that an additional booster injection of PRP did not improve rotator cuff healing. However, PRP was effective in rotator cuff healing compared to the control group, especially when the tear size was greater than 2 cm. Furthermore, in terms of functional outcomes, we found that PRP injection could help to reduce the pain of patients and improve subjective satisfaction until at least 2 years postoperative. However, there were no additional benefits on functional outcomes in those who received the PRP booster injection in comparison with PRP only group.

PRP is a platelet concentrate which contains a 3- to 5-fold increase in growth factor concentrations and is expected to improve rotator cuff healing by releasing these growth factors with higher concentrations than physiologic levels [10,38]. Several animal studies have reported that PRP may aid in the regeneration of tendon tissue through collagen synthesis, vascularization, and tendon cell proliferation when PRP is incorporated at the site of the tendon-to-bone interface in the setting of operative repair [1,23,24,34]. However, despite the theoretical advantages, clinical results of PRP in human rotator cuff healing were varied, and

previous meta-analyses did not conclude that PRP is effective in all rotator cuff repairs [2,11,34]. One of the reasons for such a difference might be due to the heterogeneity of PRP, which was used in each study [16,20,22]. There have been no properly standardized PRP preparations or activation methods [16], but several experimental studies on animals have been done with regard to PRP preparation methods. For example, one animal study reported that an increase in platelet counts was observed after using the double-centrifugation method compared with the single-centrifugation procedure while leukocytes were not concentrated [35]. Another study concluded that the double-centrifugation protocol results in higher platelet concentrations but is more likely to result in platelet morphological changes [26]. Moreover, it has been demonstrated in previous studies [31] involving 14 healthy subjects, that PRP prepared by the double-spin method generally leads to a higher concentration of platelets, relative to the single-spin method.

Regarding the activation of PRP, the kinetics of growth factor release are varied according to each commercial separation system [3,20]. As we know, platelet activation is essential for the release of growth factors, and most of these factors have short half-lives after release (minutes to a few hours) [35]. Thus, it is important to use the activated platelets at the proper time or find a way to sustain the concentration of growth factors to guarantee the clinical therapeutic efficacy of PRP. Calcium is most widely used for PRP activation due to its low cost, higher availability, and rare side effects, but doubts on its activation potential remain [8]. Several previous studies had revealed that only calcium activation [16,33] had a significant effect on increasing the overall cytokine release as well as sustaining the

concentration of growth factors (over seven days) in the double-spin PRP preparation method. Therefore, in this study, we focused on PRP preparation and activation using the double-spin centrifugation technique and calcium only activation without thrombin to evaluate the clinical efficacy of these preparation and activation methods.

Another PRP related issue deals with the delivery of PRP during arthroscopic rotator cuff repair. Although several previous systematic reviews and meta-analyses questioned the effects of PRP in rotator cuff repair [4,11,34], Salzman et al. [34] have mentioned the potential of PRP in specific situations: a solid PRP matrix [5], which could avoid a washout effect occurring with arthroscopic fluid lavage, application of PRP at the tendon-to-bone interface, double-row repair [15], and small and/or medium-sized rotator cuff tears. Therefore, the authors applied the PRP gel to the tendon-to-bone interface amid the double-row suture bridge technique during arthroscopic rotator cuff repair.

The timing of PRP application is another issue that warrants discussion, as the rotator cuff healing process continues up to 3 to 6 months after surgical repair [39]. Hence, it is also crucial to decide the timing for the postoperative delivery of the PRP booster injection. Although most PRP applications for rotator cuff healing are performed during arthroscopic rotator cuff surgery, the postoperative PRP application also has been tried [9,39]. However, there was less previous research that evaluated the efficacy of postoperative PRP application than intraoperative application. Until now, PRP application protocols during rotator cuff surgery have varied, including intraoperative administration, as well as the postoperative booster injection, and there is insufficient literature on the delivery timing of postoperative

PRP booster injections. In most previous PRP studies, PRP has been delivered at the time zero point of rotator cuff repair. However, it has been proposed that biologic augmentation of tendon repairs too early in the tendon healing process may be ineffective [13]. Moreover, intraoperative PRP injection may result in dilution [32]. To overcome this problem, a study was conducted to evaluate the effect of 2 consecutive PRP injections spaced over a week. Wang et al. [39] reported the results of repeated application of PRP to the tendon repair site after double-row arthroscopic rotator cuff repair on postoperative days 7 and 14. However, postoperative PRP injections did not improve the healing failure rate at later follow-ups. As some growth factors, like transforming growth factor-β1, have maximum expression effects at days 14 after augmentation, we decided an additional postoperative booster injection would be beneficial at 2 weeks after surgery, together with our routine visit to the clinic. However, the current study presented similar outcomes that show that an additional postoperative PRP injection after rotator cuff repair is not effective in tendon healing regardless of tear size.

The present study found that PRP was effective in enhancing rotator cuff healing in those in the PRP group, compared to the control group. The healing failure rate of the overall PRP group was significantly lower than that of the control group, however, subgroup analysis showed that this difference was only statistically significant for tear size greater than 2 cm. Several previous meta-analyses and/or systematic reviews have reported the healing failure rates according to the tear size after the application of PRP in rotator cuff repair [2,34,38,40]. These previous studies [2,34,38] suggested that the effect of PRP on

the healing rate is beneficial in small- and/or medium-sized rotator cuff tears. However, in this study, the statistical significance was not confirmed in patients with a tear size of less than 2cm. The reason for this may be due to the healing correlation to initial tear size [29,30], which means there is a lower possibility of healing failure caused by the small-sized rotator cuff itself. In other words, a small tear originally shows good healing around 90% [29,31], without PRP augmentation. However, a significantly higher failure rate (near 35%) had been revealed in patients with a tear greater than 2 cm in size [6,31], which indicates that PRP augmentation plays an apparent role in enhancing tendon healing, just as the current study showed that the healing failure rate was 12.9% in PRP group and 35.7% in the control group.

The secondary outcome of this study was to evaluate the functional outcomes of PRP augmentation at the final follow-up visit for more than 24 months. Several studies have revealed that PRP application could reduce pain [14,21], and another study showed the result of PRP application in pain and function outcomes [14]. In the present study, the pain VAS decreased significantly, while higher subjective satisfaction VAS was shown in the PRP group; however, the functional outcomes did not present significant differences. These results were similar to that of the previous studies [2,11,34,40,41]. Furthermore, PRP booster injection did not demonstrate a significantly better functional recovery result compared to the PRP only injection.

This study has several strengths. It was a prospective controlled randomized study that directly compared the efficacy of intraoperative PRP gel interposition between the tendon and bone during arthroscopic rotator cuff repair and additional

ultrasound-guided PRP booster injection around the repair site at 2 weeks after surgery. Furthermore, we compared the efficacy of intraoperative PRP augmentation with the control group that was selected by propensity score matching. Nevertheless, there were several limitations. First, the sample size was relatively small for the subgroup analysis. As the purpose of this study was to evaluate and compare the efficacy of PRP augmentation according to a postoperative booster injection, we considered that there was a sufficient number of recipients enrolled to achieve this study objective. Moreover, the randomization to compare the PRP only group and booster injection group was well balanced, and propensity score matching to evaluate the efficacy of PRP augmentation itself was performed using the essential variables. Therefore, we considered that the bias based on the small sample size was relatively well-controlled by the statistical methods.

A second limitation was that control group participants were designed to be retrospectively enrolled in the same study period. However, during the PRP study period, control group participants created by propensity score matching revealed a small number of group members. To receive a statistical power of 80% at a significance level of 5%, at least 48 participants were required to detect an MCID. Therefore, control group participants were actually enrolled with patients who underwent ARCR from June 2005 to April 2014 without any application of PRP for a sufficient number of the group, which might be a limitation of our research. However, control group participants had exactly the same surgical technique and performed by the same surgeon with the PRP study group. Furthermore, preoperative demographics and intraoperative findings of study group and group

participants enrolled show no statistical difference, which means they were well balanced. But concomitant shoulder lesions were not excluded in our study, which may be one of the limitations of this study as they could have impact on functional outcomes. Another limitation of this study is that there was no blinding of subjects in PRP group. Thus, subjective outcomes (those based on feelings such as pain or satisfaction scores) might be more at risk of bias from lack of blinding. But the visual analog scale pain and satisfaction scores were obtained by an independent researcher who was not related to this research. Furthermore, other factors that could have impact on the PRP efficacy in rotator cuff healing, such as smoking, diabetes etc. shoulder be considered to be matched in future study. If we exclude the patients with all these concomitant shoulder disease (AC arthropathy, subacromial impingement, etc.), it would be very difficult to enroll enough participants. Besides, we cannot control all other concomitant lesions in prospective study, for example, subacromial impingement is a common symptoms of rotator cuff tear. But we indeed routinely examine the biceps tendinopathy, SLAP lesion and glenohumeral osteoarthritis with a diagnostic arthroscopy at operative field, as we consider these factors could have an influence on functional outcomes after the surgery. We have run the data analysis and there was no significant difference between study group and control, which means, they are unlikely to cause statistical bias in our study. However, it may be a limitation of this study. Third, although intraoperative platelet-rich plasma (PRP) augmentation and postoperative PRP booster injection shared the same preparation, the lack of calcium activation in PRP booster delivery may result in the lack of evidence for comparison their efficacy on rotator cuff healing. However, doubts on activation

potential of calcium remain, and we were also concerned about patients' suffering from shoulder stiffness that could be caused by calcium activated gel-typed PRP booster injection, since it was delivered at the tendon repair site under subacromial place at 2 weeks postoperative when patients were still in the abduction brace. Therefore, we did not calcium gluconate activation for PRP booster injection. Additionally, intraoperative PRP gel was applied to the tendon-to-bone interface and interposed securely by double-row suture bridge technique, while postoperative PRP booster injection was sprayed on and around the repair site in subacromial space. Because it is almost impossible to deliver ultrasound-guided PRP booster injection at the tendon-to-bone interface in the clinic after repair had performed. Moreover, it is known that PRP gels under different preparations and activation protocol may show a significant difference in healing effect. Besides, we did not characterize PRP sample separately in this research. But, according to previous study about PRP preparations and activation protocols, PRP prepared by the double-spin method generally leads to a higher concentration of platelets, relative to the single-spin method [31]. And, it has also been demonstrated that only calcium activation had a significant effect on increasing the overall cytokine release as well as sustaining the concentration of growth factors (over seven days) in the double-spin PRP preparation method [33]. Therefore, in this study, we focused on PRP preparation and activation using the double-spin centrifugation technique and calcium only activation without thrombin to evaluate the clinical efficacy of these preparation and activation methods. Therefore, the protocol we used in this study requires further test including PRP characterization and comparison of various PRP preparations. Further researches on the standardization

in Platelet-Rich Plasma preparation and activation protocols are required, and comparative studies of the different PRP products are necessary.

Chapter 5. Conclusion

This study revealed that a PRP booster injection at 2 weeks after surgical repair, together with intraoperative PRP administration provided no additional benefit to the tendon integrity or functional recovery. However, intraoperative PRP augmentation during arthroscopic rotator cuff repair demonstrated superior results in anatomical healing in rotator cuff tear sizes greater than 2 cm as well as a reduction in pain and an increase in subjective satisfaction. These findings provide clinical effectiveness to support the use of PRP augmentation during ARCR of tears > 2 cm without a repeated booster injection to enhance tendon healing under arthroscopic rotator cuff repair.

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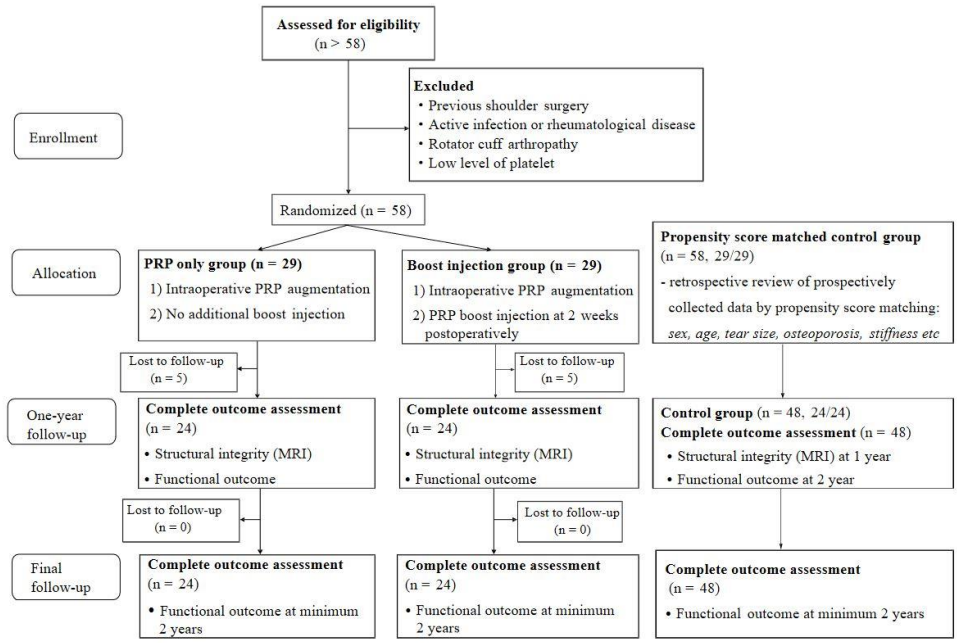
Figure legend and Figures

Figure 1. The CONSORT (Consolidated Standards of Reporting Trials) flow chart



PRP, platelet-rich plasma; MRI, magnetic resonance imaging

Figure 2. Sugaya classification of postoperative rotator cuff integrity. (A) Type I, sufficient thickness with homogeneously low intensity on each image; (B) Type II, sufficient thickness, partial high-intensity area; (C) Type III, less than half the thickness without discontinuity; (D) Type IV, minor discontinuity; (E) Type V, major discontinuity, types IV and V were regarded as healing failure.

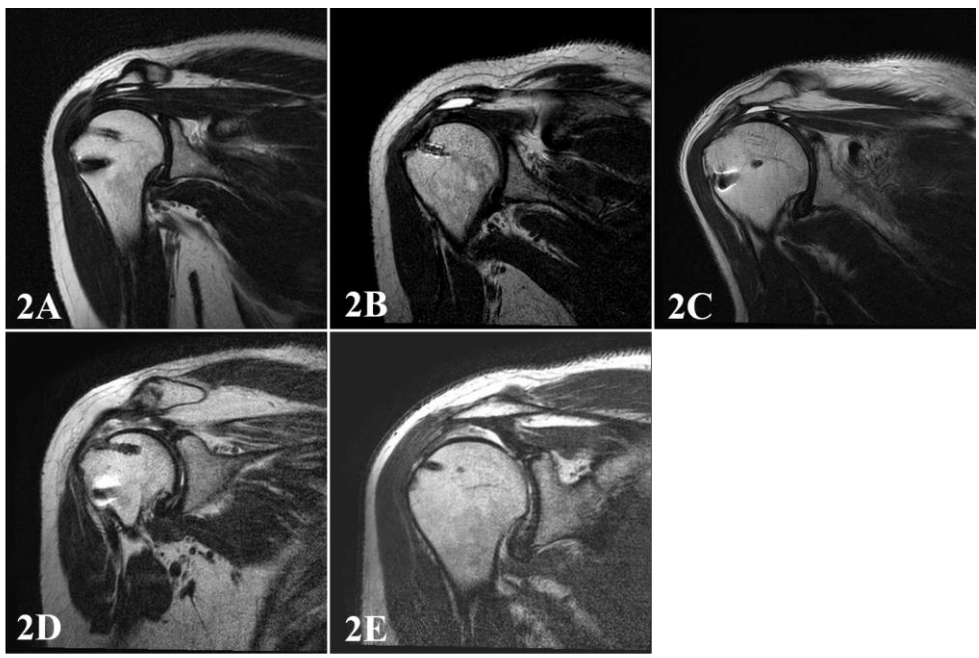


Figure 3. Preparation and activation of the platelet-rich plasma are shown. (A) The first separating centrifugation was 1889 g for 4 minutes, and the second separating centrifugation was 2009 g for 3 minutes. (B) After double spine centrifugation, 3 ml of PRP (white arrow) was collected and used to produce PRP gel. (C) The extracted PRP with 0.3 ml of 10% calcium gluconate loaded 5 ml syringe was used to produce a PRP gel. (D) Gel-formed PRP within a 5 ml syringe and (E) the final form of the PRP gel is shown.

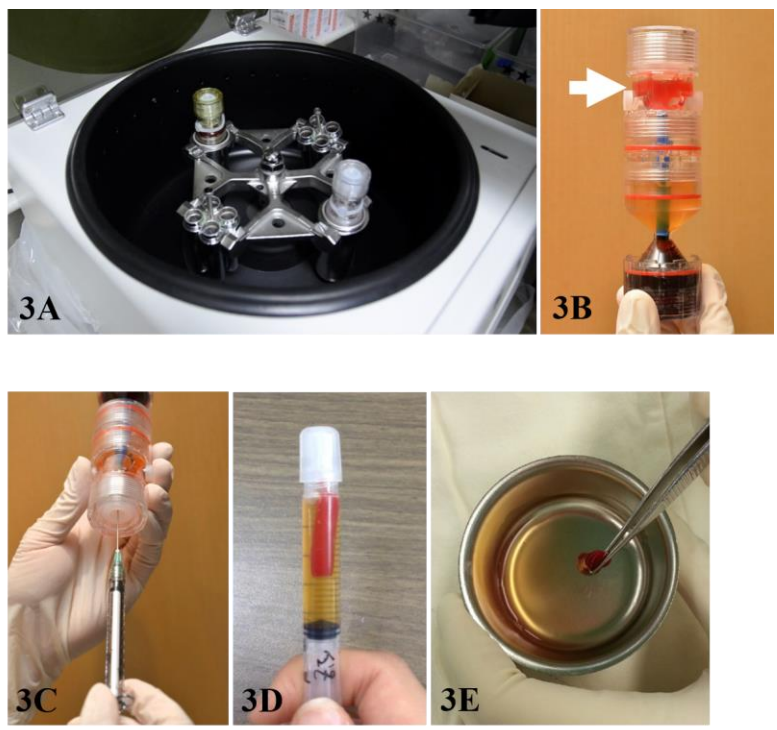


Figure 4. (A) PRP gel was applied to the tendon-to-bone interface after all medial row sutures were tied. (B) When PRP gel was placed in the proper place, the lateral row of the double-row suture bridge was secured using suture anchors. The PRP gel was interposed securely at the tendon-to-bone interface.

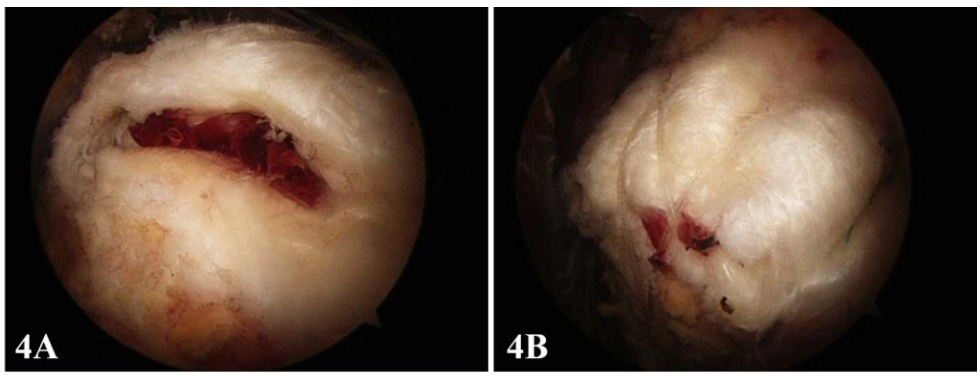


Table legend and tables

Table 1. Preoperative demographics and intraoperative findings of rotator cuff tears of the PRP (PRP only group and Booster injection group) and Control groups

	PRP group			Overall PRP group (n = 48)	Control group (n = 48)	p value
	PRP only (n = 24)	Booster injection (n = 24)	p value			
Age, year	63.9 ± 8.0	62.1 ± 11.5	0.526	63.0 ± 9.9	63.3 ± 9.0	0.863
Sex, Male: Female	10:14	14:10	0.513	24:24	24:24	>0.999
Osteoporosis	8 (33.3)	4 (16.7)	0.410	10 (20.8)	11 (22.9)	>0.999
Stiffness	8 (33.3)	2 (8.3)	0.108	12 (25.0)	13 (27.1)	>0.999
Tear size, mm						
Anteroposterior	21.8 ± 9.5	24.8 ± 15.2	0.418	23.3 ± 12.6	23.0 ± 14.8	0.573
Mediolateral	19.5 ± 8.5	20.3 ± 9.8	0.766	20.0 ± 9.1	20.6 ± 11.6	0.586
Biceps lesion	11 (45.8)	14 (58.3)	0.386	25 (52.1)	25 (52.1)	>0.999
SLAP lesion	5 (20.8)	11 (45.8)	0.066	16 (33.3)	19 (39.6)	0.525
SLBC Procedures						
None	12 (50)	9 (37.5)	0.741	21 (43.8)	17 (35.4)	0.859
Debridement	3 (12.5)	6 (25)		9 (18.8)	11 (22.9)	
Tenotomy	5 (20.8)	5 (20.8)		10 (20.8)	12 (25.0)	
Tenodesis	4 (16.7)	4 (16.7)		8 (16.7)	8 (16.7)	
Osteoarthritis	1 (4.2)	4 (16.7)	0.156	5 (10.4)	2 (4.2)	0.435
Follow-up time, month	50.1 ± 14.1	56.7 ± 10.5	0.071	53.5 ± 12.8	50.5 ± 28.0	0.508

Data are expressed as mean ± standard deviation, ratios or number (%).

PRP, platelet-rich plasma; SLAP, superior labrum anterior to posterior lesion; SLBC, SLAP and long head tendon of biceps pathologies.

Table 2. Healing failure rate in the PRP only group and Booster injection group at 1 year after rotator cuff repair

	Tear size	PRP group			Overall PRP group (n = 48)	Control group (n = 48)	p value
		PRP only (n = 24)	Booster injection (n = 24)	p value			
Healing failure, Yes: No (%)	Overall	2:22 (8.3)	4:20 (16.7)	0.383	6:42 (12.5)	14:34 (29.2)	0.038*
	≤ 2 cm	1:8 (11.1)	1:7 (12.5)	0.929	2:15 (11.8)	4:16 (20.0)	0.498
	> 2 cm	1:14 (6.7)	3:13 (18.8)	0.316	4:27 (12.9)	10:18 (35.7)	0.040*

Data are expressed as ratios (%)

PRP, platelet-rich plasma

* statistically significant

Table 3. Preoperative and postoperative functional outcomes of the PRP and control groups

		PRP group (n = 48)			Overall PRP group (n = 48)	Control group (n = 48)	p value
		PRP only (n =24)	PRP booster injection (n =24)	p value			
Pain, VAS	Preoperative	6.3 ± 2.1	5.6 ± 2.5	0.320	5.9 ± 2.3	6.6 ± 2.0	0.135
	Final FU	0.3 ± 0.8	0.8 ± 1.4	0.142	0.5 ± 1.1	1.3 ± 1.8	0.016*
	p value	< 0.001*	< 0.001*		< 0.001*	< 0.001*	
Satisfaction, VAS	Final FU	9.3 ± 1.3	9.1 ± 1.1	0.771	9.2 ± 1.2	8.6 ± 1.7	0.023*
Forward flexion, °	Preoperative	144.6 ± 23.1	152.3 ±20.0	0.273	148.4 ± 21.7	141.3 ± 39.2	0.737
	Final FU	160.8 ± 8.3	158.8 ± 26.3	0.178	160.0 ± 19.3	162.0 ± 13.5	0.854
	p value	0.006*	0.320		0.009*	0.001*	
External rotation, °	Preoperative	46.0 ± 15.5	51.3 ± 16.0	0.257	48.7 ± 15.8	52.0 ± 18.5	0.395
	Final FU	67.1 ± 12.7	71.3 ± 12.6	0.260	69.2 ± 12.7	71.4 ± 18.6	0.261
	p value	< 0.001*	< 0.001*		< 0.001*	< 0.001*	
Internal rotation, vertebral level	Preoperative	T10.8 ± 3.0	T9.7 ± 2.6	0.187	T10.3 ± 2.8	T9.8 ± 3.0	0.338
	Final FU	T8.5 ± 1.3	T8.4 ± 1.5	0.678	T8.5 ± 1.4	T8.4 ± 1.8	0.860
	p value	0.001*	0.019*		< 0.001*	0.009*	
Constant score	Preoperative	48.4 ± 9.9	55.1 ± 12.9	0.052	51.8 ± 11.9	46.9 ± 20.4	0.359
	Final FU	72.2 ± 3.3	71.3 ± 8.0	0.207	72.0 ± 6.1	69.9 ± 5.6	0.420

	p value	< 0.001*	< 0.001*		< 0.001*	0.017*	
ASES score	Preoperative	49.6 ± 19.9	51.5 ± 20.3	0.748	50.5 ± 19.9	44.8 ± 26.8	0.497
	Final FU	97.6 ± 4.8	92.9 ± 10.9	0.148	95.2 ± 8.6	90.0 ± 8.5	0.060
	p value	< 0.001*	< 0.001*		< 0.001*	0.003*	
SST score	Preoperative	3.9 ± 3.2	5.1 ± 3.3	0.204	4.5 ± 3.3	3.6 ± 2.6	0.164
	Final FU	11.2 ± 1.7	10.6 ± 1.8	0.128	10.9 ± 1.7	9.4 ± 2.4	0.185
	p value	< 0.001*	< 0.001*		< 0.001*	0.001*	

Data are expressed as mean ± standard deviation.

PRP, platelet-rich plasma; VAS, visual analogue scale; T, Thoracic vertebra; ASES, American Shoulder and Elbow Surgeons; SST, Simple Shoulder Test

Table 4. Postoperative clinical outcomes according to healing failure

	Intact	Healing failure	p value
Pain, VAS	1.0 ± 1.9	2.4 ± 2.6	0.004*
Satisfaction, VAS	8.7 ± 1.5	6.1 ± 3.5	0.001*
Forward flexion, °	162.4 ± 12.4	150.9 ± 26.7	0.041*
External rotation, °	68.1 ± 16.9	61.9 ± 19.2	0.176
Internal rotation, vertebral level	T8.0 ± 2.5	T8.5 ± 3.9	0.384
Constant score	68.9 ± 7.8	62.5 ± 8.2	0.002*
ASES score	89.4 ± 19.8	68.7 ± 33.7	0.013*
SST score	10.3 ± 2.9	7.9 ± 4.8	0.097

Data are expressed as mean ± standard deviation.

VAS, visual analogue scale; T, Thoracic vertebra; ASES, American Shoulder and Elbow Surgeons; SST, Simple Shoulder Test

국문 초록

배경: 혈소판 풍부 혈장 (Platelet Rich Plasm, PRP)은 회전근 개 유합을 향상시키기 위하여 수술적 치료와 함께 보조 치료로 최근 많이 사용되고 있지만, 어떠한 환자에서 어떻게 PRP를 적용시키는 것이 적절할 지에 대한 표준화된 지침에는 논란이 많다.

목적: 회전근 개 파열로 복원술을 시행하는 환자를 대상으로, 수술 중에 회전근 개의 봉합 부위에 PRP를 적용하는 것과, 추가로 수술 후 2주에 PRP를 초음파 유도하에 봉합 부위에 주사하는 것이, 회전근 개의 수술 후 유합을 향상시키는 지 알아보고자 하였다.

방법: 회전근 개 파열 진단 하에 수술적 치료를 시행한 환자 58명을 대상으로 수술 중 PRP를 수술 부위에 적용하였고, 이중 29명의 환자를 무작위로 배정하여 수술 후 2주째 초음파 유도 하에 회전근 개 봉합부위에 PRP를 주사하였다. PRP치료를 받지 않은 대조군은 성향점수법으로 1:1 매칭하였다. 회전근 개의 유합은 수술 후 1년에 MRI을 사용하여 판단하였고, 수술 후 최소 2년 이후에 통증과 수술에 대한 만족도를 Visual Analogue Scale (VAS)을 통해서 평가하였다. 아울러, 견관절 기능 평가를 위하여 관절 운동범위, Constant score, American Shoulder and Elbow Surgeons Shoulder Score, Simple Shoulder Test score를 사용하였다.

결과: 회전근 개 파열의 크기가 2 cm 이상인 환자에서 유합 실패율은 PRP를 수술 중에 주입한 군에서 대조군보다 유의하게 낮았다 (12.9 % vs 35.7 %; p = 0.040). 하지만, 수술 후 2주에 추가로 PRP를 추가로 주사한 군이 더 좋은 유합을 보이지는 않았다 (6.7 % vs 18.8 %; p = 0.316). 최종 추시 때의 통증은 PRP군이 대조군에 비해 유의하게 낮았고 (0.5 ± 1.1 vs 1.3 ± 1.8; P = 0.016), 수술 후 만족도는 의미있게 높았다 (9.2 ± 1.2 vs 8.6 ±

1.7; P = 0.023). 하지만, 수술 후 기능 평가 점수는 모든 군에서 유의한 차이는 없었다.

결론: 2 cm 이상의 회전근 개 파열 환자에서 수술 중 회전근 개 봉합 부위에 PRP를 주입하는 것은 회전근 개의 유합을 향상시키며 수술 후 통증과 만족도를 증가시키지만, 수술 후 추가로 주사하는 PRP는 추가적인 이득이 없는 것을 확인할 수 있었고, 이는 향후 PRP를 이용한 치료 방침 결정에 중요한 계기가 될 것으로 생각한다.

주요어 : 혈소판 풍부 혈장, 회전근 개 파열, 회전근 개 파열의 생물학적 치유, 혈소판 풍부 혈장의 임상 결과
학번 : 2019-26451