Contribution of platelet-rich plasma to the surgical treatment of rotator cuff tear: An experimental study

IOANNIS ANGELOS TRANTOS[1], ELIAS S. VASILIADIS[2], FILIPPOS S. GIANNOULIS[3], LOUKIA FRAGKOPOULOU[4] and SPYROS G. PNEUMATICOS[2]

[1]Second Department of Orthopaedic Surgery, Gennimatas General Hospital of Athens, 11527 Athens, Greece;
[2]Third Department of Orthopaedic Surgery, University of Athens, KAT Hospital, 14561 Athens, Greece;
[3]Hand, Upper Extremity and Microsurgery Department, 'Hygeia' Hospital, 15123 Athens, Greece;
[4]Department of Radiology, KAT Hospital, 14561 Athens, Greece

Received February 10, 2026; Accepted July 29, 2026

DOI: 10.3892/br.2026.2187

Abstract. Shoulder rotator cuff tears are a common condition, which under specific indications is treated with arthroscopic repair. The optimal treatment aims at alleviating shoulder pain, the return of shoulder functionality and the prevention of recurrence of symptoms. The aim of the present study was to investigate and describe the augmentation of arthroscopic repair of rotator cuff tears with platelet-rich-plasma (PRP) treatment postoperatively, and its effects on pain, shoulder functionality and risk of retear. A total of 51 patients were divided into two groups. The treatment group received a subacromial PRP injection in the direct postoperative period after arthroscopic repair of rotator cuff tears, while the control group underwent arthroscopic treatment alone. There was no statistically significant difference in the verbal numeric rating score at 30 days postoperatively and the Constant-Murley and American Shoulder and Elbow Surgeons shoulder scores at 3, 6 and 12 months postoperatively between the two groups. However, the patients in the treatment group exhibited a statistically significant improvement of both scores between the 3- and 6-month timepoints, which was not observed in the control group. A smaller portion of the treatment group had rotator cuff retears compared with the control group (42.86 vs. 75.00%), although this was not statistically significant. It has not yet been adequately established that PRP treatment can provide additional benefits when combined with surgical treatment of rotator cuff tears. Further research with larger sample sizes may provide sufficient data concerning a possible protective effect on the postoperative retear risk. The trial has been registered on ClinicalTrials.gov under number NCT07689383 (submission date, July 1, 2026) and can be accessed at: clinicaltrials.gov/study/NCT07689383?term=NCT07689383&viewType=Card&rank=1.

Correspondence to: Dr Ioannis Angelos Trantos, Second Department of Orthopaedic Surgery, Gennimatas General Hospital of Athens, Mesogeion Avenue 154, 11527 Athens, Greece
E-mail: john.aggelos@gmail.com

Abbreviations: ASES, American Shoulder and Elbow Surgeons; A-PRF, advanced platelet-rich fibrin; CGF, concentrated growth factor; CLES, common language effect size; ES, (standardized) effect size; NRS, numerical rating scale; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; TIMP, tissue inhibitor of metalloproteinases; VNRS, Verbal Numerical Rating Score

Key words: arthroscopy, growth factors, PRP, rotator cuff tears, shoulder injuries

Introduction

Shoulder rotator cuff tears, as a result of the degenerative process of tendinopathy or traumatic events, are a common condition that may cause shoulder pain and disability. The portion of the population older than 60 years of age with some form of rotator cuff injury is estimated to be about 30% (1). Treatment options vary from conservative, noninvasive, including a recovery program, to more invasive procedures such as shoulder injections and surgery. There is still debate concerning the ideal choice and timing of every treatment. A systematic review showed limited evidence that surgery is more effective in treating rotator cuff tear than conservative treatment alone (2). The patient's age and activity level, the tear's mechanism, and the tear's size and anatomic position are among the factors that determine the surgical treatment of such tears. According to Dunn *et al* (3), patients' expectations concerning the success of physical therapy are the strongest predictor of the need for surgery, along with activity level and smoking. Although surgical repair-whether arthroscopic or mini-open-is the standard approach, it is associated with concerningly high rates of retear and recurring symptoms. Reported postoperative retear rates range widely, reaching up to 70% (4), and as high as 96% in cases of massive tears (5). While patients with structural failure often experience significant relief from pain, they frequently report persistent weakness and varying levels of functional impairment (6).

Surgical failure can be influenced by numerous factors, including the patient's age, body mass, underlying conditions like diabetes, smoking habits, physical activity history, as well as characteristics of the tear-such as its size, type, and location.

Other contributing elements include the surgical technique used, tendon quality, the extent of fatty infiltration, the local biological environment for healing, the degree of tendon retraction and chronicity of the tear, any prior or simultaneous surgeries, and the postoperative rehabilitation process (7). It has to be noted that a case control study of 603 patients identified the following independent patient risk factors for poor rotator cuff healing after surgical repair: age of older than 70 years at the time of surgery, tear size in anteroposterior dimension and preoperative tendon retraction, fatty infiltration of infraspinatus muscle, low bone mineral density and high level of work activity (8). To reduce failure rates, it is essential to identify and address the 'weak links' within the current standard of care. Biomechanical research has shown that modern suture configurations are capable of withstanding forces greater than those typically imposed upon the rotator cuff tendons (9). However, the primary biomechanical 'weak link' appears to be the tendon's limited capacity for biological healing. The resulting scar tissue lacks the tensile strength of healthy tendon, making it more susceptible to retear (10). As Castricini *et al* (11) have pointed out, the rotator cuff shows a limited healing capacity at its humeral insertion following repair. This may not only be due to the poor vascular supply of tendon tissue but also because of histopathological changes that occur after rupture-such as elevated levels of metalloproteinases and their inhibitors, tissue inhibitor of metalloproteinases (TIMP)-1 and TIMP-2 (12).

The investigation and clinical implementation of biological systems that facilitate tendon repair processes have become increasingly significant, with particular emphasis on the role of growth factors. Platelet-rich plasma (PRP), an autologous blood-derived product, is characterized by a high concentration of growth factors and bioactive cytokines, including vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and epidermal growth factor (EGF) (13). These molecules contribute to the modulation of inflammation and the enhancement of tissue regeneration by promoting cellular migration, proliferation, angiogenesis, and extracellular matrix synthesis (14).

The methodology for producing platelet-rich plasma (PRP) varies considerably and remains largely unstandardized. Differences in several key factors-including the type of preparation kits and centrifugation protocols used (often applied directly at the point of care), the method of blood collection and its handling during processing, as well as the concentration of fibrinogen and the dynamics of fibrin polymerization-result in a wide range of PRP formulations. These formulations differ in their cellular and molecular composition, texture, and biological activity, which may, in turn, influence therapeutic outcomes (15). PRP can be broadly categorized based on leucocyte content into pure (leucocyte-poor) and leucocyte-rich types, and by physical consistency into liquid plasma or gel-like fibrin forms. Furthermore, PRP may be administered in an activated state-typically through the addition of autologous thrombin and/or calcium-or in a non-activated state.

The use of platelet-rich plasma (PRP) to enhance tendon healing has been explored in various contexts, including the treatment of tendinopathies affecting the patellar, Achilles, and lateral elbow tendons (16). However, with regard to rotator cuff tears, there remains a lack of scientific consensus on the clinical efficacy of PRP therapy, and its application is not currently included in the American Academy of Orthopaedic Surgeons guidelines (17). It is important to acknowledge that the centrifugation process involved in PRP preparation may also concentrate potentially deleterious agents. Moreover, the PRP products contain numerous platelet growth factors and cytokines, each with their own diverse cell sources, functions and effects (18). Consequently, further research is required to elucidate how patient-specific factors influence clinical outcomes and to determine the impact of varying PRP formulations on therapeutic efficacy (19).

The purpose of this study is to examine whether an intraarticular shoulder injection of PRP in the early postoperative period after arthroscopic rotator cuff repair offers any advantage concerning pain and functional results, as well as possible tendon retears, compared to standard arthroscopic repair alone. The primary question of the study is whether there is a difference in clinical results, as measured in Constant - Murley and American Shoulder and Elbow Surgeons (ASES) scores between the group of patients treated with arthroscopic repair augmented with postoperative PRP treatment and the group of patients treated with standard arthroscopic repair. The secondary question of the study is whether there is a difference in postoperative retear rates six months to twelve months postoperatively between these two groups. Our hypothesis is that PRP treatment would lead to better results concerning both questions mentioned above, based on our meta-analysis of similar recent studies (20).

Materials and methods

Trial design and eligibility criteria. This study was a randomized, prospective clinical trial in a hospital environment, followed by clinical and imaging follow-up in an outpatient setting. The patients enrolled had symptomatic rotator cuff tears, which were confirmed by magnetic resonance imaging (MRI). The study was approved by our hospital's institutional review board. They had failed previous conservative management and physical therapy of at least 3 months and were candidates for surgical treatment. The age of eligible patients could be between 18 and 79 years. The exclusion criteria were: (a) acute shoulder trauma, (b) any history of a previous surgical operation on their shoulder, (c) the local administration of corticosteroids up to fifteen days before the operation or systemic administration of corticosteroids up to a month before the operation, (d) the use of non-steroidal anti-inflammatory drugs during the trial, (e) any signs of infection or systematic inflammatory disease for at least fifteen days before the operation, (f) history of malignancy or chemotherapy during the previous year, (g) rotator cuff arthropathy with glenohumeral osteoarthritis and superior migration of the humeral head, (h) pregnancy or breastfeeding, and in case of any of these conditions the patients where ultimately excluded from the trial results. All patients gave written informed consent to participate in the trial.

Randomization procedure and allocation concealment. The patients were randomly assigned either to group A (treatment)

or group B (control) of the trial. The randomization method that was followed was simple randomization. Since the initial research planning included 50 patients, all numbers from 1 to 50 were randomly drawn and allocated to either the treatment or the control group by a member of our research group different from the researcher recruiting the patients. Since the participants of the research were not recruited simultaneously, each was given a sequential number based on the timing of the recruitment (the first patient took number 1, the second number 2 etc.) and were allocated to each group accordingly. After the first 50 patients were recruited, the same procedure was repeated for another 50 numbers, and the 51st patient was allocated to a group in this manner. The researcher who recruited the patients informed them about the study and examined them preoperatively in order to determine the baseline clinical scores the day before the operation was different than the operating surgeon. This researcher was not present at the allocation procedure and was informed about each patient's assignment to a group after the pre-operative examination, in order to implement allocation concealment and reduce the risk of selection bias. The randomization procedure was not stratified according to patient demographics or tear characteristics (such as size or shape in MRI imaging) and no digital randomization software was used.

Intervention details. The patients of both groups underwent arthroscopic repair of the rotator cuff by the same surgeon, who was blinded to the specific patient assignment. All patients received general anesthesia and were operated on in the 'beach chair' position. The patients of group A were administered a single intraarticular PRP injection in the operated shoulder at 10-15 days postoperatively. The patients of both groups otherwise received the same postoperative instructions and followed the same postoperative protocol. This protocol included using a shoulder sling with no active range of motion for four weeks, followed by a rehabilitation program of progressive active-assisted, active range of motion and muscle strengthening for two months.

Concerning the arthroscopic rotator cuff repair, systematic glenohumeral joint and subacromial exploration were performed, and lesions were managed as necessary. In each case, after the frayed and atrophied torn end was removed, the rotator cuff tear was carefully evaluated, and anteroposterior size, mediolateral retraction, number of involved tendons, visual tendon grade, excursion, and presence of the subscapularis tear were assessed. 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 suture anchors that were inserted through the accessory portal.

The PRP injected was prepared with the kit of Swiss Plasma Biotech® and an EBA 200® centrifuge. The anticoagulant used was Acid Citrate Dextrose Solution - A, a product commonly used in PRP preparation. Its main components are calcium gluconate, sodium citrate and dextrose. The tubes also contained a thixotropic gel, which was already prepared by the manufacturer. No further addition was made to the PRP product in order to activate it. An autologous sample of 9 ml of peripheral blood was collected, and after preparation with a relative centrifugal speed of 3,600 for 6 min, 4 ml of PRP was received and injected intraarticularly in a subacromial fashion. The part of the product of the centrifuge process that was extracted for injection was that of leucocyte-poor PRP. Our initial study design did not include the specific laboratory testing of each sample of the PRP product administered, which was prepared on-site after receiving blood from the patients. The volume of blood received was limited and the total amount of PRP produced in each session was administered to the patients. The fraction of the centrifuge product utilized was drawn manually, as per the protocol originally described by Anitua (21). In specific, after centrifugation of the patients' peripheral venous blood sample, the product typically contains three distinct layers: the lower layer rich in red blood cells, the middle 'buffy coat' and the higher layer of mainly acellular plasma. The buffy coat typically appears as a whitish layer and comprises the majority of the leucocytes. The upper part of the acellular plasma layer, designated plasma poor in growth factors (PPGF), was carefully aspirated and discarded from each tube using a pipette, with care taken to minimize turbulence. The remaining plasma fraction, referred to as plasma rich in growth factors (PRGF), was then collected by pipetting, with the collection volume determined by visual inspection. Afterwards, the patients were injected with this fraction of the centrifuge product. This technique is expected to produce a leucocyte-poor PRP product (15). The patients were not blinded and the patients of group B did not have any blood drawn.

Follow-up and outcome measurements. The patients of both groups had the same follow-up examinations. They were questioned about pain on a Numerical Rating Scale (NRS) of 0 to 15 at 1 month postoperatively. A thorough clinical examination with the calculation of Constant - Murley [as was translated and culturally adapted in Greek by Ntourantonis *et al* (22)] and ASES scores were performed at 3, 6 and 12 months postoperatively by the same examiner for all patients. In addition, the patients underwent a shoulder MRI examination at 6 months postoperatively, to assess the healing status of the rotator cuff tendons. The postoperative MRI imaging was assessed and compared to the preoperative MRI imaging concerning the anatomic location and size of both the original and a possible residual tear or the presence of any new rotator cuff tears. In addition, the degree of fatty degeneration of the rotator cuff muscles was assessed for each patient. The fatty degeneration was marked as 'notable' when it was greater or equal to stage 3 according to the Goutallier classification (23) (grade 0: normal muscle; grade 1: fatty streaks; grade 2: more muscle than fat; grade 3: equal amounts of fat and muscle; and grade 4: more fat than muscle). All MRIs were assessed by the same radiologist, who was blinded concerning the patients' group allocation.

Statistical analysis. The statistical analysis was performed using the Mann - Whitney U test for the comparison of ASES, Constant-Murley and VNRS scores among groups and Fisher's exact test for the assessment of the retear rates and fatty degeneration, with software tools from website statskingdom.com (accessed 16.4.2026). Normality of the samples was assessed using the Shapiro - Wilk test when using the Mann - Whitney U test. Outliers were identified based on Tukey's fences method

Table I. Demographics of patient groups.

Patient characteristics	Total	Conventional treatment	PRP treatment
Male, n	24	11	13
Female, n	27	15	12
Mean age, years	58.31	57.65	59.00
Right/left-sided, n	34/17	17/9	17/8
Isolated supraspinatus tear, n	37	17	20
Tear of two or more tendons (including supraspinatus), n	14	9	5

Numbers of male and female patients, dominant hand and mean age values for each group. PRP, platelet-rich plasma.

(k=1.5) and were included in all calculations concerning the ASES, Constant-Murley and verbal numerical rating score (VNRS) scores. The data processed using Fisher's exact test was also assessed with the chi-square test of independence, which did not produce a different result concerning the statistical significance of the differences observed among the groups.

Results

Patient demographics and lesion characteristics. A total of 51 patients were enrolled in this study, during three years, from November 2021 until September 2024. The control group originally consisted of 26 patients and the treatment group of 25 patients. In addition, two patients were approached for participation in the study, but one refused to participate and another was proven to be ineligible, because of a lumbar spinal fracture which occurred 9 days after the operation. Furthermore, three patients dropped out of the study before the first follow-up or PRP treatment, of which one was allocated to the control group and two to the treatment group. 24 patients were men (11 at the control and 13 at the treatment group) and 27 (15 at the control and 12 at the treatment group) were women. The age of the patients at the time of operation varied from 35 to 79 years. The average patients' age of the control group was 57.65 years and the treatment group 59 years, and there was no statistically significant difference between the two groups concerning gender composition or mean age. Specific data on other patient comorbidities that were not registered as exclusion criteria for participation in the study was not documented and analyzed statistically, as their correlation to rotator cuff healing was beyond the scope of this study. Concerning the anatomic location of rotator cuff tears according to the preoperative MRI imaging, the majority of the patients suffered from isolated supraspinatus tears (17 patients in the control group and 20 patients in the treatment group). A smaller portion of the patients had tears of 2 or more rotator cuff tendons, all of which included the supraspinatus (9 patients in the control group and 5 patients in the treatment group). No statistically significant difference between the two groups was observed concerning this characteristic as well (Table I). All of the patients in both groups had full thickness tear sizes and no patients with partial-thickness tears were included in our study. Tear size was not specifically measured and documented for each patient.

Table II. Baseline clinical scores and postoperative clinical results.

Variables	Conventional treatment	PRP treatment	P-value
Constant-Murley score			
Preoperative	40.98±18.49	48.14±18.49	0.22
3 months	55.63±23.46	62.81±11.05	0.18
6 months	71.13±20.70	77.36±14.39	0.32
12 months	90.25±11.13	91.57±11.39	0.67
ASES score			
Preoperative	36.28±18.35	44.91±17.55	0.09
3 months	64.95±22.83	66.21±13.82	0.94
6 months	73.11±19.73	79.69±15.74	0.27
12 months	92.35±8.94	90.22±14.41	0.85
VNRS-15 score			
1 month	4.46±3.69	5.67±2.74	0.20

The mean Constant-Murley and ASES scores are presented for each patient group at baseline, and 3, 6 and 12 months postoperatively. Mean VNRS-15 scores at 1 month postoperatively are also shown. The P-values shown are for the comparison of the control and treatment groups and were calculated using the Mann-Whitney U test including all patients that were examined at each interval. ASES, American Shoulder and Elbow Surgeons; PRP, platelet-rich plasma; VNRS, verbal numerical rating score.

Clinical scores. The preoperative Constant-Murley and ASES scores were assessed the day before the operation for all patients. Excluding the patients who dropped out before the first follow-up or intervention, the average baseline Constant score of the control group was 40.98 and the treatment group was 48.14, a difference which was not statistically significant (P=0.22, standardized effect size, ES=0.18, common language effect size, CLES=0.4). The average baseline ASES scores were 36.28 for the control group and 44.91 for the treatment group, a difference which was also not statistically significant (P=0.09, ES=0.24, CLES=0.36).

At 30 days postoperatively, the patients were examined for shoulder pain and the VNRS score was assessed (24). The patients were asked to rate the intensity of the pain at the

Table III. Postoperative MRI results.

Variables	Total, n (n=15)	Conventional treatment, n (%) (n=8)	PRP treatment, n (%) (n=7)	P-value
Fatty degeneration	6	2 (25.00)	4 (57.14)	0.31
Retears	9	6 (75.00)	3 (42.86)	0.31

Number and percentage of patients with significant fatty degeneration of rotator cuff tendon (Goutallier grade III or higher) and retears at the repair site at 6 months after the operation for each group. The P-values shown are for the comparison of the control and treatment groups and were calculated using Fisher's exact test, including all the patients who underwent postoperative MRI imaging. PRP, platelet-rich plasma.

shoulder operated on, ranging from 0 ('no pain') to 15 ('worst pain imaginable'). The treatment group had an average VNRS score of 5.67, while the control group had a better score of 4.46. However, this difference was not statistically significant (P=0.20, ES=0.2, CLES=0.38).

At the follow-up examinations at 3 months postoperatively, the Constant-Murley and ASES scores of both groups had a statistically significant improvement from baseline (P=0.03, ES=0.33, CLES=0.69 for the Constant-Murley and P=0.0006, ES=0.53, CLES=0.19 for the ASES scores of the control group, P=0.01, ES=0.39, CLES=0.73 for the Constant-Murley and P=0.001, ES=0.53, CLES=0.19 for the ASES scores of the treatment group). There was no statistically significant difference between the two groups at any of the aforementioned clinical scores (P=0.18, ES=0.21, CLES=0.38 for the Constant-Murley score and P=0.94, ES=0.013, CLES=0.49 for the ASES). The average Constant-Murley score for the control group was 55.63 and for the treatment group 62.81 and the average ASES scores were 64.95 and 66.21 respectively. There was further improvement at 6 months postoperatively. The average Constant - Murley scores were 71.13 for the control group and 77.36 for the treatment group, with no statistically significant difference observed (P=0.32, ES=0.17, CLES=0.4), and the average ASES scores were 73.11 for the control group and 79.69 for the treatment group, with no statistically significant difference (P=0.27, ES=0.18, CLES=0.39). However, it has to be noted that although the further improvement of Constant-Murley scores from three to six months postoperatively was not statistically significant (mean score difference of 15.09, P=0.09, ES=0.3, CLES=0.32) for the patients of the control group who participated in both follow-up examinations, it was statistically significant for the treatment group (mean score difference of 15.37, P=0.006, ES=0.54, CLES=0.18). The same results were extracted for the ASES scores as well (mean score difference of 9.44, P=0.24, ES=0.21, CLES=0.38 for the control group and mean score difference of 13.85, P=0.03, ES=0.42, CLES=0.25 for the treatment group). At 12 months postoperatively, average Constant scores were 90.25 for the control and 91.57 for the treatment group with no statistically significant difference (P=0.67, ES=0.072, CLES=0.46). The average ASES scores were 92.35 for the control and 90.22 for the treatment group, with no statistically significant difference (P=0.85, ES=0.032, CLES=0.48). These results are summarized in Table II.

In addition, a posthoc sensitivity analysis of the statistical results was performed, where the effect of patient drop-outs, excluded patients and outliers was taken into account. Concerning the patients who dropped out or were excluded from the study, the intention-to-treat analysis showed no statistically significant difference between the two patient groups at baseline Constant - Murley and ASES clinical scores. However, when dropped-out and/or excluded patients were included in the baseline clinical scores, the Constant - Murley scores did not show statistically significant improvement from baseline at 3 months postoperatively for the control group. It should be noted that the p values for these comparisons where barely above the 0.05 threshold in these calculations (P=0.055, ES=0.28, CLES=0.34 when drop-outs before the first follow-up where included, P=0.056, ES=0.27, CLES=0.34 when all excluded patients were taken into account at baseline scores). The rest of the results where robust, with no changes in statistical significance after the sensitivity analysis for patient drop-outs, exclusions and outlier values.

Postoperative imaging. Concerning the postoperative imaging of the patients' shoulders, there was a follow-up at 6 months postoperatively of a total of 15 patients, 8 from the control and 7 from the treatment group. Although the size of these groups was rather small, an interesting trend was observed after the investigation of postoperative re-tears at the suture area or different anatomic positions of the repaired tendons. In specific, six out of eight patients from the control group had postoperative tears (75%), while three out of seven patients from the treatment group had postoperative tears (42.86%). This difference was not statistically significant (P=0.31) as the sample size was small. It may also be noted that the patients from the control group had a notable fatty muscle degeneration at a lower rate than those from the treatment group (2/8 equaling 25% and 4/7 equaling 57.14%). The degree of degeneration was assessed in both pre- and postoperative MRI. A postoperative progress in Goutallier stage of fatty degeneration was not observed in any patient. These results are summarized in Table III.

Discussion

This trial attempts to add further data to the ongoing scientific research and discussion concerning biological treatments of shoulder rotator cuff conditions. There is an active scientific discussion concerning the use and the potential benefits of PRP treatment of several conditions in different anatomic areas. Two recent meta-analyses showed that PRP injections for the treatment of knee osteoarthritis produced positive results when compared to injections of hyaluronic acid (25),

as well as when they were combined with hyaluronic acid compared to PRP alone (26). Moreover, the augmentation of the suture repair of Achilles tendon rupture with platelet rich fibrin matrices improved the postoperative functional results, while there was a smaller increase of the tendon cross-sectional area (27). Quite a few studies have demonstrated good results concerning pain and functionality when PRP is utilized for the treatment of lateral epicondylitis of the elbow. In addition, there is scientific literature about PRP treatments of conditions including medial epicondylitis, biceps and triceps tendinopathy, injury of ulnar collateral ligament of the elbow, carpal tunnel syndrome, de Quervain's tenosynovitis, osteoarthritis of the hip, foot and ankle, wrist and sacroiliac joint, spine degenerative diseases, greater trochanteric bursitis of the femur, plantar fasciitis, Achilles tendinopathy and fracture non-union (28). Furthermore, recent research has shown that PRP may be used as part of the therapy process of certain non-musculoskeletal conditions, such as traumatic brain damage (29).

Several studies, where PRP has been applied for the conservative treatment of shoulder rotator cuff tears, have shown positive results concerning shoulder pain and function, as has been indicated by recent systematic reviews and/or meta-analyses (30-32). Giovannetti de Sanctis *et al* (30) reported that none of the examined treatment modalities-platelet-rich plasma (PRP), corticosteroid injections, or prolotherapy-demonstrated unequivocal superiority, as all interventions yielded statistically significant improvements from baseline across the studies reviewed. Nevertheless, PRP injections appeared to provide measurable long-term benefits compared to the other treatments, despite the difference in clinical scores being below the minimal clinically important difference. No significant differences were observed between treatments during short- and mid-term follow-ups. Furthermore, PRP consistently outperformed other interventions regarding shoulder function at all follow-up points evaluated (30).

It has not yet been adequately established that PRP treatment can provide additional benefits when combined with surgical treatment of full-thickness rotator cuff tears. A systematic review and meta-analysis of twenty-five clinical trials has shown that the combination of PRP injections and arthroscopic rotator cuff repair shows lower retear rates than arthroscopic repair alone. However, concerning the postoperative clinical scores, the statistically significant improvement of Constant-Murley, University of California, Los Angeles and Simple Shoulder Test scores were lower than the minimal clinically important difference and is therefore uncertain, if they represent a higher level of functional and activity level in the patients' everyday life (20). The results of the present study do not bolster these results, as no statistically significant improvement after the PRP treatment has been determined in any follow-up period compared to the control group. The only aspect of the study, in which an advantage of the PRP treatment was indicated concerning the clinical scores, was the statistically significant improvement of both scores from 3 to 6 months postoperatively. This result may indicate a prolonged healing process supported by the PRP injection. The protective effect of PRP against tendon re-tears was also not confirmed by the study with statistical significance, in the small number of patients that underwent a postoperative MRI. However, a strong positive trend was observed, as the retear rates in the control group were more than double those in the treatment group. It should be noted that since the patient's follow-up is still ongoing, a larger sample size may provide a result of statistical significance. In addition, the preoperative muscle degeneration rates were higher in the treatment group as observed in magnetic resonance imaging. Since muscle degeneration is an important cause of tendon repair failure (33), it can be argued that if the fatty degeneration rates were equal among the two groups, the measured difference of re-tear rates would have been even larger in favor of the treatment group.

It is understood that our study has certain limitations. First of all, the participants and the research team were not fully blinded to the allocation of the patients to either treatment or control group, since the patients of the control group did not receive any postoperative shoulder injection. This is a potential cause of a higher risk of observer bias, as well as self-report bias (34). Although a possible sham injection at the patients of the control group could protect our study from possible bias, it has to be noted that subacromial injections are not without risk of potential adverse effects. The adverse effects that have been reported in other studies concerning subacromial injections may vary and include mild and temporary symptoms such as dizziness, nausea, headache, hematoma at the injection site, increasing pain, a vasovagal reaction, and more severe conditions such as capsulitis and shoulder infection (35-37). Taking these into account, the decision was made to avoid a sham shoulder injection with saline in the control group. In addition, the randomization procedure was not stratified concerning clinical and imaging findings such as rotator cuff tear size and anatomic location, baseline pain and/or functional level. However, no statistically significant difference was reported in clinical scores between both groups, and sensitivity analysis for outliers showed that the results were robust concerning this aspect. In addition, in our study the sample of patients with tears in locations other than supraspinatus was small and diverse. The number of patients that had multiple tears was small (14 patients in total). In addition, this subgroup contained patients with tears of infraspinatus, teres minor, subscapularis and combinations of the above tears. As a result, stratification would lead to subgroups that would be too small to produce significant results. In a similar manner, stratification of patients according to specific tear size was not part of the original study design, as it would lead to very small sample sizes in each subgroup. As a result, it was not feasible to process the data in separate patient subgroups based on tear location and get any meaningful results and a possible multivariate analysis would be under-powered. Our study was not designed to incorporate further variates to our statistical analysis. However, the authors attempted to exclude possible confounding factors through the exclusion criteria for enrollment in the study. In specific, the exclusion of patients with previous shoulder trauma and/or surgical operations, present or recent infection, inflammatory disease, malignancy or under chemotherapy aims to exclude any patients, the general health and the local shoulder environment of whom may predispose them to inadequate tissue healing. In addition, patients under corticosteroid treatment were excluded, since corticosteroids have been associated with both spontaneous tendon rupture (38) and diabetes (39), which is a risk factor for postoperative failure of rotator cuff repair. Furthermore, patients with rotator cuff arthropathy,

glenohumeral osteoarthritis and superior migration of the humeral head are patients with large rotator cuff tears, severe tendon retraction and are generally considered ineligible for primary arthroscopic repair of the tendon tears due to high failure rates (40). As a result, such patients have been excluded from our study as well. In addition, no patients with osteoporosis (T-score -2.5 or lower) participated in our study, which is notable since low bone mineral density has been associated with poor postoperative rotator cuff healing (8). It also has to be noted that the study groups did not differ in a statistically significant manner concerning mean age, gender and anatomic tear location. Secondly, the size of the groups of our study may have been smaller than required to prove a potential effect of the treatment in a statistically significant degree. We recommend that future studies in this field take our findings into consideration when performing power analysis, in order to recruit sufficient number of patients for a sample size that may provide statistically significant results. This limitation of our study is most prevalent in the patient follow-up with postoperative MRI imaging, as certain patients would choose not to undergo a postoperative MRI, even though they were willing to continue the follow-up with clinical examinations. Patient claustrophobia and other anxiety linked to MRI scanning have been documented in several studies (41). The high rate of patient drop-out in this section of our study can be the reason for a high risk of bias due to missing data, as described by 'The Cochrane Handbook for Systematic Reviews of Interventions' (42). To our knowledge, the possible reluctance of certain patients to undergo a postoperative MRI is not clearly correlated to the therapeutic result. However, since the total number of patients who underwent MRI is rather small, such risk of bias cannot be excluded. In addition, it should be noted that our study was not restricted in specific rotator cuff tear size and/or shape and the allocation of patients to the study groups did not take into account the specific characteristics of their rotator cuff tears. To our knowledge, there is insufficient data in the literature so far to specify whether certain tear characteristics may benefit more from such treatments. However, there are indications that tear size is a factor to be considered, as in a meta-analysis by Xu and Xue (43) large to massive tear size was found to contribute to a significantly decreased retear rate for rotator cuff repair combined with PRP. The difference observed between the patient groups in the degree of fatty degeneration is another factor that may affect the study results concerning retear rates, pain and functional results. Fatty muscle degeneration is characterized by the accumulation of fat within and between muscle fascicles, although the exact underlying cellular mechanisms have yet to be fully investigated. It is well documented that a greater degree of muscle degeneration has an adverse effect on rotator cuff tendon healing and integrity (44). According to a study by Oh *et al* (45), the fatty degeneration of supraspinatus and infraspinatus is a predictor of potential failure of surgical repair. Interestingly, the fatty degeneration of infraspinatus was described as the most independent predictor of the postoperative integrity of the rotator cuff. In addition, a meta-analysis of 18 studies has demonstrated that fatty degeneration exerted the greatest adverse influence on tendon healing among all patient- and tear-related risk factors (46). In our study, since no visible progression of tendon degeneration was observed postoperatively, the difference between the two groups cannot be attributed to the administered treatment. It is a baseline difference between the two populations. As a result, one can suppose that had the baseline ratio of fatty degeneration been equal between the two groups, the trend towards lower postoperative retear rates in the treatment group could have reached statistical significance. Furthermore, we have to acknowledge that our study design included specific clinical scores and imaging examinations, and a choice of different measurable results, such as different quality-of-life scales or a more detailed biomechanical assessment of shoulder strength and range of motion pre- and postoperatively could hypothetically have produced data of statistical and clinical significance. It should also be noted that any statistically significant results should be correlated with the minimum clinically important difference for any relevant scale and/or score used, in order to examine whether they represent a significant improvement of the patients' status.

In our opinion, the general hypothesis that an autologous product rich in growth factors, cytokines and extracellular vesicles (47) may promote postoperative healing and accommodate rehabilitation and return of function may have not yet been rejected. PRP contains a huge array of different cells and growth factors, and the possibilities of utilizing it in treatment of different conditions have not yet been fully studied. It is understood that platelets, platelet-adhesive molecules and leucocytes contained in PRP have a pivotal role in modulation of the immune response, both innate and adaptive. In addition, platelets are involved in regulation of serotonin (5-hydroxytryptamine, 5-HT), which has a critical role in the central nervous system, including pain tolerance and in different paracrine and autocrine mechanisms. Furthermore, the components of PRP have been shown to have analgesic effects and promote angiogenesis (18). The choice of the correct biological therapy may be critical, as different autologous platelet concentrates can have different characteristics. First of all, the exact composition of PRP products can vary to a measurable degree. It is under discussion, whether gel-like fibrin or liquid plasma has superior results, as well as whether leucocyte-poor or leucocyte-rich PRP is preferable. Furthermore, there is a lack of a comprehensive classification system of PRP with wide scientific consensus (18). As highlighted by Barber (48), platelets primarily enhance anabolic signalling, whereas leucocytes contribute to catabolic signalling. This distinction arises because leucocyte-rich PRP contains elevated levels of matrix metalloproteinase-9 and interleukin-1β, both of which are inflammatory catabolic mediators potentially harmful to tendon repair. Increased inflammatory responses, as well as increased angiogenesis have been observed seven days following treatment with leucocyte-rich PRP in comparison to leucocyte-poor PRP in rat models (49). Furthermore, preparations with higher leucocyte concentrations have been associated with less favourable clinical outcomes (50), manifesting as greater early disruption of tendon architecture, increased vascularity, and fibrosis. These findings suggest that leucocyte-poor PRP may provide superior conditions for tendon healing. Such an approach can be supported by a 2020 consensus statement by French-speaking experts (51), where leucocyte-poor PRP was recommended for the treatment of knee osteoarthritis,

although the recommendation achieved relative agreement. Under the light of this information, a PRP without a high leucocyte count was preferred for the assessment of tendon healing in our study. The PRP product that was used in our study is expected to fall under the leucocyte-poor category based on the preparation technique. However, laboratory testing of cell concentration and specific composition of each dosage was not performed to have more specific data. On the other hand, there are studies in the literature with results that are conflicting to the above data. An example is the studies analyzed by Chen (19), which show improved results in the Constant-Murley score for leucocyte-rich PRP, with otherwise no statistical differences between the results after the administration of leucocyte-poor and -rich PRP. Secondly, it has been demonstrated that PRP, platelet-rich fibrin and 'advanced' platelet-rich fibrin (which is centrifuged at lower speeds for a longer time period) differ in growth factor release. In a study conducted by Kobayashi *et al* (52), platelet-rich plasma (PRP) was shown to release significantly higher concentrations of growth factors at early time points, whereas platelet-rich fibrin (PRF) and advanced platelet-rich fibrin (A-PRF) exhibited a more sustained release of growth factors over a period of up to ten days. Notably, the newer A-PRF formulation released significantly greater total amounts of growth factors compared to traditional PRF (52). Similarly, research by Masuki *et al* (53) demonstrated that both A-PRF and concentrated growth factor (CGF) extracts contained comparable or higher platelet and platelet-derived growth factor levels than PRP. Additionally, *in vitro* assays revealed that both A-PRF and CGF extracts significantly promoted the proliferation of human periosteal cells, maintaining efficacy even at higher concentrations without notable cytotoxicity (53). A quite interesting study by Chevrier *et al* (54) in large animals (ewes) using chitosan-PRP had positive results regarding rotator cuff tendon healing and the product's safety. Unfortunately, a lot of the studies in the literature do not provide enough information on their protocols for preparation of PRP, making protocol reproducibility and PRP product comparison difficult. We have to acknowledge that measuring specific cell and cytokine count of the PRP product used in such studies may provide interesting results, as it could help correlate any clinical findings to the cellular and molecular level. It could be stated that the fact that such data could not be extracted in our study is a weakness of the present study. Unfortunately, to our knowledge, most of similar studies have not reported such data. As an example, out of the 28 studies assessed in a meta-analysis published in 2023 (20), only 4 performed a laboratory test of platelets and white blood cells of the PRP product administered to the patient.

Another important consideration when comparing *in vivo* and *in vitro* studies is the variability in growth factor concentrations among different donors. Moreover, given the growing aging population increasingly undergoing regenerative treatments, it is anticipated that this variability will be further amplified due to factors associated with advanced age, including a higher prevalence of systemic diseases and concomitant medication use (52).

In addition, a prolonged postoperative healing process may require a longer therapeutic scheme than the single-dosage scheme that we have utilized. It has been indicated that multiple PRP injections are more effective than one injection for the treatment of knee osteoarthritis (55-57). To our knowledge, such data on shoulder PRP injections may be scarce and it would be worth investigating multiple dosage schemes. The disadvantage of this strategy is that it would further increase the overall therapy cost. In a meta-analysis and cost-effectiveness analysis by Vavken *et al* (50), it has been estimated that although PRP treatment may reduce retear rates of small- and medium-sized tears, its use is not cost-effective concerning its clinical benefits. As this analysis refers to the costs and prices in the United States of America (USA) more than a decade before the submission of this article (2013), this aspect needs to be taken into account by future studies, in order to determine the clinical value of such treatments. Another factor to be taken into account was the timing of the PRP treatment in accordance to the surgical repair of the rotator cuff. In a recent systematic review and meta-analysis (20) of studies assessing the PRP augmentation of surgical repair of rotator cuff tear, all of the 25 studies administered the PRP products either intraoperatively or within the first two weeks of surgery. More specifically, the majority of the reviewed studies (22 of 25 trials) employed a single-dose treatment protocol, with the biologic product administered intraoperatively following tendon repair and prior to wound closure through the arthroscopic portals. In one study, an additional postoperative dose was administered one week after surgery. Another study investigated the effects of a single dose administered 10-14 days postoperatively, whereas a separate trial evaluated a two-dose PRP regimen delivered at one and two weeks following the surgical procedure. This timing can be justified by the necessity to administer the treatment before the completion of the proliferative stage (which lasts from the first to the third week after injury or surgical repair) and the beginning of the tissue remodeling stage of tendon healing (four weeks after injury or surgical repair), as they are described in the literature (58). The timing of the postoperative MRI imaging is another factor to be taken into consideration. A systematic review and meta-analysis by Longo *et al* (59) showed postoperative rotator cuff retear rates of 15% at 3 months follow-up, 21% at 3-6 months follow-up, 16% at 6-12 months follow-up, 21% at 12-24 months follow-up, 16% at follow-up longer than 24 months. Based on these findings, imaging follow-up to assess retears seems plausible at either approximately 6 months postoperatively, as was performed in our study, or between the first and the second year after arthroscopic repair. To the authors' knowledge, there are no clinical studies that directly compare dosage schemes and timing of PRP treatment for rotator cuff pathology. As a result, the data available is too heterogeneous to have clear guidelines on the optimal treatment protocol. Since our protocol has not shown clear advantages over different protocols from previous trials, we cannot advocate for the protocol chosen over intraoperative injections, different timing or multiple injections. Since the data available is rather inconclusive, further research on the subject with high-quality studies is necessary. Furthermore, it has to be noted that the follow-up results in this study are limited to twelve months postoperatively. A continuation of the follow-up to 24 months postoperatively

is ongoing and may provide further interesting data to be published in the future.

In conclusion, the results of the present study are not sufficient to confirm that PRP augmentation of arthroscopic rotator cuff repair provides significant advantages on the clinical outcome when compared to the standard arthroscopic cuff repair. As a result, the existing evidence cannot yet sufficiently support the standardizing of PRP augmentation of rotator cuff repair. However, certain aspects of our study leave room for optimism on the matter, as the patients treated with PRP showed a trend towards less new rotator cuff tears in the postoperative period. In addition, a prolonged period of statistically significant improvement was observed on the treatment group between three and six months postoperatively. Additional, thoroughly organised future studies with larger patient samples and adequate follow-up that take into account tear characteristics, different PRP compositions, treatment timing and/or dosage schemes may provide definite results.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ESV and IAT conceived and designed the study. SGP and ESV provided the methodological framework and theoretical rationale of the study. IAT utilized the software tools required for the study. ESV, FSG, LF and IAT validated and interpreted the study results and were involved in producing the relevant conclusions. IAT oversaw the formal statistical analysis. FSG, LF and IAT collected the study evidence on site and participated in the patient interventions and the clinical examinations. FSG, LF and IAT collected and organized the resources for the study. IAT organized and archived the data relevant for the study. IAT prepared the original draft of the article. SGP, ESV, FSG and LF reviewed and edited the manuscript. IAT prepared all charts and tables relevant to the study. SGP had the overall scientific supervision of the study. SGP and ESV had administrative roles in the project. ESV and IAT confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Scientific Board (13th meeting/20-05-2021) and the Administrative Board (18th meeting/08-06-2021) of KAT General Hospital (Athens, Greece). Informed written consent was obtained from all subjects involved in the study for participation.

Patient consent for publication

Informed written consent was obtained from all subjects involved in the study for publication of the study.

Competing interests

The authors declare that they have no competing interests.

References

1. Teunis T, Lubberts B, Reilly BT and Ring D: A systematic review and pooled analysis of the prevalence of rotator cuff disease with increasing age. J Shoulder Elbow Surg 23: 1913-1921, 2014.
2. Ryösä A, Laimi K, Äärimaa V, Lehtimäki K, Kukkonen J and Saltychev M: Surgery or conservative treatment for rotator cuff tear: A meta-analysis. Disabil Rehabil 39: 1357-1363, 2017.
3. Dunn WR, Kuhn JE, Sanders R, An Q, Baumgarten KM, Bishop JY, Brophy RH, Carey JL, Harrell F, Holloway BG, *et al*: 2013 Neer Award: Predictors of failure of nonoperative treatment of chronic, symptomatic, full-thickness rotator cuff tears. J Shoulder Elbow Surg 25: 1303-1311, 2016.
4. Galatz LM, Ball CM, Teefey SA, Middleton WD and Yamaguchi K: The outcome and repair integrity of completely arthroscopically repaired large and massive rotator cuff tears. J Bone Joint Surg Am 86: 219-224, 2004.
5. Gerber C, Fuchs B and Hodler J: The results of repair of massive tears of the rotator cuff. J Bone Joint Surg 82: 505-515, 2000.
6. Jost B, Zumstein M, Pfirrmann CW and Gerber C: Long-term outcome after structural failure of rotator cuff repairs. J Bone Joint Surg Am 88: 472-479, 2006.
7. Mall NA, Tanaka MJ, Choi LS and Paletta GA Jr: Factors affecting rotator cuff healing. J Bone Joint Surg Am 96: 778-788, 2014.
8. Kwon J, Kim SH, Lee YH, Kim TI and Oh JH: The rotator cuff healing index: A new scoring system to predict rotator cuff healing after surgical repair. Am J Sports Med 47: 173-180, 2019.
9. Burkhart SS, Denard PJ, Konicek J and Hanypsiak BT: Biomechanical validation of load-sharing rip-stop fixation for the repair of tissue deficient rotator cuff tears. Am J Sports Med 42: 457-462, 2014.
10. Cheung EV, Silverio L and Sperling JW: Strategies in biologic augmentation of rotator cuff repair: A review. Clin Orthop Relat Res 468: 1476-1484, 2010.
11. Castricini R, Longo UG, De Benedetto M, Panfoli N, Pirani P, Zini R, Maffulli N and Denaro V: Platelet-Rich plasma augmentation for arthroscopic rotator cuff repair: A randomized controlled trial. Am J Sports Med 39: 258-265, 2011.
12. Castagna A, Cesari E, Gigante A, Conti M and Garofalo R: Metalloproteases and their inhibitors are altered in both torn and intact rotator cuff tendons. Musculoskelet Surg 97 (Suppl 1): S39-S47, 2013.
13. Hurley ET, Hannon CP, Pauzenberger L, Fat DL, Moran CJ and Mullett H: Nonoperative treatment of rotator cuff disease with platelet-rich plasma: A systematic review of randomized controlled trials. Arthroscopy 35: 1584-1591, 2019.
14. Baksh N, Hannon CP, Murawski CD, Smyth NA and Kennedy JG: Platelet-rich plasma in tendon models: A systematic review of basic science literature. Arthroscopy 29: 596-607, 2013.
15. Dohan Ehrenfest DM, Rasmusson L and Albrektsson T: Classification of platelet concentrates: From pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 27: 158-167, 2009.
16. Filiardo G, Di Matteo B, Kon E, Merli G and Marcacci M: Platelet-rich plasma in tendon-related disorders: Results and indications. Knee Surg Sports Traumatol Arthrosc 26: 1984-1999, 2018.
17. American Academy of Orthopaedic Surgeons: Management of Rotator Cuff Pathology Appropriate Use Criteria. https://www.aaos.org/rcauc. Accessed June 10, 2025.
18. Everts P, Onishi K, Jayaram P, Lana JF and Mautner K: Platelet-Rich plasma: New performance understandings and therapeutic considerations in 2020. Int J Mol Sci 21: 7794, 2020.
19. Chen X, Jones IA, Togashi R, Park C and Vangsness CT Jr: Use of platelet-rich plasma for the improvement of pain and function in rotator cuff tears: A systematic review and meta-analysis with bias assessment. Am J Sports Med 48: 2028-2041, 2020.

20. Trantos IA, Vasiliadis ES, Giannoulis FS, Pappa E, Kakridonis F and Pneumaticos SG: The effect of PRP augmentation of arthroscopic repairs of shoulder rotator cuff tears on postoperative clinical scores and retear rates: A systematic review and meta-analysis. J Clin Med 12: 581, 2023.
21. Anitua E: Plasma rich in growth factors: Preliminary results of use in the preparation of future sites for implants. Int J Oral Maxillofac Implants 14: 529-535, 1999.
22. Ntourantonis D, Panagopoulos A, Iliopoulos I, Tatani I, Tsoumpos P, Kouzelis A and Tyllianakis M: Translation, cultural adaptation, validity and reliability of the Greek version of the modified Constant Score. JSES Open Access 1: 45-50, 2017.
23. Goutallier D, Postel JM, Bernageau J, Lavau L and Voisin MC: Fatty muscle degeneration in cuff ruptures. Pre- and postoperative evaluation by CT scan. Clin Orthop Relat Res (304), 78-83, 1994.
24. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, Fainsinger R, Aass N and Kaasa S; European Palliative Care Research Collaborative (EPCRC): Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review. J Pain Symptom Manage 41: 1073-1093, 2011.
25. Tang JZ, Nie MJ, Zhao JZ, Zhang GC, Zhang Q and Wang B: Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: A meta-analysis. J Orthop Surg Res 15: 403, 2020.
26. Zhao J, Huang H, Liang G, Zeng LF, Yang W and Liu J: Effects and safety of the combination of platelet-rich plasma (PRP) and hyaluronic acid (HA) in the treatment of knee osteoarthritis: A systematic review and meta-analysis. BMC Musculoskelet Disord 21: 224, 2020.
27. Sánchez M, Anitua E, Azofra J, Andía I, Padilla S and Mujika I: Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. Am J Sports Med 35: 245-251, 2007.
28. Pretorius J, Habash M, Ghobrial B, Alnajjar R and Ellanti P: Current status and advancements in platelet-rich plasma therapy. Cureus 15: e47176, 2023.
29. Lin KC, Chen KH, Shao PL, Chai HT, Sung PH, Chiang JY, Ko SF and Yip HK: Combined phloretin and human platelet-rich plasma effectively preserved integrities of brain structure and neurological function in rat after traumatic brain damage. Curr Mol Pharmacol 17: e18761429316684, 2024.
30. Giovannetti de Sanctis E, Franceschetti E, De Dona F, Palumbo A, Paciotti M and Franceschi F: The efficacy of injections for partial rotator cuff tears: A systematic review. J Clin Med 10: 51, 2020.
31. A Hamid MS and Sazlina SG: Platelet-rich plasma for rotator cuff tendinopathy: A systematic review and meta-analysis. PLoS One 16: e0251111, 2021.
32. Lin MT, Wei KC and Wu CH: Effectiveness of platelet-rich plasma injection in rotator cuff tendinopathy: A systematic review and meta-analysis of randomized controlled trials. Diagnostics (Basel) 10: 189, 2020.
33. Lee YS, Jeong JY, Park CD, Kang SG and Yoo JC: Evaluation of the risk factors for a rotator cuff retear after repair surgery. Am J Sports Med 45: 1755-1761, 2017.
34. Miller LE and Stewart ME: The blind leading the blind: Use and misuse of blinding in randomized controlled trials. Contemp Clin Trials 32: 240-243, 2011.
35. Hiemstra LA, Macdonald PB and Froese W: Subacromial infection following corticosteroid injection. J Shoulder Elbow Surg 12: 91-93, 2003.
36. Gruson KI, Ruchelsman DE and Zuckerman JD: Subacromial corticosteroid injections. J Shoulder Elbow Surg 17 (1 Suppl): 118S-130S, 2008.
37. Moosmayer S, Ekeberg OM, Hallgren HB, Heier I, Kvalheim S, Juel NG, Blomquist J, Pripp AH and Brox JI: Ultrasound guided lavage with corticosteroid injection versus sham lavage with and without corticosteroid injection for calcific tendinopathy of shoulder: Randomised double blinded multi-arm study. BMJ 383: e076447, 2023.
38. Kamel SI, Rosas HG and Gorbachova T: Local and systemic side effects of corticosteroid injections for musculoskeletal indications. AJR Am J Roentgenol 222: e2330458, 2024.
39. Perez A, Jansen-Chaparro S, Saigi I, Bernal-Lopez MR, Miñambres I and Gomez-Huelgas R: Glucocorticoid-induced hyperglycemia. J Diabetes 6: 9-20, 2014.
40. Droz LG, Hurley ET, Glover MA, Lorentz SG and Dickens JF: Optimal techniques and rehabilitation protocols for rotator cuff repair: A literature review. Open Access J Sports Med 16: 119-130, 2025.
41. Oztek MA, Brunnquell CL, Hoff MN, Boulter DJ, Mossa-Basha M, Beauchamp LH, Haynor DL and Nguyen XV: Practical considerations for radiologists in implementing a patient-friendly MRI experience. Top Magn Reson Imaging 29: 181-186, 2020.
42. The Cochrane Collaboration: Cochrane Handbook for Systematic Reviews of Interventions. https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-08. Accessed May 24, 2026.
43. Xu W and Xue Q: Application of platelet-rich plasma in arthroscopic rotator cuff repair: A systematic review and meta-analysis. Orthop J Sports Med 9: 23259671211016847, 2021.
44. Feuerriegel GC, Fritz B, Marth AA, Sommer S, Wieser K and Sutter R: Assessment of the rotator cuff muscles: State-of-the-art MRI and clinical implications. Radiology 315: e242131, 2025.
45. Oh JH, Kim SH, Ji HM, Jo KH, Bin SW and Gong HS: Prognostic factors affecting anatomic outcome of rotator cuff repair and correlation with functional outcome. Arthroscopy 25: 30-39, 2009.
46. Raman J, Walton D, MacDermid JC and Athwal GS: Predictors of outcomes after rotator cuff repair-A meta-analysis. J Hand Ther 30: 276-292, 2017.
47. Anitua E, Troya M, Falcon-Pérez JM, López-Sarrio S, González E and Alkhraisat MH: Advances in platelet rich plasma-derived extracellular vesicles for regenerative medicine: A systematic-narrative review. Int J Mol Sci 24: 13043, 2023.
48. Barber FA: PRP as an adjunct to rotator cuff tendon repair. Sports Med Arthrosc Rev 26: 42-47, 2018.
49. Yuan Z, Wang Y, Li Y, Lin C, Wang S, Wang J, Ma C and Wu S: Comparison of leukocyte-rich and leukocyte-poor platelet-rich plasma on pressure ulcer in a rat model. J Burn Care Res 44: 860-868, 2023.
50. Vavken P, Sadoghi P, Palmer M, Rosso C, Mueller AM, Szoelloesy G and Valderrabano V: Platelet-Rich plasma reduces retear rates after arthroscopic repair of small- and medium-sized rotator cuff tears but is not cost-effective. Am J Sports Med 43: 3071-3076, 2015.
51. Eymard F, Ornetti P, Maillet J, Noel É, Adam P, Legré-Boyer V, Boyer T, Allali F, Gremeaux V, Kaux JF, *et al*: Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: A consensus statement from French-speaking experts. Knee Surg Sports Traumatol Arthrosc 29: 3195-3210, 2021.
52. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, Sawada K, Sculean A, Schaller B and Miron RJ: Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin Oral Invest 20: 2353-2360, 2016.
53. Masuki H, Okudera T, Watanebe T, Suzuki M, Nishiyama K, Okudera H, Nakata K, Uematsu K, Su CY and Kawase T: Growth factor and pro-inflammatory cytokine contents in platelet-rich plasma (PRP), plasma rich in growth factors (PRGF), advanced platelet-rich fibrin (A-PRF), and concentrated growth factors (CGF). Int J Implant Dent 2: 19, 2016.
54. Chevrier A, Hurtig MB and Lavertu M: Chitosan-platelet-rich plasma implants improve rotator cuff repair in a large animal model: Pivotal study. Pharmaceutics 13: 1955, 2021.
55. Yurtbay A, Say F, Çinka H and Ersoy A: Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: The 2-year results of a randomized, double-blind, placebo-controlled clinical trial. Arch Orthop Trauma Surg 142: 2755-2768, 2022.
56. Tao X, Aw AAL, Leeu JJ and Bin Abd Razak HR: Three doses of platelet-rich plasma therapy are more effective than one dose of platelet-rich plasma in the treatment of knee osteoarthritis: A systematic review and meta-analysis. Arthroscopy 39: 2568-2576.e2, 2023.
57. Görmeli G, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O and Ertem K: Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: A randomized, double-blind, placebo-controlled trial. Knee Surg Sports Traumatol Arthrosc 25: 958-965, 2017.
58. Darrieutort-Laffite C, Blanchard F, Soslowsky LJ and Le Goff B: Biology and physiology of tendon healing. Joint Bone Spine 91: 105696, 2024.
59. Longo UG, Carnevale A, Piergentili I, Berton A, Candela V, Schena E and Denaro V: Retear rates after rotator cuff surgery: A systematic review and meta-analysis. BMC Musculoskelet Disord 22: 749, 2021.