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SECEC Research Grant 2008 II: Use of platelet- and leucocyte-rich fibrin (L-PRF) does not affect late rotator cuff tendon healing: a prospective randomized controlled study

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Background: Because the retear rate after rotator cuff repairs remains high, methods to improve healing are very much needed. Platelet-rich concentrates have been shown to enhance tenocyte proliferation and promote extracellular matrix synthesis in vitro; however, their clinical benefit remains unclear. We hypothesized that arthroscopic rotator cuff repair with leucocyte- and platelet-rich fibrin (L-PRF) results in better clinical and radiographic outcome at 12 months of follow-up than without L-PRF.

Methods: Thirty-five patients were randomized to receive arthroscopic rotator cuff repair with L-PRF locally applied to the repair site (L-PRF+ group, n = 17) or without L-PRF (L-PRF− group, n = 18). Preoperative and postoperative clinical evaluation included the Subjective Shoulder Value, visual analog score for pain, Simple Shoulder Test, and Constant-Murley score. The anatomic watertight healing, tendon thickness, and tendon quality was evaluated using magnetic resonance arthrography at 12 months of follow-up.

Results: No complications were reported in either group. The mean Subjective Shoulder Value, Simple Shoulder Test, and Constant-Murley scores increased from preoperatively to postoperatively, showing no significant differences between the groups. Complete anatomic watertight healing was found in 11 of 17 in the L-PRF+ group and in 11 of 18 in the L-PRP− group ($P = .73$). The mean postoperative defect size (214 ± 130 mm^2 in the L-PRF+ group vs 161 ± 149 mm^2 in the L-PRF− group; $P = .391$) and the mean postoperative tendon quality according to Sugaya (L-PRF+ group: 3.0 ± 1.4, L-PRF− group: 3.0 ± 0.9) were similar in both groups at 12 months of follow-up.

Conclusion: Arthroscopic rotator cuff repair with application of L-PRF yields no beneficial effect in clinical outcome, anatomic healing rate, mean postoperative defect size, and tendon quality at 12 months of follow-up.

Level of evidence: Level I, Randomized Controlled Trial, Treatment Study.

Keywords: Shoulder arthroscopy; rotator cuff; leucocyte and platelet-rich fibrin (L-PRF); platelet-rich concentrates

This study complied with local ethical approval guidelines.

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Despite developments in surgical techniques and suture materials, the failure rates of open,[26,58] arthroscopic single-row,[6,24] and double-row repairs[20,31] are still very high. The incidence of failure of the tendon to heal after rotator cuff repair is variable and is reported in up to 94%.[24] Age is one of the most significant predisposing factors, with significantly higher failure rates in patients older than 65 years.[6] A possible explanation for this is decreased vascularization at the critical zone near the insertion of the rotator cuff.[41,50,52] Compared with healthier rotator cuff tissue, degenerative rotator cuff tissue has a significantly less vascular microcirculation.[4] This decrease in the vascular supply may predispose to the development of rotator cuff tendinopathy[53] and to a decreased healing rate after attempted repair.[19]

Owing to the limited ability of the rotator cuff to heal, several new strategies have been proposed, including biologic augmentation of the ruptured rotator cuff with growth factors and cytokines, gene therapy, and stem cell application.[10,32-34,48]

Platelet-rich concentrates are classified according to the presence of leucocytes and to the polymerization technique of the fibrin.[18] To our knowledge, 5 clinical studies have been published using a leucocyte- and platelet-rich plasma (L-PRP)[36,48] and a leucocyte-poor or pure platelet-rich fibrin (P-PRF)[3,10,51] in rotator cuff repair.

Conversely, autologous leucocyte- and platelet-rich fibrin (L-PRF), as described by Dohan et al,[14-16] is a bioactive component of whole blood that includes platelet activation and fibrin polymerization. This simple and open-access matrix can be produced by a standard centrifugation procedure during the surgical operation in less than 20 minutes. Its production is cost-effective because it can be produced in a glass-coated tube without any additives. Unlike PRP, L-PRF does not dissolve quickly during the hours after application.[57] Furthermore, due to the primary fibrin polymerization, the stable matrix leads to an entrapment of growth factors that allows a continuous slow release of growth factors for up to 28 days.[57] In addition to the platelets, the leucocytes produce a significant amount of growth factors that are known to promote healing.[17] The fibrin matrix in the L-PRF also may have an effect on the healing of the surrounding tissue by increasing neovascularization.[11] Our previous prospective randomized pilot study demonstrated that the application of L-PRF was technically feasible during arthroscopic rotator cuff repair and yielded higher early vascularization at 6 weeks.

To date, however, there are no data from randomized trials assessing the radiographic outcome and clinical benefit of L-PRF augmentation in rotator cuff repair. This study evaluated the clinical and radiographic outcome, with and without application of L-PRF in rotator cuff repair, of posterosuperior tears at 12 months postoperatively. We hypothesized that biologic augmentation with L-PRF would result in an increased improvement in shoulder outcome, a better anatomic healing rate, and increased tendon thickness and quality.

Materials and methods

This prospective randomized blinded study assessed the clinical and radiographic influence of intraoperative biologic augmentation of L-PRF in repair of chronic rotator cuff tendon tears.

Patient data

Thirty-five consecutive patients with chronic posterosuperior full-thickness rotator cuff tears were treated between October 2008 and March 2009 with a primary arthroscopic repair by the senior surgeon (P.B.) or under his direction.

Inclusion and exclusion criteria

Patients were included (1) if they had a posterosuperior chronic full-thickness detachment limited to the supraspinatus and infraspinatus tendon with intact insertions of the subscapularis, (2) if an arthroscopic double-row cuff repair with complete coverage of the footprint could be performed, if necessary, after release of the coracohumeral ligament from the coracoid and a supraglenoid capsular release, and (3) if they were aged older than 55 years. Also included were individuals with additional biceps pathology, including delamination, tenosynovitis, inflammation, subluxation, and dislocation.

Patients were excluded when the tear or the repair was only partial thickness and when there had been a previous operation at the rotator cuff. Diagnoses such as extension of the tear to the subscapularis tendon, which requires surgical intervention, an isolated subscapularis tear, workers' compensation claims, or a labral pathology amenable to surgical repair also resulted in the exclusion of these patients.

Contraindications to arthroscopic cuff repair were upward humeral migration (an acromiohumeral distance of <6 mm on the anteroposterior radiographs with the shoulder in neutral rotation), associated glenohumeral osteoarthritis, or severe muscle atrophy or fatty infiltration (stage 3 or 4 according to the classification system of Goutallier et al[30]) on a computed tomography arthrogram or magnetic resonance imaging (MRI) study.[22] Patients were definitively included in the study protocol after confirming the diagnosis at the beginning of the surgery when the diagnostic arthroscopy was performed.

Randomization

A block randomization was performed with a block size of 18 vs 17 patients.[44] In the test group (L-PRF+), we used an arthroscopic transosseous equivalent double-row rotator cuff repair with additional application of 4-folded L-PRF matrices in between the bone and the tendon. In the control group (L-PRF−), we used the same rotator cuff repair, without the application of L-PRF. Patients were blinded to the treatment they had received. Clinical assessments, scores, and radiographic evaluation were performed by independent observers blinded to the treatment provided.

Surgical technique and postoperative care

All patients underwent an arthroscopic mattress tension-band transosseous equivalent double-row rotator cuff repair, as previously described.[5] After bursectomy and mobilization of the cuff, the dimension, shape, and reducibility of the tear was evaluated, and a systematic release was performed if the cuff was retracted and immobile. The goal was to allow a low-tension reduction of the supraspinatus tendon to its anatomic position on the upper surface of the greater tuberosity. Finally, the surgeon performed a débridement of degenerative tendon using a basket biter or a shaver.

The soft tissue and cortical bone of the upper surface of the greater tuberosity were abraded with a shaver and burr (Acromionizer; Smith & Nephew Inc, Andover, MA, USA) to create an even, bleeding cancellous bone bed, with avoidance of trough formation, to promote tissue healing.

Medial double-loaded bioabsorbable suture anchors were placed, and the sutures were passed through the medial part of the tendon, including the often-delaminated deep layer of the tendon, if present. The sutures were knotted in such a way that they fixed the tendon to the medial part of the footprint, to avoid later dislocation of the L-PRF medial to the medial row. In our previous analysis, L-PRF showed 3 to 4 times lower growth factor content than L-PRP (unpublished data). We therefore we prepared 4 L-PRF clots to have results comparable to other studies.[49,51]

After 4 L-PRF clots were prepared according to the PRF Process (Nice, France) and the modifications by Zumstein et al,[57] the clots were folded, stacked, and sutured together with bioabsorbable polyglactin 910 sutures (Vicryl; Johnson & Johnson, Ethicon, Somerville, NJ, USA; Fig. 1).

To facilitate the application of the L-PRF clots, an 8.25-mm threaded cannula (Smith & Nephew) was inserted through the lateral portal. The stacked and sutured L-PRF conglomerate was brought in between the tendon and the decorticated greater tuberosity and positioned optimally (Fig. 2). Then, the lateral row of sutures was fixed at the lateral cortex of the humerus. This brought the tendon back on the lateral part of the footprint and put compression on the L-PRF clots between the tendon and the bone (Fig. 3).

Although 2 anchors are sufficient for single supraspinatus tears, we used 2 medial and 2 lateral anchors for supraspinatus and infraspinatus tears. A subacromial decompression with acromioplasty was performed only if needed.

Shoulders were immobilized postoperatively for 4 weeks after single-tendon tear repair and for 6 weeks after repair of massive tears of the supraspinatus and infraspinatus using a sling in adduction. Patients were encouraged to mobilize the elbow, wrist, and hand immediately after. Patients were advised to perform these exercises for 5 minutes at a time and 5 times a day for the first 3 weeks. Parallel during the immobilization period, they were sent to a physical therapist for passive motion exercises in the plane of the scapula at 3 weeks. Further passive range of motion and active-assisted range of motion exercises were allowed after gradual weaning off the sling from 4 to 6 weeks after surgery. No active motion was allowed for 6 weeks or until complete recovery of passive motion had occurred. Hydrotherapy was strongly encouraged. Patients began strengthening exercises after 3 months. Light sports activities were allowed after 3 months, and full return to sports was allowed after 6 to 9 months, according to individual recovery.

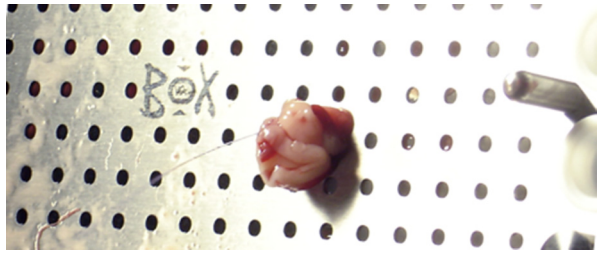

Figure 1 Preparation of 4 leucocyte platelet-rich fibrin clots.

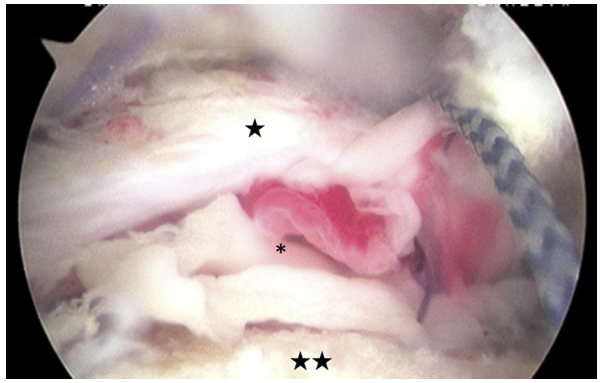

Figure 2 The leukocyte platelet-rich fibrin clots (*) are placed in between the tendon of the rotator cuff (★) and the bone (★★).

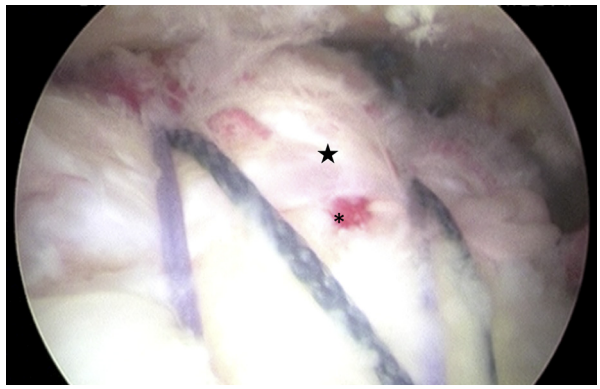

Figure 3 The rotator cuff (★) is fixed on the lateral part of the humerus (leukocyte platelet-rich fibrin clots are depicted in *).

Clinical assessment

Evaluation

Patients were assessed the day before the surgery and postoperatively at 6 and 12 weeks and at l and 6 months until a final follow-up of at least 12 months (range, 12-25 months).

Clinical outcome measures

Four outcome measures were used preoperatively and postoperatively:

1. The patient's subjective satisfaction with the clinical function of the affected shoulder was rated as very satisfied, satisfied, not satisfied, or disappointed.[21,26,37,38,58]
2. The Subjective Shoulder Value (SSV)[26,29,37,38,58] is the patient's estimated value of the involved shoulder as a percentage of an entirely healthy shoulder, with the latter being 100%.
3. The Simple Shoulder Test (SST)[6,40] was used as a patient based outcome score.
4. The absolute as well as the relative Constant and Murley (CM) score[12,13,29] was used as a clinical outcome score.

Clinical assessments and scores were performed by independent observers blinded to the treatment provided.

Radiographic outcome measures

All patients underwent a standardized radiographic evaluation, including anteroposterior and scapular lateral fluoroscopically controlled views preoperatively and postoperatively at the latest follow-up. The acromiohumeral distance[8] and the acromion index (a measure of the lateral extension of the acromion)[45,58] were measured as on a true anteroposterior shoulder radiograph. All patients preoperatively had a computed tomography arthrogram (28 patients) or MRI (7 patients). MRI scans of the shoulder were obtained at the 12-month follow-up in every patient.

The extent of the rotator cuff tear was evaluated on the preoperative scans and confirmed by direct visualization with the arthroscope in the lateral portal according to location, size, and retraction. The location of the tear was classified into 6 segments or sectors (A, B, C, D, E, or F), as according to Thomazeau et al,[56] and modified by Boileau et al.[6] The mean tear area was calculated as previously described[26,37,38,58] by measuring the anteroposterior diameter (base) and the mediolateral diameter (height) of the tear. Retraction was graded, according to Patte,[47] as 1 (not retracted), 2 (retracted to humeral head), or 3 (retracted to glenoid). Fatty infiltration of the rotator cuff muscles was assessed on a computed tomography arthrogram or on MRI scans and was classified according to Goutallier et al[30] and Fuchs et al[22] (grade 0 = no fatty infiltration, grade 1 = some fatty streaks; grade 2 = more muscle than fat; grade 3 = as much muscle as fat, or grade 4 = less muscle than fat).

The integrity of the rotator cuff tendons was assessed postoperatively using established MRI criteria.[35,42,46] The diagnosis of a full-thickness persistent tear was made when a fluid-equivalent signal or nonvisualization of the supraspinatus or infraspinatus tendon was found in 1 or more standard T2-weighted images, with or without fat suppression. The size of the persistent defect in nonhealed tears at the final follow-up assessment were compared with the initial tear sizes found preoperatively by using the maximal mediolateral and anteroposterior diameters, as previously described.[26,37,38,58]

The rotator cuff insertion quality[35,42] was postoperatively classified into 0 (normal), 1 (scar tendinopathy), 2 (partial thinning), 3 (localized transmural defect), and 4 (whole-tendon defect), as well as according to Sugaya et al[55] into 5 categories as type I: sufficient thickness with homogenous low intensity; type II: sufficient thickness with partial high intensity; type III: insufficient thickness without discontinuity (thinned cuff); type IV: presence of minor discontinuity; and type V: presence of a major discontinuity. Footprint coverage was classified into 4 categories: 100% coverage, >50% coverage, <50% coverage, and no coverage of the footprint.

The delamination of the supraspinatus tendon was evaluated in the coronal T2-weighted MRI scans. Scans were assessed by 3 independent observers blinded to the treatment provided, including a musculoskeletal radiologist and 2 fellowship-trained shoulder surgeons. Definitive radiographic diagnosis was made in consensus.

Statistics

Nonparametric statistical analyses were performed using SPSS 18.0 software (IBM Corp, Armonk, NY, USA). Data are presented as the mean ± the standard deviation of the mean. The mean values were compared using the Mann-Whitney test for unpaired groups and the Wilcoxon test for paired groups for continuous variables and the χ^2 test or the Fisher exact test for categoric variables. The Spearman correlation coefficient was used to test quantitative relationships between variables. A difference of $P < .05$ was considered to be statistically significant.

Power analysis

We determined the study sample size with a power analysis to provide sufficient statistical power (80%) at an α level of 0.05. With use of our previous data from the above-mentioned pilot study, a power analysis provided a sample size of 17 patients per group to detect a 10% difference in the CM score at the 12-month follow-up, assuming a standard deviation of 10.9.

Results

There were no intraoperative or postoperative complications or reoperations.

Baseline demographics

Thirty-five patients (18 men and 17 women) met the inclusion criteria and were randomized into 2 treatment groups. The mean age was 65.3 years (range, 57-74 years). There were no smokers in the study. The average duration of the symptoms before surgery was 29 months (range, 3-120 months). On the basis of the patient's history, the tear was associated with trauma in 9 shoulders in each group. There were no significant differences in baseline characteristics between the 2 groups (Table I).

Preoperatively, 9 patients in the L-PRF+ and 10 patients in the L-PRF− group had received at least 1 subacromial injection of cortisone (range, 1-5; $P = .909$), and 17 patients in the L-PRF+ group and 15 in the L-PRF− group had been preoperatively treated with medication or physical therapy, or both.

The mean acromiohumeral distance, measured on the preoperative anteroposterior radiograph in neutral rotation, was 10 ± 2 mm in the L-PRF+ group and 10 ± 2 mm in the L-PRF− group. The acromion was curved (type II) in 16 and hooked (type III) in 18 shoulders. The acromion index,[45,58] was 0.70 ± 0.064 for the L-PRF+ group and 0.72 ± 0.071

Table I Comparison of preoperative clinical parameters

Parameter	PRF+ group (n = 17)	PRF− group (n = 18)	*P* value*
Gender distribution			.505
Male, No.	10	8	
Female, No.	7	10	
Patients who received post-op			
Infiltration, No.	9	10	
Medication, No.	17	15	
Age at surgery, mean (range) years	65 (58-74)	66 (55-73)	.829
Follow-up, mean (range) months	14 (12-20)	15 (12-25)	.817
Acromion index, mean ± SD	0.70 ± 0.064	0.72 ± 0.071	.400
Acromiohumeral distance, mean ± SD mm	10 ± 2	10 ± 2	.637
Supraspinatus tendon			
Retraction†			
None	2	1	
To humeral head	12	12	
To glenoid	3	5	
Tear area, mean ± SD mm^2	322 ± 180	445 ± 421	.516
Location of the tear			
Stage‡			
CD	4	5	
CDE	4	7	
BCD	1	2	
BCDE	3	1	
DE	1	1	

PRF+, platelet-rich fibrin augmentation; *PRF−*, no platelet-rich fibrin augmentation; *SD*, standard deviation; *CD*, supraspinatus tear with infraspiantus delamination; *CDE*, supraspinatus tear that extended in the subscapularis (delamination) and in the infraspinatus (delamination); *BCD*, supraspinatus and infraspinatus tear; *BCDE*, supraspinatus, infraspinatus tear and teres minor tear; *DE*, supraspinatus tear that extended in the subscapularis (delamination).

* According to the Mann-Whitney test ($P < .05$ indicates statistical significance).

† According to Patte.[47]

‡ According to Thomazeau et al,[56] and modified by Boileau et al.[6]

for the L-PRF− group. There were no significant differences between the 2 groups for the acromiohumeral distance ($P = .637$) and the acromion index ($P = .400$).

In 4 patients of the L-PRF+ group and in 2 patients of the L-PRF− group, lesions affected only the supraspinatus (stage D). The supraspinatus tear was associated with infraspinatus delamination (stage CD) in 4 L-PRF+ patients (5 in L-PRF− group). In 4 cases of the L-PRF+ group and in 7 in the L-PRF− group, the supraspinatus tear was associated with anterior and posterior delamination (stage CDE). The supraspinatus and infraspinatus, including also an anterior cleavage (stage BCD), were involved in 1 tear of the L-PRF+ group and in 2 tears of the L-PRF− group. Three patients in the L-PRF+ group and 1 patient in the L-PRF− group had a complete tear of the supraspinatus and infraspinatus tendon (BCDE) with anterior (and posterior) delamination. In each group, the supraspinatus tear extended anteriorly to the rotator interval, leaving the long head of the biceps uncovered, or was associated with subscapularis delamination or fraying (stage DE) in 1 patient. The mean preoperative tear area was 322 ± 180 mm^2 in the L-PRF+ group and 445 ± 420 mm^2 in the L-PRF− group ($P = .533$).

There were also no differences in mean fatty infiltration of the supraspinatus and infraspinatus muscles (supraspinatus: 1.44 ± 0.70 in the L-PRF+ group vs 1.28 ± 0.57 in the L-PRF− group, $P = .463$; infraspinatus: 0.69 ± 0.70 in the L-PRF+ group vs 0.78 ± 0.73 in the L-PRF− group, $P = .746$). There were no significant differences in the preoperative clinical and radiographic subparameters between the 2 groups. Details are summarized in Table I.

Clinical outcomes

Overall satisfaction

At the mean 14 months of follow-up (range, 12-25 months), 13 patients of the L-PRF+ group rated the clinical result as very satisfying and 4 as satisfying. The clinical result in the L-PRF− group was rated as very satisfying by 13 patients, satisfying by 3, and not satisfying by 2. There were no significant differences between the 2 groups ($P = .650$).

Functional scores

Overall, there was a significant improvement of the SSV and the SST from preoperatively to postoperatively (46% to 69%, $P = .001$; and 6.2 points to 9.8 points, $P = .01$) in both groups.

Table II Comparison of clinical parameters preoperatively and at 12 months postoperatively

	PRF+ group			PRF− group		
	Pre-op	Post-op at 12 months	*P* value*	Pre-op	Post-op at 12 months	*P* value*
Subjective Shoulder Value, %†	46	88	**.001**	46	84	**.001**
Simple Shoulder Test, 1-12	5.4	10.7	**.001**	5.6	10.9	**.001**
Constant-Murley score						
Absolute, points‡	53	80	**.001**	55	80	**.001**
Relative, %§	70	105	**.001**	71	104	**.001**
VAS pain score, 1-10 points	6.3	13.9	**.001**	6.0	13.6	**.001**
Activity of daily living, points	9.1	18.4	**.001**	8.7	18.2	**.001**
Functional use of arm, points	30.4	36.3	**.040**	29.7	36.3	**.010**
Force, kg	7.5	12.5	**.003**	7.4	11.6	**.003**
Active mobility						
Flexion, °	156	167	**.043**	153	164	**.014**
External rotation, °	39	46	**.035**	36	39	.264
Internal rotation, points	6.4	9.1	**.001**	5.9	7.8	**.006**

PRF+, platelet-rich fibrin augmentation; *PRF−*, no platelet-rich fibrin augmentation; *VAS*, visual analog scale.

* Wilcoxon signed rank test. Bold values indicate statistical significance ($P < .05$).

† Patient's estimation of the operated shoulder in percentage compared with an entirely normal shoulder.

‡ Constant-Murley score in points.

§ Relative Constant-Murley score in percentage of an age- and gender-related normal value.

The absolute and the relative CM score increased significantly from 53 ± 12 points and 69% ± 15% preoperatively to 79 ± 9 points and 104% ± 11% postoperatively ($P = .001$ for both values) in the entire study population. All tested clinical parameters improved significantly in all patients from preoperatively to postoperatively at the 12-month follow-up. Details are reported in Table II.

The SSV, SST, and the absolute and relative CM score and its' subgroups were not significantly different between the L-PRF+ and the L-PRF− group at the 12-month follow-up (Table III).

The surgical time in the L-PRF+ group was significantly longer than in the L-PRF− group (126 ± 37 minutes vs 100 ± 33 minutes, $P = .061$).

Pain

Preoperatively, VAS pain scores for pain at night, pain on motion, and average pain level were not different in the 2 groups. After surgery, all pain scores decreased with time until the final follow-up in both groups. No significant difference between the 2 groups was found for any VAS pain measurement at any time point.

Structural outcome: integrity and quality of the rotator cuff insertion

The evaluation of the postoperative MRI scans showed no significant differences in the overall anatomic healing rate between the 2 groups, with 11 of 17 patients (65%) in the L-PRF+ and 11 of 18 patients (62%) in the L-PRF− group ($P = .73$). The mean defect size was 214 ± 130 mm^2 in the L-PRF+ group and 161 ± 149 mm^2 in the L-PRF−, with no significant difference between the 2 groups ($P = .391$). Ten of the 13 defects were smaller postoperatively compared with the preoperative size.

A similar mean footprint coverage was achieved with a 1.89 ± 1.17 in the L-PRF+ group and 1.94 ± 0.94 in the L-PRF− group ($P = .660$), which corresponds to coverage of more than 50%.

Delamination in occurred in 4 patients the L-PRF+ group and in 5 patients in the L-PRF− group ($P = .639$). The mean postoperative rotator cuff quality, according to Sugaya, was 3 ± 1.41 for the L-PRF+ group and 3 ± 0.9 for the L-PRF− group.

There was no significant increase of fatty infiltration in the supraspinatus and infraspinatus muscles from preoperatively to postoperatively in either groups (supraspinatus: 1.44 ± 0.70 to 1.76 ± 0.83 in the L-PRF+ group, $P = .819$; infraspinatus: 0.69 ± 0.70 to 1.18 ± 0.73 in the L-PRF− group, $P = .144$).

A postoperative comparison of the 2 groups revealed significantly more fatty infiltration of the supraspinatus muscle in the L-PRF+ group (1.76 ± 0.83) than in the L-PRF− group (1.11 ± 0.68; $P = .032$). No difference in the amount of fatty infiltration was found postoperatively in the infraspinatus muscle between the 2 groups (1.18 ± 0.73 in the L-PRF+ group vs 0.76 ± 0.57 in the L-PRF− group, $P = .114$).

Discussion

Tendon injuries are a significant source of pain and disability. Most research on treating tendon injuries[5-7,27,28]

Table III Comparison of clinical and radiologic parameters preoperatively and at 3, 6, and 12 months postoperatively

Parameter	Preoperatively			3 months postoperatively			6 months postoperatively			12 Months Postoperative		
	PRF+ group	*P* value*	PRF− group	PRF+ group	*P* value*	PRF− group	PRF+ group	*P* value*	PRF− group	PRF+ group	*P* value*	PRF− group
Subjective Shoulder Value,† %	46	.858	46	64.7	.684	63.6	78	.464	78.7	88	.932	84
Simple Shoulder Test	5.4	.851	5.6	9.06	.959	8.61	10.42	.113	13.78	10.7	.273	10.9
Constant-Murley score												
Absolute,‡ points	53	.883	55	63	.757	62	72	.244	77	80	.546	80
Relative,§ %	70	.807	71	81	.987	81	92	**.032**	99	105	.258	104
VAS pain score, 1-10 points	6.3	.883	6.0	11.9	.503	11.7	13.1	.986	12.7	13.9	.832	13.6
Activity of daily living, points	9.1	.103	8.7	15.6	.287	13.8	16.5	.274	17.9	18.4	.909	18.2
Functional use of arm, points	30.4	.908	29.7	29.2	.613	29.8	33	.155	36	36	.590	36
Force, kg	7.5	.708	7.4	6.9	.961	6.8	9.5	.873	10.1	12.5	.483	11.6
Active mobility												
Flexion,°	156	.935	167	137	.134	134	149	**.012**	161	153	.732	164
External rotation,°	39	.287	46	31	.525	27	37	.873	38	36	.207	39
Internal rotation, points	6.4	.386	9.1	6.8	.424	6.3	7.6	.957	7.7	5.9	.089	7.8
Tendon quality‖										2/6/3/2/4		0/3/8/6/1
Tendon homogeneity¶										1/12/4		0/13/5
Sugaya**										2/6/3/2/4		0/7/5/5/1
Delamination††										13/4		13/5
Footprint coverage‡‡										1.88		1.94
SSP fatty infiltration§§												
Stage 0: no infiltration	1		1							6		6
Stage 1: some fatty streaks	8		11							8		11
Stage 2: more muscle than fat	8		6							3		1
Stage 3: as much muscle as fat	0		0							0		0
Stage 4: less muscle than fat	0		0							0		0
ISP fatty infiltration§§												
Stage 0: no infiltration	7		7							3		5
Stage 1: some fatty streaks	8		8							8		12
Stage 2: more muscle than fat	2		3							6		1
Stage 3: as much muscle as fat	0		0							0		0
Stage 4: less muscle than fat	0		0							0		0

ISP, infraspinatus; *PRF+*, platelet-rich fibrin augmentation; *PRF−*, no platelet-rich fibrin augmentation; *SSP*, supraspinatus; *VAS*, visual analog scale.

* According to the Mann-Whitney test. Bold values indicate statistical significance ($P < .05$).

† Patient's estimation of the operated shoulder in percentage compared with an entirely normal shoulder.

‡ Constant-Murley score in points.

§ Relative Constant-Murley score in percentage of an age- and gender-related normal value.

‖ 0, normal; 1, scar tendinopathy; 2, partial thinning; 3, localized transmural defect; 4, whole-tendon defect.

¶ 0, normal; 1, inhomogeneous; 2, delaminated.

** Classification according to Sugaya et al[55] into 5 categories (I, sufficient thickness with homogenously low intensity; II, sufficient thickness with partial high intensity; III, insufficient thickness without discontinuity (thinned cuff); IV, presence of minor discontinuity; V, presence of a major discontinuity).

†† 0, no delamination; 1, delamination.

‡‡ 4 categories: 1, 100% coverage; 2, >50% coverage; 3, <50% coverage; 4, no coverage.

§§ According to Goutallier et al[30] and Fuchs et al.[22]

indicates that biologic properties, such as tissue composition[23,25,39,43] and vascularization[1,2] of the aging tendon, are key determinants, and it seems that the healing rate cannot be improved with mechanical augmentation alone. Recently, attention has turned to the biology of tendon healing as a means to improve the outcome of such injuries. Biologic augmentation using growth factors may have a potential benefit in rotator cuff surgery with, among other things, an increase in vascularization, which may improve the watertight healing rate.[2,9] However, research in this field is still inconclusive, and that there is a clinical benefit has not been sufficiently demonstrated.

Platelet concentrates for musculoskeletal injuries are innovative tools for regenerative medicine. However, many different products are available, and yet, little is known about the biologic properties of these products. There are 4

main families of platelet concentrates, each with different fibrin architecture and cellular content.[18] P-PRP and L-PRP are platelet suspensions, respectively, without and with leukocytes, that can be used as liquid injectable preparations. In an open surgical site, these products can be activated into a fibrin gel that offers additional local antihemorrhagic and sealing properties. Conversely, P-PRF and L-PRF are solid fibrin-based bioactive healing biomaterials, respectively, without and with leukocytes. The advantage of L-PRF as a solid scaffold for the long-term delivery of growth factors[57] is a innovative approach in tissue engineering of rotator cuff repairs.

The main goal of this study was to investigate the effect of the biologic augmentation with L-PRF on the clinical outcome at a mean follow-up of 14 months postoperatively. The secondary end point was to investigate the radiologic outcome of this treatment. This is the first prospective, randomized, double-blinded, controlled study to investigate the effect of L-PRF augmentation during arthroscopic rotator cuff repair. The absolute and relative CM score, the SSV, and SST improved significantly from preoperatively to postoperatively but failed to show any differences between the L-PRF+ and L-PRF− group at all time points. Furthermore, no significant improvement in structural integrity and tissue quality was evident, and overall nonhealing rates were not significantly different between the L-PRF+ and the L-PRF− groups.

To our knowledge, there are no studies in which rotator cuff repairs have been augmented with L-PRF; therefore a comparison with other studies that were using the same L-PRF preparation is not possible to date. Several studies, though, used other forms of autologous platelet-rich concentrates for rotator cuff augmentation. Castricini et al[10] showed that augmentation with leucocyte-poor or P-PRF did not provide superior clinical and structural outcomes compared with a control group. Rodeo et al[51] reported similar short-term results using also platelet-rich fibrin matrix as a leucocyte-poor or P-PRF in a prospective randomized study with 79 patients. Similar results could be found using PRP.[19,36]

In contrast, in a case-control study Barber et al[36] showed that the augmentation of the rotator cuff with leucocyte-poor or P-PRF results in lower healing defect rates without a clinical difference in outcome measures. Interestingly, the authors reported a 60% nonhealing rate in the control group, which is relatively high in a mixed tear size group. In another nonrandomized single group study with 14 patients, autologous L-PRP augmentation for arthroscopic rotator cuff repair provided good clinical results.[48,49] Comparing these studies' results with our own results, 2 aspects must be considered: the amount of growth factors released over time and the manufacturing process of the different platelet-rich preparations. Even if the preparation techniques of platelets and leucocyte concentrates are standardized, there is an immense interindividual variation in the quantity and quality of platelets and growth factors released between different patients, as shown by different authors.[17,57] In addition, different platelet-rich concentrates are prepared in different manners, which leads to a wide variation in platelet activation, growth factor release, and reaction with the cells of the tendon and bone. In this field, additional research is needed to understand the cause for the immense variability in platelet and growth factor release. A weakness of our study is the absence of information about the number or platelets in the applied L-PRF. However, we reported in previous studies the amount of platelets and growth factor release with this protocol over time.[57]

Previous studies suggest that there is a difference in the clinical outcome between nonhealed and healed rotator cuff repairs.[6,54,58] We found a slightly better patient satisfaction in the healed rotator cuffs, but the difference was without significance.

In our study, the use of autologous platelet-derived growth factors results in longer surgical time, is more expensive, and may be technically more demanding. However no local or systemic infection or other complications occurred with the intraoperative use of L-PRF. This is in accordance with previous studies.[36,48,51]

This study has some limitations, including that (1) we did not assess the number of patients who were eligible and recruited from our clinic and recorded the dropouts due to the exclusion criteria, (2) we had a small sample size determined by the power calculation according to the CM score as the primary outcome point in our previous studies with a potential type 2 error; and (3) we had still not a complete characterization of the L-PRFs used in this study. However, because we analyzed the different protocols previously[57] and were able to detect a slow release over time, we do not think that this influenced the data.

Conclusion

Our study does not support the use of autologous L-PRF for augmentation of a double-row repair of a rotator cuff. Compared with the significantly shorter and technically less demanding double-row repair without augmentation, we did not find an improved clinical or structural outcome. Because there is an immense heterogeneity of platelet-rich concentrate preparations, it is possible that other preparations may be more effective.

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