

# Arthroscopic rotator cuff repair with or without PrP: our experience

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**Summary.** *Background and aim of the work:* Arthroscopical rotator cuff repair has good results, but the rate of tendon healing is 80% in small tears with a decrease to 30% in large and massive tears. Platelets are an endogenous source of growth factors present during rotator cuff healing. Aim of the work is checking if Cascade Autologous Platelet System may improve rotator cuff healing in small sovraspinatus tears. *Methods:* Each patient enrolled in cases has surgical arthroscopical repair of sovraspinatus small tear and then treated with intraoperative Cascade. Patients of control group undergoing the same surgery with traditional arthroscopic repair. Follow-up time was at 3, 6, 12 month from surgery with evaluation of ROM, strength, Constant score, NRS. RMN was repeated at 12 month from surgery with evaluation of sovraspinatus tendon thickness, signal intensity, fat degeneration and muscle atrophy. *Results:* Between 2010 and 2013, 18 patients have undergone sovraspinatus repair in arthroscopic surgery with intraoperative Cascade and 18 patients with traditional arthroscopic repair. Only sovraspinatus tendon thickness and signal intensity were statistically difference in the cases group. In ROM, strength, Constant score, NRS, fat degeneration and muscle atrophy were not a statistically difference compared with controls. *Conclusions:* In small sovrapinsatus tears Cascade Autologous Platelet System did not result in improved ROM, strength, Constant score, NRS, tendon fat degeneration and muscle atrophy. Only sovraspinatus tendon thickness and signal intensity were improved. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** cascade, arthroscopy, sovraspinatus small tears, surgical treatment

## Introduction

Rotator cuff repair is one of the most common orthopedic pathologies, with 4.5 physician visit per year and 250.000 surgical procedures per year in USA (1, 2, 3]. Arthroscopical repair has good results, but the rate of tendon healing is 80% in small tears with a decrease to 30% in large and massive tears (4, 5, 6, 7]. In certain populations, including those with large and massive tears, re-tears rate can reach 94% (8]. A satisfactory healing depends on quality of bone, tendon and muscle: poor tissue quality is the major cause of tendon non-healing or re-tears (4, 5, 6, 7]. Difficult healing is linked to poor tendon vascularization and to histopathologic changes (production of abnormal

tendon collagen, type III) not only in the rupture area but also in the intact tendon areas, suggesting a general involvement of the tendon (2, 9, 10). On the other hand, several studies has showed that healing tendon process takes place through fibrous scar tissue formation and not with a histological normal tendon tissue: the result is a decrease in mechanical tendon properties with a higher rate of re-tear (11). Tendon is a low energy tissue. This is the cause of a slow healing after injury. Accelerate healing process allows a faster return to work, to sport and to normal activity of life, resulting useful both for professional athletes and for normal people (11).

Few data exist on biologic support to tendon healing after rotator cuff repair. Growth factor and cy-

tokines participate in tendon healing after rotator cuff repair: they represents important factors to accelerate healing process with their positive role in connective tissue formation (8).

Platelet-Rich Plasma (PRP) is a platelet concentrate, usually containing more than  $1000 \times 10^3$  platelets per microliter, 3-5 times increase as compared with whole blood. Thanks to growth factor in  $\alpha$ - granules, PRP can potentially release growth factor at high level. Most important growth factor are epidermal growth factor (EGF), transforming growth factor-beta 1 (TGF- $\beta$ 1), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I), hepatocyte growth factor (HGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF). Initially utilized in plastic and maxillo-facial surgery, today it's tested on orthopedic surgery as healing enhancer in bone, muscle, cartilage, ligament and tendon (11).

Cascade Autologous Platelet System (MTF [Musculoskeletal Transplant Foundation], Edison, New Jersey) consists in a membrane, a thin layer of autologous fibrin very rich in platelets. It's obtained by high speed centrifugation of patients own blood. It results in a Platelet-Rich-Fibrin-Matrix (PRFM), which can be utilized directly in the tear site and sutured in place, stimulating a faster tendon healing (2, 12).

Primary target of this study is comparison between 2 groups (PRP group and control group) of clinical and functional results with utilize of Constant score.

Secondary target is evaluation in post-operative follow-up of range of motion, pain, patient autonomy, tendon continuity and thickness.

## Methods

This is a case-control study. Each patient enrolled has surgical arthroscopical repair of *sovraspinatus* between 2010 and 2013 in our clinic (Clinica Ortopedica in Azienda Ospedaliero Universitaria Santa Maria della Misericordia in Udine), and then treated with intra-operative Cascade.

Patients of control group undergoing the same surgery with traditional arthroscopic repair, in the

same period and in the same place. All patients receive the treatment by the same surgeon. Eligibility criteria are showed in Table 1. Patients information have been taken with a clinic management software (G2 clinico, INSIEL SpA, Trieste, Italia).

For each patient we have studied following data:

- Peri-operative phase: age, sex, peri-operative Constant score, time of surgery, side of surgery, lesion size, retraction size, other surgery action as tenotomy or acromioplasty.
- Follow-up phase: ROM (flexion, abduction, external and internal rotation), strength, Constant score, return at normal activity of live; each data has been standardized as in Constant score. For evaluation of pain we have utilized NRS (Numeric Rating Scale, when 0 is no pain and 10 stronger pain). If NRS wasn't reported, we utilized pain scale in the Constant score (0 no pain, 15 stronger pain). Patient autonomy was evaluated in consideration of the specific part in Constant score (0 total inability, 20 total wellness)

Follow-up time was at 3, 6, 12 month from surgery.

RMN was repeated at 12 month from surgery. Thickness and signal intensity with fat degeneration and muscle atrophy were evaluated with validated literary scales (13-15) (Table 2, 3, 4, 5).

Software for all measurements for DICOM images was OsiriX Imaging Software for Macintosh (open source).

**Table 1.**

### *Inclusion criteria*

- Age between 45 and 75 years old
- Clinical and radiologic signs of *sovraspinatus* small tears
- Atraumatic lesion of *sovraspinatus*

### *Exclusion criteria*

- Previous shoulder surgery
- Traumatic lesion of *sovraspinatus*
- Lesion in other rotator cuff tendons
- Rotator cuff arthropathy
- Previous coagulation deficiency (thrombocytopenia, low fibrinogen level, anticoagulant therapy)

**Table 2.** Sovraspinatus thickness grading (13)

I	< 25% of normal thickness
II	25-50% of normal thickness
III	50-75% of normal thickness
IV	>75% of normal thickness

**Table 3.** Sovraspinatus signal intensity grading (13, 14)

I	Signal increased in all thickness
II	Intact tendon with focal increase of signal
III	Light and diffuse increase of signal

**Table 4.** Sovraspinatus signal intensity grading (13, 14)

I	Fat>Muscle
II	Fat=Muscle
III	Muscle>Fat
IV	Some fat pieces
V	Muscle without fat

**Table 5.** Sovraspinatus atrophy grading (14)

I	Tangent sign positive
II	Tangent sign negative

## Statistical analysis

Patient number ratio between two group was 1:1. T student test for impaired samples was utilized for continuous variable (age, surgery time, lesion and retraction size, pain, autonomy score). For each group was calculated mean, standard deviation and confidence interval. Range of movement, tendon thickness in RMN, tendon intensity of signal in RMN, tendon fat degeneration in RMN were analyzed with chi square test for trend. Other nominal variable (sex, side, acromioplasty or biceps tenotomy) and muscle atrophy grading in RMN were analyzed with Fisher test.

Statistical significance was for all test  $p < 0.05$ .

All data collected were elaborated in anonymous way with Excel 2011 for Macintosh (Microsoft Corporation, Redmond, USA). Software for statistical analysis was Graphpad Prism vers. 6c for Macintosh (GraphPad Software Inc., La Jolla, USA).

## Results

Between 2010 and 2013 18 patients have undergone sovrspinatus repair in arthroscopic surgery with intraoperative Cascade (cases). From historic register of our clinic, 18 patients with the same sovrspinatus tear and with arthroscopical traditional repair were enrolled randomly (controls). Three patients of each study were excluded due to a bad compliance in follow-up.

Average age was similar in 2 groups (cases 62,11±9,33 year; controls: 60,94±8,77 year;  $p=0,70$ ). Two groups were homogeneous for sex (8 woman and 10 men in cases; 8 men and 10 woman in controls;  $p=0,73$ ). The side of surgery was similar in 2 groups (cases 5 left and 13 right; controls 4 left and 14 right;  $p=1,00$ ). Surgery time in cases was longer then controls (75,83±14,58 min vs 60±20 min;  $p=0,01$ ). No statistical difference was found in tear size (cases: 1,7±0,56 cm; controls: 1,63±0,63 cm  $p=0,74$ ), in retraction size (cases: 0,9±0,73 cm; controls: 0,65±0,65  $p=0,33$ ), in biceps tenotomy incidence (16 in cases, 14 in controls;  $p=0,65$ ), in acromioplasty incidence (cases 1, controls 5;  $p=0,17$ ) (Table 6).

First target of this study doesn't show statistical difference between cases and controls. Constant score results were similar in peri-operative time (cases: 58,11±12,36; controls: 56,89±13,15  $p=0,77$ ), at 3 months follow-up (cases: 76±11,43; controls: 74,40±9,7  $p=0,68$ ), at 6 months follow-up (cases: 85,40±12,94; controls: 85,38±9,9  $p=0,99$ ), at 12 months follow-up (cases: 92,08±6,3; controls: 92,61±8,88  $p=0,86$ ) (Table 7).

Analysis of each movement of operated limb (included in Constant score) confirmed equivalence be-

**Table 6.** General patients data and intra-operative data (M: Men; W: Woman.  $p<0,05$ )

	Cases	Controls	p
Age (year)	62,11±9,33	60,94±8,77	0,7
Sex (M:W)	10:8	8:10	0,73
Side (Left:Right)	5:13	4:14	1
Time of surgery (min)	75,83±14,58	60±20	0,01
Tear size (cm)	1,7±0,56	1,63±0,63	0,74
Retraction (cm)	0,9±0,73	0,65±0,65	0,33
Tenotomy (Yes:No)	16:2	14:4	0,65
Acromioplasty (Yes:No)	1:17	5:13	0,17

**Table 7.** Patients Constant Score data (SD: standard deviation; 95% CI: confidence interval at 95%.  $p < 0,05$ )

		Cases	Controls	p
Before Surgery	<i>mean ± SD</i>	58,11±12,36	56,89±13,15	0,77
	<i>95% CI</i>	[51,96 - 64,26]	[50,35 - 63,43]	
3 months	<i>mean ± SD</i>	76±11,43	74,40±9,7	0,68
	<i>95% CI</i>	[69,67 - 82,33]	[69 - 79,8]	
6 months	<i>mean ± SD</i>	85,40±12,94	85,38±9,9	0,99
	<i>95% CI</i>	[78,23 - 92,57]	[80,1 - 90,65]	
12 months	<i>mean ± SD</i>	92,08±6,3	92,61±8,88	0,86
	<i>95% CI</i>	[88,08 - 96,09]	[88,19 - 97,03]	

tween 2 groups. In detail flexion was the same (3 months  $p=0,13$ ; 6 months  $p=0,61$ ; 12 months  $p=0,69$ ) (Table 8), as well as abduction (3 months  $p=1$ ; 6 months  $p=0,91$ ; 12 months  $p=0,31$ ) (Table 9), as internal rotation (3 months  $p=0,10$ ; 6 months  $p=0,18$ ; 12 months  $p=0,59$ ) (Table 10) and as external rotation (3 months  $p=0,44$ ; 6 months  $p=0,51$ ; 12 months  $p=0,21$ ) (Table 11).

Strength was also stackable between 2 groups (3 months  $p=1$ ; 6 month  $p=1$ ; 12 months  $p=0,99$ ) (Table 12).

NRS scale was similar in 2 groups (3 months  $p=0,76$ ; 6 months  $p=0,13$ ; 1 year  $p=0,81$ ) (Table 13).

Both cases and controls have a similar functional recovery (3 months  $p=0,54$ ; 6 months  $p=0,92$ ; 12 months  $p=0,42$ ) (Table 14).

Significant difference was found at MRI analysis between 2 groups about tendon thickness (12 months  $p=0,03$ ) (Table 15), *sovraspinatus* signal intensity (12 months  $p < 0,001$ ) (Table 16).

No difference was found in muscle fat degeneration (12 months  $p=0,62$ ) (Table 17) and atrophy (12 months  $p=0,69$ ) (Table 18).

**Table 8.** Shoulder flexion ( $p < 0,05$ )

	3 months (%)		6 months (%)		12 months (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
0°-30°	0	0	0	0	0	0
31°-60°	0	0	0	0	0	0
61°-90°	20,00	6,67	6,67	6,25	0	5,56
91°-120°	13,33	0	6,67	0	0	0
121°-150°	0	6,67	0	0	8,33	0
> 150°	66,67	86,66	86,66	93,75	91,67	94,44
p	0,13		0,61		0,69	

**Table 9.** Shoulder abduction ( $p < 0,05$ )

	3 months (%)		6 months (%)		12 months (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
0°-30°	0	0	0	0	0	0
31°-60°	0	0	0	0	0	0
61°-90°	26,67	20,00	13,33	6,25	0	5,56
91°-120°	6,67	13,33	0	12,50	0	5,56
121°-150°	0	6,67	0	0	8,33	5,56
> 150°	66,66	60,00	86,67	81,25	91,67	83,32
p	1		0,91		0,31	

**Table 10.** Level of shoulder internal rotation ( $p < 0,05$ )

	3 months (%)		6 months (%)		12 months (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
Thigh	0	0	0	0	0	0
Gluteus	6,68	20,00	0	6,25	0	5,56
Sacrum	13,33	20,00	0	6,25	0	0
L3	13,33	20,00	13,33	6,25	8,33	0
T12	33,33	26,67	20,00	37,50	33,33	44,44
T7	33,33	13,33	66,67	43,75	58,34	50,00
P	0,1		0,18		0,59	

**Table 11.** Level of shoulder external rotation. (BH: back head; OH: over head; FE: forward elbow; BE: back elbow.  $p < 0,05$ )

	3 months (%)		6 months (%)		12 months (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
BH – FE	6,67	20,00	0	6,25	8,33	0
BH – BE	33,33	26,67	26,67	12,50	16,67	5,56
OH – FE	40,00	40,00	13,33	37,50	8,33	5,56
OH – BE	0	0	6,67	6,25	8,33	27,78
Complete elevation	20,00	13,33	53,33	37,50	58,34	61,10
P	0,44		0,51		0,21	

**Table 12.** Patient pain (SD: standard deviation; 95% CI: confidence interval at 95%.  $p < 0,05$ )

	3 months (%)		6 months (%)		12 months (%)	
	Cases	Controls	Cases	Controls	Cases	Controls
Paralysys	0	0	0	0	0	0
Simple contraction	0	0	0	0	0	0
No gravity	0	0	0	0	0	0
Against gravity	0	0	0	0	0	0
Versus resistance	100,00	100,00	86,67	86,67	16,67	27,78
Normal strenght	0	0	13,33	13,33	83,33	72,22
P	1		1		0,99	

**Table 13.** Patients Constant Score data (SD: standard deviation; 95% CI: confidence interval at 95%.  $p < 0,05$ )

	Cases	Controls	p	
3 months	<i>mean ± SD</i> <i>95% CI</i>	1,66±1,54 [0,81 - 2,52]	1,53±0,74 [1,12 - 1,94]	0,76
6 months	<i>mean ± SD</i> <i>95% CI</i>	1,06±1,38 [0,29 - 1,83]	0,5±0,5 [0,22 - 0,77]	0,13
12 months	<i>mean ± SD</i> <i>95% CI</i>	0,75±0,96 [0,13 - 1,36]	0,66±0,97 [0,18 - 1,14]	0,81

**Table 14.** Grading of patient autonomy (SD: standard deviation; 95% CI: confidence interval at 95%.  $p < 0,05$ )

		Cases	Controls	p
3 months	<i>mean ± SD</i>	13,8±3,32	13±3,83	0,54
	<i>95% CI</i>	[11,96 - 15,64]	[10,88 - 15,12]	
6 months	<i>mean ± SD</i>	16±4,4	16,13±2,82	0,92
	<i>95% CI</i>	[13,56 - 18,44]	[14,62 - 17,63]	
12 months	<i>mean ± SD</i>	17,50±3,37	18,33±2,22	0,42
	<i>95% CI</i>	[15,36 - 19,64]	[17,23 - 19,44]	

**Table 15.** Grading of sovrapinatus thickness (Statistical significance for  $p < 0,05$ )

	12 months (%)	
	Cases	Controls
I	5,26	22,22
II	31,58	55,56
III	47,37	11,11
IV	15,79	11,11
V	5,26	22,22
P	0,03	

**Table 16.** Grading of sovraspinatus signal intensity ( $p < 0,05$ )

	12 months (%)	
	Cases	Controls
I	5,26	33,33
II	26,32	55,56
III	68,42	11,11
P	< 0,001	

**Table 17.** Grading of fat degeneration ( $p < 0,05$ )

	12 months (%)	
	Cases	Controls
I	0	5,26
II	5,26	10,53
III	36,84	31,58
IV	36,84	26,32
V	21,05	26,32
P	0,62	

**Table 18.** Grading of sovraspinatus atrophy ( $p < 0,05$ )

	12 months (%)	
	Cases	Controls
I	15,79	22,22
II	84,21	77,78
P	0,69	

## Discussion

In our study both groups were homogeneous, there wasn't any statistical difference in peri-operative data, except for time of surgery which was longer in cases, probably due to application of intra-operative PRP.

In post-operative evaluation no difference was found in functional values of Constant score. Same results were found in works of Nourissat, Chahal and Zhang (16-18). In Randelli study post-operative pain is better in cases, as well as the healing. This improvement was in the first 3 months, later there was no more difference as showed in Nourissat reply (19).

Constant score values observed in follow-up in our experience are a little higher in relation to literature data. This can be explained with small size of rotator cuff tear.

NRS scores were low in 2 groups in each follow-up time, confirming that pain after rotator cuff repair can be significant only in the first month after surgery. Between the two groups there wasn't statistical difference. Literature data are limited and not comparable with our study. In fact Randelli study evaluates pain only in the first month after surgery (19).

At the RMN evaluation, statistical difference were found in thickness and intensity of sovraspinatus, both bigger in Cascade group. Tendon was continuous in most of patients. Exceptions were one patient of cases with a small lesion, which was very symptomatic and four control patient with asymptomatic small lesion. According with literature, in cases group at the same post-surgery time, tendon was thicker (20). A thicker tendon doesn't mean a better tendon: it may be hyperplasia or hypertrophy or a fibrous tissue with consecutive mechanical proprieties. About relative risk of re-tears in literary data there are no statistical dif-

ference between case/control groups, but about re-tear rate it is smaller in PRP group for small/medium lesion (18); in large or massive tears re-tear rate is bigger, with or without PRP treatment (17).

According to Castricini et al (2), we utilize MRI to study post-operative tendon thickness; MRI guarantees good definition of anatomical structures and allows to differentiate re-tear from tendon degeneration. Point of strength of this study are also the use of a single surgeon and a standardize post-operative management. Weakness points are the absence on precise number of platelet injected and of course the limited number of patients.

As showed in Table 19, actually about 11 studies have been published on PRP in the last 5 years, with 6 different PRP systems.

Randelli et al. (19) showed the application of PRP with bovine thrombin on rotator cuff repair: they showed a safe and reproducible procedure in 14 patients. The same group of study (Randelli et al.), has published the results of a randomized controlled study (19); as indicate over, post-operative pain was significantly decreased in PRP group at 3, 7, 14 e 30 days after surgery. Clinical scores were significantly improved in cases group at 3 months ( $p=0.05$ ). But at 6, 12, 24 months there were no statistically significant difference. MRI after 12 months from surgery didn't showed any difference in rate re-tears (cases 40%, controls 52%;  $p>0.05$ ).

Antuna et al (21) studied 14 patients: clinical scores and re-tear rate were similar without statistically significant differences at 24 months. Same results

in study of Ruiz-Moneo et al. (22) (63 patients) and of Gumina et al. (23) (80 patients). In this last work, post-operative follow-up at 13 months showed 1 re-tear episode only in control group.

Jo et al. (11) published a control study which showed clinical scores increased in control group at 3 months, but PRP group included more patients with massive tear that started rehabilitation 6 weeks after surgery, compared with control group that started rehabilitation after 4 week from surgery. No difference was found at 6 and 12 months. Despite this non homogeneous distribution, PRP group showed a smaller re-tear rate after 9 month from surgery. Same group recently published a control randomized study which confirmed a worth re-tear rate in control group.

Next 5 study has utilized Cascade system.

Castricini et al. (2), after 16 months follow-up in a prospective randomized study (88 patients), showed no statistical difference between 2 groups (Constant score and MRI). Nevertheless, re-tear rate was almost significantly higher in control group (2.5% vs 10%;  $p=0.07$ ).

Rodeo et al. (24) (US follow-up at 6 and 12 weeks) doesn't showed any statistical difference tendon healing at MRI (intact tendon: 80.6% in controls, 66.7% in cases at 12 weeks).

Barber et al. (25), in a prospective study, compared 2 group with MRI at 4 months after surgery: tendon deficiency was higher in control (60%vs 30%); in small lesion (<3 cm) tendon healing was better in PRP group (86% vs 50%). By the way no clinical difference were found between 2 groups at 31 months.

**Table 19.**

Author	Evidence level	PRP System	Patients number
Randelli et al (2011)	1	GPS system	53
Ruiz-Moneo et al (2013)	1	PRGF Endoret system	63
Antuna et al (2013)	2	Vivostat system	28
Gumina et al (2012)	1	Regenkit-THT system	76
Jo et al (2011)	2	Cobe spectra system	42
Jo et al (2013)	1	Cobe spectra system	48
Castricini et al (2010)	1	Cascade system	88
Rodeo et al (2012)	2	Cascade system	67
Barber et al (2011)	3	Cascade system	40
Bergeson et al (2012)	3	Cascade system	37
Weber et al (2013)	1	Cascade system	60

Bergeson et al. (8) showed a re-tears rate in favor of control group: 56% in PRP group vs 38% in control group.

Weber et al. (26) showed a statistical difference in re-tears rate in control group (43% vs 29% of PRP group) at 3-5 months after surgery.

Compare these studies is very difficult. There too many variable and not all studies have all variable. In 11 study mentioned, 6 system of PRP production are utilized. Randelli et al. (27) try to gather all the information from these studies, considering all the variable, to determine a statistical significance in re-tear rate. Result was no significant difference in re-tears rate between control group and PRP group, respectively 36% and 31 % ( $p > 0.05$ ). Three study [Jo (11), Castricini (2) and Barber (25)] classified small tear as  $< 3$  cm. Randelli et al. (27) classified rotator cuff tear in relation of tendon retraction (small e medium size if humerus head was exposed without exposition of glenoid). There was a statistically significant difference in re-tear rate in small lesion: 7.9% vs 26.8% ( $p = 0.0002$ , Four square test); in 5 works there wasn't any data for small/medium lesion so they are not considerate. No difference between 2 groups was found in double row repair (PRP 30% vs control 38%) and in single row repair (PRP 32% vs 35%). In Cascade works, re-tear rate was similar (28.5% in PRP group and 27.5% in control group) and the difference was no significant.

In these studies no complication are occurred, except for 2 episodes of infection. Bergeson et al (8) find infection rate of 12% in cases (0% in control group), but this difference was not statistically significant in the study and in complication rate of all studies.

## Conclusions

As showed in literature, PRP treatment doesn't show clearly any improvement in tendon healing in patient with sovraspinatus small tears. About increasing tendon thickness, literature hasn't already cleared its meaning. It would be useful an analysis in this sense, with a clinical and functional study.

PRP represents surely a source of growth factors, but preparation, activation and application are still discussed. In this way, we need additional studies, espe-

cially one level study, to reach definitive and convinced conclusion.

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