

Efficacy of stem cells in partial rotator cuff tears

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Abstract: Background: The purpose of these study was to determine the efficiency of using placental stem cells in the treatment of partial RC (Rotator cuff) tears.

Methods: Triple-blind randomized clinical trial, patients with diagnosis of partial tearing of the supraspinatus tendon were classified into four groups: Bursal tears, articular tears, intrasubstance and full-thickness tears, all of which had an area smaller than 1.5 cm². A 50-mUC injection at the site of injury was performed. Follow up was carried for 12 weeks.

Results: A total of 42 patients were divided into two groups, 8% of the cases were identified as bursal tears, 44% of the cases were articular tears, 20% of the cases were intrasubstance tears, and 28% of the cases were full-thickness tears. We found that the bursal tear cases in the study group showed 50% improvement according to imaging and functional improvement.

Study group

In the articular tear group, 50% of the patients showed improvement. In the intrasubstance tear group, the follow-up results revealed that only 25% of the patients exhibited improvement.

Control group

The articular tear patients showed 60% of improvement. In the articular tear group, 87.5% of the cases showed improvement.

In this group, significant imaging and functional improvements were observed in the patients with articular tears; however, such improvements were not observed in the patients with bursal, intrasubstance or full-thickness tears.

Conclusion: Considering that the process of obtaining stem cells from the placenta and umbilical cord has been widely replicated, the effectiveness of stem cell therapy for muscle-tendon injury repair requires further investigation.

Keywords

Rotator cuff tears, Stem cells.

Introduction

In the United States of America, the prevalence of rotator cuff (RC) injuries is 4-5% in patients under 50 years old and 55-60% in patients older than 55 years.¹ More than 350,000 tendon repairs are estimated to be performed annually.² Extracapsular pressure and load activity constitute the underlying context of most RC injuries due to greater involvement of the joint and tendon.³

The spectrum of RC injuries ranges from partial tears to full-thickness tears, with the latter accounting for 85% of RC injury cases.⁴ Overall, 80% of injuries involve the RC supraspinatus tendon, while fewer injuries involve the infraspinatus tendon, followed by the subscapularis tendon.⁵

The RC repair strategy is determined according to the mode of injury, as described by Neer.⁶

Treatment options for both partial and full-thickness tears aim to stabilize the injury and promote its biological repair.⁷ Some evidence and reports in the literature indicate that biological factors promote the repair of tendon injuries.^{7,8} Therefore, we aim to determine the efficiency of using placental stem cells in the treatment of partial RC tears.

Methods

In a triple-blind randomized clinical trial, patients with an ultrasonographic diagnosis of partial tearing of the supraspinatus tendon from January to September 2018 were classified into four groups: partial bursal tears, partial articular tears, intrasubstance tears and full-thickness tears, all of

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	Control group	Study group	<i>p</i>
Gender, M/F	10/10	4/15	0.04
Age, years	54 (34-68)	55.4 (37-82)	0.05
Dominant extremity, R/L	20/0	18/1	0.036
Affected extremity, R/L	11/9	16/3	0.000
Frontal flexion	126° (40-180)	114°	0.620
Abduction	115° (70-180)	30°	0.001
Internal rotation	L2	L2	0.000
External rotation	31° (0-40)	28° (4-90)	0.001
Constant-Murley score	39	39	0.368
UCLA score	15 (34-74)	13 (7-24)	0.134

Table 1. Description of both groups at the beginning of the study.

which had an area smaller than 1.5 cm². Clinical, radiographic and ultrasound assessments were performed initially to evaluate and measure the tears, and functional Constant-Murley and University of California at Los Angeles (UCLA) shoulder scores as well as clinical range of motion data and specific tests for RC pathology were used to randomly assign the patients to a control group and a study group. A 50-mUC ultrasound-guided direct injection at the site of injury was performed, and a physiotherapy program was prescribed. Weekly monitoring was carried out for 12 weeks, including sonographic assessments to measure the injury and the use of functional scales.

The sonographic assessments were carried out by a blinded specialist certified in musculoskeletal sonography, and the functional scales were evaluated by a specialist with a subspecialty in shoulder surgery and clinical assessment experience. Blinding was maintained throughout the study.

We used descriptive statistics for demographic variables in addition to inferential statistics to analyze numerical variables, with *p* values <0.05 considered significant.

Results

A total of 42 patients were divided into two groups (21 in the study group and 21 in the control group). Three patients were lost to follow-up, including two patients in the study group and one patient in the control group, resulting in a total of 39 patients remaining for analysis (19 vs. 20) (Table 1).

In the overall study population, 14 male patients and 25 female patients were included, with an average age of 54.6 years. The right extremity was affected in 27 cases (70%), and the left extremity was affected in 12 cases (30%). The initial average movement ranges were 122° frontal flexion, 114° abduction, 30° external rotation and L2 internal rotation. The initial average Constant-Murley score

was 39, and the initial average UCLA score was 14 (Table 1).

Among the overall study population, 8% of the cases were identified as bursal tears, 44% of the cases were articular tears, 20% of the cases were intrasubstance tears, and 28% of the cases were full-thickness tears (Table 2).

In the study and control groups, we found statistically significant differences between the initial parameters of the injury and those at the final follow-up, indicating improvement (Figure 1). However, the full-thickness tear group exhibited persistent symptomatology and imaging evidence of tendon injury.

In our analysis of the control and study groups according to tear type, we found that the bursal tear cases in the study group showed 50% improvement according to imaging and functional improvement according to Constant-Murley scores (*p*=0.013) and UCLA scores (*p*=0.030).

	Control group	Study group
Bursal tear	1 (5%)	2 (11%)
Articular tear	8 (40%)	9 (47%)
Intrasubstance tear	4 (20%)	4 (21%)
Full-thickness tear	7 (35%)	4 (21%)
TOTAL	20 (100%)	19 (100%)

Table 2. Number of cases of each group of rotator cuff tear.

Study group

In the articular tear group, 50% of the patients showed improvement on imaging examinations, and only one patient presented progression towards a full-thickness tear. In terms of function, the average Constant-Murley score improved from 45 points to 77.8 points (*p*<0.000), while the average UCLA score improved from 12 points to 24 points (*p*<0.000).

In the intrasubstance tear group, the follow-up results revealed that only 25% of the patients exhibited improvement on imaging as indicated by the absence of injury, 25% of the patients progressed towards full-thickness tears, and 50% of the patients showed no change. Functionally, no statistically significant differences were found between the final and initial Constant-Murley (*p*=0.10) or UCLA scores (*p*=0.51).

Finally, in the full-thickness tear group, ultrasonographic data were available for 100% of the patients, and 86% of the patients presented changes on imaging only in the area of the tear, indicating persistent full-thickness tears. Only 14% of the

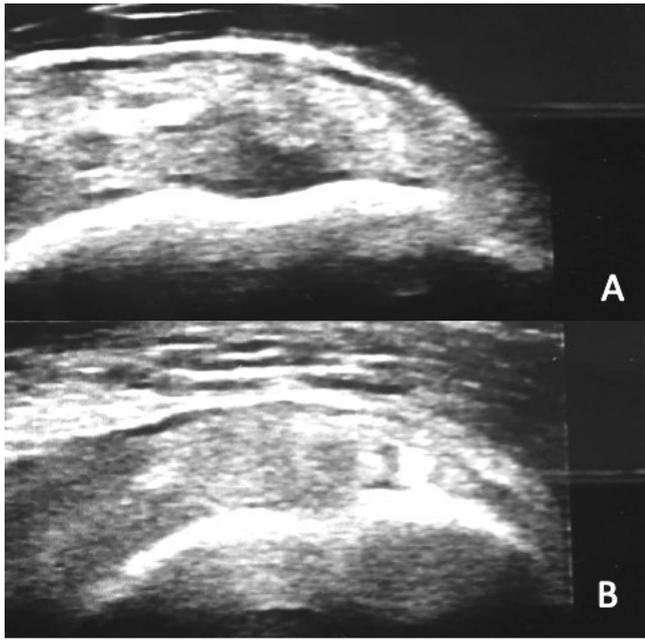


Figure 1. A. Initial image of a patient with an intra-articular tear. B. Image at 6-week follow up

patients showed progression towards bursal tears. Functionally, no statistically significant differences were found between the final and initial Constant-Murley ($p=0.89$) or UCLA scores ($p=0.70$).

Control group

The articular tear patients in the control group showed greater improvement on imaging compared to the articular tear patients in the study group (60%) as well as a 55% reduction in the average injury area. Only 15% of the patients progressed to complete tears. In terms of function, the average Constant-Murley score improved from 52 points to 74.6 points ($p<0.000$), and the average UCLA score improved from 15.4 points to 25 points ($p<0.000$).

The single patient with a bursal tear in the control group did show any changes in the injury, although a 30% reduction in the injury area was noted. Clinically, the patient's improvement was significant at the end of the follow-up, with a final Constant-Murley score of 67 points versus 18 points initially and a final UCLA score of 18 points versus 23 points initially.

In the articular tear group, 87.5% of the cases showed improvement, as indicated by the absence of injury on ultrasound images at the end of the follow-up. Only one case (12.5%) progressed towards a full-thickness tear. Functionally, the average Constant-Murley score increased from 55.2 points to 66.7 points ($p=0.005$), and the average UCLA score increased from 15.3 points to 22.6 points ($p=0.028$).

In the intrasubstance tear group, only 25% of the cases showed no injury on imaging at the end of the follow-up, and improvements varied in the

remaining cases. Functionally, the average Constant-Murley score ranged from 54 to 79 points ($p=0.87$), and the average UCLA score ranged from 12 to 23 points ($p=0.41$).

In the full-thickness tear group, ultrasonographic data were available for 85% of the cases, and 86% of these cases presented a decrease in the injury area. One patient (14%) showed a 30% increase in the injury area. Functionally, statistically significant differences were found between the initial and follow-up measurements, with a final Constant-Murley score of 46.7 points versus 78.7 points initially ($p=0.001$) and a final UCLA score of 16.5 points versus 28.8 points initially ($p=0.001$).

Discussion

In this clinical trial, we compared the radiographic and functional results of patients with different types of RC tears between those treated with placental stem cells and those in a control group. In the study group, significant imaging and functional improvements were observed in the patients with articular tears; however, such improvements were not observed in the patients with bursal, intrasubstance or full-thickness tears.

Compared with the control group, no significant improvements were observed in the study group. In the control group, improvements were observed in three of the four tear-type groups, although not on ultrasound imaging. However, improvements in function and patient satisfaction were noted.

Patients with full-thickness tears did not show improvement in either the study group or the control group, indicating the need for different treatment options for these patients.

Conclusion

Biological repair of partial RC injuries remains controversial. In our study group, the use of placental stem cells was effective in the treatment of partial tears, mainly tears of the articular side of the tendon, according to both clinical and ultrasound imaging examinations; however, the outcomes for bursal tears were not superior to those in the control group.

Multicenter studies with larger sample sizes are required to truly define the efficacy of these treatments in specific populations.

Considering that the process of obtaining stem cells from the placenta and umbilical cord has been widely replicated, the effectiveness of stem cell therapy for muscle-tendon injury repair requires further investigation.

Conflicts of interest

None.

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