

# Ultrasound-guided subacromial injections of sodium hyaluronate for the management of rotator cuff tendinopathy: a prospective comparative study with rehabilitation therapy

G. Merolla · P. Bianchi · G. Porcellini

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## Abstract

**Background** Rotator cuff (RC) tendinopathy is a common cause of pain and shoulder dysfunction. The literature evidence suggests that a combination of overuse and extrinsic compression may induce chronic RC tendinopathy. Aim of the current study was to compare the results of subacromial sodium hyaluronate injections with rehabilitation therapy.

**Materials and methods** We enrolled 48 patients (M/F: 26/22; mean age: 50 years; shoulder right/left: 29/19) with persistent shoulder pain for at least 4 months. Exclusion criteria were as follows: RC tear, calcifying tendinitis, glenohumeral instability, osteoarthritis, rheumatic diseases, physical therapy and/or injection in the previous 4 months, shoulder surgery, anesthetic nerve block, trauma, and severe medical diseases. The included subjects received either two ultrasound-guided subacromial hyaluronic acid (HA) injections (25 patients, HA group) at baseline and 14 days, or underwent rehabilitation therapy (23 patients, Physio group) including active shoulder mobilization, soft tissue stretching and humeral head positioner and propeller muscles strengthening for 30 days (3 sessions every week). Clinical assessment of shoulder function was performed with visual analog scale score for pain (0–100), Oxford Shoulder Score (OSS), and Constant–Murley Score (CS). Overall, patients were examined at baseline, week 2, week 4, week 12, and week 24. Statistical significance was set at 5 % ( $p < 0.05$ ).

**Results** Reduction in overall pain in the HA group was statistically significant at week 2 ( $p < 0.05$ ) week 4 ( $p < 0.05$ ), week 12 comparing to baseline. Similarly, pain subscores (at night and with activity) were significantly lower at week 2 ( $p < 0.05$ ), week 4 ( $p < 0.05$ ), and week 12 ( $p < 0.05$ ), respectively. In the Physio group, pain decreased significantly at week 2 ( $p < 0.05$ ) but not maintained at week 4 ( $p > 0.05$ ), week 12 ( $p > 0.05$ ), and week 24 ( $p > 0.05$ ). CS and OSS in the HA group increased significantly at week 2 ( $p < 0.05$ ), week 4 ( $p < 0.05$ ), and week 12 ( $p < 0.05$ ). A non-statistically significant increase in clinical scores was found at week 24 ( $p > 0.05$ ). A significant improvement of CS and OSS we found in the Physio group at week 2 ( $p < 0.05$ ), but not at weeks 4, 12, and 24 ( $p > 0.05$ ).

**Conclusions** Subacromial HA injections could be an effective and safe alternative treatment for patients suffering from RC tendinopathy. We believe that the results of this study are encouraging but not lasting and we might suppose that a series of three to four subacromial sodium hyaluronate injections could provide good mid- and long-term clinical benefits.

**Keywords** Shoulder · Injection · Sodium hyaluronate · Rotator cuff · Tendinopathy

## Introduction

Rotator cuff (RC) tendinopathy is a common source of pain and shoulder dysfunction that affects both the young and older population [1] mainly in arduous overhead workers [2]. The available research findings emphasize the multifactorial origin of RC tendinopathy that begins as a failure in the tendon fibers due to the overuse and cyclic loading on their internal side [1]. Under these conditions, the subunits of the RC tendons undergo internal compressive

G. Merolla (✉) · G. Porcellini  
Unit of Shoulder and Elbow Surgery, D. Cervesi Hospital,  
Via L. V. Beethoven 46, Cattolica, Italy  
e-mail: giovanni.merolla@auslrm.net;  
giovannimerolla@hotmail.com

P. Bianchi  
Department of Orthopedics, Traumatology, Rehabilitation  
and Plastic Surgery, Second University of Naples, Naples, Italy

forces which induce the development of fibrocartilage in these regions [3]; particularly, fibrocartilage develops on the articular side of the supraspinatus tendon close to its insertion, where the articular fibers are subjected to less strain than the non-articular side [4, 5]. Fibrocartilage is less capable of withstanding tension load, and joint-side fibers have half the force of the bursal-side fibers [6]. Furthermore, the supraspinatus and infraspinatus are inserted into a cable located 1.5 cm from the humeral insertion of the fibers [7], and the “crescent” region is located between the cable and the humerus insertion where the tendon fibers are thinner and close to the hypovascularized region and therefore are more susceptible to degeneration [8]. This evidence suggests that a combination of overuse and extrinsic compression may induce chronic RC tendinopathy. Conservative therapies, including rehabilitation, physical therapies analgesics, and non-steroid anti-inflammatory drugs (NSAIDs), are commonly recommended to restore shoulder function in chronic RC tendinopathy. Physiotherapy is based on the correction of the flexibility, motion, and strength that are the cause of painful shoulder [9]. Subacromial supplementation with sodium hyaluronate or hyaluronic acid (HA) has been proposed to treat RC dysfunction [10] due to its action as a lubricant [11] and suppressor of the joint inflammatory process [12]. To our knowledge, no studies in the literature have compared physiotherapy and subacromial HA injection; therefore, the purpose of the current research was to assess the efficacy and safety of sodium hyaluronate injection versus physiotherapy in a population of patients with painful chronic RC tendinopathy.

## Materials and methods

### Study population

The study was approved by the Hospital Institutional review board (Prot. 4232/2011/I.5/186), and all patients gave informed consent prior to enrollment. This was a prospective non-randomized comparative study involving a study population of 60 patients with RC tendinopathy aged from 47 to 53 years old, seen in the outpatient office of our Shoulder and Elbow Unit between June 2010 and March 2011 (Table 1).

Patients were considered eligible for subacromial therapy if they were 18 years or older, had persistent shoulder pain for at least 4 months, clinical diagnosis of RC tendinopathy detected with MRI, no previous treatment with articular or subacromial steroid injections within the last 4 months, availability for the duration of the study. Patients were excluded if they refused to consent to such a procedure, had a positive history of shoulder trauma, partial

or complete RC tears, calcifying tendinitis, previous arthroscopic or open shoulder surgery, shoulder instability, infections or neoplasm, symptomatic cervical spine disease, rheumatoid arthritis or immune diseases, gout and uric acid diseases, severe medical conditions, or were pregnant. Patients were also assessed for their mental status and excluded if they presented with cognitive limitations that could prevent them expressing a valid consent, or undergo subjective and objective evaluations. We also excluded subjects with known allergic or adverse reactions to previous nonsteroid or hyaluronan injections. All evaluations were performed by two experienced shoulder surgeons. The diagnosis of RC tendinopathy was performed by trained musculoskeletal radiologists who depicted a high tendon signal intensity that was anatomically intact on the MRI in T2-weighted images. During the screening, 10 patients were excluded because they refused the treatment or failed to comply with the inclusion criteria. We allowed a rescue medication of oral paracetamol at a maximum dosage of 4 g/day, and the amount taken by each patient was recorded at the four follow-up visits. Withdrawal of rescue medication (paracetamol) 24 h prior to each follow-up visit was recommended by the assessor and confirmed by the patients during the examination. There were no statistically significant differences between the two groups of treatment with respect to demographic characteristics at baseline (Table 1).

**Table 1** Demographic and anthropometric data of the population enrolled in the study

Variable	Data		
	HA group	Physio group	<i>p</i> value
Patients (No.)	25	23	0.9651
Mean age (years $\pm$ SD)	49 $\pm$ 2.35	51 $\pm$ 2.64	0.8947
Gender (M/F) (%)	14/11 (56/44)	12/11 (52/44)	0.7591
Mean height (cm $\pm$ SD)	172 $\pm$ 1.42	168 $\pm$ 1.67	0.9720
Mean weight (kg $\pm$ SD)	71 $\pm$ 2.42	73 $\pm$ 1.96	0.9053
Side			
Right/left (%)	16/9 (64/36)	13/10 (56/44)	0.6974
Dominant	14/11 (56/44)	14/9 (61/49)	0.9896
Interval from symptoms to treatment (months)	12 $\pm$ 1.69	11 $\pm$ 1.85	0.9531
Injection approach	Anterolateral		
Follow-up visit (days $\pm$ SD)	Week 2 (14 $\pm$ 5.6)	Week 2 (14 $\pm$ 7.5)	
	Week 4 (28 $\pm$ 7.2)	Week 4 (27 $\pm$ 8.2)	
	Week 12 (84 $\pm$ 8.6)	Week 12 (83 $\pm$ 6.6)	
	Week 24 (168 $\pm$ 7.6)	Week 24 (168 $\pm$ 6.8)	

*SD* standard deviation



**Fig. 1** Anatomical landmark with the two sites of injections drawn for the anterolateral approach to the subacromial space

### Treatment groups

We recruited an intent-to-treat population to be assigned to two treatment groups with the objective of gaining an improvement in the pain score of 4 points and in the Constant–Murley scale of 10 points. According to these parameters and a power value of 0.8, we had enrolled 50 patients consecutively: the first half in the hyaluronic acid group (HA group,  $N = 25$ ) and the second half in the physiotherapy group (Physio group,  $N = 25$ ).

### Ultrasound-guided injection

The study material was a specific preparation (SportVis™, MDT Int'l SA, Switzerland), whose main content is a STABHA™ (Soft Tissue Adapted Biocompatible Hyaluronic Acid) of 1 million of daltons contained in a pre-filled syringe (12 mg/1.2 ml).

The procedure was performed in a standardized way in the outpatients' office with the patient in the upright position using local disinfection, sterile drape, and marking the site of injection (Fig. 1). A shoulder surgeon (MG) with 10 years of experience injected all the shoulders using an ultrasound-guided anterolateral approach and the same GE Logiq 7 ultrasound machine (7.5–14 MHz). We first checked the tendon thickness and its superior limitant. Subsequently, a 22G needle was introduced beneath the anterolateral acromial edge above the tendon (Fig. 2), taking care not to overcome the superior limitant. The preparation was injected allowing it to spread over the superior tendon surface (Fig. 3).

### Physiotherapy

We set a standard protocol of physiotherapy [9] for 30 days, following three sessions a week. The loss of flexibility due to the glenohumeral internal rotation deficit



**Fig. 2** The preparation is injected under ultrasound assistance taking care to direct the needle medially and posteriorly, on the insertion area of the supraspinatus tendon

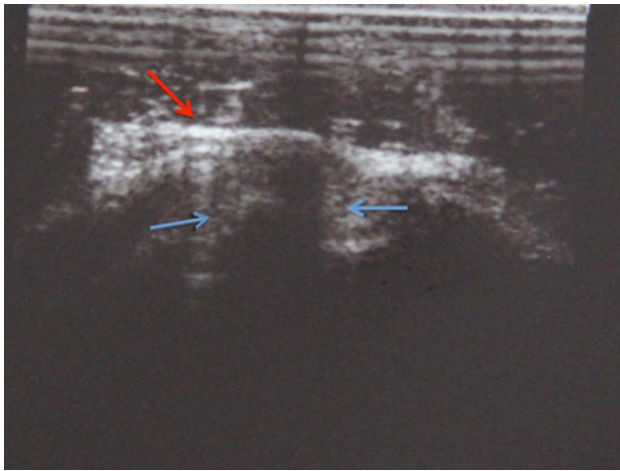
(GIRD) and the coracoid base muscles tightness was treated using open stretch in the supine position and rotation stretch exercises with the scapula stabilized. Scapula control was obtained performing exercises for lower trapezius and serratus anterior with the arm below 90° abduction. RC activation exercises were allowed after a stable scapular base was established and included horizontal and vertical closed-chain exercises, horizontal open-chain exercises, and diagonal closed-chain exercises. The final sequence was completed with open-chain plyometric exercises.

### Outcome measurements

Primary outcome measurements were the visual analog scale (VAS) for pain.

Secondary outcomes measurements were the Constant–Murley scale (CS) [13] and the Oxford Shoulder Score (OSS) [14, 15], the Patient Global Assessment (PGA), the tolerability and any adverse events after each injection.

Pain included overall pain, pain at night, pain with activity, and pain without activity and was rated subjectively on a scale ranging from 1 (no pain) to 10 (severe pain). Patients were invited to write their average pain rate for the previous 48 h. The CS included a subjective questionnaire for pain, the ability to perform daily living activity (DLA), an objective evaluation of active range of motion (ROM) and strength. Pain was scored on a 15-point scale (0 severe pain, 15 no pain), while DLA was scored on a 20-point scale, with lower scores associated with greater impairment on DLA. ROM was measured using a standard goniometer between the upper arm and the upper part of the thorax. Shoulder strength was assessed using the Lafayette handheld dynamometer (Lafayette Instruments, Lafayette, Ind, USA) that has a microprocessor with a resolution of 0.4 lb (0.2 kg) in the range 0–50 pounds



**Fig. 3** Ultrasound image showing the needle (red arrow) placed in the subacromial bursa, on the superior limitant of the supraspinatus tendon. The blue arrows emphasize the preparation that expanded above the tendon surface (color figure online)

(0–22.6 kg), 0.03 % accuracy with two calibration points: 0.25 and 50 lbs (0.11 and 22.6 kg). Data were recorded and analyzed using SPSS version 10 software (SPSS Inc, Chicago, IL, USA). We assigned 1 point for each 0.5 kg of strength registered.

The OSS is a 12-item patient-reported outcome measure specifically used for assessing the impact of RC tendinopathy on the patient's quality of life. Each question on the OSS is scored 0–4, with 4 representing the best; the twelve items are summed to produce overall scores ranging from 0 to 48. Interpreting the OSS: a score 0–19 indicates a severe shoulder condition, a score 20–29 indicates a moderate to severe shoulder condition, a score 30–39 indicates a mild to moderate shoulder condition, a score 40–48 may indicate a satisfactory shoulder function.

#### Follow-up

Overall, patients were assessed immediately before the treatment (baseline), at the time of the second injection (week 2), and subsequently at week 4, week 12, and week 24. The value of the subjective pain score was recorded by each patient using a printed analogic scale. Data were then entered on an electronic worksheet (Microsoft Excel for Mac OS 2011) which calculated the average values for pain overall and relative subscores. CS and OSS were obtained as the numeric sum of the subjective and objective evaluations using a dedicated electronic version of both scales ([www.orthopaedicscores.com](http://www.orthopaedicscores.com)) that gave the final score at the end of the questionnaire. Overall clinical scores were collected by two independent observers who had not performed the injections.

**Table 2** Overall pain scores in the HA and Physio groups

Follow-up	HA group	<i>p</i> value within HA group	Physio group	<i>p</i> value within Physio group	<i>p</i> value between HA and Physio groups
Week 0	7.48 ± 1.61	–	7.17 ± 1.23	–	0.9671
Week 2	4.22 ± 0.96	0.0161	4.43 ± 1.26	0.0103	0.7281
Week 4	4.12 ± 1.12	0.0123	6.34 ± 1.18	0.9418	0.0149
Week 12	4.01 ± 1.04	0.0114	6.17 ± 1.16	0.9942	0.0168
Week 24	6.04 ± 1.21	0.4047	6.26 ± 1.32	0.9486	0.8725

Data refer to mean ± SD values

*p* values refer to analysis versus baseline

#### Statistical analysis

Statistical analysis was performed using the Kruskal–Wallis test for the equality of populations and the ANOVA test for the variables, setting the significance at 5 %. Bravais–Pearson correlation coefficient was calculated to analyze the variability of the two independent observations.

#### Results

All the 25 patients with persistent shoulder pain due to RC tendinopathy considered for subacromial injection treatment with hyaluronic acid (HA group) from June to July 2010 completed the follow-up evaluations (Table 1).

Among the 25 patients who were assigned to the physiotherapy group (Physio group) from August to October 2010, two cases were excluded: one case because he refused to consent to the use of his data for research purposes at the time of the enrollment and one case due to incomplete evaluation (lost at last follow-up examination) (Table 1).

#### Pain score and subscores

In the HA group, we registered a remarkable decrease in overall pain score from baseline to the week 2 ( $p < 0.05$ ), week 4 ( $p < 0.005$ ), and week 12 ( $p < 0.05$ ), and it was always statistically significant. The pain reduction was recorded at week 24, but no statistically significant difference was found ( $p > 0.05$ ) (Table 2). Similarly, pain subscores (at night and with activity) were significantly lower compared with baseline values, respectively, at week 2 ( $p < 0.05$ ), week 4 ( $p < 0.05$ ), and week 12 ( $p < 0.05$ ), while at week 24, such reduction was maintained but not statistically significant ( $p > 0.05$ ) (Table 3).

In the Physio group at follow-up evaluation, we found that pain decreased significantly at week 2 ( $p < 0.05$ ) while

**Table 3** Pain with activity and pain at night in the HA and Physio groups

	Follow-up								
	Week 0	Week 2	<i>p</i> value	Week 4	<i>p</i> value	Week 12	<i>p</i> value	Week 24	<i>p</i> value
<i>HA group</i>									
Pain at night	7.81 ± 0.96	4.25 ± 1.05	0.0104	4.28 ± 1.12	0.0110	4.82 ± 1.06	0.0391	6.42 ± 1.04	0.8492
Pain with activity	8.02 ± 1.03	4.34 ± 0.96	0.0109	4.32 ± 1.07	0.0103	4.76 ± 1.11	0.0386	6.63 ± 0.98	0.9578
<i>Physio group</i>									
Pain at night	7.74 ± 1.05	5.98 ± 1.02	0.0671	6.60 ± 1.13	0.5965	6.49 ± 1.02	0.4827	6.48 ± 1.10	0.8307
Pain with activity	7.94 ± 1.04	5.96 ± 0.98	0.0798	6.65 ± 0.97	0.5984	6.60 ± 1.14	0.5879	6.69 ± 1.06	0.8966

Data refer to mean ± SD values

*p* values refer to analysis versus baseline

higher values were registered at week 4 ( $p > 0.05$ ), week 12 ( $p > 0.05$ ), and week 24 ( $p > 0.05$ ) (Table 2). Pain at night and pain with activity had similar trend with a significant decreasing at week 2 ( $p < 0.05$ ) and persistent higher values at week 4 ( $p > 0.05$ ), week 12 ( $p > 0.05$ ), and week 24 ( $p > 0.05$ ) (Table 3).

#### Constant–Murley Score and Oxford Shoulder Score

The average values of CS and OSS in the HA group increased significantly comparing to baseline at week 2 ( $p < 0.05$ ), week 4 ( $p < 0.05$ ), and week 12 ( $p < 0.05$ ). A non-statistically significant increase in clinical scores was found at week 24 ( $p > 0.05$ ). In the Physio group, we recorded significantly higher values of CS and OSS at week 2 ( $p < 0.05$ ), but at week 4, 12, and 24, there was no significant difference compared with baseline values ( $p > 0.05$ ) (Tables 4, 5).

#### Comparison between HA and Physio groups

##### Overall pain and subscores

Overall pain and subscores were stratified to evaluate the difference in pain scores between the two groups of treatment. There was no statistically significant difference in overall pain scores between the groups at baseline and at week 2 ( $p > 0.05$ ). We found an average difference of 2.22 points at week 4 ( $p = 0.0149$ ) and 2.16 points at week 12 ( $p = 0.0168$ ), while the difference at week 24 was not statistically significant ( $p > 0.05$ ) (Table 2). Subscores for pain at night were significantly different at week 4 ( $p = 0.0487$ ), and remained at week 12, while the average difference found at week 24 was not significant ( $p > 0.05$ ). A similar trend was found for pain with activity which registered a significant difference at week 4 ( $p = 0.0318$ ) and maintained at week 12 and but not at week 24 ( $p > 0.05$ ). Rescue medication consumption was found to

be similar at week 2 and 4 in both groups, and higher from the week 12 to the week 24 in the Physio group.

##### Clinical scores

The CS showed no significant difference at baseline and week 2 between the groups ( $p > 0.05$ ). There was a persistently statistically significant higher score at week 4 and week 12 in the HA group versus physiotherapy group ( $p < 0.05$ ), and maintained at week 24 follow-up but without statistical significance ( $p > 0.05$ ). The OSS in the two groups had the same values at baseline, but significantly higher scorers registered in the HA group at weeks 4 and 12 ( $p < 0.05$ ) and such improvement difference maintained at week 24 but with no significant difference ( $p > 0.05$ ). Inter-observer agreement resulted in *k* values ranging from 0.81 to 0.85 for CS and from 0.80 to 0.88 for OSS; good intra-observer agreement was registered with  $k = 0.85–0.90$ .

##### Patient global assessment and adverse events

The PGA showed good patient compliance with no serious adverse events registered during the experimentation. The anterolateral approach injections, with US assistance, proved to be safe and well tolerated by all the patients enrolled for the study.

## Discussion

Sodium hyaluronate is effective in managing acute or chronic ligaments and tendon injuries, like ankle sprains and epicondylalgia [16, 17]. HA is believed to integrate into the extracellular fibrin matrix to help realignment of fibrils thanks to electrostatic interactions. Thus, stability of form and function is then restored allowing healing to occur in structures (ligaments and tendons) and shortening the rehabilitation process. Recent research findings



**Table 4** Comparison of Constant–Murley Score in the HA and Physio groups

Follow-up	HA group	<i>p</i> value within HA group	Physio group	<i>p</i> value within Physio group	<i>p</i> value between HA and Physio groups
Week 0	53.08 ± 1.04	–	52.91 ± 2.10	–	0.9539
Week 2	70.12 ± 1.09	0.0128	66.82 ± 1.92	0.0137	0.8782
Week 4	69.72 ± 1.16	0.0196	59.21 ± 1.88	0.0891	0.0492
Week 12	67.44 ± 1.09	0.0181	59.30 ± 1.21	0.0752	0.0593
Week 24	59.04 ± 1.13	0.7652	57 ± 1.89	0.2497	0.2891

Data refer to mean ± SD values

*p* values refer to analysis versus baseline

**Table 5** Comparison of Oxford Shoulder Score in the HA and Physio groups

Follow-up	HA group	<i>p</i> value within HA group	Physio group	<i>p</i> value within Physio group	<i>p</i> value between HA and Physio groups
Week 0	23.28 ± 0.98	–	26.21 ± 1.08	–	0.7841
Week 2	38.68 ± 1.12	0.0023	37.21 ± 1.04	0.0137	0.9614
Week 4	38.12 ± 1.21	0.0076	29.13 ± 1.09	0.5931	0.0395
Week 12	38.21 ± 1.16	0.0109	29.34 ± 1.03	0.5873	0.0485
Week 24	29.36 ± 1.07	0.0847	28.82 ± 1.15	0.7942	0.9238

Data refer to mean ± SD values

*p* values refer to analysis versus baseline

demonstrated that repeated periarticular injections of the study materials were more effective in pain relief and joint function improvement, compared to placebo or standard conservative treatment for ankle sprains and lateral epicondylalgia. Long-term follow-up by investigators confirmed the therapeutic effects persist after 12 and 24 months [16, 17].

Several trials using sodium hyaluronate in the treatment for chronic shoulder pain have been documented, on shoulder osteoarthritis [18], RC tears [19], peri-arthritis [20, 21] adhesive capsulitis [22], and chronic shoulder pain of different etiologies [23].

The effectiveness of subacromial injections of HA alone in patients with chronic RC tendinopathy is also reported in the literature. In an open label multicenter study, Itokazu et al. [21] observed a significant pain and range of motion improvement after subacromial high-molecular weight sodium hyaluronate injection for 5 weeks or more, and they conclude that this treatment was effective in patients with peri-arthritis of the shoulder. Kim et al. [24], in a prospective randomized single-blind comparative study on 105 patients with subacromial impingement, found that hyaluronate injections produced more significant pain reduction and similar functional improvement comparing to corticosteroid at 12 weeks. On the contrary, respect to our results, Penning et al. [25] reported a significant reduction in pain at short- and long-term follow-up with corticosteroid injections compared with hyaluronic acid

and in the long-term placebo injections showed the best results. In the current study, physiotherapy was selected for the comparator because it is proven to be effective in shoulder tendinopathy management [26] and is recommended by the recent European guidelines (2008). A standard program of physiotherapy is recommended to correct inflexibility, loss of strength and mobility in RC, and associated structures, but it is common that these conditions persist despite a proper rehabilitation program which is phased into a maintenance program to reduce the risk of reinjury [9]. The current study compared directly the effects of HA injections and physiotherapy, and we found that both treatments produced good results in pain and clinical scores in the short term, with a significant pain decrease at week 2 of 3.3 points in the HA group and 2.8 points in the Physio group. In midterm, the pain score maintained a significant improvement at week 4 and week 12 only in the HA group, while the improvement found in the Physio group was not significant at week 4 and week 12 compared to the baseline. Pain subscores at night and during activity in the HA group showed a significant reduction from the start of the study throughout follow-up, except for week 24, while in the Physio group, the reduction in pain subscores was not significant from week 2 to week 24. CS and OSS showed a course similar to overall pain, with a significant improvement in both treatment groups at week 2, persistent pain relief in the HA group only at week 4 and week 12, and a return to lower but

non-statistically significant scores with respect to baseline, at week 24 in both groups. The consumption of rescue medication was higher in the Physio group from week 12 to week 24, but at the end of the study, such difference became not significant. These results suggest that subacromial HA injections are effective in inducing better clinical outcomes and pain relief compared to physiotherapy from the start of the study up to week 12, the therapeutic effects became less important at 6 months when symptoms gradually returned. Stratifying the results, we found that five patients in the Physio group had worsening VAS scores at the end of study, whereas this was seen in only two patients in the HA group. The two patients in the HA group were young in age and have relative high daily activities on the shoulder in life, that is, regular fitness training and therefore higher risk to develop overuse tendinopathy and subacromial bursitis. The procedure for shoulder injection was safe without any adverse events registered in all the enrolled subjects.

We used the same anterolateral approach with ultrasound assistance, to allow the injection on the superior limitant of the supraspinatus tendon as accurate as possible [27]. Using this approach, we ensured that the HA preparation was injected on the thinner crescent supraspinatus fibers, [7] located within the hypovascular region (critical zone) [8] and more at risk of degeneration and tearing.

Our research findings confirmed the good early- and midterm results of HA in RC tendinopathy and are consistent with the outcomes of Itokazu et al. [23] and with those reported by Kim et al. [24] who described a good VAS and ASES scores in patients treated with HA injections by using corticosteroids as a comparator.

The choice of two injections 2 week apart could explain the lower clinical scores observed at 6 months, and it might be reasonable to expect that the long-term results may be more favorable if the number of injections was increased using protocols similar to those already tested by other authors [24, 27]. The lack of randomization and placebo control, the limited sample size represent the limitations of this research. Taking into account these limitations, we still have to note that the combination of physiotherapy with subacromial injections showed the better results as suggested by the available literature evidence [28]. Physiotherapy can be regarded as part of the conservative treatment to be undertaken in subjects with chronic RC tendinopathy, but this treatment alone is not able to reduce pain and restore shoulder function in long term. A recent Cochrane review [29] concluded that subacromial corticosteroid injection has insufficient overall evidence to support its usage. It might be beneficial for RC disease and intra-articular injection for adhesive capsulitis, but their effect is small and not well maintained. We believe that a series of three to four subacromial sodium hyaluronate

injections could provide good mid- and long-term clinical benefits.

## Conclusions

Despite the limitations of the current research, such as no randomization and relatively small sample size, we may conclude that subacromial HA injections could be an effective and safe alternative treatment for patients suffering from RC tendinopathy. Our results are encouraging but not lasting, and we might suppose that further investigation with a larger sample size into the optimal injection regime and possible combination with current standard therapies, so as to provide long-term benefits, are warranted.

**Conflict of interest** None.

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