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# Effects of supplementing extracorporeal shockwave therapy to hyaluronic acid injection among patients with rotator cuff lesions without complete tear: a prospective double-blinded randomized study

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**Background:** The study investigates the combined efficacy of subacromial hyaluronic acid (HA) injections and extracorporeal shockwave therapy (ESWT) in managing rotator cuff lesions without complete tears.

**Materials and methods:** Eligible patients were randomized into three groups: three HA injections combined with two sham ESWT (HA), three HA injections combined with one ESWT and one sham ESWT (HA + 1 ESWT), or three HA injections combined with two ESWT (HA + 2 ESWT) with an allocation ratio of 1:1:1. Visual Analogue Scale (VAS), Constant–Murley Score (CMS), range of motion (ROM), and muscle power of shoulder abduction (MP) were assessed preintervention and at 1, 3, 6, and 12 months postinitial HA injection. Shoulder MRI was conducted before and 12 months after the intervention.

**Results:** All pertinent parameters showed no significant between-group differences at baseline but demonstrated significant within-group improvement throughout the study. The HA + 1 ESWT group demonstrated superior improvements in MP ($P = 0.011$) and CMS ($P = 0.018$) at 1 month, and in MP ($P = 0.014$) and CMS ($P = 0.005$) at 6 months, compared to the HA group. The HA + 2 ESWT group showed greater improvements in FF ($P = 0.027$), IR ($P = 0.019$), and SROM ($P = 0.025$) at 1 month, and in ABD ($P = 0.022$) at 6 months, compared to the HA group. Notably, the HA + 2 ESWT group exhibited greater improvements in FF ($P = 0.013$), IR ($P = 0.019$), and SROM ($P = 0.025$) at 1 month, and in FF ($P = 0.007$) at 3 months, than the HA + 1 ESWT group. Moreover, no deterioration in tendinopathy grading or tear status occurred in the HA + 1 ESWT group on MRI scans.

**Conclusion:** ESWT provides additional benefits when combined with HA injections for patients with rotator cuff lesions lacking complete tears.

**Keywords:** Constant–Murley score, extracorporeal shockwave therapy, hyaluronic acid, rotator cuff lesion without complete tear

## HIGHLIGHTS

- The HA + 1 ESWT group demonstrated superiority in muscle power of shoulder abduction (MP) improvement and Constant–Murley Score (CMS) improvement compared to the HA group at various intervals, while the HA + 2 ESWT group also exhibited superiority over the HA group in terms of MP improvement and CMS improvement at variable time points. However, no discernible difference was observed between the HA + 1 ESWT group and the HA + 2 ESWT group.
- Both the HA + 1 ESWT and the HA + 2 ESWT groups exhibited superiority in various aspects of range of motion compared to the HA group across different intervals. Specifically, the HA + 2 ESWT group showed better improvement in forward flexion, internal rotation, and sum of range of motion at 1 month after Day 1, as well as better improvement in forward flexion at 3 months after Day 1, in comparison to the HA + 1 ESWT group.
- None of the participants in the HA + 1 ESWT group exhibited worsening in tendinopathy grading and tear status in shoulder MRI.

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## Introduction

Rotator cuff (RC) tendinopathy is a prevalent orthopaedic disease, often causing shoulder discomforts including pain and limited range of motion[1–5]. The prevalence of RC tendinopathy increases with age, with over half of the general population experiencing a lesion in their sixth decade[4]. Risk factors for RC tears include older age, male sex, smoking, diabetes, hypertension, and a higher critical shoulder angle[6].

The prevalence of partial RC tears is substantial, ranging from 15 to 32% in the general population and increasing to 40% in the dominant shoulder of professional overhead athletes[3]. Partial RC tears are more common than complete tears, with the majority of complete tears being attributed to partial tears[7]. Partial RC tears may be more painful than full-thickness tears due to the nonphysiological tension within the remaining intact RC fibres[8]. Conservative modalities are prevalent in RC tendinopathy management, particularly in the absence of full tears. Hyaluronate acid (HA) injections and extracorporeal shockwave therapy (ESWT) have gained popularity as treatment options[9].

Hyaluronic acid (HA) constitutes a nonsulphated glycosaminoglycan comprising repetitive units of glucuronic acid and N-acetyl glucosamine. It is extensively distributed in the extracellular matrix of both vertebrates and invertebrates, providing mechanical support, viscoelasticity, hygroscopic properties, and anti-inflammatory effects to cells and tissues. While the impact of hyaluronic acid on the biomechanical characteristics of tendons remains unclear, it has been shown to augment fibroblast activity, encompassing adhesiveness, synthesis of the extracellular matrix, and proliferation[10]. Clinical studies have highlighted the therapeutic potential of exogenous HA injections in alleviating pain, enhancing function, and reducing tendon rubbing in various tendinopathies, including those affecting the RC, epicondyle, patellar, and Achilles tendons, as well as in tendon injuries and postsurgical tendon repair[11].

Extracorporeal shockwave therapy (ESWT) has been employed in treating various musculoskeletal diseases[2,12–19]. ESWT, with its diverse mechanisms, partially unleashes its therapeutic potential through a phenomenon known as 'regenerative rehabilitation', physically stimulating damaged tissue to amplify regenerative processes and enhance therapeutic efficacy[20]. ESWT delivers rapidly rising positive pressure impulses ranging from 5 to 120 MPa in ~5 ns, followed by a decrease to negative pressure values of −20 MPa at the treatment site[16]. ESWT can induce hypervascularity in the ischaemic RC tendon and may temporarily increase cell membrane permeability, facilitating the entry of treatment molecules into the cells[21]. These distinguishing advantages set ESWT apart from other potential stimulation methods.

Presently, the concurrent use of medications has emerged as a predominant strategy for managing various medical conditions, including diabetes and hypertension. However, there has been limited discourse regarding the concurrent application of ESWT and injection therapy for treating RC lesions without complete tears, and whether ESWT can manifest dose-dependent therapeutic effects remains uncertain. Our prior research has suggested that combining ESWT with platelet-rich plasma (PRP) injection may confer advantages beyond those of PRP injection alone in terms of range of motion (ROM) for cases of RC lesions without complete tears[22]. Conversely, although a retrospective study hinted at potential benefits of combining ESWT with HA over stand-alone ESWT therapy concerning the numerical rating scale (NRS) and Shoulder Pain and Disability Index (SPADI) score 1 month and 2 months post-treatment[11], these findings lack validation from prospective randomized studies. Additionally, the potential dose-dependent effects of ESWT when combined with HA remain unexplored. To address these clinical uncertainties, we conducted a prospective randomized study to investigate the combined effects of ESWT and HA and to assess whether ESWT demonstrates dose-dependent benefits when used alongside HA. The hypothesis posited by this study is that the combination of ESWT with HA injections will yield superior therapeutic outcomes compared to HA injection alone in the management of RC lesions lacking complete tears. Additionally, the study explores the potential for ESWT to demonstrate dose-dependent effects when used in conjunction with HA.

## Material and methods

### *Patient recruitment*

This study obtained approval from the Institutional Review Board of ? Medical Foundation and was conducted between 1 August 2019 and 31 July 2022 (protocol code: 201900290B0A3, approval date: 22 April 2019). The eligibility and exclusion criteria for our study were listed in Table 1. All participants provided written informed consent for the publication of this case report and accompanying images. Our study was registered on ClinicalTrials.gov (https://www.clinicaltrials.gov/), in accordance with the principles outlined in the Declaration of Helsinki and adhering to the guidelines of the Consolidated Standards of Reporting Trials (CONSORT)[23–26].

The determination of the minimum required sample size for the three groups was conducted using the G*Power 3.1.9.2 software (http://www.gpower.hhu.de/en.html, accessed on 1 January 2019) prior to participant recruitment. The 'Test family' selected 'F tests', while the 'Statistical test' opted for 'ANOVA: Fixed effects, omnibus, one-way'. The Type of power analysis was set to 'A priori', with an Effect size (f) of 0.5, an $\alpha$ error probability of 0.05, a power (1- $\beta$ error probability) of 0.8, and the number of groups set at 3. The total sample size was determined to be at least 42. After considering a dropout rate of 6%, the adjusted total sample size was at least 45.

**Table 1**

**The inclusion and exclusion criteria for the participants.**

| Inclusion criteria | Exclusion criteria |
|---|---|
| 1. VAS score > 3 | 1. Rheumatic diseases |
| 2. Positive impingement sign | 2. Glenohumeral osteoarthritis |
| 3. Pain during Hawkins' test or empty can test | 3. Full-thickness RC tear |
| 4. MRI evidence of a supraspinatus lesion without complete tear | 4. Fractures |
| 5. Pain and/or stiffness resistance to modifications in physical activity and/or therapeutic interventions under professional therapists for at least 3 months | 5. Infections |
| 6. Aged between 35 and 80 years | 6. Neoplasms |
| | 7. Pregnancy |
| | 8. Subacromial injections within the preceding 3 weeks |
| | 9. History of allergy to HA |
| | 10. Not submitting valid written informed consent |

**Table 2**

**The assigned intervention at various time points for the three groups.**

| | HA | HA + 1 ESWT | HA + 2 ESWT |
|---|---|---|---|
| Day 1 | HA | HA | HA |
| Day 1 (1 h after HA) | sham | ESWT | ESWT |
| Day 8 | HA | HA | HA |
| Day 8 (1 h after HA) | | | |
| Day 15 | HA | HA | HA |
| Day 15 (1 h after HA) | sham | sham | ESWT |

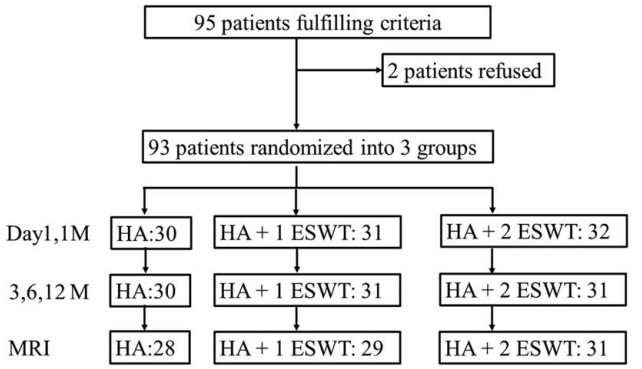


**Figure 2.** The randomisation process of the study and the number of participants at each stage.

### *Definition of participants, randomisation, and intervention*

This study utilised a parallel-group trial design comprising three arms. Participants were randomly assigned to receive one of three interventions: three HA injections combined with two sham ESWT (HA), three HA injections combined with one ESWT and one sham ESWT(HA + 1 ESWT), or three HA injections combined with two ESWT (HA + 2 ESWT) with an allocation ratio of 1:1:1 (Table 2). The Charlson comorbidity index score was calculated for every participant on Day 1, as defined in Table 2. This index has been employed in a substantial number of studies to reflect the baseline severity of participants' medical comorbidities[27–30]. Randomisation was performed using a computer-generated list, and allocation concealment was maintained through a series of numbered envelopes. Both participants and examiners conducting follow-up assessments remained blinded to the treatment allocation.

The diagnostic assessment of RC tendinopathy necessitated a consensus among a musculoskeletal radiologist proficient in interpreting MRI scans of the shoulder joint, the primary author, and the corresponding author. Tendinosis was identified by heightened intratendinous signal intensity on T2-weighted MRI images without complete disruption. Partial-thickness tears were delineated by hyperintense fluid or fluid-like signal extending into the tendon on T2-weighted images, while full-thickness tears were diagnosed when hyperintense fluid or fluid-like signal permeated the entire thickness of the disrupted RC tendon on T2-weighted images. The grading of tendinopathy was delineated as follows: Grade 1 denoted tendinopathy, characterised by heightened T2 signal intensity, covering less than one-third of the volume; Grade 2 indicated tendinopathy encompassing equal to or greater than one-third but less than two-thirds of the volume; and Grade 3 denoted tendinopathy encompassing more than two-thirds of the volume (Fig. 1). MRI assessments were conducted at baseline and 1 year after Day 1 to evaluate tear status and tendinopathy grade.

Subacromial injections of HA, ARTZ Dispo, 25 mg of sodium hyaluronate (Seikagaku), were administered by the first author, an experienced shoulder surgeon with over two decades of expertise. The injection procedure involved a posterolateral approach, positioned ~1.5 finger breadths below the posterolateral corner of the acromion, without the use of local anaesthesia. The needle was skillfully guided along the superior border of the RC into the subacromial space, and if the needle tip encountered the undersurface of the acromion, slight withdrawal of the needle facilitated the smooth delivery of the substance.

Subjects undergoing authentic ESWT received 3000 shockwave impulses calibrated at 24 kV (energy flux density

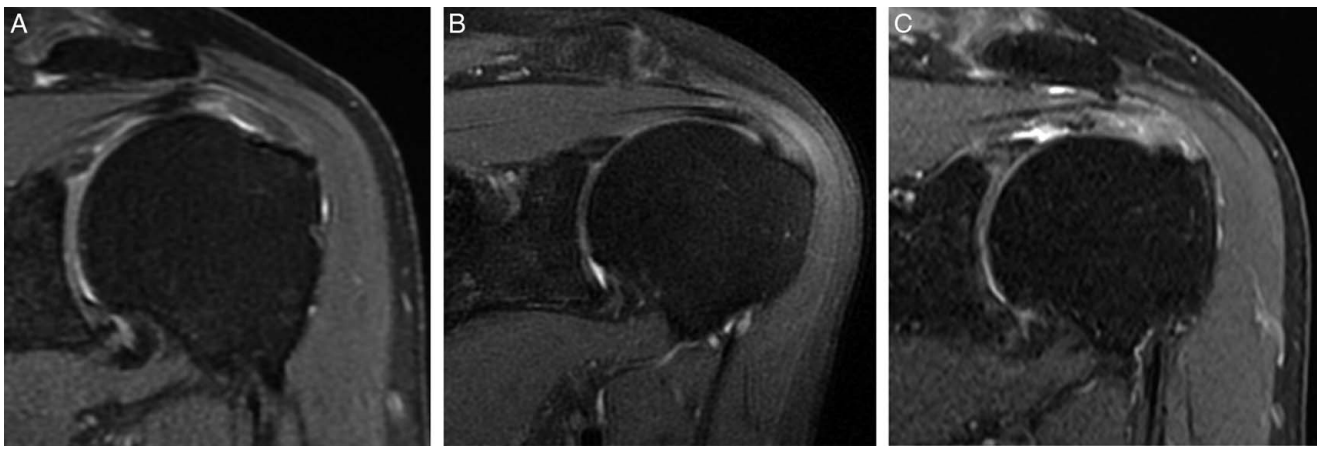


**Figure 1.** The representative images of (A) Grade 1, (B) Grade 2, and (C) Grade 3 tendinopathy in MRI. Both (C) and (A) pertain to a 77 year-old male patient participant with diabetes allocated to the HA + 1 ESWT group. Proton-weighted fat-suppressed MRI imaging revealed grade 3 diffuse supraspinatus tendinosis with a small partial tear at the distal insertion site at baseline (C). However, MRI conducted 12 months later showed a regression to grade 1 supraspinatus tendinosis and complete resolution of the partial tear (A).

**Table 3**

**The baseline demographic data of the three groups.**

| | HA | HA + 1 ESWT | HA + 2 ESWT | *P* |
|---|---|---|---|---|
| Male/female | 12/18 | 11/20 | 10/22 | 0.772 |
| Age | 61.0 ± 9.2 | 60.5 ± 7.1 | 60.3 ± 8.0 | 0.935 |
| Left/right | 14/16 | 12/19 | 10/22 | 0.460 |
| BMI | 24.3 ± 3.9 | 24.7 ± 3.9 | 24.6 ± 3.4 | 0.905 |
| CCI score (< 3/≥ 3) | 16/14 | 18/13 | 19/13 | 0.881 |
| Current smoking (− / +) | 5/25 | 6/25 | 6/26 | 0.960 |

CCI score, Charlson comorbidity index score.

$= 0.32\ mJ/mm^2$) in an 1 h session, scheduled for 1 h following HA injection. These therapeutic shockwaves were emitted by the STORZ MEDICAL (Lohstampfestrasse 8, 8274 Tägerwilen). A certified specialist oversaw this therapeutic protocol with expertise in an outpatient setting. The shockwaves were meticulously targeted, focusing clinically on the rotator interval (one finger's breadth laterally and superiorly to the coracoid process) and the rotator cable (a thick fibrous bundle transmitting applied forces to RC). Surgical lubricant was applied to facilitate the juxtaposition of the shockwave tube and the skin, while the use of local anaesthetics was intentionally avoided. Conversely, participants assigned to the sham ESWT group underwent a simulated procedure. In this simulated intervention, the device was operated without the silicone pad on the stand-off device. While participants experienced audible shockwave sounds and a tactile tingling sensation, actual energy transmission was withheld. Throughout the therapeutic procedure, vital signs were vigilantly monitored, and any potential discomfort was diligently observed and recorded. Following the intervention, the treated areas were meticulously inspected for local manifestations such as swelling, ecchymosis, or haematoma. The baseline regimen, encompassing activity modification and/or physiotherapy, was diligently maintained postintervention. As participants progressed through the postintervention phase, they were gradually introduced to a regimen of gentle pendulum exercises and carefully guided assisted shoulder movements, including elevation, external rotation, and internal rotation. Patients were advised to limit their analgesic intake to a daily dosage of 1000 mg acetaminophen and to avoid any anti-inflammatory agents after the intervention. In preparation for each assessment, patients refrained from using pain medication for three days. Surgical intervention was recommended in cases where persistent and severe shoulder discomfort or loss of function persisted.

### *Assessment after intervention*

The clinical parameters, including the visual analogue scale (VAS), muscle power for shoulder abduction (MP), Constant–Murley score (CMS), and shoulder range of motion (ROM), were assessed at 1 month (1 M), 3 months (3 M), 6 months (6 M), and 12 months (12M) following Day 1 defined in Table 2. These evaluations were performed by a research assistant who was unaware of the participant's group allocation and did not administer the ESWT procedure in the outpatient setting. The VAS functions as a pain assessment scale, with 0 indicating no pain and 10 indicating unbearable pain. Muscle power for shoulder abduction was determined by measuring the maximal isometric contraction of the abductor muscles. This evaluation employed a handheld Baseline 250 hydraulic push–pull dynamometer (Baseline Corporation, Irvington) with the shoulder positioned at 45° abduction, the elbow at 90° flexion, and the arm internally rotated without torso stabilisation. The Constant–Murley score (CMS) is a standardized scale for assessing shoulder function, with a maximum score of 100 representing optimal shoulder function. This scoring system has been utilised in numerous studies to evaluate shoulder-related outcomes. Shoulder ROM was assessed with the patient seated. A goniometer was used to measure the extent of passive forward flexion (FF) or abduction (ABD) of the shoulder. External rotation (ER) and internal rotation (IR) of the shoulders were evaluated with the patient's arm in a resting position and at a 45° flexion position, respectively. The sum of range of motion (SROM) was determined by adding the measured ROM values. The minimal clinically important difference (MCID) for VAS and CMS was set at 1.4 and 10, respectively. The patient acceptable symptom state (PASS) for VAS and CMS was identified as 3.0 and 80, respectively[31,32].

### *Statistical analyses*

Between-group differences in continuous variables were assessed using the analysis of variance (ANOVA) test, with Tukey's Honestly Significant Difference (HSD) for post-hoc analysis. Intragroup differences in continuous variables across different time points were analysed using repeated-measures ANOVA, also with Tukey's HSD for post-hoc analysis. The $\chi^2$ test was

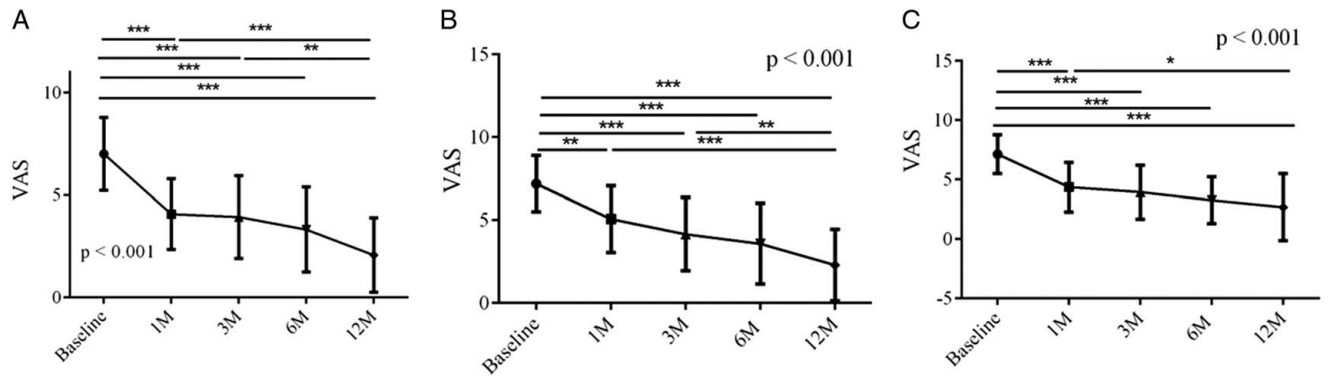


**Figure 3.** The visual analogue scale (VAS) from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

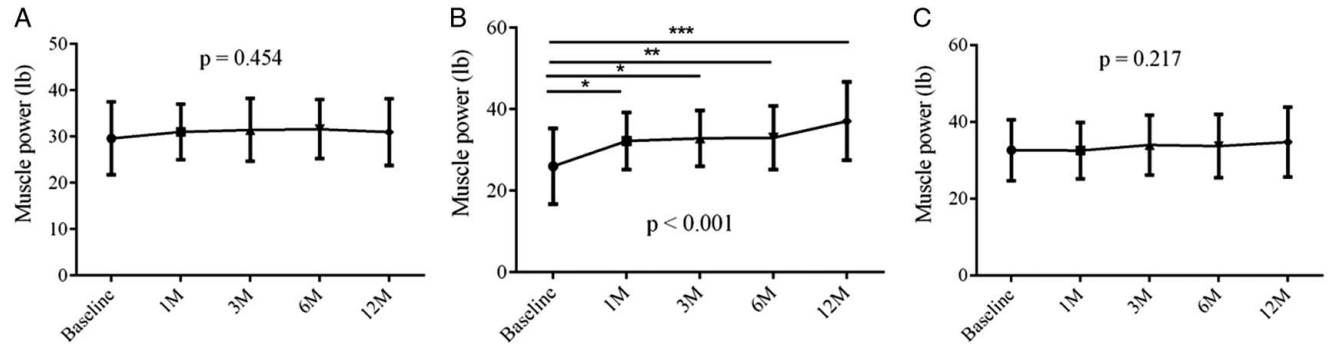


**Figure 4.** The muscle power from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

utilised to compare categorical variables between groups. All statistical analyses were performed using GraphPad Prism v5.0 (GraphPad Software Inc.).

## Results

Between 1 August 2019 and 31 July 2022, a total of 95 patients met the inclusion criteria and were not excluded based on the exclusion criteria. Out of these 95 patients, 93 agreed to participate in the study. Randomisation allocated 30 patients to the HA group, 31 patients to the HA + 1 ESWT group, and 32 patients to the HA + 2 ESWT group. Throughout the study period, there was no crossover between these groups, and all 93 patients completed the designated intervention from Day 1 to Day 15 (Table 2). Follow-up examinations were conducted with all 93 participants 1 month after Day 1. At 3, 6, and 12 months post-Day 1, 30, 31, and 31 patients, respectively, remained in the HA, HA + 1 ESWT, and HA + 2 ESWT groups. However, one patient in the HA + 2 ESWT group underwent surgery. Additionally, 28, 29, and 31 patients, respectively, completed the MRI follow-up examination 12 months after Day 1. Notably, two participants in the HA group and two patients in the HA + 1 ESWT group were unable to adhere to the MRI schedule (Fig. 2). The demographic profiles of the participants are detailed in Table 3.

All three groups demonstrated significant improvement from baseline to 12 months after Day 1 in VAS ($P < 0.001$ for all three groups) (Fig. 3). While no specific trend for muscle power was observed in the HA group ($P = 0.454$) and the HA + 2 ESWT group ($P = 0.217$), the HA + 1 ESWT group exhibited a significant trend of muscle power improvement from baseline to 12 months after Day 1 ($P < 0.001$) (Fig. 4). Similarly, all three groups showed a significant trend of improvement from baseline to 12 months after Day 1 in CMS ($P < 0.001$ for all three groups) (Fig. 5). In terms of between-group comparisons, no significant differences were observed in VAS, MP (lb), and CMS at baseline. However, at 1 month post-Day 1, significant disparities emerged in MP improvement ($P = 0.014$) and CMS improvement ($P = 0.005$). Post-hoc analysis revealed that the HA + 1 ESWT group exhibited superior MP improvement compared to the HA group ($P = 0.011$), with greater CMS improvement ($P = 0.018$) compared to the HA group. Similar findings were observed at 3 months post-Day 1, with significant differences in MP improvement ($P = 0.012$) and CMS improvement ($P = 0.008$), indicating the superiority of the HA + 1 ESWT group over the HA group. At 6 months post-Day 1, significant disparities were observed in MP improvement ($P = 0.014$) and CMS improvement ($P = 0.005$), with the HA + 1 ESWT group demonstrating greater improvement in both parameters compared to the HA group. These trends continued at 12 months post-Day 1, with significant differences in MP improvement ($P = 0.001$), with the HA + 1 ESWT group showing greater improvement compared to the HA group ($P < 0.001$). In summary, the HA + 1 ESWT group demonstrated superiority in MP improvement and CMS improvement compared to the HA group at various intervals, while the HA + 2 ESWT group also showed superiority over the

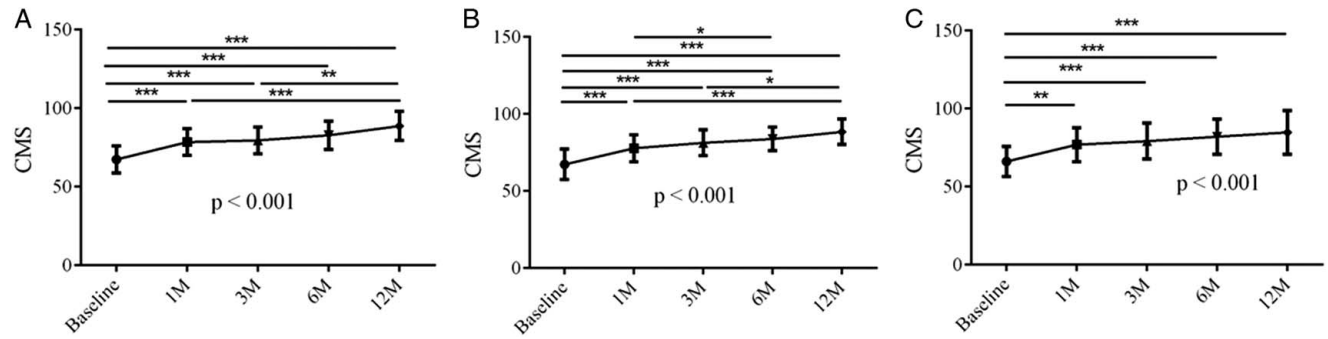


**Figure 5.** The Constant–Murley Score (CMS) from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

**Table 4**

**The visual analogue scale (VAS), muscle power (MP) of abduction, and Constant–Murley score (CMS) for subjects receiving the assigned interventions.**

| | HA | HA + 1 ESWT | HA + 2 ESWT | *P* |
|---|---|---|---|---|
| Baseline profiles | N = 30 | N = 31 | *N* = 32 | |
| VAS | 6.88 ± 1.73 | 7.27 ± 0.72 | 7.18 ± 1.59 | 0.612 |
| 95% CI | (6.26–7.50) | (7.02–7.52) | (6.63–7.73) | |
| MP (lb) | 32.02 ± 12.73 | 27.81 ± 9.76 | 32.17 ± 9.36 | 0.177 |
| 95% CI | (27.46–36.58) | (24.37–31.25) | (28.93–35.41) | |
| CMS | 67.08 ± 10.41 | 67.19 ± 9.58 | 65.52 ± 9.86 | 0.747 |
| 95% CI | (63.35–70.81) | (63.82–70.56) | (62.10–68.94) | |
| One month | *N* = 30 | *N* = 31 | *N* = 32 | |
| VAS | 4.03 ± 1.94 | 5.09 ± 1.99 | 4.52 ± 2.24 | 0.125 |
| 95% CI | (3.34–4.72) | (4.39–5.79) | (3.74–5.30) | |
| VAS improvement | 2.43 ± 2.01 | 2.40 ± 2.21 | 3.10 ± 2.02 | 0.345 |
| 95% CI | (1.71–3.15) | (1.62–3.18) | (2.40–3.80) | |
| MP (lb) | 30.93 ± 6.10 | 32.05 ± 7.57 | 32.16 ± 7.90 | 0.750 |
| 95% CI | (28.75–33.11) | (29.39–34.71) | (29.42–34.90) | |
| MP improvement (lb) | − 1.34 ± 11.28[a] | 4.52 ± 5.46[a] | 0.75 ± 5.16 | 0.014 |
| 95% CI | (− 5.38–2.70) | (2.60–6.44) | (− 1.04–2.54) | |
| CMS | 77.36 ± 9.42 | 77.64 ± 8.65 | 76.91 ± 10.71 | 0.954 |
| 95% CI | (73.99–80.73) | (74.60–80.69) | (73.20–80.62) | |
| CMS improvement | 4.05 ± 12.19[bc] | 11.35 ± 9.72[b] | 11.84 ± 8.78[c] | 0.005 |
| 95% CI | (− 0.31–8.41) | (7.93–14.77) | (8.80–14.88) | |
| Three months | *N* = 30 | *N* = 31 | *N* = 31 | |
| VAS | 3.84 ± 1.98 | 4.25 ± 2.24 | 3.94 ± 2.26 | 0.733 |
| 95% CI | (3.13–4.55) | (3.46–5.04) | (3.14–4.74) | |
| VAS improvement | 2.93 ± 2.16 | 3.23 ± 2.64 | 3.37 ± 2.17 | 0.763 |
| 95% CI | (2.16–3.70) | (2.30–4.16) | (2.61–4.13) | |
| MP (lb) | 32.25 ± 6.97 | 33.14 ± 7.25 | 34.21 ± 7.55 | 0.567 |
| 95% CI | (29.76–34.74) | (30.59–35.69) | (31.55–36.87) | |
| MP improvement (lb) | − 0.86 ± 12.94[d] | 5.92 ± 5.76[d] | 1.26 ± 5.59 | 0.012 |
| 95% CI | (− 5.49–3.77) | (3.89–7.95) | (− 0.71–3.23) | |
| CMS | 80.31 ± 8.69 | 81.09 ± 8.30 | 79.16 ± 11.52 | 0.725 |
| 95% CI | (77.20–83.42) | (78.17–84.01) | (75.10–83.22) | |
| CMS improvement | 7.05 ± 9.70[ef] | 15.02 ± 11.54[e] | 13.40 ± 9.24[f] | 0.008 |
| 95% CI | (3.58–10.52) | (10.96–19.08) | (10.15–16.65) | |
| Six months | *N* = 30 | *N* = 31 | *N* = 31 | |
| VAS | 3.26 ± 2.04 | 3.58 ± 2.43 | 3.26 ± 1.97 | 0.800 |
| 95% CI | (2.53–3.99) | (2.72–4.44) | (2.57–3.95) | |
| VAS improvement | 3.52 ± 2.46 | 3.97 ± 2.56 | 4.14 ± 1.98 | 0.584 |
| 95% CI | (2.64–4.40) | (3.07–4.87) | (3.44–4.84) | |
| MP (lb) | 32.83 ± 6.88 | 32.84 ± 8.25 | 33.67 ± 8.23 | 0.888 |
| 95% CI | (30.37–35.29) | (29.94–35.74) | (30.77–36.57) | |
| MP improvement (lb) | − 0.18 ± 12.03[g] | 5.94 ± 6.49[g] | 0.94 ± 4.37 | 0.014 |
| 95% CI | (− 4.48–4.12) | (3.66–8.22) | (− 0.60–2.48) | |
| CMS | 83.20 ± 9.06 | 83.90 ± 7.69 | 82.85 ± 10.42 | 0.902 |
| 95% CI | (79.96–86.44) | (81.19–86.61) | (79.18–86.52) | |
| CMS improvement | 9.76 ± 10.23[hi] | 17.98 ± 11.44[h] | 17.03 ± 8.51[i] | 0.005 |
| 95% CI | (6.10–13.42) | (13.95–22.01) | (14.03–20.03) | |
| Twelve months | *N* = 30 | *N* = 31 | *N* = 31 | |
| VAS | 2.06 ± 1.78 | 2.29 ± 2.16 | 2.67 ± 2.82 | 0.578 |
| 95% CI | (1.40–2.72) | (1.50–3.08) | (1.64–3.70) | |
| VAS improvement | 4.76 ± 2.36 | 5.31 ± 2.61 | 4.90 ± 2.47 | 0.679 |
| 95% CI | (3.88–5.64) | (4.35–6.27) | (3.99–5.81) | |
| MP (lb) | 31.76 ± 7.04 | 33.88 ± 8.59 | 34.39 ± 9.21 | 0.431 |
| 95% CI | (29.13–34.39) | (4.36–6.27) | (31.01–37.77) | |
| MP improvement (lb) | − 1.19 ± 12.57[j] | 7.20 ± 6.17[j] | 1.95 ± 4.50 | 0.001 |
| 95% CI | (− 5.88–3.50) | (4.94–9.46) | (0.30–3.60) | |
| CMS | 88.91 ± 9.20 | 88.05 ± 8.05 | 85.37 ± 13.74 | 0.406 |
| 95% CI | (85.47–92.35) | (85.10–91.00) | (80.33–90.41) | |
| CMS improvement | 15.19 ± 13.05 | 22.83 ± 13.07 | 20.19 ± 11.51 | 0.069 |
| 95% CI | (10.32–20.06) | (18.04–27.62) | (15.97–24.41) | |

By Tukey HSD (honestly significant difference) post-hoc tests.
[a]$P = 0.011$.
[b]$P = 0.018$.
[c]$P = 0.011$.
[d]$P = 0.010$.
[e]$P = 0.009$.
[f]$P = 0.047$.
[g]$P = 0.017$.
[h]$P = 0.008$.
[i]$P = 0.021$.
[j]$P < 0.001$.

**Table 5**

**The number of participants achieving the minimal clinically important difference (MCID) ($\geq$1.4 for VAS and $\geq$10 for CMS) and patient acceptable symptom state (PASS) ($\leq$3.0 for VAS and $\geq$80 for CMS).**

| | MCID | | | PASS | | |
|---|---|---|---|---|---|---|
| | HA | HA + 1 ESWT | HA + 2 ESWT | HA | HA + 1 ESWT | HA + 2 ESWT |
| Baseline | *N*=30 | *N*=31 | *N*=32 | *N*=30 | *N*=31 | *N*=32 |
| VAS | | | | 0 | 0 | 0 |
| CMS | | | | 1 | 2 | 1 |
| One month | *N*=30 | *N*=31 | *N*=32 | *N*=30 | *N*=31 | *N*=32 |
| VAS | 23 | 18 | 23 | 6 | 14 | 11 |
| CMS | 10 | 15 | 13 | 12 | 12 | 14 |
| Three months | *N*=30 | *N*=31 | *N*=31 | *N*=30 | *N*=31 | *N*=31 |
| VAS | 25 | 20 | 26 | 11 | 16 | 15 |
| CMS | 14 | 19 | 18 | 16 | 18 | 17 |
| Six months | *N*=30 | *N*=31 | *N*=31 | *N*=30 | *N*=31 | *N*=31 |
| VAS | 25 | 24 | 26 | 16 | 22 | 21 |
| CMS | 17 | 24 | 23 | 20 | 23 | 19 |
| Twelve months | *N*=30 | *N*=31 | *N*=31 | *N*=30 | *N*=31 | *N*=31 |
| VAS | 27 | 28 | 28 | 21 | 27 | 23 |
| CMS | 20 | 26 | 23 | 26 | 27 | 21 |

HA group in terms of MP and CMS improvement at variable time points. However, no discernible difference was observed between the HA + 1 ESWT group and the HA + 2 ESWT group (Table 4). The outcomes regarding the number of participants achieving the minimal clinically important difference (MCID) ($\geq$1.4 for VAS and $\geq$10 for CMS) and patient acceptable symptom state (PASS) ($\leq$3.0 for VAS and $\geq$80 for CMS) are presented in (Table 5).

All three groups demonstrated a significant improvement in FF ($P<0.001$ for all three groups) (Fig. 6), ABD ($P<0.001$ for all three groups) (Fig. 7), IR ($P<0.001$ for all three groups) (Fig. 8), ER ($P<0.001$ for all three groups) (Fig. 9), and SROM ($P<0.001$ for all three groups) (Fig. 10) from baseline to 12 months after Day 1. No differences were observed between the groups regarding FF (°), ABD (°), IR (°), ER (°), and SROM (°) at baseline. However, at 1 month post-Day 1, significant differences emerged in terms of FF ($P=0.027$), FF improvement ($P=0.007$), ABD ($P=0.011$), IR improvement ($P=0.005$), and SROM improvement ($P=0.011$). Post-hoc analysis revealed that the HA + 1 ESWT group exhibited superior FF ($P=0.035$) and ABD ($P=0.007$) compared to the HA group. The HA + 2 ESWT group showed superior FF improvement ($P=0.013$), IR improvement ($P=0.019$), and SROM improvement ($P=0.025$) compared to the HA group. Moreover, the HA + 2 ESWT group demonstrated better FF improvement ($P=0.020$), IR improvement ($P=0.009$), and SROM improvement ($P=0.023$) compared to the HA + 1 ESWT group. At 3 months post-Day 1, significant differences emerged in FF improvement ($P=0.004$) and ABD ($P=0.045$). Post-hoc analysis revealed that the HA + 1 ESWT group exhibited superior ABD ($P=0.042$) compared to the HA group, while the HA + 2 ESWT group showed enhanced FF improvement ($P=0.014$) compared to the HA group. The HA + 2 ESWT group demonstrated better FF improvement ($P=0.007$) compared to the HA + 1 ESWT group. At 6 months post-Day 1, significant differences emerged in ABD improvement ($P=0.036$). Post-hoc analysis revealed that the HA + 2 ESWT group displayed superior ABD improvement ($P=0.022$) compared to the HA group. In summary, both the HA + 1 ESWT and the HA + 2 ESWT groups exhibited superiority in various dimensions of ROM compared to the HA group across different intervals. Specifically, the HA + 2 ESWT group showed better FF improvement, IR improvement, and SROM improvement at 1 month after Day 1, as well as FF improvement at 3 months after Day 1, in comparison to the HA + 1 ESWT group (Table 6).

Twenty-eight, 29, and 31 patients underwent MRI follow-up twelve months after D1. Among the 28 patients in the HA group who underwent MRI study at this interval, 3 exhibited improvement, 21 remained stable, and 4 showed deterioration in terms of tendinopathy-related T2 high signalling. Additionally, 2 patients showed improvement, 24 remained stable, and 2 worsened in terms of tear status compared to the baseline MRI. Among the 29 patients in the HA + 1 ESWT group who underwent MRI study at the 12-month mark, 7 demonstrated improvement in tendinopathy grading, while 22 remained stable, with none showing worsening. Similarly, 5 patients showed improvement, 24 remained stable, and none worsened in terms of tear status compared to the baseline MRI. Among the 31 patients in the HA + 2 ESWT group who underwent MRI study at twelve months after D1, 5 displayed improvement, 24 remained stable, and 2 worsened in terms of tendinopathy grading. Additionally, 2 patients improved, 28 remained stable, and 1 worsened in terms of tear status compared to the baseline MRI. None of the participants in the HA + 1 ESWT group exhibited worsening in tendinopathy grading and tear status.

No adverse effects were documented from Day 1 up to 12 months thereafter among all participants.

## Discussion

Our team previously conducted a randomised, double-blind, placebo-controlled study employing ARTZ Dispo treatment, which is identical to the intervention used in the present study, involving 51 patients with RC lesions lacking complete tears. This prior investigation revealed that the weekly ARTZ Dispo group exhibited superior CMS ($P=0.010$) and VAS ($P=0.002$) outcomes compared to the placebo group 6 weeks after treatment, thus substantiating the therapeutic advantages of weekly ARTZ injections[33]. In line with our earlier research, the current study shows that 3HA injections with 2 sham ESWT could significantly improve almost all assessed parameters except MP. Among the 30 patients receiving 3 HA injections with 2 sham ESWT, 28 managed MRI surveys one year after Day 1, with 3 showing improvement in grade and 2 in tear status. While the exact mechanism behind HA injections' clinical improvements remains unclear, research has investigated HA's effects on subacromial-synovium fibroblasts (SSF) from patients with RC disease. HA has been shown to reduce the expression of proinflammatory cytokines and COX-2/PGE[2] production in SSF, with CD44 blocking reversing HA's effects[34]. Building upon these known benefits of HA, the current study aims to explore additional strategies to further enhance the therapeutic efficacy of weekly HA injections.

Prior research has outlined four distinct phases of ESWT reactions: physical, physicochemical, chemical, and biological. During the physical phase, shockwaves induce positive pressure, facilitating the transmission of energy to tissues and cells, while cavitation enhances cell membrane permeability[35].

**Table 6**

**The range of motion in forward flexion, abduction, internal rotation (IR), external rotation (ER), and the sum of range of motion (SROM) for the subjects who received the assigned interventions.**

| | HA | HA + 1 ESWT | HA + 2 ESWT | *P* |
|---|---|---|---|---|
| Baseline profiles | *N* = 30 | *N* = 31 | *N* = 32 | |
| FF (°) | 123.18 ± 21.86 | 132.42 ± 17.64 | 121.82 ± 25.27 | 0.105 |
| 95% CI | (115.02–131.34) | (125.95–138.89) | (112.71–130.93) | |
| ABD (°) | 111.52 ± 28.27 | 118.18 ± 24.65 | 109.58 ± 26.46 | 0.387 |
| 95% CI | (100.96–122.08) | (109.14–127.22) | (100.04–119.12) | |
| IR (°) | 39.24 ± 26.78 | 51.06 ± 23.84 | 40.30 ± 25.25 | 0.116 |
| 95% CI | (29.24–49.24) | (42.32–59.80) | (31.20–49.40) | |
| ER (°) | 72.88 ± 17.00 | 74.09 ± 17.34 | 68.03 ± 14.84 | 0.289 |
| 95% CI | (66.53–79.23) | (67.73–80.45) | (62.68–73.38) | |
| SROM (°) | 346.82 ± 73.61 | 375.76 ± 64.09 | 339.73 ± 63.19 | 0.075 |
| 95% CI | (319.33–374.31) | (352.25–399.27) | (316.95–362.51) | |
| One month | *N* = 30 | *N* = 31 | *N* = 32 | |
| FF (°) | 127.93 ± 16.45[a] | 138.79 ± 16.83[a] | 137.24 ± 15.62 | 0.027 |
| 95% CI | (122.04–133.82) | (132.87–144.71) | (131.83–142.65) | |
| FF improvement (°) | 5.00 ± 12.02[b] | 5.54 ± 9.36[c] | 16.07 ± 19.55[bc] | 0.007 |
| 95% CI | (0.70–9.30) | (2.25–8.83) | (9.30–22.84) | |
| ABD (°) | 116.55 ± 21.80[d] | 134.48 ± 20.01[d] | 125.86 ± 24.06 | 0.011 |
| 95% CI | (108.75–124.35) | (127.44–141.52) | (117.52–134.20) | |
| ABD improvement (°) | 6.33 ± 17.66 | 14.33 ± 19.11 | 15.33 ± 22.89 | 0.618 |
| 95% CI | (0.01–12.65) | (7.60–21.06) | (7.40–23.26) | |
| IR (°) | 57.33 ± 24.97 | 65.33 ± 20.42 | 64.33 ± 17.60 | 0.287 |
| 95% CI | (48.39–66.27) | (58.14–72.52) | (58.23–70.43) | |
| IR improvement (°) | 14.63 ± 20.94[e] | 13.33 ± 8.99[f] | 27.41 ± 18.52[ef] | 0.005 |
| 95% CI | (7.14–22.12) | (10.17–16.49) | (20.99–33.83) | |
| ER (°) | 78.06 ± 15.53 | 79.19 ± 16.89 | 79.68 ± 11.25 | 0.907 |
| 95% CI | (72.50–83.62) | (73.24–85.14) | (75.78–83.58) | |
| ER improvement (°) | 4.19 ± 15.23 | 6.13 ± 14.82 | 12.42 ± 13.53 | 0.072 |
| 95% CI | (– 1.26–9.64) | (0.91–11.35) | (7.73–17.11) | |
| SROM (°) | 386.45 ± 63.90 | 408.55 ± 63.83 | 397.58 ± 57.46 | 0.375 |
| 95% CI | (363.58–409.32) | (386.08–431.02) | (377.67–417.49) | |
| SROM improvement (°) | 35.69 ± 44.38[g] | 35.34 ± 37.18[h] | 64.45 ± 41.54[gh] | 0.011 |
| 95% CI | (19.81–51.57) | (22.25–48.42) | (50.06–78.84) | |
| Three months | *N* = 30 | *N* = 31 | *N* = 31 | |
| FF (°) | 138.83 ± 16.12 | 142.67 ± 14.90 | 140.17 ± 18.03 | 0.657 |
| 95% CI | (133.06–144.60) | (137.42–147.92) | (133.82–146.52) | |
| FF improvement (°) | 10.34 ± 14.59[i] | 9.46 ± 9.46[j] | 20.71 ± 15.62[ij] | 0.004 |
| 95% CI | (5.12–15.56) | (6.13–12.79) | (15.21–26.21) | |
| ABD (°) | 127.14 ± 21.79[k] | 140.36 ± 17.48[k] | 136.61 ± 20.73 | 0.045 |
| 95% CI | (119.34–134.94) | (134.21–146.51) | (129.31–143.91) | |
| ABD improvement (°) | 15.34 ± 23.18 | 18.97 ± 18.19 | 24.14 ± 21.34 | 0.282 |
| 95% CI | (7.05–23.63) | (12.57–25.37) | (16.63–31.65) | |
| IR (°) | 63.97 ± 23.28 | 75.17 ± 17.19 | 68.28 ± 20.67 | 0.117 |
| 95% CI | (55.64–72.30) | (69.12–81.22) | (61.00–75.56) | |
| IR improvement (°) | 23.00 ± 21.03 | 22.17 ± 12.50 | 24.50 ± 24.54 | 0.901 |
| 95% CI | (15.47–30.53) | (17.77–26.57) | (15.86–33.14) | |
| ER (°) | 80.86 ± 13.43 | 83.10 ± 9.86 | 83.10 ± 9.85 | 0.670 |
| 95% CI | (76.05–85.67) | (79.63–86.57) | (79.63–86.57) | |
| ER improvement (°) | 8.33 ± 15.33 | 9.17 ± 12.80 | 15.17 ± 16.99 | 0.168 |
| 95% CI | (2.84–13.82) | (4.66–13.68) | (9.19–21.15) | |
| SROM (°) | 415.17 ± 49.58 | 436.17 ± 49.61 | 419.67 ± 4.40 | 0.253 |
| 95% CI | (397.43–432.91) | (418.71–453.63) | (418.12–421.22) | |
| SROM improvement (°) | 61.00 ± 44.19 | 56.50 ± 36.13 | 78.80 ± 45.89 | 0.103 |
| 95% CI | (45.19–76.81) | (43.78–69.22) | (62.65–94.95) | |
| Six months | *N* = 30 | *N* = 31 | *N* = 31 | |
| FF (°) | 142.14 ± 14.62 | 147.86 ± 11.50 | 143.21 ± 18.37 | 0.327 |
| 95% CI | (136.91–147.37) | (143.81–151.91) | (136.74–149.68) | |
| FF improvement (°) | 17.59 ± 17.51 | 13.28 ± 12.41 | 20.86 ± 18.13 | 0.209 |
| 95% CI | (11.32–23.86) | (8.91–17.65) | (14.48–27.24) | |
| ABD (°) | 138.28 ± 22.13 | 142.24 ± 18.74 | 137.59 ± 22.56 | 0.668 |
| 95% CI | (130.36–146.20) | (135.64–148.84) | (129.65–145.53) | |
| ABD improvement (°) | 12.25 ± 16.82[l] | 22.24 ± 17.14 | 26.90 ± 22.38[l] | 0.036 |
| 95% CI | (6.23–18.27) | (16.21–28.27) | (19.02–34.78) | |
| IR (°) | 70.17 ± 21.86 | 72.41 ± 19.30 | 73.45 ± 17.73 | 0.811 |
| 95% CI | (62.35–77.99) | (65.62–79.20) | (67.21–79.69) | |
| IR improvement (°) | 28.45 ± 19.69 | 20.52 ± 22.41 | 31.03 ± 20.55 | 0.143 |
| 95% CI | (21.40–35.50) | (12.63–28.41) | (67.21–79.69) | |
| ER (°) | 85.00 ± 8.66 | 84.48 ± 8.70 | 85.69 ± 7.29 | 0.855 |
| 95% CI | (81.90–88.10) | (81.42–87.54) | (83.12–88.26) | |
| ER improvement (°) | 12.83 ± 14.48 | 9.52 ± 19.85 | 16.94 ± 15.26 | 0.222 |
| 95% CI | (7.65–18.01) | (2.53–16.51) | (11.57–22.31) | |
| SROM (°) | 436.72 ± 46.68 | 442.41 ± 46.61 | 435.34 ± 54.35 | 0.846 |
| 95% CI | (420.02–453.42) | (426.00–458.82) | (416.21–454.47) | |
| SROM improvement (°) | 83.45 ± 51.51 | 64.66 ± 48.35 | 93.76 ± 42.22 | 0.067 |
| 95% CI | (65.02–101.88) | (47.64–81.68) | (78.90–108.62) | |
| Twelve months | *N* = 30 | *N* = 31 | *N* = 31 | |
| FF (°) | 150.17 ± 19.98 | 151.72 ± 14.16 | 147.07 ± 19.89 | 0.614 |
| 95% CI | (143.02–157.32) | (146.74–156.70) | (140.07–154.07) | |

**Table 6**

**(*Continued*)**

| | HA | HA + 1 ESWT | HA + 2 ESWT | *P* |
|---|---|---|---|---|
| FF improvement (°) | 24.31 ± 22.35 | 17.76 ± 15.09 | 27.07 ± 20.72 | 0.185 |
| 95% CI | (16.31–32.31) | (12.45–23.07) | (19.78–34.36) | |
| ABD (°) | 150.34 ± 20.13 | 150.52 ± 16.66 | 142.59 ± 23.05 | 0.236 |
| 95% CI | (143.14–157.54) | (144.66–156.38) | (134.48–150.70) | |
| ABD improvement (°) | 35.86 ± 27.13 | 30.69 ± 21.41 | 31.34 ± 23.03 | 0.672 |
| 95% CI | (26.15–45.57) | (23.15–38.23) | (23.23–39.45) | |
| IR (°) | 72.76 ± 20.64 | 76.72 ± 15.37 | 74.66 ± 18.99 | 0.717 |
| 95% CI | (65.37–80.15) | (71.31–82.13) | (67.98–81.34) | |
| IR improvement (°) | 31.03 ± 28.23 | 25.00 ± 21.79 | 32.59 ± 21.45 | 0.450 |
| 95% CI | (20.93–41.13) | (17.33–32.67) | (25.04–40.14) | |
| ER (°) | 88.28 ± 4.49 | 88.62 ± 3.76 | 85.59 ± 6.21 | 0.719 |
| 95% CI | (86.67–89.89) | (87.30–89.94) | (83.40–87.78) | |
| ER improvement (°) | 14.48 ± 14.60 | 16.03 ± 17.65 | 21.55 ± 14.64 | 0.203 |
| 95% CI | (9.26–19.70) | (9.81–22.24) | (16.40–26.70) | |
| SROM (°) | 461.55 ± 51.27 | 465.00 ± 42.66 | 448.79 ± 53.48 | 0.424 |
| 95% CI | (443.20–479.90) | (449.98–480.02) | (429.96–467.62) | |
| SROM improvement (°) | 106.90 ± 70.50 | 86.72 ± 58.65 | 107.55 ± 49.44 | 0.330 |
| 95% CI | (81.67–132.13) | (66.07–107.37) | (90.15–124.95) | |

By Tukey HSD (honestly significant difference) post-hoc tests.
[a]$P = 0.035$.
[b]$P = 0.013$.
[c]$P = 0.020$.
[d]$P = 0.007$.
[e]$P = 0.019$.
[f]$P = 0.009$.
[g]$P = 0.025$.
[h]$P = 0.023$.
[i]$P = 0.014$.
[j]$P = 0.007$.
[k]$P = 0.042$.
[l]$P = 0.022$.

Subsequently, in the physicochemical phase, this physical stimulus triggers biochemical reactions, releasing biomolecules such as ATP to activate cell signalling pathways[36]. The chemical phase involves ESWT altering ion channel functions and mobilising calcium ions[37]. Finally, in the biological phase, ESWT modulates angiogenesis, demonstrates anti-inflammatory effects, and promotes tissue healing[38]. These reactions suggest that ESWT can induce hypervascularity in the ischaemic RC tendon and transiently increase cell membrane permeability, facilitating the ingress of treatment molecules such as HA. Consequently, by harnessing the diverse effects of ESWT on tissue physiology, the combination of ESWT and HA presents a synergistic therapeutic approach to enhance outcomes in RC lesions without complete tears.

Based on this mechanistic hypothesis, we conducted the current study to investigate further strategies, specifically supplementing ESWT, to augment the therapeutic outcomes of weekly HA injections. In our investigation, we observed that administering three HA injections improved clinical outcomes in patients with RC lesions lacking complete tears. Furthermore, the addition of ESWT yielded additional benefits, notably in reducing VAS scores, enhancing CMS, and improving ROM across various dimensions. Our findings also suggest a dose-dependent effect of ESWT, particularly evident in enhancing improvements in FF, IR, and SROM at 1 month postinitial treatment, as well as improvement in FF at the 3-month mark. Importantly, none of the participants in the HA + 1 ESWT group exhibited deterioration in tendinopathy

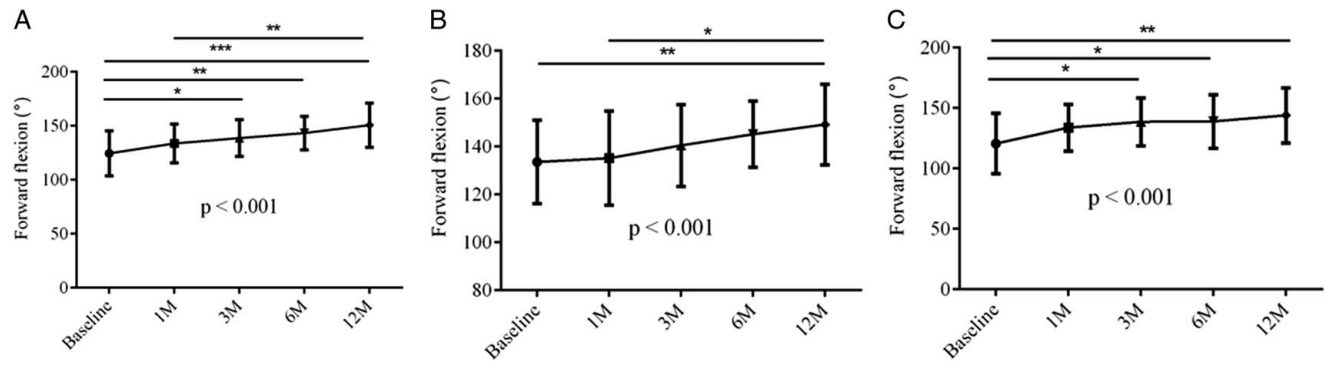


**Figure 6.** The extend of forward flexion from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

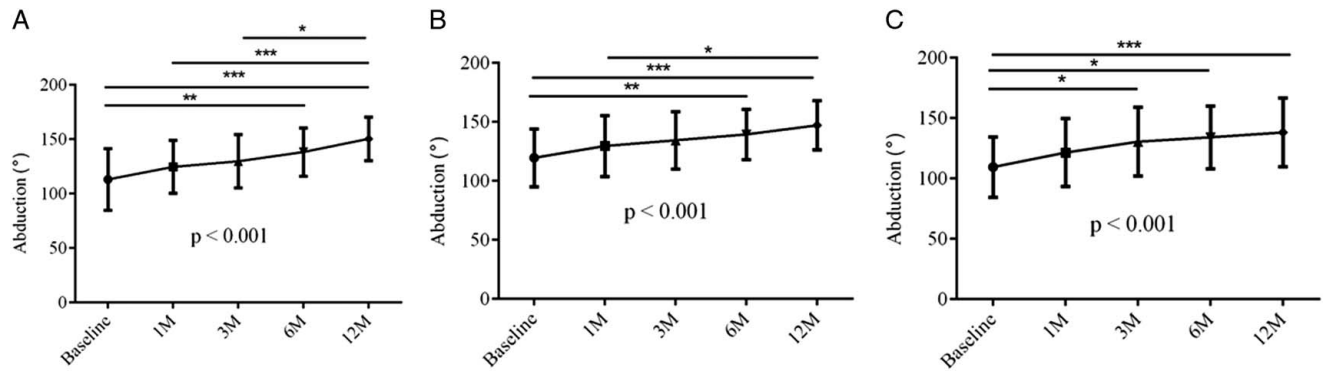


**Figure 7.** The extend of abduction from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

grading or tear status during the 1 year follow-up MRI assessment. These novel findings highlight the potential efficacy of combining ESWT and HA therapy in the management of RC lesions without complete tears.

In our present study, supplementary ESWT confers a significant benefit in dose-dependently augmenting improvements in FF, IR, and SROM. This observation aligns with prior investigations, which have consistently demonstrated the effectiveness of ESWT in enhancing ROM-related parameters. Notably, recent research has unveiled that ESWT induces a notable increase in ankle dorsiflexion among patients with plantar fasciopathy, thereby contributing to enhanced ankle ROM[39]. Similarly, multicentre randomized controlled trials focusing on patients with chronic knee pain have underscored the capacity of ESWT to alleviate knee stiffness and associated discomfort[40]. Furthermore, our previous exploration into the therapeutic potential of ESWT for RC lesions with shoulder stiffness has yielded significant enhancements in ROM, alongside other clinical parameters[41]. These collective findings underscore the efficacy of ESWT in augmenting ROM across diverse joints, encompassing the ankle, knee, and shoulder. The present study supplements these previous investigations by demonstrating that the ROM-enhancing effect of ESWT is dose-dependent, providing novel insights into its therapeutic potential.

The precise mechanism underlying the dose-dependent improvement of shoulder ROM by ESWT remains elusive. However, insights can be gleaned from the pathogenesis of frozen shoulder (FS), a condition characterised by fibroblastic and inflammatory processes. In the fibroblastic domain, synovial hyperplasia and enhanced vascularity are observable in the early stages of FS, followed by subsequent fibrosis in critical areas of the shoulder[42]. Notably, thickening of the coracohumeral ligament and glenohumeral capsule contributes significantly to ROM limitation[43]. Concurrently, the inflammatory aspect is evident through the expression of cytokines and chronic immune cell infiltration in stiff shoulders[44]. Remarkably, ESWT demonstrates dual antifibroblastic and anti-inflammatory effects. Recent research in an immobilisation-induced joint capsule fibrosis model revealed that ESWT reduces collagen deposition and improves ROM by activating adenosine A2A receptors (A2AR) and subsequent protein kinase A (PKA) and nuclear factor erythroid 2-related factor 2 (Nrf2) signalling pathways[45]. Additionally, ESWT may modulate endogenous nitric oxide (NO) production, thereby suppressing NF-κB activation and mitigating tissue inflammation[46]. These findings shed light on the therapeutic promise of ESWT in tackling the intricate pathophysiology of conditions like FS, thus partially explaining the dose-dependent enhancement of shoulder ROM by ESWT.

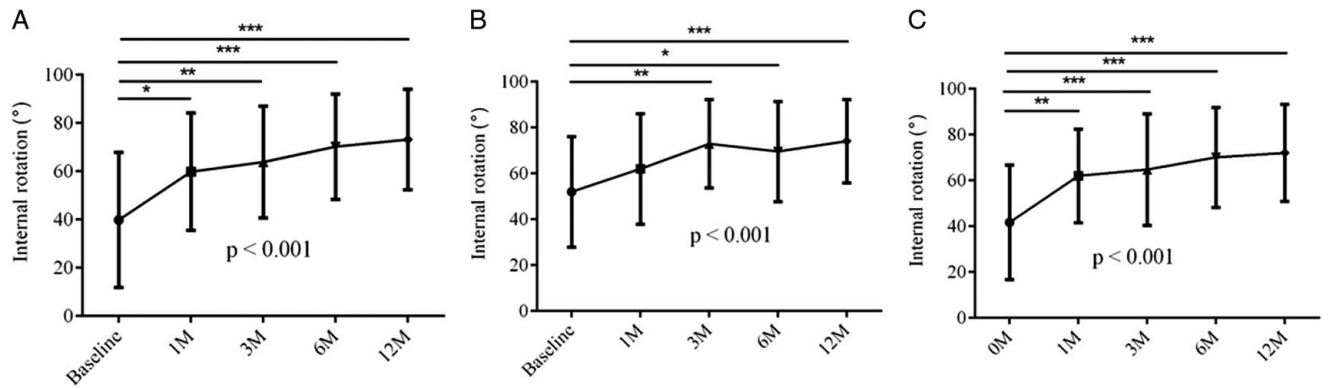


**Figure 8.** The extend of internal rotation from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$).

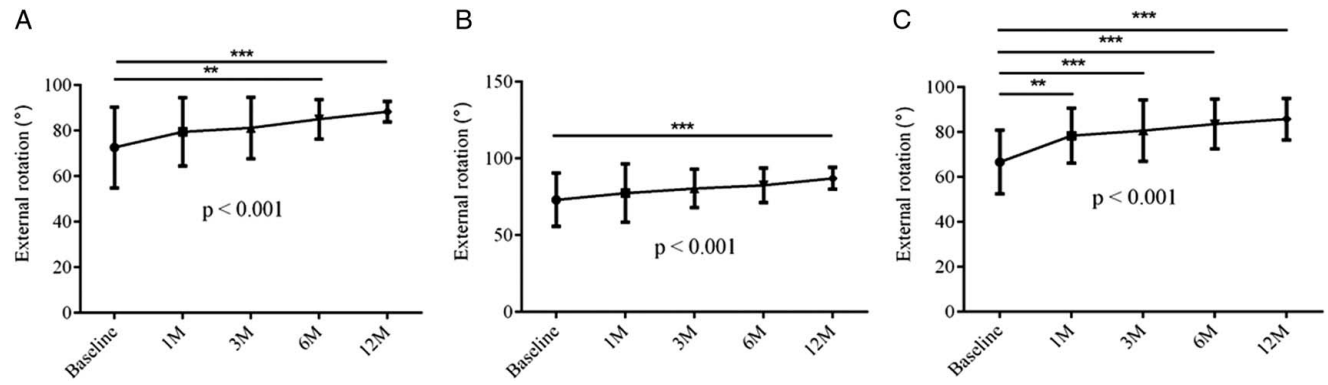


**Figure 9.** The extend of external rotation from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (**$P < 0.01$ and ***$P < 0.001$).

It is noteworthy that none of the participants in the HA + 1 ESWT group demonstrated deterioration in tendinopathy grading or tear status in MRI assessments 1 year post-intervention. Previous study in animal models of Achilles tendinopathy has illustrated the potential of ESWT in promoting tendon healing, revealing that ESWT stimulates the release of growth factors derived from tenocytes, including transforming growth factor β1 (TGF-β1) and insulin-like growth factor 1 (IGF-1), which are integral to the healing process[38]. Furthermore, ESWT has been shown to enhance the expression of lubricin, a crucial mucinous glycoprotein involved in tendon gliding and protection against friction-induced damage[47]. This upregulation of lubricin, triggered by mechanical and biochemical stimuli, supports tendon healing by facilitating movement within tendon structures and collagen fascicles. Despite the absence of worsening in tendinopathy grading and tear status among participants receiving HA + 1 ESWT, two patients experienced deteriorations in tendinopathy grading and one patient in tear status within the HA + 2 ESWT group. This suggests that while the ROM-enhancing effect of ESWT may be dose-dependent, its beneficial effects on MRI-related healing parameters do not exhibit such dependency. Further investigation into the optimal dosing of ESWT for various parameters, including ROM and MRI-related assessments of tendinopathy and tear status, is warranted.

There are limitations to our study. Firstly, although our recruited participant number exceeded the calculated minimum sample size, the reliability of our findings could still be improved with a larger sample size. Secondly, despite our efforts to retain participants, a small number of patients withdrew, introducing potential attrition bias. Thirdly, the true clinical implications of our study need to be validated by assessing the number of patients willing to undergo supplementary ESWT based on the benefits demonstrated by the present study and those who genuinely benefit from it. Finally, the generalisability of our study is limited, as the benefits of additional ESWT cannot be extrapolated to patients with full-thickness RC tears, those with conditions outside our inclusion criteria such as rheumatic diseases, or different ethnic groups, as this study is based on the Taiwanese population. Potential directions for further research include evaluating cohorts with complete tears (with and without rotator cuff tear arthropathy) and testing the effects of more than two ESWT sessions (as many patients in the clinical settings undergo more than two treatment sessions).

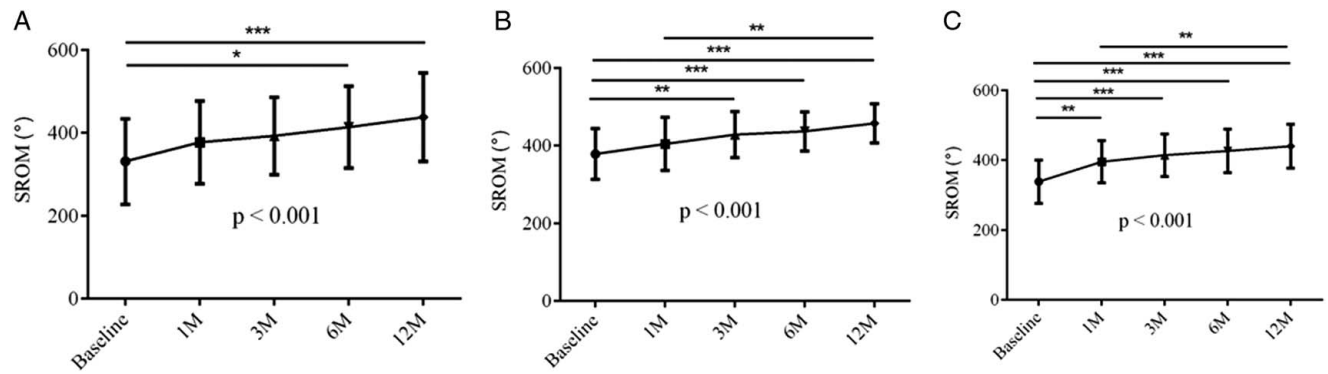


**Figure 10.** The extend of sum of range of motion (SROM) from baseline to 12 months after Day 1 for (A) HA group, (B) HA + 1 ESWT group, and (C) HA + 2 ESWT group (*$P < 0.05$, **$P < 0.01$, and *** $P < 0.001$).

## Conclusion

Both the HA + 1 ESWT and HA + 2 ESWT groups consistently demonstrated superior improvements in MP, CMS, and various aspects of ROM compared to the HA group throughout the study period. Notably, the HA + 2 ESWT group exhibited greater improvements in FF ($P = 0.013$), IR ($P = 0.019$), and SROM ($P = 0.025$) at 1 month, and in FF ($P = 0.007$) at 3 months, than the HA + 1 ESWT group. None of the HA + 1 ESWT group participants experienced worsened tendinopathy grading or tear status on MRI. These findings underscore the potential of combining HA injections with ESWT as an effective strategy for enhancing therapeutic outcomes in patients with RC lesions without complete tears.

## Ethical approval

This investigation was approved by the Institutional Review Board of Chang Gung Medical Foundation (protocol code: 201900290B0A3, date of approval: 2019/04/22).

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. Patients' and volunteers' names, initials, or hospital numbers were not be used.

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## Author contribution

J.-Y.K.: funding acquisition; C.-C.H., P.-H.H., J.-W.C., and C.-Y.L: data curation; S.-J.K.: writing – original draft and writing – review and editing.

## Conflicts of interest disclosure

The authors declare no conflicts of interest.

## Research registration unique identifying number (UIN)

This study is registered on ClinicalTrials.gov (https://www.clinicaltrials.gov/) with the unique identifying number (UIN) NCT05034757.

## Guarantor

Jih-Yang Ko (first author) and Shu-Jui Kuo (corresponding author).

## Data availability statement

The data presented in this study are available on request from the corresponding author.

## Provenance and peer review

This paper has been invited by Guest Editor Professor Kandiah Raveendran under the theme of 'shockwave treatment'. Dr. Jih-Yang Ko, the first author, is a member of ISMST.

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