Influence of Radial Extracorporeal Shock Wave Therapy on Shoulder Pain and Structural Abnormalities in Stroke Patients

Keywords
stroke, disability, Shock wave, Shoulder pain, ultra-sonography

Abstract
Introduction
To examine the efficacy of radial extracorporeal shock wave (rESWT) on pain & disability levels in stroke patients with shoulder structural abnormalities.

Material and methods
Methods: Thirty sub-acute stroke patients their ages between 40 to 60 years were randomly allocated into 2 equal groups after signing an institutional consent form. Real rESWT group (GA) underwent rESWT in addition to a designed program of physical therapy to shoulder joint. Control group (GB) received sham rESWT in addition to the same physical therapy program as for GA. The treatment protocol for both groups was two times per week for a whole month. Baseline and post intervention findings in both groups were assessed and compared for the primary outcomes including shoulder structural changes, pressure pain threshold (PPT) and shoulder disability measured by ultrasonography (USS), handheld algometer and shoulder pain disability index (SPADI) respectively.

Results
Significant reduction of all post treatment SPADI scores (pain, disability & total scores) in both groups with remarkable decrease in favor to rESWT group (GA) (P < 0.05), In addition, USS scores and PPT findings showed notable preference in favor to (GA) which was demonstrated as significant decrease in USS score with increase in PPT findings only in rESWT group (GA) (P < 0.05).

Conclusions
The addition of radial extracorporeal shock wave (rESWT) to a designed physical therapy program is more efficient in reducing shoulder structural abnormalities, pain and disability in sub-acute stroke patients

Explanation letter
Dear Dr. (Journal editor name),

First of all, I want to thank you for reviewing our submitted manuscript.

I have reviewed your comments and I will answer it one by one:

Reviewer 1:
Q1: Line 125 add years to the sentence: Patient's ages were between 40 and 60
A1: Done
Q2: Abbreviated rESWT in the first mention only and then use it for example Discussion first and 2nd paragraph and other additional mentions. In this same section, lines 328 and 330 also is needed to mention that rESWT is an add on intervention and is in sub-acute stroke patients.
A2: Done
Q3: In line 352 change pan to Pan et al.,
A3: Done
Q4: In line 356 change: However, the outcomes of our study are “more relevant”, to are “more comprehensive”
A4: Done
Q5: Don’t abbreviate VEGF is used once.
A5: Done
Q6: In the Discussion section regarding Engebretsen et al, the author mention that the difference between the outcomes in this study and the current is the addition of rESWT, however, both used rESWT so is not enough explanation to the findings.
A6: we add the following
The effect of exercises was discussed in a previous comparative study conducted by Engebretsen et al. [30]; they investigated the effect of supervised exercises versus radial extracorporeal shock-wave therapy on subacromial shoulder pain in stroke patients with 1 year follow up. Results revealed reduction of SPADI score, pain and improvement of shoulder function in both groups with no significant difference between them, also there was a recommendation on the short-term efficacy of supervised exercises (SE) than rESWT. In our study, we assessed the efficacy of adding rESWT to a designed physical therapy program, and there was significant difference in the pain, SPADI & functional scores in favor to the real rESWT group, this may be attributed to the cumulative effect of rESWT and the designed physical therapy program, in addition to the doubled number of rESWT sessions used in our study.
Q7: Change “special neurologists “to vascular or general neurologist only
A7: Done
-Didn’t find in the manuscript this response:
Q8: Who applied the scales and the intervention?
A8: Intervention (rESWT + Physical therapy program) was applied by a certain therapist and to avoid bias assessment of SPADI scale and PTT is done by another therapist.
A8: We add it at the end of intervention section.

Review 4:
Q1. It’s better introducing ischemic stroke and post-stroke complications in the Introduction part.
A1. We add the following paragraph
Stroke is the third leading cause of death and the major cause of disability worldwide. It is a focal cerebral insult that often results in neurologic and medical sequelae with long-term implications for quality of life. Ischemic stroke represents the majority of strokes (85%), and hemorrhagic stroke accounts for the rest. Impairments associated with stroke can be motor, perceptual, sensory, cognitive and psychological. (Turner et al., 2002). It is estimated that about 70% of stroke patients had upper limb residual impairments that compromise activities of daily living. The return of upper limb function has been identified as an important rehabilitation goal. (Harris and Eng 2007)
Q2. I would recommend a NIHSS score for stroke patients reflecting the severity of illness.
A2: In the primary recruitment stage of this study, Modified Ashworth’s Scale (MAS) was the way adopted to classify the stroke patients according to the degree of upper limb spasticity. We included only patients with mild to moderate upper limb spasticity (grade 1+: 2). In addition, the SPADI score was used to assess shoulder pain and functional activities.
We would recommend the use of NIHSS in future work in comparative studies to figure out the effect of rESWT on HSP in sub-acute stroke patients with different stroke severities (this part has been added to the limitation part).

Q3. Table 3, Is a BH-adjustment for comparison needed in this table since multiple comparisons have been made?  
A3. We didn't use BH-adjustment as there is no need to adjust any P-value, as there was no need to control a family-wise error-rate (FWER).

Q4. Reference 10, no page number.  
A4: We have searched for the page numbers of this article in different reference search engines but not found even the citation link for the article includes no pages (only volume and issue number). This is the DOI for this paper for more clarification (https://doi.org/10.1186/s43166-021-00068-z).

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Influence of Radial Extracorporeal Shock Wave Therapy on Shoulder Pain and Structural Abnormalities in Stroke Patients

Abstract

Introduction: Structural abnormalities in shoulder joint are a common complication post stroke, as a consequent pain and functional limitation became the most devastating quality of life problems for such patients. Shock wave therapy is a non-invasive method that can enhance the level of perfusion in ischemic tissues, relief inflammation and promote healing. Objectives: To examine the efficacy of radial extracorporeal shock wave (rESWT) on pain & disability levels in stroke patients with shoulder structural abnormalities. Methods: Thirty sub-acute stroke patients their ages between 40 to 60 years were randomly allocated into 2 equal groups after signing an institutional consent form. Real rESWT group (GA) underwent rESWT in addition to a designed program of physical therapy to shoulder joint. Control group (GB) received sham rESWT in addition to the same physical therapy program as for GA. The treatment protocol for both groups was two times per week for a whole month. Baseline and post intervention findings in both groups were assessed and compared for the primary outcomes including shoulder structural changes, pressure pain threshold (PPT) and shoulder disability measured by ultrasonography (USS), handheld algometer and shoulder pain disability index (SPADI) respectively. Results: Significant reduction of all post treatment SPADI scores (pain, disability & total scores) in both groups with remarkable decrease in favor to rESWT group (GA) (P < 0.05), In addition, USS scores and PPT findings showed notable preference in favor to (GA) which was demonstrated as significant decrease in USS score with increase in PPT findings only in rESWT group (GA) (P < 0.05) Conclusion: The addition of radial extracorporeal shock wave (rESWT) to a designed physical therapy program is more efficient in reducing shoulder structural abnormalities, pain and disability in sub-acute stroke patients

Key words: Shock wave, Shoulder pain, ultrasound, disability, stroke.

Introduction
Stroke is the third leading cause of death and the major cause of disability worldwide. It is a focal cerebral insult that often results in neurologic and medical sequelae with long-term implications for quality of life. Ischemic stroke represents most of strokes (85%), and hemorrhagic stroke accounts for the rest. Impairments associated with stroke can be motor, perceptual, sensory, cognitive and psychological. [1]. It is estimated that about 70% of stroke patients had upper limb residual impairments that compromise activities of daily living. The return of upper limb function has been identified as an important rehabilitation goal [2].

Hemiplegic shoulder pain (HSP) is considered one of the most debilitating complications following stroke [3]. Between 30 and 65% of stroke patients may experience HSP [4]. Pain can result from shoulder structural injury and abnormal posture which may damage the surrounding tissues over time [5]. Impingement of rotator cuff, subluxation or capsulitis of glenohumeral joint, bicipital tendinitis, shoulder muscles spasticity, and shoulder hand syndrome are other causes for shoulder pain post stroke. Shoulder pain is demonstrated as a predictor for decrease arm functional adequacy, high levels of depression and poorer quality of life [6].

Wide array of pathologies can potentially underly the development of HSP. Three possible mechanisms were identified; soft-tissue lesions, impaired motor control (muscle tone changes) and altered peripheral and central nervous system activity. The patho-mechanism is thought to be during the acute and sub-acute phase of stroke, flaccid paresis occurs resulting in potential subluxation of the shoulder, and/or imbalance of shoulder joint control and soft-tissue structure, resulting in altered mechanics of movement and increased susceptibility to injury. Spasticity
causes abnormal scapulohumeral rhythm and lead to impingement of the rotator cuff or other structures in the subacromial space. Several predisposing factors are linked with HSP, including incorrect handling, trauma during post-stroke rehabilitation, passive abduction greater than 90° or forced abduction without lateral rotation or immobilization of the affected limb [7, 8].

Ultrasonography (US) is an essential method in evaluation of post-stroke HSP, it is superior to other imaging techniques that were used in evaluation of shoulder soft tissue structures. A variety of advantages are associated with it, including real-time imaging, direct multi-planar evaluation, cost-effectiveness, a short examination time, the ability to compare side-by-side immediately, and the absence of ionizing radiation [9].

An extracorporeal shock wave is defined as a sequence of single sonic pulses characterized by high peak pressure (100 MPa), a fast rise in pressure ( < 10 ns) and a short lifecycle (10 μs) . A specific generator transfers the energy directly to the targeted region, with a flow density ranging from 0.003 mJ/mm2 to 0.888 mJ/mm2 [10]. Extracorporeal shock wave therapy (ESWT) can cause energy gradients and torsional tension between tissues of different densities through energy conversion and transmission, causing a cavitation effect that induces various biological effects. Many clinical studies showed that shock waves are effective in management of tendon and bone disorders, for example; pseudoarthrosis, shoulder tendinitis, plantar fasciitis, and many other tendon disorders, particularly among athletes [11].

Several studies investigated the efficacy of using extracorporeal shock wave therapy on spasticity [12,13,14,15,16] and hemiplegic shoulder pain post stroke [10]. However, displaying the therapeutic
possibilities of using extracorporeal shock wave therapy on the structural abnormalities that happen in the shoulder post stroke in relation to its effect on the level of shoulder pain and disability index post stroke were not well defined in any previous studies.

Material and methods

Design of the study

A single-blind randomized controlled study was administrated in an outpatient private clinic during the period, from September 2020 to October 2021. Prior to enrollment, an informed consent form was signed by each participant. The study was conducted in accordance with the principles of the Declaration of Helsinki and good clinical practice standards was approved by the ethics committee for clinical research of faculty of physical therapy, Cairo university with registration number (P.T.REC/012/002870). The study has an identification number on ClinicalTrials.gov: NCT04859673.

Confidentiality

All research procedures were carried out in a closed room in a private outpatient clinic, from the orientation to the actual application of the study. During the study, we made sure that only the investigators were in the room.

Declaration of interests

Other than the information and data acquired from participants for the research study, there is no interest.

Accesses to data

The patient's personal data and details were recorded in an excel spreadsheet that were only accessed by the research investigators. The sheet was on the principal password-protected investigator's PC.

Ancillary and post-trial care
There are no physical, psychological, or social dangers in this study. If subjects report any unexpected symptoms during treatment, the trial could be halted.

**Dissemination policy**

Reports and results were sent by email to each patient.

**Participants**

The study was conducted on thirty sub-acute stroke patients with hemiplegic shoulder pain. All patients were clinically diagnosed and referred from a general neurologist. Computed tomography scan and MRI were used to confirm the diagnosis of stroke in the territory of the middle cerebral artery.

Patient’s ages were between 40 and 60 years, with mild to moderate upper limb spasticity (grade 1+: 2); according to the modified Ashworth scale (MAS). All conducted patients experienced a single stroke during the last three months with cognitive capacity that enable them to comprehend and follow the instructions (Mini-Mental Scale >24).

Exclusion criteria includes patients with a history of shoulder pain, trauma, or surgery prior to stroke, patients taking warfarin with an international normalized ratio above 4.0, oral NSAIDs three days prior to study, or intra-articular injections one month prior to study were all excluded from the study. Patients who are unable to express their own pain severity, those who have a cardiac pacemaker, and those who are osteoporotic were also disqualified.

**Randomization**
Thirty-five subacute stroke patients with shoulder pain were initially evaluated for eligibility. Four patients didn’t meet our inclusion criteria, and one refused to participate. Allocation of the remaining thirty patients took place randomly via computer-generated random numbers.
into two groups of equal size. The examiners were blinded to which group the patients belong (CONSORT Flow Diagram (Figure 1)).

Outcome measures

Primary: Shoulder structural abnormalities

Samsung HS70A (Samsung medison, Seoul, Korea) ultrasonography machine was used to assess the structural changes of the hemiplegic shoulder. Ultrasonography procedures were applied while the patient seated on a chair, the affected shoulder was examined in all patients via scanning four main tendons; biceps brachii (long head), supraspinatus, infraspinatus and subscapularis, glenohumeral joint, as well as the existence of adhesive capsulitis (through measuring of coracohumeral ligament thickness) [17]. Abnormal ultrasound (USS) findings were assigned as follow: (a) Full-thickness tear of rotator cuff presented as: A full-thickness hypoechoic defect, visible hyaline cartilage or appearance of heterogeneous hypoechoic cuff due to deltoid or subacromial-subdeltoid bursa herniation into the cuff. (b) Partial-thickness tear of cuff showed as: hypoechoic defect within tendon (more than 3 mm) or in articular or bursal surface that appears in both planes (transverse & longitudinal). (c) Tendinosis was presented as diminished echogenicity with tendon enlargement (>8mm for biceps and > 2 mm for rotator cuff). (d) Long head of biceps tendon (LHBT) sheath effusion was defined as an anechoic region (>2 mm) encircling LHBT in transverse view or an anechoic/hypoechoic crescent penetrating LHBT in the longitudinal views. (e) Bursitis was diagnosed by the presence of fluid in the subacromial-subdeltoid (SASD) bursa with a thickness of more than 2 mm. (f) Shoulder subluxation was diagnosed by increase in the distance between acromion and greater tuberosity by more than 0.4 cm over the
normal value (1.91–2.84 cm) (g) **Adhesive capsulitis**: identified by increased thickness of coraco-humeral ligament more than 3 mm [17,18].

**Scoring**: If an abnormal USS finding was present, it was given a score of one (1), and if it wasn't, it was given a score of zero (0). So, presence of LHBT effusion, SASD effusion, subluxation or adhesive capsulitis all received one point a piece. The four tendons were evaluated individually per shoulder and were graded identically for tendon tear, tendinosis, or degeneration. The combination of these results produced a raw USS score, with the lowest score being zero (normal examination) and the highest score being 16. The raw USS scores were then divided into graded USS scores; with (0) for normal shoulder, (1-2) for mild damage, (3-4) for moderate damage, (5-6) for severe damage, and (>6) for intense damage [8]. All measures were taken at baseline and post intervention for both groups.

**Secondary: The pressure-pain threshold**

The pressure-pain threshold (PPT) is the lowest pressure at which the pressure sense is perceived as a pain. Pressure algometry is a valid and reliable method to evaluate deep somatic tissue sensitivity. Hand-held Baseline® Dolorimeters algometer was used to assess the Pressure-pain thresholds (PPT). It has a pistol-style grip and a rod at the tip with a pressure-sensitive gauge strain. The algometer tip was positioned on the middle of the deltoid muscle on the affected shoulder of each patient while seated. Pressure was conducted at a rate of 1 kg/cm2/sec using a 0.785 cm² rubber tip. As the algometer was pressed, the force gradually increased, the algometer display was not visible to the patients at any time, patients were instructed to say "stop" once they felt pain, after which the device was released, and the force was measured. The
threshold was assessed three times for each patient at each site, and the average was calculated and utilized for analysis. [19]

**Shoulder pain and disability index (SPADI)**

Self- administered 13-items questionnaire that involve two main domains, pain and functional activities. The pain domain consists of five questions regarding the severity of pain, functional activities are assessed with eight questions designed to measure the degree of difficulty experienced in activities of daily living that require upper-extremity use. Items of the questionnaire were demonstrated clearly then patients are asked to place a mark on a 10cm visual analogue scale for each question (Right end) indicating "worst pain imaginable/ so difficult required help", (Left end)"no pain/no difficulty". Scores were demonstrated as follow; a maximum of 50 points for the pain subscale, 80 points for the disability subscale and 130 points for the total index score. All scores were expressed as a percentage. Final score of each part was statistically analyzed separately [20].

**Intervention**

- **Radial Extracorpeal Shock Wave Therapy:**

   Shock wave was delivered using Swiss DolorClast® Master - shockwave therapy system machine. It is equipped with master console, external compressor, 15mm contact head and hand piece. Each patient was instructed to sit comfortably with the affected shoulder exposed. The stimulator head with the transmitter was applied to greater and lesser tuberosities of the humeral head to activate the rotator cuff tendons and the shoulder capsule. These
stimulation points corresponded to the insertion points of the subscapularis and supraspinatus muscles. The subscapularis insertion site was stimulated by externally rotating the shoulder and flexing the elbow at 90 degrees, while the supraspinatus insertion site was stimulated by internally rotating the shoulder and slightly extending the elbow. Each stimulation site received 3000 pulses (1500 pulses/site) at a submaximal pressure of 0.39 to 1.95 mJ/mm2 and a frequency of 12 Hz each session, according to patient's tolerance for pain without the use of local anesthetics [10].

- **Designed Physical Therapy program for shoulder:**

  It included Bobath approach for upper limb, Scapular mobilization, Stretching exercises for inward rotators, Passive range of motion, and active assisted exercises for shoulder movements [5].

Patients in real rESWT group (GA) underwent rESWT plus a designed physical therapy program for shoulder joint. The duration of session was about 75min (15 min for rESWT and 60 min for physical therapy program) according to patient's tolerance. Patients in control group (GB) received sham (rESWT) plus the same designed program of physical therapy as in (GA). Sham (rESWT) was done via applying the stimulator head to the same stimulation points, since the transmitter had been removed, stimulation was not provided, and the patients got only air pressure and sound at same frequency [10]. The treatment protocol for both groups was two times per week for a whole month. Intervention (rESWT + Physical therapy program) was applied by a certain therapist and to avoid bias assessment of SPADI scale and PTT is done by another therapist.
Sample Size Estimation

Prior to the study administration, sample size was calculated using the G*power 3.0.10 software (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). It was calculated based on previous studies (F test MANOVA: Repeated measures, within- between interaction, \( \alpha = 0.05 \), the effect size = 0.35, power = 0.95\% and large effect size) showed that the suitable for this study is about = 30 patients (15 patients for each group).

Statistical analysis

Data analyses were conducted using SPSS Version 21 (SPSS Inc., Chicago, USA). Distribution of gender and degree of spasticity in both groups were evaluated using Chi-square test. Shapiro-Wilk test was used to test the normality of data. Mann-Whitney and Wilcoxon tests were used to compare USS score pre and post treatment between and within groups respectively. 2×2 Multivariate analysis of variance (MANOVA) was used to analyze SPADI and PPT variables, with the treatment groups (GA versus GB) used as between subjects’ factor and time of assessment (pre and post treatment) used as within subjects’ factor. Independent t-test was used to compare age, duration of illness between both groups. For all statistical examinations, level of significance was \( P < 0.05 \).

Results

There was no statistically significant difference between both groups regarding age, sex, degree of spasticity and duration of illness (\( P > 0.05 \)) (Table 1).

The statistical analysis of measured variables pre and post treatment within each group revealed significant reduction of all SPADI scores
(pain, disability and total scores) in both groups (P< 0.05), the percent of changes were 41.58, 36.94 and 38.99 in (GA) compared to 10.76, 12.23 and 11.05 in (GB) respectively, while there was a significant reduction of USS score and increase of PPT only in (GA) (P= 0.001) (Table 2 & 3).

The between-groups analysis revealed no significant differences between groups before treatment (at the baseline assessment) in all measured variables (P> 0.05). While post treatment between-groups analysis was as following; significant reduction in all SPADI scores (pain, disability and total scores), USS score and significant increase of PPT in favor to (GA) (P< 0.05) (Table 2 & 3).

Table 1: Comparison of general characteristics of patients in both groups:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Real rESWT (GA) group</th>
<th>Control (GB) group</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>51.60 ± 5.32</td>
<td>50.80 ± 6.81</td>
</tr>
<tr>
<td>Sex</td>
<td>Male No. (%)</td>
<td>8 (53.30 %)</td>
<td>6 (40.00 %)</td>
</tr>
<tr>
<td></td>
<td>Female No. (%)</td>
<td>7 (46.70 %)</td>
<td>9 (60.00 %)</td>
</tr>
<tr>
<td>Degree of spasticity</td>
<td>Score 1 No. (%)</td>
<td>4 (26.70 %)</td>
<td>1 (6.67 %)</td>
</tr>
<tr>
<td></td>
<td>Score 2 No. (%)</td>
<td>11 (73.30 %)</td>
<td>14 (93.33 %)</td>
</tr>
<tr>
<td>Duration of illness (months)</td>
<td>Mean ± SD</td>
<td>5±0.845</td>
<td>5.2±0.862</td>
</tr>
</tbody>
</table>

Numerical data are expressed as mean ± SD, nominal data are expressed as number and percentage, P> 0.05: non-significant.

Table 2: Comparison of USS scores within and between both groups:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Real rESWT (GA) group</th>
<th>Control (GB) group</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>USS score</td>
<td>Pre- treatment</td>
<td>4(1)</td>
<td>3(0)</td>
</tr>
<tr>
<td></td>
<td>Post- treatment</td>
<td>1(1)</td>
<td>3(0)</td>
</tr>
<tr>
<td>P- value</td>
<td>0.0001*</td>
<td>0.99</td>
<td></td>
</tr>
</tbody>
</table>

*Significant: P- value ≤0.05, USS: Ultrasonography, IQR: interquartile range

Table 3: Comparison of SPADI and PPT variables within and between both groups:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Real rESWT</th>
<th>Control (GB)</th>
<th>P- value</th>
</tr>
</thead>
</table>


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<tr>
<td></td>
<td></td>
<td>(GA) group</td>
<td>group</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SPADI pain score</strong></td>
<td></td>
<td>Pre- treatment</td>
<td>91.53 ± 5.08</td>
<td>94.13 ± 3.96</td>
<td>0.129</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post- treatment</td>
<td>53.47 ± 11.62</td>
<td>84.00 ± 3.68</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>P- value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>SPADI disability score</strong></td>
<td></td>
<td>Pre- treatment</td>
<td>89.07 ± 3.97</td>
<td>92.76 ± 6.16</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post- treatment</td>
<td>56.17 ± 12.88</td>
<td>81.42 ± 5.77</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>P- value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>SPADI total score</strong></td>
<td></td>
<td>Pre- treatment</td>
<td>90.31 ± 3.25</td>
<td>92.62 ± 5.38</td>
<td>0.165</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post- treatment</td>
<td>55.10 ± 11.64</td>
<td>82.39 ± 4.12</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>P- value</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>Pain pressure threshold (PPT)</strong></td>
<td></td>
<td>Pre- treatment</td>
<td>1.29 ± 0.2</td>
<td>1.46 ± 0.28</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post- treatment</td>
<td>3.23 ± 0.61</td>
<td>1.77 ± 0.58</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>P- value</strong></td>
<td></td>
<td></td>
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<td></td>
<td>0.057</td>
</tr>
</tbody>
</table>

*Significant: P- value ≤0.05, SPADI: Shoulder pain and disability index

**Discussion**

This study provides evidence on the efficacy of adding radial extracorporeal shock wave (rESWT) to a designed physical therapy program on shoulder structural abnormalities as well as pain & disability level in sub-acute stroke patients. Approximately one third of all stroke patients experience shoulder pain that has a negatively impact on daily activities and the quality of life. To the best of our knowledge, this study was the first randomized controlled trial that investigated the efficacy of rESWT on shoulder structural abnormalities in accordance to pain and disability level in sub-acute stroke patients.

Findings of the current study revealed significant reduction in the ultrasonographic structural abnormalities of the hemiplegic shoulder in the real rESWT group. This may be attributed to the therapeutic effect of rESWT that facilitates tendon healing by increasing angiogenesis, promoting tenocyte proliferation and collagen metabolism, increasing collagen turnover, and enhancing neovascularization of injured tissue,
which is accompanied with release of endothelial nitric oxide, vascular endothelial growth factor, and proliferating cell antinuclear antigen [21]. Another assumption that supported our results had investigated the role of shock wave in resolving edema and reducing inflammatory cytokines into the injured tendons as well as its role in increasing the expression of growth factors like (TGF-1 and TGF-1) that play an integral role in tissue regeneration and tendon repair [22].

Results of the current study also agreed with the declaration of Pan et al. [23] who concluded that two sessions of rESWT, 14 days apart showed great therapeutic outcomes in tendinitis of the shoulders especially of the rotator cuff with arc-type calcific plaques. However, the outcomes of our study are more comprehensive, as the therapeutic efficacy of rESWT on the shoulder structural changes were examined via ultrasonographic scanning of four main tendons: biceps brachii (long head), supraspinatus, infraspinatus and subscapularis, glenohumeral joint, as well as the existence of adhesive capsulitis. Also, our findings may be correlated to the doubled number of rESWT sessions applied in our study.

The presented study is in accordance with other previous studies which provided evidence about the positive effect of rESWT on relieving pain via increasing pain pressure threshold and decreasing SPADI pain score in real rESWT group. This could be attributed to shock waves' direct suppressive effects on nociceptors, as well as the hyper stimulation mechanism that disables the gate control mechanism. Other studies declared that shock waves helped to reduce pain by lowering substance P levels in the target tissue and decreasing substance P synthesis in the dorsal root ganglia [24, 25]. Furthermore, some studies have described the efficacy of shock waves in reducing the expression of inflammatory mediators at high levels (matrix metalloproteinases and inter-leukins). In
addition, it can boost regional blood flow and reduces muscular tension and stiffness as well as pain reduction by interfering with the flow of excessive activation of nociceptors and selective destruction of nonmyelinated fibers [26].

Regarding the efficacy of rESWT on pain, the findings obtained in our study revealed significant reduction in the level of pain by the end of the treatment protocol; this is congruent to those found by Kim et al. [10], who concluded that rESWT is an effective and safe modality for pain management in people with hemiplegic shoulder pain. However, the method used to evaluate pain in our study was more objective compared to that used by Kim, we used PPT instead of the visual analogue scale. Another advantage to our study is the frequency of application as the optimum treatment protocol for rESWT is three sessions per week [27]. In our study rESWT was applied twice per week for 4 weeks compared to 4 times a week for 2 weeks applied by Kim.

In terms of the functional improvement in the shoulder after rESWT, results of the present study revealed reduction in all SPADI scores (pain, disability and total scores) for both groups, with a more pronounced effect in favor to real rESWT group (GA). This may be attributed to anti-inflammatory and anti-fibrotic effect of rESWT which helped in reducing the synovial inflammation and capsular fibrosis with a consequent improvement in shoulder ROM and function [28].

In this study, the designed physical therapy program on shoulder including (Bobath, ROM, stretching and scapular mobilization) showed improvement in pain level and functional abilities for both groups, this may be attributed to improved blood flow to the affected areas, reduced adhesions, modulated spasticity, and inhibiting nociceptors [29, 30, 31].
The effect of exercises was discussed in a previous comparative study conducted by Engebretsen et al. [32]; they investigated the effect of supervised exercises versus rESWT on subacromial shoulder pain in stroke patients with 1 year follow up. Results revealed reduction of SPADI score, pain and improvement of shoulder function in both groups with no significant difference between them, also there was a recommendation on the short-term efficacy of supervised exercises (SE) than rESWT. In our study, we assessed the efficacy of adding rESWT to a designed physical therapy program, and there was significant difference in the pain, SPADI & functional scores in favor to the real rESWT group, this may be attributed to the cumulative effect of rESWT and the designed physical therapy program, in addition to the doubled number of rESWT sessions used in our study.

On the other hand, different findings have been reported by other authors; Speed et al. [33] claimed that there is no evidence of an added benefit from rESWT compared with sham treatment. This contradiction may be attributed to different sites of stimulation, number of sessions and session's interval between the two studies. Our findings also contradicted with Kvalvaag et al. [34], who concluded that rESWT has no additional effect to the supervised exercises in the management of subacromial shoulder pain after 24 weeks, except in the subgroup of patients with calcification in the rotator cuff. The discrepancy between the two studies may be due to different duration of treatment protocol as the study of Kvalvaag et al., applied rESWT once a week for four weeks, while in our study rESWT was applied two times a week for 4 weeks.
In this study, post treatment changes of USS score and PPT in the control didn't reach significant difference which may be due to short treatment period.

**Limitation:**

It is necessary, to point out some limitations in this study. This study was limited by only reporting the immediate post treatment effect of rESWT so we cannot generalize about the long-term efficacy of rESWT after stopping our program. Also, the included patients were limited to sub-acute hemiplegic with shoulder pain so further researches are recommended to investigate the impact of rESWT of patients with different hemiplegic onsets as acute & chronic hemiplegic shoulder pain.

Further studies are recommended on a larger sample size, effect of gender should be considered in future work. Future researchers should also address various age groups in their sample and incorporate different follow-up periods in their study design. We would also recommend the use of NIHSS in future work in comparative studies to figure out the effect of rESWT on HSP in sub-acute stroke patients with different stroke severities.

**Conclusion:**

The use of the radial extracorporeal shock wave as an adjunct to a designed physical therapy program has a significant effect on reducing shoulder structural abnormalities and consequently pain and disability in sub-acute stroke patients.

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Conflict of interest
There are no conflicts of interest declared by the authors.

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