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Original Article

Efficacy and safety of Tuina and intermediate frequency electrotherapy for frozen shoulder: MRI-based observation evidence

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Abstract: Background: Tuina and Intermediate Frequency (IF) electrotherapy are commonly used treatments for frozen shoulder (FS). This study aimed to compare the clinical efficacy of Tuina and IF electrotherapy in the treatment of stage II frozen shoulder and to provide evidence-based treatment for FS. Methods: The FS patients were randomized into two groups, the observation group, which received Tuina, and the control group, which received IF electrotherapy. The total treatment duration was 20 minutes per treatment, 3 times per week; the treatment period was 6 weeks. Assessments were performed at baseline, 3 weeks, 6 weeks, and 16 weeks after follow-up. Primary assessments included visual analog scale (VAS), Constant-Murley scale (CMS), and secondary assessments included shoulder MRI, rotator cuff muscle diffusion tensor imaging (DTI). Results: A total of 57 patients participated in this study, in the observation group (n = 29) and the control group (n = 28). At the end of the 3rd and 6th weeks of treatment, Tuina was significantly more effective than IF electrotherapy in reducing the VAS score and improving the Constant-Murley total score ($P<0.05$), but there was no significant difference in scores between the two groups at the 16-week follow-up ($P>0.05$). MRI results in both groups: compared to the control group, the observation group had better results in reducing the degree of periapical edema and reducing the thickness of the axillary humeral capsule ($P<0.05$); and the observation group had significantly more efficacy than the control group in improving the diffusion state of water molecules in the rotator cuff muscles ($P<0.05$). Conclusion: Tuina is more effective than IF electrotherapy in improving the symptoms of FS patients as it can rapidly relieve the pain and restore the function of the affected shoulder, reduce the edema of the shoulder capsule, restore the function of the rotator cuff muscles, and shorten the natural course of FS. Name of the registry: This study was registered in the Shandong University of Traditional Chinese Medicine Affiliated Hospital; Grant No. (2021) Lun Audit No. (033) - KY; Date of registration: 2021.4.27.

Keywords: Frozen shoulder, Tuina, IF electrotherapy, MRI, RCT

Introduction

Frozen shoulder (FS), or adhesive capsulitis, is a chronic inflammatory disease involving the tissues surrounding the shoulder joint and the shoulder capsule, most often occurring in the 50s, and is characterized by shoulder pain and limited active or passive motion [1]. The prevalence in the general population is about 2% to 5.3% [2], and patients with diabetes and hyperlipidemia account for about 15% of all FS patients [3]. Its pathology is mainly characterized by chronic inflammation and fibrosis of the synovial membrane, based on arthroscopic findings, Neviaser divided the course of FS into four stages, i.e., acute, tumescent, frozen, and recovery [4], and regardless of the stage, physical therapy combined with self-functional exercise is the initial means of conservative treatment [5]. The natural course of the disease is long (15 months on average), and although it is self-limited [6], persistent pain and muscle protective activity disorders in the shoulder tend to cause spasticity and stiffness of the rotator cuff muscles, reduced muscle strength, and poor blood circulation. This can lead to rotator cuff muscle atrophy over time, seriously affecting the patient's quality of life. As a result,

patients seek treatment from medical professionals to reduce pain and speed up joint motion recovery.

Tuina, as a traditional external treatment method of TCM, has been widely used to treat musculoskeletal disorders related to chronic soft tissue injury [7]. After years of development, Tuina has combined modern anatomy with TCM meridians and acupoints, and the use of manipulation on shoulder tissues can relieve pain in the shoulder affected by FS, expand the range of motion of the shoulder joint, and have better clinical effect on the treatment of FS [8]. However, there are no reports on the efficacy of Tuina and IF electrotherapy in the treatment of frozen shoulder. Currently, MRI has been widely applied for FS symptoms evaluation as certain manifestations, including coracohumeral ligament (CHL) thickness, rotator cuff gap edema, fat obliteration in the sub coracoid triangle, and the degree of glenohumeral ligament edema are helpful in the diagnosis and assessment of the efficacy of FS [9]. But relevant reports from evidence-based clinical point of view are rare. The study aimed to find strong evidence for the treatment of FS with Tuina, to explore its clinical efficacy, and to provide more scientific and objective evidence-based support for clinical treatment.

Methods

Study design

This study is a two-armed, parallel-design, single-center, assessor- and analyst-blinded, randomized clinical trial comparing the clinical efficacy of Tuina treatment (group 1) versus IF electrotherapy (group 2) for frozen shoulder. It was conducted at the outpatient clinic of the Department of Tuina at the Affiliated Hospital of Shandong University of Traditional Chinese Medicine, China, and was reviewed by the hospital ethics committee, Ethics No. (2021) Ethics No. (033) - KY. All patients signed an informed consent form prior to participation in this study.

Inclusion criteria

In this prospective randomized controlled study, 60 subjects with complaints of shoulder pain that had persisted for at least 3 months and were diagnosed with FS by clinical examination and MRI were selected, 30 persons in each group. The diagnostic criteria of subjects are listed in Practical Orthopedics [10]. During the course of treatment, one female patient in the Tuina group was excluded due to a traumatic fracture in the first week that prevented further treatment. Two male patients in the IF electrotherapy alone group were excluded from the study due to poor compliance, and all patients were asked to receive no other adjunctive therapy during the study period except for the outpatient Tuina and IF electrotherapy. Inclusion criteria details are as follows: (1) Age 40-65, regardless of gender; (2) Single shoulder pain for 3-9 months, in stage II frozen shoulder; (3) Widespread shoulder pain, which worsens at night, with a VAS score between 7 and 9; (4) >50% decrease in shoulder elevation or external rotation function, with predominant limitation of activities such as external rotation, abduction and posterior extension of the affected shoulder; (5) No contraindications to acupuncture and Tuina, able to actively cooperate with the doctor and sign the consent form.

Exclusion criteria

(1) Used any medications or other treatments that may affect the efficacy of the treatment within 1 month prior to the treatment; (2) Suffering from severe nerve damage to the shoulder or other life-threatening multisystem diseases; (3) Pain and limited movement of the shoulder joint caused by other pathological inflammatory conditions; (4) Patients with contraindications to MRI.

Dropout criteria

Participants may withdraw from the study for any reason. (1) Failure to adhere to the trial; (2) Participate in other experiments during the trial; (3) Serious adverse events occurred during the trial; (4) Lost to follow-up.

Randomization and blinding

The subjects were randomly assigned to the observation and control groups in a 1:1 ratio using a randomized numerical table, with the observation group using Tuina therapy and the control group using IF electrical therapy. The randomly selected sequences were sealed in opaque envelopes and provided only to the therapist so that the participants could be assigned accordingly. Evaluators and data analysts were not aware of group assignments.

Interventions

The observation group was treated with Tuina; the control group was treated with IF electrotherapy. Patients in both groups were treated 3 times a week, 1 to 2 days apart/time. Each treatment time was about 30 min, 6 weeks was a course of treatment, a total of 18 times, and the overall efficacy evaluation of the intervention effect was conducted after 1 course of treatment. To ensure the reliability of the treatment results, all patients in the Tuina group were treated by experienced Tuina physicians, and the physicians were trained in the standardization of Tuina methods before the trial and were allowed to participate in the study after passing the test.

Tuina procedure

The operation procedure of Tuina is developed with reference to the third edition of the Chinese textbook "Tui Na Therapy" [11].

Relaxation of the tendons and the collaterals. The operator stands on one side of the patient, applying Gun Fa (rolling technique) to the patients' shoulder and scapula for around 5 to 7 min, accompanying with passive supination, abduction, posterior extension, internal rotation, and external rotation of the affected shoulder. Stretching the shoulder joint with the intensity tolerated by the patient for 2-3 min; tap and rub the acupressure points of Jianjing, Jianyu, Jianzhen, Tianzong, Quchi, Hegu, etc., until pyretic distention is felt by the shoulder. Stretching the shoulder joint. The patient is seated and the operator stands on the affected side, holding the affected shoulder with one hand, and another hold the elbow to perform the circumduction of shoulder joint from small to large amplitude, for about 2 min, as tolerated by the patient. Then, the stretching operation is applied to the affected shoulder, mostly being passive shoulder supination, abduction, adduction, posterior extension, and external rotation stretching depending on restriction degree at different angles of the affected shoulder. Stretching method: hold the shoulder with one hand, slowly stretch the upper arm with the other hand, and stay for 5-7 s when the shoulder reaches the maximum mobility and tolerance level, then relax and rest, with local pressure and passive activities of the scapula. Stretching operation: hold the patient's shoulder with one hand and another hand assists the stretching of the elbow until the reaching the maximum movement range and tolerance, then pause at this point for about 5-7 seconds. This operation can be combined with local compression and passive scapular movement, with repeated stretch of 3-5 times on each direction depending on patients' tolerance.

IF electrotherapy procedure

IF electrotherapy was performed with a computerized IF electrotherapy instrument (produced by Xiangyu Medical Equipment Co., Ltd., Model: XYZP-IE). The patient was placed in a supine position, and the doctor put 2 electrode tablets in a wet cloth bag soaked with warm water, and placed the wet cloth bag with electrode tablets on the pressure pain point of the patient's shoulder, and an elastic band was fixed. The prescription was chosen for frozen shoulder, the treatment frequency was 50 Hz, and the intensity of current stimulation (tremor and mild tightening sensation) was appropriate for the patient to tolerate. Each treatment was given for 30 min. Attention was paid to safety during operation to prevent electric shock injury.

Outcomes and measurement

The assessment results consist of 2 rating scales and MRI assessment data reports that can reflect changes in the shoulder joint of FS patients after both interventions. The scoring scales were assessed at baseline, week 3, week 6, and at the 16-week follow-up after the end of the intervention. Shoulder MRI assessments were performed at baseline and at the end of treatment at week 6, respectively.

Primary outcomes

Analysis of shoulder joint pain indicators: The visual analogue scale (VAS) was used as a criterion to evaluate the subjective pain of the patients. This method uses a figure rating scale to measure the pain level of the shoulder joints before and after treatment according to the patient's subjective judgment, and the higher the VAS score (0-10), the more severe the pain.

Constant-Murley shoulder scale: The Constant-Murley scale was used as the standard for the evaluation of shoulder function before and after treatment in both groups, with a total

score of 100 points. These points are divided into four categories: 15 points for pain, 20 points for activities of daily living (ADL), 40 points for range of motion (ROM) (10 points each for abduction, pronation, external rotation, and internal rotation), and 25 points for muscle strength. Of these, 35 points (15 for pain and 20 for ADL) come from the patient's subjective perception and 65 points (40 for ROM and 25 for muscle strength) come from the physician's objective judgment. The higher the score, the better the function of the shoulder joint.

Secondary outcome measurement

The secondary outcome measure of this experiment was the change in MRI images of the shoulder joint before and after treatment. This includes routine MRI and rotator cuff muscle DTI testing.

MRI was carried out to observe the characteristic features of FS: qualitative data (with or without) included IGHL edema, extracapsular edema, fat obliteration in the subcoracoid triangle, and periarticular fluid volume; quantitative data (refer to the measurements by Sunghoon, Mengiardi [12, 13]) including joint capsule thickness in humeral portion of the axillary capsule (mm) and in the glenoid; height and width of the axillary capsule, as well as thickness of the coracohumeral ligament and of the rotator cuff gap. Evaluation index of DTI imaging: rotator cuff muscles (supraspinatus SSP, infraspinatus ISP, teres minor TM, amd subscapularis SSC), ADC (Apparent Diffusion Coefficient) and FA (Fractional Anisotraphy) values were observed before and after treatment.

MRI examination procedure

MRI of the shoulder joint was carried out on all subjects. To ensure that the subjects were in a resting state, strenuous exercise was avoided and the patients rested for 30-40 min before the examination. Then, the imaging was performed using SIGNA Pioneer 3.0TMR (GE, USA) with a 16-channel flexible coil. The patients were in a supine position on the MRI bed, with the shoulder joint naturally relaxed and the shoulder as close as possible to the center of the magnet. The upper limb to be examined was in a standard neutral position, with the palm up; and the large flexible surface coil was wrapped around the shoulder joint to be examined. Soft pads were placed behind the upper arm and forearm, and sandbags are placed on the forearm to ensure that the shoulder joint and upper arm are at the same level, while keeping the shoulder joint braked to avoid motion artifacts.

Parameter settings: Axial scanning range covers the upper part of the acromioclavicular joint and the lower part of the subscapularis muscle; the localization line was parallel to the supraspinatus muscle. DTI is performed with axial scanning; repetition time (TR) = 6000 ms; echo time (TE) = 89 ms. 15 gradient coding directions were collected; b = 500 s/mm^2; layer thickness was 3.5 mm; layer spacing = 0 mm; 35 layers were collected. The field of view (FOV) = 240 mm × 240 mm, matrix = 128 × 128. Axial PDWI, TR/TE = 3000 ms/34 ms, layer thickness = 3.5 mm, layer spacing = 0 mm, FOV: 180 × 180 mm, scan time 3 min 18 s, 35 layers were collected; matrix = 256 × 320. The oblique coronal position included the anterior border of the coracoid process and the posterior border of the scapular spine, and the localization line was parallel to the long axis of the supraspinatus tendon. Oblique coronal T1WI, TR/TE = 500 ms/11 ms, layer thickness = 3 mm, layer spacing = 0.3 mm, FOV = 180 mm × 180 mm, matrix = 256 × 320. Oblique coronal compression lipid T2WI, TR/TE (3000 ms/80 ms), layer thickness = 3 mm, layer spacing = 0.3 mm, FOV = 180 mm × 180 mm, matrix = 256 × 320. The oblique sagittal scan covers the medial rostral process, laterally including the lateral humeral head, with the localization line perpendicular to the supraspinatus tendon, oblique sagittal compression lipid T2WI, TR/TE = 3000 ms/80 ms, layer thickness = 3 mm, layer spacing = 0.3 mm, FOV = 180 mm × 180 mm, matrix = 256 × 320.

Image processing and analysis

The acquired raw images were transferred to the GE ADW4.7 workstation, and the DTI data were post-processed using the Functool software, while the computer automatically constructed FA and ADC maps. As layer-free interval scanning was applied to DTI, the images were superimposed on the PDWI pressure lipid images to be reconstructed into oblique coronal and oblique sagittal matching scan images,

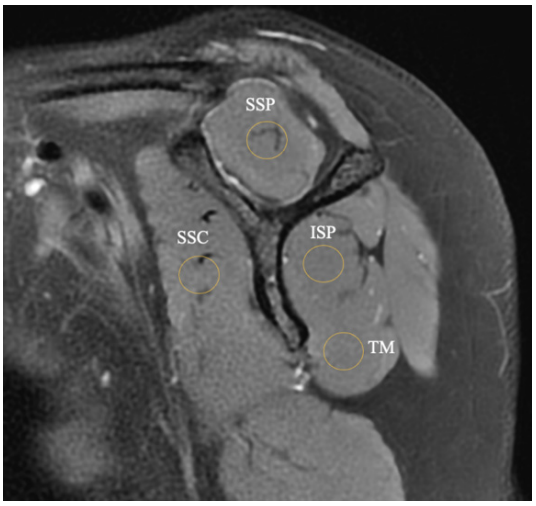

Figure 1. Oblique sagittal fat suppression T2-weighted MRI images, respectively, and ROI (35-40 mm^2) were selected at the same level for all subjects, and these are circled in yellow. The FA and ADC values of the muscles corresponding to ROI were measured.

which were more convenient for muscle identification and measurement. The images were analyzed by two physicians with more than 3 years of experience in clinical imaging diagnosis, and the region of interest (ROI) was selected to be about 35-40 mm^2, which was chosen to be as central to the muscle belly as possible, avoiding fatty infiltrated areas and artifacts (**Figure 1**). The FA and ADC values of rotator cuff muscles (SSP, ISP, TM, SSC, and DT) were measured at the same level, respectively. The average value was taken after 3 repeated measurements at each site.

Fiber bundle imaging: The scanned DTI data were transferred to the GE ADW4.7 workstation. Then the Fiber Track function was loaded, and the rotator cuff muscles in the corresponding oblique sagittal position were outlined. The bundles passing through the rotator cuff muscles respectively were selected for tracking, and finally the layers were removed to obtain a clear fiber bundle image.

Data collecting and monitoring

All participants were evaluated before treatment, 3 weeks after treatment, 6 weeks after treatment and 16 weeks after the end of the intervention at follow-up visits. The Department of Tuina of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine served as the data coordination center for the collection of case report forms (CRFs) and data transfer and analysis. All data were protected in a password-protected computer. Those responsible for data transfer and analysis had access only to the participants' non-personalized information.

Statistical analysis

Statistical analysis was performed using SPSS 20.0, and the mean ± standard deviation ($\bar{x}$ ± s) was used for normally distributed measures. For repeated measured data, repeated measures ANOVA followed by post hoc Bonferroni test. The data were compared between groups using the two independent samples t-test and the Mann-Whitney U rank sum test for non-conformity. Paired t-test was applied to compare the score values of each group before and after treatment. Wilcoxon rank sum test was used for non-conformity. Categorical variables were expressed as frequencies and rates, and qualitative information. Unordered categorical variables were tested by Pearson χ^2 or continuous corrected χ^2 test or Fisher's exact probability method. $P<0.05$ was considered significant.

Results

Since 3 patients failed to follow-up, we finally selected 57 patients with FS, including 25 males and 32 females aged 40-65 (54.04± 6.86), disease course 3-8 (4.95±1.33) months, who attended the outpatient clinic of the Department of Tuina at the Affiliated Hospital of Shandong University of TCM from June 2021 to April 2022. **Table 1** shows the basic profile of the included patients. The baseline data were similar in all aspects between the two groups except for the duration of shoulder symptoms, and the general data were not significantly different ($P>0.05$).

VAS pain score and constant-murley scores

Both groups showed a greater reduction in shoulder pain than before treatment, and similar improvements in shoulder function were achieved in both groups.

Compared to the control group, the trend of pain reduction and shoulder function improvement was more significant in the treatment group at weeks 3 and 6 ($P<0.01$), indicating that the pain reduction effect of the Tuina method group was significantly better than

Table 1. Baseline participant characteristics

Classification	Observation group (n = 29)	Control group (n = 28)	*P* value
Mean age (years)*	53.48±7.08	54.60±6.69	*0.541*
Female (%)	16 (55.1%)	16 (57.2%)	*0.705*
Mean duration of symptoms (month)	53.48±7.08	54.60±6.69	*0.541*
Diabetes (%)	5 (17%)	4 (14%)	*1.000**
Thyroid disease (%)	7 (24%)	6 (21%)	*0.870*

*Mean ± SD (standard deviation). *Indicates the use of Fisher's exact probability method.

Table 2. Comparison of VAS scores and Constant-Murley scores

Study variable	Observation group Mean ± SD	Control group Mean ± SD	*P value*
VAS pain score			
Baseline	7.07±0.65	7.10±0.79	*0.844*
3 weeks of treatment	4.46±0.97	5.67±0.94	*<0.001*
6 weeks of treatment	2.33±0.94	3.77±0.96	*<0.001*
Week 16 after the end of treatment	1.88±0.75	1.96±0.73	*0.709*
Constant-Murley Scores			
Baseline	38.62±5.27	39.82±7.15	*0.470*
3 weeks of treatment	57.2±5.39	47.93±8.0	*<0.001*
6 weeks of treatment	76.93±6.74	63.78±8.36	*<0.001*
Week 16 after the end of treatment	82.93±5.76	79.82±6.26	*0.057*

that of the MF electrotherapy group within 6 weeks of treatment. At the follow-up visit at week 16 after the end of treatment, it was found that although there were differences in VAS scores and CMS scores between the two groups, the differences were not significant (P>0.05) (**Table 2**).

Characteristic MR manifestations of frozen shoulder

The results in **Table 3** show the changes observed on MRI before and after treatment in both groups. Before treatment, about 90% of FS patients had IGHL edema and about 75% had pericapsular edema. After 6 weeks of treatment, these two percentages decreased to about 25% and 18%, respectively (P<0.05 versus pretreatment). After 6 weeks of treatment, sub-deltoid bursa effusion, fluid around the biceps tendon, and coracohumeral ligament edema were relieved or even disappeared. The difference between groups was significant (P<0.01). Comparison between groups showed that both treatments were good at eliminating edema and effusion around the shoulder capsule. However, except for the subdeltoid bursa effusion, the observation group had a significant advantage over the control in eliminating the degree of edema (P<0.05). There was about 70% chance for the obliteration of fat in the subcoracoid triangle to occur, and the difference between the groups was not significant after treatment (P>0.05).

The thickness of the axillary joint capsule in the humeral part of the observation group was reduced before (5.55±1.06) and after (4.77± 0.87) treatment (P<0.01). The thickness of the coracohumeral ligament before and after treatment in the observation group was (3.12±0.78) and (2.49±0.69), respectively. Thickness reduction after treatment was significant (P<0.05). Comparison between groups showed that the observation group was significantly better than the control group in improving the thickness of the joint capsule in the humeral part of the axilla. There were no significant differences in the intra-group and inter-group comparisons of the changes in joint capsule thickness in glenoid, the width and height of the axillary capsule, or the thickness of the rotator cuff gap before and after treatment (P>0.05) (**Table 3**, **Figures 2**-**4**).

MRI before and after FS treatment

Imaging of rotator cuff muscle DTI: We did magnetic resonance special imaging-MR-DTI on the

Table 3. Changes of nuclear magnetic parameters in patients

MRI parameter	Observation group (n = 29)		Control group (n = 26)		*P* value
Quantitative data*	Before treatment	After treatment	Before treatment	After treatment	
IGHL Edema					
Humeral portion	27 (93)	8 (27)	25 (89)	14 (50)	*0.082*
Glenoid portion	26 (89)	7 (24)	26 (92)	13 (46)	*0.078*
Extracapsular edema					
Anterior	24 (82)	5 (21)	21 (75)	12 (42)	*<0.05*
Posterior	16 (55)	4 (14)	15 (51)	9 (32)	*0.133*
subsacral effusion of the deltoid muscle	19 (65)	10 (34)	18 (64)	12 (42)	*0.516*
fluid around the biceps tendon	22 (76)	8 (28)	19 (67)	13 (46)	*0.140*
Coracohumeral ligament edema	19 (65)	6 (20)	21 (75)	11 (39)	*0.125*
Obliteration of fat in the subcoracoid triangle	11 (37)	14 (48)	13 (46)	18 (64)	*0.223*
Qualitative data*	Mean ± SD (mm)				
Joint capsule thickness in humeral portion of the axillary capsule (mm)	5.55±1.06	4.77±0.87	5.54±1.2	5.04±1.09	*<0.05*
Joint capsule thickness in glenoid	5.15±1.25	4.95±1.22	5.12±1.21	4.91±1.13	*0.903*
Width of the axillary capsule	2.34±0.89	2.31±0.83	2.7±1.17	2.44±1.03	*0.601*
Height of the axillary capsule	6.46±2.01	6.53±1.86	6.39±1.94	6.23±1.35	*0.287*
Thickness of the coracohumeral ligament	3.12±0.78	2.49± 0.69	3.06±0.79	2.63±0.69	*0.440*
Rotator cuff gap thickness	8.30±1.52	8.51±1.56	8.27±1.56	8.35±1.42	*0.649*

*Data are number of shoulders with percentage in parentheses or mean ± SD.

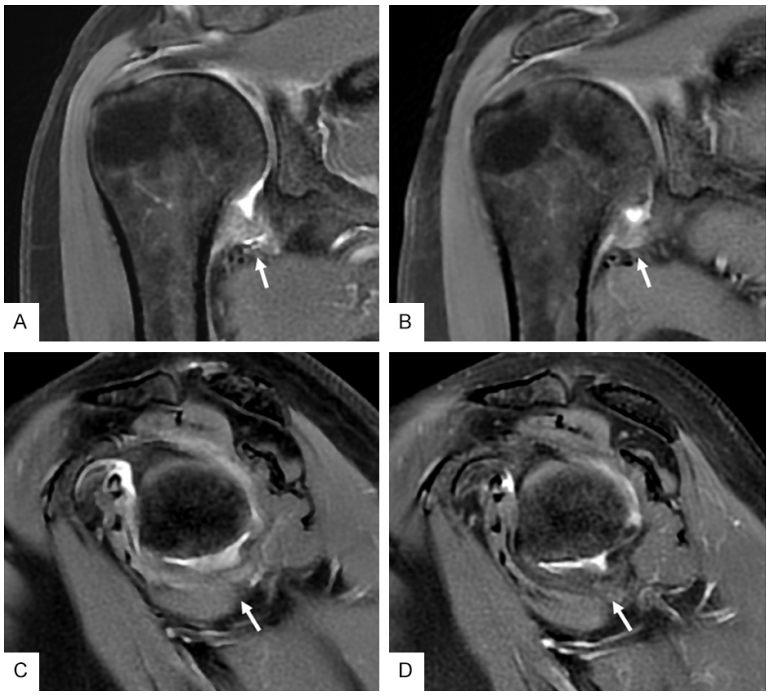

Figure 2. 49-year-old woman with FS, severe pain and limited range of motion for more than 4 months. A. Oblique coronal fat-suppressed T2-weighted MR image shows diffuse joint capsule edema of the axillary humerus with thickening of contracture (arrow). B. After 6 weeks of treatment, the edema and thickness of the axillary joint capsule were reduced (arrow). C. Oblique sagittal fat-suppressed T2-weighted MR image shows obvious axillary joint capsule edema (arrow). D. After 6 weeks of treatment, the edema of the joint capsule of the axillary humerus was better than before (arrow).

affected shoulder before and after treatment in both groups, and the computer workstation constructed FA and ADC maps and measured the corresponding FA and ADC values.

After 6 weeks of treatment, we found that the FA values of rotator cuff muscles (SSP, ISP, TM, SSC) in the observation group were significantly higher than those before treatment (P<0.01). Also, ADC values in the observation group decreased after treatment compared to before treatment, and the differences were especially significant in ISP, and SSC (P<0.01). There was no significant difference in SSP and TM (P>0.05). In the control group, there was a ssignificant difference in FA values after treatment compared to before treatment only in ISP. TM (P<0.01), and ADC values before and after treatment differed significantly only in ISP (P<0.05), while the differences in SSP, TM, and SSC were not significant (P>0.05).

Comparison between groups showed that the observation group could significantly reduce FA

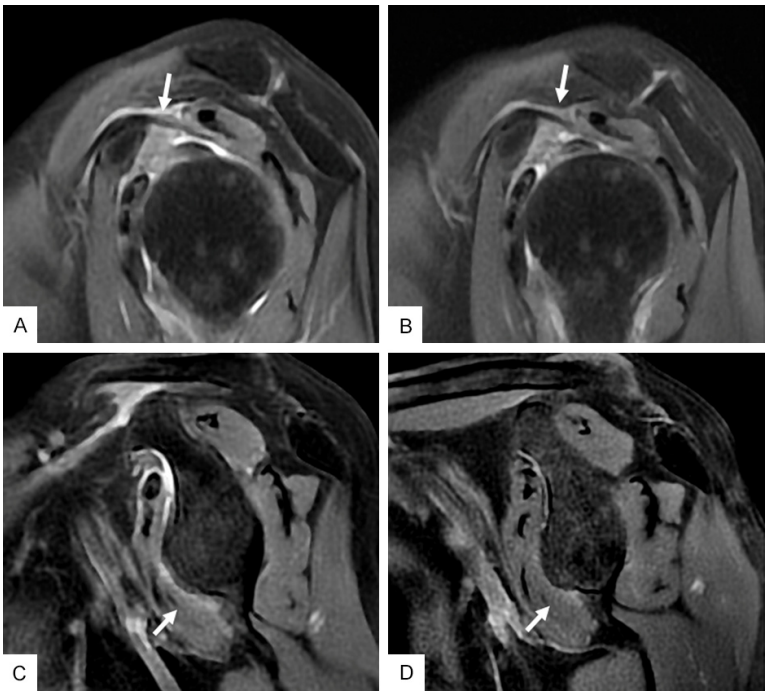

Figure 3. 63-year-old woman with FS, severe pain and limited range of motion for more than 7 months. A. Oblique sagittal fat-suppressed T2-weighted MR image shows edema and thickening (3.8 mm) of the coracohumeral ligament (arrow). B. After 6 weeks of treatment, the edema of the coracohumeral ligament was reduced and the thickness decreased to 2.7 mm (arrow). C. Oblique sagittal fat-suppressed T2-weighted MR image shows marked anterior extracapsular edema (arrow). D. After 6 weeks of treatment, showing disappearance of anterior extracapsular edema (arrow).

values in SSP and SSC compared to the control group ($P<0.05$). The observation group had higher ADC values in ISP compared to controls ($P<0.05$). In other muscles, the differences between the two groups were not significant ($P>0.05$). This indicates that the observation group was significantly more effective than the control group in improving water molecular dispersion in the rotator cuff muscle group ($P<0.05$), as shown in **Table 4**.

DTI imaging before and after treatment

The following is a comparison of the DTI fiber bundle imaging of the rotator cuff muscles before and after the Tuina intervention (the same muscle is the same shoulder before and after the massage), see **Figure 5**.

Discussion

In this study, we evaluated the clinical efficacy of Tuina and MF electrotherapy for FS using VAS scores, Constant-Murley shoulder function scores, and MRI imaging. The results showed that these scores improved after 6 weeks of treatment. Compared to MF electrotherapy, Tuina achieved better results in relieving shoulder pain and restoring shoulder function.

It is believed in modern medicine that reasonable manipulations can promote the local blood circulation, down-regulate some inflammatory cytokines, accelerate the metabolism of inflammatory substances, relieve muscle spasm, and release the adhesion of soft tissues, thus recovering the normal ROM of shoulder joints [7, 14]. Research has proven that the pain can be effectively alleviated by promoting the release of β-endorphin through Tuina [15]. In addition, manipulations can also enhance the liquidity of synovial fluid, increase the nutrition supply to intra-articular cartilages, postpone joint degeneration, potentiate the immune function, dredge channels and collaterals, and activate the immune function qi and blood by facilitating their flow [16]. Compared to oral drugs, Tuina can improve test scores and better recovery of muscle strength after treatment.

This study found that, in the early stages, Tuina provided better relief of intense tearing pain in the affected shoulder compared to MF electrotherapy. Other effects included recovery of nerve function, increased muscle strength and improved shoulder function. We evaluated the influence of Tuina and IF electrotherapy on the recovery of ROM and ADL based on CMS scores and found that the ROM was improved in both groups after treatment, with the observation group showing better recovery effects in ROM than the control group. This indicates that this therapy can restore patients' joint function while improving neurological function. Furthermore, after each operation of Tuina, the instant pain was alleviated, and the ROM was improved. During the treatment with Tuina, stretching the shoulder joints gradually and moderately is the

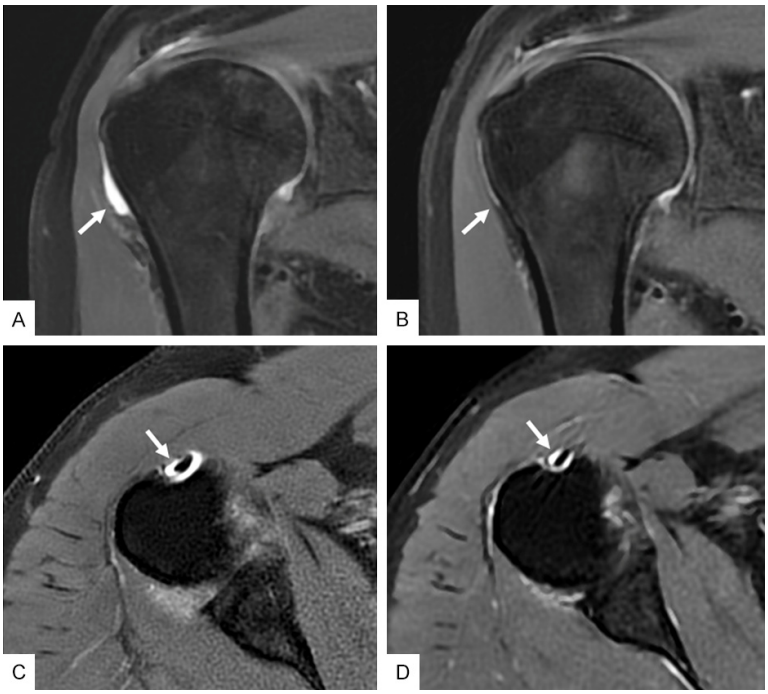

Figure 4. A. Oblique coronal fat suppression T2-weighted MR image showing subsacral effusion of the deltoid muscle (arrow). B. After 6 weeks of treatment, the deltoid subsacral fluid disappeared (arrow). C. Axial fat-suppressed T2-weighted MR image shows fluid in long head biceps tendon sheath (arrow) at humeral neck. D. After 6 weeks of treatment, the volume of fluid in the biceps tendon decreased (arrow).

optimal choice to maximize the ROM, which implies that stretching was an effective manipulation in most cases. However, during the follow-up visit in the 16th week, two groups showed similar ROM and functional scores, indicating the temporary advantages of Tuina.

MRI is an objective method to evaluate the clinical efficacy of FS, including the following manifestations: axillary capsule and CHL thickening, abnormal lesion of soft tissues in the rotator cuff gap, fat obliteration in the subcoracoid triangle, and high signals in IGHL and the outer part of axillary recesses [18, 19]. Sofka [20] found that the thickness of the axillary joint capsule was associated with clinical staging, and that axillary joint capsule edema was usually diagnosed in Stage II. In this study, it was also very common to find the thickening of this edema. FS patients' degree of pain, limited ROM, or contracture of capsule membranes may be caused by the extracapsular edema in shoulder joints [21]. Comparing the MRI of FS before and after treatment, we observed that the IGHL swelling in the affected shoulder, as well as extracapsular and CHL edemas were alleviated after treatment, which were clearly displayed in T2-weighted fat saturation MRI images. Besides, these images also showed that the volume of peri-articular fluids decreased, including subsacral effusion of the deltoid muscle, and fluid around the biceps tendon, which indicated that Tuina could relieve the peri-articular inflammation and edemas around the shoulder joint capsule. As the high signals of scapulohumeral edema were reduced, the articular cavity was less pressed, and the degree of night pain was mitigated [22]. Chellathurai [19] concluded that the thickness of IGHL edema significantly decreased in Stage IV of FS, while there was no obvious difference in the height and width of the axillary capsule, as well as the thickness of axillary glenoid cavity. Furthermore, Sunghoon [13] proposed that the joint capsule thickness of axillary humerus was positively correlated with the degree of pain. This study found that such thickness could be reduced by Tuina, but the treatment had little impact on the thickness of other articular capsules, which was in line with previous evidence. This result also indicates that Tuina can reduce the inflammation of the joint capsule and surrounding tissues, inhibit the proliferation of synovial tissues in the joint capsule, and that Tuina can reduce the fibrosis of the joint capsule, accelerate the transition to the recovery phase of frozen shoulder, and thus shorten the course of FS.

As verified by Ozaki [22], patients with chronic FS suffer from fibrosis and contracture of connective tissues in the rotator cuff gap, including the CHL, with the thickened CHL highlighting the severity of FS [23]. During therapeutic observation, the oblique sagittal CHL thickness was (3.12±0.78) mm in the FS patients in the Tuina treatment group and (2.49±0.69) mm after treatment, indicating that Tuina was able

Table 4. Rotator cuff muscle FA values, ADC values

MRI -DTI data (Mean ± SD)		Observation group (n = 29)			Control group (n = 26)		
		Before treatment	After treatment	*P value*	Before treatment	After treatment	*P value*
FA (0-1)	SSP	0.35±0.05	0.41±0.05	*0.000*	0.35±0.07	0.36±0.07	*0.242*
	ISP	0.34±0.05	0.42±0.09	*0.001*	0.35±0.06	0.43±0.08	*0.009*
	TM	0.34±0.06	0.38±0.05	*0.001*	0.36±0.08	0.40±0.08	*0.02*
	SSC	0.40±0.05	0.49±0.11	*0.000*	0.38±0.08	0.41±0.07	*0.189*
ADC ($\times 10^{-3}$ mm^2/s)	SSP	1.40±0.186	1.376±0.199	*0.552*	1.429±0.164	1.391±0.125	*0.215*
	ISP	1.551±0.20	1.356±0.164	*0.000*	1.553±0.155	1.507±0.156	*0.018*
	TM	1.543±0.153	1.549±0.169	*0.878*	1.505±0.147	1.490±0.142	*0.308*
	SSC	1.628±0.20	1.498±0.163	*0.004*	1.569±0.150	1.473±0.140	*0.33*

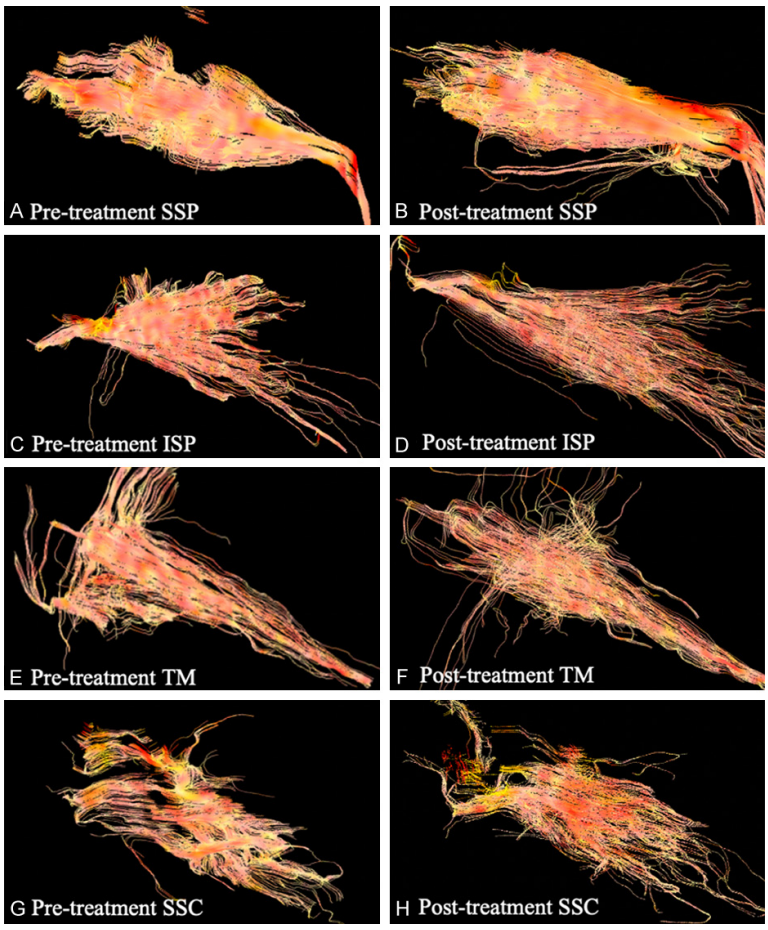

Figure 5. The upper group of pictures shows the DTI fiber bundle imaging of the shoulder muscles of 4 patients before and after treatment. Before the treatment of the shoulder muscles of patients with FS, the muscle fiber bundles were disordered, with poor integrity and compactness, or even shortened; after the treatment, the muscle fibers were full, continuous, and smooth, with good integrity and compactness.

to reduce the rostro-humeral ligament edema and reduce the CHL thickness to some extent. In addition, it was observed that the images showed a reduction in the edema of the CHL, which changed from a blurred state of edema before treatment to a clear state after treatment, which we believe is an important factor contributing to the reduction in the measured CHL thickness. We thought this was because Tuina relieved scapulohumeral edema and inflammation of the articular capsule, thus inhibiting the pathologic process of fibrillar contraction of articular capsule. This study showed that pushing achieved better results in reducing periapical edema and decreasing the thickness of the joint capsule in the humeral portion of the axilla compared to intermediate frequency electrotherapy.

FS can develop into muscular atrophy due to the limited ROM of shoulder joints. Therefore, it is necessary to perform physical therapy to restore the muscle strength and alleviating the pain [24]. In this paper, the MRI-DTI was used to detect the influence of Tuina and IF electrotherapy on rotator cuff muscles. DTI, which is an imaging technique reflecting the fine structure of viable tissues based on the principle of anisotropy for the diffusion of water molecules, can objectively present the changes of microstructures in the skeletal muscle on a micro level,

without causing any trauma [25]. Generally, FS patients will suffer from pain in shoulder joints and limitation of daily activities for several months to years, which significantly reduces the muscle strength of external rotators in shoulders and the cross-sectional area of muscle fibers [26, 27]. These fibers will become shorter due to chronic disuse of muscles and decrease of muscle strength. Under such circumstances, fatty infiltration and fibrosis are intensified [28], which changes the diffusion properties of water molecules around shoulders.

The rotator cuff muscles involved in this study mainly included supraspinatus (SSP), infraspinatus (ISP), teres minor (TM), and subscapularis (SSC). Results showed that the rotator cuff muscular tissues had higher fractional anisotropy (FA) after the treatment with Tuina; and the apparent diffusion coefficient (ADC) was reduced in TM and SSC. Thereinto, the FA value reflected the arrangement and integrity of muscle fibers. The inflammatory infiltration in FS patients' articular capsule and surrounding tissues could cause muscular tension and rigidity and increase the radius of muscle fibers. In the meantime, since patients were reluctant to move their shoulder joints due to pain, the blood could not be adequately perfused to these joints, which inhibited the anisotropic diffusion of water molecules and reduced the FA value. ADC mainly reflected the intracellular diffusion of water molecules [28]. Among FS patients, the aseptic inflammation of scapulohumeral muscles primarily caused muscle swelling around the articular capsule, exerting little impact on other muscles. As we focused on the center of muscle belly, no obvious changes were observed in the value of ADC for rotator cuff muscles. As shown in this study, compared to the IF electrotherapy, Tuina achieved better effects in supplying blood to shoulders, recovering muscle strength, excreting inflammatory mediators, lengthening the shortened or bonded connective tissues, improving muscle compliance, and relieving muscular rigidity.

Both groups of patients achieved functional improvement after 6 weeks of treatment. However, patients who received Tuina treatment recovered shoulder function faster and more effectively and improved ROM and shoulder function by pulling on the joint, similar to previous studies [29, 30]. The Tuina group showed significant pain relief in the early period (from baseline to week three). ROM of the shoulder joint improved significantly in the later period (from week three to week six). The VAS and ROM in the IF-Therapy group recovered from baseline to week six, but the effect presented relatively slowly compared to the observation group. In addition, the discomfort associated with pushing was temporary and tolerable, and no adverse effects were observed during the treatment. Therefore, this study suggests that Tuina is safe, effective, and acceptable in the treatment of FS.

There were some limitations in this study. First, the sample size was small and the follow-up period lasted only 16 weeks. Therefore, the sample size should be increased and the follow-up period extended to further evaluate the treatment effect and safety. Second, in contrast to IF electrotherapy, pushing, although effective, can cause varying degrees of painful irritation during stretching of the shoulder joint, which can easily make patients fearful of the treatment.

Conclusion

Clinical outcome of Tuina in the treatment of FS was superior to that of the IF electrotherapy group. Tuina therapy could provide more rapid pain relief, reduce shoulder capsule edema, restore rotator cuff muscle function, improve shoulder ROM, and shorten the natural course of FS.

Future research directions

We will design more rigorous randomized controlled trials by increasing the sample size, extending the follow-up period, and optimizing the treatment protocol to find out how the analgesic effect achieved by Tuina is related to molecules in specific signaling pathways, and whether Tuina can alleviate fibrosis in the shoulder capsule, so as to explore the mechanism of action of Tuina for FS and develop more efficient therapy.

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The study was approved by the Ethics Committee of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine (ethical approval number: (2021) Lun Audit No. (033) - KY). All patients signed an informed consent form before participating in this study.

Disclosure of conflict of interest

None.

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