Clinical Trial/Experimental Study

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A randomized controlled trial of ultrasound-guided pulsed radiofrequency for patients with frozen shoulder

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Abstract

Background: This study assessed the effectiveness and safety of ultrasound-guided pulsed radiofrequency (UGPRF) for patients with frozen shoulder (FS).

Methods: This study was designed as a randomized, double-blind, sham control trial. A total of 136 patients with FS were recruited and then were equally randomly allocated into a treatment group (n = 68) and a sham group (n = 68). The patients in the treatment group received UGPRF, while the subjects in the sham group underwent sham UGPRF. Patients in both groups were treated for a total of 12 weeks. The primary outcome was the pain intensity, measured by the visual analog scale (VAS). The secondary outcomes consisted of shoulder disorder, measured by the score of shoulder pain and disability index (SPADI); quality of life, assessed by the Short Form-36 questionnaire (SF-36); and any adverse events (AEs) during the treatment period. All outcomes were measured at baseline, at the end of 6-week, and 12-week treatment.

Results: At the end of 6 weeks, and 12 weeks, UGPRF showed more promising outcome results in pain relief, as measured by VAS ($P < .01$), improvement of shoulder disorder, as assessed by SPADI score (pain, $P < .01$; disability, $P < .01$; total, $P < .01$), and enhancement of quality of life, as measured by the SF-36 scale (PCS, $P < .01$; MCS, $P < .01$), compared with sham UGPRF in this study.

Conclusion: The findings of this study showed that UGPRF may benefit for patients with FS after 12 weeks treatment.

Abbreviations: AEs = adverse events, CRF = case report form, FS = frozen shoulder, RCTs = randomized clinical trials, SF-36 = Short Form-36 questionnaire, SPADI = score of shoulder pain and disability index, UGPRF = ultrasound-guided pulsed radiofrequency, VAS = visual analog scale.

Keywords: chronic shoulder pain, effectiveness, frozen shoulder, safety, ultrasound-guided pulsed radiofrequency

1. Introduction

Frozen shoulder (FS) is one of the most common disorders of the joint diseases.[1–3] It mainly manifests with shoulder pain and motion limitation.[4–6] It has been reported that this condition can affect 2% to 5% of the general population, mostly among the female population between 40 and 65 years old.[7–11] A variety of studies tried to explore its mechanism.[12–14] Unfortunately, it is still unclear.[11]

Several approaches have been reported to manage this condition. These managements consist of medication, physical therapy and exercise, location injections, manipulation under anesthesia, arthroscopic capsular release, muscle release, ultrasound therapy, massage, laser therapy, and acupuncture.[15–25] However, their efficacy is still limited.

Although ultrasound-guided pulsed radiofrequency (UGPRF) has also been reported to treat FS,[26] there is still insufficient data to support this therapy. The lacking evidence for UGPRF for the treatment of FS warrants strictly designed randomized clinical trials (RCTs). Therefore, in this RCT study, we hypothesized that for treatment of FS, the effectiveness of UGPRF would be superior to the effectiveness of sham UGPRF.

2. Methods and design

2.1. Ethical approval

The present study was approved by the ethics committee of Yanan University Affiliated Hospital, and The First People's Hospital of Xianyang City. All included patients were asked to provide the written informed consent before the study.

2.2. Study design

This study was designed as a randomized, double-blind, sham-control trial with 2 parallel groups. A total of 136 eligible patients with FS were recruited from Yanan University Affiliated Hospital and The First People's Hospital of Xianyang City by poster or advertise from January 2017 to June 2018. After screening, all included subjects were randomly allocated to a treatment group or a control group in a ratio of 1:1. Before the randomization, there was be a 1 week run-in period. Patients in both groups were

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treated for a total of 12 weeks. All outcomes were assessed at baseline, at the end of 6 weeks and 12 weeks treatment.

2.3. Patients

The inclusion criteria included patients aged between 40 and 70 years with 1 side shoulder attacked; primary idiopathic adhesive capsulitis; experiencing shoulder pain and motion limitation at least 3 months before the study.

Patients were excluded if they did not agree to participate or continue the study; having systematic diseases, bony abnormality, calcific tendonitis, shoulder osteoarthritis, psychological disorder, photoallergy, substantial local trauma history, previous shoulder surgery, local infection, relex sympathetic dystrophy, pregnancy, or breastfeeding; receiving UGPRF, or physiotherapy treatment during the last 3 months before the study; or using anti-pain medication during this study.

2.4. Randomization and blinding

A random number list was generated through SAS 9.1 package (SAS Institute Inc., Cary, NC) by a specified research assistant who was masked to the study allocation. Stratified randomization was performed to randomize and allocate the patients equally to a treatment group and a sham group in a 1:1 ratio by using concealed in sequentially numbered, opaque, sealed envelopes. Attending investigators, subjects, outcome assessors, as well as the data analysts were blinded in this study.

2.5. Intervention

The patients in the treatment group received UGPRF. Under sterile conditions and appropriate monitoring, the subjects were placed in a seated position on a chair. Local skin and soft tissues were anesthetized with 1 mL 2% lidocaine before the needles of radiofrequency inserted. After that, its needles and probes arrived at each target nerves under the guidance by ultrasound. Radiofrequency therapy was applied by using a 10 cm 22-gauge cannula with a 10 mm active. The sensorial stimulation was utilized to check and identify the nerve position with a threshold current intensity of <0.5 mA. The needles of radiofrequency were regarded to be adequately placed by ultrasound guidance; the current intensity was decreased to less than 0.2 mA. Then pulsed radiofrequency therapy was applied by using 2 Hz current at 40 volts with 20 ms active and 480 ms silent periods. The temperature was controlled to less than 42°C.

The patients in the sham group undergo the same procedure. The radiofrequency treatment was simulated without applying pulsed stimulation. Patients in both groups received once weekly for a total of 12 weeks intervention.

2.6. Outcome measurements

The primary outcome of pain intensity was measured by the visual analog scale (VAS).[27] The score ranges from 0, no pain, to 10, worst. The secondary outcomes included shoulder disorder, as measured by the score of shoulder pain and disability index (SPADI), varying from 0 to 100, with score of 0 indicating less shoulder disability and 100 indicating more shoulder dysfunction;[28] and quality of life, as assessed by the Short Form-36 questionnaire (SF-36), each item is scored on a 0 to 100 range, with a higher score indicating better quality of life.[29] All primary and secondary outcomes were measured at baseline, at the end of 6 weeks and 12 weeks treatment.

2.7. Safety evaluation

Any adverse events (AEs) were monitored, recorded, and reported by investigators at each visit. All expected and unexpected AEs were monitored. For any AEs, we documented its date of onset and cease, intensity, and also the association to the intervention. Based on those reports, the physicians decided to continue treating the subjects or not.

2.8. Data management

All data values were collected by a case report form (CRF), which specifically pre-designed by the researchers according to the standard operating procedures of the Yanan University Affiliated Hospital, and The First People's Hospital of Xianyang City. All the data were entered into electronic database of the research computer system. Any paper records were kept in locked cabinets.

2.9. Quality control

Two monitors from the Ethic Committee of Yanan University Affiliated Hospital and The First People's Hospital of Xianyang City monitored all the procedures of the study, including written informed consent, protocol compliance, data collection, CRF, and all other documents filling, as well as the other study-related procedures.

2.10. Statistical analysis

All data were analyzed by SAS 9.1 package using intent-to-treat analysis. The t test or Mann–Whitney U test was utilized to perform the continuous variables. Fisher exact test or χ^2 test was applied to analyze the categorical variables. A value of $P < .05$ was considered statistically significant.

2.11. Sample size

To detect difference between the treatment group and the control group of at least 30% in pain intensity, measured by VAS scale, and with α=0.05, power of 80%, effect value of 0.75, the desired sample size for this RCT is 136 patients, with 68 subjects in each group, including the assumed dropout rates of 15%.[30] It is the minimum required sample size to evaluate the effectiveness UGPRF for patients with FS.

3. Results

A total of 169 potential eligible patients initially entered this study for screen (Fig. 1). After selection, 33 subjects were excluded. Thus, 136 patients were included and were divided equally into the treatment group and sham group in this study. After 6 weeks treatment, no patient in either group withdrew from the study. However, after 12 weeks treatment, 1 subject in the control group withdrew from the study, because he moved to the other city and quitted the treatment.

Baseline characteristics are summarized in Table 1. At baseline, no significant differences in all characteristics values were found between 2 groups. These values included basic characteristics, demographics, and primary and secondary outcome measurement at baseline.

At the end of 6 weeks, and 12 weeks, patients in the treatment group exerted better efficacy in pain relief, as measured by VAS ($P < .01$, Table 2), improvement of shoulder disorder, as assessed by SPADI score (pain, $P < .01$; disability, $P < .01$; total, $P < .01$;

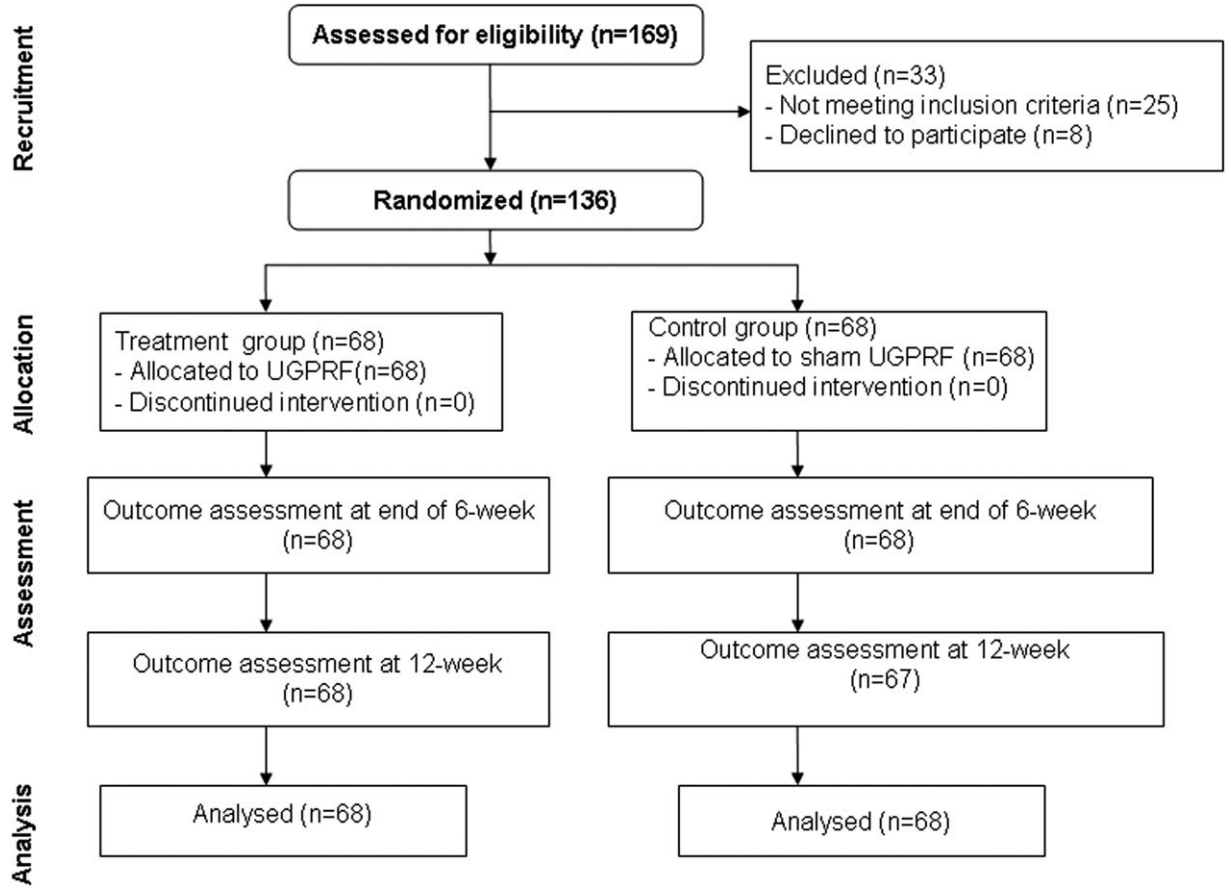

Figure 1. Flowchart of participant selection.

Table 3), and enhancement of quality of life, as measured by the SF-36 scale (PCS, $P < .01$; MCS, $P < .01$; Table 4), compared with patients in the sham group in this study.

Table 1

Patient characteristic at baseline.

Characteristics	Treatment group (n = 68)	Sham group (n = 68)	*P*
Mean age, year	51.4 (12.1)	53.0 (11.7)	.43
Gender			
Male	37 (54.1)	42 (61.8)	.39
Female	31 (45.6)	26 (38.2)	.39
BMI, kg/m^2	27.5 (3.4)	26.8 (3.0)	.20
Location			
Left	36 (52.9)	40 (58.8)	.49
Right	32 (47.1)	28 (41.2)	.49
Duration of disease, month	12.4 (6.7)	11.6 (7.8)	.52
Previous analgesic medication used	24 (35.3)	31 (45.6)	.22
Pain intensity			
VAS	6.2 (1.4)	6.4 (1.1)	.35
Shoulder disorder			
SPADI pain	59.3 (12.8)	62.1 (13.3)	.21
SPADI disability	50.1 (12.1)	51.5 (11.6)	.49
SPADI total	53.4 (12.5)	54.9 (12.7)	.49
Quality of life			
SF-36 PCS	51.9 (15.6)	54.0 (16.2)	.44
SF-36 MCS	55.7 (14.3)	56.6 (15.5)	.72

Data are present as mean ± standard deviation or number (%); BMI = body mass index, VAS = visual analogue scale, SPADI = score of shoulder pain and disability index, SF-36 = Short Form-36 questionnaire, PCS = physical component score, MCS = mental component score.

No severe AEs were recorded in either group in this study. No death related treatment occurred in both groups. However, 2 subjects reported slight pain in the treatment. Fortunately, no patients withdrew from the study because of the AEs.

4. Discussion

This randomized, double-blind, sham-control trial was designed to compare the effectiveness of UGPRF treatment with that of sham UGPRF intervention for patients suffering from FS. Reductions in pain intensity of attacked shoulders and improvement in shoulder mobility and quality of life were assessed to confirm whether the patients with FS were improved or not. Additionally, safety evaluation was also be performed by checking and monitoring any AEs that occurred during the period of the treatment, as well as the follow-up duration.

Currently, no study investigated the effectiveness of UGPRF for the treatment of FS. To our best knowledge, this study first focused on this issue. The results of this RCT may provide very valuable evidence for the potential treatment of FS. We wish to provide a scientific basis for this management according to the results of this study. However, more stringent data are still needed for further evaluating the effectiveness and safety of UGPRF for the treatment of patients with FS in the future studies.

After 12-week treatment, the results of this study showed that UGPRF can not only reduce pain intensity, as measured by VAS, but also can improve the status of shoulder disorder, as evaluated by SPADI score, as well as can enhance the quality of life, as measured by SF-36 scale. Moreover, only minor AEs of slight

Table 2

Comparison of pain intensity (change from baseline).

Pain intensity	6-week treatment				12-week treatment			
	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*
VAS	−3.1 (−4.2, −1.9)	−1.3 (−1.8, −0.7)	−1.8 (−2.7, −1.1)	<.01	−4.6 (−6.9, −2.7)	−1.7 (−3.0, −0.9)	−3.0 (−4.4, −2.0)	<.01

Data are present as mean (range), VAS = visual analogue scale.

Table 3

Comparison of shoulder disorder (change from baseline).

SPADI	6-week treatment				12-week treatment			
	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*
Pain	−30.5 (−43.7, −21.2)	−9.1 (−16.6, −4.7)	−21.4 (−39.6, −12.9)	<.01	−41.8 (−55.9, −28.6)	−14.1 (−23.4, −8.8)	−27.7 (−36.1, −19.2)	<.01
Disability	−26.4 (−35.1, −17.7)	−7.5 (−13.3, −4.2)	−18.9 (−26.5, −13.6)	<.01	−34.2 (−43.6, −22.9)	−11.5 (−19.9, −5.0)	−22.8 (−28.3, −15.4)	<.01
Total	−27.9 (−37.2, −16.4)	−8.2 (−14.5, −4.0)	−19.6 (−25.8, −14.1)	<.01	−36.6 (−46.9, −23.7)	−12.8 (−21.3, −6.7)	−24.0 (−30.9, −15.6)	<.01

Data are present as mean (range), SPADI = score of shoulder pain and disability index.

Table 4

Comparison of quality of life (change from baseline).

SF-36	6-week treatment				12-week treatment			
	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*	Treatment group (n = 68)	Sham group (n = 68)	Differences	*P*
PCS	20.3 (12.5, 31.6)	6.1 (2.9, 9.4)	14.2 (6.5, 21.7)	<.01	29.8 (18.6, 40.5)	9.5 (4.4, 15.6)	20.4 (13.9, 26.2)	<.01
MES	15.9 (8.8, 22.4)	5.5 (2.7, 7.8)	10.5 (7.1, 14.6)	<.01	21.6 (13.7, 30.1)	7.0 (4.1, 10.5)	14.7 (9.9, 18.3)	<.01

Data are present as mean (range), SF-36 = Short Form-36 questionnaire, PCS = physical component score, MCS = mental component score.

pain were recorded in this study. It results indicated that UGPRF may be utilized as an alternative intervention for FS treatment.

This study had 2 limitations. First, this study did not include follow-up assessment after the treatment quit. Thus, further studies should extend the outcome evaluation period with follow-up visit after the treatment. Second, since this study is the first study to explore the effectiveness of UGPRF for FS, therefore, more studies should be focused on this issue to further warrant the results of this study.

5. Conclusion

The results of this study demonstrated that UGPRF is more effective for patients with FS than sham UGPRF after 12 weeks treatment.

Author contributions

Conceptualization: Juan Yan, Xian-Min Zhang.
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Investigation: Xian-Min Zhang.
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Visualization: Juan Yan, Xian-Min Zhang.
Writing – original draft: Juan Yan, Xian-Min Zhang.
Writing – review & editing: Juan Yan, Xian-Min Zhang.

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