

Instant analgesic effect of radial extracorporeal shock wave therapy on primary dysmenorrhoea according to functional magnetic resonance imaging: Study protocol for a randomised placebo-controlled trial

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Study protocol

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Abstract

Background: Primary dysmenorrhoea (PDM) is defined as a series of pain-dominated symptoms during and after menstruation without organic lesions. Non-steroidal anti-inflammatory drugs and oral contraceptives are usually recommended as first-line drugs for the clinical treatment of PDM, but their widespread long-term application is controversial. Radial extracorporeal shock wave therapy (rESWT) has been widely applied in musculoskeletal rehabilitation because of its secure and non-invasive characteristics and its confirmed effect in improving pain symptoms. This research seeks to explore the efficacy of rESWT for PDM and the changes in brain function of patients with PDM. Methods: This clinical research will be a randomised, evaluated blind and sham-controlled trial. Forty-six patients with PDM will be divided into the rESWT group (n = 23) and the sham rESWT group (n = 23) at random. In the rESWT group, treatment will be applied once within 48 hours of menstruation at six abdominal myofascial trigger points. The sham rESWT group will receive sham shockwave therapy on the same sites but without energy input. Other dysmenorrhoea-related treatments in both groups will be limited. The main indicators include the short-form McGill Pain Questionnaire and the Cox Menstrual Symptom Scale. The secondary indicators include the Zung Self-rating Anxiety Scale and Self-rating Depression Scale and functional magnetic resonance imaging (fMRI) changes in brain regions. Results will be evaluated at the screening, baseline and before and after treatment, and adverse treatments will be examined. Inter- and intra-group analyses will be performed in the statistics section. Discussion: This randomised controlled study is designed to explore the immediate efficacy of rESWT for PDM. After rESWT treatment, PDM symptom tests, pain tests as well as fMRI data will be investigated for the potential connections between immediate neuroanalgesic mechanisms, which are associated with pain and brain networks. The main results will be used to assess the efficacy of rESWT, and secondary results will focus on improving the neurobiological understanding of disease treatment.

Background

Primary dysmenorrhoea (PDM) involves premenstrual or menstrual pain in the lower abdomen without pelvic organic lesions and may spread to the waist and inner thigh. PDM is also characterised by a series of symptoms, such as headache, fatigue and irritability. Although most common in pregnant women, PDM affects more than 55% of young women worldwide, often with pain so severe that it has restricted their work and daily activities[1], thus causing considerable personal and socio-economic burden[2].

Despite the importance of PDM management, clinical treatment is inadequate. According to the Primary Dysmenorrhea Consensus Guideline, non-steroidal anti-inflammatory drugs or combined hormonal contraceptives are recommended as first-line treatment for most women with PDM[3]. Non-steroidal anti-inflammatory drugs hinder the production of peripheral prostaglandins by inhibiting cyclooxygenase, thereby producing analgesic effects[4]. Combined hormonal contraceptives relieve pain by inhibiting ovulation and the growth of endometrial tissue and reducing blood flow and prostaglandins, thus decreasing stress and contractions in the uterus. The analgesic effect of such contraceptives is definite, but long-term use can cause gastrointestinal damage or abnormal hormone secretion. As an alternative

treatment, physical factor therapies, such as high-frequency electrical stimulation, ultra-short wave and hot compress[3] have weak practical application because of their obvious side effects, expensive treatment or long treatment cycle and unsatisfactory treatment outcomes.

Radial extracorporeal shock wave therapy (rESWT) involves a kind of mechanical wave that can convert mechanical signals into the target area in vitro in biochemical or molecular signals and induce changes in cell characteristics. Finally, a descending pain suppression system that plays a role in analgesia has been accepted all over the world for the extensive treatment of musculoskeletal pain, especially for intractable pain such as chronic peri-arthritis of the shoulder and stubborn plantar fasciitis[5][6]. Clinical studies have shown that the acute to chronic transformation of musculoskeletal diseases will lead to a series of peripheral nervous system lesions and even structural changes of the central nervous system, accompanied by different degrees of myofascial trigger point symptoms, such as spontaneous pain and dysmenorrhoea. Moreover, the selection of clinical treatment sites is primarily related to the location of the myofascial trigger point. The clinical study of Huang[7][8] shows that the pain and related symptoms of PDM can be effectively alleviated in patients with the trigger point of abdominal myofascial pain and who receive local dry and wet acupuncture treatment at the trigger point. Li[9] and Xing[10] confirmed that rESWT can effectively alleviate the symptoms of chronic dysmenorrhoea. In the future, rESWT may be another treatment to complement ibuprofen. However, few studies have been conducted on the immediate analgesic effect of rESWT, and evidence of its central analgesic effect is insufficient.

Tu Cheng-hao et al.[11][12][13] proved that the generation of PDM is related to the abnormal changes in metabolism in brain regions which are [related to](#) various aspects of pain management. The major manifestations include increased glucose metabolism in the thalamus, orbitofrontal area and prefrontal area. Conversely, lowered metabolism occurs in the lateral somatosensory motor area. Some imaging studies have confirmed that patients with moderate and severe PDM have structural and functional consistency changes in multiple pain-related brain regions after acupuncture or moxibustion[14][15][16]. Imaging evidence of functional changes in PDM brain areas is limited by the fact that different interventions have dissimilar effects on brain areas. A recent study[10] showed that rESWT can effectively balance the concentration of blood prostaglandin in women with dysmenorrhoea after the treatment of one menstrual cycle by trigger point shockwave and relieve dysmenorrhoea symptoms. Furthermore, no adverse events (AEs) occurred during the follow-up after six months.

Therefore, the rESWT will be used for treatment in the hope of obtaining imaging evidence of analgesia, especially immediate analgesia. In this trial, we will focus on assessing the therapeutic effect of rESWT treatment and sham rESWT treatment. For an in-depth understanding on the mechanism in terms of central analgesia of pain relief by rESWT, the changes in pain state, emotional state and local brain functional areas will be assessed before and after the therapy.

Methods

Objectives

1. To evaluate the efficacy of rESWT in the treatment of PDM compared with the placebo group.
2. To explore the central mechanism of rESWT in the treatment of PDM according to the results of resting functional magnetic resonance imaging (fMRI).

Design

This research will be a randomised, assessor and statistician-blinded and placebo-controlled trial. A total of 46 subjects with PDM who meet the guidelines of the Canadian Society of Obstetricians and Gynecologists for the diagnosis of PDM will be recruited and randomly assigned to a shockwave group or a sham shockwave group at a 1:1 ratio. Table 1 lists the recruitment process, intervention methods and evaluation, and Figure 1 depicts the experimental flow chart. The Standard Protocol Items: Recommendations for Interventional Trials 2013 Checklist is attached as Additional file 1. This study has been conducted since January 2019 at Zhongshan-Xuhui Hospital, Fudan University, Shanghai, China.

Experimental ethics

The ethics-related aspects of this research were approved by the Institutional Review Board of the Institute of Clinical Trials. The experiment was reviewed and approved by the Ethical Committee of Zhongshan-Xuhui Hospital in January 2019 (Approval No. 2018043). It was likewise registered in the Chinese Clinical Trial Registry in January 2019 (Registration No. ChiCTR1900020678). This research conforms to the Helsinki Declaration.

Demographics data, questionnaire results, magnetic resonance imaging (MRI) results and signed consent forms will be gathered. All electronic data will be stored in encrypted computers and paper data will be locked in cabinets.

Any modification of the protocol will be documented at www.chictr.org.cn. The research team will disseminate the results of this study by publishing them in peer-reviewed journals.

Participants

Recruitment

Subjects will be recruited from the Shanghai University of Sport, East China Normal University and the Shanghai University of Medicine and Health Sciences through recruitment posters.

Inclusion criteria

The inclusion criteria are as follows:

- (1) diagnosed as having PDM according to the Primary Dysmenorrhea Guidelines[3];
- (2) 18–30 years old without history of delivery[21];
- (3) regular menstrual cycle of 27–32 days;
- (4) menstrual pain for over six months;
- (5) in the past six months, the average pain level of menstruation with conventional treatment was at least four points on a verbal numerical scale (0 = no pain at all, 10 = the most serious pain)[11][16];
- (6) no oral contraceptives or drugs that act on the central nervous system drugs within six months before treatment;
- (7) right-handed;
- (8) no previous extracorporeal rESWT therapy; and
- (9) volunteers to participate in the experiment and sign the informed consent form.

Exclusion criteria

The exclusion criteria are as follows:

- (1) organic changes in the pelvic cavity;
- (2) with mental or neurological disorder and taking drugs that act on the central nervous system;
- (3) irregular menstrual cycle;
- (4) history of childbirth;
- (5) early pregnancy or immediate plans for pregnancy[16];
- (6) allergic to the coupling agent;
- (7) with histological changes in the skin or muscle of the treatment site;
- (8) severe mental illness;
- (9) serious diseases, such as those of the heart, brain, liver, kidney and haematopoietic system; and
- (10) contraindications to MRI (claustrophobia, pacemaker implants or surgical metal plate in the body).

Termination criteria

The criteria for termination for subjects with PDM are as follows:

- (1) subjects taking other forms of pain relief, such as extra pain relievers, during the rESWT treatment of this trial;
- (2) severe AEs (SAEs);
- (3) surgery or hospitalisation for an accident or other diseases; and
- (5) participant request.

A reminder will be sent the day before the appointment to ensure participant retention and adherence.

Randomisation, concealment of allocation and blinding

Participants who meet the inclusion criteria will sign the informed consent form voluntarily and will be eligible for randomisation. They will be assigned randomly to the rESWT group or sham rESWT group. The random sequence will be generated by a statistician using IBM® SPSS® Statistics version 22.0 (IBM Institute, Inc., USA) and who is not involved in the intervention or outcome evaluation.

The random number and group assignment will be sent immediately to the independent assessor by another research coordinator via an encrypted electronic file. As much as possible, evaluators will be prevented from communicating with the patients to avoid bias. This process will ensure that randomisation concealment will be competent and will be unaffected by the participants or practitioners.

To decrease the risk bias from the assigned treatment group, participants and assessors will be blinded to the treatment allocation. Prior to signing the informed consent form, subjects will be told that they will be assigned to two different groups and receive different shockwave treatments. However, practitioners will not be blinded. Before the trial begins, all researchers will be trained to ensure the successful implementation of the blinding method. An independent investigator who does not participate in the assignment and treatment process will assess the subject's blinding validity.

Interventions

The time of interventions will be within the first 48 hours of the menstrual period. Trained and qualified practitioners from the Ministry of Health of the People's Republic of China will perform real and sham rESWT therapy on the participants. Before the intervention, the myofascial trigger points in the abdominal muscles will be clinically located by the clinician, and ultrasound coupling gel will be applied on the lower

abdominal skin surface (Figure 2). In the real rESWT group, 5000 impulses of radial shock waves with a pressure of 1.5 bar and a rate of 15 impulses per second will be applied using the radial shock wave device on each participant (STORZ MEDICAL AG, MASTERPULS® MP100, C15, Ø 15 mm, Switzerland) (Figure 3)[9][10]. Patients in the sham control group will receive placebo intervention just with the same sound but no energy input[17]. Moreover, any other treatment to improve menstrual pain will be restricted in both real and sham rESWT group during the trial.

MRI scanning procedure

The Siemens 3.0T Magnetom Verio MRI system (Siemens Medical, Erlangen, Germany) with 32-channel head coil will be used to obtain MRI data of pain relief after rESWT treatment at the Department of Radiology, Zhongshan-Xuhui Hospital, Fudan University, Shanghai, China. To avoid head movement, foam pads will be used to fixed the participants' heads. The fMRI data will be acquired with a single-shot gradient recalled echo planar imaging sequence in the following parameters: repetition time (TR)/echo time (TE) = 2530 ms/2.98 ms, flip angle = 7, field of view (FOV) = 256 mm × 256 mm and slice thickness = 1 mm. To obtain the resting fMRI data, a whole-brain blood oxygenation level-dependent (BOLD) pulse sequence (TR/TE = 2000/30 ms, flip angle = 90, FOV = 192 mm × 192 mm, voxel size = 3.0 × 3.0 × 5.0 mm, slice thickness = 1 mm and 28 slices) will be used.

Outcome measurement

Primary outcome

Short-form McGill Pain Questionnaire (SF-MPQ)

The primary outcome will be the change in the SF-MPQ score (Table 1). SF-MPQ is a scale composed of the pain rating index (PRI), visual analogue scale and existing pain intensity to measure pain intensity. The PRI consists of 11 sensory and 4 emotional pain descriptors, all of which are rated from 0 to 3 points to indicate the different degrees of no, mild, medium or severe pain, respectively. This index is a sensitive and reliable pain evaluation method widely used in the assessment of dysmenorrhoea.

Cox Menstrual Symptom Scale (CMSS)

The menstrual pain symptoms of participants will be integrally evaluated by the CMSS, which consists of 18 items or symptoms, including cramps, nausea, vomiting, loss of appetite, headaches, backaches, leg aches, dizziness, weakness, diarrhoea, facial blemishes, abdominal pain, flushing, sleeplessness, general aching, depression, irritability and nervousness[18]. The table is mainly used to evaluate the severity and

duration of menstrual pain symptoms. All items use a five-level scoring method ranging from 0 to 4 points. The choices for pain severity include painless, mild pain, moderate pain, severe pain and very serious pain. Patients can evaluate the duration of their pain from among 0 hours, less than 3 hours, 3–7 hours, 7–24 hours and more than 24 hours. The CMSS will be used before and after rESWT treatment.

Secondary outcomes

Zung Self-rating Anxiety Scale (SAS)

The SAS will be used to measure anxiety-related symptoms in PDM because dysmenorrhoea is often accompanied by emotional change. It is a self-administered questionnaire, with each response using a four-point scale from 0 (none of the time) to 4 (most of the time). A total score above 40 indicates a clinically relevant anxiety disorder[19]. The SAS will be utilised before and after rESWT treatment (Table 1).

Self-rating Depression Scale (SDS)

The SDS is a scale used to evaluate participants' changes in terms of depression[19]. In this trial, participants will fill out 20 items based on their actual experience over the past week. The total score for this scale ranges from 20 to 80, with a score above 40 indicating depressive symptoms. This scale will be employed before and after rESWT treatment (Table 1).

Sample size calculation

The smallest significant differences in clinical treatment are considered to assess the effects of different treatments. The effect size will be set as 0.25 according to the literature review and preliminary experimental results. Sample size calculation showed that 38 patients are required in two groups, with two tests, 85% statistical power and 5% significance level[9]. As the minimum number of patients in each group is 20 and the estimated drop-out rate is 15%, the necessary sample size after comprehensive consideration is 46 patients (23 patients in each group).

MRI data analysis

The fMRI data processing assistant based on statistical parameter mapping will be used to preprocess the original MRI data (DPARF, Yan and Zang 2010, <http://rfmri.org/DPARF>) on MATLAB R2015b. After complete preprocessing, data processing and analysis of brain imaging of the amplitude of low-frequency fluctuation (ALFF) will be processed by the resting-state fMRI data analysis toolkit.[20]

Afterwards, a comparison, correction and acquisition of the image will be executed via the Rest Slice Viewer software, and the final result will be presented in combination with the specific anatomical position of the corresponding area of MNI coordinates.

Statistical analysis

Clinical and MRI outcomes will be obtained in this study. Among these outcomes, results from participants in both MRI scans and two clinical evaluations will be included in the results analysis; otherwise they will be considered data from drop-outs. Note that all participants will receive our instructions before participating.

Statistical analysis of the clinical outcomes will be accomplished using the SPSS 22.0 statistical software. All tests will be bilateral, and $p < 0.05$ will be statistically significant.

Demographic characteristics and baseline information for all participants will be analysed statistically. For continuous data, independent sample t test or Wilcoxon rank sum test will be applied for analysis and represented as \pm . If dichotomous data occur, we will use the chi-square test or the Friedman test and represent the outcome in percentiles.

For post-test results, the paired t test or Wilcoxon signed rank test will be employed for continuous data within the group. Conversely, the chi-square test or Fisher's exact test will be applied for two-part data to compare the differences before and after treatment. For different intervention methods, independent sample T test will be conducted to identify whether the intervention methods have differences in the relief of PDM.

The statistical comparison of MRI data will be conducted in different ways. With the use of the 3.0T Siemens Magnetom Verio MRI system, each subject will produce two resting state scans. The Data Processing Assistant for r-fMRI (DPARSF 4.4) software package will be used to process MRI Data on the MATLAB 2015b platform and obtain the ALFF values. The mean value of the amplitude of all frequency points within 0.01–0.08 Hz will be calculated. That is, the intensity of the BOLD signal changes will be calculated to obtain the brain map of the statistical parameter of amplitude, which will be used to describe the spontaneous activity of the voxel[21]. SPM12 software will be employed to perform two-sample t test on the two groups of statistical brain maps. The final results will be superimposed on standard avg152 T1 images for display. Finally, the statistical difference of low-frequency amplitudes in the resting state between the two groups will be obtained, and $p < 0.05$ will indicate a significant statistical difference.

Security

AEs will be recorded during each operation. The following conditions are defined as SAEs: (1) aggravated illness requiring hospitalisation, (2) disability and (3) other major medical events. In the event of SAEs, the lead investigator should report to the sponsor within 24 days, and the investigator will intervene as a third party to evaluate whether the AEs are connected to the intervention. If necessary, the appropriate medical services should be provided when the victim asks for compensation. Participants will be withdrawn if the AEs are too severe for them to continue with the trial. However, participants need not withdraw if the AE is unrelated to the intervention or is not a SAE, with respect to the individual wishes of the participants.

Given the safety of rESWT, no safe end point will be predefined because this is considered impossible. However, all AEs will be documented as evidence for safety assessment. Meanwhile, a meaningful number of adverse reactions will be observed.

Management of study data

In this trial, data managers will use the double-entry method to input data into the Microsoft Excel 2016 software and establish an electronic database. They will also use password protection. The Clinical Research Center of Xuhui District Central Hospital in Shanghai will conduct regular monitoring tests to ensure the integrity and authenticity of all data. Interim data analysis should not be undertaken for any reason at any time. To ensure the confidentiality of the participants, all patients will be pseudonymous using study identification numbers. Moreover, all researchers will have access to the final database.

Quality control and monitoring

This study aims to explore the efficacy and mechanism of rESWT for PDM. The data monitoring board is considered a non-essential safety consideration at this time, and similar studies often apply the same approach. Owing to the heavy variety of data tasks, inspectors must monitor the data. According to the actual situation, they will conduct evaluation of the source documents, including medical document charts, related reports and AE records, as well as additional documents, such as agreements, informed consent forms and pathological report forms, all of which will also be under unified management.

Discussion

Current first-line guidelines for treating PDM advised the use of non-steroidal anti-inflammatory drugs or oral contraceptives. However, long-term side effects limit the availability of treatments[3]. Complementary and alternative therapies include exercise, acupuncture and percutaneous electrical nerve stimulation. In recent years, acupuncture has been used to treat dysmenorrhoea, and studies have found that it can improve symptoms in women with dysmenorrhea and is more effective than traditional Chinese medicine or placebo. Other researchers found no advantage in acupuncture when compared with a placebo[3][22]. A retrospective analysis confirmed the efficacy of high-frequency percutaneous nerve electrical

stimulation for dysmenorrhoea. However, high-frequency electrical stimulation may cause local muscle tension and generate adverse reactions, such as headache, nausea, skin flushing or burning sensation[3]. Such stimulation is limited in practical application owing to its obvious side effects, expensive treatment or long treatment cycle, unsatisfactory treatment outcome and other reasons. Therefore, safer and more effective non-drug analgesic schemes must be explored to control PDM.

As far as we know, this work will be the first randomised clinical trial to evaluate the effects of rESWT on pain relief, mental health and changes in brain function in patients with PDM. Few previous studies have used rESWT as treatment for PDM and even fewer have investigated the brain function of PDM patients from the perspective of imaging.

This study aims to explore the differences in pain intensity, anxiety, depression mood and functional brain networks in patients with PDM after rESWT treatment. To accurately elucidate the effect of rESWT, we will compare the changes of MRI indexes in the rESWT and sham rESWT groups and test whether the changed pain condition is related to the changes of the brain function after rESWT treatment. Although some studies have examined the brain function in patients with PDM nervous disorders and abnormal change, they only explored the disease itself and did not examine the intervention, an approach which does not conform to the reality[21][23][24]. To our knowledge, our research will be the first to use an MRI to reflect the divergence of the efficacy of rESWT treatment for PDM and the related neural mechanisms through a random controlled trial. Existing research[24] shows that the function of the midbrain activity is closely related to the RSS (Cox pain symptom scores) ($r = 0.489$), the medial prefrontal cortex activity and RSS (pain symptom scores) showed negative correlation ($r = -0.580$), the medial prefrontal cortex aims to reduce the activity of the brain's pain regulating system. Thus, the Cox Dysmenorrhea Symptom Score is chosen as the main outcome measure for this study. This scale is usually employed to evaluate dysmenorrhoea symptoms and detect the severity of dysmenorrhoea.

The limitation of this trial is supposed to be flagged. Recall that during this study, the sham divergent extracorporeal shock wave group will function as the control group. As no research is available on reliable treatment for sham shock wave, the principle of controlling no energy output from previous clinical studies is applied. However, limitations occur with any type of sham shock wave. Firstly, this is not a double-blind trial because people who are conducting the treatment cannot blindly assign treatment without knowing the type of treatment. To minimise the risk of bias, participants and evaluators will be carefully identified as shock-wave types and trained in advance to apply a fake shock wave with the machine vibrating open and pushing into the handle with almost no energy. Secondly, shock wave often shows a large nonspecific effect and produces physiological activity, and cannot be ignored during the experiment. Nonetheless, the neural mechanisms between different groups can be compared. Therefore, by using the MRI results, we can recognise rESWT-specific pathways related to pain amelioration, even if their effects are not significantly different. Thirdly, a healthy group should not be used as a control group. Previous literature has shown differences in the brain networks of patients with PDM and healthy participants[25][26]. Conversely, our study will focus on the functional brain changes that will be confirmed by extracorporeal shock wave rather than the PDM-specific features against healthy controls.

Therefore, the comparison of the changes in brain networks between the rESWT and sham rESWT groups will be emphasised. Thus far, the RCT has only been exploratory, but the prospects look promising. In the future, we expect to collect extensive samples with higher-quality RCT.

Trial status

The study was registered with the Chinese Clinical Trial Register (Registration No. Chi CTR1900020678) registered on 13 January 2019. Participants were recruited on 31 January 2019. At the time of submission, seven patients have been selected into our Centre (which is participating in the implementation agreement of the convention in the hospital). Recruitment is expected to be completed around December 2019.

Abbreviations

rESWT: radial extracorporeal shock wave therapy

PDM: primary dysmenorrhoea

fMRI: functional magnetic resonance Imaging

SF-MPQ: short-form McGill Pain Questionnaire

CMSS: Cox Menstrual Symptom Scale

SAS: Zung Self-rating Anxiety Scale

SDS: Self-rating Depression Scale

ALFF: Amplitude of low-frequency fluctuation

Declaration

Acknowledgements

Not applicable.

Authors' contributions

YJ, LSS and WLZ contributed to the conception and design of the protocol. All three were involved in drafting and revising the manuscript. LSS and YJ approved the final version. All authors have read and approved the final manuscript.

Funding

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The research will be carried out in accordance with the ethical principles of the Helsinki Declaration concerning human research. The study protocol will include written informed consent of all subjects and the approval of the Ethical Committee of Zhongshan-Xuhui Hospital in January 2019 (Approval No. 2018043).

For publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Additional files

Additional file 1: Figure 1. Flow chart of the trial. Functional magnetic resonance imaging (PDF 188 kb)

Additional file 2: Table 1. Study design schedule (PDF 121 kb)

Additional file 3: Figure 2. Case study procedure (PDF 46.9 kb)

Additional file 4: Figure 3. Description of the shockwave instrument (PDF 81.1kb)

Additional file 5: Figure 4. Treatment site of the abdominal muscle fascia trigger point. (PDF 67.1 kb)

Additional file 6: Table 2. Details of the rESWT intervention. (PDF 72.7 kb)

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Tables

Table 1. Study design schedule

| Period | Screening | MRI scan | Treatment | MRI scan | Close-out |
|------------------------------------|-----------|----------|-----------|----------|-----------|
| Menstrual cycle | 0 month | 1 month | 1 month | 1 month | 1 month |
| Inclusion and exclusion criteria | √ | | | | |
| Informed consent | √ | | | | |
| Physical examination | √ | | | | |
| Medical history | √ | | | | |
| Comorbidities | √ | | | | |
| Pelvic MRI | √ | | | | |
| Allocation | | | √ | | |
| SF-MPQ | | √ | | √ | |
| CMSS | | √ | | √ | |
| SAS and SDS | | √ | | √ | |
| Patient compliance | | | | | √ |
| Reasons for dropout or withdrawals | | | | | √ |
| Adverse events | | | | | √ |
| Safety evaluation | | | | | √ |

SF-MPQ Short-form McGill Pain Questionnaire, *CMSS* COX Menstrual Symptom Scale, *SAS* Zung Self-rating Anxiety Scale, *SDS* Self-rating Depression Scale

Table 2. Details of rESWT intervention

| Item | Detail | Description |
|-------------------------------|---|---|
| rESWT rationale | (1a) Type of shock wave | Pneumatic ballistic extracorporeal shock wave therapy |
| | (1b) Reasoning for treatment | The best treatment option was selected according to our previous study results and other clinical trials of rESWT for PDM |
| | Extent to which treatment varies | None |
| Details of needling | (2a) Number of treatment sites per subject | 9 |
| | (2b) Names of points used | Attachment point of rectus abdominis above the symphysis pubis (bilateral) (blue dot in Fig. 4) |
| | | Intersection of the anterior superior iliac spine with the outer margin of the rectus abdominis (bilateral) *yellow dot in Figure 4 |
| | | The anterior superior iliac spine shifts inward by approximately 2 cm along the line (bilateral) (location of the red dot in Figure 4) |
| | (2c) Shock wave intensity | 1.5–2.0 bar |
| | (2d) Shock wave frequency | 10–14 Hz |
| | (2e) Number of hits from each site | 600 times |
| (2f) Response sought | None | |
| Treatment regimen | (3a) Number of treatment sessions | 1 time |
| | (3b) Treatment time | Within 24 hours of menstruating |
| Other components of treatment | (4a) Details of other interventions administered to the rESWT group | None |
| | (4b) Setting and context of the treatment | Hospital rehabilitation section: outpatient department |
| Background of practitioner | (5) Profile of the therapist | Specialist in rehabilitation medicine or a resident of more than one year under the guidance of the specialist in rehabilitation medicine |
| Control or comparator | (6) Rationale for the control or comparator in the context of the research question | As a placebo control, a non-energetic sham rESWT was used |

Figures

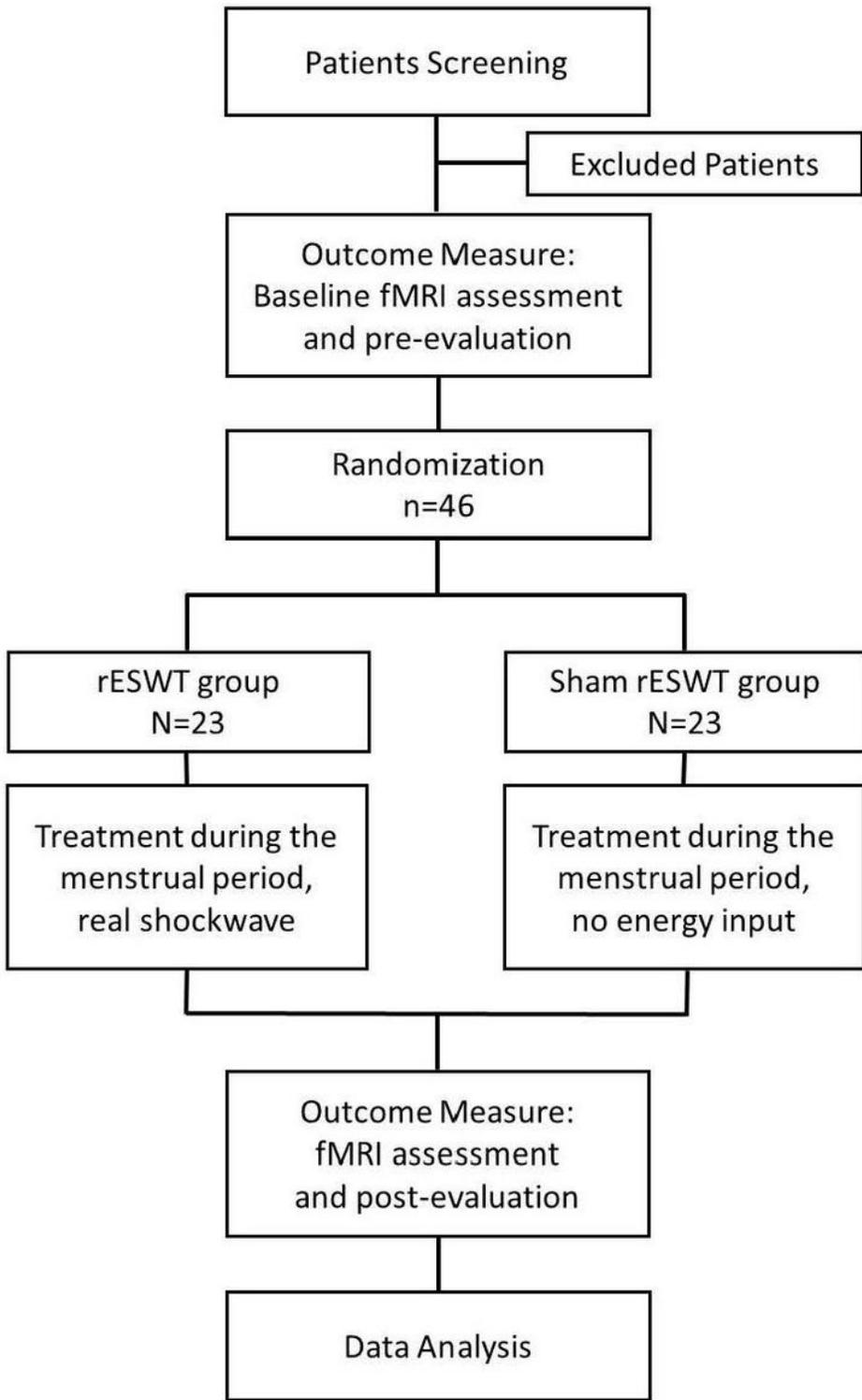


Figure 1

Flow chart of the trial. fMRI functional magnetic resonance imaging

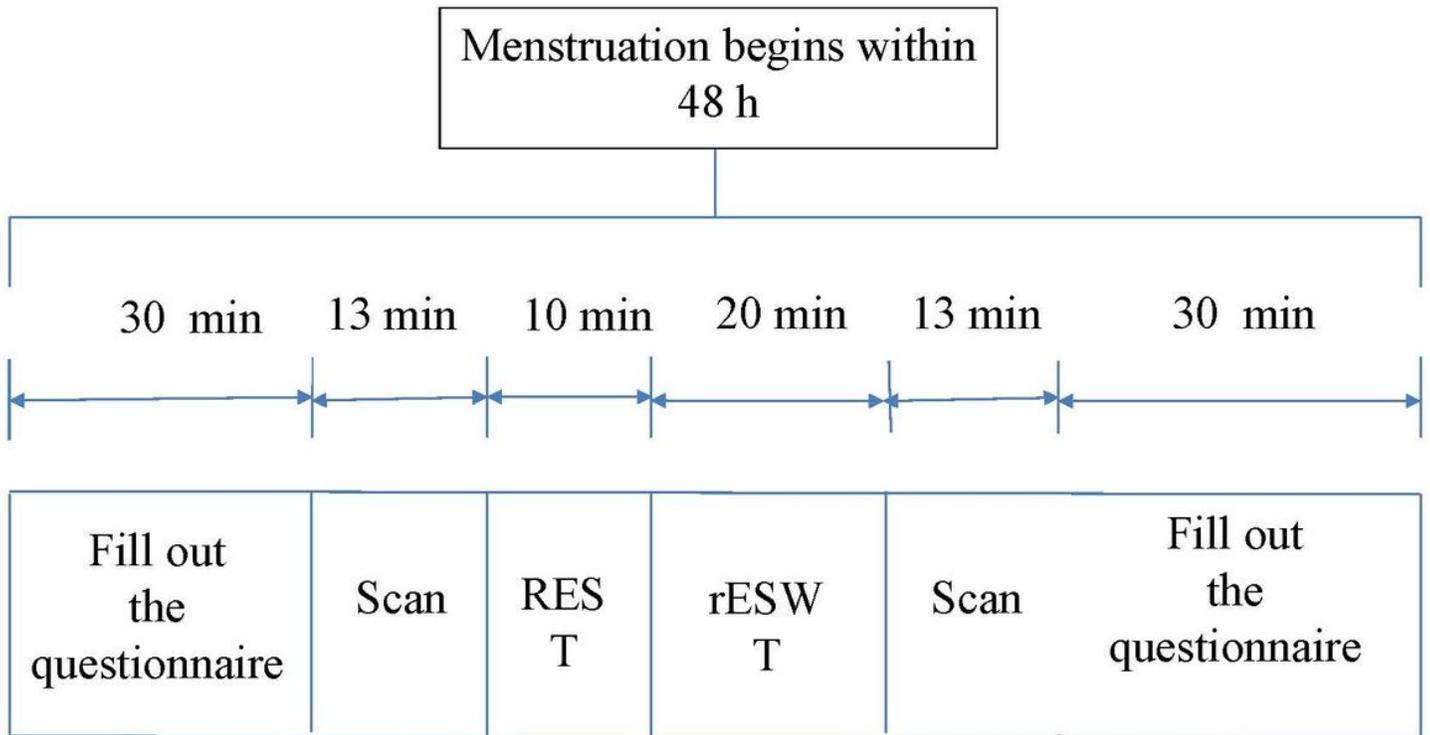


Figure 2

Case study procedure

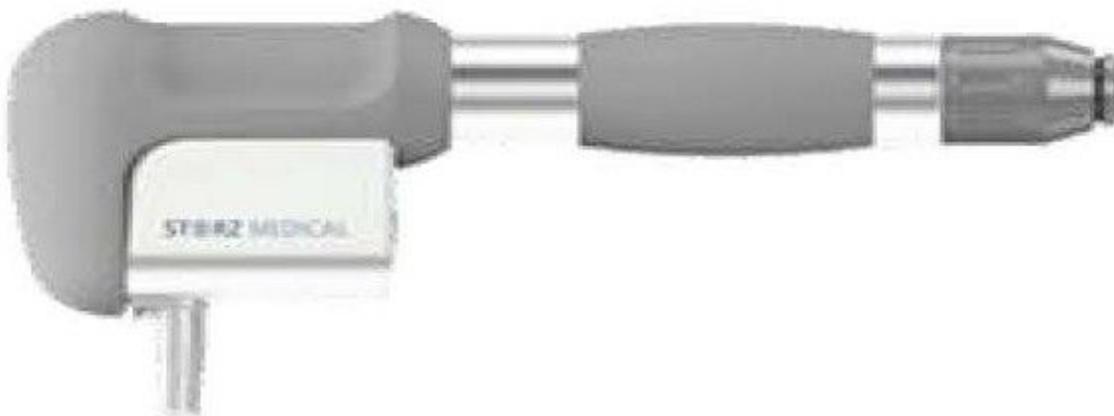


Figure 3

Above is the front view of the shockwave instrument(model: MASTERPULS MP100), and the below is the side view of the treatment handle and the ceramic probe C15 attached to the handle (model: R-SW handpiece)

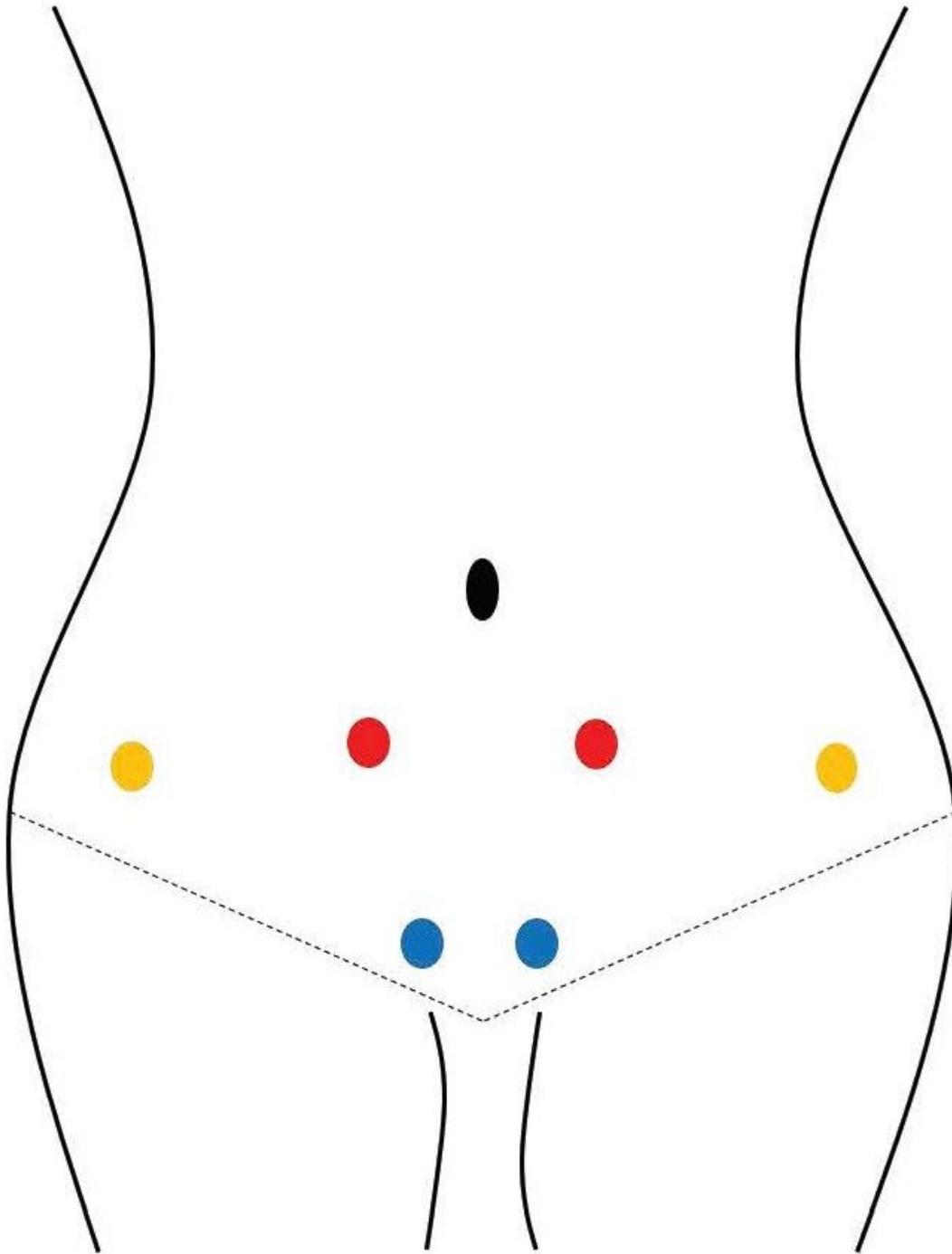


Figure 4

Treatment site of the abdominal muscle fascia trigger point. The blue dots, the rectus abdominis attachment point is located above the pubic symphysis (bilateral); the yellow dots, the intersection of the anterior superior iliac spine with the outer edge of the rectus abdominis (bilateral); the red dots, the anterior superior iliac spine moving inward about 2 cm along a straight line (bilateral)

Supplementary Files

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- [supplement1.doc](#)