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Title page

Article title:

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Abstract

Introduction: Plantar fasciitis (PF) is reported to be the most common cause of plantar heel pain. Acupuncture has been used for patients experiencing PF, but evidence of the efficacy of acupuncture on PF is limited. The primary objective of this trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist control for improving the level of pain experienced by patients suffering from chronic PF.

Methods and Analysis: This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week follow-up. Participants in the waitlist control group will not undergo treatment for a period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period. The primary outcome will be the treatment response rate 4 weeks after randomization, assessed as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. All analyses will be performed with a 2-sided *P* value of < 0.05 considered significant following the intention-to-treat principle.

Ethics and Dissemination: The study has been approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). The results will be disseminated through presentation

at a peer-reviewed medical journal, the relevant conferences and scientific meetings.

Key words: acupuncture; chronic plantar fasciitis; pain intensity; clinical trial

Trial registration: ClinicalTrials.gov identifier: NCT 04185259.

Strengths and limitations of this study:

► This study is the first randomized controlled trial comparing combined acupuncture and sham acupuncture versus waitlist control for pain relief in participants with chronic PF.

► Sham control and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control and evaluation of participants' expectation regarding acupuncture, aiming to reduce the risk of bias.

►Acupuncturists and participants in the waitlist control group will not be blinded, which may cause bias.

►A high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial.

►The 12-week follow-up will not allow the detection of the long-term effects of acupuncture on chronic PF.

Background

Plantar fasciitis (PF), which presents with heel pain and tenderness particularly at the plantar aspect of the calcaneal tuberosity [1] upon the initiation of weight bearing, is one of the most prevalent complaints encountered by foot and ankle specialists. It is reported that 1 in 10 people suffer from inferior heel pain within their lifetime [2] and this condition is attributed to PF in 80% of cases.[3] PF predominantly affects elderly and middle-aged individuals [4] and is more frequent in runners or those whose employment requires standing.[5] The exact etiology of PF is multifactorial and not completely understood. Physical-mechanical overload and micro tears within the fascia [6,7] could be involved in the development of PF, resulting in localized inflammation and degeneration of the proximal plantar aponeurosis.[8]

The available treatment options for PF mainly include non-operative treatments (e.g., plantar fascia and gastrocnemius soleus muscle stretching, heel cups, arch supports, night splints, nonsteroidal antiinflammatory drugs (NSAIDs), local corticosteroid injections), and operative management.[9] However, no consensus has been reached regarding the most beneficial treatment method for PF.[10] Although conservative treatment of PF is successful in the vast majority of cases [11] and many PF cases are self-limiting and eventually enter remission, it can take up to months or even years for patients to recover.[12] Moreover, approximately 10 to 20% of patients are recalcitrant to conventional treatments, resulting in foot pain and/or disabilities for years.[13]

Acupuncture, an integral part of traditional Chinese medicine (TCM), is a technique whereby the acupoints located on specific body areas are pierced with fine needles for therapeutic purposes based on the principles of TCM.[14] Acupuncture has been used in the management of PF and other musculoskeletal pain-related conditions

for thousands of years. Mechanistic studies have revealed that acupuncture can induce an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin, β-endorphin, and endomorphin).[15] Two recent systematic reviews [16,17] found that acupuncture may reduce pain intensity and improve plantar function for patients with PF. However, there were methodological problems with the small sample sizes, lack of control with a placebo/waitlist group, or no adjustment for the confounding effects of patients who received combination treatments in the design of the included acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous remission of PF cannot be excluded and the beneficial effects of acupuncture for PF remain in need of further assessment.

We designed a randomized controlled trial to evaluate the efficacy of acupuncture, compared with sham acupuncture (SA) or being on a waitlist control group, for patients with chronic PF for >6 months. Given that clinical and experimental results have shown that SA can induce a significant alleviation of pain similar to verum acupuncture [18] due to non-specific effects (e.g., acupuncture expectations), the primary hypothesis in this trial was that combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment in patients with chronic PF. The secondary hypothesis examined whether acupuncture can reduce heel pain intensity more effectively than SA or no acupuncture.

Methods and design

Study design

This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate. We will design the protocol in accordance with standard protocol items including the Recommendations for Interventional Trials [19] and the Standards for Reporting

Interventions in the Clinical Trials of Acupuncture [20] guidelines. The study flow chart and study schedule are shown in Figs. 1 and 2.

Study setting and recruitment

This trial is planned to be conducted at Guang'anmen Hospital, China Academy of Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from March 2020 to March 2022. A total of 120 participants will be publicly recruited through the use of posters and hospital webs in the two participating hospitals. The duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week treatment, and 12-week follow-up.

Randomization and Blinding

The eligible participants who sign an informed consent form will complete a 1-week baseline assessment before randomization. Participants will be randomized into the acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of 2:1:1 using simple randomization. Randomization will be generated with the PROC PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group allocation will be concealed on cards inside sealed opaque envelopes by the staff member responsible for the allocation. A research coordinator, who will not be involved in the treatment and outcome assessments, will be responsible for contacting participants and allocating them to their assigned group. Participants in the acupuncture and SA groups, together with efficacy evaluators and data analysts will be blinded to the group assignments. Participants in the waitlist control group and acupuncturists will not be blinded.

Participants

Participants with a diagnosis of PF by an orthopedist on clinical grounds will be included in the study only if they meet all of the following inclusion criteria and do

not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the guidelines described by the Orthopaedic Section of American Physical Therapy Association.[21] The following clinical findings will be used to diagnose PF: plantar medial heel pain during the initial steps after a period of inactivity but also worse pain following prolonged weight bearing, heel pain precipitated by a recent increase in weight-bearing activity, physical examination findings (heel pain with palpation of the proximal insertion of the plantar fascia), as well as a positive windlass test and negative tarsal tunnel tests.

Inclusion criteria:

1. Age ≥18 years and ≤75 years;
2. History of plantar medial heel pain for at least 6 months before enrolment;
3. Reported an average worst pain intensity at first steps in the morning over the last 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before enrolment;
4. Failure to respond to conservative treatment for ≥ 1 months, including any of the following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs, and orthotics;
5. Ability to comply with the study protocol, understand the medical information forms as well as having provided informed consent.

Exclusion criteria:

1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture, or having a significant foot deformity (clubfoot, pes cavus, or pes calcaneovalgus);
2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or radiation, or surgery to plantar fascia within 6 months preceding enrollment;

3. Radiculopathy or peripheral neuropathy around the ankle joint such as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
5. Joint, bone, or skin infection in the affected foot;
6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or coagulation disorder at baseline as determined by the investigator;
7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks prior to enrollment.

Interventions

Acupuncture group

The acupuncture protocol was developed by the consensus of three experts based on the meridian theory of TCM and was used in our previous trial.[22] Licensed acupuncturists with more than 2 years of acupuncture experience will perform the treatment. We will apply needles to two Ashi points (the two most severe tender points in the most sensitive area over the anteromedial aspect of the heels, according to the participant's perceived pain upon palpation) as well as the Chengshan (BL57), Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the aforementioned acupoints will be based on the Nomenclature and location of acupuncture points [23] designated by the National Standard of the People's Republic of China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used. With the patient in a prone position, the local skin will be routinely sterilized, followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected

acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar fascia layer with a depth of approximately 15-20 mm depending on the location. BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin through the pad. All needles except the Ashi points will be manually stimulated with small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi (a sensation including soreness, numbness, distention, and heaviness).[24] Needles will be retained for 30 minutes per treatment. During each treatment, every needle will be manipulated three times every 10 minutes.

SA group

In the SA group, sham Ashi (0.5 cun away from Ashi, one 'cun' is equivalent to the greatest width of the individual patients' thumb, ~1.5 cm), sham BL57 (0.5 cun lateral to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon) will be used. The treatment protocol will be similar to that of the acupuncture group. The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be inserted at the sham points through the adhesive pads attached to the skin without skin penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three times every 10 minutes. No specific De qi response will be elicited.

Waitlist control group

Participants will receive no treatment for their heel pain for a period of 16 weeks after randomization, and subsequently have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period.

The intervention will last for 30 minutes in the acupuncture and SA groups, and will be performed three times per week for a total of 12 sessions in four consecutive weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides

and evaluate the more severe side. Participants in all groups will be treated and (or) evaluated separately. Participants in all groups will be advised to use soft heel foot wear, not to stand for a long time, and not to walk barefoot during the study.

Rescue medication

Additional therapies for heel pain during the entire study period will be prohibited. However, the investigator will be permitted to prescribe ibuprofen (sustained release type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as rescue medication no more than 2 days per week up to the maximum daily dose if unbearable heel pain occurs. Participants will be required not to take rescue medication within 72 h before the baseline and outcome measurements. In the event rescue medication needs to be taken after the baseline measurement, the participant will postpone the next visit to the treatment center.

Outcome measures

Primary outcome

The primary outcome used in this trial will be the proportion of participants with a treatment response 4 weeks after randomization, defined as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. The average worst pain intensity over the last 3 days will be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS, with 0 indicating no pain and 100 indicating maximal pain. Participants who must resort to additional treatments other than rescue medication will be classified as nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be assessed.

Secondary outcomes

The secondary outcomes are as follows:

1. Changes in the VAS score for worst pain intensity during the first steps in the morning from baseline to 4, 8, and 16 weeks after randomization;
2. Changes in the VAS score for mean pain intensity during the day from baseline to 4, 8, and 16 weeks after randomization;
3. Changes in the pressure pain threshold (PPT) at the most painful area from baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the minimum pressure detected when the sensation of pressure first changes to a sensation of pain.[25] PPT will be tested with a pressure algometer (Fabrication Enterprises, Inc., White Plains, NY; from 1 kg/cm^2 to 5 kg/cm^2) using a metal probe with a 0.5 cm^2 rubber disc by a trained researcher. PPT will be measured when the participant is lying supine in a relaxed position with the affected foot hanging over the edge of the bed. When measuring the PPT, the rubber disc will be placed perpendicularly on the painful spot and pressure will be applied at a rate of approximately 0.1 kg/cm^2/s through the metal probe of the pressure algometer. Participants will be informed to report when the initial pain sensation occurs, and the readings of the algometer will be recorded. The score will be determined by averaging three repeated measurements with 30 seconds between each trial. All values below 1 kg/cm^2 will be reported as 0.5 kg/cm^2.
4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16 weeks after randomization: The examiner will measure the AROM including plantar dorsiflexion and plantar flexion using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan, from 0° to 360°). Prior to the measurement, the participant will sit in a relaxed station with the popliteal space at the edge of the table and their knees with 90° of flexion. The axis of the goniometer will be placed at the lateral malleolus. The stationary arm will be

placed parallel to the fifth metatarsal and the moving arm placed parallel to the center of the fibular head. The ankle will be passively moved from a neutral starting position into dorsiflexion and flexion until a firm end feel is elicited [26] and the readings of the goniometer will be registered. The mean score of three trials with 10 seconds between each examination will be calculated and used for analysis.

5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a self-reported questionnaire concerning 21 activities of daily living (ADL) items and eight sports subscale items.[27] Each item is scored on a 0-4 point Likert scale anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores indicating a higher level of function. The FAAM has a maximum potential score of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and sport subscale scores) is divided by the maximum potential score and multiplied by 100 to obtain a percentage. If the patient does not respond, the specific question will be left blank and not be a part of the final value of the questionnaire. In this trial, we will use the previously validated Chinese version of the FAAM.[28]
6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after randomization: PFT will be measured at the thickest point closest to the calcaneal insertion in its medial portion using ultrasound. The ultrasound scan will be performed using an 8-12 MHz linear probe with the patient in the prone position at the baseline and at 4 and 16 weeks after randomization.
7. Participant global assessment of improvement: Participants will be asked to rate their global improvement using a 7-point scale. The improvement will be scaled from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious

improvement, 3 being a little improvement, 4 being no change, 5 being a little worse, and 6 being obviously worse. The proportions of participants with different degrees of improvement will be assessed at 4, 8, and 16 weeks after randomization.

8. Participants' expectation towards acupuncture at baseline: At baseline, participants in the acupuncture and SA groups will be asked the following question: "Do you think acupuncture will be helpful to improve your chronic PF?" Participant will choose one of the following answers: "Extremely helpful", "Very helpful", "Helpful", "Not help at all", and "Unclear".
9. The proportion of participants who have maintained blinding during treatment in the acupuncture and SA groups: Participants' blindness to the mode of acupuncture will be assessed five minutes after the end of any treatment in the fourth week by asking the patients the following question: "Which of the two acupuncture modalities do you think you received, acupuncture or SA?" Participants will choose one of the following answers: "Acupuncture", "SA", or "Unclear". Prior to the question, patients will be informed that they may have received one of two modalities: acupuncture with a deeper insertion or SA with no skin penetration.

Safety assessment

The adverse events (AEs) during the entire study will be recorded and described as acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8, using VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness, vomiting, headache, palpitations). Detailed information on AEs including the name,

onset, end date, intensity, correlation with acupuncture, and outcomes will be documented in the case report form. Investigators will immediately report serious AEs (eg, requiring hospitalization, causing disability or impaired ability to work) to the Medical Ethics Committee of Guang'anmen Hospital, and stop the clinical trial until further instruction is given.

Sample size calculation

Based on the results of a previous study,[13] a sample size of 120 participants will be enrolled to provide 80% power to detect a difference of 35% between the combined acupuncture group and waiting-list group in the proportion of participants with treatment response 4 weeks after randomization at a two-sided significance level of 0.05. The proportion of participants with treatment response after 4 weeks was assumed to be roughly 12% for the waiting-list group [13], with an anticipated 10% loss to follow-up.

Statistical analysis

The null hypothesis is that the proportion of participants with treatment response 4 weeks after randomization will be the same for the combined acupuncture groups and waiting-list group. Data will be presented as mean ± standard deviation for quantitative variables and frequencies (number of cases), with relative frequencies (percentages) for categorical variables. The primary outcome analysis will use the Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the combined acupuncture groups and the waiting-list group. If the result of this analysis is significant, hierarchical testing will be applied to the acupuncture group versus waiting-list group, SA group versus waiting-list group, and acupuncture group versus SA group. For normally distributed quantitative variables, a repeated-measures analysis of variance (ANOVA) with multiple comparisons post-hoc test will be used

when comparing more than two groups and an unpaired T test when comparing two groups. For non-normally distributed quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney test will be performed. For categorical variables, the Chi square (χ^2) test will be used. A two-tailed test will be applied for all available data, and a P value < 0.05 will be considered statistically significant. All analyses in this trial will be performed using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the basis of the intention-to-treat (ITT) population, which will include participants who had been randomized. Missing data will be completed as the last value observed before dropout.

Quality control

To ensure the quality of the trial, all the relevant staff will be uniformly trained before the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF, inclusion and exclusion criteria, intervention procedures, and outcome measures). Licensed acupuncturists with at least 2 years' acupuncture experience will perform the treatment. Throughout the trial, strict three-level monitoring will be conducted for data quality control. Dropouts and withdrawals including the reasons will be recorded during the trial. Paper-based study data will be stored in locked file cabinets under the management of the investigators. Electronic records will be stored in a Structured Query Language (SQL) server database on a limited access, secure server maintained by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

Patient and public involvement

The research question of whether combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment for patients with chronic PF was first proposed by the investigator after encountering a patient who received SA and reported a similar improvement in heel pain as another patient who received

routine acupuncture in the clinic. Patients were not involved in conceiving or implementing the study.

Ethics and dissemination

This trial will be conducted in accordance with the principles of the Declaration of Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign the informed consent form prior to randomization, and they will be permitted to withdraw at any time during the trial, with or without reasons being provided. Any amendment or other change of the protocol will need to be approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Science, and agreed to by the co-researchers.

Following analysis of the data, the findings of this study will be submitted for publication in a peer-reviewed medical journal. The results will also be disseminated through presentation at the relevant conferences and scientific meetings.

Discussion

Although several reviews and RCTs [16,17,13,29] have been published that focus on acupuncture for PF, owing to the lack of a placebo control, non-specific physiology effects of needling and spontaneous remission of PF cannot be excluded. To date, this is the first randomized trial with three parallel arms, assessing whether combined acupuncture and SA compared to no treatment control produce a significant reduction in pain intensity in chronic PF. We anticipate that this study will determine the efficacy of acupuncture for patients with chronic PF, and improve the care of these patients in the clinic.

Though most PF patients will achieve significant improvement in symptoms within 1 year regardless of treatment,[30] many will seek treatment before then. Patients are often interested in alternative treatment options when they cannot obtain a satisfactory outcome from conservative treatment. In this trial, we recruited only chronic participants who had failed to respond to conservative treatment prior to participation. The results can be generalized to patients experiencing chronic refractory PF.

In this study, pain intensity measured with VAS during the first steps in the morning will be used as the primary outcome. This variable has been used in previous trials [13,22] and is a meaningful subject outcome measure for the assessment of PF improvement. In addition, we will also use PPT and PFT as objective secondary outcomes. PPT is an essential evaluation tool for patients suffering from many musculoskeletal disorders including PF and provides a reliable process for measuring participants' responses to mechanical stimuli.[31] Compared to normal asymptomatic patients, patients with PF often exhibit a thickened plantar fascia on ultrasound. [32] Therefore, a PFT evaluation would provide information to detect the anatomical changes that occur in the plantar fascia after acupuncture.

The strengths of this study include a sham control (non-penetrating at non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control, and evaluation of the participants' expectations regarding acupuncture. Several limitations to this trial need to be acknowledged. First, it will be impossible to blind the acupuncturists and participants in the waitlist control group, which is a general problem in non-pharmacological interventional trials and can cause bias. Second, a high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial. Third, the follow-up

period will not exceed 12 weeks, which will not allow for detection of the long-term effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw conclusions about the selected acupuncture points but not about individualized treatments.

Ethical Approval and Consent to participate The study has received approval from the Institutional Review Boards of Guang'anmen Hospital in China (approval NO. 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the Helsinki Declaration.

Consent for publication Not applicable.

Availability of data and materials All data are fully available without restriction.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Weiming Wang and Zhishun Liu conceived the idea and designed this trial. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang Li will be responsible for the recruitment, acupuncture, and assessment respectively. Yan Liu will be responsible for statistical analysis. This manuscript was drafted by Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All authors read and approved the final draft of the manuscript.

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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

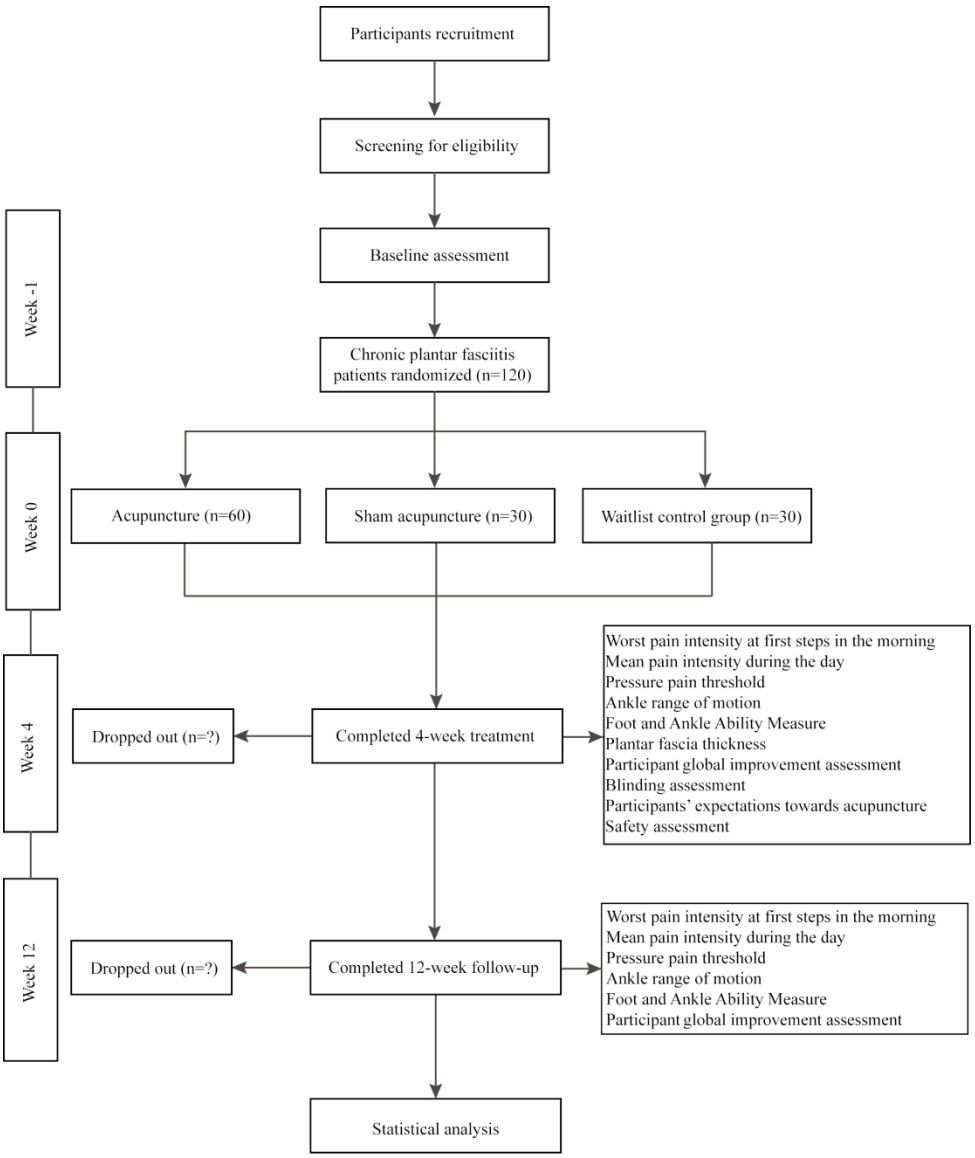

Figure 1. Trial flow diagram

Trial flow diagram

199x246mm (300 x 300 DPI)

	Study Period				
	Baseline	**Allocation**	**Treatment**	**Follow-up**	
TIME POINT (W，week)			W 4±2d	W 8±3d	W16±3d
Enrollment					
Eligibility criteria	×				
Demography characteristics	×				
Disease history of chronic plantar fasciitis	×				
Eligibility screen	×				
Informed consent	×				
Allocation		×			
Interventions					
Acupuncture			×(weeks1-4)		
Sham acupuncture			×(weeks1-4)		
Waitlist control (no treatment)			×(weeks1-4)		
Assessments					
Worst pain intensity at first steps in the morning	×		×	×	×
Mean pain intensity during the day	×		×	×	×
Pressure pain threshold	×		×	×	×
Ankle range of motion	×		×	×	×
Foot and Ankle Ability Measure	×		×	×	×
Plantar fascia thickness	×		×		
Participant global improvement assessment	×		×	×	×
Participant′ expectations towards acupuncture	×				
Blinding assessment					
Adverse events			×		
Safety assessment			×	×	×

Figure 2: study schedule

Study schedule

206x194mm (300 x 300 DPI)

Table 1

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13-14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16,19

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Title page

Article title:

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Running title: acupuncture for chronic plantar fasciitis

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Abstract

Introduction: Plantar fasciitis (PF) is reported to be the most common cause of plantar heel pain. Acupuncture has been used for patients experiencing PF, but evidence of the efficacy of acupuncture on PF is limited. The primary objective of this trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist control for improving the level of pain experienced by patients suffering from chronic PF.

Methods and Analysis: This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week follow-up. Participants in the waitlist control group will not undergo treatment for a period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period. The primary outcome will be the treatment response rate 4 weeks after randomization, assessed as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. All analyses will be performed with a 2-sided *P* value of < 0.05 considered significant following the intention-to-treat principle.

Ethics and Dissemination: The study has been approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). The results will be disseminated through presentation

at a peer-reviewed medical journal, the relevant conferences and scientific meetings.

Key words: acupuncture; chronic plantar fasciitis; pain intensity; clinical trial

Trial registration: ClinicalTrials.gov identifier: NCT 04185259.

Strengths and limitations of this study:

► This study is the first randomized controlled trial comparing combined acupuncture and sham acupuncture versus waitlist control for pain relief in participants with chronic PF.

► The advantages to this study include sham acupuncture and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control and evaluation of participants' expectation regarding acupuncture.

► The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance patient adherence by allowing more patients to receive acupuncture.

►Acupuncturists and participants in the waitlist control group will not be blinded, which may cause bias.

►A high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial.

Background

Plantar fasciitis (PF), which presents with heel pain and tenderness particularly at the plantar aspect of the calcaneal tuberosity [1] upon the initiation of weight bearing, is one of the most prevalent complaints encountered by foot and ankle specialists. It is reported that 1 in 10 people suffer from inferior heel pain within their lifetime [2] and this condition is attributed to PF in 80% of cases.[3] PF predominantly affects elderly and middle-aged individuals [4] and is more frequent in runners or those whose employment requires standing.[5] The exact etiology of PF is multifactorial and not completely understood. Physical-mechanical overload and micro tears within the fascia [6] could be involved in the development of PF, resulting in localized inflammation and degeneration of the proximal plantar aponeurosis.[7]

The available treatment options for PF mainly include non-operative treatments (e.g., plantar fascia and gastrocnemius soleus muscle stretching, heel cups, arch supports, night splints, shockwave therapy, nonsteroidal antiinflammatory drugs (NSAIDs), local corticosteroid injections), and operative management.[8] However, no consensus has been reached regarding the most beneficial treatment method for PF.[9] Although conservative treatment of PF is successful in the vast majority of cases [10] and many PF cases are self-limiting and eventually enter remission, it can take up to months or even years for patients to recover.[11] Moreover, approximately 10 to 20% of patients are recalcitrant to conventional treatments, resulting in foot pain and/or disabilities for years.[12]

Acupuncture, an integral part of traditional Chinese medicine (TCM), is a technique whereby the acupoints located on specific body areas are pierced with fine needles for therapeutic purposes based on the principles of TCM.[13]Acupuncture has been used in the management of PF and other musculoskeletal pain-related conditions

for thousands of years. Mechanistic studies have revealed that acupuncture can induce an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin, β-endorphin, and endomorphin).[14] Two recent systematic reviews [15,16] found that acupuncture may reduce pain intensity and improve plantar function for patients with PF. However, there were methodological problems with the small sample sizes, lack of control with a placebo/waitlist group, or no adjustment for the confounding effects of patients who received combination treatments in the design of the included acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous remission of PF cannot be excluded and the beneficial effects of acupuncture for PF remain in need of further assessment.

We designed a randomized controlled trial to evaluate the efficacy of acupuncture, compared with sham acupuncture (SA) or being on a waitlist control group, for patients with chronic PF for >6 months. Given that clinical and experimental results have shown that SA can induce a significant alleviation of pain similar to verum acupuncture [17]due to non-specific effects (e.g., acupuncture expectations), the primary hypothesis in this trial was that combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment in patients with chronic PF. The secondary hypothesis examined whether acupuncture can reduce heel pain intensity more effectively than SA or no acupuncture.

Methods and design

Study design

This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate. We will design the protocol in accordance with standard protocol items including the Recommendations for Interventional Trials [18] and the Standards for Reporting

Interventions in the Clinical Trials of Acupuncture [19] guidelines. The study flow chart and study schedule are shown in Figs. 1 and 2.

Study setting and recruitment

This trial is planned to be conducted at Guang'anmen Hospital, China Academy of Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from March 2020 to March 2022. A total of 120 participants will be publicly recruited through the use of posters and hospital webs in the two participating hospitals. The duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week treatment, and 12-week follow-up.

Randomization and Blinding

The eligible participants who sign an informed consent form will complete a 1-week baseline assessment (see Fig. 2) before randomization. Participants will be randomized into the acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of 2:1:1 using simple randomization. Randomization will be generated with the PROC PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group allocation will be concealed on cards inside sealed opaque envelopes by the staff member responsible for the allocation. A research coordinator, who will not be involved in the treatment and outcome assessments, will be responsible for contacting participants and allocating them to their assigned group. Participants in the acupuncture and SA groups, together with efficacy evaluators and data analysts will be blinded to the group assignments. Participants in the waitlist control group and acupuncturists will not be blinded.

Participants

Participants with a diagnosis of PF by an orthopedist on clinical grounds will be included in the study only if they meet all of the following inclusion criteria and do

not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the guidelines described by the Orthopaedic Section of American Physical Therapy Association.[20] The following clinical findings will be used to diagnose PF: plantar medial heel pain during the initial steps after a period of inactivity but also worse pain following prolonged weight bearing, heel pain precipitated by a recent increase in weight-bearing activity, physical examination findings (heel pain with palpation of the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal foot posture index, high body mass index, as well as a positive windlass test and negative tarsal tunnel tests.

Inclusion criteria:

1. Age ≥18 years and ≤75 years;
2. History of plantar medial heel pain for at least 6 months before enrolment;
3. Reported an average worst pain intensity at first steps in the morning over the last 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before enrolment;
4. Failure to respond to conservative treatment for ≥ 1 months, including any of the following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs, shockwave therapy, dry needling and orthotics;
5. Ability to comply with the study protocol, understand the medical information forms as well as having provided informed consent.

Exclusion criteria:

1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture, or having a significant foot deformity (clubfoot, pes cavus, or pes calcaneovalgus);

2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or radiation, or surgery to plantar fascia within 6 months preceding enrollment;
3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
5. Joint, bone, or skin infection in the affected foot;
6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or coagulation disorder at baseline as determined by the investigator;
7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks prior to enrollment.

Interventions

Acupuncture group

The acupuncture protocol was developed by the consensus of three experts based on the meridian theory of TCM and was used in our previous trial.[21] Licensed acupuncturists with more than 2 years of acupuncture experience will perform the treatment. We will apply needles to two Ashi points (the two most severe tender points in the most sensitive area over the anteromedial aspect of the heels, according to the participant's perceived pain upon palpation) as well as the Chengshan (BL57), Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the aforementioned acupoints will be based on the Nomenclature and location of acupuncture points [22] designated by the National Standard of the People's Republic of China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used. With the patient in a prone position, the local skin will be routinely sterilized,

followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar fascia layer with a depth of approximately 15-20 mm depending on the location. BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin through the pad. All needles except the Ashi points will be manually stimulated with small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi (a sensation including soreness, numbness, distention, and heaviness).[23] Needles will be retained for 30 minutes per treatment. During each treatment, every needle will be manipulated three times every 10 minutes.

SA group

In the SA group, sham Ashi (0.5 cun away from Ashi, one 'cun' is equivalent to the greatest width of the individual patients' thumb, ~1.5 cm), sham BL57 (0.5 cun lateral to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon) will be used. The treatment protocol will be similar to that of the acupuncture group. The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be inserted at the sham points through the adhesive pads attached to the skin without skin penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three times every 10 minutes. No specific De qi response will be elicited.

Waitlist control group

Participants will receive no treatment for their heel pain for a period of 16 weeks after randomization, and subsequently have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period.

The intervention will last for 30 minutes in the acupuncture and SA groups, and will be performed three times per week for a total of 12 sessions in four consecutive weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides and evaluate the more severe side. Participants in all groups will be treated and (or) evaluated separately. Participants in all groups will be advised to use soft heel foot wear, not to stand for a long time, and not to walk barefoot during the 17-week study period.

Rescue medication

Additional therapies for heel pain during the entire study period will be prohibited. However, the investigator will be permitted to prescribe ibuprofen (sustained release type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as rescue medication no more than 2 days per week up to the maximum daily dose if unbearable heel pain occurs. Participants will be required not to take rescue medication within 72 h before the baseline and outcome measurements. In the event rescue medication needs to be taken after the baseline measurement, the participant will postpone the next visit to the treatment center.

Outcome measures

Primary outcome

The primary outcome used in this trial will be the proportion of participants with a treatment response 4 weeks after randomization, defined as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. The average worst pain intensity over the last 3 days will be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS, with 0 indicating no pain and 100 indicating maximal pain. Participants who must resort to additional treatments other than rescue medication will be classified as

nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be assessed.

Secondary outcomes

The secondary outcomes are as follows:

1. Changes in the VAS score for worst pain intensity during the first steps in the morning from baseline to 4, 8, and 16 weeks after randomization;
2. Changes in the VAS score for mean pain intensity during the day from baseline to 4, 8, and 16 weeks after randomization;
3. Changes in the pressure pain threshold (PPT) at the most painful area from baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the minimum pressure detected when the sensation of pressure first changes to a sensation of pain.[24] PPT will be tested with a pressure algometer (Fabrication Enterprises, Inc., White Plains, NY; from 1 kg/cm^2 to 5 kg/cm^2) using a metal probe with a 0.5 cm^2 rubber disc by a trained researcher. PPT will be measured when the participant is lying supine in a relaxed position with the affected foot hanging over the edge of the bed. When measuring the PPT, the rubber disc will be placed perpendicularly on the painful spot and pressure will be applied at a rate of approximately 0.1 $kg/cm^2/s$ through the metal probe of the pressure algometer. Participants will be informed to report when the initial pain sensation occurs, and the readings of the algometer will be recorded. The score will be determined by averaging three repeated measurements with 30 seconds between each trial. All values below 1 kg/cm^2 will be reported as 0.5 kg/cm^2.
4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16 weeks after randomization: The examiner will measure the AROM including dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee)

using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan, from 0° to 360°). For the flexed-knee assessment, the participant will sit in a relaxed station with the popliteal space at the edge of the table and their knees with 90° of flexion. For the extended-knee assessment, the participant will be seated on a treatment table with the knees fully extended (0°) and the feet hanging off the end of the table. The axis of the goniometer will be placed at the lateral malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the moving arm placed parallel to the center of the fibular head. The ankle will be passively moved from a neutral starting position into dorsiflexion and plantar flexion until a firm end feel is elicited [25] and the readings of the goniometer will be registered. The mean score of three trials with 10 seconds between each examination will be calculated and used for analysis.

5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a self-reported questionnaire concerning 21 activities of daily living (ADL) items and eight sports subscale items.[26] Each item is scored on a 0-4 point Likert scale anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores indicating a higher level of function. The FAAM has a maximum potential score of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and sport subscale scores) is divided by the maximum potential score and multiplied by 100 to obtain a percentage. If the patient does not respond, the specific question will be left blank and not be a part of the final value of the questionnaire. In this trial, we will use the previously validated Chinese version of the FAAM.[27]
6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after randomization: PFT will be measured at the thickest point closest to the calcaneal

insertion in its medial portion using ultrasound. The ultrasound scan will be performed using an 8-12 MHz linear probe with the patient in the prone position at the baseline and at 4 weeks after randomization.

7. Participant global assessment of improvement: Participants will be asked to rate their global improvement using a 7-point scale. The improvement will be scaled from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious improvement, 3 being a little improvement, 4 being no change, 5 being a little worse, and 6 being obviously worse. The proportions of participants with different degrees of improvement will be assessed at 4, 8, and 16 weeks after randomization. Scales of participant global assessment of improvement with 7 response categories have been rated as relatively easy to use and show good reliability and validity.[28]
8. Participants' expectation towards acupuncture at baseline: At baseline, participants in the acupuncture and SA groups will be asked the following question: "Do you think acupuncture will be helpful to improve your chronic PF?" Participant will choose one of the following answers: "Extremely helpful", "Very helpful", "Helpful", "Not help at all", and "Unclear".
9. The proportion of participants who have maintained blinding during treatment in the acupuncture and SA groups: Participants' blindness to the mode of acupuncture will be assessed five minutes after the end of any treatment in the fourth week by asking the patients the following question: "Which of the two acupuncture modalities do you think you received, acupuncture or SA?" Participants will choose one of the following answers: "Acupuncture", "SA", or "Unclear". Prior to the question, patients will be informed that they may have received one of two modalities: acupuncture with a deeper insertion or SA with no

skin penetration.

Safety assessment

The adverse events (AEs) during the entire study will be recorded and described as acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8, using VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness, vomiting, headache, palpitations). Detailed information on AEs including the name, onset, end date, intensity, correlation with acupuncture, and outcomes will be documented in the case report form. Investigators will immediately report serious AEs (eg, requiring hospitalization, causing disability or impaired ability to work) to the Medical Ethics Committee of Guang'anmen Hospital, and stop the clinical trial until further instruction is given.

Sample size calculation

Based on the results of a previous study,[12] a sample size of 120 participants will be enrolled to provide 80% power to detect a difference of 35% between the combined acupuncture group and waiting-list group in the proportion of participants with treatment response 4 weeks after randomization at a two-sided significance level of 0.05. The proportion of participants with treatment response after 4 weeks was assumed to be roughly 12% for the waiting-list group, [12] with an anticipated 10% loss to follow-up.

Statistical analysis

The null hypothesis is that the proportion of participants with treatment response 4 weeks after randomization will be the same for the combined acupuncture groups and waiting-list group. Data will be presented as mean ± standard deviation for

quantitative variables and frequencies (number of cases), with relative frequencies (percentages) for categorical variables. The primary outcome analysis will use the Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the combined acupuncture groups and the waiting-list group. If the result of this analysis is significant, hierarchical testing will be applied to the acupuncture group versus waiting-list group, SA group versus waiting-list group, and acupuncture group versus SA group. For normally distributed quantitative variables, a repeated-measures analysis of variance (ANOVA) with multiple comparisons post-hoc test will be performed using baseline as a co-variate when comparing more than two groups and an unpaired T test when comparing two groups. For non-normally distributed quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney test will be performed. For categorical variables, the Chi square (χ^2) test will be used. Confidence intervals for the difference between treatments will be calculated at the 95% level. A two-tailed test will be applied for all available data, and a P value < 0.05 will be considered statistically significant. All analyses in this trial will be performed using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the basis of the intention-to-treat (ITT) population, which will include participants who had been randomized. Missing data will be completed as the last value observed before dropout. No adjustment will be made for multiple outcomes.

Quality control

To ensure the quality of the trial, all the relevant staff will be uniformly trained before the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF, inclusion and exclusion criteria, intervention procedures, and outcome measures). Licensed acupuncturists with at least 2 years' acupuncture experience will perform the treatment. Throughout the trial, strict three-level monitoring will be conducted for

data quality control. Dropouts and withdrawals including the reasons will be recorded during the trial. Paper-based study data will be stored in locked file cabinets under the management of the investigators. Electronic records will be stored in a Structured Query Language (SQL) server database on a limited access, secure server maintained by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

Patient and public involvement

The research question of whether combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment for patients with chronic PF was first proposed by the investigator after encountering a patient who received SA and reported a similar improvement in heel pain as another patient who received routine acupuncture in the clinic. Patients were not involved in conceiving or implementing the study.

Ethics and dissemination

This trial will be conducted in accordance with the principles of the Declaration of Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign the informed consent form prior to randomization, and they will be permitted to withdraw at any time during the trial, with or without reasons being provided. Any amendment or other change of the protocol will need to be approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Science, and agreed to by the co-researchers.

Following analysis of the data, the findings of this study will be submitted for publication in a peer-reviewed medical journal. The results will also be disseminated through presentation at the relevant conferences and scientific meetings.

Discussion

Although several reviews and RCTs [15,16,12,29] have been published that focus on acupuncture for PF, owing to the lack of a placebo control, non-specific physiology effects of needling and spontaneous remission of PF cannot be excluded. To date, this is the first randomized trial with three parallel arms, assessing whether combined acupuncture and SA compared to no treatment control produce a significant reduction in pain intensity in chronic PF. We anticipate that this study will determine the efficacy of acupuncture for patients with chronic PF, and improve the care of these patients in the clinic.

Though most PF patients will achieve significant improvement in symptoms within 1 year regardless of treatment,[30] many will seek treatment before then. Patients often choose other treatment options when they cannot obtain a satisfactory outcome from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic participants who had failed to respond to conservative treatment prior to participation. The results can be generalized to patients experiencing chronic refractory PF.

In this study, pain intensity measured with VAS during the first steps in the morning will be used as the primary outcome. This variable has been used in previous trials [12,21] and is a meaningful subject outcome measure for the assessment of PF improvement. In addition, we will also use PPT and PFT as objective secondary outcomes. PPT is an essential evaluation tool for patients suffering from many musculoskeletal disorders including PF and provides a reliable process for measuring participants' responses to mechanical stimuli.[31] Compared to normal asymptomatic patients, patients with PF often exhibit a thickened plantar fascia on ultrasound. [32]

Therefore, a PFT evaluation would provide information to detect the anatomical changes that occur in the plantar fascia after acupuncture.

The strengths of this study include a sham control (non-penetrating at non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control, and evaluation of the participants' expectations regarding acupuncture. Several limitations to this trial need to be acknowledged. First, it will be impossible to blind the acupuncturists and participants in the waitlist control group, which is a general problem in non-pharmacological interventional trials and can cause bias. Second, a high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial. Third, the follow-up period will not exceed 12 weeks, which will not allow for detection of the long-term effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw conclusions about the selected acupuncture points but not about individualized treatments.

Ethical Approval and Consent to participate The study has received approval from the Institutional Review Boards of Guang'anmen Hospital in China (approval NO. 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the Helsinki Declaration.

Consent for publication Not applicable.

Availability of data and materials Not applicable.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Weiming Wang and Zhishun Liu conceived the idea and designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang Li will be responsible for the recruitment, acupuncture, and assessment respectively. Yan Liu will be responsible for statistical analysis. This manuscript was drafted by Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All authors read and approved the final draft of the manuscript.

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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

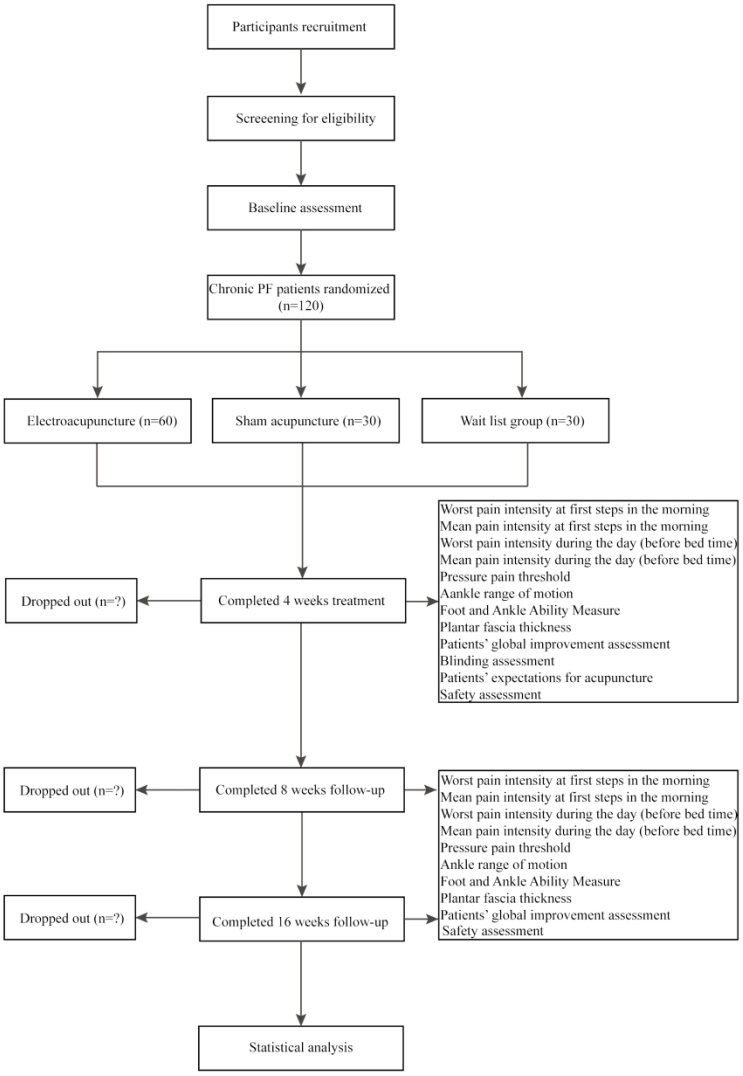

Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

	Study Period				
	Baseline	**Allocation**	**Treatment**	**Follow-up**	
TIME POINT (W，week)			W 4±2d	W 8±3d	W16±3d
Enrollment					
Eligibility criteria	×				
Demography characteristics	×				
Disease history of chronic plantar fasciitis	×				
Eligibility screen	×				
Informed consent	×				
Allocation		×			
Interventions					
Acupuncture			×(weeks1-4)		
Sham acupuncture			×(weeks1-4)		
Waitlist control (no treatment)			×(weeks1-4)		
Assessments					
Worst pain intensity at first steps in the morning	×		×	×	×
Mean pain intensity during the day	×		×	×	×
Pressure pain threshold	×		×	×	×
Ankle range of motion	×		×	×	×
Foot and Ankle Ability Measure	×		×	×	×
Plantar fascia thickness	×		×		
Participant global improvement assessment	×		×	×	×
Participant′ expectations towards acupuncture	×				
Blinding assessment					
Adverse events			×	×	×
Safety assessment			×	×	×

Figure 2: study schedule

Study schedule

206x194mm (300 x 300 DPI)

Table 1

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13-14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16,19

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Primary Subject Heading:	Medical management
Secondary Subject Heading:	Complementary medicine
Keywords:	COMPLEMENTARY MEDICINE, PAIN MANAGEMENT, Clinical trials < THERAPEUTICS

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Title page

Article title:

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Abstract

Introduction: Plantar fasciitis (PF) is reported to be the most common cause of plantar heel pain. Acupuncture has been used for patients experiencing PF, but evidence of the efficacy of acupuncture on PF is limited. The primary objective of this trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist control for improving the level of pain experienced by patients suffering from chronic PF.

Methods and Analysis: This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week follow-up. Participants in the waitlist control group will not undergo treatment for a period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period. The primary outcome will be the treatment response rate 4 weeks after randomization, assessed as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. All analyses will be performed with a 2-sided *P* value of < 0.05 considered significant following the intention-to-treat principle.

Ethics and Dissemination: The study has been approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). The results will be disseminated through presentation

at a peer-reviewed medical journal, the relevant conferences and scientific meetings.

Key words: acupuncture; chronic plantar fasciitis; pain intensity; clinical trial

Trial registration: ClinicalTrials.gov identifier: NCT 04185259.

Strengths and limitations of this study:

► This study is the first randomized controlled trial comparing combined acupuncture and sham acupuncture versus waitlist control for pain relief in participants with chronic PF.

► The advantages to this study include sham acupuncture and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control and evaluation of participants' expectation regarding acupuncture.

► The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance patient adherence by allowing more patients to receive acupuncture.

►Acupuncturists and participants in the waitlist control group will not be blinded, which may cause bias.

►A high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial.

Background

Plantar fasciitis (PF), which presents with heel pain and tenderness particularly at the plantar aspect of the calcaneal tuberosity [1] upon the initiation of weight bearing, is one of the most prevalent complaints encountered by foot and ankle specialists. It is reported that 1 in 10 people suffer from inferior heel pain within their lifetime [2] and this condition is attributed to PF in 80% of cases.[3] PF predominantly affects elderly and middle-aged individuals [4] and is more frequent in runners or those whose employment requires standing.[5] The exact etiology of PF is multifactorial and not completely understood. Physical-mechanical overload and micro tears within the fascia [6] could be involved in the development of PF, resulting in localized inflammation and degeneration of the proximal plantar aponeurosis.[7]

The available treatment options for PF mainly include non-operative treatments (e.g., plantar fascia and gastrocnemius soleus muscle stretching, heel cups, arch supports, night splints, shockwave therapy, nonsteroidal antiinflammatory drugs (NSAIDs), local corticosteroid injections), and operative management.[8] However, no consensus has been reached regarding the most beneficial treatment method for PF.[9] Although conservative treatment of PF is successful in the vast majority of cases [10] and many PF cases are self-limiting and eventually enter remission, it can take up to months or even years for patients to recover.[11] Moreover, approximately 10 to 20% of patients are recalcitrant to conventional treatments, resulting in foot pain and/or disabilities for years.[12]

Acupuncture, an integral part of traditional Chinese medicine (TCM), is a technique whereby the acupoints located on specific body areas are pierced with fine needles for therapeutic purposes based on the principles of TCM.[13]Acupuncture has been used in the management of PF and other musculoskeletal pain-related conditions

for thousands of years. Mechanistic studies have revealed that acupuncture can induce an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin, β-endorphin, and endomorphin).[14] Two recent systematic reviews [15,16] found that acupuncture may reduce pain intensity and improve plantar function for patients with PF. However, there were methodological problems with the small sample sizes, lack of control with a placebo/waitlist group, or no adjustment for the confounding effects of patients who received combination treatments in the design of the included acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous remission of PF cannot be excluded and the beneficial effects of acupuncture for PF remain in need of further assessment.

We designed a randomized controlled trial to evaluate the efficacy of acupuncture, compared with sham acupuncture (SA) or being on a waitlist control group, for patients with chronic PF for >6 months. Given that clinical and experimental results have shown that SA can induce a significant alleviation of pain similar to verum acupuncture [17]due to non-specific effects (e.g., acupuncture expectations), the primary hypothesis in this trial was that combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment in patients with chronic PF. The secondary hypothesis examined whether acupuncture can reduce heel pain intensity more effectively than SA or no acupuncture.

Methods and design

Study design

This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate. We will design the protocol in accordance with standard protocol items including the Recommendations for Interventional Trials [18] and the Standards for Reporting

Interventions in the Clinical Trials of Acupuncture [19] guidelines. The study flow chart and study schedule are shown in Figs. 1 and 2.

Study setting and recruitment

This trial is planned to be conducted at Guang'anmen Hospital, China Academy of Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from March 2020 to March 2022. A total of 120 participants will be publicly recruited through the use of posters and hospital webs in the two participating hospitals. The duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week treatment, and 12-week follow-up.

Randomization and Blinding

The eligible participants who sign an informed consent form will complete a 1-week baseline assessmentbefore randomization, which includes foot symptoms, functionality, and ultrasound examinations, as well as participants' expectation (see Fig. 2). Participants will be randomized into the acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of 2:1:1 using simple randomization. Randomization will be generated with the PROC PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group allocation will be concealed on cards inside sealed opaque envelopes by the staff member responsible for the allocation. A research coordinator, who will not be involved in the treatment and outcome assessments, will be responsible for contacting participants and allocating them to their assigned group. Participants in the acupuncture and SA groups, together with efficacy evaluators and data analysts will be blinded to the group assignments. Participants in the waitlist control group and acupuncturists will not be blinded.

Participants

Participants with a diagnosis of PF by an orthopedist on clinical grounds will be included in the study only if they meet all of the following inclusion criteria and do not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the guidelines described by the Orthopaedic Section of American Physical Therapy Association.[20] The following clinical findings will be used to diagnose PF: plantar medial heel pain during the initial steps after a period of inactivity but also worse pain following prolonged weight bearing, heel pain precipitated by a recent increase in weight-bearing activity, physical examination findings (heel pain with palpation of the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal foot posture index, high body mass index, as well as a positive windlass test and negative tarsal tunnel tests.

Inclusion criteria:

1. Age ≥18 years and ≤75 years;
2. History of plantar medial heel pain for at least 6 months before enrolment;
3. Reported an average worst pain intensity at first steps in the morning over the last 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before enrolment;
4. Failure to respond to conservative treatment for ≥ 1 months, including any of the following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs, shockwave therapy, dry needling and orthotics;
5. Ability to comply with the study protocol, understand the medical information forms as well as having provided informed consent.

Exclusion criteria:

1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture, or having a significant foot deformity (clubfoot, pes cavus, or pes calcaneovalgus);
2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or radiation, or surgery to plantar fascia within 6 months preceding enrollment;
3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
5. Joint, bone, or skin infection in the affected foot;
6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or coagulation disorder at baseline as determined by the investigator;
7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks prior to enrollment.

Interventions

Acupuncture group

The acupuncture protocol was developed by the consensus of three experts based on the meridian theory of TCM and was used in our previous trial.[21] Licensed acupuncturists with more than 2 years of acupuncture experience will perform the treatment. We will apply needles to two Ashi points (the two most severe tender points in the most sensitive area over the anteromedial aspect of the heels, according to the participant's perceived pain upon palpation) as well as the Chengshan (BL57), Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the aforementioned acupoints will be based on the Nomenclature and location of acupuncture points [22] designated by the National Standard of the People's Republic of

China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used. With the patient in a prone position, the local skin will be routinely sterilized, followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar fascia layer with a depth of approximately 15-20 mm depending on the location. BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin through the pad. All needles except the Ashi points will be manually stimulated with small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi (a sensation including soreness, numbness, distention, and heaviness).[23] Needles will be retained for 30 minutes per treatment. During each treatment, every needle will be manipulated three times every 10 minutes.

SA group

In the SA group, sham Ashi (0.5 cun away from Ashi, one 'cun' is equivalent to the greatest width of the individual patients' thumb, ~1.5 cm), sham BL57 (0.5 cun lateral to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon) will be used. The treatment protocol will be similar to that of the acupuncture group. The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be inserted at the sham points through the adhesive pads attached to the skin without skin penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three times every 10 minutes. No specific De qi response will be elicited.

Waitlist control group

Participants will receive no treatment for their heel pain for a period of 16 weeks after randomization, and subsequently have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period.

The intervention will last for 30 minutes in the acupuncture and SA groups, and will be performed three times per week for a total of 12 sessions in four consecutive weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides and evaluate the more severe side. Participants in all groups will be treated and (or) evaluated separately. Participants in all groups will be advised to use soft heel foot wear, not to stand for a long time, and not to walk barefoot during the 17-week study period.

Rescue medication

Additional therapies for heel pain during the entire study period will be prohibited. However, the investigator will be permitted to prescribe ibuprofen (sustained release type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as rescue medication no more than 2 days per week up to the maximum daily dose if unbearable heel pain occurs. Participants will be required not to take rescue medication within 72 h before the baseline and outcome measurements. In the event rescue medication needs to be taken after the baseline measurement, the participant will postpone the next visit to the treatment center.

Outcome measures

Primary outcome

The primary outcome used in this trial will be the proportion of participants with a treatment response 4 weeks after randomization, defined as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. The average worst pain intensity over the last 3 days will

be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS, with 0 indicating no pain and 100 indicating maximal pain. Participants who must resort to additional treatments other than rescue medication will be classified as nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be assessed.

Secondary outcomes

The secondary outcomes are as follows:

1. Changes in the VAS score for worst pain intensity during the first steps in the morning from baseline to 4, 8, and 16 weeks after randomization;
2. Changes in the VAS score for mean pain intensity during the day from baseline to 4, 8, and 16 weeks after randomization;
3. Changes in the pressure pain threshold (PPT) at the most painful area from baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the minimum pressure detected when the sensation of pressure first changes to a sensation of pain.[24] PPT will be tested with a pressure algometer (Fabrication Enterprises, Inc., White Plains, NY; from 1 kg/cm^2 to 5 kg/cm^2) using a metal probe with a 0.5 cm^2 rubber disc by a trained researcher. PPT will be measured when the participant is lying supine in a relaxed position with the affected foot hanging over the edge of the bed. When measuring the PPT, the rubber disc will be placed perpendicularly on the painful spot and pressure will be applied at a rate of approximately 0.1 $kg/cm^2/s$ through the metal probe of the pressure algometer. Participants will be informed to report when the initial pain sensation occurs, and the readings of the algometer will be recorded. The score will be determined by averaging three repeated measurements with 30 seconds between each trial. All values below 1 kg/cm^2 will be reported as 0.5 kg/cm^2.

4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16 weeks after randomization: The examiner will measure the AROM including dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee) using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan, from 0° to 360°). For the flexed-knee assessment, the participant will sit in a relaxed station with the popliteal space at the edge of the table and their knees with 90° of flexion. For the extended-knee assessment, the participant will be seated on a treatment table with the knees fully extended (0°) and the feet hanging off the end of the table. The axis of the goniometer will be placed at the lateral malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the moving arm placed parallel to the center of the fibular head. The ankle will be passively moved from a neutral starting position into dorsiflexion and plantar flexion until a firm end feel is elicited [25] and the readings of the goniometer will be registered. The mean score of three trials with 10 seconds between each examination will be calculated and used for analysis.
5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a self-reported questionnaire concerning 21 activities of daily living (ADL) items and eight sports subscale items.[26] Each item is scored on a 0-4 point Likert scale anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores indicating a higher level of function. The FAAM has a maximum potential score of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and sport subscale scores) is divided by the maximum potential score and multiplied by 100 to obtain a percentage. If the patient does not respond, the specific question will be left blank and not be a part of the final value of the questionnaire.

In this trial, we will use the previously validated Chinese version of the FAAM.[27]

6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after randomization: PFT will be measured at the thickest point closest to the calcaneal insertion in its medial portion using ultrasound. The ultrasound scan will be performed using an 8-12 MHz linear probe with the patient in the prone position at the baseline and at 4 weeks after randomization.
7. Participant global assessment of improvement: Participants will be asked to rate their global improvement using a 7-point scale. The improvement will be scaled from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious improvement, 3 being a little improvement, 4 being no change, 5 being a little worse, and 6 being obviously worse. The proportions of participants with different degrees of improvement will be assessed at 4, 8, and 16 weeks after randomization. Scales of participant global assessment of improvement with 7 response categories have been rated as relatively easy to use and show good reliability and validity.[28]
8. Participants' expectation towards acupuncture at baseline: At baseline, participants in the acupuncture and SA groups will be asked the following question: "Do you think acupuncture will be helpful to improve your chronic PF?" Participant will choose one of the following answers: "Extremely helpful", "Very helpful", "Helpful", "Not help at all", and "Unclear".
9. The proportion of participants who have maintained blinding during treatment in the acupuncture and SA groups: Participants' blindness to the mode of acupuncture will be assessed five minutes after the end of any treatment in the fourth week by asking the patients the following question: "Which of the two acupuncture modalities do you think you received, acupuncture or SA?"

Participants will choose one of the following answers: “Acupuncture”, “SA”, or “Unclear”. Prior to the question, patients will be informed that they may have received one of two modalities: acupuncture with a deeper insertion or SA with no skin penetration.

Safety assessment

The adverse events (AEs) during the entire study will be recorded and described as acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8, using VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness, vomiting, headache, palpitations). Detailed information on AEs including the name, onset, end date, intensity, correlation with acupuncture, and outcomes will be documented in the case report form. Investigators will immediately report serious AEs (eg, requiring hospitalization, causing disability or impaired ability to work) to the Medical Ethics Committee of Guang’anmen Hospital, and stop the clinical trial until further instruction is given.

Sample size calculation

Based on the results of a previous study,[12] a sample size of 120 participants will be enrolled to provide 80% power to detect a difference of 35% between the combined acupuncture group and waiting-list group in the proportion of participants with treatment response 4 weeks after randomization at a two-sided significance level of 0.05. The proportion of participants with treatment response after 4 weeks was assumed to be roughly 12% for the waiting-list group, [12] with an anticipated 10% loss to follow-up.

Statistical analysis

The null hypothesis is that the proportion of participants with treatment response 4 weeks after randomization will be the same for the combined acupuncture groups and waiting-list group. Data will be presented as mean ± standard deviation for quantitative variables and frequencies (number of cases), with relative frequencies (percentages) for categorical variables. The primary outcome analysis will use the Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the combined acupuncture groups and the waiting-list group. If the result of this analysis is significant, hierarchical testing will be applied to the acupuncture group versus waiting-list group, SA group versus waiting-list group, and acupuncture group versus SA group. For normally distributed quantitative variables, a repeated-measures analysis of variance (ANOVA) with multiple comparisons post-hoc test will be performed using baseline as a co-variate when comparing more than two groups and an unpaired T test when comparing two groups. For non-normally distributed quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney test will be performed. For categorical variables, the Chi square (χ^2) test will be used. Confidence intervals for the difference between treatments will be calculated at the 95% level. A two-tailed test will be applied for all available data, and a P value < 0.05 will be considered statistically significant. All analyses in this trial will be performed using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the basis of the intention-to-treat (ITT) population, which will include participants who had been randomized. Missing data will be completed as the last value observed before dropout. No adjustment will be made for multiple outcomes.

Quality control

To ensure the quality of the trial, all the relevant staff will be uniformly trained before the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF,

inclusion and exclusion criteria, intervention procedures, and outcome measures). Licensed acupuncturists with at least 2 years' acupuncture experience will perform the treatment. Throughout the trial, strict three-level monitoring will be conducted for data quality control. Dropouts and withdrawals including the reasons will be recorded during the trial. Paper-based study data will be stored in locked file cabinets under the management of the investigators. Electronic records will be stored in a Structured Query Language (SQL) server database on a limited access, secure server maintained by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

Patient and public involvement

The research question of whether combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment for patients with chronic PF was first proposed by the investigator after encountering a patient who received SA and reported a similar improvement in heel pain as another patient who received routine acupuncture in the clinic. Patients were not involved in conceiving or implementing the study.

Ethics and dissemination

This trial will be conducted in accordance with the principles of the Declaration of Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign the informed consent form prior to randomization, and they will be permitted to withdraw at any time during the trial, with or without reasons being provided. Any amendment or other change of the protocol will need to be approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Science, and agreed to by the co-researchers.

Following analysis of the data, the findings of this study will be submitted for publication in a peer-reviewed medical journal. The results will also be disseminated through presentation at the relevant conferences and scientific meetings.

Discussion

Although several reviews and RCTs [15,16,12,29] have been published that focus on acupuncture for PF, owing to the lack of a placebo control, non-specific physiology effects of needling and spontaneous remission of PF cannot be excluded. To date, this is the first randomized trial with three parallel arms, assessing whether combined acupuncture and SA compared to no treatment control produce a significant reduction in pain intensity in chronic PF. We anticipate that this study will determine the efficacy of acupuncture for patients with chronic PF, and improve the care of these patients in the clinic.

Though most PF patients will achieve significant improvement in symptoms within 1 year regardless of treatment,[30] many will seek treatment before then. Patients often choose other treatment options when they cannot obtain a satisfactory outcome from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic participants who had failed to respond to conservative treatment prior to participation. The results can be generalized to patients experiencing chronic refractory PF.

In this study, pain intensity measured with VAS during the first steps in the morning will be used as the primary outcome. This variable has been used in previous trials [12,21] and is a meaningful subject outcome measure for the assessment of PF improvement. In addition, we will also use PPT and PFT as objective secondary outcomes. PPT is an essential evaluation tool for patients suffering from many musculoskeletal disorders including PF and provides a reliable process for measuring

participants' responses to mechanical stimuli.[31] Compared to normal asymptomatic patients, patients with PF often exhibit a thickened plantar fascia on ultrasound. [32] Therefore, a PFT evaluation would provide information to detect the anatomical changes that occur in the plantar fascia after acupuncture.

The strengths of this study include a sham control (non-penetrating at non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control, and evaluation of the participants' expectations regarding acupuncture. Several limitations to this trial need to be acknowledged. First, it will be impossible to blind the acupuncturists and participants in the waitlist control group, which is a general problem in non-pharmacological interventional trials and can cause bias. Second, a high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial. Third, the follow-up period will not exceed 12 weeks, which will not allow for detection of the long-term effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw conclusions about the selected acupuncture points but not about individualized treatments. Fifth, there are multiple secondary outcomes in this trial, which may increase the risk of type I error.

Ethical Approval and Consent to participate The study has received approval from the Institutional Review Boards of Guang'anmen Hospital in China (approval NO. 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the Helsinki Declaration.

Consent for publication Not applicable.

Availability of data and materials Not applicable.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Weiming Wang and Zhishun Liu conceived the idea and designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang Li will be responsible for the recruitment, acupuncture, and assessment respectively. Yan Liu will be responsible for statistical analysis. This manuscript was drafted by Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All authors read and approved the final draft of the manuscript.

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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

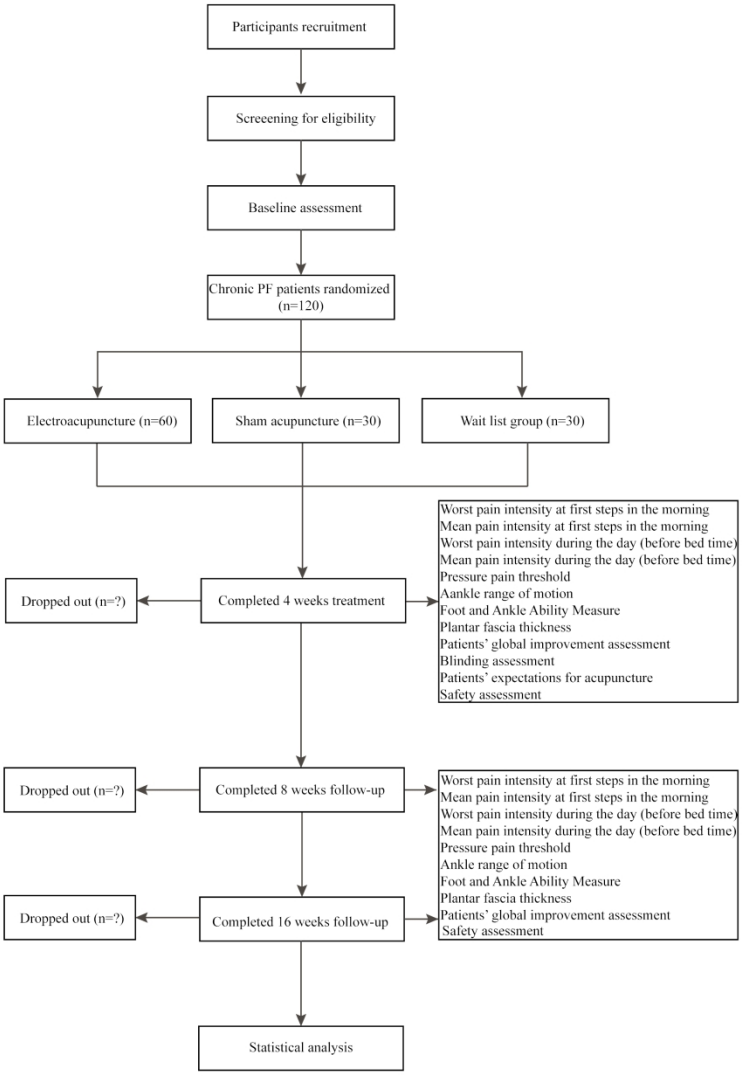

Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

	Study Period				
	Baseline	**Allocation**	**Treatment**	**Follow-up**	
TIME POINT (W, week)			W 4±2d	W 8±3d	W16±3d
Enrollment					
Eligibility criteria	×				
Demography characteristics	×				
Disease history of chronic plantar fasciitis	×				
Eligibility screen	×				
Informed consent	×				
Allocation		×			
Interventions					
Acupuncture			×(weeks1-4)		
Sham acupuncture			×(weeks1-4)		
Waitlist control (no treatment)			×(weeks1-4)		
Assessments					
Worst pain intensity at first steps in the morning	×		×	×	×
Mean pain intensity during the day	×		×	×	×
Pressure pain threshold	×		×	×	×
Ankle range of motion	×		×	×	×
Foot and Ankle Ability Measure	×		×	×	×
Plantar fascia thickness	×		×		
Participant global improvement assessment			×	×	×
Participants′ expectation towards acupuncture	×				
Blinding assessment					
Adverse events			×	×	×
Safety assessment			×	×	×

Figure 2: study schedule

Study schedule

199x194mm (300 x 300 DPI)

Table 1

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13-14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16,19

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Title page

Article title:

Efficacy of acupuncture vs sham acupuncture or waitlist control for patients with chronic plantar fasciitis: study protocol for a 2-center randomized controlled trial

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Running title: acupuncture for chronic plantar fasciitis

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Abstract

Introduction: Plantar fasciitis (PF) is reported to be the most common cause of plantar heel pain. Acupuncture has been used for patients experiencing PF, but evidence of the efficacy of acupuncture on PF is limited. The primary objective of this trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist control for improving the level of pain experienced by patients suffering from chronic PF.

Methods and Analysis: This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week follow-up. Participants in the waitlist control group will not undergo treatment for a period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period. The primary outcome will be the treatment response rate 4 weeks after randomization, assessed as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning compared with the baseline. All analyses will be performed with a 2-sided *P* value of < 0.05 considered significant following the intention-to-treat principle.

Ethics and Dissemination: The study has been approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). The results will be disseminated through presentation

at a peer-reviewed medical journal, the relevant conferences and scientific meetings.

Key words: acupuncture; chronic plantar fasciitis; pain intensity; clinical trial

Trial registration: ClinicalTrials.gov identifier: NCT 04185259.

Strengths and limitations of this study:

► This study is the first randomized controlled trial comparing combined acupuncture and sham acupuncture versus waitlist control for pain relief in participants with chronic PF.

► The advantages to this study include sham acupuncture and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control and evaluation of participants' expectation regarding acupuncture.

► The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance patient adherence by allowing more patients to receive acupuncture.

►Acupuncturists and participants in the waitlist control group will not be blinded, which may cause bias.

►A high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial.

Background

Plantar fasciitis (PF), which presents with heel pain and tenderness particularly at the plantar aspect of the calcaneal tuberosity [1] upon the initiation of weight bearing, is one of the most prevalent complaints encountered by foot and ankle specialists. It is reported that 1 in 10 people suffer from inferior heel pain within their lifetime [2] and this condition is attributed to PF in 80% of cases.[3] PF predominantly affects elderly and middle-aged individuals [4] and is more frequent in runners or those whose employment requires standing.[5] The exact etiology of PF is multifactorial and not completely understood. Physical-mechanical overload and micro tears within the fascia [6] could be involved in the development of PF, resulting in localized inflammation and degeneration of the proximal plantar aponeurosis.[7]

The available treatment options for PF mainly include non-operative treatments (e.g., plantar fascia and gastrocnemius soleus muscle stretching, heel cups, arch supports, night splints, shockwave therapy, nonsteroidal antiinflammatory drugs (NSAIDs), local corticosteroid injections), and operative management.[8] However, no consensus has been reached regarding the most beneficial treatment method for PF.[9] Although conservative treatment of PF is successful in the vast majority of cases [10] and many PF cases are self-limiting and eventually enter remission, it can take up to months or even years for patients to recover.[11] Moreover, approximately 10 to 20% of patients are recalcitrant to conventional treatments, resulting in foot pain and/or disabilities for years.[12]

Acupuncture, an integral part of traditional Chinese medicine (TCM), is a technique whereby the acupoints located on specific body areas are pierced with fine needles for therapeutic purposes based on the principles of TCM.[13]Acupuncture has been used in the management of PF and other musculoskeletal pain-related conditions

for thousands of years. Mechanistic studies have revealed that acupuncture can induce an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin, β-endorphin, and endomorphin).[14] Two recent systematic reviews [15,16] found that acupuncture may reduce pain intensity and improve plantar function for patients with PF. However, there were methodological problems with the small sample sizes, lack of control with a placebo/waitlist group, or no adjustment for the confounding effects of patients who received combination treatments in the design of the included acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous remission of PF cannot be excluded and the beneficial effects of acupuncture for PF remain in need of further assessment.

We designed a randomized controlled trial to evaluate the efficacy of acupuncture, compared with sham acupuncture (SA) or being on a waitlist control group, for patients with chronic PF for >6 months. Given that clinical and experimental results have shown that SA can induce a significant alleviation of pain similar to verum acupuncture [17]due to non-specific effects (e.g., acupuncture expectations), the primary hypothesis in this trial was that combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment in patients with chronic PF. The secondary hypothesis examined whether acupuncture can reduce heel pain intensity more effectively than SA or no acupuncture.

Methods and design

Study design

This will be a two-center, parallel-group, sham and no-treatment controlled, assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate. We will design the protocol in accordance with standard protocol items including the Recommendations for Interventional Trials [18] and the Standards for Reporting

Interventions in the Clinical Trials of Acupuncture [19] guidelines. The study flow chart and study schedule are shown in Figs. 1 and 2.

Study setting and recruitment

This trial is planned to be conducted at Guang'anmen Hospital, China Academy of Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from March 2020 to March 2022. A total of 120 participants will be publicly recruited through the use of posters and hospital webs in the two participating hospitals. The duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week treatment, and 12-week follow-up.

Randomization and Blinding

The eligible participants who sign an informed consent form will complete a 1-week baseline assessmentbefore randomization, which includes foot symptoms(i.e., worst pain intensity at first steps in the morning, mean pain intensity during the day), functionality, and ultrasound examinations (see Fig. 2). Participants' expectation towards acupuncture will be assessed in the acupuncture and SA groups at baseline by asking participants: Do you think acupuncture will be helpful to improve your chronic PF? Participant will choose one of the following answers: "Extremely helpful", "Very helpful", "Helpful", "Not help at all", and "Unclear". Participants will be randomized into the acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of 2:1:1 using simple randomization. Randomization will be generated with the PROC PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group allocation will be concealed on cards inside sealed opaque envelopes by the staff member responsible for the allocation. A research coordinator, who will not be involved in the treatment and outcome assessments, will be responsible for contacting participants and allocating them to their assigned group. Participants in the

acupuncture and SA groups, together with efficacy evaluators and data analysts will be blinded to the group assignments. Participants in the waitlist control group and acupuncturists will not be blinded.

Participants

Participants with a diagnosis of PF by an orthopedist on clinical grounds will be included in the study only if they meet all of the following inclusion criteria and do not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the guidelines described by the Orthopaedic Section of American Physical Therapy Association.[20] The following clinical findings will be used to diagnose PF: plantar medial heel pain during the initial steps after a period of inactivity but also worse pain following prolonged weight bearing, heel pain precipitated by a recent increase in weight-bearing activity, physical examination findings (heel pain with palpation of the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal foot posture index, high body mass index, as well as a positive windlass test and negative tarsal tunnel tests.

Inclusion criteria:

1. Age ≥18 years and ≤75 years;
2. History of plantar medial heel pain for at least 6 months before enrolment;
3. Reported an average worst pain intensity at first steps in the morning over the last 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before enrolment;
4. Failure to respond to conservative treatment for ≥ 1 months, including any of the following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs, shockwave therapy, dry needling and orthotics;
5. Ability to comply with the study protocol, understand the medical information

forms as well as having provided informed consent.

Exclusion criteria:

1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture, or having a significant foot deformity (clubfoot, pes cavus, or pes calcaneovalgus);
2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or radiation, or surgery to plantar fascia within 6 months preceding enrollment;
3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
5. Joint, bone, or skin infection in the affected foot;
6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or coagulation disorder at baseline as determined by the investigator;
7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks prior to enrollment.

Interventions

Acupuncture group

The acupuncture protocol was developed by the consensus of three experts based on the meridian theory of TCM and was used in our previous trial.[21] Licensed acupuncturists with more than 2 years of acupuncture experience will perform the treatment. We will apply needles to two Ashi points (the two most severe tender points in the most sensitive area over the anteromedial aspect of the heels, according to the participant's perceived pain upon palpation) as well as the Chengshan (BL57), Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the

aforementioned acupoints will be based on the Nomenclature and location of acupuncture points [22] designated by the National Standard of the People's Republic of China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used. With the patient in a prone position, the local skin will be routinely sterilized, followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar fascia layer with a depth of approximately 15-20 mm depending on the location. BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin through the pad. All needles except the Ashi points will be manually stimulated with small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi (a sensation including soreness, numbness, distention, and heaviness).[23] Needles will be retained for 30 minutes per treatment. During each treatment, every needle will be manipulated three times every 10 minutes.

SA group

In the SA group, sham Ashi (0.5 cun away from Ashi, one 'cun' is equivalent to the greatest width of the individual patients' thumb, ~1.5 cm), sham BL57 (0.5 cun lateral to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon) will be used. The treatment protocol will be similar to that of the acupuncture group. The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be inserted at the sham points through the adhesive pads attached to the skin without skin penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three times every 10 minutes. No specific De qi response will be elicited.

Waitlist control group

Participants will receive no treatment for their heel pain for a period of 16 weeks after randomization, and subsequently have the option of 4 weeks (12 sessions) of acupuncture free of charge at the end of the follow-up period.

The intervention will last for 30 minutes in the acupuncture and SA groups, and will be performed three times per week for a total of 12 sessions in four consecutive weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides and evaluate the more severe side. Participants in all groups will be treated and (or) evaluated separately. Participants in all groups will be advised to use soft heel foot wear, not to stand for a long time, and not to walk barefoot during the 17-week study period.

Rescue medication

Additional therapies for heel pain during the entire study period will be prohibited. However, the investigator will be permitted to prescribe ibuprofen (sustained release type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as rescue medication no more than 2 days per week up to the maximum daily dose if unbearable heel pain occurs. Participants will be required not to take rescue medication within 72 h before the baseline and outcome measurements. In the event rescue medication needs to be taken after the baseline measurement, the participant will postpone the next visit to the treatment center.

Outcome measures

Primary outcome

The primary outcome used in this trial will be the proportion of participants with a treatment response 4 weeks after randomization, defined as a minimum of 50% improvement in the worst pain intensity during the first steps in the morning

compared with the baseline. The average worst pain intensity over the last 3 days will be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS, with 0 indicating no pain and 100 indicating maximal pain. Participants who must resort to additional treatments other than rescue medication will be classified as nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be assessed.

Secondary outcomes

The secondary outcomes are as follows:

1. Changes in the VAS score for worst pain intensity during the first steps in the morning from baseline to 4, 8, and 16 weeks after randomization;
2. Changes in the VAS score for mean pain intensity during the day from baseline to 4, 8, and 16 weeks after randomization;
3. Changes in the pressure pain threshold (PPT) at the most painful area from baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the minimum pressure detected when the sensation of pressure first changes to a sensation of pain.[24] PPT will be tested with a pressure algometer (Fabrication Enterprises, Inc., White Plains, NY; from 1 kg/cm^2 to 5 kg/cm^2) using a metal probe with a 0.5 cm^2 rubber disc by a trained researcher. PPT will be measured when the participant is lying supine in a relaxed position with the affected foot hanging over the edge of the bed. When measuring the PPT, the rubber disc will be placed perpendicularly on the painful spot and pressure will be applied at a rate of approximately 0.1 kg/cm^2/s through the metal probe of the pressure algometer. Participants will be informed to report when the initial pain sensation occurs, and the readings of the algometer will be recorded. The score will be determined by averaging three repeated measurements with 30 seconds between each trial. All

values below 1 kg/cm^2 will be reported as 0.5 kg/cm^2.

4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16 weeks after randomization: The examiner will measure the AROM including dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee) using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan, from 0° to 360°). For the flexed-knee assessment, the participant will sit in a relaxed station with the popliteal space at the edge of the table and their knees with 90° of flexion. For the extended-knee assessment, the participant will be seated on a treatment table with the knees fully extended (0°) and the feet hanging off the end of the table. The axis of the goniometer will be placed at the lateral malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the moving arm placed parallel to the center of the fibular head. The ankle will be passively moved from a neutral starting position into dorsiflexion and plantar flexion until a firm end feel is elicited [25] and the readings of the goniometer will be registered. The mean score of three trials with 10 seconds between each examination will be calculated and used for analysis.
5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a self-reported questionnaire concerning 21 activities of daily living (ADL) items and eight sports subscale items.[26] Each item is scored on a 0-4 point Likert scale anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores indicating a higher level of function. The FAAM has a maximum potential score of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and sport subscale scores) is divided by the maximum potential score and multiplied by 100 to obtain a percentage. If the patient does not respond, the specific

question will be left blank and not be a part of the final value of the questionnaire. In this trial, we will use the previously validated Chinese version of the FAAM.[27]

6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after randomization: PFT will be measured at the thickest point closest to the calcaneal insertion in its medial portion using ultrasound. The ultrasound scan will be performed using an 8-12 MHz linear probe with the patient in the prone position at the baseline and at 4 weeks after randomization.
7. Participant global assessment of improvement: Participants will be asked to rate their global improvement using a 7-point scale. The improvement will be scaled from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious improvement, 3 being a little improvement, 4 being no change, 5 being a little worse, and 6 being obviously worse. The proportions of participants with different degrees of improvement will be assessed at 4, 8, and 16 weeks after randomization. Scales of participant global assessment of improvement with 7 response categories have been rated as relatively easy to use and show good reliability and validity.[28]
8. Participants' expectation towards acupuncture at baseline: At baseline, participants in the acupuncture and SA groups will be asked the following question: "Do you think acupuncture will be helpful to improve your chronic PF?" Participant will choose one of the following answers: "Extremely helpful", "Very helpful", "Helpful", "Not help at all", and "Unclear".
9. The proportion of participants who have maintained blinding during treatment in the acupuncture and SA groups: Participants' blindness to the mode of acupuncture will be assessed five minutes after the end of any treatment in the fourth week by asking the patients the following question: "Which of the two

acupuncture modalities do you think you received, acupuncture or SA?" Participants will choose one of the following answers: "Acupuncture", "SA", or "Unclear". Prior to the question, patients will be informed that they may have received one of two modalities: acupuncture with a deeper insertion or SA with no skin penetration.

Safety assessment

The adverse events (AEs) during the entire study will be recorded and described as acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8, using VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness, vomiting, headache, palpitations). Detailed information on AEs including the name, onset, end date, intensity, correlation with acupuncture, and outcomes will be documented in the case report form. Investigators will immediately report serious AEs (eg, requiring hospitalization, causing disability or impaired ability to work) to the Medical Ethics Committee of Guang'anmen Hospital, and stop the clinical trial until further instruction is given.

Sample size calculation

Based on the results of a previous study,[12] a sample size of 120 participants will be enrolled to provide 80% power to detect a difference of 35% between the combined acupuncture group and waiting-list group in the proportion of participants with treatment response 4 weeks after randomization at a two-sided significance level of 0.05. The proportion of participants with treatment response after 4 weeks was assumed to be roughly 12% for the waiting-list group, [12] with an anticipated 10% loss to follow-up.

Statistical analysis

The null hypothesis is that the proportion of participants with treatment response 4 weeks after randomization will be the same for the combined acupuncture groups and waiting-list group. Data will be presented as mean ± standard deviation for quantitative variables and frequencies (number of cases), with relative frequencies (percentages) for categorical variables. The primary outcome analysis will use the Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the combined acupuncture groups and the waiting-list group. If the result of this analysis is significant, hierarchical testing will be applied to the acupuncture group versus waiting-list group, SA group versus waiting-list group, and acupuncture group versus SA group. For normally distributed quantitative variables, a repeated-measures analysis of variance (ANOVA) with multiple comparisons post-hoc test will be performed using baseline as a co-variate when comparing more than two groups and an unpaired T test when comparing two groups. For non-normally distributed quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney test will be performed. For categorical variables, the Chi square (χ^2) test will be used. Confidence intervals for the difference between treatments will be calculated at the 95% level. A two-tailed test will be applied for all available data, and a P value < 0.05 will be considered statistically significant. All analyses in this trial will be performed using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the basis of the intention-to-treat (ITT) population, which will include participants who had been randomized. Missing data will be completed as the last value observed before dropout. Only the analysis of primary outcome will be considered in a confirmatory manner. No adjustment will be made for multiple comparisons as those analyses of secondary outcomes will be interpreted as exploratory.

Quality control

To ensure the quality of the trial, all the relevant staff will be uniformly trained before the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF, inclusion and exclusion criteria, intervention procedures, and outcome measures). Licensed acupuncturists with at least 2 years' acupuncture experience will perform the treatment. Throughout the trial, strict three-level monitoring will be conducted for data quality control. Dropouts and withdrawals including the reasons will be recorded during the trial. Paper-based study data will be stored in locked file cabinets under the management of the investigators. Electronic records will be stored in a Structured Query Language (SQL) server database on a limited access, secure server maintained by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

Patient and public involvement

The research question of whether combined acupuncture and SA will result in larger improvements in heel pain than no acupuncture treatment for patients with chronic PF was first proposed by the investigator after encountering a patient who received SA and reported a similar improvement in heel pain as another patient who received routine acupuncture in the clinic. Patients were not involved in conceiving or implementing the study.

Ethics and dissemination

This trial will be conducted in accordance with the principles of the Declaration of Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign the informed consent form prior to randomization, and they will be permitted to withdraw at any time during the trial, with or without reasons being provided. Any

amendment or other change of the protocol will need to be approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of Chinese Medical Science, and agreed to by the co-researchers.

Following analysis of the data, the findings of this study will be submitted for publication in a peer-reviewed medical journal. The results will also be disseminated through presentation at the relevant conferences and scientific meetings.

Discussion

Although several reviews and RCTs [15,16,12,29] have been published that focus on acupuncture for PF, owing to the lack of a placebo control, non-specific physiology effects of needling and spontaneous remission of PF cannot be excluded. To date, this is the first randomized trial with three parallel arms, assessing whether combined acupuncture and SA compared to no treatment control produce a significant reduction in pain intensity in chronic PF. We anticipate that this study will determine the efficacy of acupuncture for patients with chronic PF, and improve the care of these patients in the clinic.

Though most PF patients will achieve significant improvement in symptoms within 1 year regardless of treatment,[30] many will seek treatment before then. Patients often choose other treatment options when they cannot obtain a satisfactory outcome from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic participants who had failed to respond to conservative treatment prior to participation. The results can be generalized to patients experiencing chronic refractory PF.

In this study, pain intensity measured with VAS during the first steps in the morning will be used as the primary outcome. This variable has been used in previous trials [12,21] and is a meaningful subject outcome measure for the assessment of PF

improvement. In addition, we will also use PPT and PFT as objective secondary outcomes. PPT is an essential evaluation tool for patients suffering from many musculoskeletal disorders including PF and provides a reliable process for measuring participants' responses to mechanical stimuli.[31] Compared to normal asymptomatic patients, patients with PF often exhibit a thickened plantar fascia on ultrasound. [32] Therefore, a PFT evaluation would provide information to detect the anatomical changes that occur in the plantar fascia after acupuncture.

The strengths of this study include a sham control (non-penetrating at non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT, PFT), strict quality control, and evaluation of the participants' expectations regarding acupuncture. We chose sham acupuncture as a placebo treatment for this study to confirm the specific physiological effect of needling because sham acupuncture may be preferable, particularly for Chinese patients who are familiar with the general procedure of acupuncture. Several limitations to this trial need to be acknowledged. First, it will be impossible to blind the acupuncturists and participants in the waitlist control group, which is a general problem in non-pharmacological interventional trials and can cause bias. Second, a high dropout rate may exist in the waitlist group because participants expect to receive acupuncture treatment when they join the trial. Third, the follow-up period will not exceed 12 weeks, which will not allow for detection of the long-term effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw conclusions about the selected acupuncture points but not about individualized treatments.

Ethical Approval and Consent to participate The study has received approval from the Institutional Review Boards of Guang'anmen Hospital in China (approval NO. 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the Helsinki Declaration.

Consent for publication Not applicable.

Availability of data and materials Not applicable.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions Weiming Wang and Zhishun Liu conceived the idea and designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang Li will be responsible for the recruitment, acupuncture, and assessment respectively. Yan Liu will be responsible for statistical analysis. This manuscript was drafted by Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All authors read and approved the final draft of the manuscript.

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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

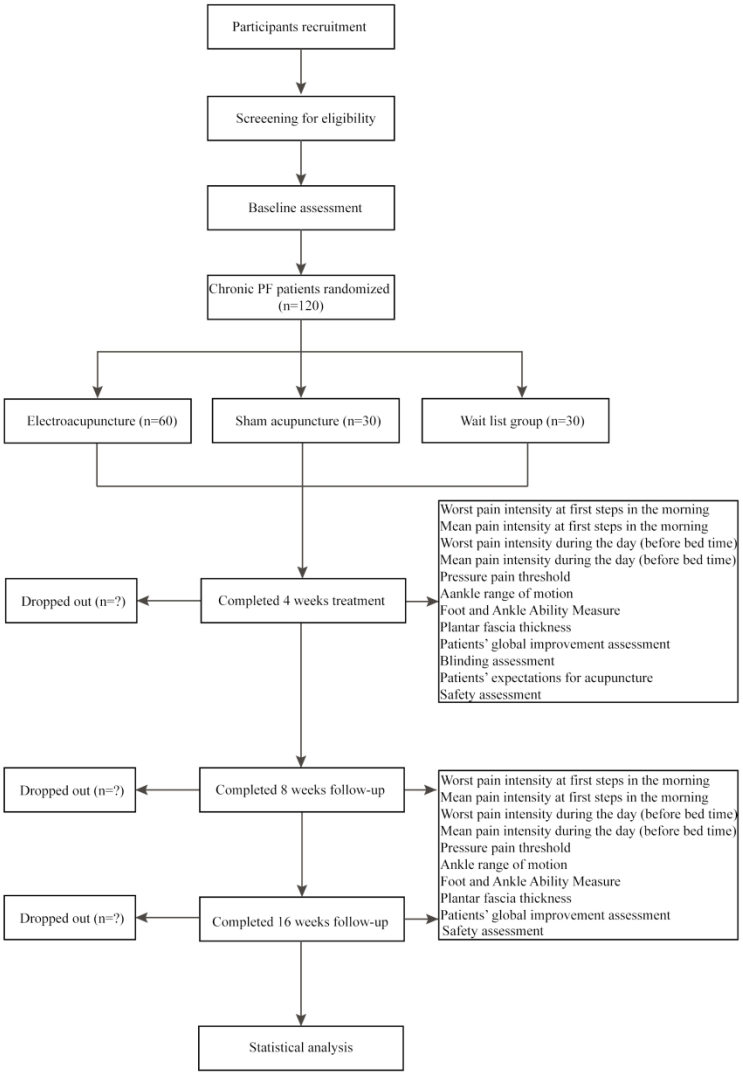

Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

	Study Period				
	Baseline	**Allocation**	**Treatment**	**Follow-up**	
TIME POINT (W, week)			W 4±2d	W 8±3d	W16±3d
Enrollment					
Eligibility criteria	×				
Demography characteristics	×				
Disease history of chronic plantar fasciitis	×				
Eligibility screen	×				
Informed consent	×				
Allocation		×			
Interventions					
Acupuncture			×(weeks1-4)		
Sham acupuncture			×(weeks1-4)		
Waitlist control (no treatment)			×(weeks1-4)		
Assessments					
Worst pain intensity at first steps in the morning	×		×	×	×
Mean pain intensity during the day	×		×	×	×
Pressure pain threshold	×		×	×	×
Ankle range of motion	×		×	×	×
Foot and Ankle Ability Measure	×		×	×	×
Plantar fascia thickness	×		×		
Participant global improvement assessment			×	×	×
Participants′ expectation towards acupuncture	×				
Blinding assessment					
Adverse events			×	×	×
Safety assessment			×	×	×

Figure 2: study schedule

Study schedule

199x194mm (300 x 300 DPI)

Table 1

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	3
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	14
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13

Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	6
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	6
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	6

	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14-15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	14
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13-14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	16,19

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	19
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
	31b	Authorship eligibility guidelines and any intended use of professional writers	19
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.