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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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3 Title page
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7 Article title:
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10 **Efficacy of acupuncture vs sham acupuncture or waitlist control for**
11 **patients with chronic plantar fasciitis: study protocol for a 2-center**
12 **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

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4 at a peer-reviewed medical journal, the relevant conferences and scientific meetings.
5

6 **Key words:** acupuncture; chronic plantar fasciitis; pain intensity; clinical trial
7

8
9 **Trial registration:** ClinicalTrials.gov identifier: NCT 04185259.
10

11 **Strengths and limitations of this study:**
12

13
14 ▶ This study is the first randomized controlled trial comparing combined
15
16 acupuncture and sham acupuncture versus waitlist control for pain relief in
17
18 participants with chronic PF.
19

20
21
22 ▶ Sham control and waitlist control design, objective measurements (i.e. PPT, PFT),
23
24 strict quality control and evaluation of participants' expectation regarding
25
26 acupuncture, aiming to reduce the risk of bias.
27

28
29
30 ▶ Acupuncturists and participants in the waitlist control group will not be blinded,
31
32 which may cause bias.
33

34
35 ▶ A high dropout rate may exist in the waitlist group because participants expect to
36
37 receive acupuncture treatment when they join the trial.
38

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40 ▶ The 12-week follow-up will not allow the detection of the long-term effects of
41
42 acupuncture on chronic PF.
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Background

Plantar fasciitis (PF), which presents with heel pain and tenderness particularly at the plantar aspect of the calcaneal tuberosity¹ 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 lifetime² and this condition is attributed to PF in 80% of cases.³ PF predominantly affects elderly and middle-aged individuals⁴ 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 cases¹¹ 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

1
2
3 for thousands of years. Mechanistic studies have revealed that acupuncture can induce
4 an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin,
5 β -endorphin, and endomorphin).¹⁵ Two recent systematic reviews ^{16,17} found that
6 acupuncture may reduce pain intensity and improve plantar function for patients with
7 PF. However, there were methodological problems with the small sample sizes, lack
8 of control with a placebo/waitlist group, or no adjustment for the confounding effects
9 of patients who received combination treatments in the design of the included
10 acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous
11 remission of PF cannot be excluded and the beneficial effects of acupuncture for PF
12 remain in need of further assessment.
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26 We designed a randomized controlled trial to evaluate the efficacy of acupuncture,
27 compared with sham acupuncture (SA) or being on a waitlist control group, for
28 patients with chronic PF for >6 months. Given that clinical and experimental results
29 have shown that SA can induce a significant alleviation of pain similar to verum
30 acupuncture ¹⁸ due to non-specific effects (e.g., acupuncture expectations), the
31 primary hypothesis in this trial was that combined acupuncture and SA will result in
32 larger improvements in heel pain than no acupuncture treatment in patients with
33 chronic PF. The secondary hypothesis examined whether acupuncture can reduce heel
34 pain intensity more effectively than SA or no acupuncture.
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47 **Methods and design**

48 **Study design**

49 This will be a two-center, parallel-group, sham and no-treatment controlled,
50 assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate.
51 We will design the protocol in accordance with standard protocol items including the
52 Recommendations for Interventional Trials ¹⁹ and the Standards for Reporting
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2
3 Interventions in the Clinical Trials of Acupuncture²⁰ guidelines. The study flow chart
4
5 and study schedule are shown in Figs. 1 and 2.
6
7

8 **Study setting and recruitment**

9
10 This trial is planned to be conducted at Guang'anmen Hospital, China Academy of
11
12 Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from
13
14 March 2020 to March 2022. A total of 120 participants will be publicly recruited
15
16 through the use of posters and hospital webs in the two participating hospitals. The
17
18 duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week
19
20 treatment, and 12-week follow-up.
21
22

23 **Randomization and Blinding**

24
25 The eligible participants who sign an informed consent form will complete a 1-week
26
27 baseline assessment before randomization. Participants will be randomized into the
28
29 acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of 2:1:1
30
31 using simple randomization. Randomization will be generated with the PROC PLAN
32
33 in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group allocation will
34
35 be concealed on cards inside sealed opaque envelopes by the staff member
36
37 responsible for the allocation. A research coordinator, who will not be involved in the
38
39 treatment and outcome assessments, will be responsible for contacting participants
40
41 and allocating them to their assigned group. Participants in the acupuncture and SA
42
43 groups, together with efficacy evaluators and data analysts will be blinded to the
44
45 group assignments. Participants in the waitlist control group and acupuncturists will
46
47 not be blinded.
48
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53 **Participants**

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55 Participants with a diagnosis of PF by an orthopedist on clinical grounds will be
56
57 included in the study only if they meet all of the following inclusion criteria and do
58
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1
2
3 not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the
4
5 guidelines described by the Orthopaedic Section of American Physical Therapy
6
7 Association.²¹ The following clinical findings will be used to diagnose PF: plantar
8
9 medial heel pain during the initial steps after a period of inactivity but also worse pain
10
11 following prolonged weight bearing, heel pain precipitated by a recent increase in
12
13 weight-bearing activity, physical examination findings (heel pain with palpation of
14
15 the proximal insertion of the plantar fascia), as well as a positive windlass test and
16
17 negative tarsal tunnel tests.
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22 **Inclusion criteria:**

- 23
24 1. Age ≥ 18 years and ≤ 75 years;
25
26 2. History of plantar medial heel pain for at least 6 months before enrolment;
27
28 3. Reported an average worst pain intensity at first steps in the morning over the last
29
30 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before
31
32 enrolment;
33
34 4. Failure to respond to conservative treatment for ≥ 1 months, including any of the
35
36 following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs,
37
38 and orthotics;
39
40 5. Ability to comply with the study protocol, understand the medical information
41
42 forms as well as having provided informed consent.
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46

47
48 **Exclusion criteria:**

- 49
50 1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture,
51
52 or having a significant foot deformity (clubfoot, pes cavus, or pes
53
54 calcaneovalgus);
55
56 2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or
57
58 radiation, or surgery to plantar fascia within 6 months preceding enrollment;
59
60

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- 2
- 3 3. Radiculopathy or peripheral neuropathy around the ankle joint such as nerve
- 4
- 5 entrapment tarsal tunnel syndrome or Achilles tendinopathy;
- 6
- 7
- 8 4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2
- 9
- 10 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
- 11
- 12
- 13 5. Joint, bone, or skin infection in the affected foot;
- 14
- 15 6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or
- 16
- 17 coagulation disorder at baseline as determined by the investigator;
- 18
- 19 7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks
- 20
- 21 prior to enrollment.
- 22

23 **Interventions**



24 **Acupuncture group**

25

26 The acupuncture protocol was developed by the consensus of three experts based on

27

28 the meridian theory of TCM and was used in our previous trial.²² Licensed

29

30 acupuncturists with more than 2 years of acupuncture experience will perform the

31

32 treatment. We will apply needles to two Ashi points (the two most severe tender

33

34 points in the most sensitive area over the anteromedial aspect of the heels, according

35

36 to the participant's perceived pain upon palpation) as well as the Chengshan (BL57),

37

38 Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the

39

40 aforementioned acupoints will be based on the Nomenclature and location of

41

42 acupuncture points ²³ designated by the National Standard of the People's Republic of

43

44 China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand,

45

46 Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used.

47

48 With the patient in a prone position, the local skin will be routinely sterilized,

49

50 followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato

51

52 brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected

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1
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3 acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar
4 fascia layer with a depth of approximately 15-20 mm depending on the location.
5
6 BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin
7
8 through the pad. All needles except the Ashi points will be manually stimulated with
9
10 small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi
11
12 (a sensation including soreness, numbness, distention, and heaviness).²⁴ Needles will
13
14 be retained for 30 minutes per treatment. During each treatment, every needle will be
15
16 manipulated three times every 10 minutes.
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20

21 **SA group**

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23 In the SA group, sham Ashi (0.5 cun away from Ashi, one ‘cun’ is equivalent to the
24 greatest width of the individual patients’ thumb, ~1.5 cm), sham BL57 (0.5 cun lateral
25 to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the
26 heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon)
27
28 will be used. The treatment protocol will be similar to that of the acupuncture group.
29
30 The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be
31
32 inserted at the sham points through the adhesive pads attached to the skin without skin
33
34 penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three
35
36 times every 10 minutes. No specific De qi response will be elicited.
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45 **Waitlist control group**

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47 Participants will receive no treatment for their heel pain for a period of 16 weeks after
48 randomization, and subsequently have the option of 4 weeks (12 sessions) of
49
50 acupuncture free of charge at the end of the follow-up period.
51
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53
54 The intervention will last for 30 minutes in the acupuncture and SA groups, and
55
56 will be performed three times per week for a total of 12 sessions in four consecutive
57
58 weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides
59
60

1
2
3 and evaluate the more severe side. Participants in all groups will be treated and (or)
4
5 evaluated separately. Participants in all groups will be advised to use soft heel foot
6
7 wear, not to stand for a long time, and not to walk barefoot during the study.
8
9

10 **Rescue medication**

11
12 Additional therapies for heel pain during the entire study period will be prohibited.
13
14 However, the investigator will be permitted to prescribe ibuprofen (sustained release
15
16 type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as
17
18 rescue medication no more than 2 days per week up to the maximum daily dose if
19
20 unbearable heel pain occurs. Participants will be required not to take rescue
21
22 medication within 72 h before the baseline and outcome measurements. In the event
23
24 rescue medication needs to be taken after the baseline measurement, the participant
25
26 will postpone the next visit to the treatment center.
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30 **Outcome measures**

31 **Primary outcome**

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33 The primary outcome used in this trial will be the proportion of participants with a
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35 treatment response 4 weeks after randomization, defined as a minimum of 50%
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37 improvement in the worst pain intensity during the first steps in the morning
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39 compared with the baseline. The average worst pain intensity over the last 3 days will
40
41 be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS,
42
43 with 0 indicating no pain and 100 indicating maximal pain. Participants who must
44
45 resort to additional treatments other than rescue medication will be classified as
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47 nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be
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49 assessed.
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55 **Secondary outcomes**

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57 The secondary outcomes are as follows:
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3 1. Changes in the VAS score for worst pain intensity during the first steps in the
4 morning from baseline to 4, 8, and 16 weeks after randomization;
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- 8 2. Changes in the VAS score for mean pain intensity during the day from baseline to
9
10 4, 8, and 16 weeks after randomization;
11
12
- 13 3. Changes in the pressure pain threshold (PPT) at the most painful area from
14 baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the
15 minimum pressure detected when the sensation of pressure first changes to a
16 sensation of pain.²⁵ PPT will be tested with a pressure algometer (Fabrication
17 Enterprises, Inc., White Plains, NY; from 1 kg/cm² to 5 kg/cm²) using a metal
18 probe with a 0.5 cm² rubber disc by a trained researcher. PPT will be measured
19 when the participant is lying supine in a relaxed position with the affected foot
20 hanging over the edge of the bed. When measuring the PPT, the rubber disc will
21 be placed perpendicularly on the painful spot and pressure will be applied at a rate
22 of approximately 0.1 kg/cm²/s through the metal probe of the pressure algometer.
23 Participants will be informed to report when the initial pain sensation occurs, and
24 the readings of the algometer will be recorded. The score will be determined by
25 averaging three repeated measurements with 30 seconds between each trial. All
26 values below 1 kg/cm² will be reported as 0.5 kg/cm².
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- 45 4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16
46 weeks after randomization: The examiner will measure the AROM including
47 plantar dorsiflexion and plantar flexion using a digital goniometer (Tangxia
48 Electronic Instrument Factory, Dongguan, from 0° to 360°). Prior to the
49 measurement, the participant will sit in a relaxed station with the popliteal space at
50 the edge of the table and their knees with 90° of flexion. The axis of the
51 goniometer will be placed at the lateral malleolus. The stationary arm will be
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3 placed parallel to the fifth metatarsal and the moving arm placed parallel to the
4
5 center of the fibular head. The ankle will be passively moved from a neutral
6
7 starting position into dorsiflexion and flexion until a firm end feel is elicited²⁶ and
8
9 the readings of the goniometer will be registered. The mean score of three trials
10
11 with 10 seconds between each examination will be calculated and used for
12
13 analysis.
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- 16
17 5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale
18
19 scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a
20
21 self-reported questionnaire concerning 21 activities of daily living (ADL) items
22
23 and eight sports subscale items.²⁷ Each item is scored on a 0-4 point Likert scale
24
25 anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores
26
27 indicating a higher level of function. The FAAM has a maximum potential score
28
29 of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and
30
31 sport subscale scores) is divided by the maximum potential score and multiplied
32
33 by 100 to obtain a percentage. If the patient does not respond, the specific
34
35 question will be left blank and not be a part of the final value of the questionnaire.
36
37 In this trial, we will use the previously validated Chinese version of the FAAM.²⁸
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41
42 6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after
43
44 randomization: PFT will be measured at the thickest point closest to the calcaneal
45
46 insertion in its medial portion using ultrasound. The ultrasound scan will be
47
48 performed using an 8-12 MHz linear probe with the patient in the prone position
49
50 at the baseline and at 4 and 16 weeks after randomization.
51
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54 7. Participant global assessment of improvement: Participants will be asked to rate
55
56 their global improvement using a 7-point scale. The improvement will be scaled
57
58 from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious
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60

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3 improvement, 3 being a little improvement, 4 being no change, 5 being a little
4
5 worse, and 6 being obviously worse. The proportions of participants with different
6
7 degrees of improvement will be assessed at 4, 8, and 16 weeks after
8
9 randomization.
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11

- 12 8. Participants' expectation towards acupuncture at baseline: At baseline,
13
14 participants in the acupuncture and SA groups will be asked the following
15
16 question: "Do you think acupuncture will be helpful to improve your chronic PF?"
17
18 Participant will choose one of the following answers: "Extremely helpful", "Very
19
20 helpful", "Helpful", "Not help at all", and "Unclear".
21
22
- 23 9. The proportion of participants who have maintained blinding during treatment in
24
25 the acupuncture and SA groups: Participants' blindness to the mode of
26
27 acupuncture will be assessed five minutes after the end of any treatment in the
28
29 fourth week by asking the patients the following question: "Which of the two
30
31 acupuncture modalities do you think you received, acupuncture or SA?"
32
33 Participants will choose one of the following answers: "Acupuncture", "SA", or
34
35 "Unclear". Prior to the question, patients will be informed that they may have
36
37 received one of two modalities: acupuncture with a deeper insertion or SA with no
38
39 skin penetration.
40
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44 **Safety assessment**

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46 The adverse events (AEs) during the entire study will be recorded and described as
47
48 acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs
49
50 include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8 , using
51
52 VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or
53
54 symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness,
55
56 vomiting, headache, palpitations). Detailed information on AEs including the name,
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2
3 onset, end date, intensity, correlation with acupuncture, and outcomes will be
4
5 documented in the case report form. Investigators will immediately report serious AEs
6
7 (eg, requiring hospitalization, causing disability or impaired ability to work) to the
8
9 Medical Ethics Committee of Guang'anmen Hospital, and stop the clinical trial until
10
11 further instruction is given.
12
13

14 **Sample size calculation**

15
16 Based on the results of a previous study,¹³ a sample size of 120 participants will be
17
18 enrolled to provide 80% power to detect a difference of 35% between the combined
19
20 acupuncture group and waiting-list group in the proportion of participants with
21
22 treatment response 4 weeks after randomization at a two-sided significance level of
23
24 0.05. The proportion of participants with treatment response after 4 weeks was
25
26 assumed to be roughly 12% for the waiting-list group¹³, with an anticipated 10% loss
27
28 to follow-up.
29
30
31

32 **Statistical analysis**

33
34 The null hypothesis is that the proportion of participants with treatment response 4
35
36 weeks after randomization will be the same for the combined acupuncture groups and
37
38 waiting-list group. Data will be presented as mean \pm standard deviation for
39
40 quantitative variables and frequencies (number of cases), with relative frequencies
41
42 (percentages) for categorical variables. The primary outcome analysis will use the
43
44 Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the
45
46 combined acupuncture groups and the waiting-list group. If the result of this analysis
47
48 is significant, hierarchical testing will be applied to the acupuncture group versus
49
50 waiting-list group, SA group versus waiting-list group, and acupuncture group versus
51
52 SA group. For normally distributed quantitative variables, a repeated-measures
53
54 analysis of variance (ANOVA) with multiple comparisons post-hoc test will be used
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3 when comparing more than two groups and an unpaired T test when comparing two
4
5 groups. For non-normally distributed quantitative variables, the non-parametrical
6
7 Kruskal-Wallis test and Mann-Whitney test will be performed. For categorical
8
9 variables, the Chi square (χ^2) test will be used. A two-tailed test will be applied for all
10
11 available data, and a *P* value < 0.05 will be considered statistically significant. All
12
13 analyses in this trial will be performed using SPSS software V.20.0 (IBM SPSS
14
15 Statistics; IBM Corp, Somers, NY) on the basis of the intention-to-treat (ITT)
16
17 population, which will include participants who had been randomized. Missing data
18
19 will be completed as the last value observed before dropout.
20
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23 24 **Quality control**

25
26 To ensure the quality of the trial, all the relevant staff will be uniformly trained before
27
28 the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF,
29
30 inclusion and exclusion criteria, intervention procedures, and outcome measures).
31

32
33 Licensed acupuncturists with at least 2 years' acupuncture experience will perform
34
35 the treatment. Throughout the trial, strict three-level monitoring will be conducted for
36
37 data quality control. Dropouts and withdrawals including the reasons will be recorded
38
39 during the trial. Paper-based study data will be stored in locked file cabinets under the
40
41 management of the investigators. Electronic records will be stored in a Structured
42
43 Query Language (SQL) server database on a limited access, secure server maintained
44
45 by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.
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49 **Patient and public involvement**

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51 The research question of whether combined acupuncture and SA will result in larger
52
53 improvements in heel pain than no acupuncture treatment for patients with chronic PF
54
55 was first proposed by the investigator after encountering a patient who received SA
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57 and reported a similar improvement in heel pain as another patient who received
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3 routine acupuncture in the clinic. Patients were not involved in conceiving or
4
5 implementing the study.
6

7 **Ethics and dissemination**

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10 This trial will be conducted in accordance with the principles of the Declaration of
11
12 Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and
13
14 approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of
15
16 Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign
17
18 the informed consent form prior to randomization, and they will be permitted to
19
20 withdraw at any time during the trial, with or without reasons being provided. Any
21
22 amendment or other change of the protocol will need to be approved by the Ethical
23
24 Committee of the Guang'anmen Hospital, China Academy of Chinese Medical
25
26 Science, and agreed to by the co-researchers.
27
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31 Following analysis of the data, the findings of this study will be submitted for
32
33 publication in a peer-reviewed medical journal. The results will also be disseminated
34
35 through presentation at the relevant conferences and scientific meetings.
36

37 **Discussion**

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39 Although several reviews and RCTs ^{16,17,13,29} have been published that focus on
40
41 acupuncture for PF, owing to the lack of a placebo control, non-specific physiology
42
43 effects of needling and spontaneous remission of PF cannot be excluded. To date, this
44
45 is the first randomized trial with three parallel arms, assessing whether combined
46
47 acupuncture and SA compared to no treatment control produce a significant reduction
48
49 in pain intensity in chronic PF. We anticipate that this study will determine the
50
51 efficacy of acupuncture for patients with chronic PF, and improve the care of these
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53 patients in the clinic.
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3 Though most PF patients will achieve significant improvement in symptoms
4
5 within 1 year regardless of treatment,³⁰ many will seek treatment before then. Patients
6
7 are often interested in alternative treatment options when they cannot obtain a
8
9 satisfactory outcome from conservative treatment. In this trial, we recruited only
10
11 chronic participants who had failed to respond to conservative treatment prior to
12
13 participation. The results can be generalized to patients experiencing chronic
14
15 refractory PF.
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18
19 In this study, pain intensity measured with VAS during the first steps in the
20
21 morning will be used as the primary outcome. This variable has been used in previous
22
23 trials^{13,22} and is a meaningful subject outcome measure for the assessment of PF
24
25 improvement. In addition, we will also use PPT and PFT as objective secondary
26
27 outcomes. PPT is an essential evaluation tool for patients suffering from many
28
29 musculoskeletal disorders including PF and provides a reliable process for measuring
30
31 participants' responses to mechanical stimuli.³¹ Compared to normal asymptomatic
32
33 patients, patients with PF often exhibit a thickened plantar fascia on ultrasound.³²
34
35 Therefore, a PFT evaluation would provide information to detect the anatomical
36
37 changes that occur in the plantar fascia after acupuncture.
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41 The strengths of this study include a sham control (non-penetrating at
42
43 non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT,
44
45 PFT), strict quality control, and evaluation of the participants' expectations regarding
46
47 acupuncture. Several limitations to this trial need to be acknowledged. First, it will be
48
49 impossible to blind the acupuncturists and participants in the waitlist control group,
50
51 which is a general problem in non-pharmacological interventional trials and can cause
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53 bias. Second, a high dropout rate may exist in the waitlist group because participants
54
55 expect to receive acupuncture treatment when they join the trial. Third, the follow-up
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3 period will not exceed 12 weeks, which will not allow for detection of the long-term
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5 effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw
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7 conclusions about the selected acupuncture points but not about individualized
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9 treatments.
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For peer review only

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6 **Ethical Approval and Consent to participate** The study has received approval from
7
8 the Institutional Review Boards of Guang'anmen Hospital in China (approval NO.
9
10 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the
11
12 Helsinki Declaration.
13
14

15
16 **Consent for publication** Not applicable.
17

18
19 **Availability of data and materials** All data are fully available without restriction.
20

21
22 **Competing interests** The authors declare that they have no competing interests.
23

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25 No. ZZ13-YQ-019). The funding agency has no role in the design of the study; data
26 collection, management, analysis, and interpretation of the data; preparation, review,
27 or approval of the manuscript.
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30

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33
34 **Authors' contributions** Weiming Wang and Zhishun Liu conceived the idea and
35 designed this trial. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang Li will be
36 responsible for the recruitment, acupuncture, and assessment respectively. Yan Liu
37 will be responsible for statistical analysis. This manuscript was drafted by Weiming
38 Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All authors read
39 and approved the final draft of the manuscript.
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52 **Acknowledgments** The authors appreciate the support and efforts from people who
53 will be included in this study.
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4 **Figure legends**

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6 Figure 1: Trial flow diagram

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9 Figure 2: Study schedule

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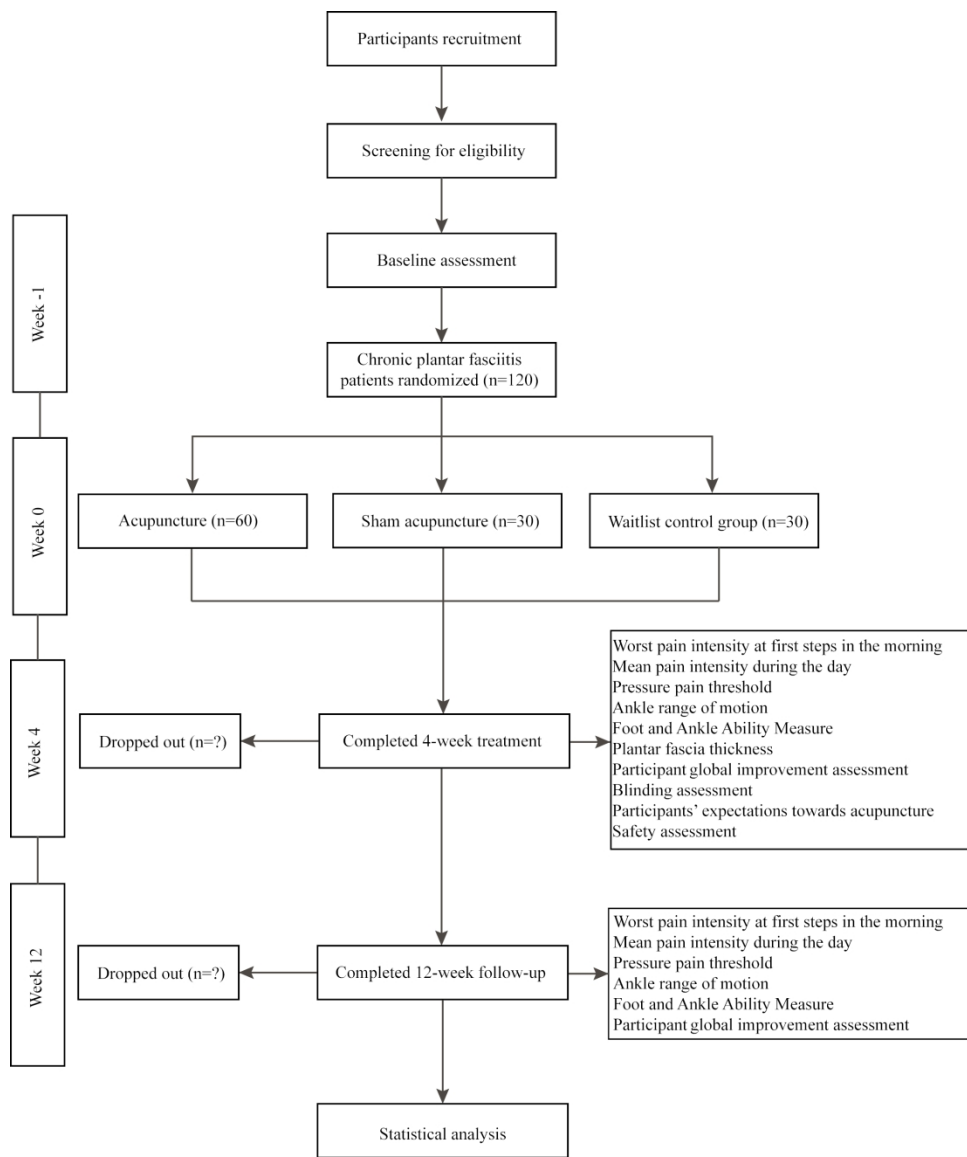


Figure 1. Trial flow diagram

Trial flow diagram

199x246mm (300 x 300 DPI)

TIME POINT (W, week)	Study Period				
	Baseline	Allocation	Treatment	Follow-up	
			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
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	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
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5	Protocol	25	Plans for communicating important protocol modifications (eg, changes to	16
6	amendments		eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators,	
7			REC/IRBs, trial participants, trial registries, journals, regulators)	
8				
9	Consent or	26a	Who will obtain informed consent or assent from potential trial participants	6
10	assent		or authorised surrogates, and how (see Item 32)	
11				
12		26b	Additional consent provisions for collection and use of participant data and	NA
13			biological specimens in ancillary studies, if applicable	
14				
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16	Confidentiality	27	How personal information about potential and enrolled participants will be	19
17			collected, shared, and maintained in order to protect confidentiality before,	
18			during, and after the trial	
19				
20	Declaration of	28	Financial and other competing interests for principal investigators for the	19
21	interests		overall trial and each study site	
22				
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24	Access to	29	Statement of who will have access to the final trial dataset, and disclosure	19
25	data		of contractual agreements that limit such access for investigators	
26				
27	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for compensation to	NA
28	post-trial care		those who suffer harm from trial participation	
29				
30	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to	16
31	policy		participants, healthcare professionals, the public, and other relevant groups	
32			(eg, via publication, reporting in results databases, or other data sharing	
33			arrangements), including any publication restrictions	
34				
35				
36		31b	Authorship eligibility guidelines and any intended use of professional	19
37			writers	
38				
39		31c	Plans, if any, for granting public access to the full protocol, participant-level	NA
40			dataset, and statistical code	
41				
42				
43	Appendices			
44				
45	Informed	32	Model consent form and other related documentation given to participants	NA
46	consent		and authorised surrogates	
47	materials			
48				
49	Biological	33	Plans for collection, laboratory evaluation, and storage of biological	NA
50	specimens		specimens for genetic or molecular analysis in the current trial and for	
51			future use in ancillary studies, if applicable	
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5 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &
6 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.
7 The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-
8 NonCommercial-NoDerivs 3.0 Unported](#)" license.
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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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-036773.R1
Article Type:	Protocol
Date Submitted by the Author:	05-Mar-2020
Complete List of Authors:	Wang, Weiming; Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Department of acupuncture Liu, Sixing; Guizhou University of Traditional Chinese Medicine, School of Acupuncture-Moxibustion and Tuina, Liu, Yan Zang, Zhiwei; Yantai Hospital of Traditional Chinese Medicine, Department of Acupuncture Zhang, Weina; Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Department of Acupuncture Li, Liang; Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Department of Ultrasound Liu, zhishun; Guang'an men Hospital Affiliated to China Academy of Chinese Medical Sciences, acupuncture and moxibustion department
Primary Subject Heading:	Medical management
Secondary Subject Heading:	Complementary medicine
Keywords:	COMPLEMENTARY MEDICINE, PAIN MANAGEMENT, Clinical trials < THERAPEUTICS

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3 1 Title page
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7 3 Article title:
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10 4 **Efficacy of acupuncture vs sham acupuncture or waitlist control for**
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12
13 5 **patients with chronic plantar fasciitis: study protocol for a 2-center**
14
15 6 **randomized controlled trial**

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53 25 **Running title:** acupuncture for chronic plantar fasciitis
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57 27 **Word count: abstract 268; main text 4069.**
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1
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3
4 29 **Abstract**

5
6 30 **Introduction:** Plantar fasciitis (PF) is reported to be the most common cause of
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9 31 plantar heel pain. Acupuncture has been used for patients experiencing PF, but
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11
12 32 evidence of the efficacy of acupuncture on PF is limited. The primary objective of this
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14
15 33 trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist
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18 34 control for improving the level of pain experienced by patients suffering from chronic
19
20 35 PF.

21
22 36 **Methods and Analysis:** This will be a two-center, parallel-group, sham and
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24
25 37 no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate
26
27
28 38 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a
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31 39 ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute
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34 40 acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week
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37 41 follow-up. Participants in the waitlist control group will not undergo treatment for a
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40 42 period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of
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42
43 43 acupuncture free of charge at the end of the follow-up period. The primary outcome
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45
46 44 will be the treatment response rate 4 weeks after randomization, assessed as a
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48
49 45 minimum of 50% improvement in the worst pain intensity during the first steps in the
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51
52 46 morning compared with the baseline. All analyses will be performed with a 2-sided *P*
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54
55 47 value of < 0.05 considered significant following the intention-to-treat principle.

56
57 48 **Ethics and Dissemination:** The study has been approved by the Ethical Committee
58
59 49 of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences
60
50 (approval No: 2019-210-KY). The results will be disseminated through presentation

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3
4 51 at a peer-reviewed medical journal, the relevant conferences and scientific meetings.
5

6 52 **Key words:** acupuncture; chronic plantar fasciitis; pain intensity; clinical trial
7

8
9 53 **Trial registration:** ClinicalTrials.gov identifier: NCT 04185259.
10

11 54 **Strengths and limitations of this study:**
12

13
14 55 ▶ This study is the first randomized controlled trial comparing combined
15
16 56 acupuncture and sham acupuncture versus waitlist control for pain relief in
17
18 57 participants with chronic PF.
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21
22 58 ▶ The advantages to this study include sham acupuncture and waitlist control design,
23
24 59 objective measurements (i.e. PPT, PFT), strict quality control and evaluation of
25
26 60 participants' expectation regarding acupuncture.
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30 61 ▶ The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance
31
32 62 patient adherence by allowing more patients to receive acupuncture.
33

34
35 63 ▶ Acupuncturists and participants in the waitlist control group will not be blinded,
36
37 64 which may cause bias.
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39
40 65 ▶ A high dropout rate may exist in the waitlist group because participants expect to
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42 66 receive acupuncture treatment when they join the trial.
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69 **Background**

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

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

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

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3 94 for thousands of years. Mechanistic studies have revealed that acupuncture can induce
4
5 95 an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin,
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7 96 β -endorphin, and endomorphin).¹⁴ Two recent systematic reviews ^{15,16} found that
8
9 97 acupuncture may reduce pain intensity and improve plantar function for patients with
10
11 98 PF. However, there were methodological problems with the small sample sizes, lack
12
13 99 of control with a placebo/waitlist group, or no adjustment for the confounding effects
14
15 100 of patients who received combination treatments in the design of the included
16
17 101 acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous
18
19 102 remission of PF cannot be excluded and the beneficial effects of acupuncture for PF
20
21 103 remain in need of further assessment.

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25
26 104 We designed a randomized controlled trial to evaluate the efficacy of acupuncture,
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28 105 compared with sham acupuncture (SA) or being on a waitlist control group, for
29
30 106 patients with chronic PF for >6 months. Given that clinical and experimental results
31
32 107 have shown that SA can induce a significant alleviation of pain similar to verum
33
34 108 acupuncture ¹⁷due to non-specific effects (e.g., acupuncture expectations), the primary
35
36 109 hypothesis in this trial was that combined acupuncture and SA will result in larger
37
38 110 improvements in heel pain than no acupuncture treatment in patients with chronic PF.
39
40 111 The secondary hypothesis examined whether acupuncture can reduce heel pain
41
42 112 intensity more effectively than SA or no acupuncture.

43 113 **Methods and design**

44 114 **Study design**

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46
47 115 This will be a two-center, parallel-group, sham and no-treatment controlled,
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49 116 assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate.
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51 117 We will design the protocol in accordance with standard protocol items including the
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53 118 Recommendations for Interventional Trials ¹⁸ and the Standards for Reporting
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3 119 Interventions in the Clinical Trials of Acupuncture¹⁹ guidelines. The study flow chart
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5
6 120 and study schedule are shown in Figs. 1 and 2.

7 8 121 **Study setting and recruitment**

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10 122 This trial is planned to be conducted at Guang'anmen Hospital, China Academy of
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12 123 Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from
13
14 124 March 2020 to March 2022. A total of 120 participants will be publicly recruited
15
16
17 125 through the use of posters and hospital webs in the two participating hospitals. The
18
19 126 duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week
20
21
22 127 treatment, and 12-week follow-up.

23 24 128 **Randomization and Blinding**

25
26 129 The eligible participants who sign an informed consent form will complete a 1-week
27
28 130 baseline assessment (see Fig. 2) before randomization. Participants will be
29
30 131 randomized into the acupuncture group, SA group, or waitlist (no acupuncture) group
31
32
33 132 at a ratio of 2:1:1 using simple randomization. Randomization will be generated with
34
35 133 the PROC PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the
36
37 134 group allocation will be concealed on cards inside sealed opaque envelopes by the
38
39 135 staff member responsible for the allocation. A research coordinator, who will not be
40
41
42 136 involved in the treatment and outcome assessments, will be responsible for contacting
43
44 137 participants and allocating them to their assigned group. Participants in the
45
46 138 acupuncture and SA groups, together with efficacy evaluators and data analysts will
47
48
49 139 be blinded to the group assignments. Participants in the waitlist control group and
50
51
52 140 acupuncturists will not be blinded.

53 54 141 **Participants**

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56 142 Participants with a diagnosis of PF by an orthopedist on clinical grounds will be
57
58 143 included in the study only if they meet all of the following inclusion criteria and do
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1
2
3 144 not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the
4
5 145 guidelines described by the Orthopaedic Section of American Physical Therapy
6
7
8 146 Association.²⁰ The following clinical findings will be used to diagnose PF: plantar
9
10 147 medial heel pain during the initial steps after a period of inactivity but also worse pain
11
12 148 following prolonged weight bearing, heel pain precipitated by a recent increase in
13
14 149 weight-bearing activity, physical examination findings (heel pain with palpation of
15
16 150 the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal
17
18 151 foot posture index, high body mass index, as well as a positive windlass test and
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20 152 negative tarsal tunnel tests.
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24 153 **Inclusion criteria:**

- 25
26 154 1. Age ≥ 18 years and ≤ 75 years;
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28 155 2. History of plantar medial heel pain for at least 6 months before enrolment;
29
30 156 3. Reported an average worst pain intensity at first steps in the morning over the last
31
32 157 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before
33
34 158 enrolment;
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36 159 4. Failure to respond to conservative treatment for ≥ 1 months, including any of the
37
38 160 following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs,
39
40 161 shockwave therapy, dry needling and orthotics;
41
42 162 5. Ability to comply with the study protocol, understand the medical information
43
44 163 forms as well as having provided informed consent.
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49 164 **Exclusion criteria:**

- 50
51 165 1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture,
52
53 166 or having a significant foot deformity (clubfoot, pes cavus, or pes
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55 167 calcaneovalgus);
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3 168 2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or
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5 169 radiation, or surgery to plantar fascia within 6 months preceding enrollment;
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8 170 3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such
9
10 171 as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
11
12 172 4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2
13
14 173 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
15
16
17 174 5. Joint, bone, or skin infection in the affected foot;
18
19 175 6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or
20
21 176 coagulation disorder at baseline as determined by the investigator;
22
23
24 177 7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks
25
26 178 prior to enrollment.

179 **Interventions**

180 **Acupuncture group**

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

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3 193 followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato
4
5 194 brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected
6
7 195 acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar
8
9 196 fascia layer with a depth of approximately 15-20 mm depending on the location.
10
11 197 BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin
12
13 198 through the pad. All needles except the Ashi points will be manually stimulated with
14
15 199 small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi
16
17 200 (a sensation including soreness, numbness, distention, and heaviness).²³ Needles will
18
19 201 be retained for 30 minutes per treatment. During each treatment, every needle will be
20
21 202 manipulated three times every 10 minutes.

26 203 **SA group**

28 204 In the SA group, sham Ashi (0.5 cun away from Ashi, one ‘cun’ is equivalent to the
29
30 205 greatest width of the individual patients’ thumb, ~1.5 cm), sham BL57 (0.5 cun lateral
31
32 206 to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the
33
34 207 heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon)
35
36 208 will be used. The treatment protocol will be similar to that of the acupuncture group.
37
38 209 The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be
39
40 210 inserted at the sham points through the adhesive pads attached to the skin without skin
41
42 211 penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three
43
44 212 times every 10 minutes. No specific De qi response will be elicited.

49 213 **Waitlist control group**

51 214 Participants will receive no treatment for their heel pain for a period of 16 weeks after
52
53 215 randomization, and subsequently have the option of 4 weeks (12 sessions) of
54
55 216 acupuncture free of charge at the end of the follow-up period.
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3 217 The intervention will last for 30 minutes in the acupuncture and SA groups, and
4
5 218 will be performed three times per week for a total of 12 sessions in four consecutive
6
7 219 weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides
8
9 220 and evaluate the more severe side. Participants in all groups will be treated and (or)
10
11 221 evaluated separately. Participants in all groups will be advised to use soft heel foot
12
13 222 wear, not to stand for a long time, and not to walk barefoot during the 17-week study
14
15 223 period.

19 224 **Rescue medication**

21 225 Additional therapies for heel pain during the entire study period will be prohibited.
22
23 226 However, the investigator will be permitted to prescribe ibuprofen (sustained release
24
25 227 type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as
26
27 228 rescue medication no more than 2 days per week up to the maximum daily dose if
28
29 229 unbearable heel pain occurs. Participants will be required not to take rescue
30
31 230 medication within 72 h before the baseline and outcome measurements. In the event
32
33 231 rescue medication needs to be taken after the baseline measurement, the participant
34
35 232 will postpone the next visit to the treatment center.

39 233 **Outcome measures**

41 234 **Primary outcome**

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43 235 The primary outcome used in this trial will be the proportion of participants with a
44
45 236 treatment response 4 weeks after randomization, defined as a minimum of 50%
46
47 237 improvement in the worst pain intensity during the first steps in the morning
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49 238 compared with the baseline. The average worst pain intensity over the last 3 days will
50
51 239 be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS,
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53 240 with 0 indicating no pain and 100 indicating maximal pain. Participants who must
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55 241 resort to additional treatments other than rescue medication will be classified as
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3 242 nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be
4
5 243 assessed.

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8 244 **Secondary outcomes**

9
10 245 The secondary outcomes are as follows:

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12 246 1. Changes in the VAS score for worst pain intensity during the first steps in the
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14 247 morning from baseline to 4, 8, and 16 weeks after randomization;
- 15
16
17 248 2. Changes in the VAS score for mean pain intensity during the day from baseline to
18
19 249 4, 8, and 16 weeks after randomization;
- 20
21 250 3. Changes in the pressure pain threshold (PPT) at the most painful area from
22
23 251 baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the
24
25 252 minimum pressure detected when the sensation of pressure first changes to a
26
27 253 sensation of pain.²⁴ PPT will be tested with a pressure algometer (Fabrication
28
29 254 Enterprises, Inc., White Plains, NY; from 1 kg/cm² to 5 kg/cm²) using a metal
30
31 255 probe with a 0.5 cm² rubber disc by a trained researcher. PPT will be measured
32
33 256 when the participant is lying supine in a relaxed position with the affected foot
34
35 257 hanging over the edge of the bed. When measuring the PPT, the rubber disc will
36
37 258 be placed perpendicularly on the painful spot and pressure will be applied at a rate
38
39 259 of approximately 0.1 kg/cm²/s through the metal probe of the pressure algometer.
40
41 260 Participants will be informed to report when the initial pain sensation occurs, and
42
43 261 the readings of the algometer will be recorded. The score will be determined by
44
45 262 averaging three repeated measurements with 30 seconds between each trial. All
46
47 263 values below 1 kg/cm² will be reported as 0.5 kg/cm².
- 48
49 264 4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16
50
51 265 weeks after randomization: The examiner will measure the AROM including
52
53 266 dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee)
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3 267 using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan,
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5 268 from 0° to 360°). For the flexed-knee assessment, the participant will sit in a
6
7
8 269 relaxed station with the popliteal space at the edge of the table and their knees
9
10 270 with 90° of flexion. For the extended-knee assessment, the participant will be
11
12 271 seated on a treatment table with the knees fully extended (0°) and the feet hanging
13
14 272 off the end of the table. The axis of the goniometer will be placed at the lateral
15
16
17 273 malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the
18
19 274 moving arm placed parallel to the center of the fibular head. The ankle will be
20
21
22 275 passively moved from a neutral starting position into dorsiflexion and plantar
23
24 276 flexion until a firm end feel is elicited²⁵ and the readings of the goniometer will
25
26 277 be registered. The mean score of three trials with 10 seconds between each
27
28 278 examination will be calculated and used for analysis.

29
30 279 5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale
31
32 280 scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a
33
34 281 self-reported questionnaire concerning 21 activities of daily living (ADL) items
35
36 282 and eight sports subscale items.²⁶ Each item is scored on a 0-4 point Likert scale
37
38 283 anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores
39
40 284 indicating a higher level of function. The FAAM has a maximum potential score
41
42 285 of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and
43
44 286 sport subscale scores) is divided by the maximum potential score and multiplied
45
46 287 by 100 to obtain a percentage. If the patient does not respond, the specific
47
48 288 question will be left blank and not be a part of the final value of the questionnaire.
49
50 289 In this trial, we will use the previously validated Chinese version of the FAAM.²⁷
51
52
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54 290 6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after
55
56 291 randomization: PFT will be measured at the thickest point closest to the calcaneal
57
58
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3 292 insertion in its medial portion using ultrasound. The ultrasound scan will be
4
5 293 performed using an 8-12 MHz linear probe with the patient in the prone position
6
7
8 294 at the baseline and at 4 weeks after randomization.
9

10 295 7. Participant global assessment of improvement: Participants will be asked to rate
11
12 296 their global improvement using a 7-point scale. The improvement will be scaled
13
14 297 from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious
15
16 298 improvement, 3 being a little improvement, 4 being no change, 5 being a little
17
18 299 worse, and 6 being obviously worse. The proportions of participants with different
19
20 300 degrees of improvement will be assessed at 4, 8, and 16 weeks after
21
22 301 randomization. Scales of participant global assessment of improvement with 7
23
24 302 response categories have been rated as relatively easy to use and show good
25
26 303 reliability and validity.²⁸
27
28
29

30 304 8. Participants' expectation towards acupuncture at baseline: At baseline,
31
32 305 participants in the acupuncture and SA groups will be asked the following
33
34 306 question: "Do you think acupuncture will be helpful to improve your chronic PF?"
35
36 307 Participant will choose one of the following answers: "Extremely helpful", "Very
37
38 308 helpful", "Helpful", "Not help at all", and "Unclear".
39
40
41

42 309 9. The proportion of participants who have maintained blinding during treatment in
43
44 310 the acupuncture and SA groups: Participants' blindness to the mode of
45
46 311 acupuncture will be assessed five minutes after the end of any treatment in the
47
48 312 fourth week by asking the patients the following question: "Which of the two
49
50 313 acupuncture modalities do you think you received, acupuncture or SA?"
51
52 314 Participants will choose one of the following answers: "Acupuncture", "SA", or
53
54 315 "Unclear". Prior to the question, patients will be informed that they may have
55
56 316 received one of two modalities: acupuncture with a deeper insertion or SA with no
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1
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3 317 skin penetration.
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5 318 **Safety assessment**
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7
8 319 The adverse events (AEs) during the entire study will be recorded and described as
9
10 320 acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs
11
12 321 include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8 , using
13
14 322 VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or
15
16 323 symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness,
17
18 324 vomiting, headache, palpitations). Detailed information on AEs including the name,
19
20 325 onset, end date, intensity, correlation with acupuncture, and outcomes will be
21
22 326 documented in the case report form. Investigators will immediately report serious AEs
23
24 327 (eg, requiring hospitalization, causing disability or impaired ability to work) to the
25
26 328 Medical Ethics Committee of Guang'anmen Hospital, and stop the clinical trial until
27
28 329 further instruction is given.
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31

32
33 330 **Sample size calculation**
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35 331 Based on the results of a previous study,¹² a sample size of 120 participants will be
36
37 332 enrolled to provide 80% power to detect a difference of 35% between the combined
38
39 333 acupuncture group and waiting-list group in the proportion of participants with
40
41 334 treatment response 4 weeks after randomization at a two-sided significance level of
42
43 335 0.05. The proportion of participants with treatment response after 4 weeks was
44
45 336 assumed to be roughly 12% for the waiting-list group,¹² with an anticipated 10% loss
46
47 337 to follow-up.
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50
51 338 **Statistical analysis**
52

53 339 The null hypothesis is that the proportion of participants with treatment response 4
54
55 340 weeks after randomization will be the same for the combined acupuncture groups and
56
57 341 waiting-list group. Data will be presented as mean \pm standard deviation for
58
59
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2
3 342 quantitative variables and frequencies (number of cases), with relative frequencies
4
5 343 (percentages) for categorical variables. The primary outcome analysis will use the
6
7 344 Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the
8
9 345 combined acupuncture groups and the waiting-list group. If the result of this analysis
10
11 346 is significant, hierarchical testing will be applied to the acupuncture group versus
12
13 347 waiting-list group, SA group versus waiting-list group, and acupuncture group versus
14
15 348 SA group. For normally distributed quantitative variables, a repeated-measures
16
17 349 analysis of variance (ANOVA) with multiple comparisons post-hoc test will be
18
19 350 performed using baseline as a co-variate when comparing more than two groups and
20
21 351 an unpaired T test when comparing two groups. For non-normally distributed
22
23 352 quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney
24
25 353 test will be performed. For categorical variables, the Chi square (χ^2) test will be used.
26
27 354 Confidence intervals for the difference between treatments will be calculated at the
28
29 355 95% level. A two-tailed test will be applied for all available data, and a *P* value < 0.05
30
31 356 will be considered statistically significant. All analyses in this trial will be performed
32
33 357 using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the
34
35 358 basis of the intention-to-treat (ITT) population, which will include participants who
36
37 359 had been randomized. Missing data will be completed as the last value observed
38
39 360 before dropout. No adjustment will be made for multiple outcomes.

361 **Quality control**

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

1
2
3 367 data quality control. Dropouts and withdrawals including the reasons will be recorded
4
5 368 during the trial. Paper-based study data will be stored in locked file cabinets under the
6
7 369 management of the investigators. Electronic records will be stored in a Structured
8
9
10 370 Query Language (SQL) server database on a limited access, secure server maintained
11
12 371 by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.

14 372 **Patient and public involvement**

16
17 373 The research question of whether combined acupuncture and SA will result in larger
18
19 374 improvements in heel pain than no acupuncture treatment for patients with chronic PF
20
21 375 was first proposed by the investigator after encountering a patient who received SA
22
23 376 and reported a similar improvement in heel pain as another patient who received
24
25 377 routine acupuncture in the clinic. Patients were not involved in conceiving or
26
27 378 implementing the study.

30 379 **Ethics and dissemination**

32
33 380 This trial will be conducted in accordance with the principles of the Declaration of
34
35 381 Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and
36
37 382 approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of
38
39 383 Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign
40
41 384 the informed consent form prior to randomization, and they will be permitted to
42
43 385 withdraw at any time during the trial, with or without reasons being provided. Any
44
45 386 amendment or other change of the protocol will need to be approved by the Ethical
46
47 387 Committee of the Guang'anmen Hospital, China Academy of Chinese Medical
48
49 388 Science, and agreed to by the co-researchers.

51
52
53 389 Following analysis of the data, the findings of this study will be submitted for
54
55 390 publication in a peer-reviewed medical journal. The results will also be disseminated
56
57 391 through presentation at the relevant conferences and scientific meetings.
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3 392 **Discussion**
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5 393 Although several reviews and RCTs^{15,16,12,29} have been published that focus on
6
7 394 acupuncture for PF, owing to the lack of a placebo control, non-specific physiology
8
9 395 effects of needling and spontaneous remission of PF cannot be excluded. To date, this
10
11 396 is the first randomized trial with three parallel arms, assessing whether combined
12
13 397 acupuncture and SA compared to no treatment control produce a significant reduction
14
15 398 in pain intensity in chronic PF. We anticipate that this study will determine the
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17 399 efficacy of acupuncture for patients with chronic PF, and improve the care of these
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19 400 patients in the clinic.
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24 401 Though most PF patients will achieve significant improvement in symptoms
25
26 402 within 1 year regardless of treatment,³⁰ many will seek treatment before then. Patients
27
28 403 often choose other treatment options when they cannot obtain a satisfactory outcome
29
30 404 from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night
31
32 405 splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic
33
34 406 participants who had failed to respond to conservative treatment prior to participation.
35
36 407 The results can be generalized to patients experiencing chronic refractory PF.
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40 408 In this study, pain intensity measured with VAS during the first steps in the
41
42 409 morning will be used as the primary outcome. This variable has been used in previous
43
44 410 trials^{12,21} and is a meaningful subject outcome measure for the assessment of PF
45
46 411 improvement. In addition, we will also use PPT and PFT as objective secondary
47
48 412 outcomes. PPT is an essential evaluation tool for patients suffering from many
49
50 413 musculoskeletal disorders including PF and provides a reliable process for measuring
51
52 414 participants' responses to mechanical stimuli.³¹ Compared to normal asymptomatic
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54 415 patients, patients with PF often exhibit a thickened plantar fascia on ultrasound.³²
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3 416 Therefore, a PFT evaluation would provide information to detect the anatomical
4
5 417 changes that occur in the plantar fascia after acupuncture.
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8 418 The strengths of this study include a sham control (non-penetrating at
9
10 419 non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT,
11
12 420 PFT), strict quality control, and evaluation of the participants' expectations regarding
13
14 421 acupuncture. Several limitations to this trial need to be acknowledged. First, it will be
15
16 422 impossible to blind the acupuncturists and participants in the waitlist control group,
17
18 423 which is a general problem in non-pharmacological interventional trials and can cause
19
20 424 bias. Second, a high dropout rate may exist in the waitlist group because participants
21
22 425 expect to receive acupuncture treatment when they join the trial. Third, the follow-up
23
24 426 period will not exceed 12 weeks, which will not allow for detection of the long-term
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26 427 effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw
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28 428 conclusions about the selected acupuncture points but not about individualized
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33 429 treatments.
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5 431 **Ethical Approval and Consent to participate** The study has received approval from
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7 432 the Institutional Review Boards of Guang'anmen Hospital in China (approval NO.
8
9 433 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the
10
11
12 434 Helsinki Declaration.

13
14 435 **Consent for publication** Not applicable.

15
16 436 **Availability of data and materials** Not applicable.

17
18
19 437 **Competing interests** The authors declare that they have no competing interests.

20
21 438 **Funding** This RCT is funded by China Academy of Chinese Medical Sciences (Grant
22
23 439 No. ZZ13-YQ-019). The funding agency has no role in the design of the study; data
24
25 440 collection, management, analysis, and interpretation of the data; preparation, review,
26
27 441 or approval of the manuscript.
28
29

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31 442

32
33 443 **Authors' contributions** Weiming Wang and Zhishun Liu conceived the idea and
34
35 444 designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the
36
37 445 acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang
38
39 446 Li will be responsible for the recruitment, acupuncture, and assessment respectively.
40
41 447 Yan Liu will be responsible for statistical analysis. This manuscript was drafted by
42
43 448 Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All
44
45 449 authors read and approved the final draft of the manuscript.
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54 451 **Acknowledgments** The authors appreciate the support and efforts from people who
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56 452 will be included in this study.
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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

For peer review only

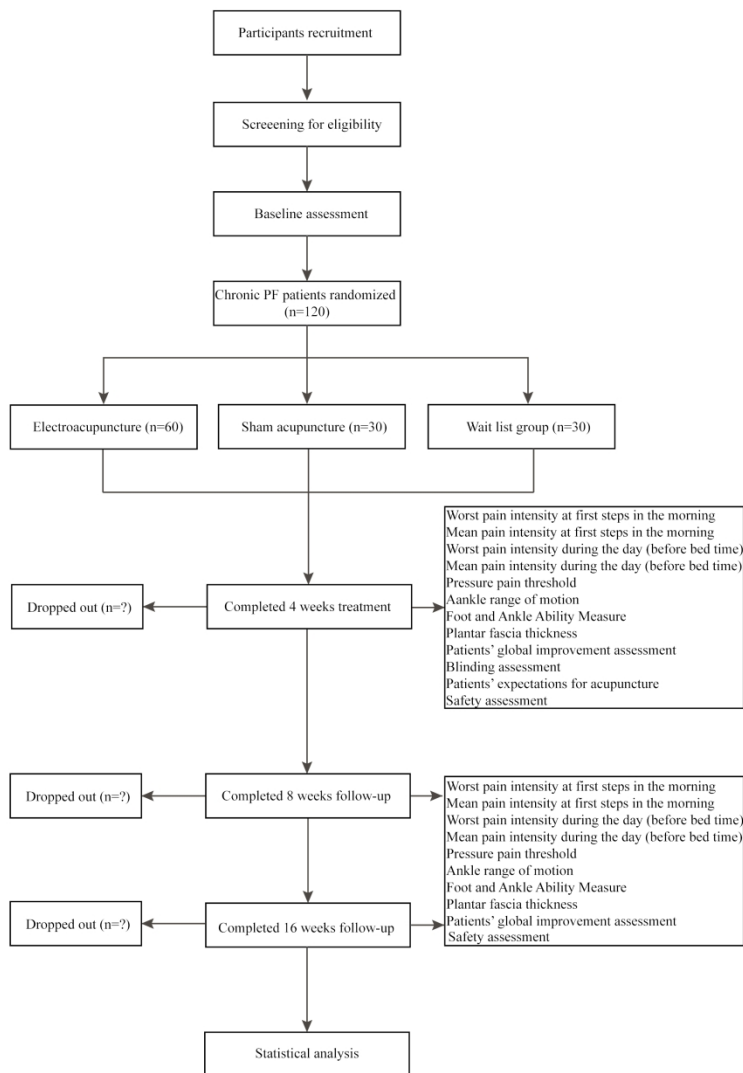


Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

TIME POINT (W, week)	Study Period				
	Baseline	Allocation	Treatment	Follow-up	
			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
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5		18b	Plans to promote participant retention and complete follow-up, including list 15
6			of any outcome data to be collected for participants who discontinue or
7			deviate from intervention protocols
8			
9			
10	Data	19	Plans for data entry, coding, security, and storage, including any related 15
11	management		processes to promote data quality (eg, double data entry; range checks for
12			data values). Reference to where details of data management procedures
13			can be found, if not in the protocol
14			
15	Statistical	20a	Statistical methods for analysing primary and secondary outcomes. 14-15
16	methods		Reference to where other details of the statistical analysis plan can be
17			found, if not in the protocol
18			
19			
20		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) NA
21			
22		20c	Definition of analysis population relating to protocol non-adherence (eg, as
23			randomised analysis), and any statistical methods to handle missing data 14-15
24			(eg, multiple imputation)
25			
26			

Methods: Monitoring

27			
28			
29	Data	21a	Composition of data monitoring committee (DMC); summary of its role and NA
30	monitoring		reporting structure; statement of whether it is independent from the sponsor
31			and competing interests; and reference to where further details about its
32			charter can be found, if not in the protocol. Alternatively, an explanation of
33			why a DMC is not needed
34			
35			
36		21b	Description of any interim analyses and stopping guidelines, including who 14
37			will have access to these interim results and make the final decision to
38			terminate the trial
39			
40	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and 13-14
41			spontaneously reported adverse events and other unintended effects of
42			trial interventions or trial conduct
43			
44			
45	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether 15
46			the process will be independent from investigators and the sponsor
47			

Ethics and dissemination

48			
49			
50	Research	24	Plans for seeking research ethics committee/institutional review board 16,19
51	ethics		(REC/IRB) approval
52	approval		
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5	Protocol	25	Plans for communicating important protocol modifications (eg, changes to	16
6	amendments		eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators,	
7			REC/IRBs, trial participants, trial registries, journals, regulators)	
8				
9	Consent or	26a	Who will obtain informed consent or assent from potential trial participants	6
10	assent		or authorised surrogates, and how (see Item 32)	
11				
12		26b	Additional consent provisions for collection and use of participant data and	NA
13			biological specimens in ancillary studies, if applicable	
14				
15				
16	Confidentiality	27	How personal information about potential and enrolled participants will be	19
17			collected, shared, and maintained in order to protect confidentiality before,	
18			during, and after the trial	
19				
20	Declaration of	28	Financial and other competing interests for principal investigators for the	19
21	interests		overall trial and each study site	
22				
23				
24	Access to	29	Statement of who will have access to the final trial dataset, and disclosure	19
25	data		of contractual agreements that limit such access for investigators	
26				
27	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for compensation to	NA
28	post-trial care		those who suffer harm from trial participation	
29				
30	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to	16
31	policy		participants, healthcare professionals, the public, and other relevant groups	
32			(eg, via publication, reporting in results databases, or other data sharing	
33			arrangements), including any publication restrictions	
34				
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36		31b	Authorship eligibility guidelines and any intended use of professional	19
37			writers	
38				
39		31c	Plans, if any, for granting public access to the full protocol, participant-level	NA
40			dataset, and statistical code	
41				
42				
43	Appendices			
44				
45	Informed	32	Model consent form and other related documentation given to participants	NA
46	consent		and authorised surrogates	
47	materials			
48				
49	Biological	33	Plans for collection, laboratory evaluation, and storage of biological	NA
50	specimens		specimens for genetic or molecular analysis in the current trial and for	
51			future use in ancillary studies, if applicable	
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5 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &
6 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.
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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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3 1 Title page
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7 3 Article title:
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10 4 **Efficacy of acupuncture vs sham acupuncture or waitlist control for**
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12 5 **patients with chronic plantar fasciitis: study protocol for a 2-center**
13
14 6 **randomized controlled trial**

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53 25 **Running title:** acupuncture for chronic plantar fasciitis
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57 27 **Word count: abstract 268; main text 4100.**
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1
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3
4 29 **Abstract**

5
6 30 **Introduction:** Plantar fasciitis (PF) is reported to be the most common cause of
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8
9 31 plantar heel pain. Acupuncture has been used for patients experiencing PF, but
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12 32 evidence of the efficacy of acupuncture on PF is limited. The primary objective of this
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15 33 trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist
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18 34 control for improving the level of pain experienced by patients suffering from chronic
19
20 35 PF.

21
22 36 **Methods and Analysis:** This will be a two-center, parallel-group, sham and
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24
25 37 no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate
26
27
28 38 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a
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31 39 ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute
32
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34 40 acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week
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37 41 follow-up. Participants in the waitlist control group will not undergo treatment for a
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40 42 period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of
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42
43 43 acupuncture free of charge at the end of the follow-up period. The primary outcome
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46 44 will be the treatment response rate 4 weeks after randomization, assessed as a
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48
49 45 minimum of 50% improvement in the worst pain intensity during the first steps in the
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51
52 46 morning compared with the baseline. All analyses will be performed with a 2-sided *P*
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54
55 47 value of < 0.05 considered significant following the intention-to-treat principle.

56
57 48 **Ethics and Dissemination:** The study has been approved by the Ethical Committee
58
59 49 of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences
60
50 (approval No: 2019-210-KY). The results will be disseminated through presentation

1
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4 51 at a peer-reviewed medical journal, the relevant conferences and scientific meetings.
5
6

7 52 **Key words:** acupuncture; chronic plantar fasciitis; pain intensity; clinical trial
8

9 53 **Trial registration:** ClinicalTrials.gov identifier: NCT 04185259.
10

11 54 **Strengths and limitations of this study:**
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13
14 55 ▶ This study is the first randomized controlled trial comparing combined
15
16
17 56 acupuncture and sham acupuncture versus waitlist control for pain relief in
18
19
20 57 participants with chronic PF.
21

22 58 ▶ The advantages to this study include sham acupuncture and waitlist control design,
23
24
25 59 objective measurements (i.e. PPT, PFT), strict quality control and evaluation of
26
27
28 60 participants' expectation regarding acupuncture.
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30 61 ▶ The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance
31
32
33 62 patient adherence by allowing more patients to receive acupuncture.
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35 63 ▶ Acupuncturists and participants in the waitlist control group will not be blinded,
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37
38 64 which may cause bias.
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40 65 ▶ A high dropout rate may exist in the waitlist group because participants expect to
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43 66 receive acupuncture treatment when they join the trial.
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69 **Background**

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

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

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

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3 94 for thousands of years. Mechanistic studies have revealed that acupuncture can induce
4
5 95 an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin,
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7 96 β -endorphin, and endomorphin).¹⁴ Two recent systematic reviews ^{15,16} found that
8
9 97 acupuncture may reduce pain intensity and improve plantar function for patients with
10
11 98 PF. However, there were methodological problems with the small sample sizes, lack
12
13 99 of control with a placebo/waitlist group, or no adjustment for the confounding effects
14
15 100 of patients who received combination treatments in the design of the included
16
17 101 acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous
18
19 102 remission of PF cannot be excluded and the beneficial effects of acupuncture for PF
20
21 103 remain in need of further assessment.

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26 104 We designed a randomized controlled trial to evaluate the efficacy of acupuncture,
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28 105 compared with sham acupuncture (SA) or being on a waitlist control group, for
29
30 106 patients with chronic PF for >6 months. Given that clinical and experimental results
31
32 107 have shown that SA can induce a significant alleviation of pain similar to verum
33
34 108 acupuncture ¹⁷due to non-specific effects (e.g., acupuncture expectations), the primary
35
36 109 hypothesis in this trial was that combined acupuncture and SA will result in larger
37
38 110 improvements in heel pain than no acupuncture treatment in patients with chronic PF.
39
40 111 The secondary hypothesis examined whether acupuncture can reduce heel pain
41
42 112 intensity more effectively than SA or no acupuncture.

43 113 **Methods and design**

44 114 **Study design**

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47 115 This will be a two-center, parallel-group, sham and no-treatment controlled,
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49 116 assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate.
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51 117 We will design the protocol in accordance with standard protocol items including the
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53 118 Recommendations for Interventional Trials ¹⁸ and the Standards for Reporting
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3 119 Interventions in the Clinical Trials of Acupuncture¹⁹ guidelines. The study flow chart
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5
6 120 and study schedule are shown in Figs. 1 and 2.

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8 121 **Study setting and recruitment**

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10 122 This trial is planned to be conducted at Guang'anmen Hospital, China Academy of
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12 123 Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from
13
14 124 March 2020 to March 2022. A total of 120 participants will be publicly recruited
15
16
17 125 through the use of posters and hospital webs in the two participating hospitals. The
18
19 126 duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week
20
21
22 127 treatment, and 12-week follow-up.

23
24 128 **Randomization and Blinding**

25
26 129 The eligible participants who sign an informed consent form will complete a 1-week
27
28 130 baseline assessment before randomization, which includes foot symptoms,
29
30 131 functionality, and ultrasound examinations, as well as participants' expectation (see
31
32
33 132 Fig. 2). Participants will be randomized into the acupuncture group, SA group, or
34
35 133 waitlist (no acupuncture) group at a ratio of 2:1:1 using simple randomization.
36
37 134 Randomization will be generated with the PROC PLAN in SAS 9.4 (SAS Institute
38
39 135 Inc., Cary, NC, USA). Details of the group allocation will be concealed on cards
40
41
42 136 inside sealed opaque envelopes by the staff member responsible for the allocation. A
43
44 137 research coordinator, who will not be involved in the treatment and outcome
45
46 138 assessments, will be responsible for contacting participants and allocating them to
47
48 139 their assigned group. Participants in the acupuncture and SA groups, together with
49
50 140 efficacy evaluators and data analysts will be blinded to the group assignments.
51
52
53 141 Participants in the waitlist control group and acupuncturists will not be blinded.

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56 142 **Participants**

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3 143 Participants with a diagnosis of PF by an orthopedist on clinical grounds will be
4
5 144 included in the study only if they meet all of the following inclusion criteria and do
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7
8 145 not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the
9
10 146 guidelines described by the Orthopaedic Section of American Physical Therapy
11
12 147 Association.²⁰ The following clinical findings will be used to diagnose PF: plantar
13
14 148 medial heel pain during the initial steps after a period of inactivity but also worse pain
15
16 149 following prolonged weight bearing, heel pain precipitated by a recent increase in
17
18 150 weight-bearing activity, physical examination findings (heel pain with palpation of
19
20 151 the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal
21
22 152 foot posture index, high body mass index, as well as a positive windlass test and
23
24 153 negative tarsal tunnel tests.

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28 154 **Inclusion criteria:**

- 29
30 155 1. Age ≥ 18 years and ≤ 75 years;
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32 156 2. History of plantar medial heel pain for at least 6 months before enrolment;
33
34 157 3. Reported an average worst pain intensity at first steps in the morning over the last
35
36 158 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before
37
38 159 enrolment;
39
40 160 4. Failure to respond to conservative treatment for ≥ 1 months, including any of the
41
42 161 following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs,
43
44 162 shockwave therapy, dry needling and orthotics;
45
46 163 5. Ability to comply with the study protocol, understand the medical information
47
48 164 forms as well as having provided informed consent.
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53 165 **Exclusion criteria:**
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- 166 1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture,
167 or having a significant foot deformity (clubfoot, pes cavus, or pes
168 calcaneovalgus);
- 169 2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or
170 radiation, or surgery to plantar fascia within 6 months preceding enrollment;
- 171 3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such
172 as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
- 173 4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2
174 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
- 175 5. Joint, bone, or skin infection in the affected foot;
- 176 6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or
177 coagulation disorder at baseline as determined by the investigator;
- 178 7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks
179 prior to enrollment.

180 **Interventions**

181 **Acupuncture group**

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

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2
3 191 China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand,
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5 192 Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used.
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7
8 193 With the patient in a prone position, the local skin will be routinely sterilized,
9
10 194 followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato
11
12 195 brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected
13
14 196 acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar
15
16 197 fascia layer with a depth of approximately 15-20 mm depending on the location.
17
18 198 BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin
19
20 199 through the pad. All needles except the Ashi points will be manually stimulated with
21
22 200 small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi
23
24 201 (a sensation including soreness, numbness, distention, and heaviness).²³ Needles will
25
26 202 be retained for 30 minutes per treatment. During each treatment, every needle will be
27
28 203 manipulated three times every 10 minutes.

204 **SA group**

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

214 **Waitlist control group**

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3 215 Participants will receive no treatment for their heel pain for a period of 16 weeks after
4
5 216 randomization, and subsequently have the option of 4 weeks (12 sessions) of
6
7 217 acupuncture free of charge at the end of the follow-up period.
8
9

10 218 The intervention will last for 30 minutes in the acupuncture and SA groups, and
11
12 219 will be performed three times per week for a total of 12 sessions in four consecutive
13
14 220 weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides
15
16 221 and evaluate the more severe side. Participants in all groups will be treated and (or)
17
18 222 evaluated separately. Participants in all groups will be advised to use soft heel foot
19
20 223 wear, not to stand for a long time, and not to walk barefoot during the 17-week study
21
22 224 period.
23
24

25 225 **Rescue medication**

26
27
28 226 Additional therapies for heel pain during the entire study period will be prohibited.
29
30 227 However, the investigator will be permitted to prescribe ibuprofen (sustained release
31
32 228 type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as
33
34 229 rescue medication no more than 2 days per week up to the maximum daily dose if
35
36 230 unbearable heel pain occurs. Participants will be required not to take rescue
37
38 231 medication within 72 h before the baseline and outcome measurements. In the event
39
40 232 rescue medication needs to be taken after the baseline measurement, the participant
41
42 233 will postpone the next visit to the treatment center.
43
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46 234 **Outcome measures**

47 235 **Primary outcome**

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50 236 The primary outcome used in this trial will be the proportion of participants with a
51
52 237 treatment response 4 weeks after randomization, defined as a minimum of 50%
53
54 238 improvement in the worst pain intensity during the first steps in the morning
55
56 239 compared with the baseline. The average worst pain intensity over the last 3 days will
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3 240 be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS,
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5 241 with 0 indicating no pain and 100 indicating maximal pain. Participants who must
6
7 242 resort to additional treatments other than rescue medication will be classified as
8
9
10 243 nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be
11
12 244 assessed.

15 245 **Secondary outcomes**

17 246 The secondary outcomes are as follows:

- 19 247 1. Changes in the VAS score for worst pain intensity during the first steps in the
21 248 morning from baseline to 4, 8, and 16 weeks after randomization;
- 24 249 2. Changes in the VAS score for mean pain intensity during the day from baseline to
26 250 4, 8, and 16 weeks after randomization;
- 28 251 3. Changes in the pressure pain threshold (PPT) at the most painful area from
30 252 baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the
32 253 minimum pressure detected when the sensation of pressure first changes to a
34 254 sensation of pain.²⁴ PPT will be tested with a pressure algometer (Fabrication
36 255 Enterprises, Inc., White Plains, NY; from 1 kg/cm² to 5 kg/cm²) using a metal
38 256 probe with a 0.5 cm² rubber disc by a trained researcher. PPT will be measured
40 257 when the participant is lying supine in a relaxed position with the affected foot
42 258 hanging over the edge of the bed. When measuring the PPT, the rubber disc will
44 259 be placed perpendicularly on the painful spot and pressure will be applied at a rate
46 260 of approximately 0.1 kg/cm²/s through the metal probe of the pressure algometer.
48 261 Participants will be informed to report when the initial pain sensation occurs, and
50 262 the readings of the algometer will be recorded. The score will be determined by
52 263 averaging three repeated measurements with 30 seconds between each trial. All
54 264 values below 1 kg/cm² will be reported as 0.5 kg/cm².

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3 265 4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16
4
5 266 weeks after randomization: The examiner will measure the AROM including
6
7 267 dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee)
8
9 268 using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan,
10
11 269 from 0° to 360°). For the flexed-knee assessment, the participant will sit in a
12
13 270 relaxed station with the popliteal space at the edge of the table and their knees
14
15 271 with 90° of flexion. For the extended-knee assessment, the participant will be
16
17 272 seated on a treatment table with the knees fully extended (0°) and the feet hanging
18
19 273 off the end of the table. The axis of the goniometer will be placed at the lateral
20
21 274 malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the
22
23 275 moving arm placed parallel to the center of the fibular head. The ankle will be
24
25 276 passively moved from a neutral starting position into dorsiflexion and plantar
26
27 277 flexion until a firm end feel is elicited²⁵ and the readings of the goniometer will
28
29 278 be registered. The mean score of three trials with 10 seconds between each
30
31 279 examination will be calculated and used for analysis.
32
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37 280 5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale
38
39 281 scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a
40
41 282 self-reported questionnaire concerning 21 activities of daily living (ADL) items
42
43 283 and eight sports subscale items.²⁶ Each item is scored on a 0-4 point Likert scale
44
45 284 anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores
46
47 285 indicating a higher level of function. The FAAM has a maximum potential score
48
49 286 of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and
50
51 287 sport subscale scores) is divided by the maximum potential score and multiplied
52
53 288 by 100 to obtain a percentage. If the patient does not respond, the specific
54
55 289 question will be left blank and not be a part of the final value of the questionnaire.
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- 1
2
3 290 In this trial, we will use the previously validated Chinese version of the FAAM.²⁷
4
5
6 291 6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after
7
8 292 randomization: PFT will be measured at the thickest point closest to the calcaneal
9
10 293 insertion in its medial portion using ultrasound. The ultrasound scan will be
11
12 294 performed using an 8-12 MHz linear probe with the patient in the prone position
13
14
15 295 at the baseline and at 4 weeks after randomization.
16
17 296 7. Participant global assessment of improvement: Participants will be asked to rate
18
19 297 their global improvement using a 7-point scale. The improvement will be scaled
20
21 298 from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious
22
23 299 improvement, 3 being a little improvement, 4 being no change, 5 being a little
24
25 300 worse, and 6 being obviously worse. The proportions of participants with different
26
27 301 degrees of improvement will be assessed at 4, 8, and 16 weeks after
28
29 302 randomization. Scales of participant global assessment of improvement with 7
30
31 303 response categories have been rated as relatively easy to use and show good
32
33 304 reliability and validity.²⁸
34
35
36
37 305 8. Participants' expectation towards acupuncture at baseline: At baseline,
38
39 306 participants in the acupuncture and SA groups will be asked the following
40
41 307 question: "Do you think acupuncture will be helpful to improve your chronic PF?"
42
43 308 Participant will choose one of the following answers: "Extremely helpful", "Very
44
45 309 helpful", "Helpful", "Not help at all", and "Unclear".
46
47
48
49 310 9. The proportion of participants who have maintained blinding during treatment in
50
51 311 the acupuncture and SA groups: Participants' blindness to the mode of
52
53 312 acupuncture will be assessed five minutes after the end of any treatment in the
54
55 313 fourth week by asking the patients the following question: "Which of the two
56
57 314 acupuncture modalities do you think you received, acupuncture or SA?"
58
59
60

1
2
3 315 Participants will choose one of the following answers: “Acupuncture”, “SA”, or
4
5 316 “Unclear”. Prior to the question, patients will be informed that they may have
6
7
8 317 received one of two modalities: acupuncture with a deeper insertion or SA with no
9
10 318 skin penetration.

319 **Safety assessment**

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

331 **Sample size calculation**

332 Based on the results of a previous study,¹² a sample size of 120 participants will be
333 enrolled to provide 80% power to detect a difference of 35% between the combined
334 acupuncture group and waiting-list group in the proportion of participants with
335 treatment response 4 weeks after randomization at a two-sided significance level of
336 0.05. The proportion of participants with treatment response after 4 weeks was
337 assumed to be roughly 12% for the waiting-list group,¹² with an anticipated 10% loss
338 to follow-up.

339 **Statistical analysis**

1
2
3 340 The null hypothesis is that the proportion of participants with treatment response 4
4
5 341 weeks after randomization will be the same for the combined acupuncture groups and
6
7 342 waiting-list group. Data will be presented as mean \pm standard deviation for
8
9 343 quantitative variables and frequencies (number of cases), with relative frequencies
10
11 344 (percentages) for categorical variables. The primary outcome analysis will use the
12
13 345 Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the
14
15 346 combined acupuncture groups and the waiting-list group. If the result of this analysis
16
17 347 is significant, hierarchical testing will be applied to the acupuncture group versus
18
19 348 waiting-list group, SA group versus waiting-list group, and acupuncture group versus
20
21 349 SA group. For normally distributed quantitative variables, a repeated-measures
22
23 350 analysis of variance (ANOVA) with multiple comparisons post-hoc test will be
24
25 351 performed using baseline as a co-variate when comparing more than two groups and
26
27 352 an unpaired T test when comparing two groups. For non-normally distributed
28
29 353 quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney
30
31 354 test will be performed. For categorical variables, the Chi square (χ^2) test will be used.
32
33 355 Confidence intervals for the difference between treatments will be calculated at the
34
35 356 95% level. A two-tailed test will be applied for all available data, and a *P* value < 0.05
36
37 357 will be considered statistically significant. All analyses in this trial will be performed
38
39 358 using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the
40
41 359 basis of the intention-to-treat (ITT) population, which will include participants who
42
43 360 had been randomized. Missing data will be completed as the last value observed
44
45 361 before dropout. No adjustment will be made for multiple outcomes.
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362 **Quality control**

54
55 363 To ensure the quality of the trial, all the relevant staff will be uniformly trained before
56
57 364 the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF,
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1
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3 365 inclusion and exclusion criteria, intervention procedures, and outcome measures).
4
5 366 Licensed acupuncturists with at least 2 years' acupuncture experience will perform
6
7 367 the treatment. Throughout the trial, strict three-level monitoring will be conducted for
8
9 368 data quality control. Dropouts and withdrawals including the reasons will be recorded
10
11 369 during the trial. Paper-based study data will be stored in locked file cabinets under the
12
13 370 management of the investigators. Electronic records will be stored in a Structured
14
15 371 Query Language (SQL) server database on a limited access, secure server maintained
16
17 372 by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.
18
19
20

21 373 **Patient and public involvement**

22
23
24 374 The research question of whether combined acupuncture and SA will result in larger
25
26 375 improvements in heel pain than no acupuncture treatment for patients with chronic PF
27
28 376 was first proposed by the investigator after encountering a patient who received SA
29
30 377 and reported a similar improvement in heel pain as another patient who received
31
32 378 routine acupuncture in the clinic. Patients were not involved in conceiving or
33
34 379 implementing the study.
35
36

37 380 **Ethics and dissemination**

38
39
40 381 This trial will be conducted in accordance with the principles of the Declaration of
41
42 382 Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and
43
44 383 approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of
45
46 384 Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign
47
48 385 the informed consent form prior to randomization, and they will be permitted to
49
50 386 withdraw at any time during the trial, with or without reasons being provided. Any
51
52 387 amendment or other change of the protocol will need to be approved by the Ethical
53
54 388 Committee of the Guang'anmen Hospital, China Academy of Chinese Medical
55
56 389 Science, and agreed to by the co-researchers.
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3 390 Following analysis of the data, the findings of this study will be submitted for
4
5 391 publication in a peer-reviewed medical journal. The results will also be disseminated
6
7
8 392 through presentation at the relevant conferences and scientific meetings.
9

10 393 **Discussion**

11
12 394 Although several reviews and RCTs^{15,16,12,29} have been published that focus on
13
14 395 acupuncture for PF, owing to the lack of a placebo control, non-specific physiology
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16
17 396 effects of needling and spontaneous remission of PF cannot be excluded. To date, this
18
19 397 is the first randomized trial with three parallel arms, assessing whether combined
20
21 398 acupuncture and SA compared to no treatment control produce a significant reduction
22
23 399 in pain intensity in chronic PF. We anticipate that this study will determine the
24
25 400 efficacy of acupuncture for patients with chronic PF, and improve the care of these
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27 401 patients in the clinic.
28
29

30 402 Though most PF patients will achieve significant improvement in symptoms
31
32 403 within 1 year regardless of treatment,³⁰ many will seek treatment before then. Patients
33
34 404 often choose other treatment options when they cannot obtain a satisfactory outcome
35
36 405 from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night
37
38 406 splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic
39
40 407 participants who had failed to respond to conservative treatment prior to participation.
41
42 408 The results can be generalized to patients experiencing chronic refractory PF.
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46
47 409 In this study, pain intensity measured with VAS during the first steps in the
48
49 410 morning will be used as the primary outcome. This variable has been used in previous
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51 411 trials^{12,21} and is a meaningful subject outcome measure for the assessment of PF
52
53 412 improvement. In addition, we will also use PPT and PFT as objective secondary
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55 413 outcomes. PPT is an essential evaluation tool for patients suffering from many
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57 414 musculoskeletal disorders including PF and provides a reliable process for measuring
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3 415 participants' responses to mechanical stimuli.³¹ Compared to normal asymptomatic
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5 416 patients, patients with PF often exhibit a thickened plantar fascia on ultrasound.³²
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7
8 417 Therefore, a PFT evaluation would provide information to detect the anatomical
9
10 418 changes that occur in the plantar fascia after acupuncture.

11
12 419 The strengths of this study include a sham control (non-penetrating at
13
14 420 non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT,
15
16 421 PFT), strict quality control, and evaluation of the participants' expectations regarding
17
18 422 acupuncture. Several limitations to this trial need to be acknowledged. First, it will be
19
20 423 impossible to blind the acupuncturists and participants in the waitlist control group,
21
22 424 which is a general problem in non-pharmacological interventional trials and can cause
23
24 425 bias. Second, a high dropout rate may exist in the waitlist group because participants
25
26 426 expect to receive acupuncture treatment when they join the trial. Third, the follow-up
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28 427 period will not exceed 12 weeks, which will not allow for detection of the long-term
29
30 428 effects of acupuncture for chronic PF. Fourth, our approach will enable us to draw
31
32 429 conclusions about the selected acupuncture points but not about individualized
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34 430 treatments. Fifth, there are multiple secondary outcomes in this trial, which may
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36 431 increase the risk of type I error.
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5 433 **Ethical Approval and Consent to participate** The study has received approval from
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7 434 the Institutional Review Boards of Guang'anmen Hospital in China (approval NO.
8
9 435 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the
10
11
12 436 Helsinki Declaration.

13
14 437 **Consent for publication** Not applicable.

15
16 438 **Availability of data and materials** Not applicable.

17
18
19 439 **Competing interests** The authors declare that they have no competing interests.

20
21 440 **Funding** This RCT is funded by China Academy of Chinese Medical Sciences (Grant
22
23 441 No. ZZ13-YQ-019). The funding agency has no role in the design of the study; data
24
25 442 collection, management, analysis, and interpretation of the data; preparation, review,
26
27 443 or approval of the manuscript.
28
29

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31 444

32
33 445 **Authors' contributions** Weiming Wang and Zhishun Liu conceived the idea and
34
35 446 designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the
36
37 447 acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang
38
39 448 Li will be responsible for the recruitment, acupuncture, and assessment respectively.
40
41 449 Yan Liu will be responsible for statistical analysis. This manuscript was drafted by
42
43 450 Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All
44
45 451 authors read and approved the final draft of the manuscript.
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54 453 **Acknowledgments** The authors appreciate the support and efforts from people who
55
56 454 will be included in this study.
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Figure legends

Figure 1: Trial flow diagram

Figure 2: Study schedule

For peer review only

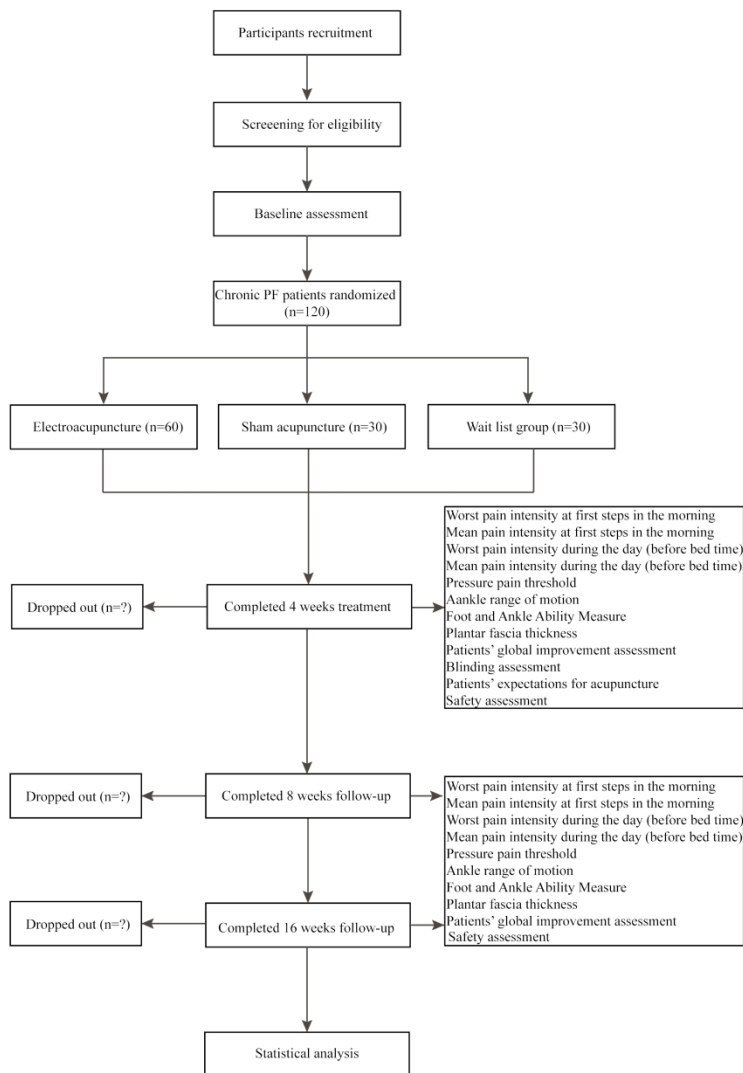


Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

TIME POINT (W, week)	Study Period				
	Baseline	Allocation	Treatment	Follow-up	
			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
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	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
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1				
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4				
5	Protocol	25	Plans for communicating important protocol modifications (eg, changes to	16
6	amendments		eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators,	
7			REC/IRBs, trial participants, trial registries, journals, regulators)	
8				
9	Consent or	26a	Who will obtain informed consent or assent from potential trial participants	6
10	assent		or authorised surrogates, and how (see Item 32)	
11				
12		26b	Additional consent provisions for collection and use of participant data and	NA
13			biological specimens in ancillary studies, if applicable	
14				
15				
16	Confidentiality	27	How personal information about potential and enrolled participants will be	19
17			collected, shared, and maintained in order to protect confidentiality before,	
18			during, and after the trial	
19				
20	Declaration of	28	Financial and other competing interests for principal investigators for the	19
21	interests		overall trial and each study site	
22				
23				
24	Access to	29	Statement of who will have access to the final trial dataset, and disclosure	19
25	data		of contractual agreements that limit such access for investigators	
26				
27	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for compensation to	NA
28	post-trial care		those who suffer harm from trial participation	
29				
30	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to	16
31	policy		participants, healthcare professionals, the public, and other relevant groups	
32			(eg, via publication, reporting in results databases, or other data sharing	
33			arrangements), including any publication restrictions	
34				
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36		31b	Authorship eligibility guidelines and any intended use of professional	19
37			writers	
38				
39		31c	Plans, if any, for granting public access to the full protocol, participant-level	NA
40			dataset, and statistical code	
41				
42				
43	Appendices			
44				
45	Informed	32	Model consent form and other related documentation given to participants	NA
46	consent		and authorised surrogates	
47	materials			
48				
49	Biological	33	Plans for collection, laboratory evaluation, and storage of biological	NA
50	specimens		specimens for genetic or molecular analysis in the current trial and for	
51			future use in ancillary studies, if applicable	
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5 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &
6 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.
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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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3 1 Title page
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10 4 **Efficacy of acupuncture vs sham acupuncture or waitlist control for**
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13 5 **patients with chronic plantar fasciitis: study protocol for a 2-center**
14
15 6 **randomized controlled trial**

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53 25 **Running title:** acupuncture for chronic plantar fasciitis
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57 27 **Word count: abstract 268; main text 4203.**
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3
4 29 **Abstract**

5
6 30 **Introduction:** Plantar fasciitis (PF) is reported to be the most common cause of
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9 31 plantar heel pain. Acupuncture has been used for patients experiencing PF, but
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12 32 evidence of the efficacy of acupuncture on PF is limited. The primary objective of this
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15 33 trial is to compare combined acupuncture and sham acupuncture (SA) versus waitlist
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18 34 control for improving the level of pain experienced by patients suffering from chronic
19
20 35 PF.

21
22 36 **Methods and Analysis:** This will be a two-center, parallel-group, sham and
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25 37 no-treatment controlled, assessor-blinded randomized trial. We will randomly allocate
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28 38 120 participants with chronic PF to acupuncture, SA, and waitlist control groups at a
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31 39 ratio of 2:1:1. Participants in the acupuncture and SA groups will receive a 30-minute
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34 40 acupuncture or SA treatment for a total of 12 sessions over 4 weeks, with a 12-week
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37 41 follow-up. Participants in the waitlist control group will not undergo treatment for a
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40 42 period of 16 weeks but instead will have the option of 4 weeks (12 sessions) of
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43 43 acupuncture free of charge at the end of the follow-up period. The primary outcome
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46 44 will be the treatment response rate 4 weeks after randomization, assessed as a
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49 45 minimum of 50% improvement in the worst pain intensity during the first steps in the
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52 46 morning compared with the baseline. All analyses will be performed with a 2-sided *P*
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54
55 47 value of < 0.05 considered significant following the intention-to-treat principle.

56
57 48 **Ethics and Dissemination:** The study has been approved by the Ethical Committee
58
59 49 of the Guang'anmen Hospital, China Academy of Chinese Medical Sciences
60
50 50 (approval No: 2019-210-KY). The results will be disseminated through presentation

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4 51 at a peer-reviewed medical journal, the relevant conferences and scientific meetings.
5

6
7 52 **Key words:** acupuncture; chronic plantar fasciitis; pain intensity; clinical trial
8

9
10 53 **Trial registration:** ClinicalTrials.gov identifier: NCT 04185259.
11

12 54 **Strengths and limitations of this study:**
13

14 55 ▶ This study is the first randomized controlled trial comparing combined
15
16 56 acupuncture and sham acupuncture versus waitlist control for pain relief in
17
18 57 participants with chronic PF.
19

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21
22 58 ▶ The advantages to this study include sham acupuncture and waitlist control design,
23
24 59 objective measurements (i.e. PPT, PFT), strict quality control and evaluation of
25
26 60 participants' expectation regarding acupuncture.
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30 61 ▶ The 2:1:1 allocation ratio used in this trial could facilitate recruitment and enhance
31
32 62 patient adherence by allowing more patients to receive acupuncture.
33

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35 63 ▶ Acupuncturists and participants in the waitlist control group will not be blinded,
36
37 64 which may cause bias.
38

39
40 65 ▶ A high dropout rate may exist in the waitlist group because participants expect to
41
42 66 receive acupuncture treatment when they join the trial.
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69 **Background**

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

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

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

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3 94 for thousands of years. Mechanistic studies have revealed that acupuncture can induce
4
5 95 an analgesic response via the release of neuropeptides (e.g., enkephalin, dynorphin,
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7 96 β -endorphin, and endomorphin).¹⁴ Two recent systematic reviews ^{15,16} found that
8
9 97 acupuncture may reduce pain intensity and improve plantar function for patients with
10
11 98 PF. However, there were methodological problems with the small sample sizes, lack
12
13 99 of control with a placebo/waitlist group, or no adjustment for the confounding effects
14
15 100 of patients who received combination treatments in the design of the included
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17 101 acupuncture literature. Therefore, the placebo effects of acupuncture and spontaneous
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19 102 remission of PF cannot be excluded and the beneficial effects of acupuncture for PF
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21 103 remain in need of further assessment.

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26 104 We designed a randomized controlled trial to evaluate the efficacy of acupuncture,
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28 105 compared with sham acupuncture (SA) or being on a waitlist control group, for
29
30 106 patients with chronic PF for >6 months. Given that clinical and experimental results
31
32 107 have shown that SA can induce a significant alleviation of pain similar to verum
33
34 108 acupuncture ¹⁷due to non-specific effects (e.g., acupuncture expectations), the primary
35
36 109 hypothesis in this trial was that combined acupuncture and SA will result in larger
37
38 110 improvements in heel pain than no acupuncture treatment in patients with chronic PF.
39
40 111 The secondary hypothesis examined whether acupuncture can reduce heel pain
41
42 112 intensity more effectively than SA or no acupuncture.

43 113 **Methods and design**

44 114 **Study design**

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47 115 This will be a two-center, parallel-group, sham and no-treatment controlled,
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49 116 assessor-blinded randomized trial comprising three arms with a 2:1:1 allocation rate.
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51 117 We will design the protocol in accordance with standard protocol items including the
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53 118 Recommendations for Interventional Trials ¹⁸ and the Standards for Reporting
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3 119 Interventions in the Clinical Trials of Acupuncture¹⁹ guidelines. The study flow chart
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5
6 120 and study schedule are shown in Figs. 1 and 2.

7 8 121 **Study setting and recruitment**

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10 122 This trial is planned to be conducted at Guang'anmen Hospital, China Academy of
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12 123 Chinese Medical Sciences, and Yantai Hospital of Traditional Chinese Medicine from
13
14 124 March 2020 to March 2022. A total of 120 participants will be publicly recruited
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16
17 125 through the use of posters and hospital webs in the two participating hospitals. The
18
19 126 duration of the trial for each participant will be 17 weeks: 1-week baseline, 4-week
20
21
22 127 treatment, and 12-week follow-up.

23 24 128 **Randomization and Blinding**

25
26 129 The eligible participants who sign an informed consent form will complete a 1-week
27
28 130 baseline assessment before randomization, which includes foot symptoms (i.e., worst
29
30 131 pain intensity at first steps in the morning, mean pain intensity during the day),
31
32 132 functionality, and ultrasound examinations (see Fig. 2). Participants' expectation
33
34 133 towards acupuncture will be assessed in the acupuncture and SA groups at baseline by
35
36 134 asking participants: Do you think acupuncture will be helpful to improve your chronic
37
38 135 PF? Participant will choose one of the following answers: "Extremely helpful", "Very
39
40 136 helpful", "Helpful", "Not help at all", and "Unclear". Participants will be randomized
41
42 137 into the acupuncture group, SA group, or waitlist (no acupuncture) group at a ratio of
43
44 138 2:1:1 using simple randomization. Randomization will be generated with the PROC
45
46 139 PLAN in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Details of the group
47
48 140 allocation will be concealed on cards inside sealed opaque envelopes by the staff
49
50 141 member responsible for the allocation. A research coordinator, who will not be
51
52 142 involved in the treatment and outcome assessments, will be responsible for contacting
53
54 143 participants and allocating them to their assigned group. Participants in the
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3 144 acupuncture and SA groups, together with efficacy evaluators and data analysts will
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5 145 be blinded to the group assignments. Participants in the waitlist control group and
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7
8 146 acupuncturists will not be blinded.
9

10 147 **Participants**

11
12 148 Participants with a diagnosis of PF by an orthopedist on clinical grounds will be
13
14 149 included in the study only if they meet all of the following inclusion criteria and do
15
16
17 150 not fulfill any of the exclusion criteria. Diagnosis of PF will be made according to the
18
19 151 guidelines described by the Orthopaedic Section of American Physical Therapy
20
21 152 Association.²⁰ The following clinical findings will be used to diagnose PF: plantar
22
23 153 medial heel pain during the initial steps after a period of inactivity but also worse pain
24
25 154 following prolonged weight bearing, heel pain precipitated by a recent increase in
26
27 155 weight-bearing activity, physical examination findings (heel pain with palpation of
28
29 156 the proximal insertion of the plantar fascia, limited ankle range of motion,), abnormal
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31 157 foot posture index, high body mass index, as well as a positive windlass test and
32
33 158 negative tarsal tunnel tests.
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37 159 **Inclusion criteria:**

- 38 160 1. Age ≥ 18 years and ≤ 75 years;
- 39 161 2. History of plantar medial heel pain for at least 6 months before enrolment;
- 40 162 3. Reported an average worst pain intensity at first steps in the morning over the last
41
42 163 7 days of at least 50 mm on a 100-mm visual analog scale (VAS) before
43
44 164 enrolment;
- 45 165 4. Failure to respond to conservative treatment for ≥ 1 months, including any of the
46
47 166 following modalities: stretching exercises, nonsteroidal anti-inflammatory drugs,
48
49 167 shockwave therapy, dry needling and orthotics;
- 50
51 168 5. Ability to comply with the study protocol, understand the medical information
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3 169 forms as well as having provided informed consent.
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5 170 **Exclusion criteria:**
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- 7
8 171 1. History of calcaneus fracture, calcaneal bone tumor or cyst, plantar fascia rupture,
9
10 172 or having a significant foot deformity (clubfoot, pes cavus, or pes
11
12 173 calcaneovalgus);
13
14 174 2. Previous injection (corticosteroid, platelet-rich plasma, lidocaine needling), or
15
16 175 radiation, or surgery to plantar fascia within 6 months preceding enrollment;
17
18 176 3. Lumbosacral radiculopathy or peripheral neuropathy around the ankle joint such
19
20 177 as nerve entrapment tarsal tunnel syndrome or Achilles tendinopathy;
21
22 178 4. Systemic disorders like rheumatoid arthritis, gout, Reiter syndrome, type 1 or 2
23
24 179 diabetes mellitus, osteoporosis, spondyloarthritis, or osteomyelitis;
25
26 180 5. Joint, bone, or skin infection in the affected foot;
27
28 181 6. Clinically significant cardiovascular disorder, severe hepatic/renal insufficiency or
29
30 182 coagulation disorder at baseline as determined by the investigator;
31
32 183 7. Known phobia to acupuncture or receiving acupuncture treatment within 4 weeks
33
34 184 prior to enrollment.
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40 185 **Interventions**

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42 186 **Acupuncture group**
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44 187 The acupuncture protocol was developed by the consensus of three experts based on
45
46 188 the meridian theory of TCM and was used in our previous trial.²¹ Licensed
47
48 189 acupuncturists with more than 2 years of acupuncture experience will perform the
49
50 190 treatment. We will apply needles to two Ashi points (the two most severe tender
51
52 191 points in the most sensitive area over the anteromedial aspect of the heels, according
53
54 192 to the participant's perceived pain upon palpation) as well as the Chengshan (BL57),
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56 193 Taixi (KI3), and Kunlun (BL60) acupoints in this trial. The position of the
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3 194 aforementioned acupoints will be based on the Nomenclature and location of
4
5 195 acupuncture points ²² designated by the National Standard of the People's Republic of
6
7 196 China (GB/T 12 346-2006). Sterile disposable stainless steel needles (Hwato brand,
8
9 197 Suzhou Medical Appliance Factory, Suzhou, China; 0.3 mm × 40 mm) will be used.
10
11
12 198 With the patient in a prone position, the local skin will be routinely sterilized,
13
14 199 followed by pasting a 10-mm diameter and 5-mm thick sterile adhesive pad (Hwato
15
16 200 brand, Suzhou Medical Appliance Factory, Suzhou, China) onto each selected
17
18 201 acupoint. Ashi points will be perpendicularly inserted through the pad to the plantar
19
20 202 fascia layer with a depth of approximately 15-20 mm depending on the location.
21
22 203 BL57, KI3, and BL60 will be punched perpendicularly 10-15 mm deep into the skin
23
24 204 through the pad. All needles except the Ashi points will be manually stimulated with
25
26 205 small, equal manipulations of lifting, thrusting, twirling, and rotating to achieve De qi
27
28 206 (a sensation including soreness, numbness, distention, and heaviness).²³ Needles will
29
30 207 be retained for 30 minutes per treatment. During each treatment, every needle will be
31
32 208 manipulated three times every 10 minutes.

37 209 **SA group**

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39
40 210 In the SA group, sham Ashi (0.5 cun away from Ashi, one 'cun' is equivalent to the
41
42 211 greatest width of the individual patients' thumb, ~1.5 cm), sham BL57 (0.5 cun lateral
43
44 212 to the true BL57 horizontally), sham KI3 (midway between the true KI3 and the
45
46 213 heel tendon) and sham BL60 (midway between the true BL60 and the heel tendon)
47
48 214 will be used. The treatment protocol will be similar to that of the acupuncture group.
49
50 215 The Hwato-brand disposable blunt-tipped needles (size 0.30 × 25 mm) will be
51
52 216 inserted at the sham points through the adhesive pads attached to the skin without skin
53
54 217 penetration. The needles will then be lifted, thrust, twirled, and rotated evenly three
55
56 218 times every 10 minutes. No specific De qi response will be elicited.
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3 219 **Waitlist control group**
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5 220 Participants will receive no treatment for their heel pain for a period of 16 weeks after
6
7 221 randomization, and subsequently have the option of 4 weeks (12 sessions) of
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9 222 acupuncture free of charge at the end of the follow-up period.

10
11
12 223 The intervention will last for 30 minutes in the acupuncture and SA groups, and
13
14 224 will be performed three times per week for a total of 12 sessions in four consecutive
15
16 225 weeks. If participants suffer pain bilaterally, the acupuncturists will treat both sides
17
18 226 and evaluate the more severe side. Participants in all groups will be treated and (or)
19
20 227 evaluated separately. Participants in all groups will be advised to use soft heel foot
21
22 228 wear, not to stand for a long time, and not to walk barefoot during the 17-week study
23
24 229 period.

25
26
27
28 230 **Rescue medication**
29

30 231 Additional therapies for heel pain during the entire study period will be prohibited.
31
32 232 However, the investigator will be permitted to prescribe ibuprofen (sustained release
33
34 233 type, 300 mg/T, Tianjin Smith Kline & French Laboratories Ltd., Tianjin, China) as
35
36 234 rescue medication no more than 2 days per week up to the maximum daily dose if
37
38 235 unbearable heel pain occurs. Participants will be required not to take rescue
39
40 236 medication within 72 h before the baseline and outcome measurements. In the event
41
42 237 rescue medication needs to be taken after the baseline measurement, the participant
43
44 238 will postpone the next visit to the treatment center.

45
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48 239 **Outcome measures**
49

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51 240 **Primary outcome**
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53 241 The primary outcome used in this trial will be the proportion of participants with a
54
55 242 treatment response 4 weeks after randomization, defined as a minimum of 50%
56
57 243 improvement in the worst pain intensity during the first steps in the morning
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3 244 compared with the baseline. The average worst pain intensity over the last 3 days will
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5 245 be used for analysis in this trial. Pain intensity will be measured using a 0-100 VAS,
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7 246 with 0 indicating no pain and 100 indicating maximal pain. Participants who must
8
9 247 resort to additional treatments other than rescue medication will be classified as
10
11 248 nonresponders. In addition, the responder rate at weeks 8 and weeks 16 will also be
12
13 249 assessed.
14
15

16 250 **Secondary outcomes**

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18
19 251 The secondary outcomes are as follows:
20

- 21 252 1. Changes in the VAS score for worst pain intensity during the first steps in the
22
23 253 morning from baseline to 4, 8, and 16 weeks after randomization;
- 24
25 254 2. Changes in the VAS score for mean pain intensity during the day from baseline to
26
27 255 4, 8, and 16 weeks after randomization;
- 28
29 256 3. Changes in the pressure pain threshold (PPT) at the most painful area from
30
31 257 baseline to 4, 8, and 16 weeks after randomization. PPT is defined as the
32
33 258 minimum pressure detected when the sensation of pressure first changes to a
34
35 259 sensation of pain.²⁴ PPT will be tested with a pressure algometer (Fabrication
36
37 260 Enterprises, Inc., White Plains, NY; from 1 kg/cm² to 5 kg/cm²) using a metal
38
39 261 probe with a 0.5 cm² rubber disc by a trained researcher. PPT will be measured
40
41 262 when the participant is lying supine in a relaxed position with the affected foot
42
43 263 hanging over the edge of the bed. When measuring the PPT, the rubber disc will
44
45 264 be placed perpendicularly on the painful spot and pressure will be applied at a rate
46
47 265 of approximately 0.1 kg/cm²/s through the metal probe of the pressure algometer.
48
49 266 Participants will be informed to report when the initial pain sensation occurs, and
50
51 267 the readings of the algometer will be recorded. The score will be determined by
52
53 268 averaging three repeated measurements with 30 seconds between each trial. All
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3 269 values below 1 kg/cm² will be reported as 0.5 kg/cm².
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5
6 270 4. Changes in the ankle range of motion (AROM) from baseline to 4, 8, and 16
7
8 271 weeks after randomization: The examiner will measure the AROM including
9
10 272 dorsiflexion and plantar flexion in 2 positions (flexed knee and extended knee)
11
12 273 using a digital goniometer (Tangxia Electronic Instrument Factory, Dongguan,
13
14 274 from 0° to 360°). For the flexed-knee assessment, the participant will sit in a
15
16
17 275 relaxed station with the popliteal space at the edge of the table and their knees
18
19 276 with 90° of flexion. For the extended-knee assessment, the participant will be
20
21 277 seated on a treatment table with the knees fully extended (0°) and the feet hanging
22
23
24 278 off the end of the table. The axis of the goniometer will be placed at the lateral
25
26 279 malleolus. The stationary arm will be placed parallel to the fifth metatarsal and the
27
28
29 280 moving arm placed parallel to the center of the fibular head. The ankle will be
30
31 281 passively moved from a neutral starting position into dorsiflexion and plantar
32
33 282 flexion until a firm end feel is elicited²⁵ and the readings of the goniometer will
34
35 283 be registered. The mean score of three trials with 10 seconds between each
36
37 284 examination will be calculated and used for analysis.
38
39
40 285 5. Changes in the Foot and Ankle Ability Measure (FAAM) total score and subscale
41
42 286 scores from baseline to 4, 8, and 16 weeks after randomization: The FAAM is a
43
44 287 self-reported questionnaire concerning 21 activities of daily living (ADL) items
45
46
47 288 and eight sports subscale items.²⁶ Each item is scored on a 0-4 point Likert scale
48
49 289 anchored by 0 (unable to do) and 4 (no difficulty at all), with higher total scores
50
51 290 indicating a higher level of function. The FAAM has a maximum potential score
52
53 291 of 116 (84 ADL and 32 sport subscales). The obtained score (total, ADL, and
54
55 292 sport subscale scores) is divided by the maximum potential score and multiplied
56
57
58 293 by 100 to obtain a percentage. If the patient does not respond, the specific
59
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1
2
3 294 question will be left blank and not be a part of the final value of the questionnaire.
4

5 295 In this trial, we will use the previously validated Chinese version of the FAAM.²⁷
6

7
8 296 6. Change in plantar fascia thickness (PFT) from baseline to 4 weeks after
9
10 297 randomization: PFT will be measured at the thickest point closest to the calcaneal
11
12 298 insertion in its medial portion using ultrasound. The ultrasound scan will be
13
14 299 performed using an 8-12 MHz linear probe with the patient in the prone position
15
16 300 at the baseline and at 4 weeks after randomization.
17

18
19 301 7. Participant global assessment of improvement: Participants will be asked to rate
20
21 302 their global improvement using a 7-point scale. The improvement will be scaled
22
23 303 from 1 (complete recovery) to 7 (vastly worse), with 2 being obvious
24
25 304 improvement, 3 being a little improvement, 4 being no change, 5 being a little
26
27 305 worse, and 6 being obviously worse. The proportions of participants with different
28
29 306 degrees of improvement will be assessed at 4, 8, and 16 weeks after
30
31 307 randomization. Scales of participant global assessment of improvement with 7
32
33 308 response categories have been rated as relatively easy to use and show good
34
35 309 reliability and validity.²⁸
36
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40 310 8. Participants' expectation towards acupuncture at baseline: At baseline,
41
42 311 participants in the acupuncture and SA groups will be asked the following
43
44 312 question: "Do you think acupuncture will be helpful to improve your chronic PF?"
45
46 313 Participant will choose one of the following answers: "Extremely helpful", "Very
47
48 314 helpful", "Helpful", "Not help at all", and "Unclear".
49

50
51 315 9. The proportion of participants who have maintained blinding during treatment in
52
53 316 the acupuncture and SA groups: Participants' blindness to the mode of
54
55 317 acupuncture will be assessed five minutes after the end of any treatment in the
56
57 318 fourth week by asking the patients the following question: "Which of the two
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3 319 acupuncture modalities do you think you received, acupuncture or SA?”
4
5 320 Participants will choose one of the following answers: “Acupuncture”, “SA”, or
6
7 321 “Unclear”. Prior to the question, patients will be informed that they may have
8
9
10 322 received one of two modalities: acupuncture with a deeper insertion or SA with no
11
12 323 skin penetration.

14 324 **Safety assessment**

16 325 The adverse events (AEs) during the entire study will be recorded and described as
17
18 326 acupuncture-related AEs and non-acupuncture-related AEs. Acupuncture-related AEs
19
20 327 include fainting, broken needle, unbearable pain during acupuncture (VAS ≥ 8 , using
21
22 328 VAS from 0 [no pain] to 10 [worst pain imaginable]), and other unintended signs or
23
24 329 symptoms after acupuncture (e.g., localized hematoma or infection, nausea, dizziness,
25
26 330 vomiting, headache, palpitations). Detailed information on AEs including the name,
27
28 331 onset, end date, intensity, correlation with acupuncture, and outcomes will be
29
30 332 documented in the case report form. Investigators will immediately report serious AEs
31
32 333 (eg, requiring hospitalization, causing disability or impaired ability to work) to the
33
34 334 Medical Ethics Committee of Guang’anmen Hospital, and stop the clinical trial until
35
36 335 further instruction is given.

37 336 **Sample size calculation**

38 337 Based on the results of a previous study,¹² a sample size of 120 participants will be
39
40 338 enrolled to provide 80% power to detect a difference of 35% between the combined
41
42 339 acupuncture group and waiting-list group in the proportion of participants with
43
44 340 treatment response 4 weeks after randomization at a two-sided significance level of
45
46 341 0.05. The proportion of participants with treatment response after 4 weeks was
47
48 342 assumed to be roughly 12% for the waiting-list group,¹² with an anticipated 10% loss
49
50 343 to follow-up.

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3 344 **Statistical analysis**
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5 345 The null hypothesis is that the proportion of participants with treatment response 4
6
7 346 weeks after randomization will be the same for the combined acupuncture groups and
8
9 347 waiting-list group. Data will be presented as mean \pm standard deviation for
10
11 348 quantitative variables and frequencies (number of cases), with relative frequencies
12
13 349 (percentages) for categorical variables. The primary outcome analysis will use the
14
15 350 Cochran-Mantel-Haenszel (CMH) test to compare the response rate between the
16
17 351 combined acupuncture groups and the waiting-list group. If the result of this analysis
18
19 352 is significant, hierarchical testing will be applied to the acupuncture group versus
20
21 353 waiting-list group, SA group versus waiting-list group, and acupuncture group versus
22
23 354 SA group. For normally distributed quantitative variables, a repeated-measures
24
25 355 analysis of variance (ANOVA) with multiple comparisons post-hoc test will be
26
27 356 performed using baseline as a co-variate when comparing more than two groups and
28
29 357 an unpaired T test when comparing two groups. For non-normally distributed
30
31 358 quantitative variables, the non-parametrical Kruskal-Wallis test and Mann-Whitney
32
33 359 test will be performed. For categorical variables, the Chi square (χ^2) test will be used.
34
35 360 Confidence intervals for the difference between treatments will be calculated at the
36
37 361 95% level. A two-tailed test will be applied for all available data, and a *P* value < 0.05
38
39 362 will be considered statistically significant. All analyses in this trial will be performed
40
41 363 using SPSS software V.20.0 (IBM SPSS Statistics; IBM Corp, Somers, NY) on the
42
43 364 basis of the intention-to-treat (ITT) population, which will include participants who
44
45 365 had been randomized. Missing data will be completed as the last value observed
46
47 366 before dropout. Only the analysis of primary outcome will be considered in a
48
49 367 confirmatory manner. No adjustment will be made for multiple comparisons as those
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51 368 analyses of secondary outcomes will be interpreted as exploratory.
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3 369 **Quality control**
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5 370 To ensure the quality of the trial, all the relevant staff will be uniformly trained before
6
7 371 the trial on the purpose and content of the trial (e.g., diagnosis of chronic PF,
8
9 372 inclusion and exclusion criteria, intervention procedures, and outcome measures).
10
11 373 Licensed acupuncturists with at least 2 years' acupuncture experience will perform
12
13 374 the treatment. Throughout the trial, strict three-level monitoring will be conducted for
14
15 375 data quality control. Dropouts and withdrawals including the reasons will be recorded
16
17 376 during the trial. Paper-based study data will be stored in locked file cabinets under the
18
19 377 management of the investigators. Electronic records will be stored in a Structured
20
21 378 Query Language (SQL) server database on a limited access, secure server maintained
22
23 379 by the Guang'anmen Hospital, China Academy of Chinese Medical Sciences.
24
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27

28 380 **Patient and public involvement**
29

30 381 The research question of whether combined acupuncture and SA will result in larger
31
32 382 improvements in heel pain than no acupuncture treatment for patients with chronic PF
33
34 383 was first proposed by the investigator after encountering a patient who received SA
35
36 384 and reported a similar improvement in heel pain as another patient who received
37
38 385 routine acupuncture in the clinic. Patients were not involved in conceiving or
39
40 386 implementing the study.
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44 387 **Ethics and dissemination**
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46 388 This trial will be conducted in accordance with the principles of the Declaration of
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48 389 Helsinki. The study has been registered at the ClinicalTrials.gov (NCT04185259) and
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50 390 approved by the Ethical Committee of the Guang'anmen Hospital, China Academy of
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52 391 Chinese Medical Sciences (approval No: 2019-210-KY). All participants must sign
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54 392 the informed consent form prior to randomization, and they will be permitted to
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56 393 withdraw at any time during the trial, with or without reasons being provided. Any
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3 394 amendment or other change of the protocol will need to be approved by the Ethical
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5 395 Committee of the Guang'anmen Hospital, China Academy of Chinese Medical
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8 396 Science, and agreed to by the co-researchers.
9

10 397 Following analysis of the data, the findings of this study will be submitted for
11
12 398 publication in a peer-reviewed medical journal. The results will also be disseminated
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14
15 399 through presentation at the relevant conferences and scientific meetings.
16

17 400 **Discussion**

18
19 401 Although several reviews and RCTs^{15,16,12,29} have been published that focus on
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21 402 acupuncture for PF, owing to the lack of a placebo control, non-specific physiology
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23 403 effects of needling and spontaneous remission of PF cannot be excluded. To date, this
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25
26 404 is the first randomized trial with three parallel arms, assessing whether combined
27
28 405 acupuncture and SA compared to no treatment control produce a significant reduction
29
30 406 in pain intensity in chronic PF. We anticipate that this study will determine the
31
32 407 efficacy of acupuncture for patients with chronic PF, and improve the care of these
33
34 408 patients in the clinic.
35
36

37 409 Though most PF patients will achieve significant improvement in symptoms
38
39 410 within 1 year regardless of treatment,³⁰ many will seek treatment before then. Patients
40
41 411 often choose other treatment options when they cannot obtain a satisfactory outcome
42
43 412 from conservative treatment (e.g., muscle stretching, heel cups, arch supports, night
44
45 413 splints, shockwave therapy, NSAIDs). In this trial, we recruited only chronic
46
47 414 participants who had failed to respond to conservative treatment prior to participation.
48
49 415 The results can be generalized to patients experiencing chronic refractory PF.
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52 416 In this study, pain intensity measured with VAS during the first steps in the
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54 417 morning will be used as the primary outcome. This variable has been used in previous
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56 418 trials^{12,21} and is a meaningful subject outcome measure for the assessment of PF
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3 419 improvement. In addition, we will also use PPT and PFT as objective secondary
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5 420 outcomes. PPT is an essential evaluation tool for patients suffering from many
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7 421 musculoskeletal disorders including PF and provides a reliable process for measuring
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9 422 participants' responses to mechanical stimuli.³¹ Compared to normal asymptomatic
10
11 423 patients, patients with PF often exhibit a thickened plantar fascia on ultrasound.³²
12
13 424 Therefore, a PFT evaluation would provide information to detect the anatomical
14
15 425 changes that occur in the plantar fascia after acupuncture.
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19 426 The strengths of this study include a sham control (non-penetrating at
20
21 427 non-acupuncture point) and waitlist control design, objective measurements (i.e. PPT,
22
23 428 PFT), strict quality control, and evaluation of the participants' expectations regarding
24
25 429 acupuncture. We chose sham acupuncture as a placebo treatment for this study to
26
27 430 confirm the specific physiological effect of needling because sham acupuncture may
28
29 431 be preferable, particularly for Chinese patients who are familiar with the general
30
31 432 procedure of acupuncture. Several limitations to this trial need to be acknowledged.
32
33 433 First, it will be impossible to blind the acupuncturists and participants in the waitlist
34
35 434 control group, which is a general problem in non-pharmacological interventional trials
36
37 435 and can cause bias. Second, a high dropout rate may exist in the waitlist group
38
39 436 because participants expect to receive acupuncture treatment when they join the trial.
40
41 437 Third, the follow-up period will not exceed 12 weeks, which will not allow for
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43 438 detection of the long-term effects of acupuncture for chronic PF. Fourth, our approach
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45 439 will enable us to draw conclusions about the selected acupuncture points but not about
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47 440 individualized treatments.
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5 442 **Ethical Approval and Consent to participate** The study has received approval from
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7 443 the Institutional Review Boards of Guang'anmen Hospital in China (approval NO.
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9 444 2019-210-KY, TEL +86-10-88001552), and all investigators complied with the
10
11
12 445 Helsinki Declaration.

13
14 446 **Consent for publication** Not applicable.

15
16 447 **Availability of data and materials** Not applicable.

17
18 448 **Competing interests** The authors declare that they have no competing interests.

19
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21
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23
24 451 collection, management, analysis, and interpretation of the data; preparation, review,
25
26 452 or approval of the manuscript.
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32

33 454 **Authors' contributions** Weiming Wang and Zhishun Liu conceived the idea and
34
35 455 designed this trial. Weiming Wang, Zhiwei Zang and Zhishun Liu developed the
36
37 456 acupuncture protocol to this article. Weina Zhang, Zhiwei Zang, Sixing Liu and Liang
38
39 457 Li will be responsible for the recruitment, acupuncture, and assessment respectively.
40
41 458 Yan Liu will be responsible for statistical analysis. This manuscript was drafted by
42
43 459 Weiming Wang and Sixing Liu, and was revised by Yan Liu and Zhishun Liu. All
44
45 460 authors read and approved the final draft of the manuscript.
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55
56 463 will be included in this study.
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4 **Figure legends**
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6 Figure 1: Trial flow diagram
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9 Figure 2: Study schedule
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For peer review only

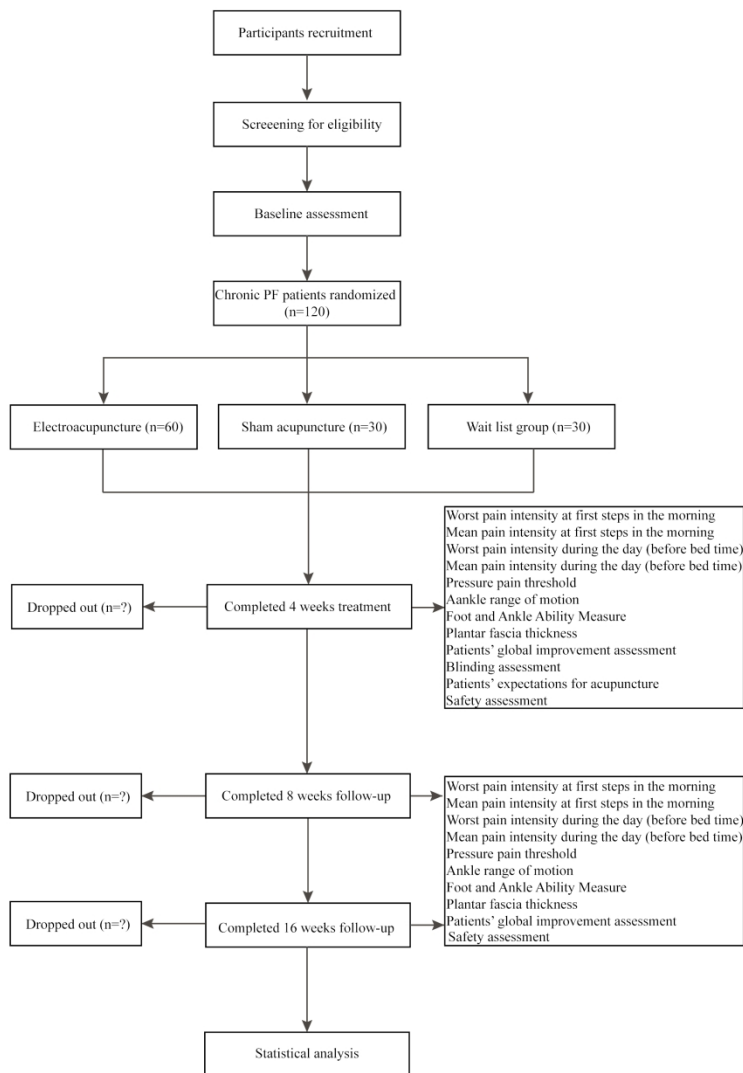


Figure 1. Trial flow diagram

Trial flow diagram

234x301mm (300 x 300 DPI)

TIME POINT (W, week)	Study Period				
	Baseline	Allocation	Treatment	Follow-up	
			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
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5		18b	Plans to promote participant retention and complete follow-up, including list 15
6			of any outcome data to be collected for participants who discontinue or
7			deviate from intervention protocols
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10	Data	19	Plans for data entry, coding, security, and storage, including any related 15
11	management		processes to promote data quality (eg, double data entry; range checks for
12			data values). Reference to where details of data management procedures
13			can be found, if not in the protocol
14			
15	Statistical	20a	Statistical methods for analysing primary and secondary outcomes. 14-15
16	methods		Reference to where other details of the statistical analysis plan can be
17			found, if not in the protocol
18			
19			
20		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) NA
21			
22		20c	Definition of analysis population relating to protocol non-adherence (eg, as
23			randomised analysis), and any statistical methods to handle missing data 14-15
24			(eg, multiple imputation)
25			
26			

Methods: Monitoring

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29	Data	21a	Composition of data monitoring committee (DMC); summary of its role and NA
30	monitoring		reporting structure; statement of whether it is independent from the sponsor
31			and competing interests; and reference to where further details about its
32			charter can be found, if not in the protocol. Alternatively, an explanation of
33			why a DMC is not needed
34			
35			
36		21b	Description of any interim analyses and stopping guidelines, including who 14
37			will have access to these interim results and make the final decision to
38			terminate the trial
39			
40	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and 13-14
41			spontaneously reported adverse events and other unintended effects of
42			trial interventions or trial conduct
43			
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45	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether 15
46			the process will be independent from investigators and the sponsor
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Ethics and dissemination

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50	Research	24	Plans for seeking research ethics committee/institutional review board 16,19
51	ethics		(REC/IRB) approval
52	approval		
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5	Protocol	25	Plans for communicating important protocol modifications (eg, changes to	16
6	amendments		eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators,	
7			REC/IRBs, trial participants, trial registries, journals, regulators)	
8				
9	Consent or	26a	Who will obtain informed consent or assent from potential trial participants	6
10	assent		or authorised surrogates, and how (see Item 32)	
11				
12		26b	Additional consent provisions for collection and use of participant data and	NA
13			biological specimens in ancillary studies, if applicable	
14				
15				
16	Confidentiality	27	How personal information about potential and enrolled participants will be	19
17			collected, shared, and maintained in order to protect confidentiality before,	
18			during, and after the trial	
19				
20	Declaration of	28	Financial and other competing interests for principal investigators for the	19
21	interests		overall trial and each study site	
22				
23				
24	Access to	29	Statement of who will have access to the final trial dataset, and disclosure	19
25	data		of contractual agreements that limit such access for investigators	
26				
27	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for compensation to	NA
28	post-trial care		those who suffer harm from trial participation	
29				
30	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to	16
31	policy		participants, healthcare professionals, the public, and other relevant groups	
32			(eg, via publication, reporting in results databases, or other data sharing	
33			arrangements), including any publication restrictions	
34				
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36		31b	Authorship eligibility guidelines and any intended use of professional	19
37			writers	
38				
39		31c	Plans, if any, for granting public access to the full protocol, participant-level	NA
40			dataset, and statistical code	
41				
42				
43	Appendices			
44				
45	Informed	32	Model consent form and other related documentation given to participants	NA
46	consent		and authorised surrogates	
47	materials			
48				
49	Biological	33	Plans for collection, laboratory evaluation, and storage of biological	NA
50	specimens		specimens for genetic or molecular analysis in the current trial and for	
51			future use in ancillary studies, if applicable	
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5 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &
6 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.
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