

SWE and SMI Ultrasound Techniques for Monitoring Needling Treatment of Ankylosing Spondylitis: Study Protocol for a Single-blinded Randomized Controlled Trial

Mengyu Wang

The Second Clinical College of Guangzhou University of Chinese Medicine

Wen Fu

Guangzhou University of Chinese Medicine <https://orcid.org/0000-0001-7261-2506>

Lingcui Meng

The Second Affiliated Hospital of Guangzhou University of Chinese Medicine

Jiajia Liu

The Second Affiliated Hospital of Guangzhou University of Chinese Medicine

Lihua Wu

Guangzhou University of Chinese Medicine

Yingjun Peng

The Second Clinical College of Guangzhou University of Chinese Medicine

Ziping Li (✉ lzip_008@163.com)

The Second Affiliated Hospital of Guangzhou University of Chinese Medicine

Study protocol

Keywords: Acupuncture, Ankylosing spondylitis, Musculoskeletal ultrasound, Physical dysfunction

Posted Date: March 25th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-354903/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Ankylosing spondylitis (AS) is a high-incidence disease in young men that interferes with patients' physical and mental wellbeing and overall quality of life (QoL) (7). It is often accompanied by arthralgia, stiffness and limited lumbar flexibility. Acupuncture is safe and effective for reducing the symptoms of AS, but the underlying mechanisms by which it does so are not fully understood. Therefore, to objectively assess acupuncture efficacy, which is critical for patients making informed decisions about appropriate treatments, we will use shear-wave elastography (SWE) and superb microvascular imaging (SMI) ultrasound techniques to evaluate elasticity of lumbar paraspinal muscles and blood flow to the sacroiliac joint (SIJ) in AS.

Methods: We will recruit a total of 70 participants diagnosed with AS and 30 healthy subjects. Participants will be randomly allocated 1:1 to either an acupuncture group or a sham control acupuncture group. Primary-outcome measures will be musculoskeletal ultrasound and the Bath Ankylosing Spondylitis Metrology Index (BASMI). Secondary-outcome measures will be the Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Function Index (BASFI), Fatigue Scale-14 (FS-14), Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS). We will monitor the effect of acupuncture or sham acupuncture on blood flow and SIJ inflammation using SMI, lumbar-muscle stiffness using SWE and the lumbar paraspinal-muscle cross-sectional area (CSA) using two-dimensional (2D) grayscale imaging. QoL, physical function and fatigue will be assessed using an evaluation scale or questionnaire developed for this study, with outcomes measured by the ASQoL, BASMI, BASDAI, BASFI and FS-14. Mental state will be evaluated using the SAS and SDS. Healthy subjects will not receive acupuncture but undergo only musculoskeletal ultrasound at baseline. Acupuncture and sham control acupuncture interventions will be conducted for 30 min, 2–3 times/week for 12 weeks. Musculoskeletal ultrasound will be conducted at baseline and post-intervention, while other outcomes will be measured at baseline, 6 weeks and post-intervention. The statistician, outcome assessor and participants will be blinded to treatment allocation.

Discussion: The results of this single-blinded, randomized trial with sham controls could help demonstrate the efficacy of acupuncture and clarify whether musculoskeletal ultrasound could be used to evaluate AS.

Trial registration: Chinese Clinical Trial Registry, ChiCTR2000031476. Registered April 3, 2020. <http://www.chictr.org.cn/index.aspx>.

Background

Ankylosing spondylitis (AS) is a systemic disease characterized by chronic inflammation of the axial joint, involving the sacroiliac joint (SIJ), with primary clinical symptoms of arthralgia, stiffness and limited flexibility [1]. Over the past 15 years, total prevalence of AS in mainland China has been 0.29%, ranging from 0.42% in males to 0.15% in females [2]. The primary pathology includes inflammation of the

bony attachments of tendons, ligaments or joint capsules [3]. Physical dysfunction in AS can potentiate serious health conditions and lead to fatigue, depression, anxiety and decreased quality of life (QoL) [4, 5]. The disease imposes substantial physical and social burdens on patients and can interfere with work and schooling [6, 7]. The goals of treatment are to alleviate symptoms, improve functioning, decrease disease complications and forestall skeletal damage as much as possible [8]. Use of non-steroidal anti-inflammatory drugs (NSAIDs) and very expensive biologics is recommended for treatment [9]. However, due to the significant side effects [10], development of therapeutic resistance to drug treatment [11] and high drug costs, such use places a huge burden on patients. Thus, nonpharmacological intervention has become one of the most important options for AS [12]. Alternative therapies play an important role in treating this disease; for example, a combination of Traditional Chinese Medicine (TCM) with, especially, acupuncture can achieve better effect.

Acupuncture is a safe alternative therapy with minimal side effects that has shown benefits in alleviating symptoms, reducing complications and accelerating recovery in AS [13]; it has been shown to improve joint functional flexibility when used in the management of pain and rheumatic diseases [14–17]. Previous systematic studies support that acupuncture could be an option for treating AS [18, 19].

The 2019 guidelines of the American College of Rheumatology (ACR) [8] state that magnetic resonance imaging (MRI) is not suitable for detecting subclinical inflammation in patients with stable disease and recommend against patients obtaining spine radiographs at scheduled intervals to monitor progression, as the practice entails radiation exposure and will not lead to alteration of treatment in most cases. Therefore, it is particularly important to find a method that is safe and can be used at short intervals to detect subclinical inflammation in a timely manner. Ultrasound has become part of the fundamental Outcome Measures in Rheumatology (OMERACT) methodology validation by repeatedly exercises across various domains, including inflammatory burden and structural damage [20, 21]. Musculoskeletal ultrasound is a reliable evaluation method that directly visualizes characteristics of rheumatic conditions such as synovitis, tenosynovitis, bursitis, enthesitis, crystal depositions, bone erosions or osteophytes/enthesophytes. It is more sensitive than X-ray or MRI in physical tendons, ligaments or joint capsules [22, 23]. Early detection of subclinical lesions can help decision makers improve the quality of their daily clinical practice in rheumatic diseases.

Although musculoskeletal ultrasound is less sensitive than MRI and X-ray in early detection of synovitis and tenosynovitis [24], it is suitable for short-term evaluation of stable rheumatic diseases, offering highly accessible, low-cost, real-time imaging without radiation [25, 26]. The OMERACT Ultrasound Working Group has engaged in the validation of ultrasound as an outcome measurement instrument (OMI) by defining ultrasound manifestations of spondyloarthritis (SpA) [27].

This high-quality, randomized controlled trial (RCT) was designed via a pragmatic trial approach to objectively assess the efficacy of acupuncture using musculoskeletal ultrasound and a sham acupuncture group.

Objectives

Our research hypotheses are as follows: (1) Musculoskeletal ultrasound will be used as a short-term effective-examination method and objective auxiliary-examination method for AS. (2) Acupuncture will reduce subjective pain rating, the use of pain relievers and the effect of pain on ASQoL.

Methods/design

Study setting

The study will follow the principles of the Consolidated Standards of Reporting Trials (CONSORT) for randomized, parallel studies, as well as the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) statement for acupuncture. [28,29]. This will be a single-blinded RCT with a sample size based on published evidence in comparative studies. Seventy AS patients will be blinded to study conditions. The study will be conducted at Guangdong Provincial Hospital of Chinese Medicine (GPHCM), Department of Acupuncture, Guangdong, China, following the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT). For the participant timeline, see Figure 1.

Recruitment

A total of 70 AS patients age 18–60 years and 30 healthy volunteers will be recruited for this study. AS participants will be recruited from both the outpatient and inpatient departments of the GPHCM, Department of Rheumatology. Study flyers, bulletin boards at the hospital and online advertisements will also be used for patient recruitment. Healthy volunteers will be recruited from among students of Guangzhou University of Chinese Medicine. Treatment and measurements will be performed at the GPHCM.

Inclusion criteria

Recruitment conditions are as follows: 1) a definite diagnosis of axial AS during a stable disease period; 2) 18–60 years of age, onset age <40 years; 3) currently being treated at a stable dose of medication for ≥ 4 weeks prior to randomization and have received no biologic therapy within the past 3 months; 4) course of disease ≤ 10 years; and 5) willingness to sign the informed-consent form. Potential participants who satisfy the inclusion criteria will be sent a more detailed information leaflet for informed consent. They will be contacted few days later to determine whether they are interested in participating, and, if so, an appointment will be made for them to visit the GPHCM.

Exclusion criteria

Potential participants will be excluded for the following reasons: 1) clinically important fracture of the spine; 2) spinal deformity or disability; 3) blood coagulation disorder; 4) presence of viral hepatitis, human immunodeficiency virus (HIV) or other blood infection; 5) pregnancy or lactation; 6) previous

history of stroke or transient ischemic attacks; 7) pacemaker or other electrical device implanted; or 8) lack of consent, active pursuit of compensation or with pending litigation.

Dropout criteria

1) Patients who have severe adverse reactions after acupuncture and cannot successfully complete the course of treatment; 2) The participant was unable to follow the protocol treatment for personal reasons during the course, or use other traditional Chinese medicine therapies.

Randomization

A computer algorithm [30] generated a permuted block randomization sequence that will allocate participants to either the acupuncture or sham control acupuncture group to ensure balanced group sizes and allocation concealment. We will use opaque, sealed envelopes in sequential order to contain allocation information.

Blinding

As this is a single-blinded trial, patients will not know which treatment approach they will undergo. During the data collection and analysis stages, the clinical researcher, assessor and statistician will not share study information with each other. Blinding will be assessed after the last treatment using a questionnaire that asks participants if they were in the real treatment group or the sham treatment group. The possible responses are “real treatment group,” “sham group” or “do not know.”

INTERVENTION

All practitioners in this trial are licensed TCM acupuncture therapists with at least 5 years' clinical experience, and they will be trained to master the study protocol. The acupuncturist will be asked to administer the sham intervention as they would administer standard manipulation, with the same enthusiasm. All participants will continue to receive standard rheumatological care.

Acupuncture group

The acupuncture intervention program was designed by a senior acupuncturist. The acupoints will be *Shenshu* (BL23), *Ganshu* (BL18), *Yanglingquan* (GB34), *Jizhong* (DU6), *Jinsuo* (DU8), *Mingmen* (DU4) and *Yaoyangguan* (DU3). We will use sterile, disposable stainless-steel needles 0.3 mm in diameter and 25 or 40 mm in length, depending on the acupoints. After eliciting the Deqi response, the researcher will apply electro-acupuncture by connecting an acupoint nerve stimulator (HANS-200A) to *Shenshu* (BL23) and *Ganshu* (BL18) at a frequency of 2 Hz for 30 min. Electro-acupuncture intensity will be set according to the maximum intensity tolerated by each subject (0.9–3.0 mA). Other needles will be stimulated manually every 10 min. All needles will be left in place for 30 min.

Sham control acupuncture group

The acupuncture points will be lateral to those in the *verum* acupuncture group. However, instead of using 0.25-mm diameter, 25-mm long, sterile disposable stainless-steel needles inserted into acupoints 2–3 mm deep without manipulation and into non-acupoints, we will include NP1 (1 cm outward horizontally of *Shenshu* [BL23]), NP2 (*Ganshu* [BL18] level outward by 1 cm), NP3 (1 cm behind *Yanglingquan* [GB34]), NP4 (1 cm to the right horizontally of *Jizhong* [DU6]), NP5 (1 cm to the right horizontally of *Jinsuo* [DU8]), NP6 (1 cm outward horizontally of *Mingmen* [DU4]) and NP7 (1 cm outward horizontally of *Yaoyangguan* [DU3]). Next, electro-acupuncture will be applied to *Shenshu* (BL23) and *Ganshu* (BL18; 0.1–0.3 mA). All needles will be left in place for 30 min. The inclusion of a placebo group will allow for comparison of active acupuncture care effects with manifestations of either sham treatment or psychic solace.

Health control group

No acupuncture intervention will be conducted in healthy controls.

OUTCOMES

Primary outcomes

Primary outcomes will be musculoskeletal-ultrasound, ASQoL and BASMI results. Musculoskeletal ultrasound will use two-dimensional (2D) grayscale, SWE and SMI techniques. The 2D grayscale technique will capture muscle thickness changes in the paraspinal and multifidus muscles. Changes in lumbar-muscle thickness can reflect muscle morphological change due to acupuncture treatment for somatic disorders. The lumbar paraspinal muscles play important roles in movement and control of the spine; studies have shown an inverse relationship between lumbar paraspinal-muscle CSA and lower-back disability but not between lumbar paraspinal-muscle CSA and pain intensity, suggesting that treatment strategies directed at increasing paraspinal-muscle size might be effective in reducing lower-back disability [31]. Later, a blinded tester will measure thickness at the levels of the L4–5 zygapophyseal joints using onscreen calipers [32]. SWE is an ultrasound technique that characterizes tissue mechanical properties based on the propagation of remotely induced shear waves [33]. It provides semiquantitative (color map) and quantitative (absolute SWE value) imaging biomarkers that are useful in assessing the elasticity of tendon and muscle composition and stiffness [34,35] and in helping to distinguish between asymptomatic and symptomatic [36], with diseased tendons being significantly softer than healthy ones [37]. SMI is an ultrasound technique for vascular and microvascular examination. It can diagnose diseases associated with angiogenesis in their early phases and has value in grading disease activities and monitoring therapeutic responses [38]. SMI uses an intelligent algorithm that efficiently separates low-speed flow signals from motion artifacts and successfully extracts clinically relevant information [39]. We will test AS participants using SMI, record resistance index (RI), peak systolic velocity (PSV) and end diastolic velocity (EDV) to reflect SIJ inflammation in this trial. Ultrasound tests will be performed at baseline and week 12.

The ASQoL and BASMI scales have anchors of 0 (none) to 10 (severe). Participants will evaluate their conditions over the preceding week. ASQoL records the impact of AS on health-related QoL from the

patient's perspective in terms of sleep, mood, motivation, coping, activities of daily living, independence, relationships and social life [40]. BASMI [41] is associated with QoL, physical function and psychological status and reflect the change of lumbar side flexion sensitive and reproducible.

Secondary outcomes

Secondary outcomes will be BASDAI, BASFI, FS-14, SAS and SDS results. The BASDAI and BASFI were developed in 1994 using the Visual Analog Scale (VAS) [42,43]. The BASDAI is a patient-generated index measuring disease activity in patients with AS. Scores depend on what patients perceive as being related to their AS. The BASFI measures patients' functional ability to cope with everyday life in terms of bending, reaching, changing position, standing, turning and climbing steps. The FS-14 measures severity of physical and mental fatigue, which correlates positively with fatigue severity in AS. The SAS and SDS, self-evaluation scales that analyze the patient's emotional state, are widely used in research and in clinical practice for the detection of anxiety and depression.

Other outcomes

Participant characteristics of age, weight, body mass index, current medical issues, current medications and back pain history will be collected using electronic case report forms. Participants will be asked for number and types of medications taken, medication scheduling and the dose used to self-manage AS symptoms at baseline and at weeks 6 and 12.

Follow-up

Follow-up will occur 12 weeks after completion of the treatment program. This time point was selected to assess sustained long-term effectiveness of the intervention.

The trial work plan is summarized in Figure 2.

Sample size

Based on published evidence in comparative studies, a sample size of 24 per group will yield a power of 90% at an alpha (α) value of 0.05. To account for an anticipated dropout rate of 15%, the enrollment target will be 70.

Data analysis

We will use SPSS software version 18.0 (IBM Corp, Armonk, New York, US) to perform data analysis. Demographic and baseline data will be analyzed with standard descriptive statistics. Data will be presented as the mean \pm standard deviation (SD). Between-group differences will be tested using repeated-measure analyses of variance (ANOVAs). The entire data analysis process will be performed by statisticians who are independent from the research team and blinded to the group settings. The accepted level of significance for all analyses will be $P < 0.05$.

Ethics and dissemination

Any participant who discontinues treatment will be asked their reasons for poor compliance or dropout. If a participant reports a severe adverse event, they will be withdrawn from the study and, depending on the nature of the event, referred to the emergency department or receive appropriate treatment. We will collect, assess and report any spontaneously described adverse events from participants.

We will be monitored by the Institutional Ethics Committee (IEC) of GPHCM, which will audit trial conduct every December. The IEC of GPHCM will be independent from the investigators and sponsor. Ethical approval has been obtained from the IEC of GPHCM (YF2019-232-01). All candidates who agree to participate and who meet all of the inclusion criteria and none of the exclusion criteria will be provided informed consent to obtain full understanding of what study participation will entail and the potential risks. Participants have the right to discontinue participation at any time. Data will be used in the aggregate only, and no identifying characteristics of individuals will be published or presented.

Discussion

The purpose of this trial is to assess the impact of acupuncture in the management of AS. It is clear that increased muscle stiffness is associated with poor range of motion [44], and a chronic inflammatory condition has significant impact on QoL. Patients report that back pain, arthralgia and stiffness influence their daily work productivity and nocturnal sleep quality [45]. Acupuncture is used to reduce muscle stiffness and increase somatic activity in AS patients, it is monitored by musculoskeletal-ultrasound techniques that, if less operator dependent, could obtain more-stable and reliable results [46]. The design of an appropriate control group for a clinical trial is critical. We will set a healthy-control group for baseline comparison, as there is currently no standardized for musculoskeletal-ultrasound measurement of AS [47]. However, it is difficult to use placebo needles for controls. Therefore, we will use non-acupoints and superficial puncturing, which are considered ineffective, in the sham acupuncture group.

NSAIDs are often first-line treatment for AS, and biologics are the next step up. However, patients who have inadequate response to NSAIDs but cannot afford biologics often experience significant pain and impairment of their QoL [48]. This trial would provide evidence for acupuncture care for this group of patients.

Despite the measures taken to ensure a well-controlled trial, there are several methodological limitations to this study. The treatment intervention duration of 12 weeks might make it difficult to ensure patient compliance. Other aspects such as the trial results are meant to describe an approach to treatment for the typical patient and cannot anticipate all possibilities; clinicians must make careful clinical assessments based on sound clinical judgment of each patient's circumstances and consideration of the patient's preferences. In spite of its limitations, we hope that the trial will help provide new insights into the value of acupuncture and the evidence of musculoskeletal-ultrasound measures in AS.

Trial status

This trial is currently recruiting participants. Participants will be recruited for this study started in June 2020 and expected finish in May 2021. The protocol version number is 2019103103, date 14 January 2020.

Abbreviations

AS: Ankylosing Spondylitis; QoL: quality of life; SWE: Wave Elastography; SMI: Superb Microvascular Imaging; SIJ: sacroiliac joint; BASMI: Bath Ankylosing Spondylitis Metrology Index; ASQoL: Ankylosing Spondylitis Quality of Life Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Function Index; FS-14: Fatigue scale-14; SAS: Self-Rating Anxiety Scale; SDS: Self-rating depression scale; CSA: cross-sectional area; NSAIDs: Non-Steroidal Antiinflammatory Drugs; TCM: Traditional Chinese Medicine; ACR: American College of Rheumatology; MRI: Magnetic Resonance Imaging; OMERACT: Outcome Measures in Rheumatology; OMI: outcome measurement instrument; SpA: spondyloarthritis; RCT: randomized controlled trial; CONSORT: Consolidated Standards of Reporting Trials; STRICTA: Standards for Reporting Interventions in Clinical Trials of Acupuncture; GPHCM: Guangdong Provincial Hospital of Chinese Medicine; SPIRIT: Recommendations for Interventional Trials; HIV: human immunodeficiency virus; 2D: two-dimensional; RI: resistance index; PSV: peak systolic velocity; EDV: end diastolic velocity; VAS: Visual Analog Scale; SD: standard deviation; ANOVAs: analyses of variance; IEC: Institutional Ethics Committee;

Declarations

Ethics approval and consent to participate

This study was approved by the Institution Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine (No.YF2019-232-01). Written informed consent is required for participation. Protocol amendments, adverse event reporting and annual review will be overseen by the CIRB.

Consent

Written informed consent was obtained from the patient(s) for publication of this manuscript and accompanying images. A copy of the written consent is available for review by the editor of this journal.

Availability of data and materials

Not applicable.

Competing interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Funding

This trial is funded by National Natural Science Foundation of China (No. 81573827), and Studio of Southern China Acupuncture and Herbal Medicine Combination School in Guangdong Provincial Hospital of Chinese Medicine (No. E43612). The funder has not taken part in the study design, data collection and analysis, the decision to publish, or the preparation of the manuscript.

Authors' contributions

ZPL conceived and designed the trial and obtained funding for the trial. MYW and WF drafted the manuscript and performed the trial registration. LCM and JJL performed musculoskeletal ultrasound operation and provided critical revision of the manuscript. LHW designed the statistical analysis. YJP participated in the data collection. All authors have read and approved the final manuscript.

Acknowledgments

We thank LetPub (www.letpub.com) for its linguistic assistance during the preparation of this manuscript.

References

1. Taurog JD, Chhabra A, Colbert RA. Ankylosing spondylitis and axial spondyloarthritis. *N Engl J Med* 2016; 374: 2563–74.
2. Zhao J, Huang C, Huang H, et al. Prevalence of ankylosing spondylitis in a Chinese population: a systematic review and meta-analysis. *Rheumatol Int*. 2020;40(6):859-872.
3. Dougados M, Baeten D. Spondyloarthritis. *Lancet* 2011; 377:2127–37.
4. Ramonda R, Marchesoni A, Carletto A, Bianchi G, Cutolo M, Ferraccioli G, Fusaro E, De Vita S, Galeazzi M, Gerli R, et al. Patient-reported impact of spondyloarthritis on work disability and working life: the ATLANTIS survey. *Arthritis Res Ther*. 2016; 18:78.
5. Kwan YH, Fong W, How P, Wee H-L, Leung YY, Phang JK, Lui NL, Tan CS, Malhotra R, Østbye T, Thumboo J. The impact of axial spondyloarthritis on quality of life (QoL): a comparison with the impact of moderate to end-stage chronic kidney disease on QoL. *Qual Life Res*. 2018; 27:2321–7.
6. Boonen A, Sieper J, van der Heijde D, Dougados M, Bukowski JF, Valluri S, et al. The burden of non-radiographic axial spondyloarthritis. *Sem Arthritis Rheum* 2015; 44:556–62.
7. Ward MM. Quality of life in patients with ankylosing spondylitis. *Rheum Dis Clin North Am* 1998; 24:815–27.
8. Ward Michael M, Deodhar Atul, Gensler Lianne S, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis.[J], 2019, 71(10): 1599-1613.

9. Kiltz U, Baraliakos X, Braun J. Management of axial spondyloarthritis. *Internist Berl*. 2016; 57:1060–8.
10. Galloway JB, Mercer LK, Moseley A, et al. Risk of skin and soft tissue infections (including shingles) in patients exposed to anti-tumour necrosis factor therapy: results from the British Society for Rheumatology Biologics Register. *Ann Rheum Dis*. 2013; 72:229–34.
11. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis*. 2009;68(Suppl 2): ii1–44.
12. Grazio S, Grubišić F, Brnić V. Rehabilitation of patients with spondyloarthritis: a narrative review. *Med Glas (Zenica)*. 2019;16(2):10.17392/1047-19.
13. Ning H, Wang Y, Yuan Y, et al. Nursing and safety of silver needle diathermy treating ankylosing spondylitis. *Pak J Pharm Sci*. 2015;28(2 Suppl):725-729.
14. Efthimiou P, Kukar M. Complementary and alternative medicine use in rheumatoid arthritis: proposed mechanism of action and efficacy of commonly used modalities. *Rheumatol Int*. 2010; 30:571–86.
15. Ernst E, Lee MS. Acupuncture for rheumatic conditions: an overview of systematic reviews. *Rheumatology (Oxford)*. 2010; 49:1957–61.
16. Phang JK, Kwan YH, Goh H, et al. Complementary and alternative medicine for rheumatic diseases: a systematic review of randomized controlled trials. *Complement Ther Med*. 2018; 37:143–57.
17. Ledford C. Spine Conditions: Mechanical and Inflammatory Low Back Pain. *FP Essent*. 2017; 461:15-20.
18. Nishishinya Aquino MB, Pereda CA, Muñoz-Ortego J. Efficacy of acupuncture in rheumatic diseases with spine involvement: Systematic review. *Med Clin (Barc)*. 2019;153(6):250-255.
19. Lv ZT, Zhou X, Chen AM. Acupuncture Therapy versus Disease-modifying Antirheumatic Drugs for the Treatment of Ankylosing Spondylitis—a Meta-analysis. *Forsch Komplementmed*. 2015;22(6):395-402.
20. Boers M, Kirwan JR, Wells G, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. *J Clin Epidemiol* 2014; 67:745-53.
21. Mandl P, Naredo E, Wakefield RJ, et al. OMERACT Ultrasound Task Force. A systematic literature review analysis of ultrasound joint count and scoring systems to assess synovitis in rheumatoid arthritis according to the OMERACT filter. *J Rheumatol* 2011; 38:2055-62.
22. Ikeda K. Roles of Musculoskeletal Ultrasonography in the Management of Rheumatic Diseases. *Rinsho Byori*. 2015;63(5):580-589.
23. Siddle HJ, Mandl P, Aletaha D, et al. The EULAR points to consider for health professionals undertaking musculoskeletal ultrasound for rheumatic and musculoskeletal diseases. *Ann Rheum Dis*. 2018;77(2):311-313.
24. Ohrndorf S, Boer AC, Boeters DM, et al. Do musculoskeletal ultrasound and magnetic resonance imaging identify synovitis and tenosynovitis at the same joints and tendons? A comparative study in early inflammatory arthritis and clinically suspect arthralgia. *Arthritis Res Ther*. 2019;21(1):59.

25. Enache L, Popescu CC, Micu M, et al. Ankle involvement in rheumatoid arthritis - a comparison of inflammatory signs on musculoskeletal ultrasound and magnetic resonance imaging. *Med Ultrason*. 2019;21(3):265-272.
26. Delle Sedie A, Riente L, Bombardieri S. Limits and perspectives of ultrasound in the diagnosis and management of rheumatic diseases. *Mod Rheumatol*. 2008;18(2):125-131.
27. Bruyn GA, Iagnocco A, Naredo E, et al. OMERACT Definitions for Ultrasonographic Pathologies and Elementary Lesions of Rheumatic Disorders 15 Years On. *J Rheumatol*. 2019;46(10):1388-1393.
28. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332.
29. MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, Moher D. Revised STAndards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. *J Evid Based Med*. 2010; 3:140–55.
30. Doig GS, Simpson F. Randomization and allocation concealment: a practical guide for researchers. *J Crit Care*. 2005;20(2):187–91.
31. Ranger TA, Cicuttini FM, Jensen TS, Heritier S, Urquhart DM. Paraspinal muscle cross-sectional area predicts low back disability but not pain intensity. *Spine J*. 2019;19(5):862-868.
32. Wasser J G, Herman D C, Horodyski M B, et al. Exercise intervention for unilateral amputees with low back pain: study protocol for a randomised, controlled trial. *Trials*, 2017, 18(1):630.
33. Eby SF, Song P, Chen S, et al. Validation of shear wave elastography in skeletal muscle. *J Biomech*. 2013;46(14):2381-2387.
34. Pingel J, Lu Y, Starborg T, et al. 3-D ultrastructure and collagen composition of healthy and overloaded human tendon: evidence of tenocyte and matrix buckling. *J Anat* 2014; 224:548–555.
35. Roskopf Andrea B, Ehrmann Christine, Buck Florian M, et al. Quantitative Shear-Wave US Elastography of the Supraspinatus Muscle: Reliability of the Method and Relation to Tendon Integrity and Muscle Quality. *Radiology*, 2016, 278(2): 465-74.
36. De Zordo T, Fink C, Feuchtner GM, et al. Real-time sonoelastography findings in healthy Achilles tendons. *AJR Am J Roentgenol* 2009; 193:134–138.
37. Dirrachs T, Quack V, Gatz M, et al. Shear wave elastography (SWE) for the evaluation of patients with tendinopathies. *Acad Radiol* 2016; 23:1204–1213.
38. Jiang ZZ, Huang YH, Shen HL, et al. Clinical Applications of Superb Microvascular Imaging in the Liver, Breast, Thyroid, Skeletal Muscle, and Carotid Plaques. *J Ultrasound Med*. 2019;38(11):2811-2820.
39. Fu Z, Zhang J, Lu Y, et al. Clinical Applications of Superb Microvascular Imaging in the Superficial Tissues and Organs: A Systematic Review. *Acad Radiol*. 2020: S1076-6332(20)30178-1.
40. Zochling J. Measures of symptoms and disease status in ankylosing spondylitis: Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional

- Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), and Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S). *Arthritis Care Res (Hoboken)*. 2011;63 Suppl 11: S47-S58.
41. Jenkinson T, Mallorie P, Whitelock H, Kennedy G, Garret S, Calin A. Defining spinal mobility in ankylosing spondylitis (AS). The Bath Metrology Index. *J Rheumatol* 1994; 21:1694–8.
 42. Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994; 21:2286-91.
 43. Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994; 21:2281–5.
 44. Johns R J, Verna W. Relative importance of various tissues in joint stiffness. *Journal of Applied Physiology*, 1962, 17(5):824-828.
 45. Martindale J, Shukla R, Goodacre J. The impact of ankylosing spondylitis/axial spondyloarthritis on work productivity. *Best Pract Res Clin Rheumatol*. 2015,29(3):512-523.
 46. Alfuraih Abdulrahman M, O'Connor Philip, Hensor Elizabeth, et al. The effect of unit, depth, and probe load on the reliability of muscle shear wave elastography: Variables affecting reliability of SWE. *J Clin Ultrasound*, 2018, 46: 108-115.
 47. Alfuraih AM, O'Connor P, Hensor E, et al. The effect of unit, depth, and probe load on the reliability of muscle shear wave elastography: Variables affecting reliability of SWE. *J Clin Ultrasound*. 2018;46(2):108-115.
 48. Kwan YH, Fong W, Tan VIC, et al. A systematic review of quality-of-life domains and items relevant to patients with spondyloarthritis. *Semin Arthritis Rheum*. 2017;47(2):175-182.

Figures

	STUDY PERIOD						
	Enrollment	Allocation	Post-allocation				Closeout
	-1	0	1	6	12	24	24
ENROLLMENT:							
Eligibility screen	X						
Informed consent	X						
Baseline assessment	X						
Allocation		X					
INTERVENTIONS:							
Standard rheumatological care			←-----→				
Acupuncture group			←-----→				
Sham acupuncture group			←-----→				
Healthy-control group							
ASSESSMENTS:							
ASQoL	X			X	X	X	
BASFI	X			X	X	X	
BASMI	X			X	X	X	
BASDAI	X			X	X	X	

	STUDY PERIOD						
	Enrollment	Allocation	Post-allocation				Closeout
	-1	0	1	6	12	24	24
FS-14	X			X	X	X	
SAS	X			X	X	X	
SDS	X			X	X	X	
Musculoskeletal ultrasound	X				X		
Adverse events			X	X	X	X	X

Figure 1

SPIRIT figure for schedule of enrollment, interventions and assessments. ASQoL, Ankylosing Spondylitis Quality of Life; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; FS-14, Fatigue Scale-14; SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale.

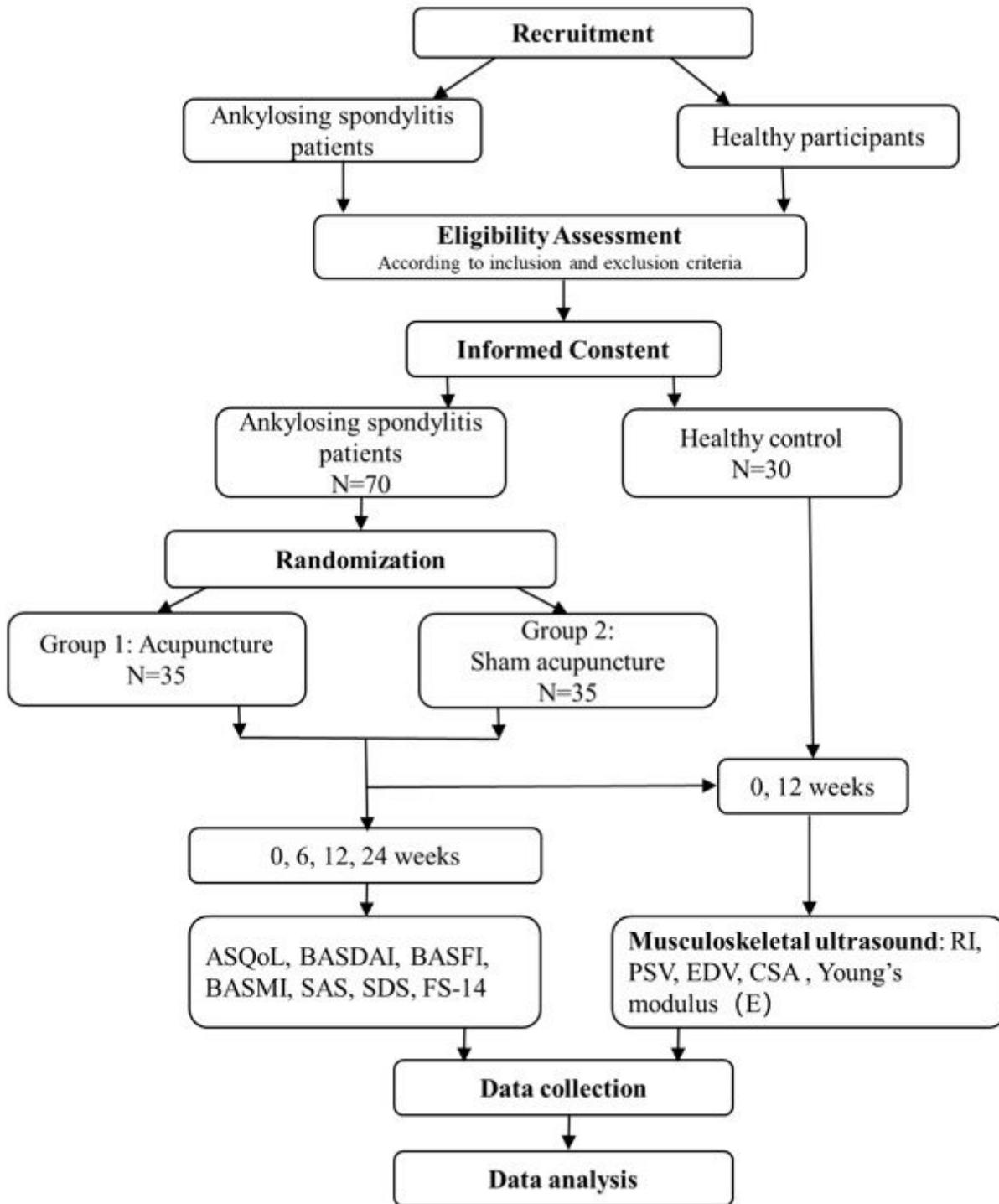


Figure 2

Trial work plan. Primary-outcomes measures will be musculoskeletal-ultrasound, ASQoL and BASMI results. The remaining outcome measures will be for secondary outcomes. Follow-up will be performed at 24 weeks.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SPIRITFillablechecklist15Aug2013.doc](#)
- [InformationLeafletforInformedConsentinchinese.doc](#)