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Efficacy and safety of two-step acupuncture therapy for symptom relief in adults with mild to moderate ulcerative colitis: rationale and design of the TSA-UC randomised controlled trial

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ABSTRACT

Introduction Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterised by episodes of symptoms including rectal bleeding, increased stool frequency and abdominal pain, impacting quality of life significantly. Conventional treatments often come with potential side effects and may not be sufficient. Acupuncture is increasingly recognised for its potential benefits in UC. This study aims to assess the efficacy and safety of acupuncture for symptom relief in mild to moderate UC.

Methods and analysis This single-centre, parallel-arm, randomised, sham-controlled, the two-step acupuncture (TSA)-UC trial, will involve 64 adults with mild to moderate UC, randomly assigned in a 1:1 ratio to either the acupuncture or sham acupuncture group. Participants will receive 20 sessions of two-step acupuncture or sham acupuncture therapy over 8 weeks. Blinding will be applied to participants, outcome assessors and statisticians. The primary outcome measure is the change in Patient-Reported Outcome 2 (PRO2) from baseline at week 8. Secondary outcomes include changes from baseline in the following scales: PRO2 at other time points, weekly average Numeric Rating Scale (NRS) for bowel urgency, weekly average NRS for abdominal pain (both associated and not associated with bowel movement), the 32-item Inflammatory Bowel Disease Questionnaire, Work Productivity and Activity Impairment Questionnaire-IBD, Pittsburgh Sleep Quality Index and Hospital Anxiety and Depression Scale. The Patient Global Impression of Change will also be assessed. Long-term effects of acupuncture will be explored. Adverse events and additional treatments will be monitored throughout the study. The modified intention-to-treat population including participants who complete baseline assessments and receive at least one treatment session will be analysed.

Ethics and dissemination The study has received ethical approval from the Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences (2024-190-KY). The results will be published in a peer-reviewed medical journal.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study represents the first rigorously designed, randomised, sham-controlled trial assessing the effects and safety of acupuncture for mild to moderate ulcerative colitis.
⇒ We will adopt a series of validated outcome measures to assess stool frequency, rectal bleeding, bowel urgency, abdominal pain and quality of life, which may provide valuable insights into the patient's symptoms and facilitate tracking symptoms over time and evaluate treatment effectiveness. Long-term effects of acupuncture will be investigated.
⇒ This trial will focus on the clinical symptoms, while endoscopy and biomarkers will not be employed, which may affect the clinical relevance of the results.
⇒ The inability to blind acupuncturists may introduce a risk of performance bias.
⇒ The single-centre design may constrain the external validity of the study results.

Trial registration number NCT06615765.

INTRODUCTION

Ulcerative colitis (UC) is one of the two primary forms of inflammatory bowel disease (IBD).[1 2] This condition is characterised by continuous mucosal inflammation that begins in the rectum and extends proximally throughout the colon.[1 3] Various factors, including genetic predisposition, environmental influences and dysregulation of mucosal immunity, are thought to contribute to the pathogenesis.[4] Diagnosis relies on a combination of gastrointestinal symptoms, biochemical markers, colonoscopy and pathological findings.[5 6] The global burden of UC is increasing significantly, with an

incidence of 9–20 cases per 100 000 individuals annually.[7] Its prevalence ranges from 156 to 291 cases per 100 000 individuals per year.[7] The average lifetime incremental cost associated with UC is US$230 102, encompassing hospitalisations, surgeries, pharmacotherapy, medical services, laboratory tests, procedures and visits to clinics and emergency departments.[8]

The presenting symptoms of UC vary depending on the location and severity of colonic inflammation. A hallmark symptom is rectal bleeding (RB), reported by over 90% of patients, ranging from mild to severe.[9] More than 90% of patients experience changes in faecal consistency (from loose to watery stools) and/or increased stool frequency (SF), with bowel movements occurring more than three times daily.[5 9] Bowel urgency is another important symptom affecting 75%–90% of individuals with UC.[10] Common intestinal symptoms also include tenesmus, nocturnal bowel movements and crampy abdominal pain.[5 9] In cases of severe colonic inflammation, systemic symptoms such as fatigue, fever, dehydration and weight loss may occur.[11] Extraintestinal manifestations are present in approximately 27% of individuals with UC[12] and can include arthritis, mucocutaneous lesions, ocular issues and hepatobiliary diseases.[13 14] Potential complications of UC include toxic megacolon, intestinal perforation, massive lower gastrointestinal bleeding, intraepithelial neoplasia and colorectal cancer.

UC follows a relapsing-remitting course, requiring tailored therapeutic strategies to induce and sustain remission.[15] As there is no known cure for UC, the primary treatment objectives are symptom management, enhancement of quality of life, and prevention and treatment of complications.[16] Natural history studies reveal that within 5 years of diagnosis, approximately 20% of UC patients are hospitalised,[17] and 7% undergo colectomy.[18] The risk of colorectal cancer after 20 years of UC is 4.5%,[19] and UC patients have a 1.7-fold increased risk of colorectal cancer compared with the general population.[20] Additionally, the life expectancy for individuals with UC is approximately 80.5 years for females and 76.7 years for males, which is about 5 years shorter than that of individuals without UC.[21]

According to the Selecting Therapeutic Targets in Inflammatory Bowel Disease initiative by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD),[16] clinical response is the immediate treatment target for UC, defined as a reduction of at least 50% in PRO2 (Patient-Reported Outcome 2, consisting of RB and SF subscale of Mayo score). Clinical remission, an intermediate (ie, medium-term) target, is defined as a PRO2 score of 0. Endoscopic healing is the long-term target. For the induction and maintenance of remission in mild to moderate UC, 5-aminosalicylic acid is recommended as the first-line therapy.[22] Moderate to severe UC may necessitate the use of oral corticosteroids for induction of remission as a bridge to other medications that sustain remission, such as infliximab, vedolizumab and ustekinumab, as well as oral small molecules like tofacitinib (which inhibits Janus kinase) or ozanimod (which modulates sphingosine-1-phosphate).[22] Despite advancements in medical therapies, the highest response rates in clinical trials range from 30% to 60%.[23]

In the management of UC, long-term medication use is often necessary but may lead to a range of adverse effects. Additionally, patients may develop drug tolerance over time, potentially reducing treatment efficacy. Adherence to medication is another significant challenge, with evidence indicating that less than 50% of patients consistently use oral 5-aminosalicylates, despite their efficacy in preventing disease relapse.[24] Consequently, there is a critical need for effective alternative and complementary therapies for UC. Acupuncture has shown potential benefits for IBD.[25–29] The International Clinical Practice Guideline on Traditional Chinese Medicine for UC, developed by the Board of Specialty Committee of Digestive System Disease of the World Federation of Chinese Medicine Societies, recommends considering acupuncture for UC patients.[30] However, the certainty of the existing evidence is limited due to a paucity of studies and methodological limitations. To address this gap, we plan to conduct this single-centre, parallel, two-arm, randomised, sham-controlled, the two-step acupuncture (TSA)-UC trial to evaluate the efficacy and safety of acupuncture for symptom relief in adult patients with mild to moderate UC. This trial will mark the first rigorously designed, randomised, sham-controlled study on this topic. It aims to provide valuable insights for the management of UC, potentially offering a promising complementary and alternative treatment option.

METHODS

Study design

This study is a single-centre, parallel-arm, randomised, sham-controlled trial. Eligible participants will be randomly assigned in a 1:1 ratio to either the acupuncture or sham acupuncture group. The trial protocol complies with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[31] and the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture.[32] The study involves a 33-week observational period, which includes a 1-week baseline phase, an 8-week treatment phase and a 24-week follow-up phase post-treatment. The study design and overview of schedule are illustrated in figures 1 and 2, and the schedule for enrolment, interventions and assessments is detailed in online supplemental file 1.

Study setting and recruitment

The study will be conducted at Guang'anmen Hospital, China Academy of Chinese Medical Sciences, in Beijing, China, a tertiary healthcare facility. Recruitment efforts, which will span from October 2024 to June 2026, will encompass a variety of approaches including the use of posters, the internet and social media.

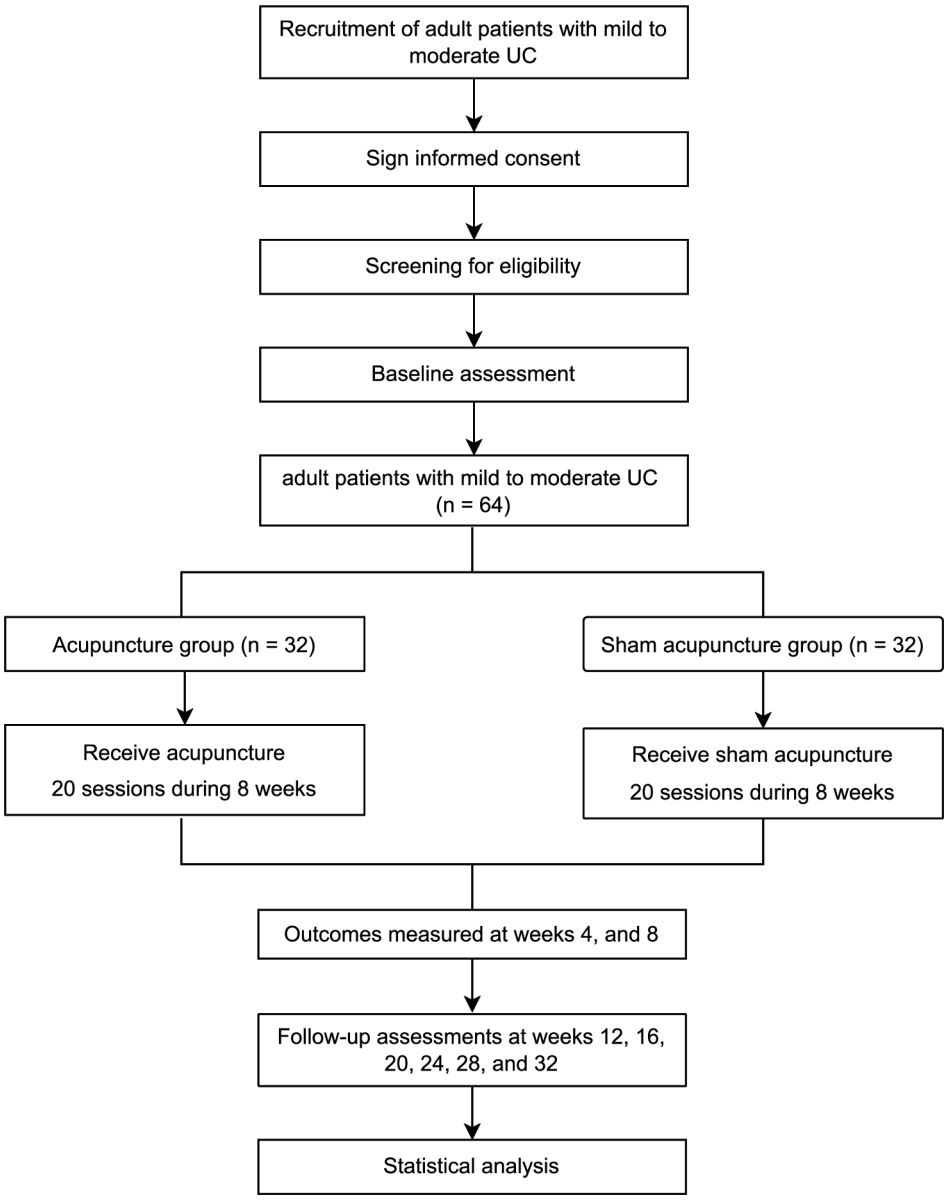

Figure 1 Flow diagram of the trial. UC, ulcerative colitis.

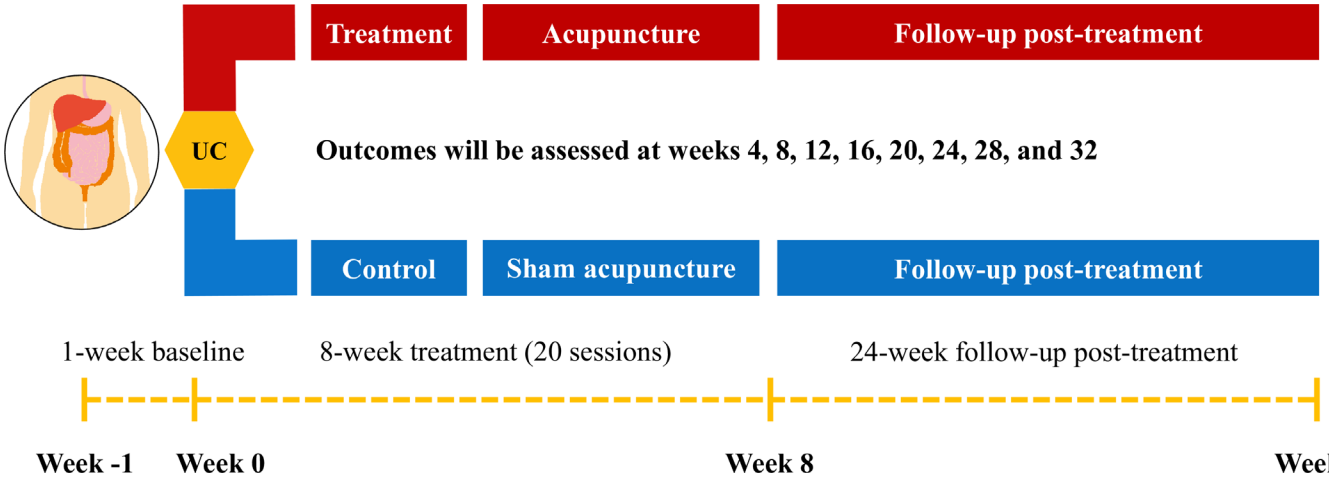

Figure 2 Trial schedule overview. UC, ulcerative colitis.

Informed consent

Prior to any study-specific procedures, participants will be required to provide written, informed consent. This consent document will detail the study's objectives, procedures, potential risks and benefits, as outlined in online supplemental file 2. Participants may withdraw from the study at any time. They will be fully informed and encouraged by the researchers, who are responsible for obtaining consent, to complete the treatment and follow-up procedures.

Randomisation, allocation concealment and blinding

Eligible patients with mild to moderate UC will be randomly assigned in a 1:1 ratio to either the acupuncture or sham acupuncture group. An independent statistician, who will not be involved in statistical analysis, will generate the randomisation sequence using the blockrand package in R software (V.4.4.1).[33] The sequence will be concealed within sealed, opaque and sequentially numbered envelopes, which will be opened only after the completion of baseline assessments. Allocation will be conducted by a research assistant who is not involved in treatment or outcome assessments. Blinding will be maintained for participants, outcome assessors and statisticians to prevent bias. However, the acupuncturists administering the intervention will not be blinded.

Participants

Individuals diagnosed with mild to moderate UC by gastroenterologists will be eligible for enrolment. Diagnosis will be based on a comprehensive assessment including medical history, clinical symptoms, endoscopic evaluation, histological analysis and the exclusion of other potential differential diagnoses such as infections and other forms of colitis. Participants must provide colonoscopy reports conducted within 1 month prior to enrolment and have Mayo scores ranging from 3 to 10. Additional laboratory tests may be performed to exclude other disorders, such as bacterial, viral and parasitic infections.

Inclusion criteria

Eligible participants are those aged 18–70 years who meet the diagnostic criteria for mild to moderate UC, have a PRO2 score of ≥2 points and provide written informed consent. Patients currently receiving oral and/or topical 5-aminosalicylic acid (such as mesalamine) may continue their treatment during the study period.

Exclusion criteria

Participants will be excluded if they meet any of the following criteria:

1. Diagnosis of Crohn's disease, intestinal tuberculosis, chronic intestinal infections or intestinal malignancies.
2. Current treatment with corticosteroids, thiopurines, biologics or oral small molecules.
3. Severe skin conditions or infections.
4. Presence of severe underlying medical conditions, including but not limited to cardiovascular diseases, hepatobiliary diseases, kidney diseases, haematologic disorders, autoimmune diseases, communicable diseases, severe malnutrition or malignancies.
5. Mental illness, cognitive dysfunctionor severe speech and language impairment.
6. Prior acupuncture treatment for UC within 30 days before enrolment.
7. Presence of substance abuse issues.
8. Current pregnancy, pregnancy planning, lactation, or postpartum status within 12 months of delivery.

Interventions

The acupuncture protocol has been developed based on previous studies[25–30] and clinical expertise. Licensed acupuncturists (≥5 years' clinical experience) who have completed protocol-specific training will administer interventions. Patients will be treated in separate rooms to avoid interaction and communication between them. The acupuncture group will receive standardised needling at the following acupuncture points: CV12 (Zhongwan), ST25 (Tianshu), SP15 (Daheng), SP14 (Fujie), CV4 (Guanyuan), ST36 (Zusanli), ST37 (Shangjuxu), SP6 (Sanyinjiao), BL32 (Ciliao), BL33 (Zhongliao) and BL35 (Huiyang). The location of these acupuncture points will adhere to the nomenclature and meridian point locations outlined in the National Standard of the People's Republic of China (GB/T 12 346–2021).[34] Detailed information can be found in table 1 and figure 3.

Notably, the use of oral and/or topical 5-aminosalicylic acid is permitted during both the intervention and follow-up periods. However, other treatments, including corticosteroids, thiopurines, biologics and oral small molecules, are not allowed during these periods. Any deviations from the permitted treatments or the use of concomitant treatments for symptom relief (which is discouraged) will be documented.

Acupuncture group

Sterile, disposable stainless steel needles (0.30×40 mm and 0.30×75 mm; Hwato, Suzhou Medical Appliance Factory, Suzhou, China) will be employed. Each treatment session comprises two steps. Initially, the patient assumes the supine position, followed by the prone position.

Step 1: When participants are in the supine position, needles measuring 0.30×75 mm will be inserted vertically and slowly, to a depth of 30–70 mm, into ST25, ST15 and SP14, until they reach the abdominal muscle layer. Needles measuring 0.30×40 mm will be inserted vertically to a depth of approximately 30 mm into CV12, CV4, ST36, ST37 and SP6. Each needle will be manipulated to evoke the deqi sensation, characterised by soreness, heaviness and distension.[35] Electroacupuncture (EA) stimulation will be applied using paired alligator clips from the EA apparatus, attached transversely to the needles at bilateral ST25, SP15 and ST36. EA stimulation will be administered for 20 min using a continuous wave of 5 Hz, with a current intensity ranging from 0.1 to 2.0 mA, adjusted to the participant's comfort level, ideally producing a mild, painless shiver around the acupuncture points.

Table 1 Locations of selected acupuncture points in the acupuncture group

Acupuncture points	Meridian	Location
CV12 (Zhongwan)	Conception vessel	On the anterior midline, midway between the xiphosternal joint and the umbilicus.
ST25 (Tianshu)	Stomach	2 cun lateral to the umbilicus.
SP15 (Daheng)	Spleen	4 cun lateral to the centre of the umbilicus, in the lateral abdominal region.
SP14 (Fujie)	Spleen	1.3 cun below the centre of the umbilicus, 4 cun lateral to the midline.
CV4 (Guanyuan)	Conception vessel	On the anterior midline, 3 cun inferior to the umbilicus.
ST36 (Zusanli)	Stomach	On the anterior aspect of the lower leg, 3 cun below ST35 (*Dubi*), one finger-breadth lateral to the anterior crest of the tibia.
ST37 (Shangjuxu)	Stomach	On the anterior aspect of the lower leg, 3 cun below ST35 (Dubi), one finger-breadth lateral to the anterior crest of the tibia.
SP6 (Sanyinjiao)	Spleen	On the medial leg, 3 cun directly above the medial malleolus, posterior to the tibia.
BL32 (Ciliao)	Bladder	In the sacral region, at the level of the second posterior sacral foramen.
BL33 (Zhongliao)	Bladder	In the sacral region, at the level of the third posterior sacral foramen.
BL35 (Huiyang)	Bladder	In the sacral region, 0.5 cun lateral to the sacrococcygeal hiatus.

1 cun≈20 mm. According to traditional Chinese acupuncture theory, 1 cun is approximately equivalent to the width of the patient's thumb at the knuckle.

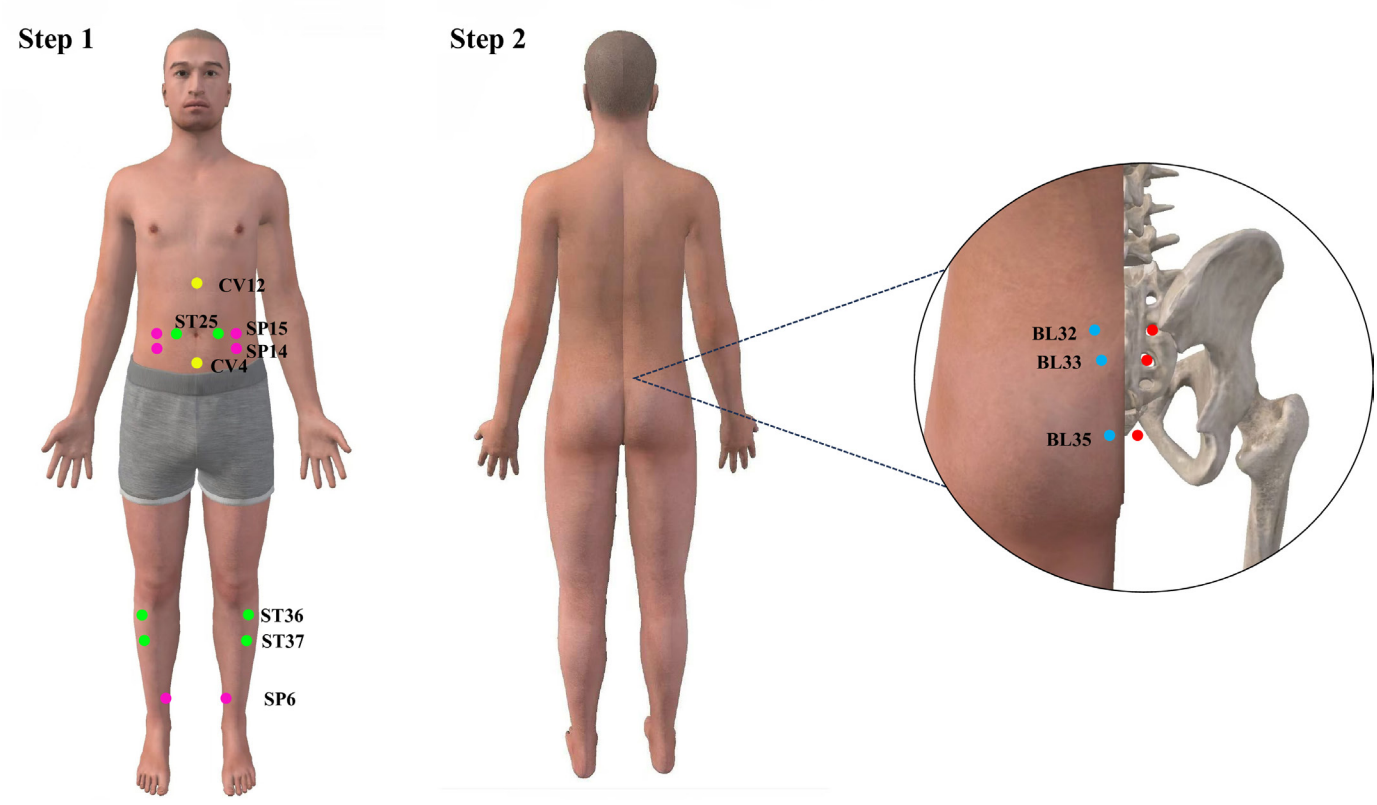

Figure 3 Locations of the acupuncture points used in the acupuncture group.

Step 2: After 20-min treatment in the supine position, participants will assume the prone position. After skin disinfection, needles will be inserted at BL32, BL33 and BL35 to a depth of approximately 60–70 mm. For BL32 and BL33, needles will be angled 30°–45° inferomedially. For BL35, the needle will be inserted at the lateral margin of the coccyx, angled slightly outward and superiorly to a depth of 60–70 mm. When inserting the needle, the depth and angle will be carefully adjusted to achieve deqi. EA will be administered to BL32, BL33 and BL35 using paired electrodes attached transversely to the needle handles. EA stimulation for these points will last 20 min, with a continuous wave of 5 Hz and a current intensity of 2.0–6.5 mA, adjusted to produce a mild, painless shiver of muscle.

Acupuncture sessions will be delivered three times a week (preferably every other day) during the first 4 weeks, and twice a week from week 5 to week 8, with each session lasting 40 min. A total of 20 sessions will be administered.

Sham acupuncture group

The sham acupuncture points used in the sham acupuncture group are located 1 cun (approximately 20 mm) lateral to the acupuncture points used in the acupuncture group, away from the body's midline. Specifically, sham CV12 and CV4 points are located 1 cun lateral to the right of CV12 and CV4. Sterile, disposable stainless steel needles (0.30×25 mm; Hwato, Suzhou Medical Appliance Factory, Suzhou, China) will be used. Following skin sterilisation, needles will be inserted into the sham acupuncture points in the depth of 2–3 mm. Needles will be manipulated slightly to enhance blinding. Paired alligator clips from a specially constructed EA apparatus will be attached to the corresponding sham points, ie, sham ST25, SP15 and ST36, and sham BL32, BL33 and BL35. The EA apparatus in the sham group will have the same working power indicator and sound as the active EA apparatus but will not deliver actual current output. All other procedures including the two-step procedure will mirror those of the acupuncture group, with needles retained in place without additional manipulation. Sham acupuncture sessions will be delivered three times a week (preferably every other day) during the first 4 weeks and twice a week from week 5 to week 8, with each session lasting 40 min. A total of 20 sessions will be administered.

Outcome measurements

Stool diary

Patients will maintain a stool diary to document bowel movements and symptoms. They should record the timing of bowel movements, stool consistency (using the Bristol Stool Chart),[36 37] RB severity (categorised as mild, moderate or severe), severity of bowel urgency and abdominal pain using the Numeric Rating Scale (NRS). Specifically, the NRS will assess bowel urgency (U-NRS; scale 0–10, with higher scores indicating worsen urgency), abdominal pain associated with bowel movements (scale 0–10, with higher scores indicating more severe pain), and abdominal pain not associated with bowel movements (scale 0–10, with higher scores indicating more severe pain).

Data on daily bowel movements and RB will be summarised from the stool diaries. The PRO2 score, assessed at weeks 4, 8, 12, 16, 20, 24, 28 and 32, comprises the SF and RB subscales of the Mayo score. The SF subscale is rated as follows: 0 (normal SF), 1 (1–2 stools more than normal), 2 (3–4 stools more than normal) and 3 (5 or more stools more than normal).[38] The RB subscale is rated as: 0 (no blood), 1 (streaks of blood less than half the time), 2 (obvious blood most of the time) and 3 (blood alone).[38]

PRO2 is a valid and practical tool for assessing disease activity in UC patients, performing comparably to the full Mayo score in identifying patient-perceived clinical responses.[39 40] It does not require laboratory tests or direct clinician interaction and correlates well with other measures of disease severity.[39 41 42] The PRO2 achieves a maximal sensitivity of 88% and specificity of 80% for detecting patient-reported improvements with a change cut-off of 1.5 points.[39]

Bowel urgency and abdominal pain are significant symptoms affecting quality of life and psychological well-being in UC patients.[43–45] Bowel urgency, in particular, is linked to higher rates of depression, anxiety, fatigue, pain and social impairment compared with patients without urgency.[45 46] Both symptoms contribute to sleep disturbances and IBD-related fatigue.[47 48]

Since bowel urgency is an independent and critical symptom impacting patients' quality of life and productivity,[49 50] this study will assess bowel urgency severity using the NRS (U-NRS) (0=no urgency, 10=worst possible urgency). The minimal clinically important difference (MCID) is defined as a ≥3-point decrease in U-NRS from baseline, while bowel urgency remission is defined as a U-NRS score of 0 or 1.[49] In this study, patients will be instructed to record their scores for each bowel movement. The average U-NRS score will be calculated weekly by summing the U-NRS scores for the week and dividing by the total number of bowel movements.

For the NRS score for abdominal pain associated with bowel movements, patients will record their scores for each bowel movement. The weekly average NRS score will be derived by summing these scores and dividing by the total number of bowel movements. For the NRS score for abdominal pain not associated with bowel movements, patients will record daily scores, which will then be summed over the week and divided by 7 to obtain the weekly average NRS score.

32-item Inflammatory Bowel Disease Questionnaire

The 32-item Inflammatory Bowel Disease Questionnaire (IBDQ-32) is the predominant tool for assessing disease-specific quality of life in randomised clinical trials for UC.[51] Studies support the efficacy of IBDQ-32 in capturing treatment impacts on the quality of life of UC patients.[51] The questionnaire encompasses four domains reflecting

the impact of UC on patients: symptoms, psychological and social functioning, and physical and emotional well-being.[52] Reviews have confirmed its reliability and validity, highlighting its superiority in measuring IBD-specific health-related quality of life (HRQoL) among available instruments.[53–55] Consequently, the IBDQ-32 has been widely recommended as a primary outcome measure in UC clinical trials, particularly where patient HRQoL is a key endpoint.[56 57]

The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (version 4)

The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale, version 4, consists of 13 items that evaluate self-reported fatigue and its impact on daily activities.[58] The scale assesses fatigue experienced over the past 7 days. A change of 5 or more points in the FACIT-F score is deemed a MCID.[59]

Work Productivity and Activity Impairment questionnaire: IBD version 2.0

The Work Productivity and Activity Impairment-IBD (WPAI-IBD) (version 2.0) (www.reillyassociates.net) is a validated tool designed to assess impairments in work and daily activities in IBD patients. This 6-item questionnaire evaluates impairments experienced over the past 7 days and provides four key metrics: (1) absenteeism (percentage of work time missed); (2) presenteeism (percentage of impairment while at work); (3) overall work productivity loss (combined estimate of absenteeism and presenteeism) and (4) activity impairment (percentage of impairment in daily activities). WPAI-IBD results are reported as percentages, with higher values reflecting greater impairment and reduced productivity.

Other measurements

The Pittsburgh Sleep Quality Index (PSQI) is a self-administered questionnaire that assesses sleep quality and disturbances over the past month, with higher scores indicating worse sleep quality.[60] The Hospital Anxiety and Depression Scale (HADS) is a self-report tool designed to identify symptoms of depression and anxiety,[61] with higher scores reflecting more severe symptoms. The Patient Global Impression of Change (PGIC) will be used to evaluate overall improvement. It measures participants' perceptions of changes in their condition using a 7-point scale: 'very much improved', 'much improved', 'minimally improved', 'no change', 'minimally worse', 'much worse' or 'very much worse'.

Primary and secondary outcomes

The primary outcome is the change from baseline in the PRO2 score at week 8. Secondary outcomes include:

1. Changes from baseline in the PRO2 score at weeks 4, 12, 16, 20, 24, 28 and 32.
2. The proportion of patients achieving a ≥50% reduction in PRO2 score at weeks 4, 8, 12, 16, 20, 24, 28 and 32.
3. The proportion of patients with a PRO2 score of 0 at weeks 4, 8, 12, 16, 20, 24, 28 and 32.
4. Changes from baseline in weekly average U-NRS scores at weeks 4, 8, 12, 16, 20, 24, 28 and 32.
5. Changes from baseline in weekly average NRS scores for abdominal pain associated with bowel movements at weeks 4, 8, 12, 16, 20, 24, 28 and 32.
6. Changes from baseline in weekly average NRS scores for abdominal pain not associated with bowel movements at weeks 4, 8, 12, 16, 20, 24, 28 and 32.
7. Changes from baseline in IBDQ-32 scores at weeks 4, 8, 12, 20 and 32.
8. Changes from baseline in WPAI-IBD scores at weeks 4, 8, 20 and 32.
9. Changes from baseline in PSQI scores at weeks 8, 20 and 32.
10. Changes from baseline in HADS scores at weeks 8, 20 and 32.
11. PGIC at weeks 4, 8, 20 and 32.

Other outcomes

Blinding assessment

To assess the effectiveness of blinding, participants will be asked to speculate about their treatment assignment at week 8, following treatment completion. Options for response include 'unsure', 'acupuncture' or 'sham acupuncture'. The success of blinding will be evaluated using Bang's Blinding Index (BI),[62] computed with the BI package in R. The BI ranges from −1 to 1, where 1 indicates a complete lack of blinding, 0 represents perfect blinding, and −1 suggests complete blinding, albeit, this may indicate unblinding in the opposite direction.[62] In general, if $-0.2 \leq \text{Bang BI} \leq 0.2$, blinding is considered to be successful.[62] This index is sensitive to even minor degrees of unblinding, response biases and behavioural differences between the groups.

Credibility and expectancy

The Credibility/Expectancy Questionnaire[63] will be administered within 5 min after the initial treatment to assess participants' perceptions of treatment credibility and their expectations.

Safety assessment

Adverse events will be recorded throughout the trial by patients, outcome assessors and acupuncturists using a specialised questionnaire. Within 24 hours of occurrence, adverse events will be classified by acupuncturists and researchers as either treatment-related or unrelated. Common acupuncture-related adverse events include subcutaneous haematoma, pain or discomfort at needle insertion sites and dizziness.

Patients' compliance assessment

Patient compliance will be monitored throughout the observation period. Detailed records will be maintained for any loss to follow-up or withdrawals, including the reasons for these occurrences.

Sample size

Based on previous research[64 65] and clinical experience, we estimate a mean difference of 1.50 in the change from baseline in PRO2 between groups, with a standard deviation (SD) of 1.85. To achieve 80% power with a two-sided significance level of 0.05, a sample size of 25 patients per group is required to detect statistically significant differences. To account for an anticipated 20% loss to follow-up, the sample size was adjusted to 32 patients per group. Thus, we plan to recruit a total of 64 patients.

Statistical analysis

An independent statistician, blinded to group assignments, will conduct all statistical analyses. Continuous variables will be reported as mean (SD). If normality assumptions are not met, median (IQR) will be used instead, and comparisons will be made using Student's t-test or the Wilcoxon Mann-Whitney test, as appropriate. Categorical variables will be summarised by number (proportion) and compared via the χ^2 test or Fisher's exact test.

The analyses will adhere to the modified intention-to-treat protocol, encompassing participants who complete baseline assessments and undergo at least one treatment session. Changes from baseline in various scores, including PRO2, weekly average U-NRS, weekly average NRS for abdominal pain (both associated and not associated with bowel movement), IBDQ-32, WPAI-IBD, PSQI and HADS will be evaluated using linear mixed-effects models. For outcomes involving the proportion of patients reporting a ≥50% reduction in PRO2 score or a PRO2 score of 0, generalised linear mixed models will be applied. PGIC outcomes will be assessed using Mann-Whitney U test or ordinal logistic regression. Safety outcomes and any additional interventions received by patients will be described narratively. Subgroup analyses will be conducted to assess the impact of concomitant treatments on the efficacy and safety of the interventions.

All statistical analyses will be performed using R software (V.4.4.1),[33] with a two-sided statistical significance level set at 0.05. It is important to note that comparisons of secondary outcomes will not be adjusted for multiple testing and should therefore be considered exploratory.

Data management and quality control

Data will be recorded in case report forms (CRFs). Before the study begins, comprehensive training will be provided to all research team members, covering study objectives, treatment protocols and quality control procedures. Rigorous confidentiality measures will safeguard all study documents, including informed consent forms, screening forms, CRFs and treatment records. A dedicated monitor will perform weekly reviews of CRFs and acupuncture treatment records to ensure accuracy and completeness. Regular meetings will be held by the principal investigator to identify, discuss and resolve any issues that arise during the observation period, thereby maintaining the highest standards of data quality and integrity.

Patient and public involvement

We will involve patient and public advisors both prior to the study's initiation and after its completion. Their feedback will inform study design, recruitment strategies and interpretation of results to enhance participant experience, adherence and study validity.

Ethics and dissemination

This study protocol has been approved by the Medical Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences (Approval No. 2024-190-KY). The study will follow the principles set forth in the Declaration of Helsinki and is registered with ClinicalTrials.gov (NCT06615765). To maintain confidentiality, personal information will be anonymised and replaced with unique identification numbers throughout the study. No personal details will appear in any dissemination materials. The findings of this study will be submitted for publication in peer-reviewed journals following completion of the research. The raw dataset generated and analysed during this study will be made available to qualified researchers upon reasonable request to the corresponding author.

DISCUSSION

UC is a chronic IBD characterised by periods of relapse and remitting phases, imposing substantial burdens on patients' daily lives including mental health, recreational activities, productivity and employment, and healthcare systems.[66 67] As a lifelong condition requiring continuous management, UC underscores the need for complementary therapeutic strategies. This study will conduct a single-centre, parallel, two-arm, randomised, sham-controlled trial to evaluate the efficacy and safety of acupuncture in alleviating clinical symptoms among adults with mild to moderate UC.

Current research on acupuncture for UC is limited, and its efficacy remains uncertain.[26 27] A review of multiple databases identified only a few randomised controlled trials published in Chinese, such as those by Li *et al*[64] and Qian *et al*,[65] as well as a few English-language studies.[28 29] These studies often suffer from methodological flaws and inadequate reporting.[26 27] Common issues include poorly described randomisation and allocation processes, absence of placebo controls, unblinded participants and potential biases in treatment effect assessments. The design of both experimental and control interventions has been problematic, introducing confounding variables and impacting the reliability of results. Some experimental groups received acupuncture combined with Chinese herbal medicine or moxibustion without appropriate controls, complicating the assessment of acupuncture's effects. Additionally, many studies had employed inadequate or unvalidated outcome measures.

This trial will be the first rigorously designed randomised sham-controlled study assessing the efficacy and safety of acupuncture for mild to moderate UC. A TSA therapy will

be delivered, aiming to provide sufficient stimulation and optimal benefits. Sham acupuncture will be used to blind participants and assess the specific effects of acupuncture. PROs will be gathered through interviews, self-completed questionnaires and diaries. We will use a stool diary to record bowel movement frequency, stool consistency, RB and its severity, as well as NRS for bowel urgency, abdominal pain associated with bowel movements, and abdominal pain not associated with bowel movements. This approach will enable us to monitor symptoms over time and evaluate treatment efficacy. Additionally, other validated outcome measures will be employed, including the IBDQ-32, FACIT Fatigue Scale, WPAI-IBD, PSQI and HADS. These instruments will assess quality of life, work productivity and mental health, providing comprehensive insights into the patient's symptoms and overall well-being.

UC is characterised by a relapsing-remitting course, requiring sustained management to achieve and maintain remission. Previous studies have demonstrated the long-term effects of acupuncture in various conditions.[68–70] This study will follow up the patients for 24 weeks post-treatment to assess the long-term efficacy of acupuncture for mild to moderate UC.

However, there are limitations to this study. First, acupuncturists cannot be blinded due to the nature of the intervention. Second, the single-centre design may limit the generalisability of the findings. Third, though validated PROs will be used for assessing symptom changes, endoscopic assessments and biomarkers, such as C reactive protein and fecal calprotectin, will not be evaluated, which may affect the clinical relevance of the results.

TRIAL STATUS

Recruitment for the trial will begin on 1 October 2024, with an anticipated completion date of 30 June 2026.

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