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Acupuncture-assisted anaesthesia for catheter ablation of atrial fibrillation to reduce the consumption of morphine hydrochloride and postoperative nausea and vomiting (PONV): study protocol for a randomised controlled trial

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ABSTRACT

Background Patients often experience postoperative nausea and vomiting (PONV) after catheter ablation of atrial fibrillation (AF) because of the use of opioids for anaesthesia and analgesia during the procedure. Some clinical trials have demonstrated that acupuncture-assisted anaesthesia (AAA) reduces opioid consumption and prevents PONV. Although several studies have been conducted on AAA, its safety and efficacy in AF catheter ablation remain unclear due to small sample sizes and a paucity of methodologically rigorous designs. Therefore, this trial was designed to evaluate the safety and efficacy of AAA in reducing PONV and morphine hydrochloride consumption during catheter ablation.

Methods This single-centre, patient-blinded, randomised, non-penetrating sham-controlled trial will be conducted in China. A total of 100 patients will be randomly assigned to the AAA and conventional anaesthesia (CA) groups in a ratio of 1:1. The patients will receive AAA or CA plus sham acupuncture during catheter ablation and will be followed up for 30 days. The primary outcomes include the total amount of morphine hydrochloride consumed during catheter ablation and PONV within the first 24 hours after the procedure. The secondary outcomes include pain, nausea and vomiting, anxiety, patient's ability to cope during catheter ablation, AF recurrence and quality of life, as assessed using the numeric rating scale. Adverse events will be recorded and their influence will be analysed at the end of the trial.

Discussion This study will help in evaluating the safety and efficacy of AAA applied for AF catheter ablation in reducing opioid doses during the procedure and the occurrence of PONV.

Ethics and dissemination The study has been approved by the Medical Ethics Committee of Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine. The results of the study will be published in peer-reviewed journals and presented at conferences if possible.

Trial registration number ChiCTR 2100042646; Chinese Clinical Trial Registry.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first randomised controlled trial to evaluate the safety and efficacy of acupuncture-assisted anaesthesia applied for atrial fibrillation (AF) catheter ablation in reducing morphine hydrochloride consumption and preventing postoperative nausea and vomiting (PONV).
⇒ This study will explore a potential sedation method for patients with AF undergoing radiofrequency catheter ablation with decreased PONV.
⇒ Considering the convenience and comfort of patients and clinicians, PC6 (Neiguan) located below the elbow indicates more operability in AF catheter ablation.
⇒ In this study, blinding the acupuncturists is difficult because acupuncture requires manual intervention.

INTRODUCTION

The prevalence and incidence of atrial fibrillation (AF) are gradually increasing, with an incidence rate of 2%–4% in adults.[1] Catheter ablation is the first-line treatment for patients with AF to maintain sinus rhythm and improve symptoms,[2] and it has become one of the most common electrophysiological procedures worldwide. During the complex and lengthy procedure of AF ablation, patients often experience unbearable pain when ablation reaches the autonomic nerve distribution area or the oesophageal area. Therefore, anaesthesia and analgesia are required to reduce pain, avoid body movements and maintain catheter stability. In China, the most commonly used drugs in AF ablation include fentanyl, morphine[3] and other opioids. However, opioids produce adverse effects, such as postoperative nausea and vomiting (PONV), respiratory depression, dependence

and abuse liability.[4] Using higher opioid doses is usually related to higher risks of adverse reactions, morbidity, longer recovery time and higher costs.[5 6] PONV causes pain and suffering among affected patients. Although PONV is not life threatening and self limiting, it is sometimes perceived to be more undesirable than incisional pain.[4 7] The use of more than one modality has gained increasing attention to achieve better anaesthetic and analgesic effects while reducing adverse effects.

Acupuncture-assisted anaesthesia (AAA) is a procedure in which anaesthetists combine acupuncture and anaesthetic techniques to enhance the sedative and analgesic effects of pharmaceuticals.[8] AAA is generally considered safe, with only mild adverse events (AEs), including haematoma, bleeding and pain.[9] It is an important part of multimodal non-opioid analgesia and has been applied to parturition, surgery and minimally invasive procedures.[10 11] Such analgesic effects might be mediated by encephalin and endorphin following the use of AAA with electrical stimulation. Encephalin and endorphin relieve pain-related emotions by upregulating the expression of neuropeptide S and its receptor in the anterior cingulate cortex and hypothalamus.[12] While the mechanism of acupuncture underlying PONV prevention has not been well elucidated, it may reduce PONV by releasing beta-endorphin or altering the transmission of serotonin.[13] Clinical trials and existing reviews indicate that AAA helps reduce the consumption of anaesthetic and analgesic agents, prevent PONV and relieve anxiety during surgery.[8 14 15] Although several studies have been conducted on AAA applied for catheter ablation, the safety and effectiveness of AAA in AF catheter ablation remain unclear due to small sample sizes and a paucity of methodologically rigorous designs.[16–18]

For these reasons, we designed a randomised controlled trial (RCT) to evaluate the safety and efficacy of AAA applied for radiofrequency catheter ablation (RFCA). The study aims to (1) determine differences in the occurrence of PONV and the consumption of opioids during AF catheter ablation between patients receiving AAA and those receiving conventional anaesthesia (CA) plus sham acupuncture and (2) examine the safety of AAA in patients during AF catheter ablation.

METHODS

Study design

This single-centre, patient-blinded, analyst-blinded, randomised, non-penetrating sham-controlled trial will be conducted at a tertiary hospital in China, the Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine. The patients will be randomly assigned to the AAA group or the CA group in a 1:1 ratio and will be followed up for 30 days from the day of ablation. Patients in the AAA and CA groups will receive AAA and CA plus non-penetrating sham acupuncture, respectively. The trial flow diagram is presented in figure 1. The consort statement[19] and Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture[20] will be used as the guiding frameworks for the study design. The protocol is reported following the Standard Protocol Items for Clinical Trials (SPIRIT) guidelines[21] (the SPIRIT checklist is shown in online supplemental file 1) and SPIRIT with Traditional Chinese Medicine Extension.[22] The study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine (approval no. 2020-046-01) and registered at the Chinese Clinical Trial Registry.

Sample size

CA was used as a positive control. We hypothesised that the incidence of PONV in patients received AAA would be lower than that in patients received CA. The alpha level will be set at 0.05 and the 1-β level will be set at 80%. The ratio of patients in the two groups will be 1:1. According to the results of a previous study,[23] the incidence of PONV was approximately 63% in the CA group and approximately 33% in the AAA group, and 40 patients should be enrolled in each group. Assuming a loss-to-follow-up rate of 20%, 100 patients (50 in the AAA group and 50 in the CA group) should be enrolled in this study. The sample size was calculated using Power Analysis & Sample Size (V.15.0).

Recruitment

Patients diagnosed with paroxysmal AF during their visit to the Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine from August 2022 to July 2023 and scheduled to undergo AF catheter ablation in this hospital will be recruited in this RCT. The potential patients will be referred to cardiologists and screened by dedicated examiners according to the inclusion and exclusion criteria. A research assistant will obtain written informed consent from the patients who meet the inclusion criteria. The included patients will be randomly assigned to the AAA or CA group(online supplemental file 2). The schedule of enrollment, intervention and assessments is detailed in table 1.

Patients

Patients with paroxysmal AF will be diagnosed and managed according to the 2020 European Society of Cardiology Guidelines.[24] Paroxysmal AF is defined as AF that terminates spontaneously or with intervention within 7 days of onset.

The inclusion criteria are as follows: (1) patients diagnosed with paroxysmal AF and already scheduled for AF catheter ablation within the next 2 weeks, (2) those with American Society of Anesthesiologists physical status of I–II, (3) those aged between 18 and 75 years (men or women) and (4) those who provided written informed consent to participate in the trial.

The exclusion criteria are as follows: (1) patients with severe coagulation disorders and a tendency of spontaneous bleeding, (2) pregnant or lactating patients, (3) patients allergic to morphine hydrochloride, (4) patients

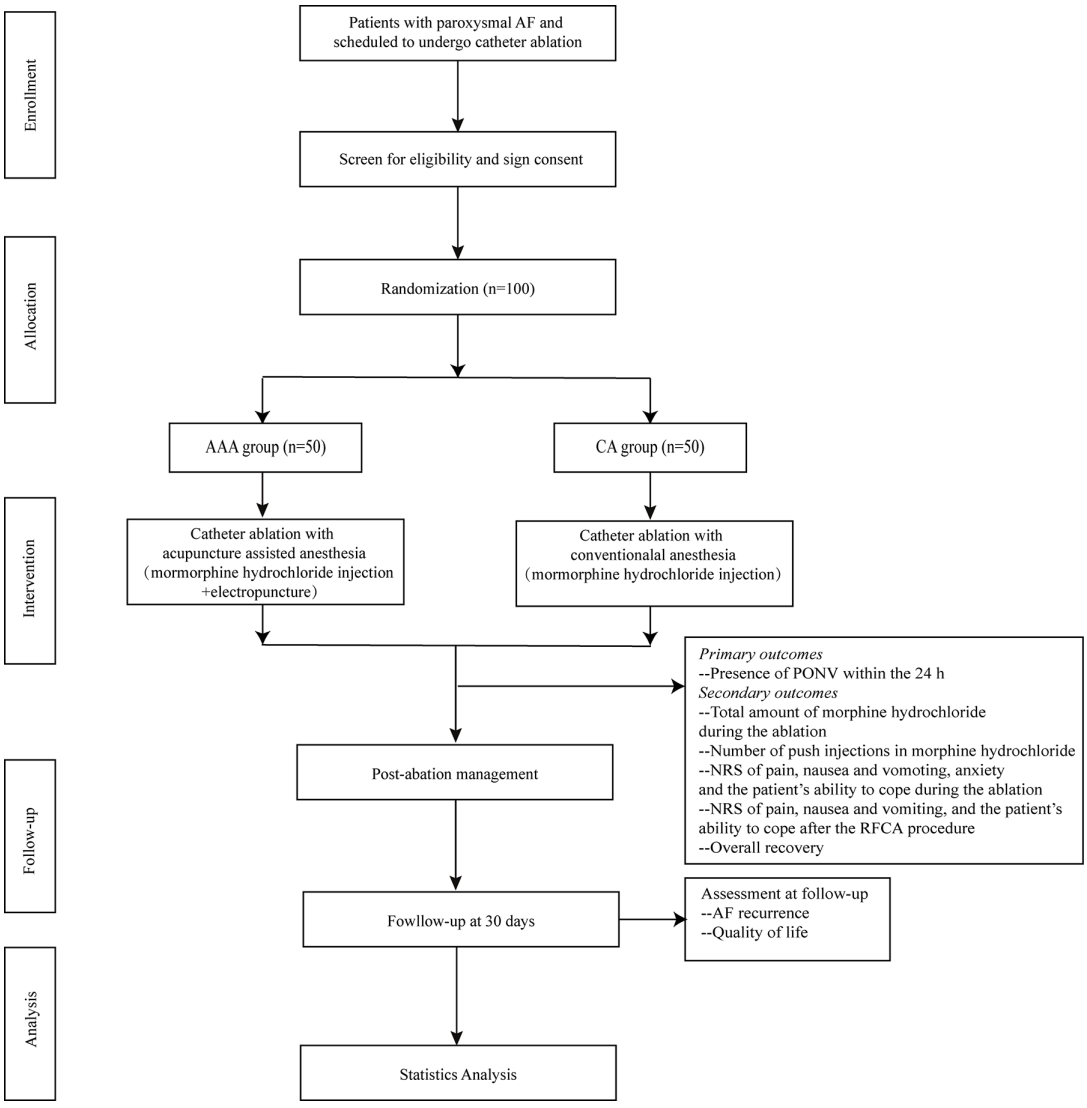

Figure 1 Trial flow diagram. AAA, acupuncture-assisted AF, atrial fibrillation; CA, conventional anaesthesia; PONY, postoperative nausea and vomiting.

with a severe psychiatric disease or cognitive impairment, (5) patients who are unable to understand the trial and provide responses about the outcome measurement, (6) patients who had received acupuncture treatment within a month, (7) patients with severe lung, liver or kidney disease or other serious primary diseases and (8) patients who cannot receive acupuncture.

Randomisation and blinding

A random sequence will be generated by an independent statistician using the R statistical package, and the randomised cards will be sealed in ordered envelopes. After completion of the screening process and baseline assessment, the patients will be randomly assigned to the AAA or CA group in a 1:1 ratio according to the random numbers in opaque envelopes. The acupuncturist who will perform the treatment will know the group allocation 2 hours before catheter ablation; the envelopes will not be opened before that time. The patients will not be informed of their group and will be instructed to wear an eye mask during catheter ablation. The principal investigator, data analysts and statisticians will remain blinded.

Ablation procedure

Senior physicians who have at least 10 years of experience and have completed more than 100 RFCA procedures will perform ablations in this trial. Patients with CHA_2DS_2-VASc scores ≥3, either women or men, will be administered warfarin or novel oral anticoagulants for at least 3 weeks before RFCA. All enrolled patients will receive lidocaine injections for local anaesthesia before the RFCA procedure. Transesophageal echocardiography will be performed on the day of the RFCA procedure or 1 day before RFCA administration to rule out left atrial thrombosis. All patients will undergo pulmonary vein isolation (PVI). The selection of the type of ablation catheter, settings of power and irrigation and the use of three-dimensional mapping systems will be determined by the physician performing the RFCA procedure. Complete

Table 1 Study schedule

	Study period							
	Enrolment	Allocation	RFCA procedure	After the procedure				Follow-up
Time point	Day 7	0		0 hour	6 hours	24 hours	48 hours	30 day
Enrolment:								
(Eligiblility screen)	×							
(Informed consent)	×							
(Randomisation)	×							
(Allocation)		×						
Intervention:								
(Acupuncture-assisted anaesthesia)			◆·····	·····◆				
(Conventional anesthesia)			◆·····	·····◆				
Assessment:								
(Consumption amount of morphine hydrochloride)			×	×				
(Presence of PONV within the 24 hours)							×	
(Number of push injections in morphine hydrochloride)								
(NRS of pain)				×	×	×	×	
(NRS of nausea and vomoting)				×	×	×	×	
(NRS of anxiety)				×	×	×	×	
(NRS of patient's ability to cope during the procedure)				×	×	×	×	
(Overall recovery)				×	×	×	×	
(Blinding assessment)				×				
(AF recurrence)								×
(AFEQT)								×
(Adverse events)			×	×	×	×	×	×

AF, atrial fibrillation; AFEQT, Atrial Fibrillation Effect and Quality of Life Scale; NRS, numeric rating scale; PONV, postoperative nausea and vomiting; RFCA, radiofrequency catheter ablation.

entrance and exit block of all pulmonary vein antra in PVI will be considered as the endpoint.

Following transseptal puncture, the patients will be given half of the standard dose of intravenous morphine hydrochloride (0.005 mg/kg). The anaesthesiologist will add a dose of morphine hydrochloride and administer injections when the patients report the pain or show significant limb movement. Morphine hydrochloride injections (Shenyang First Pharmaceutical Factory, Shenyang, China) will be used in this study. The heart rhythm, blood pressure, ECG and oxygen saturation will be monitored during the procedure to ensure patient safety and prompt detection of anomalies. The patients will remain conscious under partial sedation throughout the procedure. Electrical cardioversion will be performed if the patient remains in a state of AF after PVI. In addition, oxygen saturation and mean arterial pressure will be recorded at the time when the patient enters the operating room, at the beginning of the procedure, at the time of ablation, and at the end of the procedure. The operation time of the entire RFCA procedure will also be recorded.

Interventions

Training will be imparted to trial examiners, assessors and acupuncturists by the principal investigator (HJ) before the formal implementation to ensure the quality of this trial. This training will cover the screening criteria and electroacupuncture (EA) operation during the ablation procedure.[25] Registered acupuncturists who have at least 3 years of experience in practicing acupuncture will perform all acupuncture operations. They will be particularly trained in the standardised operating procedure of EA, which includes the timing of acupuncture during the ablation procedure, accurate positioning of acupoints, depth of needling and so on. Detailed information of the

standardised operation will be compiled and provided to the acupuncturist for reference.

The AAA group

The acupuncture protocol is based on previous clinical studies and case reports of acupuncture anaesthesia.[9 16] During the ablation procedure, the patients will be placed in the supine position and will be asked to expose their left upper arm and wear an eye mask. Before the ablation procedure and local anaesthesia, the upper limb will be massaged along the pericardium and lung meridians for 5 min. After routine disinfection, the patients will receive stimulation at Neiguan (PC 6) with disposable acupuncture needles (0.30×40 mm, Huatuo Brand; Suzhou Medical Appliance, Suzhou, Jiangsu, China). Acupoints will be selected based on previous clinical studies. According to the National Standard of People's Republic of China, 2006 (GB/T 12 346–2006), Neiguan (PC 6) is located in the anterior aspect of the forearm, which is between the tendons of the palmaris longus and the flexor carpi radialis and two cun proximal to the palmar wrist crease. Acupuncture needles will be inserted to a depth of 30–40 mm at an angle of 90°. A reinforcing–reducing technique, which includes lifting, thrusting, twisting and rotating the needles moderately, will be performed manually to achieve needling sensations (deqi sensation). Then, the needles will be connected to an EA apparatus (type GB6805-2, Huayi Medical Instrument, China), with a continuous wave frequency of 15 Hz and comfortable current intensity. AAA will be used throughout the operation. The diagram of the operation of AAA group has been shown in online supplemental file 3. At the end, the acupuncturist will switch off the EA apparatus and remove the needles using dry sterilised cotton balls by pressing the needles on the skin area to avoid bleeding.

The CA group

Patients in the CA group will receive CA with non-penetrating sham acupuncture. The settings of the CA group will be similar to those of the AAA group. The patients in the CA group will also be asked to expose their left upper arm and wear an eye mask. The tip of blunt-tipped needles will touch the area 1.5 cun lateral and posterior to PC6 (Neiguan) without penetrating the skin.[26] This sham acupuncture device, called the Streitberger placebo needle, has been broadly used and validated.[27] The EA apparatus will be placed besides the patient and will be switched on. However, the electrodes will not be connected to the needles.

Postablation management

All patients will receive a routine medication regimen after the RFCA procedure. The medication regimen includes anticoagulants (continued for at least 8 weeks after RFCA), antiarrhythmic drugs (continued for 3 months after RFCA) and proton pump inhibitors (continued for 4 weeks after RFCA). Patients who experience AF recurrence and those with recurrent AF will be allowed to restart or resume AAA or undergo another ablation. In addition, data on concomitant medication after ablation, including name, duration and dose, will be recorded.

Study withdrawal

The patients can cancel their consent for any reason without harm or penalty in any way and at any time, even during the AF ablation procedure. If a patient withdraws consent during the AF ablation procedure, all acupuncture procedures would be immediately stopped or cancelled according to their intention. The researchers may remove the participant from the study at any time for the following reasons: (1) the acupuncturists or physicians did not follow the study procedures, (2) for the benefits of the patients and (3) the physicians believe that it is not safe for the patient to continue the study. Withdrawal reasons and process details will be recorded.

Outcome measures

The primary outcomes are the presence of PONV within the first 24 hours after the procedure. The secondary outcomes include the total amount of morphine hydrochloride consumed, pain, anxiety, participant's ability to cope during and after the RFCA procedure, overall recovery, AF recurrence and quality of life, as assessed using the numeric rating scale (NRS).

Primary outcome measurement

Presence of PONV within the 24 hour

PONV is defined as at least one episode of nausea or vomiting within 24 hour after leaving the operating room. The patients will be asked whether they experienced PONV during this period, and the proportion of patients who experience PONV will be calculated at the end of the study.

Key secondary outcome measurement

Total consumption amount of morphine hydrochloride

The difference in the total amount of intravenous morphine hydrochloride consumed during the procedure is one of the primary outcome measures. The total amount of morphine hydrochloride consumed will be recorded immediately after the procedure and will be checked by the anaesthetist.

Other secondary outcome measurements

Number of push injections of morphine hydrochloride

The number of push injections of morphine hydrochloride during RFCA will also be recorded by the assessor.

Pain, nausea and vomiting, anxiety and patient's ability to cope during the procedure

Immediately after the procedure, the patients will be asked to rate how much pain, anxiety and nausea they experienced and their ability to cope during the procedure. These outcomes will be measured using the NRS, which is a commonly used scale to grade pain degree. A score of 0 on NRS indicates no pain and a score of 10 indicates the worst possible pain. The NRS will also be used

to measure nausea, anxiety levels and patient's ability to cope during the procedure. Regarding nausea and anxiety levels, a score of 0 indicates absence of nausea and anxiety and a score of 10 indicates the highest nausea and anxiety levels. Furthermore, regarding the patient's ability to cope during the procedure, a score of 0 indicates 'no ability to cope' and a score of 10 indicates 'completely able to cope'. The NRS scores for pain, nausea and vomiting and patient's ability to cope will be assessed at 6 hours, 24 hours and 48 hours after the procedure.

Overall recovery

The overall recovery will be rated on a 7-point Likert scale, which ranges from 'completely recovered from catheter ablation' to 'worse than ever'. The scale details are shown in online supplemental file 4 . The patients will be asked to rate their recovery experience on the scale at 6 hours, 24 hours and 48 hours after the procedure.

AF recurrence

All patients will be followed up for 30 days after discharge via phone calls or outpatient visits, and postoperative recurrence will be evaluated based on ECG or ambulatory ECG results.

Quality of life

The quality of life will be assessed using the Atrial Fibrillation Effect and Quality of Life Scale (AFEQT) at the 1-month follow-up.[28] A Chinese translated version of AFEQT will be used in this study.[29] AFEQT consists of 20 items, which are evaluated by four dimensions (measure patients' symptoms, daily activities, treatment concern and satisfaction). All items will be rated on a 7-point Likert scale. The total raw scores of the first three dimensions will be transformed into a scale of 0–100, and a higher score indicates a better quality of life.

Safety assessment

Possible AEs include broken needles, local haematoma, abscess, palpitations, dizziness, headache and any other symptoms after acupuncture treatment. Any AEs during the study will be recorded by the researchers. The heart rate, blood pressure and respiratory rate will be recorded at the time when AEs occur during the procedure. The details of AEs will be reported in a case report form (CRF). If any severe AE occurs during the procedure, the acupuncturist will stop the EA or sham acupuncture immediately. Serious AEs will be reported within 48 hours to the principal investigator and the ethics committee. In the event of an unexpectedly high AE rate, a decision may be made by the steering committee to unblind, pause or stop the trial at any time, as necessary. At the end of the trial, independent clinical researchers will judge the degree of severity (low, medium and high) and the relationship between AEs and acupuncture (unrelated, probably related and related). The occurrence rate of AEs in the two groups will be calculated and compared.

Blinding assessment

After the RFCA procedure, the patients will be asked to guess which group they have been assigned to evaluate the blinding success.

Data management and quality control

In addition to the aforementioned training for intervention-related personnel, we will train all researchers in data recording, CRF filling and data management. We will hold regular meetings to discuss the difficulties arising from the trial to obtain appropriate solutions. The patients' information collected in this study will not be publicly available and will only be reviewed by the researchers. To ensure data security, two independent inspectors will review each original CRF every month and write a data security report after each review. The Data Monitoring Committee of the Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine will periodically monitor the recruitment and screening of patients, data collection and entry and the monitoring of AEs to ensure that the trial is conducted according to the approved protocol.

Statistical analyses

An independent statistician blinded to group assignment will perform all statistical analyses using Statistical Package for the Social Sciences, V.25.0. The analyses will be based on the intention-to-treat principle and include data from any patients who dropped out of the trial. Data will be presented as means with SD, medians and ranges or medians with SD, as appropriate. All demographic and baseline characteristics of the patients will be analysed using descriptive statistics. The homogeneity of demographic characteristics and study variables between the two groups will be identified. The primary outcomes, total amount of morphine hydrochloride consumed and the incidence of PONV will be determined using independent samples t test or Wilcoxon rank-sum test and χ^2 test. The area under the curve of the NRS scores will be calculated using the trapezoidal method. The secondary outcomes and incidence of AEs will be compared between the two groups using χ^2 test, t test or Wilcoxon rank-sum test. All reported p values will be two-sided, and p values of <0.05 will be used to denote statistical significance.

All data in the main statistical analysis will be collected within 24 hours after the RFCA procedure and by the 30-day follow-up. If data cannot be collected, the time and reason for missing information will be recorded and the assumed missing data mechanism will be analysed. For these missing data, a multiple imputation adjustment approach will be used. After the main analysis, sensitivity analysis will be performed for various data sets to assess the impact of missing data on the results.

Patient and public involvement

Patients and the public will not be involved in design of this study.

DISCUSSION

The anaesthetic and analgesic effects of opioids in AF catheter ablation remain to be improved, particularly in terms of reducing the consumption of anaesthetic and analgesic agents and the occurrence of AEs. We chose to study AAA applied to AF catheter ablation because it can potentially provide an analgesic effect similar to that of opioids, with reduced anaesthetic drug use and fewer AEs, according to evidence from existing clinical trials.

This study will be the first RCT to evaluate the safety of AAA applied for AF catheter ablation and its efficacy to reduce the consumption of morphine hydrochloride and the occurrence of PONV. If this study shows that AAA is effective and safe in AF catheter ablation, its potential indication could be explored as a sedation method for patients with AF undergoing RFCA. It could provode a better RFCA experience with less PONV for these patients. Since AAA reduces the opioid dose for anaesthesia and lowers the incidence of AEs, it is considered a cost-effective procedure. The lower incidence of PONV is expected to reduce the use of rescue antiemetics and overall expenditure.

For this clinical trial protocol, we selected EA at the PC6 (Neiguan) acupoint to achieve AAA. In previous studies, the acupoint selection methods and techniques used to stimulate acupoints applied to AAA were not the same in each study. PC6 (Neiguan) is the most frequently used point in AAA, and its analgesic efficacy and ability to reduce PONV have been widely proven.[11 14] Considering the convenience and the comfort of patients and clinicians, PC6 (Neiguan) located below the elbow is also suitable in AF catheter ablation. Furthermore, studies have shown that electrical stimulation provides better analgesia.[30] This is a major reason why we chose EA.

This study has several limitations and challenges. First, the number of morphine hydrochloride injections is controlled by the anesthesiologist. After the standard initial injection, the number will be increased or decreased according to the pain experienced by the patient. Because this control is artificial, there may be deviations in the injection volume, leading to additional bias. We will analyse pain during the procedure using NRS to explore the influence of potential deviations on the primary outcomes. Second, blinding the acupuncturists is difficult because acupuncture requires manual intervention. Furthermore, it is not easy to blind patients during acupuncture. The patients who had received acupuncture treatment within a month will be excluded because these individuals are more likely to notice whether they have received sham acupuncture. For the same purpose, all patients will be required to wear an eye mask during ablation. Third, there may be some difficulties in patient recruitment; we will recruit more patients from other new clinical centres, if necessary.

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Competing interests The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained directly from patient(s)

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement This is a protocol. No data are available.

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REFERENCES

1 Chugh SS, Havmoeller R, Narayanan K, *et al*. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation* 2014;129:837–47.
2 Kalla M, Sanders P, Kalman JM, *et al*. Radiofrequency catheter ablation for atrial fibrillation: approaches and outcomes. *Heart Lung Circ* 2017;26:941–9.
3 CSoPa E, CSo A, AFCUo C. Current knowledge and management of atrial fibrillation:consensus of Chinese experts 2021 2022;26:15–88.
4 Dinges H-C, Otto S, Stay DK, *et al*. Side effect rates of opioids in Equianalgesic doses via intravenous patient-controlled analgesia: a systematic review and network meta-analysis. *Anesth Analg* 2019;129:1153–62.
5 Tan M, Law LS-C, Gan TJ. Optimizing pain management to facilitate enhanced recovery after surgery pathways. *Can J Anaesth* 2015;62:203–18.
6 Oderda GM, Gan TJ, Johnson BH, *et al*. Effect of opioid-related adverse events on outcomes in selected surgical patients. *J Pain Palliat Care Pharmacother* 2013;27:62–70.

7 Macario A, Weinger M, Carney S, *et al*. Which clinical anesthesia outcomes are important to avoid? the perspective of patients. *Anesth Analg* 1999;89:652–8.
8 Lu Z, Dong H, Wang Q, *et al*. Perioperative acupuncture modulation: more than anaesthesia. *Br J Anaesth* 2015;115:183–93.
9 Ang J-Y, Bhojwani K, Chan H-K, *et al*. A Malaysian retrospective study of acupuncture-assisted anesthesia in breast lump excision. *Acupunct Med* 2021;39:64–8.
10 Wang H, Xie Y, Zhang Q, *et al*. Transcutaneous electric acupoint stimulation reduces intra-operative remifentanil consumption and alleviates postoperative side-effects in patients undergoing sinusotomy: a prospective, randomized, placebo-controlled trial. *Br J Anaesth* 2014;112:1075–82.
11 Yuan W, Wang Q. Perioperative acupuncture medicine: a novel concept instead of acupuncture anesthesia. *Chin Med J* 2019;132:707–15.
12 Xu Z, Fang J, Xiang X, *et al*. Electroacupuncture alleviates pain-related emotion by upregulating the expression of NPS and its receptor NPSR in the anterior cingulate cortex and hypothalamus. *Evid Based Complement Alternat Med* 2020;2020:1–16.
13 Gouveia F, Oliveira C, Losa N. Acupuncture in the management of intraoperative nausea and vomiting. *J Acupunct Meridian Stud* 2016;9:325–9.
14 Lee A, Chan SKC, Fan LTY. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. *Cochrane Database Syst Rev* 2015;2015:CD003281.
15 Sim C-K, Xu P-C, Pua H-L, *et al*. Effects of electroacupuncture on intraoperative and postoperative analgesic requirement. *Acupunct Med* 2002;20:56–65.
16 Cui H-M, Wu F, Wang W-T, *et al*. Acupuncture anesthesia for radiofrequency catheter ablation in treatment of persistent atrial fibrillation: a case report. *Chin J Integr Med* 2021;27:137–40.
17 Shen H, Yan Y, Ma S. Effect of Acupuncture-combined anesthesia on analgesia and stress reactions in benign thyroid nodule ablation. *Shanghai J Acu-mox* 2019;38:772–5.
18 Chen G. Application effects of acupuncture anesthesia and local anesthesia to radiofrequency ablation surgery for chronic Nasosinusitis. *Western Journal of Traditional Chinese Medicine* 2019;32:112–4.
19 Schulz KF, Altman DG, Moher D. Consort 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ (Clinical research)* 2010;340.
20 MacPherson H, Altman DG, Hammerschlag R, *et al*. Revised standards for reporting interventions in clinical trials of acupuncture (stricta): extending the CONSORT statement. *PLoS Med* 2010;7:e1000261.
21 Chan A-W, Tetzlaff JM, Altman DG, *et al*. Spirit 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200–7.
22 Dai L, Cheng C-W, Tian R, *et al*. Standard protocol items for clinical trials with traditional Chinese medicine 2018: recommendations, explanation and elaboration (SPIRIT-TCM extension 2018). *Chin J Integr Med* 2019;25:71–9.
23 Frey UH, Scharmann P, Löhlein C, *et al*. P6 acustimulation effectively decreases postoperative nausea and vomiting in high-risk patients. *Br J Anaesth* 2009;102:620–5.
24 Hindricks G, Potpara T, Dagres N. Esc guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European association for Cardio-Thoracic surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of cardiology (ESC) developed with the special contribution of the European heart rhythm association (EHRA) of the ESC. *Eur Heart J* 20202021;42:373–498.
25 Witt CM. Clinical research on acupuncture - Concepts and guidance on efficacy and effectiveness research. *Chin J Integr Med* 2011;17:166–72.
26 Yang X-G, Ying L, Tian X-P, *et al*. Comments on selection of non-acupoints beyond meridians in studies of acupuncture and moxibustion. *J Tradit Chin Med* 2010;30:309–13.
27 Zhu D, Gao Y, Chang J, *et al*. Placebo acupuncture devices: considerations for acupuncture research. *Evid Based Complement Alternat Med* 2013;2013:1–9.
28 Spertus J, Dorian P, Bubien R, *et al*. Development and validation of the atrial fibrillation effect on quality-of-life (AFEQT) questionnaire in patients with atrial fibrillation. *Circ Arrhythm Electrophysiol* 2011;4:15–25.
29 Zhang H, Zhong L, Chen X. The chinesization of atrial fibrillation effect on quality-of-life questionnaire and its reliability and validity.. *Modern Preventive Medicine* 2020;47:471–3.
30 Zhang R, Lao L, Ren K, *et al*. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology* 2014;120:482–503.

Supplement File 1: SPIRIT 2013 Checklist

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	2
	2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	10
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	10
	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	10
	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)	8

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	2,3
	6b	Explanation for choice of comparators	2,3
Objectives	7	Specific objectives or hypotheses	2,3
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)	3

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	3
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)	3,4,5
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	5,6
	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)	6,8
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6,7
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	6,7,8
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)	6,figure1

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	3
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	3,9,10
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	4,7,8
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	4
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4,5
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	3,4,5
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	6
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	6,7,table 1
	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	6,7,8

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	7,8
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	8
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	8
	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)	8
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	7,8
	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	7
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	7
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	7,8
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	3,11
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	2,9,11

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3,4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	9
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	7,8,9,11
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	10
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	6,7
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	9,11
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplement 4
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Supplement File 2. Informed consent form

Informed Consent Form

Name of participant: Gender: Age: Registry No:

Dear participant,

The purpose of this study is to evaluate the safety and efficacy of acupuncture-assisted anesthesia applied for catheter ablation in reducing the morphine hydrochloride consumption during the procedure and postoperative nausea and vomiting.

This study is designed as a randomized controlled study.If you agree to participate, you will have a 50% chance of receiving the treatment of halving the initial dose of analgesics combined with acupuncture at Neiguan during catheter radiofrequency ablation.We will review the use of morphine hydrochloride within 24 hours after your surgery, number of PONV episodes, pain, numerical rating scale for anxiety, your ability to cope during and after RFCA surgery, overall recovery, AF recurrence and quality of life were recorded and scored.Before collection, you will receive training on how to collect samples.

The participation in this study is entirely voluntary. Participants may be withdrawn at any time during the study without affecting the relationship between you and researchers. There is no loss in economic aspect for you.

All information in this study will be kept confidential, and your private information will not appear in the research summary and published literature. This study has been ethically reviewed by the Chinese Ethics Committee of Registering Clinical Trials (Ethical review document number: ChiCTR2100042646)

Voluntary Subject Statement

I have learned about the requirements of the randomized controlled study in detail and fully understand the possible risks and benefits of participating in this study. I volunteered for this study.If there is any discomfort, I will report to the researcher in time. At the same time, I know that the researcher will give positive response for my possible discomfort. I am also entitled to withdraw from the study at any time for any reason. However, if there are no special circumstances, I will cooperate with the researcher to complete the study. My participation and the personal data in the trial are confidential. I agree with my researcher, the relevant regulatory authorities, and the ethics committee to review my information as required.

I (signature) relative (signature) (Relationship)

Date: D M Y

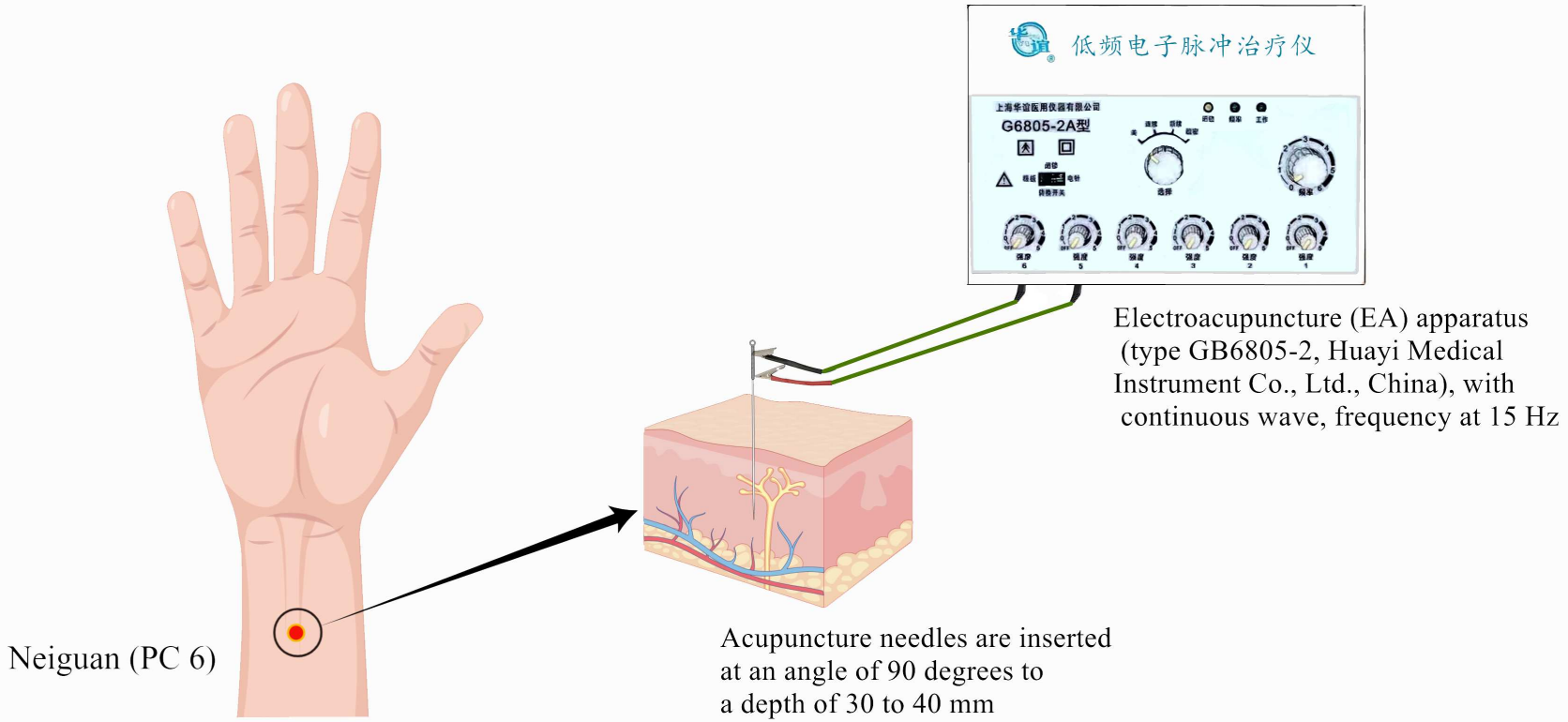
Researcher Declaration

I have fully elaborated the requirements of the randomized controlled study in detail and the potential risks or discomforts to the above participant/relative and answered their questions. To the best of my knowledge, the participant/relative has been informed adequately and has consented.

Researcher's signature Date: D M Y

In the event of inconsistency or discrepancy between the Chinese version and the English version, the Chinese language version shall prevail.

Supplement File 3. Diagram of the operation of AAA group



Supplementary File 4 Likert Scale of Overall recovery

Table Likert Scale of Overall recovery

Value	Description
0	Completely recovered from the catheter ablation
1	much recovered from the catheter ablation
2	slightly recovered from the catheter ablation
3	no change from the catheter ablation
4	slightly worse from the catheter ablation
5	much worse from the catheter ablation
6	worse than ever from the catheter ablation