

# BMJ Open Efficacy and safety of transcutaneous electrical acupoints stimulation for preoperative anxiety in thoracoscopic surgery: study protocol for a randomised controlled trial

Xindi Wu <sup>1,2</sup>, Tongyu Chen,<sup>2</sup> Ke Wang <sup>3</sup>, Xuqiang Wei,<sup>3</sup> Jijie Feng,<sup>2</sup> Jia Zhou<sup>2</sup>

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For numbered affiliations see end of article.

**Correspondence to**  
Professor Jia Zhou;  
pdzhoujia@163.com

## ABSTRACT

**Introduction** Preoperative anxiety occurs at a very high rate in patients undergoing video-assisted thoracoscopic surgery (VATS). Moreover, it will result in poor mental state, more analgesic consumptions, rehabilitation delay and extra hospitalisation costs. Transcutaneous electrical acupoints stimulation (TEAS) is a convenient intervention for pain control and anxiety reduction. Nevertheless, TEAS efficacy of preoperative anxiety in VATS is unknown.

**Methods and analysis** This single-centre randomised sham-controlled trial will be conducted in cardiothoracic surgery department of the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine in China. A total of 92 eligible participants with pulmonary nodules (size  $\geq 8$  mm) who are arranged for VATS will be randomly assigned to a TEAS group and a sham TEAS (STEAS) group in a 1:1 ratio. Daily TEAS/STEAS intervention will be administered starting on 3 days before the VATS and continued once per day for three consecutive days. The primary outcome will be the generalised anxiety disorder scale score change between the day before surgery with the baseline. The secondary outcomes will include serum concentrations of 5-hydroxytryptamine, norepinephrine and gamma-aminobutyric acid, intraoperative anaesthetic consumption, time to postoperative chest tube removal, postoperative pain, and length of postoperative hospital stay. The adverse events will be recorded for safety evaluation. All data in this trial will be analysed by the SPSS V.21.0 statistical software package.

**Ethics and dissemination** Ethics approval was obtained from the Ethics Committee of the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine affiliated to Shanghai University of Traditional Chinese Medicine (approval number: 2021-023). The results of this study will be distributed through peer-reviewed journals.

**Trial registration number** NCT04895852.

## BACKGROUND

Preoperative anxiety is common and is perceived by many patients as the worst aspect of a surgical intervention.<sup>1</sup> Despite the fact that the level of preoperative anxiety varies with different types of surgery, the

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ A randomised controlled trial of 92 patients undergoing video-assisted thoracoscopic surgery (VATS) will be conducted to evaluate the efficacy and safety of transcutaneous electrical acupoints stimulation (TEAS) for preoperative anxiety.
- ⇒ TEAS has the advantages of being non-invasive, no risk of needle induced infections, no fear of needle stimulation compared with acupuncture or electroacupuncture treatment, which would be a potential strategy for preoperative anxiety control.
- ⇒ TEAS is an extremely reductionist acupuncture technique that can potentially be applied by any acupuncturist or preoperative personnel with minimal training.
- ⇒ This study protocol is limited by the impracticability of blinding because we are unable to blind the acupuncturists due to the limits of the existing technology.
- ⇒ It is necessary to study the effect of TEAS on perioperative anxiety management in large-scale multi-centre studies and other types of surgery since we only collected data on 3-day preoperative period of VATS.

overall prevalence of preoperative anxiety in adults ranges from 11% to 90%.<sup>2</sup> Furthermore, 34% of patients referred for thoracic surgery require psychological intervention, and are more likely to develop an increased level of anxiety.<sup>3</sup> Anxiety before surgery not only increases the risk and difficulty of the management of surgery and anaesthesia, but also causes persistent anxiety after surgery, increases postoperative sensitivity to pain, suppresses immune function, increases postoperative infection and prolonging postoperative recovery time. Preoperative anxiety not only increases the risk and difficulty of the management of surgery and anaesthesia but also contributes to persistent anxiety after the surgery, which enhances the sensitivity of

postoperative pain, suppresses the function of immune system, increases the incidence of postoperative infection and prolongs the recovery time after surgery.<sup>4-6</sup> Thoracic surgery is usually accompanied by a plethora of complications and pathophysiological changes that can be aggravated by increased preoperative anxiety.<sup>7</sup> Video-assisted thoracoscopic surgery (VATS) is the most common minimally invasive surgical method in thoracic surgery.<sup>8 9</sup> However, even with VATS, several postoperative complications are still unavoidable.<sup>10 11</sup>

Currently, clinical effective intervention methods for anxiety mainly include pharmacotherapy and psychotherapy.<sup>12</sup> Medications registered with China's National Administration of Medical Products for indications of anxiety disorders include selective 5-hydroxytryptamine 1A (5-HT1A) receptor agonists and benzodiazepines.<sup>12</sup> However, frequent application of benzodiazepines easily leads to drug dependence, excessive sedation and cross-tolerance between multiple drugs.<sup>13</sup> Psychotherapy is an individualised high intensity psychological intervention that consists of 12–15 weekly sessions (fewer if the person recovers sooner; more if clinically required), each lasting 1 hour delivered by trained and competent practitioners.<sup>14</sup> Therefore, psychotherapy takes a considerable amount of time and treatment compliance is often low, while the use of healthcare service is higher and the associated costs are more cumbersome and less applicable in the preoperative period.<sup>15</sup>

Multiple studies have confirmed that acupuncture therapies are potential perioperative strategies that stabilise the patient's mental state, relieve anxiety and promote long-term recovery.<sup>16-23</sup> Among numerous acupuncture stimulation methods, transcutaneous electrical acupoint stimulation (TEAS) technology seems to be a promising strategy for preoperative anxiety management. Developed from electroacupuncture, TEAS achieve therapeutic effect by delivering low-frequency pulse currents with peripheral stimulation.<sup>24</sup> TEAS has the advantages of being noninvasive, easily accepted, having an extremely low infection rate, avoids fear of needles, easy to repeat and having a lower cost compared with penetrating acupuncture.<sup>25</sup> Our previous study also indicated that moderate intensity TEAS achieved a similar analgesic effect and mechanism of electroacupuncture.<sup>26</sup> Moreover, one clinical study concluded that TEAS is a convenient modality for postoperative pain control and anxiety reduction.<sup>27</sup> Most trials have focused on perioperative analgesia,<sup>4 28</sup> adjustment of gastrointestinal function<sup>29</sup> and early recovery<sup>30</sup> from TEAS. However, there is limited evidence available regarding TEAS and its ability to alleviate preoperative anxiety in VATS.

Based on the prior mentioned findings, we hypothesise that TEAS would be an effective and safe treatment for preoperative anxious patients scheduled to undergo VATS. This trial will obtain more reliable information on the efficacy and safety of TEAS for the treatment of preoperative anxiety of VATS.

## METHODS AND DESIGN

### Study design

We will conduct a single-centre, randomised, sham-controlled, participant-blinded and assessor-blinded trial in the inpatient ward of cardiothoracic surgery department of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine affiliated to Shanghai University of Traditional Chinese Medicine (TCM). This trial will commence following ethics approval and registration protocol. Patient enrolment started in late June 2021 and is expected to end in March 2023. It is expected that 92 participants will be recruited and randomly assigned to accept TEAS or sham TEAS (STEAS) at a 1:1 ratio using SPSS V.21.0 software. During the development of the standard protocol, the Standards for Reporting Interventions in Clinical Trials for Acupuncture and the Standard Protocol Items: Recommendations for Interventional Trials reporting guidelines will be followed to clarify the treatment procedures explicitly and transparently.<sup>31</sup> Figure 1 is the study flow chart and table 1 shows the schedule of enrolment, interventions and assessments.

### Participation and recruitment

Patients who are arranged for VATS with pulmonary nodules will be screened. The clinical trial coordinator will interview potential subjects preoperatively to assess their eligibility according to inclusion and exclusion criteria. Eligible patients should provide written informed consent prior to randomisation voluntarily.

### Diagnostic criteria

Pulmonary nodules (over or equal to 8 mm in size) that found on chest CT examination and VATS is required after evaluation by the thoracic surgeon.<sup>32</sup>

### Inclusion criteria

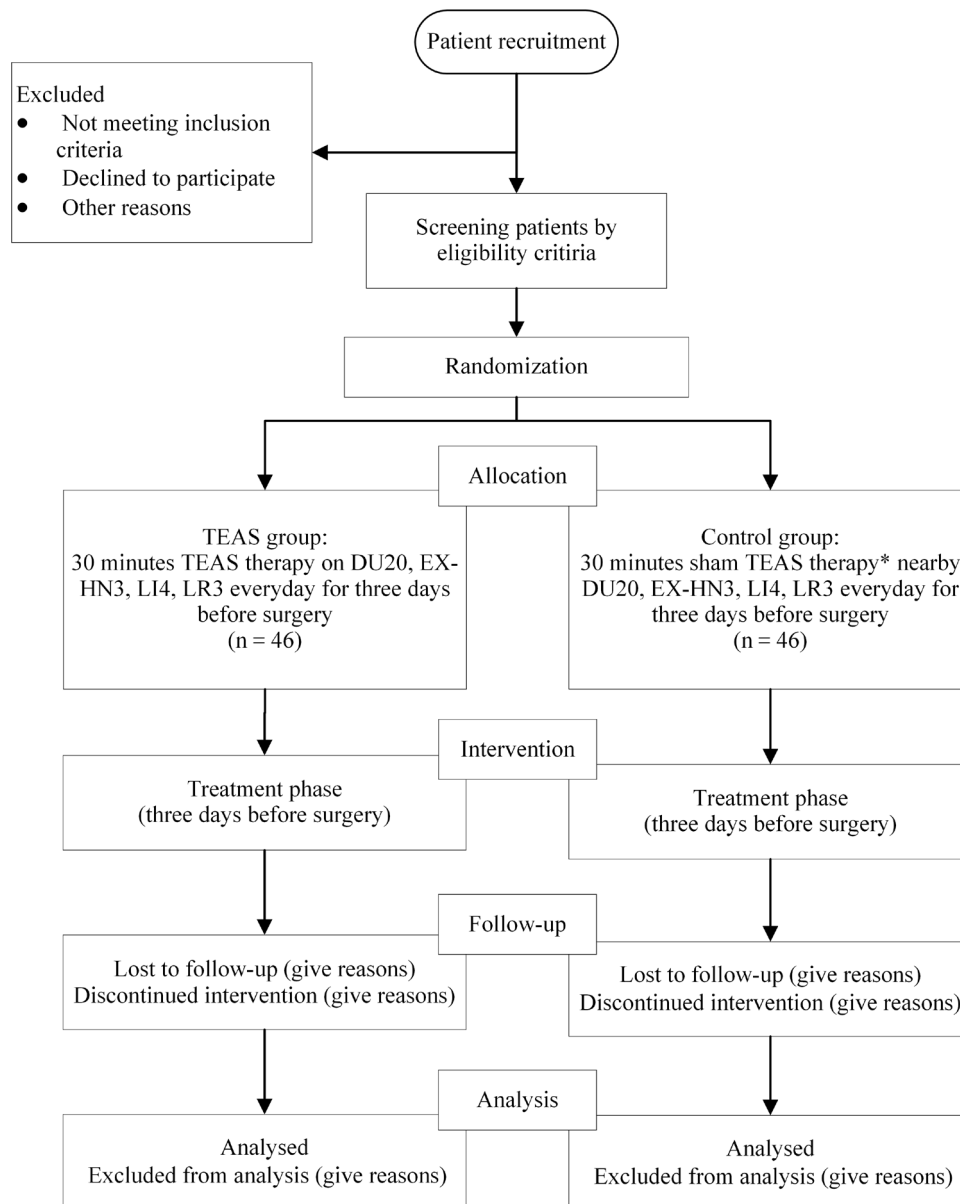
1. Those diagnosed as pulmonary nodules requiring VATS.<sup>32</sup>
2. Age ranges from 18 to 75 years old.
3. 4 ≤ Generalised Anxiety Disorder-7 (GAD-7) score ≤ 9 and those who have no previous mental illness and no use of anti-anxiety medications or psychotropic drugs within 2 weeks.<sup>33</sup>
4. Patients who have clear consciousness, normal understanding, no expression disorder, are capable of cooperating with treatment and sign the informed consent.
5. Patients who have not previously received TEAS treatment.
6. Patients who were not enrolled in or were participating in other clinical trials 1 month prior to the enrolment.

### Exclusion criteria

1. Patients with local acupoint skin infection.
2. Patients with upper or lower limb nerve injury.
3. Patients with implanted pacemaker.

### Rejection, suspension and dropout criteria

1. Those with serious adverse reactions.



**Figure 1** Study flow chart. Transcutaneous electrical acupoints stimulation. \*Sham TEAS therapy: The acupoints selection and intervention measures are the same as the TEAS group except for the current intensity is set to 0 mA. TEAS, transcutaneous electrical acupoints stimulation.

2. Those who presented worsen symptoms or life-threatening illnesses that cannot be continued during treatment.
3. The principal investigator identified an unacceptable risk of serious adverse events (AEs) during the study period.
4. Patients unable to complete the study plan, including speech difficulties, infectious diseases and other medical history.
5. Patients quit by themselves.

### Randomisation and blinding

A single-blind design will be applied to this trial. All participants are blinded to the group allocation and are informed that they might or might not feel a sensation when the apparatus is working. Acupoint stimulations will

be carried out by the acupuncturist who is not implicated in the process of data collection. The TEAS instrument is covered with an opaque box for adequate blinding. The randomised numbers were generated with SPSS V.21.0 (IBM SPSS Statistics, V.21) software. Groups in random order will be sealed in confidential envelopes. Eligible participants will be assigned to TEAS group or STEAS group randomly at a ratio of 1:1. Only the acupuncturist in charge of the operation can reveal the grouping from the sealed envelope. Participants will be treated separately to prevent communication. Efficacy assessments will be performed blinded to group assignment. The efficacy evaluators and statisticians will be separated and blinded. To test the participant-blinding effects, all participants will be asked to guess whether they had received

**Table 1** Schedule of trial enrolment, interventions and assessments

Study periods	Enrolment (screening)	Allocation (baseline)	Intervention period			Follow-up		
	Admission	Day 0	PED 3	PED 2	PED 1	VATS Day	POD 1	POD 2
Enrolment								
Eligibility screen	√							
Informed consent	√							
Randomisation		√						
Intervention								
TEAS			√	√	√			
STEAS			√	√	√			
Assessments								
GAD-7	√		√		√			
5-HT			√		√			
NE			√		√			
GABA			√		√			
Intraoperative anaesthetic consumption						√		
Chest tube removal time							√	√
VAS							√	√
Length of postoperative hospital stay							√	√
Blinding			√	√	√			
Safety variables								
Skin reaction assessment			√	√	√	√	√	√
Mood disturbance assessment			√	√	√	√	√	√
Adverse events			√	√	√	√	√	√

.GABA, gamma-aminobutyric acid; GAD-7, Generalised Anxiety Disorder Scale-7; 5-HT, 5-hydroxytryptamine; NE, norepinephrine; PED, preoperative day; POD, postoperative day; STEAS, sham TEAS; TEAS, transcutaneous electrical acupoints stimulation; VAS, Visual Analogue Scale.

TEAS or STEAS within 5 min after one of the treatment sessions before VATS.

### Interventions

The TEAS/STEAS treatment will be performed in the treatment bed. All acupuncturists will receive training on standardised operating procedures to fully understand the location of acupoints and the operation of the TEAS apparatus before the ignition of trial.

Self-adhesive gel electrode pads (Hwato physiotherapy electrode; Suzhou, Jiangsu, China) in sizes of 50×50 mm will be used for the TEAS/STEAS treatment. The electrode pads will be reused by the same patient and discarded after the final treatment session. The eligible participant will receive TEAS or STEAS once a day for three consecutive days starting on 3 days before VATS. Each treatment session will last 30 min from the moment the electrode pad is connected to the TEAS apparatus.

Except for TEAS, other therapies to reduce the level of anxiety include anxiolytic-sedative drugs such as benzodiazepines, cognitive-behavioural therapy, music therapy and massage therapy are not allowed during study period.

In accordance with the consensus statement of VATS for the thoracic surgical community,<sup>34</sup> each patient will receive the identical standardised surgical protocol and perioperative management.

### Transcutaneous electrical acupoints stimulation/STEAS

TEAS/STEAS therapy is based on the consensus of TCM theory and experts of acupuncture. Stimulation at particular acupoints can be used to treat certain diseases. Preoperative anxiety is often accompanied by excessive autonomic dysfunction and motor restlessness.<sup>35</sup> The principle of acupoint selection is to calm the nerves and relieve tension so as to help patients to relax both physically and mentally.<sup>36–40</sup> Hence, DU20 (Baihui), EX-HN3 (Yintang) and both sides of LI4 (Hegu), LR3 (Taichong) are selected for this trial. [Figure 2](#) demonstrates the locations of the acupoints.

Electric stimulation will be used with a TEAS apparatus (HANS200A Beijing Huawei) as is shown in [figure 3](#). The electrode pad will be placed at the centre of the acupoints in strict accordance with the WHO Standardised Acupuncture Location ([figure 4](#)). Alternating frequency of 2/100 Hz will be set to relieve anxiety.<sup>41</sup> The current intensity will be adjusted individually, starting at 1 mA and increasing gradually to the maximum current tolerated by the patient (ideally slight twitching of local muscles without pain).<sup>42</sup>

In the STEAS group, the same acupoints are selected as those in the TEAS group, and other intervention measures are also the same as those in the TEAS group, except that the current intensity is set to 0 mA. The acupuncturist



**Figure 2** Location of DU20, EX-HN3, LI4 and LR3.

responsible for the operation will tell patients in STEAS group that this is a type of stimulus without perception.

### Outcome measurement

#### Primary outcome

The primary outcome is the GAD-7 scale change between the day before surgery with the baseline. GAD-7 is a seven-item designed to simply measure or assess anxiety disorders. GAD-7 is a valid and efficient tool which is sensitive to detect change in anxiety-specific therapies over the



**Figure 3** HANS200A.



**Figure 4** Application of TEAS. TEAS, transcutaneous electrical acupoints stimulation.

course of treatment.<sup>43 44</sup> GAD-7 score (figure 5) ranges from 0 to 21 and score of each item ranges from 0 to 4. An overall score of GAD-7 indicates 0–4 as no anxiety, 5–9 as possibly mild anxiety, 10–14 as potentially moderate anxiety, and more than 15 as probably severe anxiety.<sup>43</sup> Frankly, higher scores suggest more severe symptoms of anxiety.<sup>45</sup>

### Evaluation criteria of curative effect

#### Minimal clinically important difference

We will adopt minimal clinically important difference (MCID) of the GAD-7 to evaluate the curative effect. The concept of MCID refers to the smallest difference in score in the domain of interest that is considered to be worthwhile or clinically important.<sup>46</sup> MCID could convey the information about whether changes in clinical interventions are meaningful for patients.<sup>47</sup> Determining the MCID value for GAD-7 could aid us in judging the efficacy of TEAS/STEAS treatment. To estimate the intraindividual MCID for the GAD-7, we used the SE of measurement (SEM, SD of baseline scores multiplied by the square root of one minus the reliability coefficient), which can be regarded as the SD of an individual score.<sup>44</sup>

$$SEM = S\sqrt{1 - r_{xx}}$$

SPSS V.21 was employed to accomplish all statistical analyses.  $S=1.98$ ,  $r_{xx}=0.60$ ,  $SEM=1.25$ . To achieve an intraindividual MCID that reflects the 95% CI, the SEM was multiplied by 1.96.<sup>44</sup> Accordingly,  $MCID=2.45$ . We set 3 as more appropriate for conservation in order to define the efficacy better. Compared with the range of possible GAD-7 scores (0–21), patients with a decrease of more than 3 points reflecting a clinically significant change value in individual over the course of treatment.

#### Secondary outcomes

Serum concentration changes of 5-HT, norepinephrine (NE) and gamma-aminobutyric acid (GABA) between the day before VATS with 3 days before VATS will be evaluated.

GAD-7

Over the <u>last 2 weeks</u> , how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total Score \_\_\_\_\_

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat Difficult	Very Difficult	Extremely Difficult
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Figure 5** The Generalised Anxiety Disorder 7-item (GAD-7) scale.

This may further identify its potential as a biomarker for monitoring the effects of TEAS on treating preoperative anxiety. Intraoperative anaesthetic consumption, time to postoperative chest tube removal, postoperative pain and length of postoperative hospital stay will also be assessed.

### Neurotransmitter indicators

The levels of neurotransmitter indexes (5-HT, NE, GABA) in the peripheral blood will be detected by the immunoturbidimetric method. The possible mechanisms of TEAS in relieving preoperative anxiety may be the regulating effect of 5-HT, NE, cortisol and other endogenous factors level.<sup>48</sup> Patients with GAD indicate dysregulation of GABA, 5-HT and NE by reason of these neurotransmitters are involved in the putative pathophysiology of anxiety.<sup>49</sup> The serum level of 5-HT and NE are negatively correlated with the inhibition of anxiety while GABA is positively related.<sup>50 51</sup>

### Intraoperative anaesthetic consumption

Preoperative anxiety is positively correlated with intraoperative analgesics consumption.<sup>52</sup> The types and cumulative doses of intraoperative analgesics will be assessed.

### Chest tube removal time

The time from the lung resection to the removal of chest tube is regarded as the chest tube removal time. Preoperative anxiety would lead to sustained anxiety after VATS that prolong the postoperative recovery time.<sup>53</sup> Early removal of the chest tube after VATS lung resection could decrease morbidity and postoperative complications which is closely related to postoperative recovery time.<sup>54 55</sup>

### Postoperative pain

Preoperative anxiety may contribute to increased sensitivity to postoperative pain.<sup>6 56</sup> The degree of postoperative pain will be evaluated once per day for 2 days after the

VATS by Visual Analogue Scale of pain (VAS). VAS ranges from 0 (no pain) to 10 (unbearable pain).<sup>57</sup>

### Length of postoperative hospital stay

Enhanced recovery after surgery (ERAS) pathways were considered to be effective in shortening the length of hospital stay.<sup>58</sup> The indications with ERAS trend in VATS lung resection which influence a reduced length of hospital stay are early mobilisation, less amount of pleural fluid drainage, earlier removal of chest tubes and urinary catheters and quickly break loose intravenous fluids.<sup>58</sup> Thus, the hospitalisation length will be calculated from the VATS day to the discharge day.

### Safety outcomes

The participants are free to inform of any AE to the outcome assessors during this trial. AEs are any unexpected symptoms, signs or health conditions that occur after starting the treatment of this study, which may not be causally related to the treatment of this study. Health condition or disease that existed before the start of the treatment in this study can only be considered an AE if it deteriorates further after the start of the treatment in this study. Abnormal laboratory test values or test results can only be considered AE when they cause clinical symptoms or signs that are considered clinically significant or require treatment.

Adverse reactions associated with TEAS, especially skin itching, rash or swelling attached to the electrodes and mood disturbance will be closely monitored through spontaneous reports by participants, or clinical observation by acupuncturists and surgeons, or by inquiring participants about AE with open questions. In that case, TEAS/STEAS will be discontinued instantly; moreover, corrective treatment will be implemented appropriately. The participant will be referred on to receive expectant treatment for the symptom if necessary. As a matter of

course, this participant will be withdrawn from the trial. Acupuncturists and surgeons will evaluate the intensity and causality with TEAS or VATS. Postoperative complications will be classified and graded in line with the Clavien-Dindo classification.<sup>59</sup> Time of occurrence, duration, symptoms severity, possible causes and corresponding AE management should be documented in detail in the electronic case report form (eCRF). Severe AEs will be reported promptly to the ethics committee.

### Data management and monitoring

Each participant's CRF will be recorded by trained clinical investigators. Two investigators will enter the participant data into the eCRF independently as soon as the data are collected on the original CRF. An independent supervisor will verify the consistency and accuracy of the data. All paper documents and eCRFs will be stored securely and separately for at least 5 years after completion of the study.

The quality of the studies and regulatory compliance will be monitored. The monitoring personnel does not participate in our research. The ethics committee has approved the supervision to verify the qualifications of investigators and research team members, and to monitor sound and appropriate documents.

### Quality control

In order to ensure that the procedure is strictly followed before the trial official starts, the launching meeting will be arranged to train all related investigators, including research goals and content, participants recruitment, treatment procedures, physician-patient communication skills and outcome evaluation.<sup>60</sup> At the same time, a coordinated and standardised procedure will be formulated to inform the team. Independent monitor will check the intervention procedure and completed cases regularly during the trial.

Only acupuncturists licensed in TCM with at least 5 years of clinical experience are allowed to operate TEAS/STEAS. Furthermore, the principal investigator will guide the acupuncturists through all the details of acupoint selection and TEAS/STEAS operating mode.

### Sample size

Primary outcome indicator in this trial is the GAD-7 score variation between the day before VATS with the baseline. The sample size was calculated on the grounds of our preliminary trial (online supplemental material 1). Reference for optimal effectiveness in clinical trials of two sample mean comparison, using formula for calculating sample size of clinical trials as follow.

$$n_1 = n_2 = 2 \left[ \frac{(u_\alpha + u_\beta)}{\delta/\sigma} \right]^2 + \frac{1}{4} u_\alpha^2$$

GAD-7 score change in TEAS group increase the divergence between the STEAS group and the SD by 73%.  $\delta/\sigma=0.73$ , test level bilateral  $\alpha=0.05$ , test power  $1-\beta = 0.9$ . Through calculation, each group required sample size is 40 samples. The submitted trial will demand 92

participants to be divided into two groups of 46 in consideration of the 15% probability of lost to follow-up.

### Statistical analysis

All results will be evaluated according to the principles of intentional treatment.<sup>61</sup> We will make use of the last-observation-carried-forward analyses to fill the missing value. Independent statisticians who are unaware of treatment allocation will analyse all the data by SPSS V.21.0. Mean $\pm$ SD will represent continuous variables with standard normal distribution, while median and IQR will be presented for biased distributed data. Classification variables will be expressed as percentage with  $\chi^2$  test. Intergroup discrepancy will be compared by Independent two-sample t-tests. The paired t-tests and the Mann-Whitney rank sum test are going to perform for intragroup comparison, corresponding to the normal distribution of continuous variables and the skewed distribution of continuous variables, respectively. The measurement of continuous variables will be repeated by the generalised linear models. Two-sided  $p<0.05$  with CIs at the 95% level will be defined as statistical significance. Kappa analysis will be employed to determine whether participants guessed their group allocation correctly at a higher rate than would be expected by chance.<sup>62</sup>

### Patient and public involvement

Neither the participants nor the public were implicated in the project of the protocol design.

### DISCUSSION

Following admission to hospital for VATS due to the presence of pulmonary nodules, the change in identity and environment and concern for a lung cancer diagnosis inevitably makes a patient anxious.<sup>63 64</sup> Although not fatal, preoperative anxiety is considered one of the core threats to extended hospitalisation along with higher medical care costs.<sup>35</sup> Presently, therapies of diverse kinds have been evolved to relieve preoperative anxiety, but none are entirely satisfactory.<sup>15</sup>

There is evidence that acupuncture therapy aimed at reducing preoperative anxiety has some beneficial effects compared with placebo or non-treatment alternatives.<sup>19</sup> As an easily operable acupuncture point stimulation method which has proven its efficacy by the increasing clinical studies, TEAS has gradually been accepted and recommended by the surgeons.<sup>25 48</sup> As far as we are aware, this clinical trial is the first to perform a safety evaluation of TEAS for alleviating preoperative anxiety of VATS. Ninety-two patients with mild anxiety prior to VATS with identical standardised protocols for surgical plan and perioperative management will be enrolled in the cardiothoracic surgery department of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine in this well-designed trial.

Specific points on meridians affected by the disease have been shown to have better benefits for patients with situational anxiety and GAD.

The exclusive combination of acupoints can greatly enhance the effects of TEAS on physical and mental relaxation according to the TCM theory. Specific acupoints on meridians affected by situational anxiety and GADs are more beneficial for patients.<sup>65–66</sup> TEAS is non-invasive and relatively safe compared with acupuncture or electroacupuncture. Although very rare, AEs have been reported, including skin itching, rash, or swelling in the area attached to electrodes, and mood disturbance.<sup>67–68</sup> Therefore, all adverse reactions will be closely monitored, but will also be subject to safeguarding procedures. Patients will receive the expected treatment of symptoms if an adverse reaction occurs.

Our trial has a few ineluctable limitations. To differ the particular effects of TEAS from its nonspecific effects, we plan to employ a 0 mA current intensity as a sham control. It is possible for participants to have a mental effect in the STEAS group, even though the acupuncturist responsible for the operation will inform the patients in advance of the stimulus type without sensing. Nevertheless, STEAS procedure for sham control has been successfully devoted to several TEAS trials for various healthcare service.<sup>67–72</sup> Another limitation is that we included participants with mild anxiety. However, including patients with GAD-7 score less than 9 may be a limitation, the level of anxiety symptoms at the beginning of the study should be of sufficient severity to allow the detection of the change. Finally, due to a single-centre clinical trial with a limited number of patients, the therapeutic effect of TEAS may be restricted by simplex ethnicity and region. Thus, it will be necessary to conduct large-sample multicentre multinational studies to demonstrate the efficacy and safety of TEAS from an extended perspective that involves other types of surgery in the future.

Our trial will provide proof for the efficacy and safety of TEAS in the intervention of anxious patients before VATS of lung resection which will support the application of TEAS as a pretreatment strategy for patients undergoing VATS.

### Ethics and dissemination

The study protocol (V.2.0, 2 April 2021) and applied informed consent forms have been approved by the Ethics Committee of the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine. Since February 2022, the number of inpatients has significantly decreased due to the novel corona virus epidemic prevention and control in Shanghai. Potential participants could not be recruited until August 2022. Therefore, we have applied to and received approval from the ethics committee for an extension until 31 March 2023. We plan to disseminate and publish the trial outcomes in a peer-reviewed journal.

### Author affiliations

<sup>1</sup>Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China

<sup>2</sup>Cardiothoracic Surgery Department, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China

<sup>3</sup>Clinical Research Institute of Acupuncture and Anaesthetic, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China

**Contributors** JZ and TC conceived the idea behind the trial. JZ, TC and KW designed the study. JF is responsible for statistical analysis. This manuscript was drafted by XW and revised by JZ, TC, KW, X-QW and JF. All authors read and approved the final manuscript.

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### ORCID iDs

Xindi Wu <http://orcid.org/0000-0002-4307-7222>

Ke Wang <http://orcid.org/0000-0002-5845-7228>

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