




BMJ Open Electroacupuncture versus sham electroacupuncture in the treatment of postoperative ileus after laparoscopic surgery for colorectal cancer: study protocol for a multicentre, randomised, sham-controlled trial

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ABSTRACT

Introduction Postoperative ileus (POI) is an inevitable complication of almost all abdominal surgeries, which results in prolonged hospitalisation and increased healthcare costs. Various treatment strategies have been developed for POI but with limited success. Electroacupuncture (EA) might be a potential therapy for POI. However, evidence from rigorous trials that evaluated the effectiveness of EA for POI is limited. Thus, the aim of this study was to examine whether EA can safely reduce the time to the first defecation after laparoscopic surgery in patients with POI.

Methods and analysis This multicentre randomised sham-controlled trial will be conducted in four hospitals in China. A total of 248 eligible participants with colorectal cancer who will undergo laparoscopic surgery will be randomly allocated to an EA group and a sham EA group in a 1:1 ratio. Treatment will be performed starting on postoperative day 1 and continued for four consecutive days, once per day. If the participant is discharged within 4 days after surgery, the treatment will cease on the day of discharge. The primary outcome will be the time to first defecation. The secondary outcome measures will include time to first flatus, tolerability of semiliquid and solid food, length of postoperative hospital stay, postoperative nausea and vomiting, abdominal distension, postoperative pain, postoperative analgesic, time to first ambulation, blinding assessment, credibility and expectancy and readmission rate.

Ethics and dissemination Ethics approval was obtained from the Ethics Committee of Beijing University of Chinese Medicine (number 2020BZHLL0116) and the institutional review board of each hospital. The results will be disseminated through peer-reviewed publications. This study protocol (V.3.0, 6 March 2020) involves human participants and was approved by the ethics committees of Beijing University of Chinese Medicine (number 2020BZHLL0116), Beijing Friendship Hospital Affiliated to Capital Medical University (number 2020-P2-069-01), Beijing Chao-Yang Hospital Affiliated to Capital Medical University (number 2020-3-11-2), National Cancer Center/

Strengths and limitations of this study

- In this clinical trial, 248 participants experiencing postoperative ileus after laparoscopic resection with different types of procedures will be enrolled from four hospitals, and a subgroup analysis based on primary surgical procedures is planned.
- The trial will be conducted in an enhanced recovery after surgery environment, which is the major difference from previous clinical studies.
- On the basis of the results of our pilot trial of 108 participants, electroacupuncture on specific acupoints is expected to yield greater benefits than those demonstrated in previous acupuncture trials.
- The patients with previous acupuncture experience may increase the possibility of lack of successful blinding.

National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (number 20/163-2359), and the Affiliated Hospital of Qingdao University (number QYFYKYL711311920). The participants gave informed consent to participate in the study before taking part. **Trial registration number** ChiCTR2000038444.

BACKGROUND

Postoperative ileus (POI) is generally defined as a transient delay of recovery of coordinated intestinal peristalsis due to nonmechanical causes within 2–6 days after a surgical intervention.^{1–3} Despite the use of minimally invasive surgical techniques, POI is typically regarded as an inevitable complication after abdominal surgery (especially colorectal resection).^{4,5} Its principal clinical features include disappearance of bowel sounds, delayed passage of

flatus and stool, inability to tolerate an oral diet, nausea, vomiting, abdominal distension and pain.⁶ POI can lower patient satisfaction and quality of life, increase the risk of other postoperative complications, prolong hospital stay, and increase readmission rates and hospital costs.^{7–9} In patients undergoing anterior lumbar interbody fusion, POI can prolong hospital stay by 3 days and increase hospitalisation costs by \$2400.¹⁰ Reducing the mean length of hospital stay by just 1 day could reduce the cost of the healthcare system in the USA by approximately \$1 billion annually.¹¹ This highlights the importance of treating and decreasing the duration of POI.

No specific interventions to prevent or treat POI have been approved by the National Medical Products Administration, and clinically relevant therapeutic strategies are lacking. Alvimopan, a peripherally acting opioid antagonist, is currently the only medication approved by the US Food and Drug Administration to accelerate the return of bowel function after colorectal resection.¹² However, owing to the increased risk of myocardial infarction and limited effect in laparoscopic surgery associated with the use of alvimopan, it has not been routinely administered. In addition, the benefits of postoperative gum chewing, coffee, nasogastric tube removal and minimally invasive surgery for reducing the risk of POI have been reported, although the data remain inconclusive.^{13–15} As such, novel and effective therapeutic options for POI must be developed urgently.

Acupuncture has been widely used for various functional gastrointestinal diseases in clinical practice.^{16–19} In terms of the recovery of gastrointestinal function after colorectal surgery, the response to acupuncture was inconsistent across trials. A review of acupuncture for treatment of POI in colorectal cancer found evidence of improvement in gastrointestinal function.²⁰ Notably, acupuncture with or without electrostimulation was the most commonly used acupuncture intervention among the 21 trials. A recent systematic review²¹ concluded that electroacupuncture (EA) could accelerate the resumption of bowel transit as a potential treatment option for POI after abdominal surgeries, including laparoscopic surgery. Owing to the scarcity of meta-analysis studies and the poor methodological quality of the trials, no definite conclusion could be reached. A sham-controlled trial²² was deemed low risk of bias by the systematic review in all domains, including selection, performance, detection, attrition and reporting. It is notable that the sample size and power of this trial may not be adequate to show a significant difference in the time to defecation between the EA and the sham electroacupuncture (SA) groups. Thus, our trial with a sample size of 248 is more adequately powered for a smaller difference in time to defecation.

On the basis of the aforementioned findings, we hypothesise that EA would be an effective treatment for POI in patients who had undergone elective laparoscopic surgery for colorectal cancer. This trial will be completed to gain more reliable insights into the efficacy and safety of EA for postoperative patients with POI.

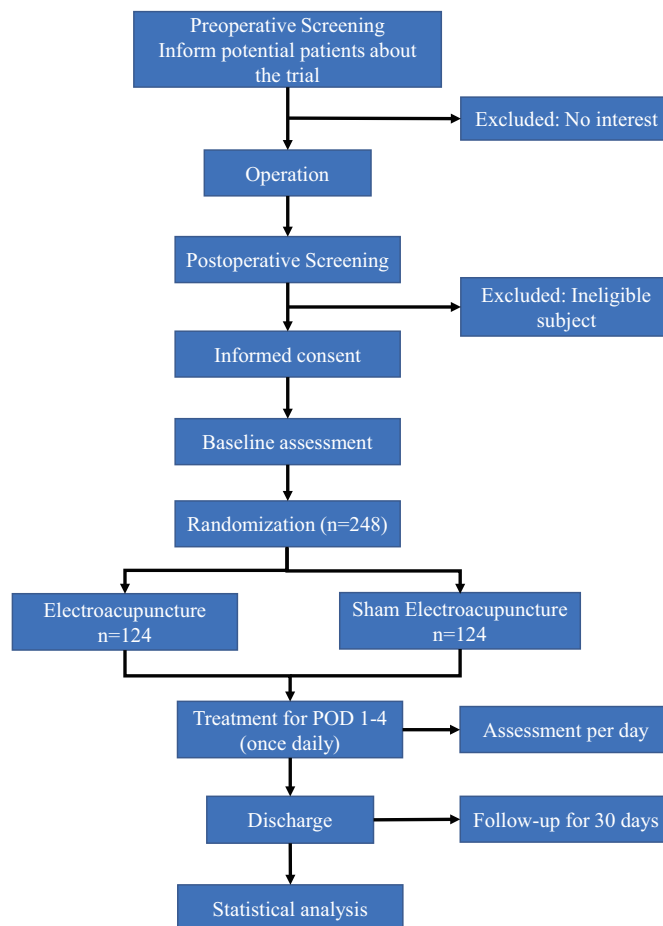


Figure 1 Study flow diagram. POD, postoperative day.

METHODS AND DESIGN

Study design

This multicentre, randomised, sham-controlled, participant-blinded and assessor-blinded trial will be conducted at the inpatient ward of four hospitals in China (Beijing Friendship Hospital Affiliated to Capital Medical University, Beijing Chao-Yang Hospital Affiliated to Capital Medical University, Cancer Hospital Chinese Academy of Medical Sciences and the Affiliated Hospital of Qingdao University). The trial will commence after ethical approval has been obtained and the protocol has been registered. An estimated 248 participants will be recruited and randomly assigned to receive EA or SA in a 1:1 ratio using stratified blocked randomisation. During the development of the standard protocol, the Consolidated Standards of Reporting Trials statements²³ and the Standards for Reporting Interventions in Clinical Trials of Acupuncture²⁴ will be followed to explicitly and transparently explain the therapeutic processes involved. The study flow diagram is shown in figure 1, while the schedules of the trial enrolment, interventions and assessments are illustrated in figure 2.

Participant recruitment

Participants who will undergo elective laparoscopic surgery for colorectal cancer will be informed of the

The schedule of trial enrolment, interventions and assessments

Enrolment	Enrolment		Intervention period				Follow-up	
	POD 0	POD 1	POD 2	POD 3	POD 4	Discharge	30-day after discharge	
Eligibility screening	●							
Informed consent	●							
Randomization	●							
Medical history	●							
Intervention*								
EA		←	→					
SA		←	→					
Assessments								
Time to first defecation		←	→					
Time to first flatus		←	→					
Length of hospital stay						●		
Time to tolerability of food		←	→					
Postoperative nausea and vomiting	●		●	●	●			
Postoperative pain	●		●	●	●			
Abdominal distension	●		●	●	●			
Time to first ambulation	●		●	●	●			
Blinding, credibility and expectancy		←	→					
readmission rate							●	
Adverse events		←	→					

Figure 2 Schedule of trial enrolment, interventions and assessments. EA, electroacupuncture; SA, sham electroacupuncture; POD, postoperative day.

trial prior to the surgery. Participants who show interest in study participation will be considered as potential subjects, and their basic information will be recorded. Potential subjects will be interviewed postoperatively by the clinical research coordinator to assess whether they meet the inclusion and exclusion criteria. Eligible participants will voluntarily provide written informed consent prior to randomisation.

Inclusion criteria

1. Male or female patients aged >18 years.
2. Patients diagnosed with colorectal cancer who have been scheduled for laparoscopic surgery.
3. Patients with American Society of Anesthesiologists grades I–III.²⁰
4. Patients who have undergone abdominal surgery for the first time.
5. Patients who sign the informed consent.

Exclusion criteria

1. Patients who received epidural anaesthesia.
2. Patients whose laparoscopic surgery should be synchronised with organ resection.
3. Patients who require conversion from laparoscopic surgery to open surgery or underwent total colorectal resection.
4. Patients with intraoperative and postoperative complications requiring long-term intensive care (>1 day).
5. Patients who require stoma creation.
6. Patients with a history of mental disorders or alcohol or drug abuse.

7. Patients who have been receiving acupuncture treatment within 1 month prior to the study.
8. Patients with electrical stimulation devices (pacemaker or implantable defibrillator).
9. Patients who have participated in other clinical studies.

Randomisation and allocation concealment

After the participants complete the baseline assessment, they will be randomised with equal probability into the EA and SA groups by using a central web-based randomisation system (SJTU-Yale Joint Center for Biostatistics). The computer-generated random sequences in R (R Project for Statistical Computing) will be compiled by an independent statistician with no direct clinical role in the trial. Randomisation will be stratified among the four enrolment hospitals, and the random block design will be adopted, in which the block sizes will be changed randomly.

Blinding

Owing to the characteristics of the interventions, the acupuncturists involved will not be blinded to the treatment allocation. To avoid the unblinding of the assessment of outcomes, the appearance of the EA apparatus in the two groups will be the same basically but with different marks. The apparatus in the EA group can be used normally, whereas the internal wires inside the apparatus in the SA group are cut so that no electric pulse will be delivered to the participants even while its lights are on. Only the acupuncturist who will operate the apparatus will know if it is working properly.

During the trial period, the participants, assessors and statistician, who will perform the statistical analysis, will be unaware of the group assignments throughout data collection and analysis to compensate for potential bias.

Intervention

The acupuncture treatments will be performed in the participant's bed. The acupuncturists involved in the study hold a Chinese medicine practitioner licence from the Ministry of Health of the People's Republic of China and have >3 years of acupuncture experience. Before the trial officially starts, all the acupuncturists will be trained in a standardised operating procedure to acquire a full understanding of the locations of acupoints and non-acupoints and the manipulation of needles. During the intervention, the acupuncturists will maintain minimal verbal communication with the participants.

Single-use, sterile needles (Hwato disposable acupuncture needle; Suzhou, Jiangsu, China) in sizes of 0.30×40 mm or 0.25×30 mm will be used for the acupuncture treatment. The eligible participant will receive EA or SA once per day for four consecutive days starting on postoperative day 1. Each session will continue for 30 min, starting from the moment the electrode is connected to the needle. The last treatment will be performed on postoperative day 4 or the day of discharge, whichever comes first.

In accordance with the Chinese consensus and clinical guidelines for Enhanced Recovery After Surgery (ERAS),²⁵ each participant will receive identical standardised protocols for perioperative management and postoperative care, namely, ERAS. During the study period, the patients' medications, such as analgesics, prokinetics and herbal medicine, should be recorded in detail.

Electroacupuncture

The treatment strategy was developed on the basis of the traditional Chinese medicine theory and a consensus of acupuncture experts. Specific acupoints are believed to be associated with certain regional effects.¹⁸ POI is considered to be closely related to the stomach and large intestine meridians. Hence, Zusanli (ST-36, bilateral), Shangjuxu (ST37, bilateral), Zhongwan (RN12) and Tianshu (ST25, bilateral) will be identified before needle insertion. The locations of the acupoints are presented in [table 1](#) and [figure 3](#).

Acupuncture needles will be inserted perpendicular to the skin. Twirling and rotating, and lifting and thrusting manipulations will be applied for 30s at each acupoint after the onset of the de qi sensation (a unique sensation of combined numbness, tingling, fullness and aching in response to acupuncture).²⁶ Electric stimulation will be used with an EA apparatus (HANS-200A acupoint nerve stimulator, Nanjing Jisheng Medical Co). The paired electrodes from the EA device will be attached to the needle handles at the bilateral ST-36 acupoints. The frequency of the electrical stimulation will be set as alternating 2/100 Hz,^{27 28} which has been shown to be effective in reducing chemotherapy-induced nausea and vomiting, and treating visceral pain. The electric current will be adjusted in strength until the patient can perceive and tolerate it (preferably with the skin around the acupoints shivering mildly without pain).²⁹

Sham electroacupuncture

A superficial skin penetration (2–3 mm in depth) at non-acupoints will be performed in the SA group. 'De qi' and manual stimulation in the group should be avoided. Non-acupoints deviate from the conventional acupoints or meridians. The locations of the four non-acupoints are shown in [table 2](#) and [figure 3](#). A sham electrical stimulation device with a broken internal wire will be applied. The paired electrodes will be connected to the needles at bilateral non-acupoint 1 for 30 min without actual current output.

Outcome measurement

The time to first defecation and flatus, time to tolerability of semiliquid and solid food, and time to first ambulation should be assessed daily during hospitalisation until the endpoints occur. The participants and their family members or caregivers will be required to record the time of postoperative outcomes and inform the assessors as soon as possible. If the outcomes do not occur during hospitalisation, the participants and their family members should be instructed to record the time of occurrence after discharge and inform the assessors by telephone. Then, the results will be transcribed in electronic case report forms (eCRFs) by the assessors. In view of the medical environment in China, caregivers are encouraged to assist in recording outcome indicators.

Table 1 Locations of the acupoints for the EA group

Acupoint	Location
Zusanli (ST36)	3 cun* directly below Dubi (ST35) and one finger breadth lateral to the anterior border of the tibia
Shangjuxu (ST37)	3 cun directly below Zusanli (ST36) and one finger breadth lateral to the anterior border of the tibia
Zhongwan (RN12)	On the anterior midline, 4 cun above the umbilicus
Tianshu (ST25)	At the same level of the umbilicus and 2 cun lateral to the anterior midline

*1 cun (≈20 mm) is defined as the width of the interphalangeal joint of the thumb.
EA, electroacupuncture; ST, stomach; RN, Ren channel.

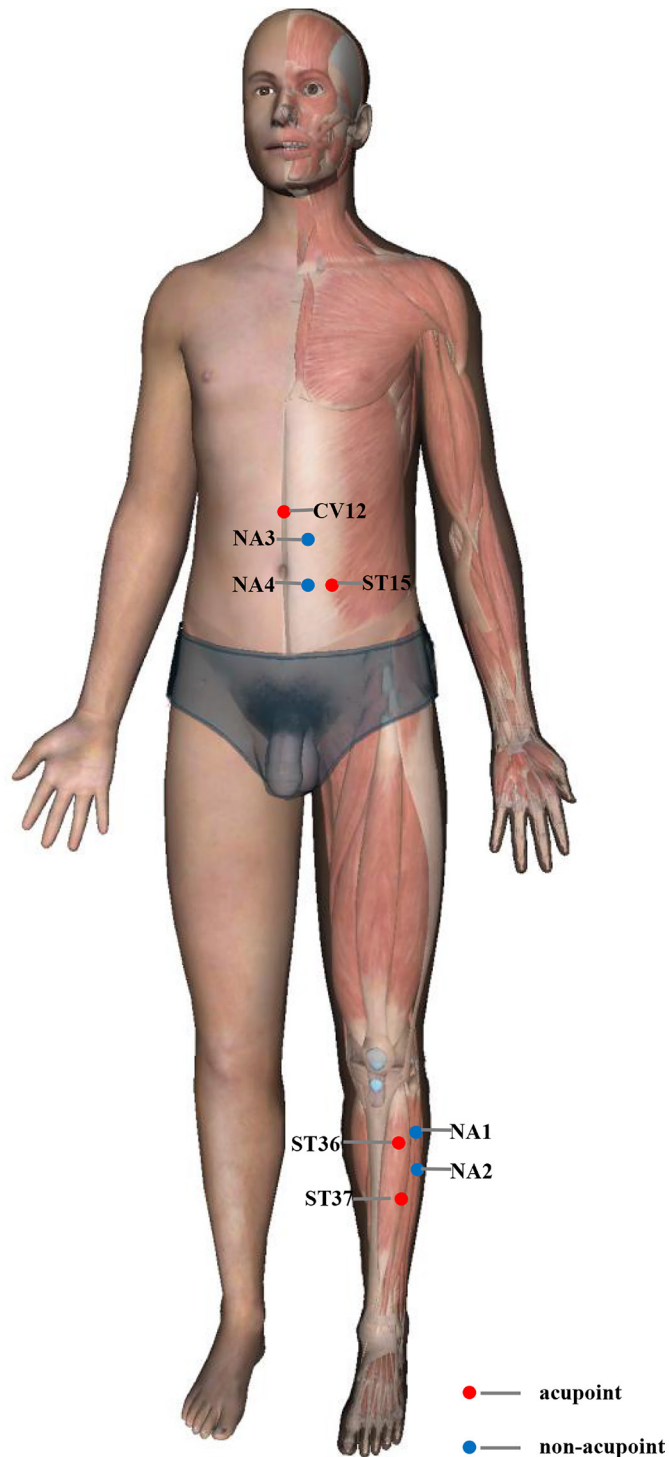


Figure 3 Locations of acupoints and NAs. NA, non-acupoint.

Primary outcome

The primary outcome is the time to first defecation,²⁰ defined as the interval between the end of the operation and the first observed passage of stool. The minimum clinical significance of the primary outcome is 12 hours.³⁰

Secondary outcomes

The severity of nausea, pain and abdominal distension will be evaluated using a self-made Visual Analogue Scale

Table 2 Locations of the non-acupoints for the SA group

Non-acupoint	Location
Non-acupoint 1	In the middle of the Yanglingquan (GB34) and Zusanli (ST36) points, between the gallbladder and stomach meridian
Non-acupoint 2	3 cun* below Yanglingquan (GB34), between the gallbladder and stomach meridian
Non-acupoint 3	3 cun above the umbilicus, and 1.0 cun to the left of the anterior midline, between the spleen and stomach meridian
Non-acupoint 4	1.0 cun lateral to the umbilicus, between the spleen and stomach meridians

*1 cun (≈ 20 mm) is defined as the width of the interphalangeal joint of the thumb.

SA, sham electroacupuncture; GB, gallbladder; ST, stomach.

(VAS) scorecard. The participants will be informed of the meaning and usage of the VAS in advance and will be required to place a mark on the line at a point representing the severity of their symptoms.^{31 32} Then, the assessors will measure the scale with a ruler and record the value in the eCRFs.

Time to first flatus

The time to first flatus refers to the time from the end of laparoscopic surgery to the first passage of exhaust.²⁰ Only when the participant feels bowel motion will the flatulence be considered clinically significant.³³

Length of postoperative hospital stay

The length of hospital stay will be calculated from the time of colorectal resection to the time of discharge.³⁴ Generally, the criteria for hospital discharge include good organ function with the ability of free movement, oral analgesics with good analgesia, ability to tolerate a semi-liquid diet, good wound healing, no sign of infection, absence of other postoperative complications, the home care provided and the participant's agreement on discharge.²⁵

Time to tolerability of semiliquid and solid food

The time to first tolerance of semiliquid and solid food³⁵ is regarded as the time from the end of the operation to the first tolerance of the two different kinds of food without nausea, vomiting and other gastrointestinal adverse reactions. Tolerability refers to the absence of nausea and vomiting within 4 hours after eating food. The semiliquid diet includes rice porridge, egg soup, and chicken custard, while the solid diet refers to the normal diet. The physician will determine which type the food belongs.

Postoperative nausea and vomiting

Nausea and vomiting will be evaluated once per day for 4 days starting on postoperative day 1. The degree of nausea will be measured on a 0–100 mm VAS with scores ranging from 0 (no nausea at all) to 100 (worst nausea). In addition, the number of episodes of postoperative

nausea and vomiting per day should be recorded by the assessors, respectively. Nausea or vomiting with an interval of more than 5 min is considered an independent event and should be recorded separately.³¹

Postoperative pain

During postoperative days 1–4, the extent of postoperative pain will be measured once per day using a VAS with scores ranging 0–100, with 0 representing absence of pain and 100 representing the worst pain imaginable.

Extent of abdominal distention

During postoperative days 1–4, the extent of postoperative abdominal distention will be assessed daily on a 0–100 mm VAS, with scores ranging from 0 (no feeling of abdominal distention) to 100 (oppressive distention).

Time to first ambulation

The time to first ambulation is defined as the time from the end of the operation to first getting out of bed and ambulation.

Blinding assessment

Nowadays, blinding is a critical component in randomised clinical trials to demonstrate internal validity. Once the first treatment session is completed, we will test the participant-blinding effects by asking them to answer the question, ‘Which type of acupuncture do you think you received, EA or SA?’³⁶

Credibility and expectancy

Treatment credibility refers to how believable, persuasive and logical the treatment seems to the participant, whereas treatment expectancy refers to the improvement the participant believes to personally achieve.³⁷ After the first treatment, treatment credibility and expectation will be evaluated using the Credibility/Expectancy Questionnaire.

Readmission rate

Readmission has long been recognised as a key endpoint in healthcare systems.^{38 39} To enquire whether the participant has been readmitted for surgical complications within 30 days after discharge, the assessors will conduct a follow-up telephone call 30 days after discharge.³¹ The proportion of participants who are readmitted for surgical complications within 30 days after discharge is regarded as the 30-day readmission rate.

Safety outcomes

During the trial, the participants will be required to report any adverse events (described as unfavourable symptoms or diseases) to the outcome assessors. The causality with acupuncture or surgery will be analysed by the acupuncturists and surgeons. On the basis of the Clavien-Dindo classification, postoperative complications will be classified and graded.⁴⁰ The occurrence, duration, severity (symptoms and signs) and corresponding solution of the adverse events should be recorded in detail in eCRFs.

Furthermore, serious adverse events will be reported to the data and safety monitoring board (DSMB) within 24 hours.

Data management

The electronic data capture (EDC) system created by a third-party corporation (SJTU-Yale Joint Center for Biostatistics) will be used for data acquisition and management. Data will be entered on tablets. Each hospital has only one outcome assessor who will be responsible for data entry. The EDC system will be tested, and the assessors will be trained on how to fill out the eCRFs using the system before the commencement of the study. The participants’ information will be stored in the EDC system with limited access to ensure that the information will not be disclosed to anyone.

On the basis of the premise of the inspection function in the EDC, dynamic management will be implemented to ensure complete, timely and accurate data collection. To enhance internal authenticity, an independent DSMB has been established to review and interpret the trial data. The board consists of experts in acupuncture, gastroenterology, methodology and statistics, and will be responsible for monitoring the overall quality and completeness of the data. The members of the board will interview assessors, examine original data (both paper and electronic) and ensure that the trial is conducted in accordance with the protocol. They will be qualified to decide on any premature closure of the study.

When the trial is completed, the database will be locked. Thereafter, the researchers will be unable to modify the data. The research documents will be safely preserved for at least 5 years after publication. If readers and reviewers have any confusion about our trial, they can contact the corresponding author to request the original data.

Quality control

To ensure that the procedure is consistent across all hospitals before the trial is officially started, a start-up conference will be arranged to train all staff on relevant content, including the objective and content of the study, participant recruitment, treatment strategies, moderate physician–patient communication and outcome evaluation. Meanwhile, a unified and standardised operation procedure will be developed and provided to the staff at each hospital. Independent monitoring staff will regularly check the completed cases and acupuncture operations during the treatment period.

Sample size

The sample size was calculated on the basis of the results of our pilot study. This study included 105 participants with colorectal cancer who underwent laparoscopic surgery, enrolled from November 2019 to September 2020. The participants were randomly assigned to receive EA at Tianshu (ST25) or Zusanli (ST36) or no acupuncture. The mean time to first defecation in the two EA groups was 76 hours. We estimated that the time to first

defecation in the EA group will be 12 hours²⁹ earlier than that in the SA group, assumed to be 88 hours, with an SD between of 32 between the two groups. On the basis of a statistical power of 80% at a two-sided significance level of 5%, the calculated number of subjects is 112 in each group. With the consideration of a 10% dropout rate, 12 additional subjects will be recruited to offset the potential attrition. Hence, we expect to enrol a target number of participants of 248 (124 per group).

Statistical analysis

The intention-to-treat analysis population, consisting of all participants who will pass the randomisation stage, will be the primary population for efficacy and safety analyses. The outcome of the primary analysis will be the difference in time to first defecation between the EA and SA groups. The outcomes of the secondary efficacy analyses include the time to first flatus; time to tolerability of semiliquid and solid food; time to first ambulation; length of hospital stay; postoperative nausea and vomiting, pain and abdominal distention; blinding assessment; treatment credibility and expectancy; and readmission rate. Kaplan-Meier curves will be used to analyse differences in time-to-event variables, and statistical significance will be calculated using log-rank tests. Differences in postoperative nausea, pain, abdominal distention and analgesic use will be analysed using an independent t-test or a rank-sum test. The χ^2 test will be used to compare differences in the blinding success of the subjects, the incidence of adverse events, and treatment credibility and expectancy between the groups.

Missing data on the primary outcome will be imputed using the multiple imputation method. Secondary outcomes in the observed cases will be analysed without imputation of missing data. To determine the independent factors, multiple linear regression analysis will be used. The following confounding factors including age, sex, body mass index, medical comorbidities and surgical time, which could have affected the gastrointestinal motility, will be regarded as the clinically relevant factors taken into account in the multiple linear regression. A predetermined subgroup analysis will be performed to determine whether the primary procedure (left-sided colectomy, right-sided colectomy or rectal resection) affects the clinical response to EA.

Continuous data will be described as mean \pm SDs for normally distributed data or median and IQR for skewed data. Categorical data will be presented using frequencies and proportions (as percentages). All statistical analyses will be processed in SAS V.9.4, with the significance threshold defined as a two-sided p value of <0.05.

Patient and public involvements

Neither the patients nor the public were involved in the design, conduct, reporting or dissemination plans of the research. The study results will be disseminated to all patients at the end of the trial.

DISCUSSION

Almost all the participants who underwent abdominal surgery, including laparoscopic surgery, had transient impairment of gastrointestinal motility, known as POI.^{4,5} Although not life-threatening, POI is regarded as one of the main contributors to prolonged hospital stay, which also means higher healthcare costs. Currently, various strategies have been developed to reduce the duration of POI, but none is entirely satisfactory.¹²⁻¹⁵ With the continuation of significant research to identify the therapeutic options for POI, EA has gradually gained acceptance from physicians, as clinical studies and basic research have demonstrated its efficacy.⁴¹ The present trial has been designed to evaluate whether EA will prompt restoration of bowel function (time to stool and time to flatus).

Previous clinical research studies had inconsistent results due to some existing limitations, including illogical design, small sample size, imperfect blinding method, and allocation concealment. In this well-designed clinical trial, 248 participants with POI after laparoscopic resection with different types of procedures will be enrolled from four hospitals. A subgroup analysis based on primary surgical procedures is also planned. To our knowledge, the use of ERAS has been reported to decrease the development of POI,⁴² but little is known about the effect of EA combined with ERAS on clinical outcomes after laparoscopic colorectal surgery. Thus, this trial will be conducted in an ERAS environment.

According to the theory of traditional Chinese medicine, the special acupoint combination can greatly enhance the effect of acupuncture on the gastrointestinal tract. Acupuncture at the acupoints on the disease-affected meridian has been demonstrated to provide superior benefits to patients with temporomandibular disorders, chronic stable angina, functional dyspepsia and migraine.⁴³⁻⁴⁶ Therefore, this trial is likely to yield greater benefits than previous similar trials.

Our study has several unavoidable limitations. Postoperative defecation and tolerance of solid food intake seem to be the best clinical endpoints of POI,⁴⁷ which reflect recovery of gastrointestinal transit and indicate readiness for discharge. Considering the ERAS situation in China, participants are encouraged to eat semiliquid food before gradually adjusting to a solid food. Participant can discharge as long as they resume taking a semiliquid food.²⁵ Hence, eating solid food is impossible for some participants until discharge. In this study, the time to first defecation is set as the primary outcome, while the time to tolerability of semiliquid and solid food is set as the second outcome. This may limit the applicability of the findings to other settings where early oral solid diet is more aggressively advocated in an ERAS setting. To isolate the specific effects of EA from its non-specific effect, we will use superficial penetrating on non-acupoints as a sham control. Compared with the non-penetrating placebo acupuncture, there is a possibility of having a physiological effect even if the non-acupoints are away from the conventional meridians or acupoints and the

depth of insertion is superficial.⁴⁸ We hypothesise that EA will have a better effect so that there is no need for a placebo control. Furthermore, this sham control procedure has been successfully applied to acupuncture studies for various medical issues.^{22 49} This may be discerned by some Chinese with previous acupuncture experience. However, all the participants will be asked to guess whether the treatment they have received was EA or SA to assess the success of the blinding. Another limitation is that patients' and their family members' postdischarge reporting of time-to-event outcomes may be subject to reporting and measurement errors. It is notable that only a small minority of outcomes will be reported after discharge.

Notwithstanding the limitations of our study, we hypothesise that EA can promote the recovery of gastrointestinal function and shorten the time to first defecation and time to first flatus. If the results meet our expectations, these will elucidate the superiority of EA over SA in terms of efficacy for the treatment of POI. Moreover, we will recommend EA as a treatment option for patients who develop POI after undergoing laparoscopic surgery for colorectal cancer.

Ethics and dissemination

The study protocol (V.3.0, 6 March 2020) has been approved by the ethics committees of Beijing University of Chinese Medicine (number 2020BZHLYL0116), Beijing Friendship Hospital Affiliated to Capital Medical University (number 2020-P2-069-01), Beijing Chao-Yang Hospital Affiliated to Capital Medical University (number 2020-3-11-2), National Cancer Centre/National Clinical Research Centre for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (number 20/163–2359) and the Affiliated Hospital of Qingdao University (number QYFYKYL711311920). Written informed consent will be obtained from all participants before the study is officially started. The results will be disseminated through peer-reviewed publications.

Trial status

Recruitment for the trial has been completed. The first participant was recruited on 12 October 2020, and the last participant was recruited on 17 October 2021.

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assisting in the monitoring and verification of the accuracy of data. We thank the researchers from the four hospitals for their joint effort to promote the future success of the study.

Contributors C-ZL, J-WY and S-YY conceived the idea behind the trial. C-ZL, J-WY, XZ, Y-CY and YW designed the study. S-YY is responsible for the statistical analysis. Y-CY, WP, J-GH, YL, M-SZ, JFT, LLL, L-QW and GXS helped with the implementation of the study. XZ, J-WY, C-ZL and Y-CY drafted and strictly revised the manuscript for important intellectual content. C-ZL sought funding. Y-CY, WP, J-GH and YL obtained the ethical approval. All authors have read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

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Data availability statement Data are available upon reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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