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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 use, 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 2020BZHYLL0116) 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 2020BZHYLL0116), Beijing Friendship Hospital Affiliated to Capital Medical University (number 2020-02-069-01), 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.

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. 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. In patients undergoing anterior lumbar interbody fusion, POI can prolong hospital stay by 3 days and increase hospitalisation costs by $2400. 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. 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. 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. 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. 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. Notably, acupuncture with or without electrostimulation was the most commonly used acupuncture intervention among the 21 trials. A recent systematic review 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 trial 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.

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 statements and the Standards for Reporting Interventions in Clinical Trials of Acupuncture 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
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 (ST36, bilateral), Shangjuxu (ST37, bilateral), Zhongwan (RN12) and Tianzhu (ST25, bilateral) will be identified before needle insertion. The locations of the acupoints are presented in table 1 and figure 3.

**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 |
| Tianzhu (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.

Acupuncture needles will be inserted perpendicular to the skin. Twirling and rotating, and lifting and thrusting manipulations will be applied for >30 s 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 ST36 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.
Primary outcome
The primary outcome is the time to first defecation, 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.

Secondary outcomes
The severity of nausea, pain and abdominal distension will be evaluated using a self-made Visual Analogue Scale (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. 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. Only when the participant feels bowel motion will the flatus be considered clinically significant.

Length of postoperative hospital stay
The length of hospital stay will be calculated from the time of colorectal resection to the time of discharge. 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.

Time to tolerability of semiliquid and solid food
The time to first tolerance of semiliquid and solid food 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 will be recorded.

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.
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.\textsuperscript{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 distension**
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 distension) to 100 (oppressive distension).

**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?’\textsuperscript{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.\textsuperscript{37} After the first treatment, treatment credibility and expectancy will be evaluated using the Credibility/Expectancy Questionnaire.

**Readmission rate**
Readmission has long been recognised as a key endpoint in healthcare systems.\textsuperscript{58, 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.\textsuperscript{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.\textsuperscript{66} 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.

One 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 hours 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 semi-liquid 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; 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 χ² 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±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. 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. 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. 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, but little is known about the effect of EA combined with ERAS on clinical outcomes after laparoscopic colorectal surgery. This, the 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. Therefore, this trial is likely to yield greater benefits than previous similar trials.

Our study has several unavoidable limitations. Postoperative defecation and tolerability of solid food intake seem to be the best clinical endpoints of POI, 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. Participants can discharge as long as they resume taking a semiliquid food. 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.\textsuperscript{18} We hypothesize 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.\textsuperscript{22, 26} 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 hypothesize 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 2020BZHYYLL0116), 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 QFYKYLL71311920). 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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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.

Provenance and peer review

Not commissioned; externally peer reviewed.

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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REFERENCES

1 Hannsberger CR, Maykel JA, Alavi K. Postoperative ileus. \textit{Clin Colon Rectal Surg} 2019;32:166–70.
2 Stakenborg N, Gomez-Pinilla PJ, Bolecxkaetns GE. Postoperative ileus: pathophysiology, current therapeutic approaches. \textit{Handb Exp Pharmacol} 2017;239:39–57.
3 Venara A, Neunlist M, Slim K, et al. Postoperative ileus: pathophysiology, incidence, and prevention. \textit{J Visc Surg} 2016;153:439–46.
4 Peters EG, Pattamma M, Smeets BJJ, et al. The clinical and economical impact of postoperative ileus in patients undergoing colorectal surgery. \textit{Neuromuscul Disord} 2020;32:e13862.
5 Doorly MG, Senagore AJ. Pathogenesis and clinical and economic consequences of postoperative ileus. \textit{Surg Clin North Am} 2012;92:259–72.
6 Sun D-L, Qi Y-K, Yang T, et al. Early oral nutrition improves postoperative ileus through the TRPA1/CCK1-R-mediated mast cell-nerve axis. \textit{Ann Transl Med} 2020;8:179.
7 Tevis SE, Carchman EH, Foley EF, et al. Postoperative ileus--More than Just Prolonged Length of Stay? \textit{J Gastrointest Surg} 2015;19:1684–90.
8 Brown SR, Mathew R, Keding A, et al. The impact of postoperative complications on long-term quality of life after curative colorectal cancer surgery. \textit{Ann Surg} 2014;259:916–23.
9 Li LT, Mills WL, White DL, et al. Causes and prevalence of unplanned readmissions after colorectal surgery: a systematic review and meta-analysis. \textit{J Am Genit Surg Soc} 2013;61:1175–81.
10 Horowitz JA, Jain A, Puvanesarajah V, et al. Risk factors, additional length of stay, and cost associated with postoperative ileus following anterior lumbar interbody fusion in elderly patients. \textit{World Neurosurg} 2018;115:e185–9.
11 Person B, Wexner SD. The management of postoperative ileus. \textit{Curr Probl Surg} 2006;43:6–65.
12 Sultani S, Coles B, Dahr P, Alvimopan for recovery of bowel function after radical cystectomy. \textit{Cochrane Database Syst Rev} 2017;5:CD012111.
13 Chapman SJ, Pericleous A, Downey C, et al. Postoperative ileus following major colorectal surgery. \textit{Br J Surg} 2018;105:797–810.
14 van Bree SHW, Nemethova A, Cailotto C, et al. New therapeutic strategies for postoperative ileus. *Nat Rev Gastroenterol Hepatol* 2012;9:675–83.

15 Gekgkas ID, Minis EE, Iavazzo C. Effect of caffeine intake on postoperative ileus: a systematic review and meta-analysis. *Dig Surg* 2020;37:22–31.

16 Fang J-F, Fang J-Q, Shao X-M, et al. Electroacupuncture treatment partly promotes the recovery time of postoperative ileus by activating the vagus nerve but not regulating local inflammation. *Sci Rep* 2017;7:37826.

17 Chen JDZ, Ni M, Yin J. Electroacupuncture treatments for gut motility disorders. *Neurogastroenterol Motil* 2018;30:e13393.

18 Yin J, Chen JDZ. Gastrointestinal motility disorders and acupuncture. *Auton Neurosci* 2010;157:31–7.

19 Kim KH, Kim DH, Kim HY, et al. Acupuncture for recovery after surgery in patients undergoing colorectal cancer resection: a systematic review and meta-analysis. *Acupunct Med* 2016;34:248–56.

20 Liu Y, May BH, Zhang AL, et al. Acupuncture and related therapies for treatment of postoperative ileus in colorectal cancer: a systematic review and meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med* 2018;2018:1–18.

21 Chen K-B, Huang Y, Jin X-L, et al. Electroacupuncture or transcutaneous electroacupuncture for postoperative ileus after abdominal surgery: a systematic review and meta-analysis. *Int J Surg* 2019;70:93–101.

22 Ng SSM, Leung WW, Mak TWC, et al. Electroacupuncture reduces duration of postoperative ileus after laparoscopic surgery for colorectal cancer. *Gastroenterology* 2013;144:307–13.

23 Bian Z-xiang, Shang H-cai. Consort 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med* 2011;154:290–1.

24 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.

25 Chen L, Chen YJ, Dong HL. Chinese consensus and clinical guidelines for enhanced recovery after surgery (2018 edition). *Chinese Journal of Clinical Surgery* 2018;38:1–20.

26 Xu S-bei, Huang B, Zhang C-yan, et al. Effectiveness of strengthened stimulation during acupuncture for the treatment of Bell palsy: a randomized controlled trial. *CMAJ* 2013;185:473–9.

27 Zhang X, Jin H-F, Fan Y-H, et al. Effects and mechanisms of transcutaneous electroacupuncture on chemotherapy-induced nausea and vomiting. *Evid Based Complement Alternat Med* 2014;2014:1–6.

28 Zhou J, Li S, Wang Y, et al. Inhibitory effects and mechanisms of electroacupuncture via chronically implanted electrodes on stress-induced gastric hypersensitivity in rats with neonatal treatment of iodoacetamide. *Neuromodulation* 2017;20:767–73.

29 Liu Z, Liu Y, Xu H, et al. Effect of electroacupuncture on urinary leakage among women with stress urinary incontinence: a randomized clinical trial. *JAMA* 2017;317:2493–501.

30 Rollins KE, Javanmard-Emamghissi H, Acheson AG, et al. The role of oral antibiotic preparation in elective colorectal surgery: a meta-analysis. *Ann Surg* 2019;270:43–58.

31 DREAMS Trial Collaborators and West Midlands Research Collaborative. Dexamethasone versus standard treatment for postoperative nausea and vomiting in gastrointestinal surgery: randomised controlled trial (dreams trial). *BMJ* 2017;357:j1455.

32 Aun C, Lam YM, Collett B. Evaluation of the use of visual analogue scale in Chinese patients. *Pain* 1986;25:215–21.

33 Yang Y, Zuo H-Q, Li Z, et al. Comparison of efficacy of simo decoction and acupuncture or chewing gum alone on postoperative ileus in colorectal cancer resection: a randomized trial. *Sci Rep* 2017;7:37826.

34 You X-M, Mo X-S, Ma L, et al. Randomized clinical trial comparing efficacy of Simo decoction and acupuncture or chewing gum alone on postoperative ileus in patients with hepatocellular carcinoma after hepatectomy. *Medicine* 2017;96:e7644.

35 Wu Z, Boersema GSA, Dereci A, et al. Clinical endpoint, early detection, and differential diagnosis of postoperative ileus: a systematic review of the literature. *Eur Surg Res* 2015;54:127–38.

36 Hou Y-Q, Zhang X, Tu J-F, et al. Efficacy of acupuncture versus sham acupuncture for postprandial distress syndrome: study protocol for a randomized controlled trial. *Trials* 2019;20:65.

37 Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *J Behav Ther Exp Psychiatry* 2000;31:73–86.

38 Wong ELY, Cheung AWL, Leung MCM, et al. Unplanned readmission rates, length of hospital stay, mortality, and medical costs of ten common medical conditions: a retrospective analysis of Hong Kong hospital data. *BMJ Health Caring Res* 2011;11:149.

39 Landrum L, Weinrich S. Readmission data for outcomes measurement: identifying and strengthening the empirical base. *Qual Manag Health Care* 2006;15:83–95.

40 Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6366 patients and results of a survey. *Ann Surg* 2004;240:205–13.

41 Yang N-N, Ye Y, Tian Z-X, et al. Effects of electroacupuncture on the intestinal motility and local inflammation are modulated by acupoint selection and stimulation frequency in postoperative ileus mice. *Neurogastroenterol Motil* 2020;32:e13808.

42 Yang H, Wang Y, Xing H, et al. Laparoscopic surgery within an enhanced recovery after surgery (ERAS) protocol reduced postoperative ileus by increasing postoperative Treg levels in patients with right-side colon carcinoma. *Med Sci Monit* 2018;24:7231–7.

43 Sen S, Orhan G, Sertel S, et al. Comparison of acupuncture on specific and non-specific points for the treatment of painful temporomandibular disorders: a randomised controlled trial. *J Oral Rehabil* 2020;47:783–95.

44 Zhao L, Li D, Zheng H, et al. Acupuncture as adjunctive therapy for chronic stable angina: a randomized clinical trial. *JAMA Intern Med* 2019;179:1388–97.

45 Ma TT, Yu SY, Li Y, et al. Randomised clinical trial: an assessment of acupuncture on specific meridian or specific acupoint vs. sham acupuncture for treating functional dyspepsia. *Aliment Pharmacol Ther* 2012;35:552–61.

46 Li Y, Zheng H, Witt CM, et al. Acupuncture for migraine prophylaxis: a randomized controlled trial. *CMAJ* 2012;184:401–10.

47 van Bree SHW, Berelman WA, Hollmann MW, et al. Identification of clinical outcome measures for recovery of gastrointestinal motility in postoperative ileus. *Ann Surg* 2014;259:708–14.

48 Moffet HH. Sham acupuncture may be as efficacious as true acupuncture: a systematic review of clinical trials. *J Altern Complement Med* 2009;15:213–8.

49 Jang J, Wang L-Q, Zou X, et al. Effect of acupuncture for postoperative distress syndrome: a randomized clinical trial. *Ann Intern Med* 2020;172:777–85.