

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Transcutaneous electrical acupoint stimulation combined with electroacupuncture for rapid recovery of patients after laparotomy for gastrointestinal surgery: A study protocol for a randomized controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-053309
Article Type:	Protocol
Date Submitted by the Author:	11-May-2021
Complete List of Authors:	Li, Hao; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Wen, Qian; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Lu, Lingyun; Sichuan University West China Hospital, Department of Integrated Traditional Chinese and Western Medicine Hu, Hangqi; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department He, Ying; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Zhou, Yaming; Sichuan University West China Hospital, Gastrointestinal Surgery Wu, Xiaoting; Sichuan University West China Hospital, Gastrointestinal Surgery Li, Ning; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department
Keywords:	COMPLEMENTARY MEDICINE, PAIN MANAGEMENT, GASTROENTEROLOGY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **Transcutaneous electrical acupoint stimulation combined with**
5
6 **electroacupuncture for rapid recovery of patients after laparotomy for**
7
8 **gastrointestinal surgery: A study protocol for a randomized controlled trial**
9
10

11
12
13
14 Hao Li[#], Qian Wen^{1#}, Lingyun Lu¹, Hangqi Hu¹, Ying He¹, Yaming Zhou², Xiaoting
15
16 Wu^{2*}, Ning Li^{1*}
17
18
19

20
21
22 # Hao Li and Qian Wen contributed equally to this work.
23

24
25 *** Correspondence authors:**
26

27 Dr. Xiaoting Wu, wxt1@medmail.com.cn
28

29 Dr. Ning Li, zhenjiuhuaxi@163.com
30

31
32 1. Department of Integrated Traditional and Western Medicine, West China Hospital
33
34 of Sichuan University, Chengdu, China
35
36

37
38 2. Department of Gastrointestinal Surgery, West China Hospital of Sichuan
39
40 University, Chengdu, China
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Introduction: Abdominal surgery is associated with common complications, including decreased or poor appetite, abdominal distension, abdominal pain caused by decreased or absent gastrointestinal motility, anal arrest with flatus and defecation, and nausea and vomiting resulting from the use of anaesthetics and opioid analgesics. These complications seriously affect postoperative recovery, prolong hospital stay, and aggravate patient burden. This study aims to investigate for the first time the efficacy of transcutaneous electrical acupoint stimulation (TEAS) combined with electroacupuncture (EA) therapy for rapid recovery after laparotomy for gastrointestinal surgery. There have been no clinical studies of this combination therapy.

Methods and analysis: This will be a prospective, single-centre, three-arm, randomised controlled trial. A total of 480 patients undergoing abdominal surgery will be stratified according to surgery type (i.e. gastric or colorectal procedure) and randomised into three groups; namely, the EA, TEAS+EA, and control groups. The control group will receive enhanced recovery after surgery (ERAS)-standardised perioperative management, including preoperative education, optimising the anaesthesia scheme, avoiding intraoperative hypothermia, restrictive fluid infusion, and reducing surgical trauma. The EA group will receive electroacupuncture stimulation at L14, PC6, ST36, ST37, and ST39 based on the ERAS-standardised perioperative management. Moreover, the TEAS+EA group will receive ERAS-standardised perioperative management; electroacupuncture stimulation at the L14, PC6, ST36, ST37, and ST39;

1
2
3
4 and TEAS stimulation at ST21 and SP15. The primary outcome will be the time of the
5
6 first postoperative spontaneous anal exhaust. Secondary outcomes will include the time
7
8 of first postoperative voluntary defecation, time to tolerance of a solid diet, time to first
9
10 ambulation, hospital duration from operation to discharge, pain and nausea vomiting
11
12 scores on the visual analogue scale (from 0 [no at all] to 10 [the worst]), medication
13
14 use, incidence of postoperative complications, and evaluation of treatment modality
15
16 acceptability. All statistical analyses will be performed based on the intention-to-treat
17
18 principle.
19
20
21
22
23

24
25 **Ethics and dissemination** Ethics approval has been granted by the Ethics Committee
26
27 on Biomedical Research, West China Hospital of Sichuan University (approval number:
28
29 2021; number 52). The results are expected to be published in peer-reviewed journals.
30
31
32

33
34 **Trial registration number:** ChiCTR2100045646 (Chinese Clinical Trial Registry)
35
36

37 **Strengths and limitations of this study**

38
39

- 40 • A randomised controlled trial of 480 patients will be conducted to evaluate the
41 efficacy of TEAS combined with EA therapy for rapid recovery after
42 laparotomy for gastrointestinal surgery.
43
44
- 45 • The trial feasibility has been examined in a pilot randomised trial of 60 patients.
46
47
- 48 • This trial will be conducted using rigorous methods; for example, the patients
49 will be randomly assigned to three groups; the data will undergo blind statistical
50 analysis; and the interventionists, efficacy evaluators, and statisticians will be
51 separated.
52
53
54
55
56
57
58
59
60

- There is no placebo effect in the control group.

INTRODUCTION

The most common postoperative complications in laparotomy for gastrointestinal surgery include gastrointestinal dysfunction, pain, postoperative nausea and vomiting (PONV), etc. These result from numerous factors, including the intraoperative use of anaesthetic drugs, surgical trauma, peritoneal irritation or inflammatory response, and postoperative use of analgesic drugs¹⁻³. Rapid postoperative rehabilitation can prevent or reduce intraperitoneal adhesion; reduce the incidence of complications, including intestinal obstruction and intestinal infection; prevent secondary surgery, reduce opioid usage, and alleviate pain. Moreover, it can promote prompt recovery of the patients' oral diet, reduce the use of parenteral nutrition, shorten the hospitalisation duration, and reduce hospitalisation costs⁴⁻⁸.

Enhanced recovery after surgery (ERAS) is based on evidence-based medicine and is a standardised, collaborative, and multidisciplinary optimisation management protocol for the perioperative period. It allows a reduction in the physiological and psychological traumatic stress response, as well as postoperative complications; a faster postoperative recovery; a shorter postoperative hospitalisation time; and a reduction in patient costs⁹. This concept was initially proposed by the Danish Medical Scientist Kehlet in 1997¹⁰. After > 20 years of practice and optimisation, the ERAS concept and pathway have been popularised and rapidly applied worldwide¹¹. Although a series of perioperative ERAS measures can accelerate recovery, there remains room for

1
2
3
4 improvement in the prevention and treatment of postoperative gastrointestinal
5
6 dysfunction and PONV, as well as in the reduction of opioid use.
7
8

9 Acupuncture exerts therapeutic effects by regulating gastrointestinal dynamics,
10
11 analgesia, and antiemetics. It is widely considered that a degree of postoperative
12
13 gastrointestinal dysfunction is an inevitable normal physiological response after
14
15 abdominal surgery¹². Several studies have demonstrated that acupuncture can
16
17 significantly relieve postoperative abdominal pain and distension, promote intestinal
18
19 ventilation, and promptly restore the patient's diet^{13 14}. Acupuncture can enhance gastric
20
21 dilatation through the sympathetic nerve to promote gastric emptying^{15 16}; moreover,
22
23 the vasoactive intestinal peptide is involved in electroacupuncture-mediated gastric
24
25 motility regulation.
26
27
28
29
30
31

32 Additionally, acupuncture can facilitate postoperative multimodal analgesia.
33
34 Postoperative analgesia is among the core ERAS components. Its principles include
35
36 sufficient analgesia and minimisation of opioid usage. Adequate postoperative
37
38 analgesia can reduce excessive stress, help patients get out of bed quickly, and promote
39
40 recovery. Opioids, which are the main traditional postoperative analgesic drugs, can
41
42 easily cause postoperative nausea, vomiting, and other complications. Reducing opioid
43
44 usage allows early recovery of patients. There have been numerous studies on the
45
46 mechanisms underlying acupuncture analgesia from the perspectives of
47
48 electrophysiology, neurochemistry, molecular biology, and brain imaging¹⁷⁻¹⁹.
49
50
51 Moreover, numerous clinical studies have shown that acupuncture can significantly
52
53 reduce postoperative pain and opioid use after total hip replacement, craniotomy,
54
55
56
57
58
59
60

1
2
3
4 abdominal surgery, and kidney stone surgery²⁰⁻²³. Therefore, based on the ERAS
5
6 clinical pathway, acupuncture analgesia may better control wound pain and reduce the
7
8 use of analgesics, including opioids, and therefore accelerate patient recovery.
9

10
11 PONV is a common complication after surgical anaesthesia and analgesia with
12
13 opioids that can cause dehydration, electrolyte imbalance, wound cracking, and
14
15 discharge delay. PONV is another important factor that affects the recovery of patients²⁴.
16
17 Studies have shown that Neiguan (PC6) stimulation can effectively prevent PONV^{25,26}.
18
19 Transcutaneous electrical acupoint stimulation (TEAS) is more effective than
20
21 intravenous ondansetron; additionally, using TEAS combined with drugs can enhance
22
23 the anti-emetic effects of ondansetron²⁷.
24
25
26
27
28

29
30 Numerous studies have supported the application of acupuncture in postoperative
31
32 rehabilitation; however, there are differences in efficacy across different acupuncture
33
34 schemes. Currently, EA is the most common acupuncture scheme for rapid
35
36 postoperative rehabilitation, with TEAS being the second most common scheme.
37
38 Although TEAS avoids pain resulting from acupuncture needles, its efficacy is slightly
39
40 worse than that of EA and it has relatively limited clinical application. However, our
41
42 previous clinical experience and preliminary trials suggested that combining TEAS
43
44 with EA may have a better curative effect than the conventional electroacupuncture
45
46 treatment. Moreover, this combination could provide an improved acupuncture
47
48 treatment protocol for rapid rehabilitation after laparotomy for gastrointestinal surgery.
49
50
51 It may promote the recovery of gastrointestinal function more quickly, reduce pain
52
53
54
55
56
57
58
59
60

1
2
3
4 more obviously, shorten the duration of postoperative hospital stay, and reduce patient
5
6 hospitalization costs, etc.
7

8
9 Therefore, this prospective, single-centre, three-arm, single-blind, randomised
10
11 controlled trial (RCT) aims to evaluate the efficacy of TEAS combined with EA therapy
12
13 for rapid recovery after laparotomy for gastrointestinal surgery.
14
15

16 17 18 **METHODS AND ANALYSIS**

19 20 21 **Design**

22
23 This will be a single-centre, prospective RCT with a three-arm parallel grouping design.

24
25 The trial protocol version number: 2.0, date 31th March,2021.The study will be
26
27 conducted at the West China Hospital of Sichuan University (WCHSU) from April
28
29 2021 to March 2023. All the participants will be required to provide written informed
30
31 consent in accordance with the most recent version of the Declaration of Helsinki.
32
33

34
35
36 Figure 1 presents the study flowchart.
37
38
39
40
41
42
43
44

45 46 47 **Patient population and setting**

48
49 A total of 480 Chinese patients undergoing laparotomy for gastrointestinal surgery will
50
51 be sequentially enrolled at the WCHSU after fulfilling the eligibility criteria and signing
52
53 informed consent. A clinical assistant with institutional review board training will be in
54
55 charge of patient enrolment.
56

57 58 59 **Eligibility criteria**

60

1
2
3
4 *The inclusion criteria will be as follows:* (1) male and female patients aged 18–70 years;
5
6 (2) laparotomy tumour resection under general anaesthesia (stomach, colon, and
7
8 rectum); and (3) volunteering to participate in this study and signing an informed
9
10 consent form.
11
12

13
14 *The exclusion criteria will be as follows:* (1) surgical incision or scar on the
15
16 meridian of ST21/SP15, (2) local skin infection at acupoints, (3) inability to complete
17
18 the visual analogue scale (VAS), and (4) allergy to metal or severe needle fear,
19
20 intolerance of TEAS or EA treatment, (5) uncontrolled diabetes, severe cardiac, central
21
22 nervous, psychiatric disorders, or coagulopathy; (6) cardiac pacemaker; and (7)
23
24 participation in other clinical trials.
25
26
27
28

29
30 *Withdrawal criteria:* Participants meeting any of the following criteria will be
31
32 withdrawn from the study: (1) occurrence of serious adverse events; (2) participants
33
34 with serious complications or other serious diseases requiring emergency measures, (3)
35
36 being required to withdraw during the test, and (4) violation of the test program.
37
38
39
40 Withdrawn patients will not be replaced.
41
42
43
44
45

46 **Randomisation and blinding**

47
48 This study will have a single-blind design. The patient will be blinded to the group
49
50 allocation; moreover, patients in the same ward will be separated by a bed curtain when
51
52 receiving acupuncture treatment, with only the research leader and acupuncturist being
53
54 aware of the treatment allocation. The randomised grouping plan will be designed using
55
56 SPSS 22.0. According to the plan, 480 patients will be randomly divided into three
57
58
59
60

1
2
3
4 groups according to a ratio of 1:1:1: EA, TEAS+EA, and control groups. The group
5
6 scheme will be kept in a confidential envelope; further, the research leader will
7
8 randomly distribute the included patients to each group following the distribution plan
9
10 in the envelope. Additionally, the research leader will only inform the acupuncturist
11
12 responsible for the operation. Efficacy evaluation will be conducted blinded to the
13
14 grouping allocation. Blind statistical analysis will be used in the data summary stage.
15
16
17 Operators, efficacy evaluators, and statisticians will be separated.
18
19
20
21
22
23
24

25 **INTERVENTION**

26
27 All acupoints will be determined based on the National Standard of Location of
28
29 Acupoints (GB 12346-90). All practitioners performing the treatment must have an
30
31 acupuncturist qualification certificate with independent clinical experience for > 2 years.
32
33
34 The acupuncturists will not be replaced during the experiments.
35
36
37

38 All patients will receive standardised perioperative management by ERAS,
39
40 including preoperative education, optimisation of anaesthesia scheme, avoidance of
41
42 intraoperative hypothermia, restrictive fluid infusion, and reduction of surgical trauma.
43
44 Regarding the electronic acupuncture treatment instrument (Hwato, SDZ-V, Suzhou
45
46 Medical Supplies Factory Co., Ltd), the current frequency will be continuous wave 2
47
48 Hz, the current intensity will be measured in degrees as tolerated by the patient;
49
50 moreover, the treatment duration will last 30 min (figure 2). The treatment will be
51
52 initiated from the first postoperative day, once daily in the morning, until the patient
53
54 recovered spontaneous flatus from the anus and could tolerate transoral solid food.
55
56
57
58
59
60

1
2
3
4
5
6
7 In the EA group (electroacupuncture is added at the base of basic treatment),
8
9 treatment will be bilaterally performed at five acupoint pairs: Hegu (LI4), Neiguan
10
11 (PC6), Zusanli (ST36), Shangjuxu (ST37), and Xiajuxu (ST39). LI4 is an acupoint of
12
13 the large intestine meridian and is located on the dorsum of the hand between the first
14
15 and second metacarpal bones. PC6 belongs to the pericardium meridian and is located
16
17 between the flexor carpi radialis muscle tendon and the palmaris longus tendon, 2 Cun
18
19 above the wrist crease. ST36, ST37, and ST39 are acupoints of the stomach meridian.
20
21 ST36 is located on the lateral side of the lower leg, 3 Cun below the lateral border of
22
23 the knee and one finger width lateral to the anterior border of the tibia. ST37 is located
24
25 3 Cun below ST36. ST39 is located 3 Cun below ST37. After skin disinfection with a
26
27 disposable disinfecting cotton swab, sterile and disposable stainless steel needles
28
29 (0.25×40 mm, Suzhou Jiajian, Jiangsu, China) will be quickly and perpendicularly
30
31 inserted into the skin acupoints at a depth of 25–30 mm. The duration of reinforcing-
32
33 reducing manipulation of twirling and rotating needles should be used for 1 min to
34
35 achieve de qi (a composite of sensations including soreness, numbness, distention,
36
37 heaviness, and other sensations), which significantly contributes to acupuncture
38
39 efficacy. The ipsilateral Neiguan, Hegu, Zusanli, and Xiajuxu will be separately
40
41 connected to one electrode set, and therefore yielding four electrode sets (figure 3 a, b).
42
43
44
45
46
47
48
49
50
51

52
53 For the TEAS+EA group, treatment will be based on the EA group with the
54
55 addition of two pairs of bilateral abdominal acupoints: Liangmen (ST21) and Daheng
56
57 (SP15). Additionally, ST21 is an acupoint of the stomach meridian that is located 4 Cun
58
59
60

1
2
3
4 above the umbilicus and 2 Cun open next to the anterior median line. SP15 is an
5
6 acupoint of the spleen meridian, located 4 Cun beside the umbilicus and lateral to the
7
8 rectus abdominis muscle. Abdominal acupoints will be stimulated using a self-adhesive
9
10 electrode pad with electrical conductivity; additionally, the ipsilateral Liangmen will
11
12 be connected to the Daheng set of electrodes. The ipsilateral Neiguan, Hegu, Zusanli,
13
14 and Xiajuxu acupoints will be connected to one electrode set to yield a total of six sets
15
16 of electrodes (figure 3 a, b, c).
17
18
19
20
21

22 The control group will receive ERAS-standardised perioperative management
23
24 without acupuncture treatment.
25
26
27
28
29

30 **OUTCOME MEASURES**

31 **Main outcome**

32
33
34
35 The primary outcome will be the time of the first postoperative spontaneous anal
36
37 exhaust. The observer will be assessments and visits for participants after each treatment.
38
39

40 **Secondary outcome**

41
42
43 The secondary outcomes include the time of first postoperative voluntary defecation,
44
45 time to tolerance of a solid diet, time to first ambulation, hospital duration from
46
47 operation to discharge, pain and nausea vomiting scores on the VAS (from 0 [no at all]
48
49 to 10 [the worst]), medication use, incidence of postoperative complications, and
50
51 evaluation of treatment modality acceptability. The observer will be assessments and
52
53 visits for participants after each treatment.
54
55
56
57

58 **Safety evaluation**

1
2
3
4 All adverse events will be recorded on the adverse event record sheet by the
5
6 acupuncturist and participants at any time during the study period. Adverse events to
7
8 be recorded include fainting during acupuncture treatment, needle breaking, unbearable
9
10 acupuncture pain, local hematoma, infection, and any other discomfort or accident. The
11
12 intensity and causality of each adverse event will be evaluated and recorded. If any
13
14 serious adverse events occur due to an intervention, the intervention will be
15
16 immediately stopped; further, appropriate corrective action will be taken. Serious
17
18 adverse events will be promptly reported to the institutional review board within 24 h
19
20 until 30 days after the end of the trial.
21
22
23
24
25

26 27 **Sample size calculation** 28

29
30 The stratification factors will be gastrectomy and colorectal resection, with each layer
31
32 being divided into three groups: the group ratio will be 1:1:1. The main efficacy
33
34 indicator will be the time from the laparotomy surgery to the first flatus. Given the lack
35
36 of reports on TEAS+EA for promoting postoperative recovery, we conducted a
37
38 preliminary experiment. The preliminary experimental results indicated that the time
39
40 spent from laparotomy gastrectomy surgery to the first flatus in the control, EA, and
41
42 TEAS+EA groups was 62.5 ± 26.7 h, 48 ± 24.5 h, and 45.7 ± 28.2 h, respectively,
43
44
45 Additionally, in the control group, the time from the laparotomy colorectal surgery to
46
47 the first flatus was the control, EA, and TEAS+EA groups was 63.6 ± 24.6 h, $50.5 \pm$
48
49 23.6 h, and 47.5 ± 25.2 h, respectively. The sample size was determined using PASS 11
50
51 with $\alpha = 0.05$ (two-sided) and $\beta = 0.1$ (90% power). The required sample size will be
52
53
54
55
56
57
58
59
60 72 patients per group. Assuming that 10% of patients will be lost to follow-up, we chose

1
2
3
4 a sample size of 80 participants for each group, with a total sample size of 480
5
6 participants.
7

8 9 **Statistical analyses**

10
11 Statistical analysis will be conducted by independent third-party professional
12
13 statisticians. All data will be collected by statisticians. Data analysis will be performed
14
15 using the intention processing principle in SPSS 22.0. Statistical results will be reported
16
17 using a two-sided test, with statistical significance being set at P-value < 0.05. The
18
19 results will be expressed as mean \pm standard deviation. The t-test will be used for
20
21 normally distributed homogenous variables, with the hypothesis test of superiority
22
23 being used for major outcome indicators, the chi-square test for normally distributed
24
25 data, and the rank-sum test or Fisher's exact probability method for non-normally
26
27 distributed data.
28
29
30
31
32
33

34 35 **Patient and public involvement**

36
37 The patients and the public were not involved in the planning and design of this study.
38
39 The present trial was developed by acupuncturists based on previous clinical experience
40
41 and literature. The expected outcomes are commonly used to assess rapid postoperative
42
43 recovery in clinical practice. The cost of interventions and outcome measurements will
44
45 be maintained using the study funding; therefore, it was not considered a significant
46
47 burden and met the patient preferences. The results will be disseminated to the
48
49 participants via the WCHSU website.
50
51
52
53
54
55
56
57
58
59
60

DISCUSSION

Several studies have demonstrated the efficacy of acupuncture in rapid postoperative rehabilitation²⁸. Previous clinical experience and studies have shown that acupuncture on the distal limb acupoints is mostly selected for rehabilitation after abdominal surgery, which may be associated with several factors, including the presence of surgical wounds after abdominal surgery, postoperative changes in the structure and state of abdominal organs affecting acupuncture needle manipulation, and safety. However, recent studies have shown that abdominal and limb acupoints facilitate improvement of abdominal pain and the distension degree; moreover, abdominal acupoints have a more optimal effect on improving the degree of abdominal pain²⁹. In this study, based on extensive clinical practice, TEAS will be applied to abdominal acupoints, which is safer than electroacupuncture based on acupuncture on the meridians of the distal extremities; moreover, the bilateral beam gate and large transverse acupoints chosen for abdominal surgery are unconventional incision positions that facilitate manipulation. Additionally, they are both antiemetic, promote gastrointestinal motility, and relieve abdominal pain. Therefore, this randomised controlled study will evaluate whether TEAS combined with EA therapy is effective at allowing rapid recovery after laparotomy for gastrointestinal surgery is more effective and beneficial, and therefore further improving patient satisfaction.

ETHICS AND DISSEMINATION

Personal information and study data of all participants will be recorded in case report forms. Moreover, data involving patient privacy will be anonymized, protected by code, and securely kept in a locked cabinet in the WCHSU accessed only by the research team. Upon completion of the trial and data verification, the case report forms will be transferred to the Science and Technology Department of Sichuan Province for safe archival purposes for 10 years before being destroyed. Data for use or analysis following study completion will be available from the corresponding author upon reasonable request. The study results will be presented at national and international scientific conferences and submitted for publication in a peer-reviewed journal.

This study has been approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University in April 2021. The approval number is 2021 (52).

The trial protocol strictly adheres to the principles of the latest Declaration of Helsinki.

Patient consent for publication is not required.

Authors' contributions: HL and QW contributed equally to this article, participated in the study design, drafted the manuscript, and recruited patients. L-y L and Y-m Z are responsible for the treatment of patients. H-q H and YH are responsible for collecting the data. NL and X-d W are responsible for monitoring this study. All authors contributed to manuscript revision and have read and approved the submitted version.

1
2
3
4 **Funding:** This study will be supported by the Sichuan Science and Technology
5
6 Program (grant number: 2021YFS0254).
7
8
9

10
11 **Disclaimer:** The funding bodies are not involved in study design, data collection,
12
13 analysis, interpretation of results, and the manuscript.
14
15
16
17

18
19 **Competing interests:** The authors declare that they have no competing interests.
20
21
22

23
24 **Provenance and peer review:** Not commissioned; externally peer-reviewed.
25
26
27
28
29
30

31 REFERENCES

- 32 1. Leslie JB, Viscusi ER, Pergolizzi JV, Jr., et al. Anesthetic Routines: The Anesthesiologist's Role in GI
33 Recovery and Postoperative Ileus. *Adv Prev Med* 2011;2011:976904. doi:
34 10.4061/2011/976904 [published Online First: 2011/10/13]
35
- 36 2. Gan TJ, Belani KG, Bergese S, et al. Fourth Consensus Guidelines for the Management of
37 Postoperative Nausea and Vomiting. *Anesth Analg* 2020;131(2):411-48. doi:
38 10.1213/ANE.0000000000004833 [published Online First: 2020/05/30]
39
- 40 3. Bragg D, El-Sharkawy AM, Psaltis E, et al. Postoperative ileus: Recent developments in
41 pathophysiology and management. *Clinical nutrition (Edinburgh, Scotland)* 2015;34(3):367-76.
42 doi: 10.1016/j.clnu.2015.01.016 [published Online First: 2015/03/31]
43
- 44 4. Ni CY, Wang ZH, Huang ZP, et al. Early enforced mobilization after liver resection: A prospective
45 randomized controlled trial. *International journal of surgery (London, England)* 2018;54(Pt
46 A):254-58. doi: 10.1016/j.ijssu.2018.04.060 [published Online First: 2018/05/13]
47
- 48 5. Ren QP, Luo YL, Xiao FM, et al. Effect of enhanced recovery after surgery program on patient-reported
49 outcomes and function recovery in patients undergoing liver resection for hepatocellular
50 carcinoma. *Medicine* 2020;99(20):e20062. doi: 10.1097/md.00000000000020062 [published
51 Online First: 2020/05/24]
52
- 53 6. Harryman C, Plymale MA, Stearns E, et al. Enhanced value with implementation of an ERAS protocol
54 for ventral hernia repair. *Surgical endoscopy* 2020;34(9):3949-55. doi: 10.1007/s00464-019-
55 07166-2 [published Online First: 2019/10/03]
56
57
58
59
60

- 1
2
3 7. Medbery RL, Fernandez FG, Khullar OV. ERAS and patient reported outcomes in thoracic surgery: a
4 review of current data. *Journal of thoracic disease* 2019;11(Suppl 7):S976-s86. doi:
5 10.21037/jtd.2019.04.08 [published Online First: 2019/06/12]
6
- 7 8. Noba L, Rodgers S, Chandler C, et al. Enhanced Recovery After Surgery (ERAS) Reduces Hospital Costs
8 and Improve Clinical Outcomes in Liver Surgery: a Systematic Review and Meta-Analysis.
9 *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary*
10 *Tract* 2020;24(4):918-32. doi: 10.1007/s11605-019-04499-0 [published Online First:
11 2020/01/05]
12
- 13 9. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA surgery*
14 2017;152(3):292-98. doi: 10.1001/jamasurg.2016.4952 [published Online First: 2017/01/18]
15
- 16 10. Wilmore DW, Kehlet H. Management of patients in fast track surgery. *BMJ (Clinical research ed)*
17 2001;322(7284):473-6. doi: 10.1136/bmj.322.7284.473 [published Online First: 2001/02/27]
18
- 19 11. McLeod RS, Aarts MA, Chung F, et al. Development of an Enhanced Recovery After Surgery Guideline
20 and Implementation Strategy Based on the Knowledge-to-action Cycle. *Annals of surgery*
21 2015;262(6):1016-25. doi: 10.1097/sla.0000000000001067 [published Online First:
22 2015/02/19]
23
- 24 12. Miedema BW, Johnson JO. Methods for decreasing postoperative gut dysmotility. *Lancet Oncol*
25 2003;4(6):365-72. doi: 10.1016/s1470-2045(03)01118-5 [published Online First: 2003/06/06]
26
- 27 13. Li H, He T, Xu Q, et al. Acupuncture and regulation of gastrointestinal function. *World journal of*
28 *gastroenterology* 2015;21(27):8304-13. doi: 10.3748/wjg.v21.i27.8304 [published Online First:
29 2015/07/29]
30
- 31 14. Ng SS, Leung WW, Mak TW, et al. Electroacupuncture reduces duration of postoperative ileus after
32 laparoscopic surgery for colorectal cancer. *Gastroenterology* 2013;144(2):307-13.e1. doi:
33 10.1053/j.gastro.2012.10.050 [published Online First: 2012/11/13]
34
- 35 15. Takahashi T. Mechanism of acupuncture on neuromodulation in the gut--a review.
36 *Neuromodulation : journal of the International Neuromodulation Society* 2011;14(1):8-12;
37 discussion 12. doi: 10.1111/j.1525-1403.2010.00295.x [published Online First: 2011/10/14]
38
- 39 16. Tada H, Fujita M, Harris M, et al. Neural mechanism of acupuncture-induced gastric relaxations in
40 rats. *Digestive diseases and sciences* 2003;48(1):59-68. doi: 10.1023/a:1021730314068
41 [published Online First: 2003/03/21]
42
- 43 17. Zhao ZQ. Neural mechanism underlying acupuncture analgesia. *Progress in neurobiology*
44 2008;85(4):355-75. doi: 10.1016/j.pneurobio.2008.05.004 [published Online First: 2008/06/28]
45
- 46 18. Hauck M, Schröder S, Meyer-Hamme G, et al. Acupuncture analgesia involves modulation of pain-
47 induced gamma oscillations and cortical network connectivity. *Scientific reports*
48 2017;7(1):16307. doi: 10.1038/s41598-017-13633-4 [published Online First: 2017/11/28]
49
- 50 19. Cui X, Liu K, Xu D, et al. Mast cell deficiency attenuates acupuncture analgesia for mechanical pain
51 using c-kit gene mutant rats. *Journal of pain research* 2018;11:483-95. doi:
52 10.2147/jpr.S152015 [published Online First: 2018/03/20]
53
- 54 20. Wu MS, Chen KH, Chen IF, et al. The Efficacy of Acupuncture in Post-Operative Pain Management:
55 A Systematic Review and Meta-Analysis. *PloS one* 2016;11(3):e0150367. doi:
56 10.1371/journal.pone.0150367 [published Online First: 2016/03/10]
57
- 58 21. Capodice JL, Parkhomenko E, Tran TY, et al. A Randomized, Double-Blind, Sham-Controlled Study
59 Assessing Electroacupuncture for the Management of Postoperative Pain after Percutaneous
60

- 1
2
3 Nephrolithotomy. *Journal of endourology* 2019;33(3):194-200. doi: 10.1089/end.2018.0665
4 [published Online First: 2019/01/30]
5
6 22. Chen CC, Yang CC, Hu CC, et al. Acupuncture for pain relief after total knee arthroplasty: a
7 randomized controlled trial. *Regional anesthesia and pain medicine* 2015;40(1):31-6. doi:
8 10.1097/aap.000000000000138 [published Online First: 2014/08/28]
9
10 23. Asmussen S, Maybauer DM, Chen JD, et al. Effects of Acupuncture in Anesthesia for Craniotomy: A
11 Meta-Analysis. *Journal of neurosurgical anesthesiology* 2017;29(3):219-27. doi:
12 10.1097/ana.000000000000290 [published Online First: 2016/03/12]
13
14 24. Kovac AL. Update on the management of postoperative nausea and vomiting. *Drugs*
15 2013;73(14):1525-47. doi: 10.1007/s40265-013-0110-7 [published Online First: 2013/09/24]
16
17 25. Lee A, Chan SK, Fan LT. Stimulation of the wrist acupuncture point PC6 for preventing postoperative
18 nausea and vomiting. *The Cochrane database of systematic reviews* 2015;2015(11):Cd003281.
19 doi: 10.1002/14651858.CD003281.pub4 [published Online First: 2015/11/03]
20
21 26. Kim YH, Kim KS, Lee HJ, et al. The efficacy of several neuromuscular monitoring modes at the P6
22 acupuncture point in preventing postoperative nausea and vomiting. *Anesth Analg*
23 2011;112(4):819-23. doi: 10.1213/ANE.0b013e31820f819e [published Online First:
24 2011/03/10]
25
26 27. Gan TJ, Jiao KR, Zenn M, et al. A randomized controlled comparison of electro-acupoint stimulation
27 or ondansetron versus placebo for the prevention of postoperative nausea and vomiting.
28 *Anesth Analg* 2004;99(4):1070-5, table of contents. doi:
29 10.1213/01.Ane.0000130355.91214.9e [published Online First: 2004/09/24]
30
31 28. Xin C, Sun JH. [The value of acupuncture-moxibustion in enhance recovery after surgery]. *Zhongguo*
32 *Zhen Jiu* 2020;40(6):679-82. doi: 10.13703/j.0255-2930.20190501-0005 [published Online
33 First: 2020/06/17]
34
35 29. Li HJ, Zhao Y, Wen Q, et al. [Comparison of Clinical Effects of Electroacupuncture of Abdominal and
36 Limb Acupoints in the Treatment of Acute Pancreatitis]. *Zhen Ci Yan Jiu* 2018;43(11):725-9.
37 doi: 10.13702/j.1000-0607.170351 [published Online First: 2018/12/27]
38
39
40
41

42 **Figure Legends**

43
44 Figure 1: Flowchart of the study protocol.

45
46 Figure 2: Instrument and parameter.

47
48 Figure 3a: Location and electrode connection of upper limb acupoints.

49
50 Figure 3b: Location and electrode connection of lower limb acupoints.

51
52 Figure 3c: Location and electrode connection of abdominal acupoints.
53
54
55
56
57
58
59
60

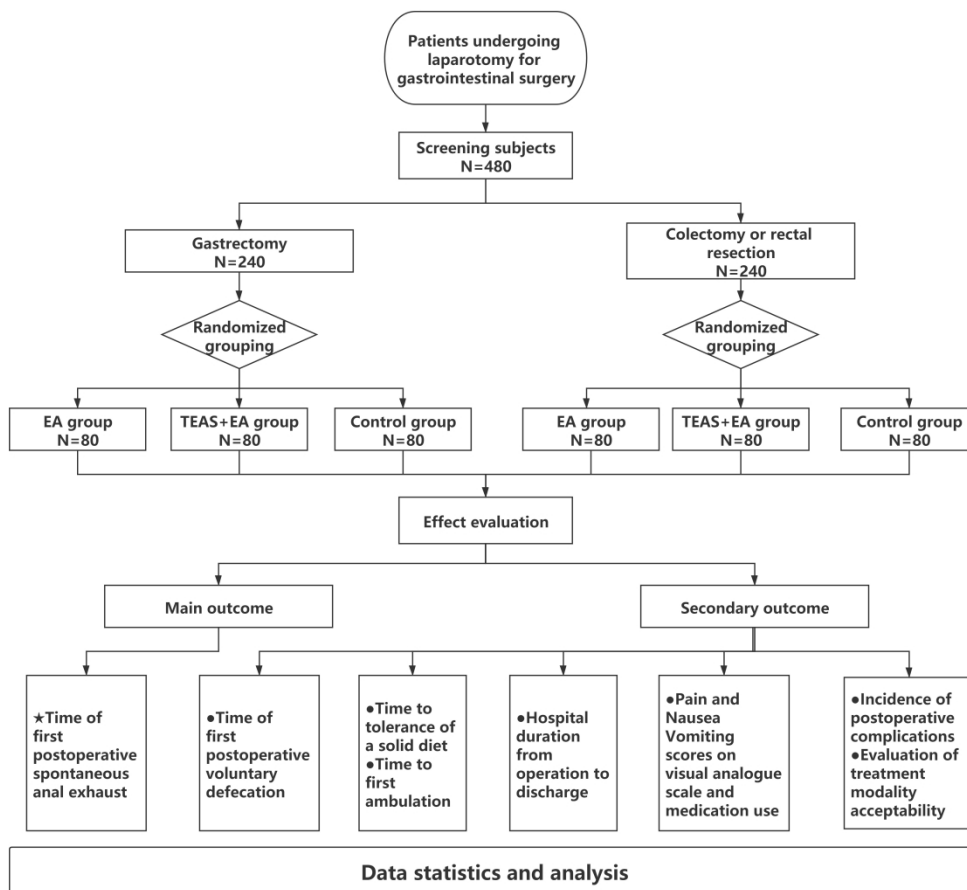


Figure 1: Flowchart of the study protocol.

1709x1560mm (72 x 72 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

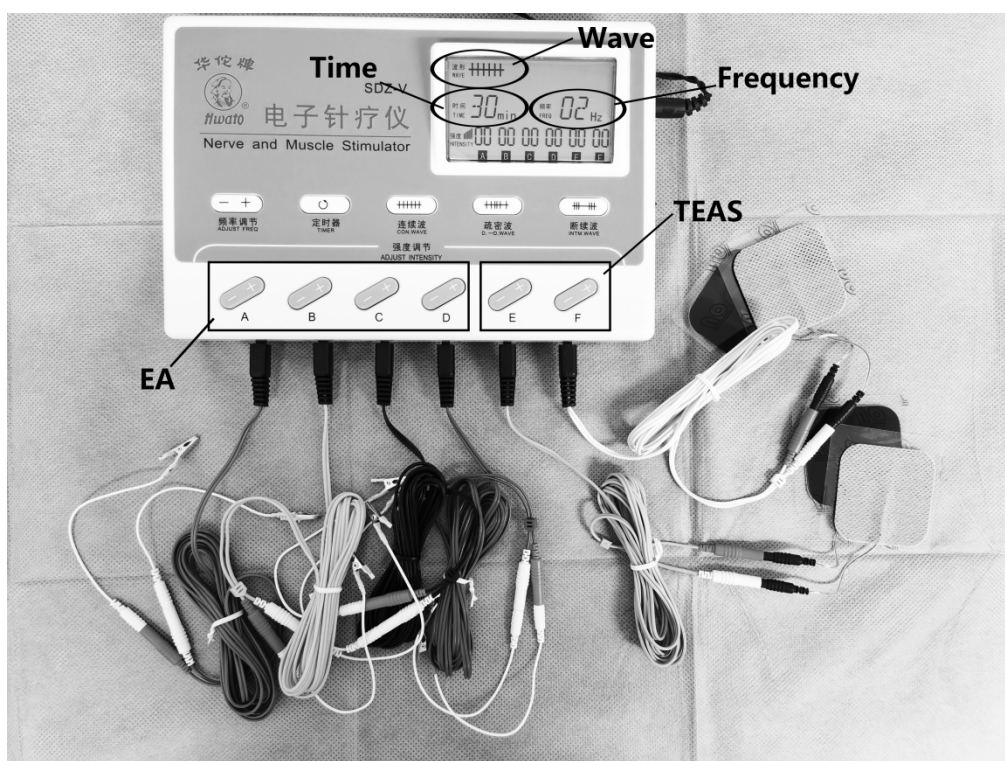


Figure 2: Instrument and parameter.

1286x965mm (72 x 72 DPI)

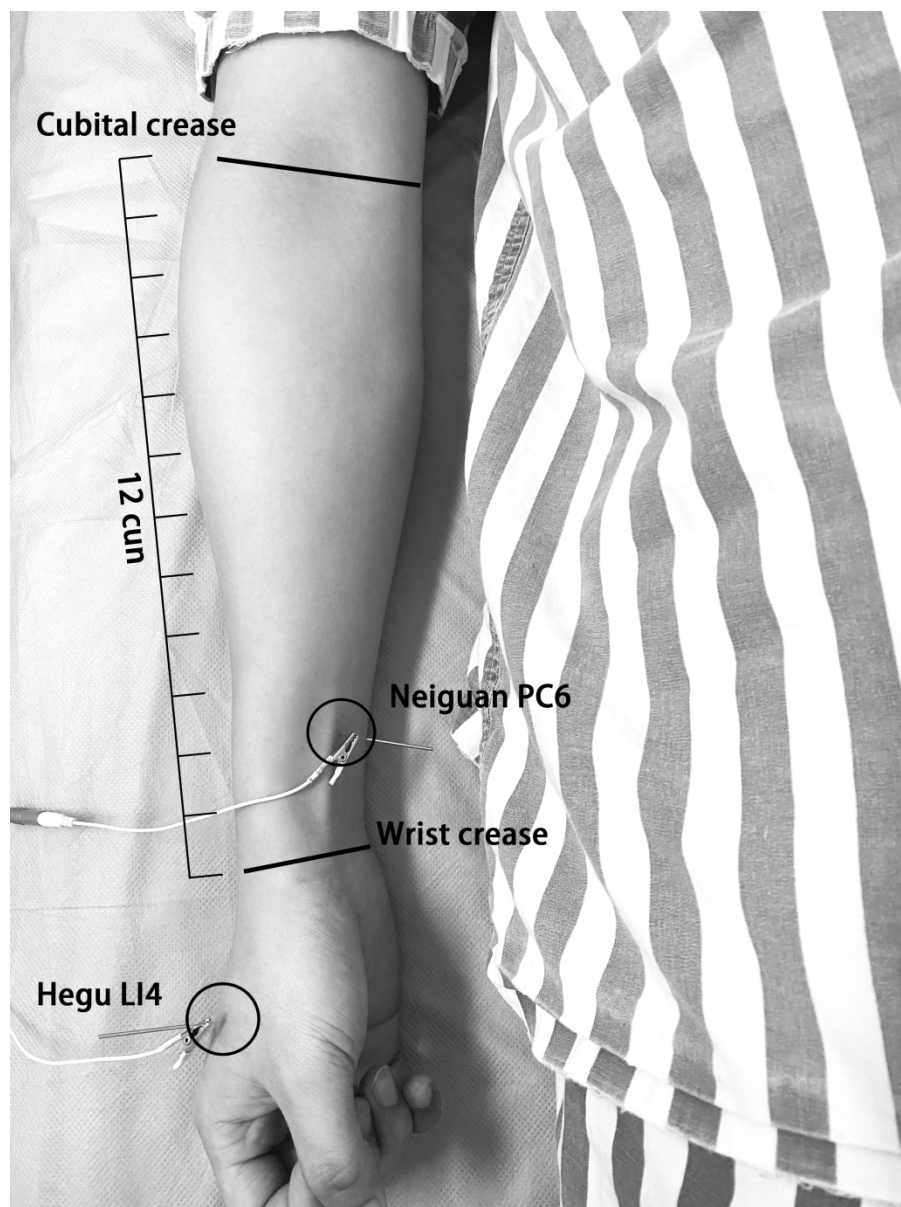


Figure 3a: Location and electrode connection of upper limb acupoints.

1066x1422mm (72 x 72 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

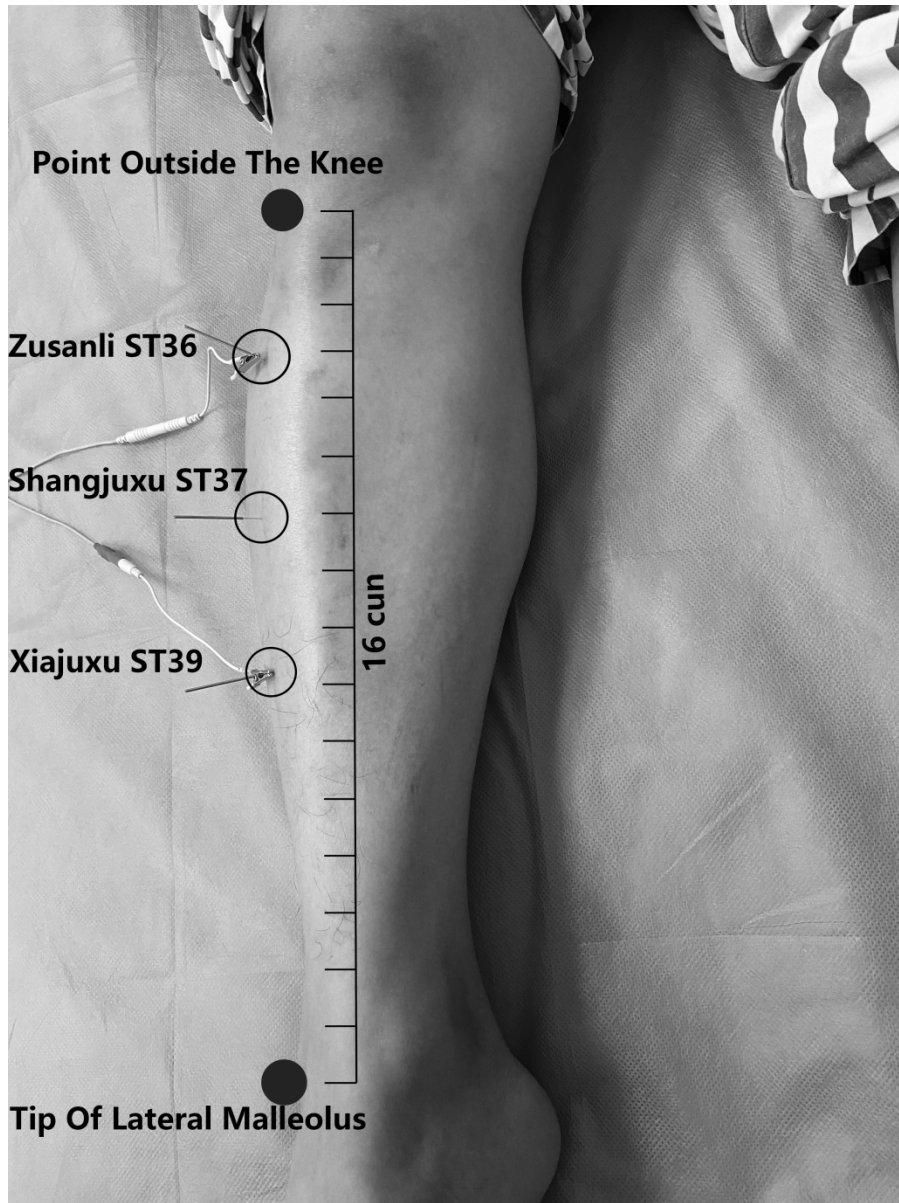
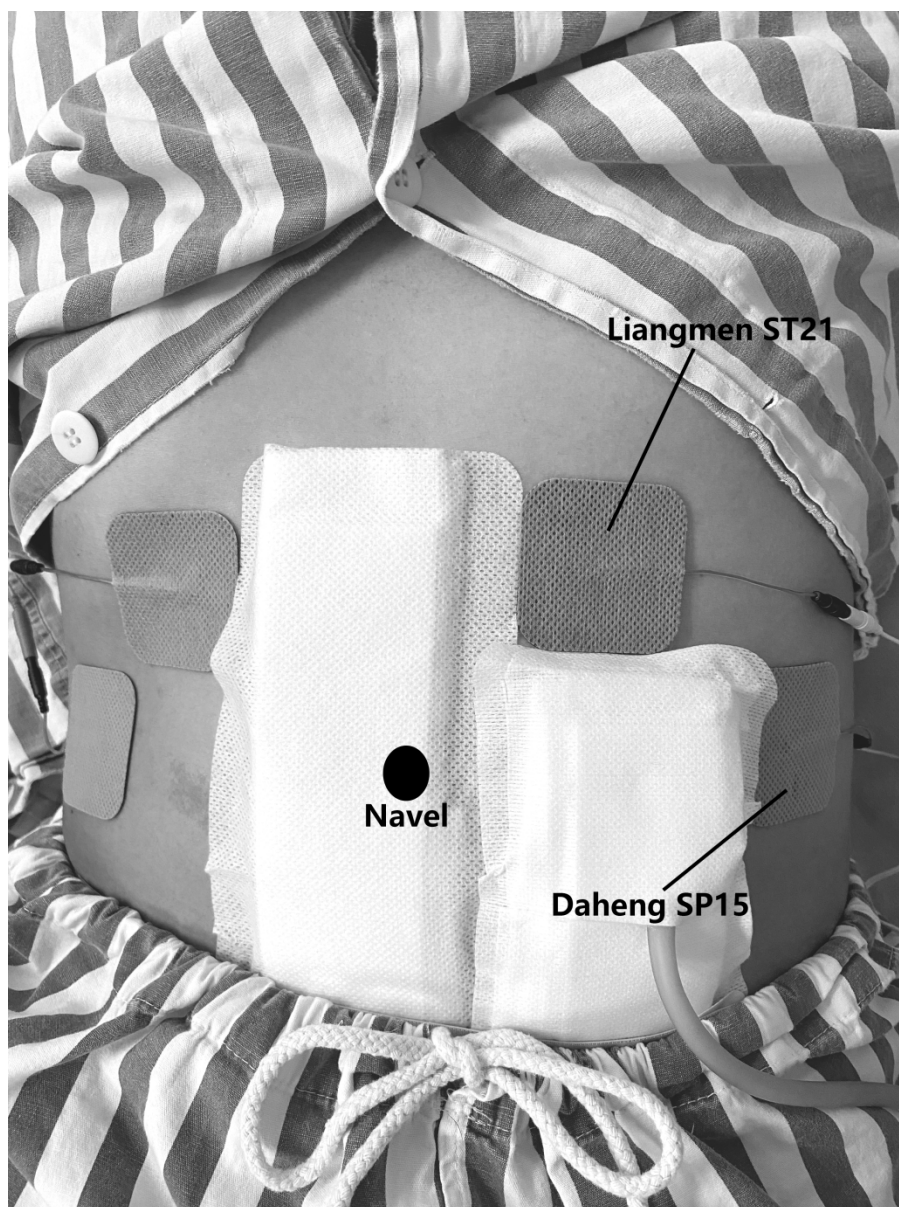


Figure 3b: Location and electrode connection of lower limb acupoints.

1066x1422mm (72 x 72 DPI)



45 Figure 3c: Location and electrode connection of abdominal acupoints.

46 1066x1422mm (72 x 72 DPI)



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page Number on which item is reported
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	3	Date and version identifier	7
Funding	4	Sources and types of financial, material, and other support	16
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	15

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-7
	6b	Explanation for choice of comparators	5
Objectives	7	Specific objectives or hypotheses	2
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	9-11
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9-11

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	9-11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9-11
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	9-11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8-9

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8-9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8-9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8-9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15

1	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13
2		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	13
3		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	13
4	Methods: Monitoring			
5	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
6		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
7	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11-12
8	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
9	Ethics and dissemination			
10	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15

Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	N/A
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7-8
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	16
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	13
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
	31b	Authorship eligibility guidelines and any intended use of professional writers	15
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	15

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

BMJ Open

Transcutaneous electrical acupoint stimulation combined with electroacupuncture for rapid recovery of patients after laparotomy for gastrointestinal surgery: A study protocol for a randomized controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-053309.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Sep-2021
Complete List of Authors:	Li, Hao; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Wen, Qian; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Lu, Lingyun; Sichuan University West China Hospital, Department of Integrated Traditional Chinese and Western Medicine Hu, Hangqi; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department He, Ying; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department Zhou, Yaming; Sichuan University West China Hospital, Gastrointestinal Surgery Wu, Xiaoting; Sichuan University West China Hospital, Gastrointestinal Surgery Li, Ning; Sichuan University West China Hospital, Integrated Traditional and Western Medicine Department
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Gastroenterology and hepatology
Keywords:	COMPLEMENTARY MEDICINE, PAIN MANAGEMENT, GASTROENTEROLOGY

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **Transcutaneous electrical acupoint stimulation combined with electroacupuncture for rapid**
5
6 **recovery of patients after laparotomy for gastrointestinal surgery: A study protocol for a**
7
8 **randomized controlled trial**
9
10

11
12
13
14 Hao Li^{1#}, Qian Wen^{1#}, Lingyun Lu¹, Hangqi Hu¹, Ying He¹, Yaming Zhou², Xiaoting Wu^{2*}, Ning
15
16
17 Li^{1*}
18
19
20
21

22 # Hao Li and Qian Wen contributed equally to this work.
23
24

25 *** Correspondence authors:**
26

27 Dr. Xiaoting Wu, wxt1@medmail.com.cn
28
29

30 Dr. Ning Li, zhenjiuhuaxi@163.com
31

32 1. Department of Integrated Traditional and Western Medicine, West China Hospital of Sichuan
33
34 University, Chengdu, China
35
36

37 2. Department of Gastrointestinal Surgery, West China Hospital of Sichuan University, Chengdu,
38
39
40 China
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Introduction: Abdominal surgery is associated with common complications, including decreased or poor appetite, abdominal distension, abdominal pain caused by decreased or absent gastrointestinal motility, anal arrest with flatus and defecation, and nausea and vomiting resulting from the use of anaesthetics and opioid analgesics. These complications seriously affect postoperative recovery, prolong hospital stay, and aggravate patient burden. This study aims to investigate for the first time the efficacy of transcutaneous electrical acupoint stimulation (TEAS) combined with electroacupuncture (EA) therapy for rapid recovery after laparotomy for gastrointestinal surgery. There have been no clinical studies of this combination therapy.

Methods and analysis: This will be a prospective, single-centre, three-arm, randomised controlled trial. A total of 480 patients undergoing abdominal surgery will be stratified according to surgery type (i.e. gastric or colorectal procedure) and randomised into three groups; namely, the EA, TEAS+EA, and control groups. The control group will receive enhanced recovery after surgery (ERAS)-standardised perioperative management, including preoperative education, optimising the anaesthesia scheme, avoiding intraoperative hypothermia, restrictive fluid infusion, and reducing surgical trauma. The EA group will receive electroacupuncture stimulation at LI4, PC6, ST36, ST37, and ST39 based on the ERAS-standardised perioperative management. Moreover, the TEAS+EA group will receive ERAS-standardised perioperative management; electroacupuncture stimulation at the LI4, PC6, ST36, ST37, and ST39;

1
2
3
4 and TEAS stimulation at ST21 and SP15. The primary outcome will be the GI-2
5
6 (composite outcome of time to first defaecation and time to tolerance of a solid diet).
7

8
9 Secondary outcomes will include the time of first passage of flatus, time to first
10
11 defaecation , time to tolerance of a solid diet, time to first ambulation, hospital duration
12
13 from operation to discharge, pain and nausea vomiting scores on the VAS, medication
14
15 use, incidence of postoperative complications, and evaluation of treatment modality
16
17 acceptability. All statistical analyses will be performed based on the intention-to-treat
18
19 principle.
20
21
22
23

24
25 **Ethics and dissemination** Ethics approval has been granted by the Ethics Committee
26
27 on Biomedical Research, West China Hospital of Sichuan University (approval number:
28
29 2021; number 52). The results are expected to be published in peer-reviewed journals.
30
31

32
33
34 **Trial registration number:** ChiCTR2100045646 (Chinese Clinical Trial Registry)
35
36

37 **Strengths and limitations of this study**

38
39

- 40 • A randomised controlled trial of 480 patients will be conducted to evaluate the
41 efficacy of TEAS combined with EA therapy for rapid recovery after
42 laparotomy for gastrointestinal surgery.
43
44
- 45 • The trial feasibility has been examined in a pilot randomised trial of 120 patients,
46 included 60 patients with laparotomy stomach tumor resection and 60 patients
47 with laparotomy colon tumor resection.
48
49
- 50 • This trial will be conducted using rigorous methods; for example, the patients
51 will be randomly assigned to three groups; the data will undergo blind statistical
52
53
54
55
56
57
58
59
60

1
2
3
4 analysis; and the interventionists, efficacy evaluators, and statisticians will be
5
6 separated.

- 7
8
9
- 10 • This trial did not include a sham control arm, the analysis of the placebo
11 response or effect was lacking.
12
13
14

15 16 **INTRODUCTION**

17
18 The most common postoperative complications in laparotomy for gastrointestinal surgery include
19 gastrointestinal dysfunction, pain, postoperative nausea and vomiting (PONV), etc. These result
20 from numerous factors, including the intraoperative use of anaesthetic drugs, surgical trauma,
21 peritoneal irritation or inflammatory response, and postoperative use of analgesic drugs¹⁻³. Rapid
22 postoperative rehabilitation can prevent or reduce intraperitoneal adhesion; reduce the incidence of
23 complications, including intestinal obstruction and intestinal infection; prevent secondary surgery,
24 reduce opioid usage, and alleviate pain. Moreover, it can promote prompt recovery of the patients'
25 oral diet, reduce the use of parenteral nutrition, shorten the hospitalisation duration, and reduce
26 hospitalisation costs⁴⁻⁸.
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41
42 Enhanced recovery after surgery (ERAS) is based on evidence-based medicine and is a
43 standardised, collaborative, and multidisciplinary optimisation management protocol for the
44 perioperative period. It allows a reduction in the physiological and psychological traumatic stress
45 response, as well as postoperative complications; a faster postoperative recovery; a shorter
46 postoperative hospitalisation time; and a reduction in patient costs⁹. This concept was initially
47 proposed by the Danish Medical Scientist Kehlet in 1997¹⁰. After > 20 years of practice and
48 optimisation, the ERAS concept and pathway have been popularised and rapidly applied
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 worldwide¹¹. Although a series of perioperative ERAS measures can accelerate recovery, there
5
6 remains room for improvement in the prevention and treatment of postoperative gastrointestinal
7
8 dysfunction and PONV, as well as in the reduction of opioid use¹².

9
10
11 Acupuncture exerts therapeutic effects by regulating gastrointestinal dynamics, analgesia, and
12
13 antiemetics. It is widely considered that a degree of postoperative gastrointestinal dysfunction is an
14
15 inevitable normal physiological response after abdominal surgery¹³. Several studies have
16
17 demonstrated that acupuncture can significantly relieve postoperative abdominal pain and
18
19 distension, promote intestinal ventilation, and promptly restore the patient's diet^{14 15}. Acupuncture
20
21 can enhance gastric dilatation through the sympathetic nerve to promote gastric emptying^{16 17};
22
23 moreover, the vasoactive intestinal peptide is involved in electroacupuncture-mediated gastric
24
25 motility regulation.
26
27
28
29
30

31
32 Studies have shown that Zusanli (ST36), Shangjuxu (ST37), and Xiajuxu (ST39) stimulation
33
34 can effectively improve gastrointestinal transit by reducing local inflammation of the intestinal
35
36 musculature¹⁸. Hegu(LI4) is a pair of acupoints belonging to the Large Intestinal meridian,
37
38 Daheng(SP15) is a pair of acupoints belonging to the Spleen meridian, Liangmen(ST21) is a pair of
39
40 acupoints belonging to the Stomach meridian. They have the effect of assisting gastrointestinal
41
42 function recovery, so they are also commonly used in clinical practice¹⁹⁻²¹.
43
44
45
46
47

48 Additionally, acupuncture can facilitate postoperative multimodal analgesia. Postoperative
49
50 analgesia is among the core ERAS components. Its principles include sufficient analgesia and
51
52 minimisation of opioid usage. Adequate postoperative analgesia can reduce excessive stress, help
53
54 patients get out of bed quickly, and promote recovery. Opioids, which are the main traditional
55
56 postoperative analgesic drugs, can easily cause postoperative nausea, vomiting, and other
57
58
59
60

1
2
3
4 complications. Reducing opioid usage allows early recovery of patients. There have been numerous
5
6 studies on the mechanisms underlying acupuncture analgesia from the perspectives of
7
8 electrophysiology, neurochemistry, molecular biology, and brain imaging²²⁻²⁴. Moreover, numerous
9
10 clinical studies have shown that acupuncture can significantly reduce postoperative pain and opioid
11
12 use after total hip replacement, craniotomy, abdominal surgery, and kidney stone surgery²⁵⁻²⁸.
13
14 Therefore, based on the ERAS clinical pathway, acupuncture analgesia may better control wound
15
16 pain and reduce the use of analgesics, including opioids, and therefore accelerate patient recovery²⁹.
17
18
19
20
21

22 PONV is a common complication after surgical anaesthesia and analgesia with opioids that
23
24 can cause dehydration, electrolyte imbalance, wound cracking, and discharge delay. PONV is
25
26 another important factor that affects the recovery of patients³⁰. Studies have shown that Neiguan
27
28 (PC6) stimulation can effectively prevent PONV^{31,32}. Transcutaneous electrical acupoint
29
30 stimulation (TEAS) is more effective than intravenous ondansetron; additionally, using TEAS
31
32 combined with drugs can enhance the anti-emetic effects of ondansetron³³.
33
34
35
36
37

38 Numerous studies have supported the application of acupuncture in postoperative rehabilitation;
39
40 however, there are differences in efficacy across different acupuncture schemes. Currently, EA is
41
42 the most common acupuncture scheme for rapid postoperative rehabilitation, with TEAS being the
43
44 second most common scheme. Although TEAS avoids pain resulting from acupuncture needles, its
45
46 efficacy is slightly worse than that of EA and it has relatively limited clinical application³⁴. However,
47
48 our previous clinical experience and preliminary trials suggested that combining TEAS with EA
49
50 may have a better curative effect than the conventional electroacupuncture treatment³⁵⁻³⁷. Moreover,
51
52 this combination could provide an improved acupuncture treatment protocol for rapid rehabilitation
53
54 after laparotomy for gastrointestinal surgery. It may promote the recovery of gastrointestinal
55
56
57
58
59
60

1
2
3
4 function more quickly, reduce pain more obviously, shorten the duration of postoperative hospital
5
6 stay, and reduce patient hospitalization costs, etc.
7

8
9 Therefore, this prospective, single-centre, three-arm, single-blind, randomised controlled trial
10
11 (RCT) aims to evaluate the efficacy of TEAS combined with EA therapy for rapid recovery after
12
13 laparotomy for gastrointestinal surgery.
14
15

16 17 18 **METHODS AND ANALYSIS**

19 20 21 **Design**

22
23 This will be a single-centre, prospective RCT with a three-arm parallel grouping design. The trial
24
25 protocol version number: 2.0, date 31th March,2021. The study will be conducted at the West China
26
27 Hospital of Sichuan University (WCHSU) from April 2021 to March 2023. All the participants will
28
29 be required to provide written informed consent in accordance with the most recent version of the
30
31 Declaration of Helsinki. Figure 1 presents the study flowchart.
32
33
34
35
36
37
38
39
40
41

42 43 **Patient population and setting**

44
45 A total of 480 Chinese patients undergoing laparotomy for gastrointestinal surgery will be
46
47 sequentially enrolled at the WCHSU after fulfilling the eligibility criteria and signing informed
48
49 consent. A clinical assistant with institutional review board training will be in charge of patient
50
51 enrolment.
52
53

54 55 **Eligibility criteria**

56
57 *The inclusion criteria will be as follows:* (1) male and female patients aged 18–70 years; (2)
58
59 laparotomy tumour resection under general anaesthesia (stomach, colon, and rectum); and (3)
60

1
2
3
4 volunteering to participate in this study and signing an informed consent form.
5

6 *The exclusion criteria will be as follows:* (1) surgical incision or scar on the meridian of
7
8
9 ST21/SP15, (2) local skin infection at acupoints, (3) inability to complete the visual analogue scale
10
11 (VAS), and (4) allergy to metal or severe needle fear, intolerance of TEAS or EA treatment, (5)
12
13 uncontrolled diabetes, severe cardiac, central nervous, psychiatric disorders, or coagulopathy; (6)
14
15 cardiac pacemaker; and (7) participation in other clinical trials.
16
17

18
19 *Withdrawal criteria:* Participants meeting any of the following criteria will be withdrawn from
20
21 the study: (1) occurrence of serious adverse events; (2) participants with serious complications or
22
23 other serious diseases requiring emergency measures, (3) being required to withdraw during the test,
24
25 and (4) violation of the test program. Withdrawn patients will not be replaced.
26
27
28
29
30
31

32 **Randomisation and blinding**

33
34 This study will have a single-blind design. The patient will be blinded to the group allocation;
35
36 moreover, patients in the same ward will be separated by a bed curtain when receiving acupuncture
37
38 treatment, with only the research leader and acupuncturist being aware of the treatment allocation.
39
40
41 The randomised grouping plan will be designed using SPSS 22.0. According to the plan, 480
42
43 patients will be randomly divided into three groups according to a ratio of 1:1:1: EA, TEAS+EA,
44
45 and control groups. The group scheme will be kept in a confidential envelope; further, the research
46
47 leader will randomly distribute the included patients to each group following the distribution plan
48
49 in the envelope. Additionally, the research leader will only inform the acupuncturist responsible for
50
51 the operation. Efficacy evaluation will be conducted blinded to the grouping allocation. Blind
52
53 statistical analysis will be used in the data summary stage. Operators, efficacy evaluators, and
54
55
56
57
58
59
60

1
2
3
4 statisticians will be separated.
5
6
7

8 9 **INTERVENTION**

10
11 All acupoints will be determined based on the National Standard of Nomenclature and Location of
12
13 Acupuncture Points (GB/T 12346-2006)³⁸. All practitioners performing the treatment must have an
14
15 acupuncturist qualification certificate with independent clinical experience for > 2 years. The
16
17 acupuncturist qualification certificate with independent clinical experience for > 2 years. The
18
19 acupuncturists will not be replaced during the experiments.
20
21

22 All patients will receive standardised perioperative management by ERAS, including
23
24 preoperative education, optimisation of anaesthesia scheme, avoidance of intraoperative
25
26 hypothermia, restrictive fluid infusion, and reduction of surgical trauma. Regarding the electronic
27
28 acupuncture treatment instrument (Hwato, SDZ-V, Suzhou Medical Supplies Factory Co., Ltd), the
29
30 current frequency will be continuous wave 2 Hz, the current intensity will be measured in degrees
31
32 as tolerated by the patient; moreover, the treatment duration will last 30 min (Figure 2). The
33
34 treatment will be initiated from the first postoperative day, once daily in the morning, until the
35
36 patient regains defecation and could tolerate transoral solid food.
37
38
39
40
41

42
43 In the EA group (electroacupuncture is added at the base of basic treatment), treatment will be
44
45 bilaterally performed at five acupoint pairs: Hegu (LI4), Neiguan (PC6), Zusanli (ST36), Shangjuxu
46
47 (ST37), and Xiajuxu (ST39). LI4 is an acupoint of the large intestine meridian and is located on the
48
49 dorsum of the hand between the first and second metacarpal bones. PC6 belongs to the pericardium
50
51 meridian and is located between the flexor carpi radialis muscle tendon and the palmaris longus
52
53 tendon, 2 Cun above the wrist crease. ST36, ST37, and ST39 are acupoints of the stomach meridian.
54
55
56
57
58 ST36 is located on the lateral side of the lower leg, 3 Cun below the lateral border of the knee and
59
60

1
2
3
4 one finger width lateral to the anterior border of the tibia. ST37 is located 3 Cun below ST36. ST39
5
6 is located 3 Cun below ST37. After skin disinfection with a disposable disinfecting cotton swab,
7
8 sterile and disposable stainless steel needles (0.25×40 mm, Suzhou Jiajian, Jiangsu, China) will be
9
10 quickly and perpendicularly inserted into the skin acupoints at a depth of 25–30 mm. The duration
11
12 of reinforcing-reducing manipulation of twirling and rotating needles should be used for 1 min to
13
14 achieve de qi (a composite of sensations including soreness, numbness, distention, heaviness, and
15
16 other sensations), which significantly contributes to acupuncture efficacy. The ipsilateral Neiguan,
17
18 Hegu, Zusanli, and Xiajuxu will be separately connected to one electrode set, and therefore yielding
19
20 four electrode sets (Figure 3 a, b).
21
22
23
24
25
26

27 For the TEAS+EA group, treatment will be based on the EA group with the addition of two
28
29 pairs of bilateral abdominal acupoints: Liangmen (ST21) and Daheng (SP15). Additionally, ST21
30
31 is an acupoint of the stomach meridian that is located 4 Cun above the umbilicus and 2 Cun open
32
33 next to the anterior median line. SP15 is an acupoint of the spleen meridian, located 4 Cun beside
34
35 the umbilicus and lateral to the rectus abdominis muscle. Abdominal acupoints will be stimulated
36
37 using a self-adhesive electrode pad with electrical conductivity; additionally, the ipsilateral
38
39 Liangmen will be connected to the Daheng set of electrodes. The ipsilateral Neiguan, Hegu, Zusanli,
40
41 and Xiajuxu acupoints will be connected to one electrode set to yield a total of six sets of electrodes
42
43 (Figure 3 a, b, c).
44
45
46
47
48
49

50 The control group will receive ERAS-standardised perioperative management without
51
52 acupuncture treatment.
53
54
55
56
57

58 **OUTCOME MEASURES**

59
60

Main outcome

The primary outcome will be the GI-2 (composite outcome of time to first defaecation and time to tolerance of a solid diet). Participants will be visited and evaluated by efficacy evaluators at the end of each treatment.

Secondary outcome

The secondary outcomes include the time of first passage of flatus, time to first defaecation, time to tolerance of a solid diet, time to first ambulation, hospital duration from operation to discharge, pain and nausea vomiting scores on the VAS (from 0 [no at all] to 10 [the worst]), medication use (name, frequency and dosage of analgesic drugs and antiemetic agents), incidence of postoperative complications (include intra-abdominal infection, intestinal ischemia and necrosis, anastomotic leak, pulmonary infection, etc), and evaluation of treatment modality acceptability (classified into five grades: very acceptable, moderately acceptable, somewhat acceptable, moderately unacceptable, and totally unacceptable). Participants will be visited and evaluated by efficacy evaluators at the end of each treatment.

We add GI-2 as a primary outcome to the original protocol after recruitment of the study had already begun. GI-2 is a time indicator, which will be calculated from two existing outcomes (time to first defaecation and time to tolerance of oral diet). There will be no harm to subjects, no additional cost and no more work.

Safety evaluation

All adverse events will be recorded on the adverse event record sheet by the acupuncturist and participants at any time during the study period. Adverse events to be recorded include fainting during acupuncture treatment, needle breaking, unbearable acupuncture pain, local hematoma,

1
2
3
4 infection, and any other discomfort or accident. The intensity and causality of each adverse event
5
6 will be evaluated and recorded. If any serious adverse events occur due to an intervention, the
7
8 intervention will be immediately stopped; further, appropriate corrective action will be taken.
9
10 Serious adverse events will be promptly reported to the institutional review board within 24 h until
11
12
13
14 30 days after the end of the trial.

17 **Sample size calculation**

18
19 The stratification factors will be gastrectomy and colorectal resection, with each layer being divided
20
21 into three groups: the group ratio will be 1:1:1. The main efficacy indicator will be the GI-2
22
23 (composite outcome of time to first postoperativedefaecation and time to tolerance of a solid diet).
24
25 Given the lack of reports on TEAS+EA for promoting postoperative recovery, we conducted a
26
27 preliminary experiment. The preliminary experimental results indicated that the GI-2 of laparotomy
28
29 gastrectomy surgery in the control, EA, and TEAS+EA groups was 113.1 ± 37.5 h, 86.9 ± 36.1 h,
30
31 and 80.1 ± 33.2 h, respectively, Additionally, in the control group, the GI-2 of laparotomy colorectal
32
33 surgery in the control, EA, and TEAS+EA groups was 106.2 ± 35.9 h, 85.6 ± 33.1 h, and $78.5 \pm$
34
35 36.3 h, respectively. The sample size was determined using PASS 11 with $\alpha = 0.05$ (two-sided) and
36
37 $\beta = 0.1$ (90% power). The required sample size will be 60 patients per group. Assuming that 20%
38
39 of patients will be lost to follow-up, we chose a sample size of 80 participants for each group, with
40
41 a total sample size of 480 participants.
42
43
44
45
46
47
48
49

51 **Statistical analysis**

52
53 Statistical analysis will be conducted by independent third-party professional statisticians. All data
54
55 will be collected by efficacy evaluators. Data analysis will be performed using the intention
56
57 processing principle in SPSS 22.0. Statistical results will be reported using a two-sided test, with
58
59
60

1
2
3
4 statistical significance being set at P-value < 0.05. Continuous variables will be expressed as: mean
5
6 (SD), median (interquartile range (IQR)), or minimum and maximum. For comparisons between
7
8 treatment groups, analyses of variance (ANOVAs) will be used for normally distributed variables,
9
10 and the Kruskal–Wallis H test will be used for non-normally distributed variables. Categorical
11
12 variables will be expressed as numbers (%), and will be analyzed via chi-square tests for between-
13
14 group comparisons.
15
16
17
18

19 **Patient and public involvement**

20
21 Patients and/or the public were not involved in study design or conduct of the study. The present
22
23 trial was developed by acupuncturists based on previous clinical experience and literature. The
24
25 expected outcomes are commonly used to assess rapid postoperative recovery in clinical practice.
26
27
28 The cost of interventions and outcome measurements will be maintained using the study funding;
29
30 therefore, it was not considered a significant burden and met the patient preferences. The results
31
32 will be disseminated to the participants via the WCHSU website.
33
34
35
36
37
38
39
40
41
42

43 **DISCUSSION**

44
45 Several studies have demonstrated the efficacy of acupuncture in rapid postoperative
46
47 rehabilitation³⁹. Previous clinical experience and studies have shown that acupuncture
48
49 on the distal limb acupoints is mostly selected for rehabilitation after abdominal surgery,
50
51 which may be associated with several factors, including the presence of surgical
52
53 wounds after abdominal surgery, postoperative changes in the structure and state of
54
55 abdominal organs affecting acupuncture needle manipulation, and safety. However,
56
57
58
59
60

1
2
3
4 recent studies have shown that abdominal and limb acupoints facilitate improvement of
5
6 abdominal pain and the distension degree; moreover, abdominal acupoints have a more
7
8 optimal effect on improving the degree of abdominal pain⁴⁰. In this study, based on
9
10 extensive clinical practice, TEAS will be applied to abdominal acupoints, which is safer
11
12 than electroacupuncture based on acupuncture on the meridians of the distal extremities;
13
14 moreover, the SP15 and ST21 chosen for abdominal surgery are unconventional
15
16 incision positions that facilitate manipulation. Additionally, they are both antiemetic,
17
18 promote gastrointestinal motility, and relieve abdominal pain. Some previous studies
19
20 on acupuncture for gastrointestinal symptoms have shown that SA although have some
21
22 placebo effect, but EA might have greater benefits than SA(Sham-acupuncture)^{15 41 42},
23
24 so we did not include sham control in this study. Therefore, the main purpose of this
25
26 three-arm randomised controlled study is to evaluate whether TEAS combined with EA
27
28 therapy is effective at allowing rapid recovery after laparotomy for gastrointestinal
29
30 surgery is more effective and beneficial, and further improving patient satisfaction.
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

47 **ETHICS AND DISSEMINATION**

48
49 Personal information and study data of all participants will be recorded in case report forms.
50
51 Moreover, data involving patient privacy will be anonymized, protected by code, and securely kept
52
53 in a locked cabinet in the WCHSU accessed only by the research team. Upon completion of the trial
54
55 and data verification, the case report forms will be transferred to the Science and Technology
56
57 Department of Sichuan Province for safe archival purposes for 10 years before being destroyed.
58
59
60

1
2
3
4 Data for use or analysis following study completion will be available from the corresponding author
5
6 upon reasonable request. The study results will be presented at national and international scientific
7
8 conferences and submitted for publication in a peer-reviewed journal.
9

10
11 This study has been approved by the Ethics Committee on Biomedical Research, West China
12
13 Hospital of Sichuan University in April 2021. The approval number is 2021 (52). The trial protocol
14
15 strictly adheres to the principles of the latest Declaration of Helsinki. Patient consent for publication
16
17 is not required.
18
19
20
21
22
23
24
25
26

27 **Authors' contributions:** HL and QW contributed equally to this article, participated in the study
28
29 design, drafted the manuscript, and recruited patients. L-y L and Y-m Z are responsible for the
30
31 treatment of patients. H-q H and YH are responsible for collecting the data. NL and X-t W are
32
33 responsible for monitoring this study. All authors contributed to manuscript revision and have read
34
35 and approved the submitted version.
36
37
38
39
40
41
42

43 **Funding:** This study will be supported by the Sichuan Science and Technology Program (grant
44
45 number: 2021YFS0254).
46
47
48
49

50 **Disclaimer:** The funding bodies are not involved in study design, data collection, analysis,
51
52 interpretation of results, and the manuscript.
53
54
55
56
57

58 **Competing interests:** The authors declare that they have no competing interests.
59
60

1
2
3
4
5
6
7 **Provenance and peer review:** Not commissioned; externally peer-reviewed.
8
9
10
11
12

13 REFERENCES

- 14 1. Leslie JB, Viscusi ER, Pergolizzi JV, Jr., et al. Anesthetic Routines: The Anesthesiologist's Role in GI
15 Recovery and Postoperative Ileus. *Adv Prev Med* 2011;2011:976904. doi:
16 10.4061/2011/976904 [published Online First: 2011/10/13]
- 17 2. Gan TJ, Belani KG, Bergese S, et al. Fourth Consensus Guidelines for the Management of
18 Postoperative Nausea and Vomiting. *Anesth Analg* 2020;131(2):411-48. doi:
19 10.1213/ANE.0000000000004833 [published Online First: 2020/05/30]
- 20 3. Bragg D, El-Sharkawy AM, Psaltis E, et al. Postoperative ileus: Recent developments in
21 pathophysiology and management. *Clinical nutrition (Edinburgh, Scotland)* 2015;34(3):367-76.
22 doi: 10.1016/j.clnu.2015.01.016 [published Online First: 2015/03/31]
- 23 4. Ni CY, Wang ZH, Huang ZP, et al. Early enforced mobilization after liver resection: A prospective
24 randomized controlled trial. *International journal of surgery (London, England)* 2018;54(Pt
25 A):254-58. doi: 10.1016/j.ijso.2018.04.060 [published Online First: 2018/05/13]
- 26 5. Ren QP, Luo YL, Xiao FM, et al. Effect of enhanced recovery after surgery program on patient-reported
27 outcomes and function recovery in patients undergoing liver resection for hepatocellular
28 carcinoma. *Medicine* 2020;99(20):e20062. doi: 10.1097/md.00000000000020062 [published
29 Online First: 2020/05/24]
- 30 6. Harryman C, Plymale MA, Stearns E, et al. Enhanced value with implementation of an ERAS protocol
31 for ventral hernia repair. *Surgical endoscopy* 2020;34(9):3949-55. doi: 10.1007/s00464-019-
32 07166-2 [published Online First: 2019/10/03]
- 33 7. Medbery RL, Fernandez FG, Khullar OV. ERAS and patient reported outcomes in thoracic surgery: a
34 review of current data. *Journal of thoracic disease* 2019;11(Suppl 7):S976-s86. doi:
35 10.21037/jtd.2019.04.08 [published Online First: 2019/06/12]
- 36 8. Noba L, Rodgers S, Chandler C, et al. Enhanced Recovery After Surgery (ERAS) Reduces Hospital Costs
37 and Improve Clinical Outcomes in Liver Surgery: a Systematic Review and Meta-Analysis.
38 *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary
39 Tract* 2020;24(4):918-32. doi: 10.1007/s11605-019-04499-0 [published Online First:
40 2020/01/05]
- 41 9. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. *JAMA surgery*
42 2017;152(3):292-98. doi: 10.1001/jamasurg.2016.4952 [published Online First: 2017/01/18]
- 43 10. Wilmore DW, Kehlet H. Management of patients in fast track surgery. *BMJ (Clinical research ed)*
44 2001;322(7284):473-6. doi: 10.1136/bmj.322.7284.473 [published Online First: 2001/02/27]
- 45 11. McLeod RS, Aarts MA, Chung F, et al. Development of an Enhanced Recovery After Surgery Guideline
46 and Implementation Strategy Based on the Knowledge-to-action Cycle. *Annals of surgery*
47 2015;262(6):1016-25. doi: 10.1097/sla.0000000000001067 [published Online First:
48 2015/02/19]
- 49
50
51
52
53
54
55
56
57
58
59
60

12. Prabhakaran S, Misra S, Magila M, et al. Randomized Controlled Trial Comparing the Outcomes of Enhanced Recovery After Surgery and Standard Recovery Pathways in Laparoscopic Sleeve Gastrectomy. *Obes Surg* 2020;30(9):3273-79. doi: 10.1007/s11695-020-04585-2 [published Online First: 2020/04/16]
13. Miedema BW, Johnson JO. Methods for decreasing postoperative gut dysmotility. *Lancet Oncol* 2003;4(6):365-72. doi: 10.1016/s1470-2045(03)01118-5 [published Online First: 2003/06/06]
14. Li H, He T, Xu Q, et al. Acupuncture and regulation of gastrointestinal function. *World journal of gastroenterology* 2015;21(27):8304-13. doi: 10.3748/wjg.v21.i27.8304 [published Online First: 2015/07/29]
15. Ng SS, Leung WW, Mak TW, et al. Electroacupuncture reduces duration of postoperative ileus after laparoscopic surgery for colorectal cancer. *Gastroenterology* 2013;144(2):307-13.e1. doi: 10.1053/j.gastro.2012.10.050 [published Online First: 2012/11/13]
16. Takahashi T. Mechanism of acupuncture on neuromodulation in the gut--a review. *Neuromodulation : journal of the International Neuromodulation Society* 2011;14(1):8-12; discussion 12. doi: 10.1111/j.1525-1403.2010.00295.x [published Online First: 2011/10/14]
17. Tada H, Fujita M, Harris M, et al. Neural mechanism of acupuncture-induced gastric relaxations in rats. *Digestive diseases and sciences* 2003;48(1):59-68. doi: 10.1023/a:1021730314068 [published Online First: 2003/03/21]
18. Yang NN, Ye Y, Tian ZX, 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(5):e13808. doi: 10.1111/nmo.13808 [published Online First: 2020/03/03]
19. Jie Ma, Yunxiao Wang, Dan Fan, et al. Clinical Study of Acupoint Catgut Embedding in the treatment of Chronic Functional Constipation. *Journal of Sichuan of Traditional Chinese Medicine* 2015;33(10):161-162. [published Online First: 2015/10/15]
20. Jian-hua. S. Clinical Observation of Acupuncture plus Flash Cupping for Gastroparesis in Senile Type 2 Diabetes. *Shanghai J Acu-mox* 2018;37(10):1132-1135. doi: 10.13460/j.issn.1005-0957.2018.10.1132 [published Online First: 2018/10/16]
21. Zhang WB, Wu A, Litscher G, et al. Effects and mechanism of acupuncture based on the principle of meridians. *Evid Based Complement Alternat Med* 2013;2013:684027. doi: 10.1155/2013/684027 [published Online First: 2014/01/01]
22. Zhao ZQ. Neural mechanism underlying acupuncture analgesia. *Progress in neurobiology* 2008;85(4):355-75. doi: 10.1016/j.pneurobio.2008.05.004 [published Online First: 2008/06/28]
23. Hauck M, Schröder S, Meyer-Hamme G, et al. Acupuncture analgesia involves modulation of pain-induced gamma oscillations and cortical network connectivity. *Scientific reports* 2017;7(1):16307. doi: 10.1038/s41598-017-13633-4 [published Online First: 2017/11/28]
24. Cui X, Liu K, Xu D, et al. Mast cell deficiency attenuates acupuncture analgesia for mechanical pain using c-kit gene mutant rats. *Journal of pain research* 2018;11:483-95. doi: 10.2147/jpr.S152015 [published Online First: 2018/03/20]
25. Wu MS, Chen KH, Chen IF, et al. The Efficacy of Acupuncture in Post-Operative Pain Management: A Systematic Review and Meta-Analysis. *PloS one* 2016;11(3):e0150367. doi: 10.1371/journal.pone.0150367 [published Online First: 2016/03/10]
26. Capodice JL, Parkhomenko E, Tran TY, et al. A Randomized, Double-Blind, Sham-Controlled Study Assessing Electroacupuncture for the Management of Postoperative Pain after Percutaneous

- Nephrolithotomy. *Journal of endourology* 2019;33(3):194-200. doi: 10.1089/end.2018.0665 [published Online First: 2019/01/30]
27. Chen CC, Yang CC, Hu CC, et al. Acupuncture for pain relief after total knee arthroplasty: a randomized controlled trial. *Regional anesthesia and pain medicine* 2015;40(1):31-6. doi: 10.1097/aap.000000000000138 [published Online First: 2014/08/28]
28. Asmussen S, Maybauer DM, Chen JD, et al. Effects of Acupuncture in Anesthesia for Craniotomy: A Meta-Analysis. *Journal of neurosurgical anesthesiology* 2017;29(3):219-27. doi: 10.1097/ana.000000000000290 [published Online First: 2016/03/12]
29. Mitra S, Carlyle D, Kodumudi G, et al. New Advances in Acute Postoperative Pain Management. *Curr Pain Headache Rep* 2018;22(5):35. doi: 10.1007/s11916-018-0690-8 [published Online First: 2018/04/06]
30. Kovac AL. Update on the management of postoperative nausea and vomiting. *Drugs* 2013;73(14):1525-47. doi: 10.1007/s40265-013-0110-7 [published Online First: 2013/09/24]
31. Lee A, Chan SK, Fan LT. Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting. *The Cochrane database of systematic reviews* 2015;2015(11):Cd003281. doi: 10.1002/14651858.CD003281.pub4 [published Online First: 2015/11/03]
32. Kim YH, Kim KS, Lee HJ, et al. The efficacy of several neuromuscular monitoring modes at the P6 acupuncture point in preventing postoperative nausea and vomiting. *Anesth Analg* 2011;112(4):819-23. doi: 10.1213/ANE.0b013e31820f819e [published Online First: 2011/03/10]
33. Gan TJ, Jiao KR, Zenn M, et al. A randomized controlled comparison of electro-acupoint stimulation or ondansetron versus placebo for the prevention of postoperative nausea and vomiting. *Anesth Analg* 2004;99(4):1070-5, table of contents. doi: 10.1213/01.Ane.0000130355.91214.9e [published Online First: 2004/09/24]
34. Chen KB, Huang Y, Jin XL, 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. doi: 10.1016/j.ijsu.2019.08.034 [published Online First: 2019/09/09]
35. Chen J, Zhang Y, Li X, et al. Efficacy of transcutaneous electrical acupoint stimulation combined with general anesthesia for sedation and postoperative analgesia in minimally invasive lung cancer surgery: A randomized, double-blind, placebo-controlled trial. *Thorac Cancer* 2020;11(4):928-34. doi: 10.1111/1759-7714.13343 [published Online First: 2020/02/18]
36. Hou L, Xu L, Shi Y, et al. Effect of electric acupoint stimulation on gastrointestinal hormones and motility among geriatric postoperative patients with gastrointestinal tumors. *J Tradit Chin Med* 2016;36(4):450-5. doi: 10.1016/s0254-6272(16)30061-9 [published Online First: 2017/05/02]
37. Sun K, Xing T, Zhang F, et al. Perioperative Transcutaneous Electrical Acupoint Stimulation for Postoperative Pain Relief Following Laparoscopic Surgery: A Randomized Controlled Trial. *Clin J Pain* 2017;33(4):340-47. doi: 10.1097/ajp.0000000000000400 [published Online First: 2016/07/21]
38. Committee CNSA, Committee CISM. National standard of the people's Republic of China "Nomenclature and Location of Acupuncture Points"(GB / T 12346-2006). Beijing: China Standards Press, 2006.
39. Xin C, Sun JH. [The value of acupuncture-moxibustion in enhance recovery after surgery]. *Zhongguo Zhen Jiu* 2020;40(6):679-82. doi: 10.13703/j.0255-2930.20190501-0005 [published Online First: 2020/06/17]

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
40. Li HJ, Zhao Y, Wen Q, et al. [Comparison of Clinical Effects of Electroacupuncture of Abdominal and Limb Acupoints in the Treatment of Acute Pancreatitis]. *Zhen Ci Yan Jiu* 2018;43(11):725-9. doi: 10.13702/j.1000-0607.170351 [published Online First: 2018/12/27]
41. Liu Z, Yan S, Wu J, et al. Acupuncture for Chronic Severe Functional Constipation: A Randomized Trial. *Ann Intern Med* 2016;165(11):761-69. doi: 10.7326/m15-3118 [published Online First: 2016/09/13]
42. Wang CP, Kao CH, Chen WK, et al. A single-blinded, randomized pilot study evaluating effects of electroacupuncture in diabetic patients with symptoms suggestive of gastroparesis. *J Altern Complement Med* 2008;14(7):833-9. doi: 10.1089/acm.2008.0107 [published Online First: 2008/08/30]

Figure Legends

Figure 1: Flowchart of the study protocol.

Figure 2: Instrument and parameter.

Figure 3: Localization of acupoints and electrode connection.

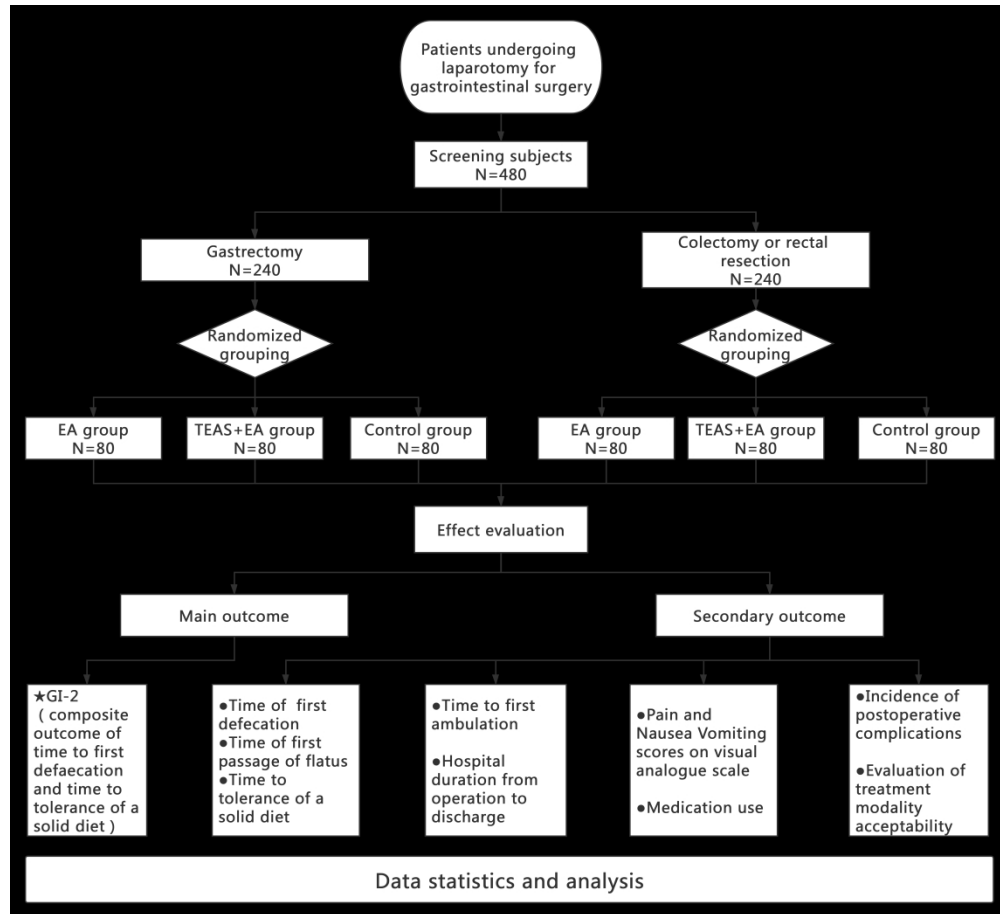


Figure 1: Flowchart of the study protocol.

1711x1560mm (72 x 72 DPI)

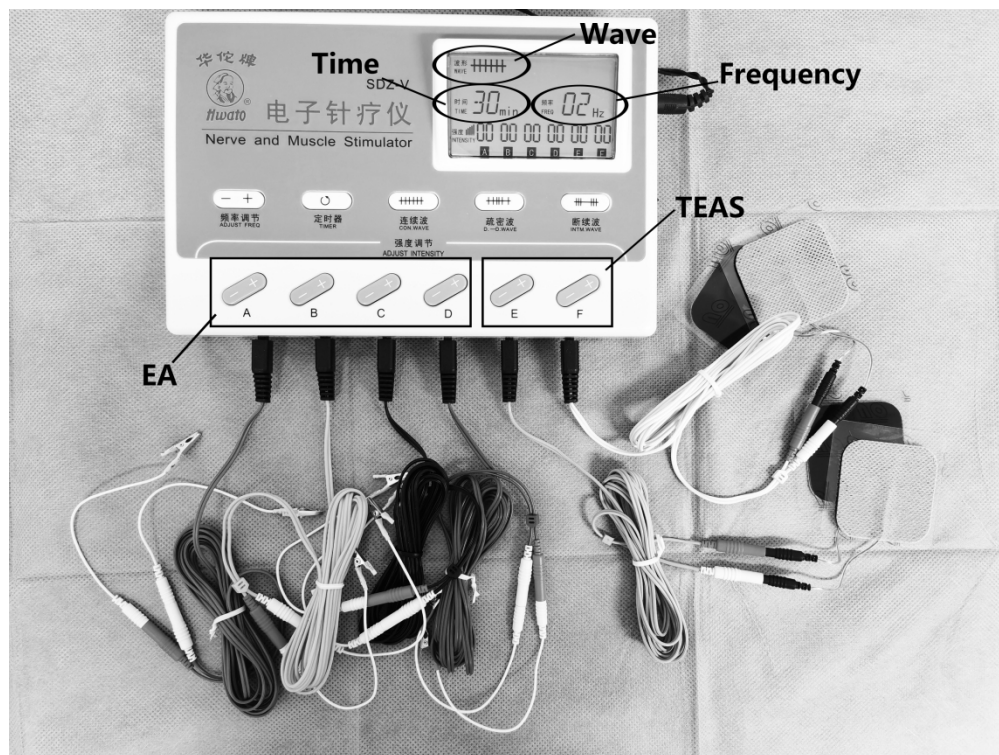


Figure 2: Instrument and parameter.

1286x965mm (72 x 72 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

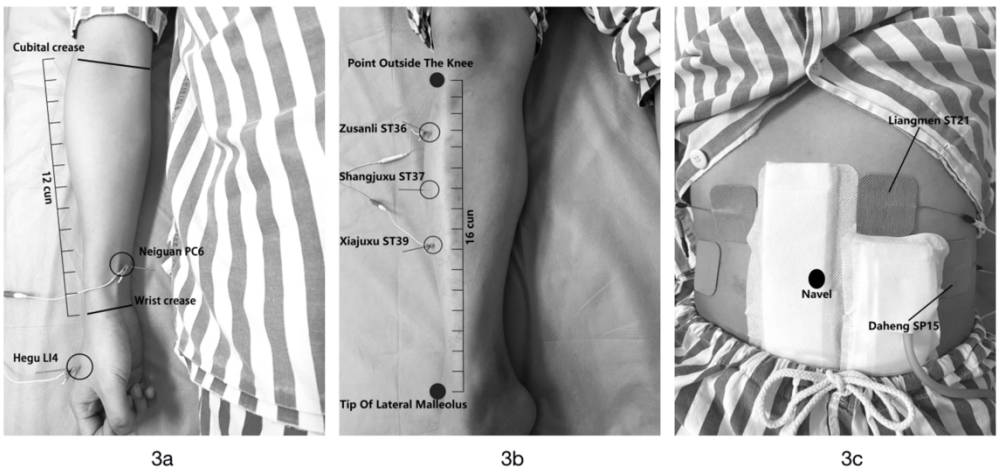


Figure 3: Localization of acupoints and electrode connection.

1492x704mm (72 x 72 DPI)



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page Number on which item is reported
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	3	Date and version identifier	7
Funding	4	Sources and types of financial, material, and other support	16
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	15

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-7
	6b	Explanation for choice of comparators	5
Objectives	7	Specific objectives or hypotheses	2
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	9-11
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9-11

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	9-11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9-11
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	9-11
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8-9

Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8-9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8-9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8-9
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15

1 2 3 4 5 6 7	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13
8 9 10 11		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	13
12 13 14 15 16 17 18		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	13
19 20 21	Methods: Monitoring			
22 23 24 25 26 27 28 29 30 31	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
32 33 34 35 36 37 38		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
39 40 41 42 43 44	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11-12
45 46 47 48 49	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
50 51 52 53	Ethics and dissemination			
54 55 56 57 58 59 60	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	15

1 2 3 4 5 6 7 8	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	N/A
9 10 11 12 13 14	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7-8
15 16 17 18 19		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
20 21 22 23 24 25 26	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
27 28 29 30	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	16
31 32 33 34 35	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15
36 37 38 39 40	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	13
41 42 43 44 45 46 47 48 49	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	15
50 51 52 53 54		31b	Authorship eligibility guidelines and any intended use of professional writers	15
55 56 57 58 59 60		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	15

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.