Study Protocol

Electroacupuncture for the prevention of postoperative gastrointestinal dysfunction in patients undergoing vascular surgery under general anesthesia: study protocol for a prospective practical randomized controlled trial

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BACKGROUND: Postoperative gastrointestinal dysfunction (PGD) is one of the most common complications following major surgeries under general anesthesia (GA). Despite ongoing research and new drug treatments, abdominal distension within 24 h postoperatively occurs in 8% – 28% of all surgeries. We aim to analyze the effectiveness of preventing PGD by preoperatively stimulating Neiguan (PC6), Zusanli (ST36) and Shangjuxu (ST37) bilaterally twice a day compared with sham-acupuncture treatment and standard treatment.

METHODS AND DESIGN: This is a single-center, prospective practical randomized controlled trial. All groups will be given standard treatments. Patients undergoing vascular surgery under GA will be included from the Vascular Surgery Unit in West China Hospital of Sichuan University, China, and divided into three groups. The experimental group will receive routine treatments and acupuncture at PC6, ST36 and ST37 bilaterally with electrical stimulation twice a day for 20 min preoperatively. The sham-acupuncture group will receive pseudo-electroacupuncture at sham acupoints of PC6, ST36 and ST37, which are 1 cun away from the real acupoints. The routine-treatment group will not receive electroacupuncture. The outcomes include the incidence of abdominal distention, abdominal circumference, the degree of abdominal distension, the first time of flatus and defecation, and hospitalization duration.

DISCUSSION: The results from this study will demonstrate whether preoperative electroacupuncture is an effective method for the prevention of PGD in patients undergoing vascular surgery under GA. This study may also provide a standardized acupuncture treatment for reduction of PGD.

TRIAL REGISTRATION: This study is registered with the Chinese Clinical Trial Registry: ChiCTR-TRC-13003649.

KEYWORDS: electroacupuncture; gastrointestinal dysfunction; vascular surgery; study protocol.

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1 Introduction

Postoperative gastrointestinal dysfunction (PGD) is one of the most common complications in patients suffered from major surgeries under general anesthesia (GA)\(^{(1)}\). It is caused by intraoperative wound traction, abdominal adhesions or lack of visceral perfusion\(^{(2)}\) and may lead to abdominal distension, constipation and other symptoms. Incidence of opioid-induced gastrointestinal dysfunction is as high as 81% in the United States\(^{(3)}\). Despite ongoing research and new drug treatments, abdominal distension within 24 h of operation occurs with 8%–28% of all surgeries\(^{(4)}\). In general, complication rates associated with endovascular surgery have decreased. For example, complications associated with respiratory procedures decreased by 77.27% from 2000 to 2003\(^{(5)}\). However, incidence rates of PGD have not decreased, and in fact, the incidence rate of PGD remained the same between 1974 and 2011 in China\(^{(6)}\) and increased by 10% in Japan over a 5-year stretch at the turn of the 21st century\(^{(7)}\). Analysis of more than 5000 records of patients undergoing major vascular surgery in 206 National Surgical Quality Improvement Program (NSQIP) hospitals from 2008 to 2009\(^{(8)}\) showed that more than 25% of cases of endovascular treatment, regardless of the severity, suffered postoperative complications, postoperative intestinal obstruction and other gastrointestinal dysfunctions within 30 d of surgery. Patients suffering from PGD have longer hospital stays, greater financial burdens\(^{(9)}\) and higher risks for other complications, like infections.

Because there are few effective treatments for PGD, prevention is paramount\(^{(10)}\). Acupuncture has gradually gained acceptance from physicians as an alternative therapy as clinical studies and basic research have demonstrated its efficacy. For example, a clinical study which enrolled 165 patients demonstrated that electroacupuncture (EA) could reduce the duration of postoperative ileus\(^{(11)}\), a small-sample-size trial found that acupoint stimulation is useful for postoperative recovery of intestinal function\(^{(12)}\), and another study showed that acupuncture helps in the recovery from stomach distension\(^{(13)}\). Animal experiments have identified factors that contribute to PGD, including reduction in the number of interstitial cells of Cajal and atrophy of their structure\(^{(14)}\), activation of sympathetic nervous system and postoperative inflammatory cytokines\(^{(15)}\) and leukocyte cell-induced nitrous oxide (NO) release, which restrains gastrointestinal peristalsis and causes intestinal inflammation\(^{(16)}\). Other animal studies have shown that acupuncture can ameliorate PGD by regulating these pathologic changes\(^{(17)}\).

Acupuncture is widely used in departments of obstetrics and gynecology\(^{(18)}\), gastrointestinal surgery\(^{(19)}\) and orthopedics. In this study, our aim is to collect details about patients scheduled for vascular surgical procedures under GA, and to evaluate whether preoperative EA is an effective method for reducing PGD incidence in patients undergoing vascular surgery under GA. This study will also define a standard acupuncture treatment for reducing incidence of PGD.

2 Methods

2.1 Trial design

This is a single-center, prospective randomized controlled trial (RCT). Using a balanced random approach (section 2.6), all participants will be assigned to three groups: Group A (EA), Group B (sham-acupuncture) and Group C (routine-treatment).

2.2 Participants

We will recruit 159 cases scheduled to receive vascular surgery with GA within 24 h. These patients will be recruited from West China Hospital of Sichuan University (WCHSU), China, after meeting the eligibility criteria, and signing the informed consent. We plan to enroll the first patient on November 1, 2014 and end on November 1, 2016.

2.2.1 Inclusion criteria

Patients who meet all of the following conditions will be considered for enrollment: age ≥ 18 years; and patients scheduled for vascular surgical procedures under GA within 24 h.

2.2.2 Exclusion criteria

The exclusion criteria are as follows: patients with a history of hypo- or hyperthyroidism, cardiopulmonary disease, or psychological disorder; patients with history of EA; patients with cardiac pacemaker; menstruating phase of the menstrual cycle; refusal to accept acupuncture; unconscious before surgery; inability to communicate; participation in another clinical trial which could interfere with the primary endpoint of this study; bleeding disorders (hemophilia or fibrinogenemia); serious systemic disease (AIDS or sepsis); initial body temperature > 38.0 °C or < 36.0 °C; known history of alcohol or substance abuse; necessity of systemic sedation for other reasons; emergency procedures; and pregnant or lactating women.

2.2.3 Withdrawal criteria

All withdrawn patients will be reported in the final results to guarantee maximum transparency. The withdrawal criteria are as follows: at the patient’s own request or at the request of the legal representative; if, in the investigator’s opinion (physician performing the acupuncture or physician performing the examination), continuation of the trial would be detrimental to the subject’s wellbeing (e.g., strong pain at the insertion points, allergic reactions, and other independent acute health problems).

2.3 Interventions

Patients receiving acupuncture therapy will be treated bilaterally at three distal acupoints: Neiguan (PC6), Zusanli
Patients in the Group A will receive the following treatment: each insertion site will be disinfected with 75% alcohol before EA treatment. Sterile single-use 0.25 mm × 38 mm needles (Wuxi Jiajian Medical Instrument Co., Ltd, Jiangsu, China) will be inserted vertically to a depth of 1–1.5 cun. At the appropriate depth, the acupuncturist will manipulate the needles for Deqi then connect a Nerve and Muscle Stimulator (Suzhou Medical Appliance Factory, Suzhou, China) to PC6 (positive electrode) and ST36 (negative electrode) on the same side of the body. In each treatment session, EA stimulation will be performed for 20 min at a frequency of 15 Hz with continuous wave.

Patients in the Group B will be treated at three sham acupoints of PC6, ST36 and ST37. These three pseudo acupoints are located 1 cun from the real acupoints (Figures 1 and 2). After sterilizing as above, fixation mats will be pasted at each point. Blunt tipped needles will be inserted vertically through the mats to the skin surfaces, but will not penetrate the skin. A visually identical, but modified electro-stimulator, with electrodes disconnected at the plug, will then be connected to sham acupoint of PC6 (positive electrode) and sham acupoint of ST36 (negative electrode) on the same side of the body. Stimulation of the sham points will be conducted for 20 min at a frequency of 15 Hz with continuous wave.

Patients in the Group A and Group B will individually receive two EA treatments (real and sham, respectively) 24 h before surgery, one at 10 AM and another at 4 PM. Patients in the Groups A, B and C will receive similar treatment after surgery, such as gastrointestinal decompression, 3 L intravenous fluids, nutritional support, routine nursing care and rehabilitation exercises (Table 1). All patients undergo supervision and evaluation of curative effect at 10 AM daily, until discharge. A third party will perform all data analysis. The flow chart of this trial is shown in Figure 3.

All participating acupuncturists will have been qualified for at least 3 years and have more than 4 years experience in acupuncture practice.

2.4 Outcome measurement

A blinded observer will receive postoperative data including abdominal circumference, degree of abdominal distension, time of first flatus and defecation and hospitalization duration. As a subjective sensation, abdominal distension will be measured using a Likert-type scale (Table 2). To improve the experimental accuracy, the objective indicator of abdominal circumference is chosen to reflect signs of PGD. In this study, the incidence of abdominal distension after surgery is the main outcome indicator.

The secondary outcomes are: 1) abdominal circumference and score of abdominal distension after vascular surgery under general anesthesia; 2) the difference between the two groups in time to first flatus and defecation; and 3)
Table 1  Intervention of three groups

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Method</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine treatment</td>
<td>Gastrointestinal decompression</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>3 L intravenous fluids or nutritional support</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Routine nursing care</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>Rehabilitation exercises</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Intervention</td>
<td>Real acupoints of PC6, ST36 and ST37</td>
<td>√</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td></td>
<td>Sham acupoints of PC6, ST36 and ST37</td>
<td>×</td>
<td>√</td>
<td>×</td>
</tr>
<tr>
<td></td>
<td>Electroacupuncture in an energized state</td>
<td>√</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td></td>
<td>Special electrostimulator with electricity</td>
<td>×</td>
<td>√</td>
<td>×</td>
</tr>
<tr>
<td></td>
<td>Electroacupuncture for 20 min at a frequency of 15 Hz with continuous wave</td>
<td>√</td>
<td>√</td>
<td>×</td>
</tr>
</tbody>
</table>

Table 2  The illustration of Likert-type scale

<table>
<thead>
<tr>
<th>Score</th>
<th>The feeling of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I feel no abdominal distension at all.</td>
</tr>
<tr>
<td>1</td>
<td>I feel a little of abdominal distension.</td>
</tr>
<tr>
<td>2</td>
<td>I feel abdominal distension but I can bear.</td>
</tr>
<tr>
<td>3</td>
<td>I feel obvious abdominal distension that I cannot bear but it does not affect my life.</td>
</tr>
<tr>
<td>4</td>
<td>I feel horrible abdominal distension that needs to be addressed.</td>
</tr>
</tbody>
</table>

Figure 3  The flow chart of study
hospitalization duration. The abdominal circumference is measured at the navel on a supine position, with relaxed breathing, using an inextensible tape graduated in millimeters (Figure 4)\(^\text{[21]}\).

The study aim is to prevent PGD; therefore, the incidence of PGD is our primary concern. However, due to the subjectivity of some of the study data, there is potential for bias. To overcome subjective bias, we chose abdominal circumference as an objective indicator. To the best of our knowledge, the study of vascular surgery-related PGD is rare and not standardized. Most previous studies used a VAS\(^\text{[3]}\) scale, while some used the MOS 36-Item Short-Form Health Survey (SF-36)\(^\text{[22]}\). Therefore, we hope that through comprehensive data collection, we will define a new standard measure for PGD.

### 2.5 Sample size calculation

Due to a lack of previous reports on PGD-related acupuncture and vascular surgery, we refer to literature describing acupuncture treatment of other diseases leading to PGD. Combined with the main outcome indicators and the abdominal distension rate, we believe that preoperative acupuncture can be shown to reduce the incidence of PGD by up to 15%, compared with the reported PGD incidence of 25%–60% without acupuncture including endovascular treatment\(^\text{[7]}\) and laparotomy\(^\text{[22]}\).

We set unilateral \(\alpha = 0.05\), power = 0.90, and \(\beta = 0.10\), providing an estimated sample size of 48 cases in each group, using Package for Encyclopedia of Medical Statistics 3.1 (PEMS 3.1, Guangzhou, China). Assuming 10% patient loss, a minimum of 159 cases is required. Therefore, we set the desired number of cases in this study at 159 cases. Our Vascular Surgery Department performs at least 100 cases of surgery per year and this study’s research period is set at 2 years. We also believe that a larger sample size will provide more useful results, another reason for selecting 159 cases in our study. Because this experiment is a prospective RCT, reasons for not completing the study, such as death and postoperative disturbances of consciousness, will still be included in the medical record analysis to provide guidance for further studies.

### 2.6 Randomization and blinding

All participants are randomly assigned to three groups on the basis of a concealed allocation approach using SPSS 13.0 (IBM SPSS, Chicago, IL, USA). A computerized random number table is used to determine the allocation of groups, with numbered opaque sealed envelopes containing the randomization schedule. The envelopes are kept by an investigator who is not an assessor in the study, and who is informed of the outcomes at the end of the study.

Both the researchers recording the outcomes and those making conclusions are blinded to the patient group assignments.

### 2.7 Data management

The study includes a period from 24 h preoperatively to 7 d postoperatively. A graduate student, not participating in patient management, will record details of patient treatment, including demographic data, anesthesia time, surgery duration, the dosage of opioids, and the operation methods (open surgery or endovascular therapy). The demographic data collected will include: age, gender, race, marriage status, job, educational background, height, weight and telephone number. Though the type of intravenous fluid given during and post surgery is a factor in postoperative recovery, all patients in this study will only under GA and the postsurgery routine treatments for them are all the same.

### 2.8 Data analysis

All data will be analyzed by a blinded statistician using SPSS 13.0 at a location separate from the WCHSU. The intention-to-treat principal will be used in the data analysis. Statistical treatments are one-sided tests, and a \(P\)-value < 0.05 is considered statistically significant. Measurement data are expressed as mean ± standard deviation. Those that meet normality and homogeneity of the variance demander are compared with each other by \(t\)-test, while those that do not are compared by the Wilcoxon rank-sum test. Enumeration data assembled by frequency, constituent ratio and other parameters are evaluated using the chi-square test or Fisher’s exact probability method.

### 2.9 Adverse events

All adverse events, such as hematoma, stuck needle and fainting, must be reported. In case of serious adverse events, experimental intervention should be ceased at once, and proper treatments must be provided.

### 3 Discussion

For preventing PGD by EA, three acupoints, PC6, ST36...
and ST37, are selected based on traditional Chinese medicine Zangfu-organ theory, known as the stomach and spleen.

Both animal and human research has shown that each of the selected acupoints is useful for recovering from PGD\cite{10,23}. ST36 can ameliorate gastric peristalsis by improving gastrointestinal blood flow distribution, regulating motilin via somatostatin\cite{24} and increasing angiotensin via NO\cite{16,25}. Clinical studies support that stimulating ST36 can significantly reduce the degree of PGD and improve gastrointestinal function recovery\cite{26,27}. However, in most previous clinical studies, the acupuncture intervention is given after surgery. It remains unclear whether pre-operation EA provides better recovery for PGD.

PC6 is an acupoint for preventing gastrointestinal dysfunction caused by opioid drugs\cite{28}. Stimulating PC6 can regulate endocrine function, especially adrenaline and vasopressin, to decrease gastric acid and adjust gastrointestinal function\cite{28}. PC6 is often used in preventing postoperative nausea and vomiting caused by opioid anesthesia and other agents\cite{29}. PC6 is also used in preventing PGD based on clinical observations.

In traditional Chinese medicine, ST37 is termed a low-sea point, and is used predominantly in treating large intestinal diseases, such as abdominal distension and irritable bowel syndrome. It is always used in conjunction with other low-sea points, like ST36, PC6 and ST38\cite{30,31}.

Although a large number of clinical studies suggest that postoperative acupuncture at ST36 and PC6 can treat PGD and postoperative nausea and vomiting, there are no known reports of preoperative EA affecting PGD. Recently, with advances in vascular surgical technology, improved quality of life during postoperative recovery has become even more important. Therefore, this study is carried out to determine if a preventive intervention program can reduce PGD after vascular surgery under GA.

In the WCHSU, we usually use gastrointestinal decompression or early walking to treat PGD, and these methods will apply to all study participants. For prevention of PGD, previous published studies state that EA should be applied from anesthesia induction to the end of the surgery\cite{32}. However, we chose 24 h before surgery for the following reasons:

(1) For research purposes: as a pre-validation study, this experiment focuses on whether the prevention interventions have an impact on PGD.

(2) For safety: this experiment uses EA, which may interfere with direct current equipment used during operation, such as the electric knife.

(3) For simplification of the setting: rehabilitation or acupuncture is often prescribed after surgery and patient numbers can be smaller. Therefore, for a more detailed analysis of the effect of acupuncture, a larger sample size is required, which led us to choose preoperative EA.

As an RCT, the purpose of this study is to provide the best EA therapeutic schedule. Researchers rarely use placebo-controlled trials when comparing interventions with general routine therapy\cite{28}. However, the potential bias among consenting participants induced by the Hawthorne effect, requires inclusion of the sham acupuncture group.

Our focus in this study is on the prevention of PGD. Therefore, the incidence of abdominal distension is our primary concern. Because this is a prospective RCT, collecting every detail during this research is helpful in making useful conclusions for subsequent studies. The degree of abdominal distension might determine whether EA is useful for preventing PGD and help to draw accurate conclusions; thus a comparison of abdominal circumferences is necessary. The three minor outcomes that will be monitored are times to first flatus and defecation and the duration of hospitalization. These parameters are used extensively for evaluating functional recovery. It is important to consider that for participants recovering from GA, their state of consciousness can be unclear and may lead to the incorrect time of first flatus. Using wake-up time can help better analyze the relationship with first flatus time.

In conclusion, we hope that rigorous clinical research can provide scientific evidence for using EA to prevent and treat PGD related to vascular surgeries under GA, thus leading to regular use of EA to treat this disorder.

4 Ethics

We will strictly follow the principles of the medical ethics of the Declaration of Helsinki with the approval of the Ethics and Research Committee of WCHSU (No. 2013(105)), China. All patients will be recruited from the Vascular Surgery Departement of WCHSU, and shall sign written informed consent in advance.

5 Authors’ contributions

M-YL, C-WW, Z-PW, and NL contributed to the design and development of the study protocol. M-YL prepared the initial draft of the manuscript. NL is the general supervisor for this research. All authors critically reviewed the content and approved the final version.

6 Acknowledgements

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7 Competing interests

The authors declare that they have no competing interests.

REFERENCES