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Research Article

Electroacupuncture or Transcutaneous Electroacupuncture for the Treatment of Postoperative Ileus after Abdominal Surgery: A Systematic Review and Meta-Analysis

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Abstract

Background & Aim: Postoperative ileus (POI) is a common status after abdominal surgery. At present, there is no ideal effective treatment for these patients. Electroacupuncture (EA) and transcutaneous electroacupuncture (TEA) are chosen as novel alternative treatments. The aim of this study is to evaluate the efficacy of EA or TEA to improve POI status of postoperative patients.

Methods: We systematically screened all randomized controlled trials (RCTs) on databases including PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang, EBSCO, Scopus and Ovid. We finally included fifteen-five high quality RCTs. Two reviewers independently conducted risk of bias assessment using Cochrane risk of bias tool, data extraction and statistical analysis. The primary outcomes included time to first flatus and time to first defecation, and the secondary outcomes included time to bowel sound recovery, time to first oral feeding, length of hospital stay and postoperative analgesic consumption. And subgroup analysis was conducted for laparoscopic surgery patients. All meta-analysis was performed by a random or fixed effect model with RevMan 5.3.

Results: A total of 15 trials involving 965 participates were included. Meta-analysis favored EA or TEA treatment for POI status including time to first flatus (MD -11.60h, 95%CI -16.19h to -7.02h, I^2=94%, REM), time to first defecation (MD -12.94h, 95%CI -18.82h to -7.06h, I^2=90%, REM), time to bowel sound recovery (MD -7.25h, 95%CI -10.27h to -4.24h, I^2=85%, REM), time to first oral feeding (MD -15.76h, 95%CI -23.91h to -7.61h, I^2=47%, REM) and length of hospital stay (MD -1.19d, 95%CI -1.78d to -0.6d, I^2=44%, REM). There was no significant difference of postoperative analgesic consumption between EA and control group (P=0.39). Subgroup analysis also favoured EA or TEA including time to first flatus (MD -2.46h, 95%CI -3.96h to -0.96h, I^2=0%, FIXED), time to first oral feeding (MD -10.73h, 95%CI -16.91h to -4.55h, I^2=0%, FIXED) and length of hospital stay (MD -1.30d, 95%CI -2.10d to -0.51d, I^2=32%, REM).

Conclusion: This meta-analysis suggests that EA or TEA is an effective and safe treatment for POI after abdominal surgery. Considering the methodology of included trials is not satisfactory due to the high risk of bias and the trials were basically performed in mainland China, more high-quality clinical trials should be conducted worldwide to confirm this conclusion. The mechanism of EA or TEA needs further investigation in the future.

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Introduction

Postoperative Ileus (POI) is a common status of gastrointestinal motility disturbance after abdominal surgery including cancer resection surgery, which causes symptoms of distension, nausea, and vomiting and diet intolerance in the patients [1]. Despite most of them can recover from POI, it is necessary to shorten the time of POI to relieve these symptoms, decrease the length of hospital stay and medical expense. The contributing factors of POI include surgical inflammation, activated sympathetic tone, patient's mental status and bowel edema [2].

Prokinetic agent is controversial on alleviating POI, especially it is not allowed to be applied on the fasting patient early after upper gastrointestinal surgery. Enhanced Recovery After Surgery (ERAS) is proved to be available and effective [3,4]. However, ERAS is an additional comprehensive strategy with various medical care and techniques such as early ambulation, early enteral nutrition, pain control and minimal invasive surgery.

Acupuncture is widely accepted in China, although its mechanism has not been well addressed. As a single effective treatment option, Electroacupuncture (EA) and Transcutaneous Electroacupuncture (TEA) at selected acupoionts are emerging in treating POI after abdominal surgery [5-8]. Our recent randomized clinical trial also showed that TEA could accelerate bowel function recovery, and it was an effective and safe way to recover post-gastrectomy patients from POI [9]. However, it is still lack of sufficient evidence to come to a conclusion. Hence, we searched for published articles related to this aspect and carried on this systematic review. As far as I am concerned, it is the first meta-analysis review focusing on the roles of EA and TEA in the treatment of POI after abdominal surgery.

Methods and Materials

Including and excluding criteria

Including criteria: (1) The participants in each study should be over 18 and undergoing abdominal surgery including open and laparoscopic surgery; (2) The intervention consisted of perioperative EA or TEA at single or combined acupoints, with or without acupoint drug injection; (3) The control group was given no electroacupuncture, sham electroacupuncture or drug therapy; (4) Articles were included with outcomes evaluating time to first flatus and/or defecation and/or bowel sound recovery, and/or time to first oral feeding, and/or length of hospital stay, and/or postoperative analgesic consumption; (5) Only RCTs were included in the study.

Excluding criteria: (1) Animal studies; (2) Did not meet inclusion criteria; (3) Reviews, letters, protocols; (4) Duplicate articles; (5) There were no sufficient outcomes related to POI.

Search strategy

The PubMed, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang, EBSCO, Scopus and Ovid databases were searched by two independent researchers for high-quality RCTs using following combinated items (1# AND 2# OR 3#):

1# "electroacupuncture", OR "transcutaneous electroacupuncture", OR "transcutaneous electrical nerve stimulation" OR "electrical acustimulation"

2# "postoperative", OR "postoperative ileus", OR "postoperative gastrointestinal motility disorder", OR "postoperative gastrointestinal function recovery", OR "postoperative gastrointestinal dysfunction".

3# "surgery", OR "abdominal surgery".

Risk of bias assessment and data extraction

The methodological qualities of the included trials were performed by two researchers according to the Cochrane risk of bias tool. The contents included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, selective reporting, and incomplete outcome data. Risk of bias was classified as low, high or unclear. Disagreements were resolved through discussion and consensus with a third researcher.

Statistical analysis

A meta-analysis was performed by a random or fixed effect model with RevMan 5.3. Continuous variables were expressed as mean difference (MD) with 95% CI with $P < 0.05$ as significant. Heterogeneity of the data was assessed using I^2 values. If I^2 value is < 25%, we will use fixed effect model to pool the data. If I^2 value is ≥ 25% %, random effect model will be used in meta-analysis. Funnel plots were generated to detect publication bias. Subgroup analysis was done for data of laparoscopic surgery.

Results

Study selection

A total of 231 articles were indentified during the initial study selection. 26 duplicates were removed. After screening by abstracts and titles, 151 studies were excluded. Then 11 animal studies, 4 reviews, 3 letters, and 2 protocols were excluded. Then 20 studies were excluded because of their low quality and insufficient data for analysis. Eventually, 15 studies were included in the final meta-analysis. Flow diagram of the screening process is summarized in Figure 1.

Risk of bias assessment

We assessed risk of bias in all included trials by the Cochrane risk of bias tool, the majority of the trials were well-designed randomly performed, however, the quality of these researches was not satisfactory because the performance and detection biases were quite high (Figure 2).

Characteristics of included studies

A total of 15 trials were included in this systematic review and meta-analysis. All trials were carried out in China including one trial in Hong Kong. There were 489 participants in EA or TEA group and 476 participants in control group (Table 1).

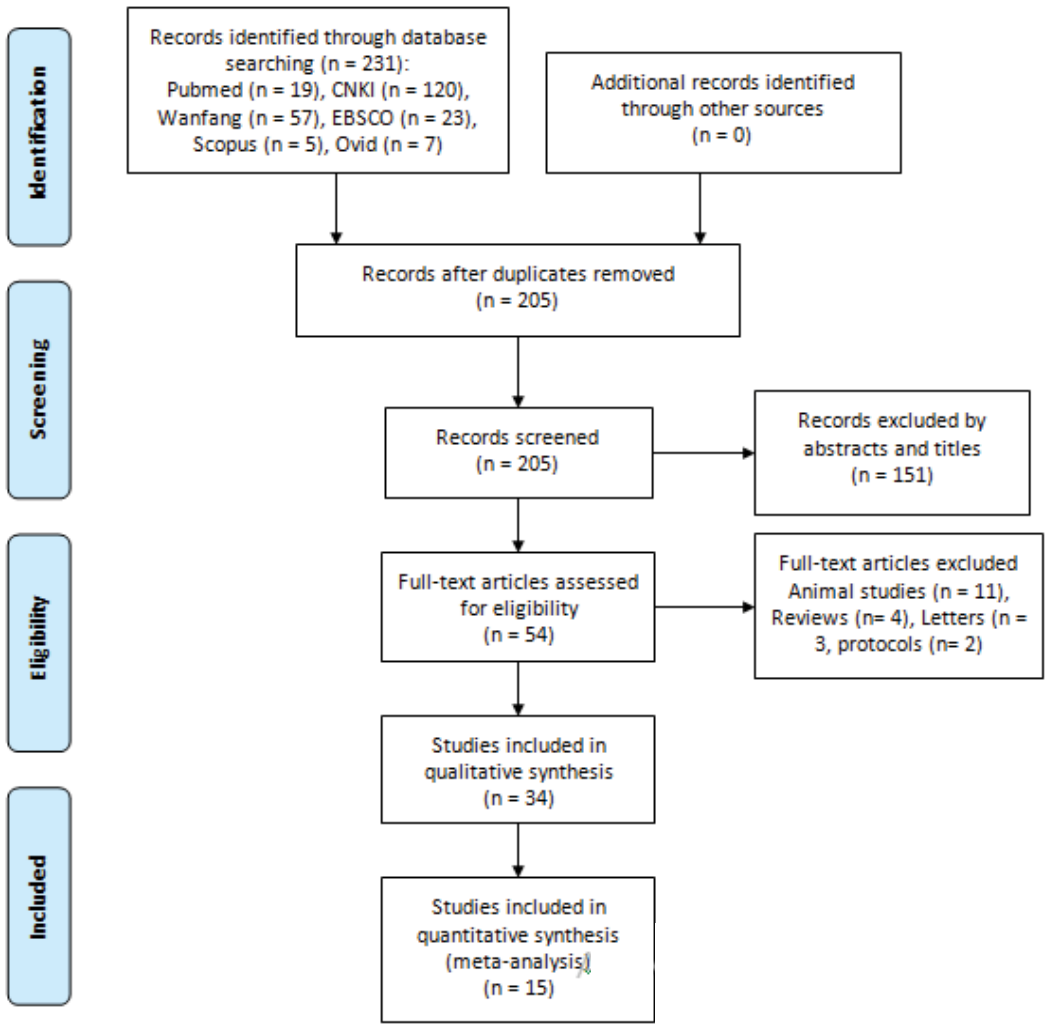

Figure 1: PRISMA Flow diagram of studies included in the review.

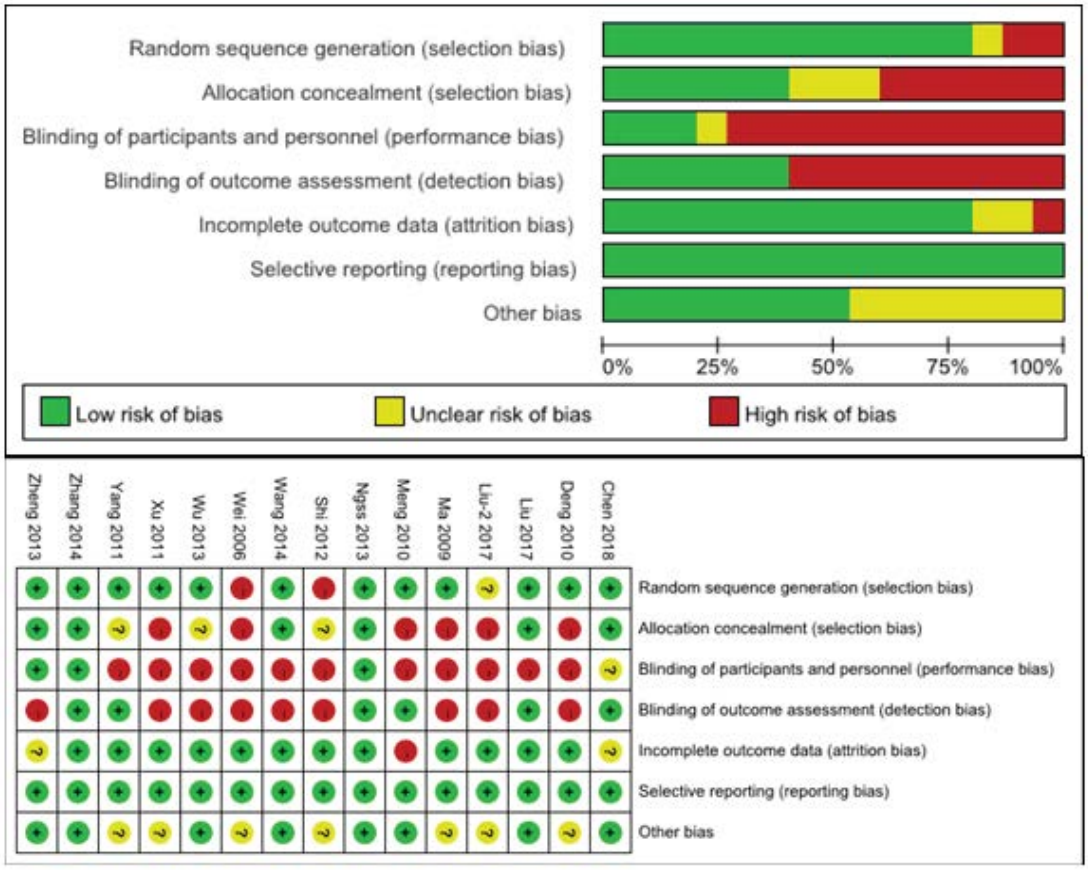

Figure 2: (a) Risk of bias: review authors' judgements about each risk of bias item presented as percentages across all included studies. (b) Risk of bias summary: review authors' judgements about each risk of bias for each included studies.

There were various differences among these trials. 3 trials underwent laparoscopic surgeries, while the rest of 12 trials underwent open surgeries. In terms of surgery type, There were colorectal (40%, 6/15), gastrointestinal (40%, 6/15), hepatobiliary (26.7%, 4/15) surgeries, vascular laparotomy (6.7%, 1/15) and undefined surgeries (20%, 3/15) involved in the research. Notably, the abdominal surgery type in 7 trials was single (one surgery type), and mixed (≥2 surgery types) in another 8 trials.

Only 1 trials performed TEA procedure, and 12 trials performed EA procedures. The most selected acupoints were ST36 (93.3%, 14/15), ST37 (40%, 6/15) and ST39 (20%, 3/15), while, less selected acupoints were PC6, SP6, LR3, SJ6, GB34, LI4 and LI11. The majority of the studies (93.3%, 14/15) applied EA or TEA postoperatively until first flatus or defecation, 1 study applied EA within 24h before surgery. The control interventions were routine treatment or sham EA.

Primary outcomes

All trials analyzed time to first flatus, Meta-analysis showed that time to first flatus in EA or TEA group significantly shorter than that in control group (MD -11.60h, 95%CI -16.19h to -7.02h, I^2=94%, REM) (Figure 3). 13 trials analyzed time to first defecation. Meta-analysis showed that time to first defecation in EA or TEA group significantly shorter than that in control group (MD -12.94h, 95%CI -18.82h to -7.06h, I^2=90%, REM) (Figure 4).

Secondary outcomes

Time to bowel sound recovery in 9 trials (MD -7.25h, 95%CI -10.27h to -4.24h, I^2=85%, REM) (Figure 5), time to first oral feeding in 6 trials (MD -15.76h, 95%CI -23.91h to -7.61h, I^2=47%, REM) (Figure 6) and length of hospital stay in 8 trials (MD -1.19d, 95%CI -1.78d to -0.6d, I^2=44%, REM) (Figure 7) was significantly shorter than that in control group.

Only 2 trials reported the pain scores, and 3 trials reported postoperative analgesic consumption. There was no significant difference of postoperative analgesic consumption between EA and control group (P=0.39) (Figure 8).

3 trials underwent laparoscopic surgeries including minimally invasive surgeries of cholelithiasis, laparoscopic colorectal surgery and laparoscopic gastrectomy. So we analyzed the outcomes in this aspect. Time to first flatus (MD -2.46h, 95%CI -3.96h to -0.96h, I^2=0%, FIXED) (Figure 8), time to first oral feeding (MD -10.73h, 95%CI -16.91h to -4.55h, I^2=0%, FIXED) (Figure 9) and length of hospital stay (MD -1.30d, 95%CI -2.10d to -0.51d, I^2=32%, REM) (Figure 10) were significantly shorter than that in control group.

Discussion and Conclusion

Acupuncture has been applied on treating various gastrointestinal disorders since over two thousand years ago in China, and EA and TEA are modern developed treatments which apply electrical current stimulation simultaneously along with acupuncture. Nowadays, they are regarded as an emerging way to promote early gastrointestinal function recovery. This systemic review concluded that EA or TEA is effective in treating POI after abdominal surgery in clinical application. EA or TEA is associated to shorter time to first flatus, first defecation, bowel sound, first oral feeding and hospital stay. In addition, EA or TEA turns out beneficial for laparoscopic surgery patients as well.

Author year (Ref.)	Sample size (E/C)	Age (years) (E/C)	Abdominal surgery type	EA or TEA procedures	Timing	Control interventions
Chen 2018 [9]	63(33/30)	63.0±9.70/59.0± 8.30	Open & laparoscopic gastrectomy	TEA at unilateral ST36 and PC6 1h twice/day	Post-Postoperative day1	Routine treatment
Deng 2010 [10]	70(35/35)	49.11 ±16.23/44.66 ±19.53	Gastrointestinal and hepatobiliary surgery	EA at bilateral ST36, SP6 and LR3 30min twice/day	Post-Not exactly	Routine treatment
Liu 2017 [11]	42(21/21)	56.0±11.31/56.8±12.16	vascular laparotomy	EA at bilateral ST36, PC6 and ST37 20min twice/day	Pre-Within 24h before sugery	Routine treatment
Liu-2 2017 [12]	60(30/30)	49.00 ±15.78/49.53±11.97	minimally invasive surgery of cholelithiasis	EA at bilateral ST36 and ST37, with heat cornel applied to abdomen 30min twice/day	Post-2h after surgery	Routine treatment
Ma 2009 [13]	60(30/30)	43.2 ±14.3/42.5 ±12.4	appendectomy, colon cancer surgery, cholecystectomy	EA at bilateral ST36 30min three times/day	Post-12h after surgery	Routine treatment
Meng 2010 [14]	85(44/41)	54.3/53.1	colon cancer surgery	EA at bilateral SJ6 and GB34 20min once/day	Post-Postoperative day1	Routine treatment
Ngss 2013 [5]	110(55/55)	67.4±9.7/68.5±10.6	laparoscopic colorectal surgery	EA at ST36, SP6, LI4 and SJ6 20min once/day	Post-Postoperative day1	Routine treatment
Shi 2012 [15]	60(30/30)	53.17±13.49/53.77±13.32	subtotal gastrectomy, colon cancer surgery	EA at bilateral ST36, ST37 and ST39 30min twice/day	Post-6h after surgery	Routine treatment
Wang 2014 [16]	60(30/30)	43.79±11.73/43.93±13.47	abdominal surgery	EA at ST36, ST37, ST39, LI4 and LI11 30min twice/day	Post-Postoperative day1	Routine treatment
Wei 2006 [17]	60(30/30)	37.27±14.69/37.59±13.83	appendectomy, cholecystectomy, subtotal gastrectomy	EA at bilateral ST36, ST37 30min twice/day	Post-6h after surgery	Routine treatment
Wu 2013 [18]	60(30/30)	53.13 ±3.37/57.03±3.23	total/subtotal gastrectomy, colon cancer surgery	EA at bilateral ST36 30min twice/day	Post-Postoperative day1	Routine treatment
Xu 2011 [19]	45(24/21)	57.5 ±12.38/57.91±14.11	abdominal surgery	EA at bilateral ST36 30min twice/day	Post-Postoperative day1	Routine treatment
Yang 2011 [20]	60(31/29)	60.9 ±6.63/62±6.89	colorectal surgery	EA at bilateral ST36, ST37 and ST39 30min once/day	Post-Postoperative day1	Routine treatment
Zhang 2014 [21]	39(19/20)	63±9/60±10	colorectal surgery	EA at bilateral ST36 30min once/day	Post-30min after surgery	Sham EA on bilateral sham ST36 30min once/day
Zheng 2013 [22]	91(47/44)	51.57±17.35/48.13±17.02	abdominal surgery	EA at bilateral ST36 30min once/day	Post-Within 2h after surgery	Routine treatment

Table 1: Characteristics of included clinical EA or TEA trials on treating POI.

The underlying therapeutic mechanism has not been totally revealed. There might be five interpretations as follows: (1) EA at ST36 is possible to protect interstitial cells of Cajal and regulate immunity [23-27]. (2) EA has anti-inflammatory effect such as TNF-α and NO activity [8,24] or anti-stress effect [28]. (3) EA can regulate the secretion of hormones related to small intestinal and colonic motility [8,29,30]. (4) EA or TEA at ST 36 activates the vagus nerve [6,7,31,32] and accelerates jejunal or colonic motility via parasympathetic efferent pathway [33,34]. (5) EA promotes gastric motility via PKC and MAPK signal transduction pathways [35].

The most selected acupoints were ST36 (93.3%, 14/15), ST37 (40%,6/15) and ST39 (20%,3/15). These three acupoints all locate along "Stomach Meridian" on lateral crural region nearby. Based on Chinese acupuncture theory, ST36 called Zusanli is the junction of Stomach Meridian of Foot-Yangming, which plays an important role in balance between Yin and Yang Qi (two opposing principles in nature) in abdomen and relieve distention and constipation. ST37 called Shangjuxu is an acupoint that mainly regulates the colon motility to assist passing gas. Liang et al demonstrated that EA stimulation at ST37 improved function of the enteric nervous system in mouse constipation model [36]. Similarly, Zhu et al. showed that EA at Li11 and/or ST37 improved colonic motility by increased TPH and 5-HT in a cold saline-induced rat model of constipation [30]. ST39 called Xiajuxu is in charge of small intestinal motility, which was traditionally applied to treating intestinal spasm. Shen et al proved that EA and acupoint injection with neostigmine at ST36, ST37/ST39 and Dachangshu acupoint (BL25) could shorten the recovery time of bowel sound and passing gas [37]. So these three

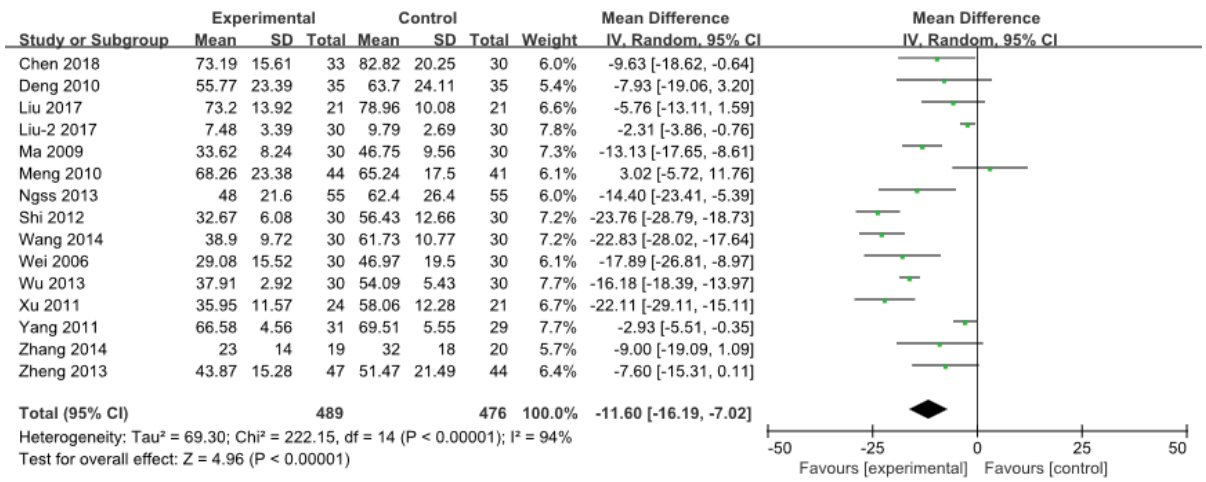

Figure 3: Forest plot of time to first flatus in EA or TEA compared with control group.

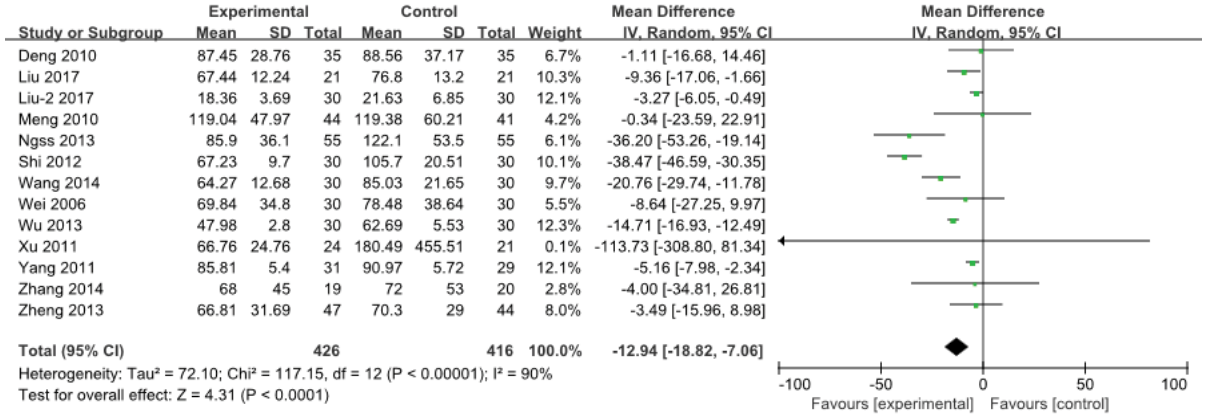

Figure 4: Forest plot of time to first defecation in EA or TEA compared with control group.

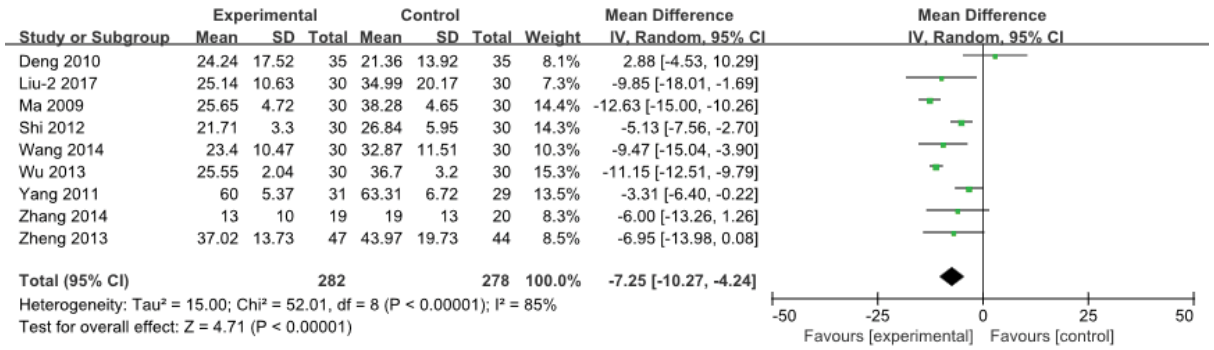

Figure 5: Forest plot of time to bowel sound recovery in EA or TEA compared with control group.

acupoints are most frequently chosen to treating gastrointestinal dysfunction.

The timing of EA stimulation is not inconsistent among the trials. Postoperative day 1 (7/15) was the most chosen one, while only 1 trial applied EA within 24h before surgery. Either pre- or post- surgery EA showed benefit to POI. Interestingly, one animal research showed that EA had a long-lasting effect on gastric activity by increased extracellular ion levels [38]. Based on our clinical experience, it is more feasible to start EA or TEA from postoperative day 1.

To the best of our knowledge, this is the first meta-analysis review focusing on the effectiveness of TEA or EA on treating POI. And our review concluded primary and secondary outcomes that related to POI. However, there are several limitations in this review. First of all, the assessed risk of bias is generally high mostly due to allocation concealment, blinding of participants and personnel and blinding of outcome assessment, which makes the evidence less convincing.

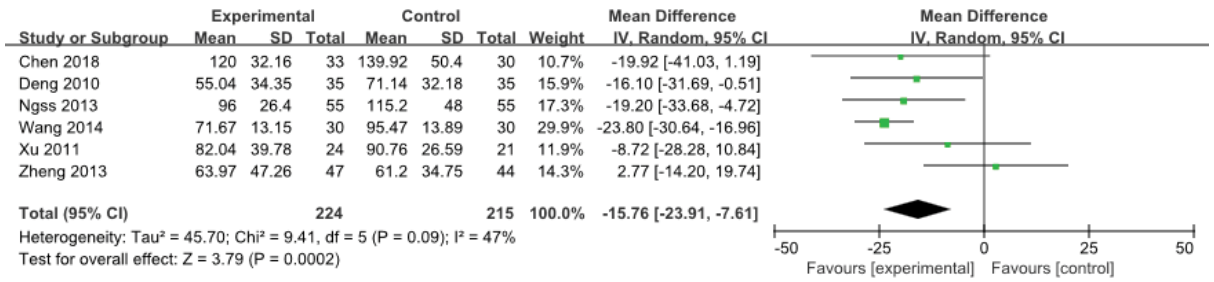

Figure 6: Forest plot of time to time to first oral feeding in EA or TEA compared with control group.

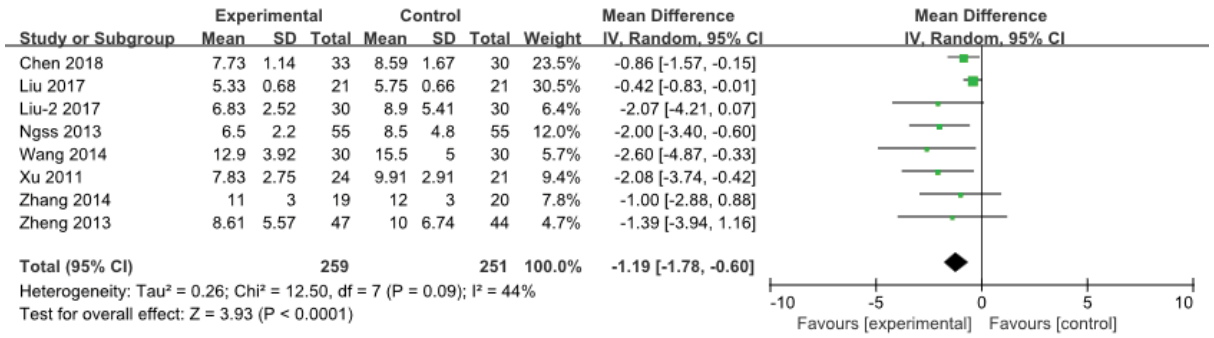

Figure 7: Forest plot of length of hospital stay in EA or TEA compared with control group.

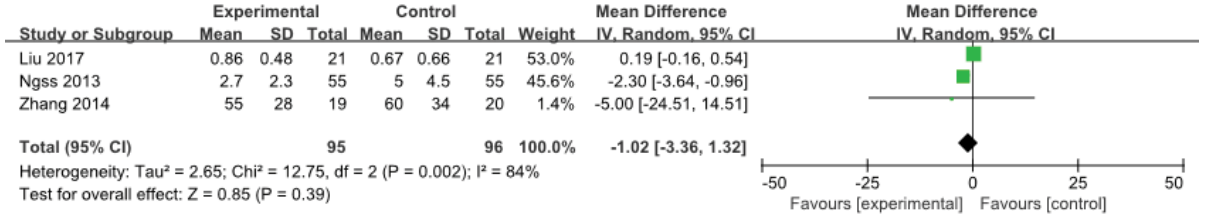

Figure 8: Forest plot of postoperative analgesic consumption in EA or TEA compared with control group.

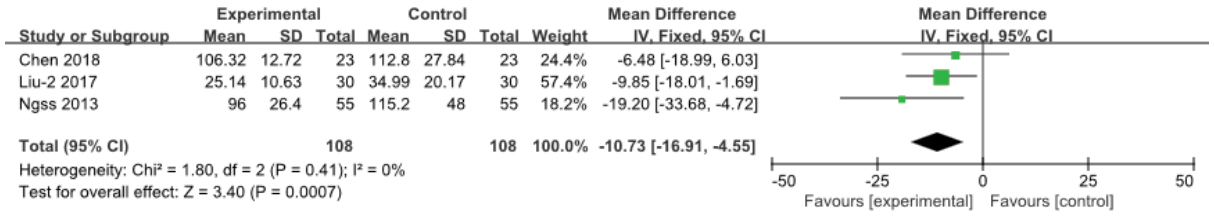

Figure 9: Forest plot of time to first oral feeding in EA or TEA compared with control group by subgroup analysis for laparoscopic surgery.

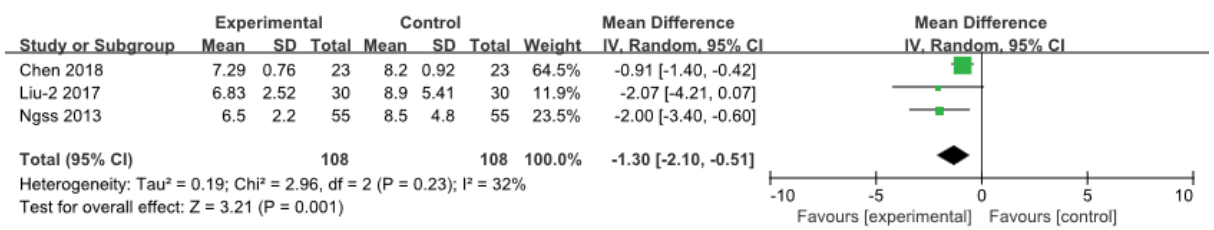

Figure 10: Forest plot of length of hospital stay in EA or TEA compared with control group by subgroup analysis for laparoscopic surgery.

Secondly, there is significant heterogeneity when analyzing primary and secondary outcomes. As table 1 showed, the abdominal surgery type is quite different. Besides, the electroacupuncture protocols are various, such as acupoint selection, EA timing, parameter and duration. Meanwhile, the baseline characteristics of each trial are different. In particular, we divided laparoscopic surgery into subgroup analysis. Laparoscopic surgery is considered as a part of ERAS protocol, whereas, EA or TEA is still capable to accelerate the gastrointestinal motility recovery in additional to minimally invasive surgery. This review failed to analyze pain relief effect by EA because the insufficient data in all included trials. And postoperative analgesic consumption indirectly reflected that EA was not able to relieve postoperative pain after abdominal surgery. Epidural anesthesia is selectively utilized to decrease the pain score of postoperative patients by blocking the afferent and efferent neural pathways [14]. There is a meta-analysis that concluded that acupuncture-point stimulation was effective in pain control for abdominal surgery patients [39]. A prospective study found that intraoperative EA could reduce postoperative pain and analgesic requirement in gynaecological surgery [40]. However, the underlying mechanism has not been determined. As we mentioned before, EA acts as a possible role in regulating parasympathetic efferent pathway. So we remind that future clinical EA or TEA study on pain relief should not perform epidural anesthesia as a confound factor.

Furthermore, there was no adverse event happened except one trial reported acupoint bruise among all these 15 clinical trials. Generally, EA or TEA seems quite safe.

TEA as a novel needless technique has an obvious advantage over EA, it is non-invasive, more convenient and portable, and postoperative patients are prone to accept it mentally. TEA has initially been applied in treatment of functional dyspepsia [41], gastric dysrhythmia [42] and chemotherapy nausea and vomiting [43], and our center recently presented that it could recover post-gastrectomy patients from POI [9]. As far as I am concerned, TEA was an very promising method in the future.

In conclusion, EA or TEA is effective and safe in treating POI after abdominal surgery regardless surgery type. TEA instead of EA is promising in the future. It is still of uncertainty whether EA or TEA is capable of relieving postoperative pain after abdominal surgery. Considering the methodology of included trials is not satisfactory due to the high risk of bias and the trials were basically performed in mainland China, we hope more high-quality clinical trials will be conducted worldwide to confirm its efficacy. The EA protocol or procedure is too diverse, we call on that there will be a professional consensus on this aspect soon. The therapeutic mechanism of EA is controversial, interstitial cells of Cajal function preservation and vagus nerve activation are the most recognized ones. Therefore, more basic researches are desired to be done to give deeper interpretation to this technique.

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Author contribution: CKB, CGF and CJ contributed to the study design, data analysis and Risk of bias assessment and writing, JXL and HY contributed to literature search and screening, WZW, SDK and ZYY contributed to manuscript revision, XWJ and SQM contributed to data extraction and analysis. All authors read and approved the final version of manuscript. CKB and CGF contributed equally to this study.

Research registration number: The protocol of this systematic review was registered in the PROSPERO database (PROSPERO ID: CRD42018084676).

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