

Effects of moxibustion on gastrointestinal function recovery in preventing early postoperative small-bowel obstruction: a meta-analysis

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Background: Moxibustion is widely used in the recovery of gastrointestinal function in East Asian countries, especially in China. This systematic review aims to evaluate the recovery effects of moxibustion on gastrointestinal function in preventing early postoperative small-bowel obstruction (EPSBO).

Methods: The Medline, Embase, PubMed, and the other seven databases were searched independently by two authors. Randomized controlled trials (RCTs) were selected using the PICOS method. The methodological quality was appraised with the Cochrane's risk of bias tool, and the reporting quality of included studies was evaluated by Consolidated Standards of Reporting Trials (CONSORT) and STandards for Reporting Interventions in Clinical Trials of Moxibustion (STRICTOM), respectively. Revman 5.2.0 was used for statistical analysis, and the mean difference (MD) with 95% confidence interval (CI) was performed for effect estimation. Random effects model (REM) and fixed effects model (FEM) were used for pooling data.

Results: A total of 8 RCTs with 693 participants were included. Meta-analysis showed that moxibustion combined with usual care had favorable effects on the time to first flatus (MD –15.15 h, 95% CI: –19.14 to –11.15, 8 studies, I²=85%, P<0.00001, REM), the time to bowel sound recovery (MD –10.35 h, 95% CI: –11.65 to –9.06, 7 studies, I²=0%, P=0.91, FEM), the time to first defecation (MD –18.94 h, 95% CI: –24.53 to –13.36, 3 studies, I²=45%, P=0.16, FEM), and the duration time to abdominal distention (MD –11.7 h, 95% CI: –15.32 to –8.09, 3 studies, I²=0%, P=0.70, FEM) when compared to the controls. No adverse events were reported in the included studies.

Conclusions: Moxibustion may have a beneficial effect on the recovery of gastrointestinal function in preventing EPSBO. However, positive findings should be treated carefully. And rigorous studies with high quality and large samples are warranted.

Keywords: Moxibustion; recovery of gastrointestinal function; early postoperative small bowel obstruction; metaanalysis

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Introduction

Early postoperative small bowel obstruction (EPSBO) is a normal response to tissue injury that occurs within two weeks after abdominal surgeries (1,2). It is usually related to the dysfunction of gastrointestinal motility (3). Patients with small-bowel obstruction often cannot eat, pass flatus, or defecate within five days after a laparotomy or minimally invasive surgery (4). Its clinical features include abdominal pain, vomit, abdominal distension, dyschezia, and radiographic confirmation (5). It is reported that the incidence rates of EPSBO ranged from 0.69% in 1987 (6) to 9.5% in 2002 (1). And it is estimated that the mortality rates widely ranged from 2.4% to 15% (7-9).

Pickleman *et al.* (10) suggested that EPSBO is caused by adhesion, inflammation, and that non-operative therapy should be treated first. Currently, effective prevention and treatment is nasogastric decompression (11). If EPSBO is not resolved, eventual re-operation will be needed. It is not easy to find obstruction sites. And the re-operation can also cause intestinal injury and expand the extent of the operation, thereby resulting in postoperative bleeding, infection, intestinal fistula, and other complications. Moreover, it may reoccur or aggravate bowel obstruction. It not only extends hospitalization (12) and increases costs (13), but also creates discomfort and increases related postoperative complications (e.g., pulmonary complications) (14,15). Therefore, early prevention and treatment of EPSBO are essential.

Thus far, complementary, and alternative therapies, especially Chinese therapy represented by moxibustion, have gained more and more attention from researchers due to their significant therapeutic potency in preventing and treating diseases. Moxibustion (moxa) is a kind of traditional oriental medicine, which originated from the meridian-collateral theory of traditional Chinese medicine (TCM). It has been used in East Asian medicine for more than a thousand years (16). It is a type of thermal therapy that stimulates specific acupoints through healing. This therapy is generated by burning dried herbs called mugwort leaves (*Artemisia vulgaris*). Moxibustion is widely accepted in East Asian countries, as well as throughout the world. Increasing evidence indicates that it can unblock the meridians and collaterals, and regulate the qi and blood function of the spleen and stomach (17), thereby preventing nausea and vomiting (18), improving dyschezia and other main gastrointestinal symptoms (19). As the study reported that moxibustion could improve intestinal motility (20), indicating a potential method in preventing EPSBO. However, insufficient evidence is still lacking to reach a conclusion on this issue.

Herein, this systematic review aims to increase the existing level of evidence by evaluating the critical effects of moxibustion on preventing EPSBO. To our knowledge, this is the first meta-analysis using randomized controlled trials (RCTs) to review the gastrointestinal outcomes on this subject. We presented the following study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting checklist (available at http://dx.doi.org/10.21037/apm-20-1266).

Methods

Search strategy

A total of 10 electronic databases ranging from their inception dates to April 30, 2019, i.e., Cochrane Central Register of Controlled Trials, Manual, Alternative and Natural Therapy Index System, Allied and Complementary Medicine Database (AMED), PubMed, Embase, Medline, and four Chinese medicine databases, including China National Knowledge Infrastructure (CNKI) Database, Wanfang database, Chinese Science and Technology Periodical Database (VIP), and Chinese Biomedical Database (CBM) were searched, as well as databases that contained relevant ongoing trials, such as US equivalent clinical trial registry (http://www.clinicaltrials.gov). The search language was restricted to English and Chinese. The keywords used to search for RCTs were: "moxibustion" OR "moxibustion therapy" OR "moxa-moxibustion" OR "warm-moxibustion" OR "complementary therapies" OR "Chinese medicine" OR "traditional medicine" OR "alternative medicine" OR "complementary medicine" AND "postoperative small-bowel obstruction" OR "postoperative ileus" OR "EPSBO" OR "gastrointestinal function recovery" OR "gastrointestinal disorder" AND

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"randomiz*". All eligible studies were reviewed, and all relevant data were identified by two review authors (L Yang and Y Bian). Any unresolved disagreements were discussed with a third review author (Z Li).

Inclusion criteria

Studies that met the PICOS (population, intervention, comparator, outcome, study type) criteria were included: (I) participants: patients regardless of age, gender, original disease, or type of surgery and anesthesia, who underwent abdominal or gastrointestinal surgery without experiencing postoperative small-bowel obstruction or any complications; (II) interventions: moxibustion at the acupoints alone or moxibustion combined with usual care; (III) comparators: usual care, e.g., fasting, gastrointestinal decompression, postoperative early mobilization and parenteral nutrition support; (IV) outcomes: the time to first flatus, the time to bowel sound recovery, the time to first defecation, and the duration time of abdominal distention. Bowel sounds were recorded at four quadrants of the abdomen with a standard interval (often every 2 h) after operation; and (V) study type: RCTs.

Exclusion criteria

Studies that met the following criteria were excluded: (I) quasi-RCTs and non-RCTs; (II) reviews, case series, case reports, or animal studies; (III) participants who received diagnostic surgery for definite diagnosis (e.g., endoscopy); (IV) intervention, including moxibustion combined with other traditional therapies (e.g., acupuncture, retention enema with Chinese herbal medicine, and acupoint massage); and (V) studies with insufficient outcome data or unsuitable for analysis.

Data extraction and quality assessment

The two reviewers (Y Bian and L Yang) extracted the relevant data independently according to a predefined form. The characteristics of the included studies were author information, date of publication, participant characteristics, sample size, interventions, outcomes, and results. A consensus was reached through a discussion with the third reviewer (Z Li) in case of any discrepancies. The author was contacted to obtain the relevant data if the information was inadequate. The primary effectiveness outcomes assessed were the time to first flatus, the time to bowel sound

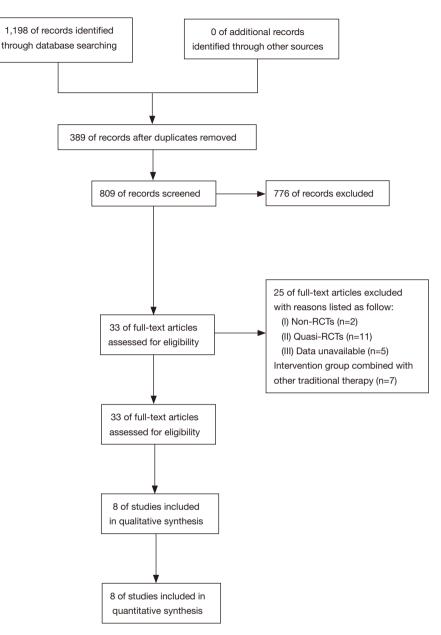
recovery, and the time to first defecation; the secondary effectiveness outcome was the duration time of abdominal distention. The safety outcomes were the adverse events including any complications caused by moxibustion.

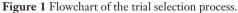
Cochrane's risk of bias tool was used to assess the methodological quality of RCTs (version 5.1.0) (21). The seven items followed a random sequence generation (selection bias), allocation concealment (selection bias), blinding of outcome assessment (selection bias), blinding of participants and personnel (performance bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases. Each research result was judged as "low" for low-degree bias, "high" for high-degree bias, and "unclear" for uncertain bias conditions. Quality of reporting was performed using the Consolidated Standards of Reporting Trials (CONSORT) 2010 (available from http://www.consort-statement.org/) and STandards for Reporting Interventions in Clinical Trials of Moxibustion (STRICTOM) (22) on full-texts. STRICTOM is developed based on the CONSORT, a statement for RCTs, and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) (available from http://www. stricta.info/), a wide guideline for RCTs of acupuncture. Each item of the statements was judged as "Yes" for adequately reported, and "NO" for not adequately reported. Two review authors (Y Bian and L Yang) crossverified the methodological and reporting quality of the eligible studies, respectively. Disagreements were resolved through a discussion with a third review author (Z Li) and consensus.

Statistical analysis

Revman 5.2.0 software (available from the website for free: http://www.ccims.net/revman/download) was used for data analyses. For continuous outcomes of moxibustion, the mean difference (MD) with 95% confidence interval (CI) was used to calculate the effect size. Before merging the statistics, all studies were tested for heterogeneity using the chi-square and I² tests. Forest plots were constructed for each outcome. The fixed-effect model was used if P>0.1 and I²<50%, which indicated homogeneity. Otherwise, a random-effect model was applied for the analysis (23). Subgroup analysis was presented based on the pre-specified study-level characteristics (e.g., type of surgery, type of intervention, and type of comparators). Besides, Egger tests were generated to examine the publication bias, and the trim-and-fill computation was used to estimate the effect of

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publication bias on the interpretation of the results (24).

Results

Study selection

Totally, 1,198 relevant articles were identified, in which 389 duplicate records were excluded. The remaining 809 studies were selected based on their titles and/or abstracts. A total of 776 studies were removed according to the inclusion

criteria, leaving 33 full-text publications for further screening. Finally, eight RCTs (25-32) were included in this review, all of which were published in Chinese. *Figure 1* shows the entire process of trial selection.

Study characteristics

The characteristics of the included trials are presented in *Table 1*. A total of 693 abdominal postoperative participants (345 in the intervention group and 348 in the controls) were

(55)								
	(n) (M/F)	6 30 6 0 6 0	anesthesia		point)			measure
Guo <i>et al.</i> , 2010 (25)	l: 25; C: 25	18-65	General anesthesia, 110–210 min	Colon, rectum	(A) Moxibustion (RN12, ST25, ST37, ST36), plus (B)	(B) Usual care	1 session =5 min, 6 h after surgery, once a day until the first flatus	TFF, TBSR
Guo <i>et al.</i> , 2011 (26)	l: 30; C: 30	18-65	General anesthesia, 65–210 min	Colon, rectum	(A) Moxibustion (RN12, RN8, ST25, ST37, ST36), plus (B)	(B) Usual care	1 session =5 min, 6 h after surgery, once a day until the first flatus	TFF, TBSR
Luo <i>et al.</i> , 2008 (27)	l: 60 (39/21); C: 60 (37/23)	l: 26–65 (42.6); C: 25–64 (43.4)	R	Gall bladder, stomach, spleen, appendix	(A) Moxibustion (RN8), plus (B)	(B) Usual care	1 session =30 min, 6 h after surgery, twice a day until the first flatus	TFF, TBSR
Pan <i>et al.</i> , 2015 (28)	l: 60; C: 66	Я	R	ЯN	(A) Moxibustion (ST36, PC6, RN12), plus (B)	(B) Usual care	1 session =30 min, twice a day, 7 d for one course	tff, tfd, dtad
Wang <i>et al.</i> , 2015 (29)	I: 48 (23/25); C: 47 (24/23)	18–80; I: 45.89±16.02, C: 41.15±18.69	R	Stomach, intestine, appendix, gall bladder	(A) Moxibustion (ST36, SP6), plus (B)	(B) Usual care	1 session =15-20 min, 1 d after surgery, twice a day until the first flatus	TFF, TBSR, TFD
Xia <i>et al.</i> , 2014 (30)	l: 60 (31/29); C: 60 (33/27)	l: 38–85; C: 37–83	R	Stomach, colon, liver, rectum, gall bladder	(A) Moxibustion (ST36, SP6), plus (B)	(B) Usual care	1 session =3-5 min, 6 h after surgery, twice a day until the first flatus	tff, tbsr, dtad
Xu <i>et al.</i> , 2009 (31)	l: 22; C: 20	36–78	NR, 110–240 min	Uterus, ovary	(A) Moxibustion (RN12, RN9, RN8, ST37), plus (B)	(B) Usual care	1 session =20 min, twice a day until the first defecation	TFF, TBSR, TFD
Zhang et al., 2014 (32) I: 40 (28/12); C: 40 (30/10)	l: 40 (28/12); C: 40 (30/10)	l: 36–76 (53≟7.3); C: 50–78 (48±9.6)	R	Stomach	(A) Moxibustion (ST36, ST37, LI4), plus (B)	(B) Usual care	1 session =10–15 min, 6 h after surgery, once a day until 3 days after the first flatus	TFF, TBSR

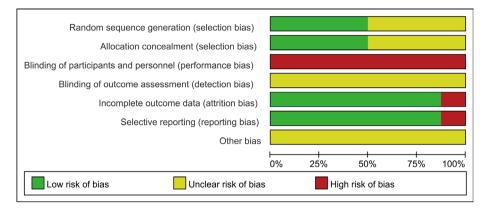


Figure 2 Risk of bias graph.

included.

The experimental interventions of all studies (25-32) used the moxibustion combined with usual care. The controls were usual care, including fasting, gastrointestinal decompression, parenteral nutrition support, and postoperative early mobilization. All studies reported the time to first flatus, seven studies (25-27,29-32) reported the time to bowel sound recovery with clear reporting standards, three studies (28,29,31) reported the time to first defecation, and two studies (28,30) reported the duration time to abdominal distention.

Risk of bias assessment

Although all studies mentioned "random allocation", only four studies (27,29,30,32) reported appropriate methods of sequence generation for the randomization. The remaining studies (25,26,28,31) did not describe the methods of sequence generation. None of the studies stated allocation concealment and dropout/withdrawal or mentioned blinding of outcome assessors. And none of the studies performed blinding to participants and personnel. This approach might be considered as a high risk of bias. The Cochrane risk of bias is presented in *Figures 2,3*.

Reporting quality

All RCTs were appraised based on the 25 standards of the CONSORT statement. In general, the included studies have poor reporting quality. All eligible studies mentioned demographic and clinical baseline characteristics. And most studies reported complete scientific background, intervention, statistical methods, and definition of the

pre-specified primary outcome measures. However, the description of trial design, sample size estimate, methods of random allocation, concealment and blinding, trial limitations, and protocol registering were not fully reported in all included studies. The main detailed results based on CONSORT are listed in Table S1.

All RCTs were also assessed based on the 7 items and 16 sub-items of the STRICTOM. Two items (moxibustion rationale about the type of moxibustion, reasoning for choosing, and treatment regimen about the number, frequency, and duration of moxibustion corresponding with STRICTOM 1a, 1b, and 3) were well-stated in all studies. And all studies mentioned details of moxibustion including names of acupoints, and the time per acupoint. Most studies (25-27,29-31) reported detailed features, procedures, or techniques for moxibustion intervention, as well as control treatment in detail. However, none of the included studies stated the background of the practitioner, information/ explanations to patients, and reasoning for choosing the control treatment. In addition, patient posture, treatment environment, and any precaution measures were not reported in any studies. The detailed findings based on STRICTOM are presented in Table S2.

Meta-analysis

Time to first flatus

All studies reported the time to first flatus, and a randomeffects model was used. The meta-analysis showed that moxibustion combined with usual care had statistically significant effects on shortening the time to first flatus than usual care alone [MD -15.15 h, 95% CI: -19.14 to -11.15, 8 studies, I²=85%, P<0.00001, random effects

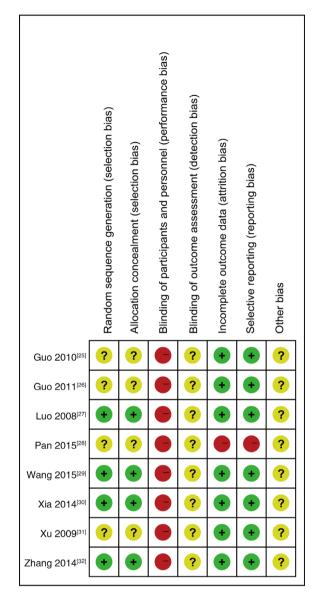


Figure 3 Risk of bias summary.

model (REM)]. The forest plots of the time to first flatus are shown in *Figure 4*. Excluding two studies (28,32), the remaining studies were used for sensitivity analysis, and the heterogeneity disappeared. A fixed-effect model was used for further analysis, which showed that the time to first flatus in the intervention group was still shorter than the time in the controls. Statistical heterogeneity was found among the remaining six studies (25-27,29-31) [MD -11.31 h, 95% CI: -12.84 to -9.78, 6 studies, I²=11%, P=0.35, fixed effects model (FEM); Figure 5].

Time to bowel sound recovery

Seven studies (25-27,29-32) reported the time to bowel sound recovery and a fixed effect model was used. The meta-analysis suggested that moxibustion combined with usual care had statistically significant effects on shortening the time to bowel sound recovery than usual care alone (MD –10.35 h, 95% CI: –11.65 to –9.06, 7 studies, I^2 =0%, P=0.91, FEM; *Figure 6A*).

Time to first defecation

Three studies (28,29,31) reported the time to first defecation and a fixed-effect model was utilized. The result suggested that moxibustion combined with usual care showed better effects on reducing the time to first defecation when compared to the usual care alone (MD -18.94 h, 95% CI: -24.53 to -13.36, 3 studies, I²=45%, P=0.16, FEM; *Figure 6B*).

Duration time of abdominal distention

Two studies (28, 30) reported the duration of abdominal distention, and a fixed-effect model was employed. The meta-analysis showed that moxibustion combined with usual care had better effects on decreasing the duration time of abdominal distention in comparison with the usual care alone (MD –11.7 h, 95% CI: –15.32 to –8.09, 3 studies, I^2 =0%, P=0.70, FEM; *Figure 6C*).

Safety outcomes

No study reported adverse events.

Publication bias

We assessed the possible publication bias using Egger tests, and defined significant publication bias as a P value < 0.1. The results of Egger tests showed P=0.180 for the time to first flatus and P=0.329 for the time to first defecation when compared with the controls, indicating no potential publication bias in the selected studies. In this analysis, there was publication bias in the time to bowel sound recovery (P=0.053). However, further analysis with the trim-and-fill test indicated that this publication bias did not affect the estimates (i.e., no trimming done because data were unchanged).

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Guo 2010 ^[25] 49.33 5.01 25 59.39 4.56 25 15.0% -10.06 [-12.72, -7.40] Guo 2011 ^[26] 48.61 5.25 30 59.19 4.04 30 15.2% -10.58 [-12.95, -8.21] Luo 2008 ^[27] 28.57 12.91 60 44.12 15.22 60 12.8% -15.55 [-20.60, -10.50] Pan 2015 ^[28] 96.5 14.6 60 125.3 15.62 66 12.6% -28.80 [-34.08, -23.52] Wang 2015 ^[29] 36.81 31.93 48 50.34 30.15 47 6.3% -13.53 [-26.02, -1.04] Xia 2014 ^[30] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59, -6.21] Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.61, -9.19] Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83]		mo	xibustio	on	C	ontrol			Mean Difference	Mean Difference
Guo 2010[23] 49.33 5.01 25 59.39 4.56 25 15.0% -10.06 [-12.72, -7.40] Guo 2011[26] 48.61 5.25 30 59.19 4.04 30 15.2% -10.58 [-12.95, -8.21] Luo 2008[27] 28.57 12.91 60 44.12 15.22 60 12.8% -15.55 [-20.60, -10.50] Pan 2015[28] 96.5 14.6 60 125.3 15.62 66 12.6% -28.80 [-34.08, -23.52] Wang 2015[28] 36.81 31.93 48 50.34 30.15 47 6.3% -13.53 [-26.02, -1.04] Xia 2014 ^[30] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59, -6.21] Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.57, -12.83] Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83] -	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Gub 2011 ^[1:43] 48.61 5.25 50 59.19 4.04 50 15.2% -10.58 [-12.95 , -8.21] Luo 2008 ^[27] 28.57 12.91 60 44.12 15.22 60 12.8% -15.55 [-20.60 , -10.50] Pan 2015 ^[28] 96.5 14.6 60 125.3 15.62 66 12.6% -28.80 [-34.08 , -23.52] Wang 2015 ^[29] 36.81 31.93 48 50.34 30.15 47 6.3% -13.53 [-26.02 , -1.04] Xia 2014 ^[40] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59 , -6.21] Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.57 , -12.83] Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57 , -12.83] -12.83	Guo 2010 ^[25]	49.33	5.01	25	59.39	4.56	25	15.0%	-10.06 [-12.72, -7.40]	+
Pan 2015 ^[28] 96.5 14.6 60 125.3 15.62 66 12.6% -28.80 [-34.08, -23.52] Wang 2015 ^[29] 36.81 31.93 48 50.34 30.15 47 6.3% -13.53 [-26.02, -1.04] Xia 2014 ^[30] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59, -6.21] - Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.61, -9.19] - Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83] -	Guo 2011 ^[26]	48.61	5.25	30	59.19	4.04	30	15.2%	-10.58 [-12.95, -8.21]	+
Wang 2015 ^[29] 36.81 31.93 48 50.34 30.15 47 6.3% -13.53 [-26.02, -1.04] Xia 2014 ^[30] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59, -6.21] Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.61, -9.19] Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83]	Luo 2008 ^[27]	28.57	12.91	60	44.12	15.22	60	12.8%	-15.55 [-20.60, -10.50]	
Xia 2014 ^[30] 40.5 15.6 60 52.4 16.2 60 12.1% -11.90 [-17.59, -6.21] - Xu 2009 ^[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.61, -9.19] - Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83] -	Pan 2015 ^[28]	96.5	14.6	60	125.3	15.62	66	12.6%	-28.80 [-34.08, -23.52]	-
Xu 2009[31] 34.2 7.5 22 49.1 10.9 20 12.1% -14.90 [-20.61, -9.19] Zhang 2014[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83]	Wang 2015 ^[29]	36.81	31.93	48	50.34	30.15	47	6.3%	-13.53 [-26.02, -1.04]	
Zhang 2014 ^[32] 72.3 9.5 40 89 8.1 40 14.0% -16.70 [-20.57, -12.83]	Xia 2014 ^[30]	40.5	15.6	60	52.4	16.2	60	12.1%	-11.90 [-17.59, -6.21]	
Zhang 2014 72.5 9.5 40 69 6.1 40 14.0% -16.70 [-20.57, -12.63]	Xu 2009 ^[31]	34.2	7.5	22	49.1	10.9	20	12.1%	-14.90 [-20.61, -9.19]	-
Total (95% CI) 345 348 100.0% -15.15 [-19.14, -11.15]	Zhang 2014 ^[32]	72.3	9.5	40	89	8.1	40	14.0%	-16.70 [-20.57, -12.83]	-
	Total (95% CI)			345			348	100.0%	-15.15 [-19.14, -11.15]	◆
	Test for overall effect:	Z = 7.43	8 (P < 0.	00001)						-50 -25 0 25 50 Favours [moxibustion] Favours [control]

Figure 4 Forest plots of time to first flatus.

	Mo	kibustio	on	c	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean SD Total Mean SD				SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Guo 2010 ^[25]	49.33	5.01	25	59.39	4.56	25	33.2%	-10.06 [-12.72, -7.40]	-
Guo 2011 ^[26]	48.61	5.25	30	59.19	4.04	30	41.7%	-10.58 [-12.95, -8.21]	+
Luo 2008 ^[27]	28.57	12.91	60	44.12	15.22	60	9.2%	-15.55 [-20.60, -10.50]	
Wang 2015 ^[29]	36.81	31.93	48	50.34	30.15	47	1.5%	-13.53 [-26.02, -1.04]	
Xia 2014 ^[30]	40.5	15.6	60	52.4	16.2	60	7.2%	-11.90 [-17.59, -6.21]	
Xu 2009 ^[31]	34.2	7.5	22	49.1	10.9	20	7.2%	-14.90 [-20.61, -9.19]	
Total (95% CI)			245			242	100.0%	-11.31 [-12.84, -9.78]	•
Heterogeneity: Chi ² =	5.60, df =	= 5 (P =	0.35);	l ² = 119	6			-	
Test for overall effect:									-20 -10 0 10 20 Favours [moxibustion] Favours [control]

Figure 5 Sensitivity analysis of time to first flatus.

Discussion

EPSBO is defined as "epigastric pain," "qi stagnancy," "intestinal mass," and "accumulation" in TCM theory. It is a common condition after abdominal surgery. EPSBO is caused by viscera dysfunction, intestinal obstruction, qi stagnation, and blood stasis, which is called "hindering pain." Meanwhile, it is also caused by the consumption of qiand blood, the nutritional deficiency of the viscera, which is also called "deficiency pain." *Danxi Zhu*, a traditional Chinese physician, suggested that the blood runs through the blood vessels smoothly when it's warm. Conversely, the blood will be blocked when it's cold. It's reported that all diseases caused by the stagnation of qi and blood can be treated with moxibustion (33).

Moxibustion therapy is an integral part of TCM, which has been used to treat and prevent diseases for more than 2,500 years. It is less well known in western countries than acupuncture due to the lack of modern medical evidence. Moxibustion is a traditional therapeutic remedy that is performed to obtain heat irritation by burning crushed dry moxa near or on the skin at certain acupoints. This therapy warms the interior and dissipates the cold, regulates qiand resolves stasis, softens and dissolves mass, resuscitates *yang*, and warms the meridians. Modern studies (34,35) found that moxibustion can obtain excellent lasting effects on regulating gastrointestinal motility and promoting gastrointestinal function recovery, which is consistent with our study.

The review of 8 RCTs (693 participants) evaluated the gastrointestinal function of moxibustion on preventing EPSBO. Moxibustion combined with usual care could effectively shorten the time to first flatus, the time to bowel sound recovery, and the time to first defecation. Meanwhile, moxibustion could shorten the duration time to abdominal distention than usual care alone, suggesting that moxibustion may improve the recovery effects of gastrointestinal function and have beneficial effects on preventing EPSBO.

Although the intervention of the studies was about moxibustion, the selection of the moxibustion acupoints was different. The main points were ST36 (6 articles), ST37 (4 articles), RN12 (4 articles), RN8 (3 articles), and ST25 (2 articles). ST36 is located on the stomach meridian. It can

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A	Мо	xibustio	on	c	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Guo 2010 ^[25]	23.42	4.63	25	33.43	4.02	25	29.0%	-10.01 [-12.41, -7.61]	+
Guo 2011 ^[26]	22.8	4.6	30	32.7	4.2	30	33.7%	-9.90 [-12.13, -7.67]	+
Luo 2008 ^[27]	20.98	7.83	60	30.5	10.66	60	15.0%	-9.52 [-12.87, -6.17]	
Wang 2015 ^[29]	34.85	31.89	48	48.34	30.15	47	1.1%	-13.49 [-25.97, -1.01]	
Xia 2014 ^[30]	35.4	13.8	60	46.5	14.3	60	6.6%	-11.10 [-16.13, -6.07]	
Xu 2009 ^[31]	28.3	8.1	22	40.8	12.3	20	4.1%	-12.50 [-18.87, -6.13]	
Zhang 2014 ^[32]	42.5	8.5	40	54.8	9.7	40	10.5%	-12.30 [-16.30, -8.30]	
Total (95% CI)			285			282	100.0%	-10.35 [-11.65, -9.06]	•
Heterogeneity: Chi ² =	2.15, df	= 6 (P =	: 0.91);	l ² = 0%					
Test for overall effect:	Z = 15.6	68 (P < 0	0.0000	1)					-20 -10 0 10 20 Favours [moxibustion] Favours [control]
В									
	Mox	kibustic	on	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Pan 2015 ^[28]	130.5	20.5	60	152.6	17.1	66	71.0%	-22.10 [-28.73, -15.47]	H
Wang 2015 ^[29]	65.52	32.11	48	81.36	42.75	47	13.5%	-15.84 [-31.07, -0.61]	
Xu 2009 ^[31]	108.5	22.5	22	115.7	24.2	20	15.5%	-7.20 [-21.37, 6.97]	
Total (95% CI)			130			133	100.0%	-18.94 [-24.53, -13.36]	•

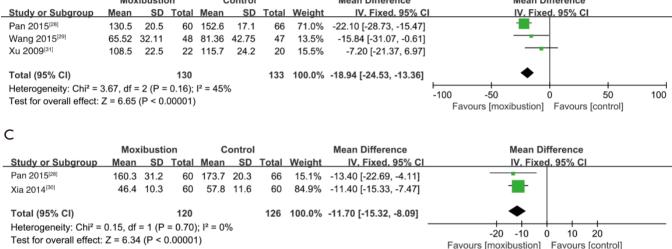


Figure 6 Forest plots within two groups. (A) Time to bowel sound recovery; (B) time to first defecation; (C) duration time of abdominal distention.

adjust the intestine and stomach, harmonize qi and blood, and calm the rising of *qi* in the stomach, thereby promoting gastrointestinal function. RN12 is an intersecting acupoint of the ren channel, small intestine meridian, triple energizer meridian, and stomach channel of foot-yangming. Moxibustion on RN12 can harmonize meridians and collaterals of the intestine and stomach. ST37 is the lower confluent acupoint of large and small intestines with the function of regulating the intestine, promoting the flow of qi, and removing qi stagnation. RN8 is an acupoint of ren meridian that smoothens the qi of the intestine and stomach, regulates *yin-yang* and *qi*-blood, promotes gastrointestinal functions, and alleviates abdomen distention. ST25 is the front *mu* acupoint of the large intestine that can adjust the functions of *zang-fu and* regulate the flow of *qi* to activate stagnancy. Moxibustion on the above acupoints has warm stimulating effects to run qi-blood and meridian, thereby

recovering gastrointestinal function.

This study was the first review about moxibustion for gastrointestinal function recovery in preventing EPSBO. All eligible studies were appraised by Cochrane's risk of bias tool for methodological quality, and assessed by the CONSORT and STRICTOM checklists for reporting quality, respectively. Thus, certain limitations can still be observed.

First, significant heterogeneity of the time to first flatus was observed. This could be explained by the clinical heterogeneity. The outcome of the first flatus, a subjective indicator, was highly dependent on the participant's selfreporting that is difficult to measure with an objective assessment tool. When assessing the outcomes, the clinicians could not rule out the subjective factors and individual differences of the participants. It may eventually cause high heterogeneity. The other subjective outcomes (e.g.,

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abdominal distention or first defecation) were also likely to have the same problem. These factors might influence the credibility of the results to a certain extent. Thus, objective assessment methods are required for future study of EPSBO prevention. Additionally, based on the CONSORT checklist and Cochrane's risk of bias, most studies did not report the methods on how to generate a random sequence. The unclear or less rigorous "randomization" may due to insufficient reporting of generation methods of allocation sequence, allocation concealment, and blinding. It may also influence internal validity and cause the overestimation of the actual therapeutic effect, which might cause selection bias. Because of the specificity of moxibustion therapy, it is hard to perform blinding methods and allocation concealment to participants and personnel. Furthermore, the patient can easily distinguish the sham moxibustion from the real one. That is why all included studies in our review used usual care as a control rather than sham moxibustion. However, a kind of sham moxa device as placebo made it possible to conduct randomized doubleblind, placebo-controlled clinical trials of moxibustion (36). Due to the lack of double-blind control, moxibustion can be easier to achieve a beneficial effect than controls. Hence, more rigorous RCTs with adequate allocation concealment, double-blinding methods, and using sham moxibustion as a placebo are needed to evaluate the true effect of moxibustion in enhancing gastrointestinal function in preventing EBPSO. Moreover, future studies with sample size estimates and adverse events in detail are also recommended.

Second, concerning the STRICTOM statement, none of the studies reported the patient's posture, treatment environment, and background of the treatment providers. The first two aspects are very important external factors that affect the whole process of moxibustion. Because the details of the patient's posture and treatment environment determine whether the results can be repeated. The background of the treatment providers in detail is one of the preconditions of moxibustion procedures to reach standardization and normalization. Any differences regarding qualification or affiliation of practitioners, experience in moxibustion practice may influence the therapeutic effect of moxibustion directly. Moreover, the effect of moxibustion on gastrointestinal function is also associated with details of moxibustion, e.g., the type of moxibustion, the selection of acupoints, the frequency of treatment session, and responses sought. Although the

studies in our review had mentioned the above details, the various kinds of acupoints selected and the intensity of stimulation sought are not equivalent among the studies. The diversity of factors will lead to the incomparability of the outcomes and a high risk of bias among studies. So we suggested that researchers should consider the guideline of STRICTOM to design more rigorous RCTs with high quality about moxibustion.

Third, no studies reported adverse events; thus, the safety of moxibustion on gastrointestinal function cannot be assessed because of insufficient evidence. Only one study (28) reported that three participants in the control group had eventual reoperation, whereas the remaining studies did not report the adverse events. If EPSBO cannot be resolved, when will the subsequent reoperation be needed? Hence, the duration of moxibustion therapy for recovering gastrointestinal function in preventing EPSBO needs to be further studied.

Fourth, all studies were conducted in China, which might cause language bias. Considering that moxibustion is also one of the most widely used medical technology in Korea and Japan. Further studies should include subjects from East Asian countries. Besides, all the studies were selected from the conference paper or academic thesis, and the negative trials might not be reported. Additional databases, including gray literature, should be considered to avoid publication bias.

Fifth, the sample size was relatively small for a country of 1.4 billion people, and the smallest one had 20 cases in the control group (31). To avoid false-positive conclusions, further study should require a large sample size for RCTs to provide high levels of evidence.

Conclusions

In this systematic review, moxibustion might have a beneficial effect on gastrointestinal function recovery in preventing EPSBO. However, the small sample size, high risk of bias, low methodological quality, and poor reporting quality among the included studies influenced the credibility of the positive findings. Future rigorous studies with high quality and large samples are warranted to support the clinical benefit of moxibustion therapy on gastrointestinal function. We also suggest that clinical investigators refer to the extension of the CONSORT and STRICTOM standards for clinical trials of moxibustion to standardize the quality of RCTs and improve research transparency.

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Footnote

Reporting Checklist: The authors have completed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. Available at http://dx.doi.org/10.21037/apm-20-1266

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/apm-20-1266). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table S1 Reporting quality of RCTs based on CONSORT

Section/topic		Checklist item	Guo 2010	Guo 2011	Luo 2008	Pan 2015	Wang 2015	Xia 2014	Xu 2009	Zhang 2014
Title and abstract				000 2011	2000	1 411 2010	Wang 2010	710 2014	Au 2000	2110119 2014
	1a	Identification as a randomized trial in the title	Ν	N	N	N	N	N	N	Ν
	1b		Y	Y	Y	N	Y	Y	N	Y
	ID	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	T	T	T	IN	T	T	IN	T
Introduction										
Background and	2a	Scientific background and explanation of rationale	Y	Y	Y	N	Y	Y	N	Y
objectives	2b	Specific objectives or hypotheses	N	N	N	N	N	Y	N	N
Methods										
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Ν	Ν	Ν	N	Ν	Ν	Ν	Ν
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Participants	40	Eligibility criteria for participants	Y	Y	Y	Y	Y	Y	Y	N
Fanicipants	4a 4b	Settings and locations where the data were collected	r Y	r Y	r Y	r Y	Y	r Y	r Y	Y
Interventions	4b 5	The interventions for each group with sufficient details to	r Y	r Y	Υ Υ	r Y	Υ Υ	r Y	r Y	Y
Interventions	5	allow replication, including how and when they were actually administered	I	1	I	I	I		1	I
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Y	Y	Y	Y	Y	Υ	Y	Υ
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Sample size	7a	How sample size was determined	Ν	N	N	N	Ν	Ν	Ν	Ν
	7b	When applicable, explanation of any interim analyses and	Ν	N	N	N	Ν	Ν	Ν	Ν
		stopping guidelines.								
Randomization										
Sequence generation	8a	Method used to generate the random allocation sequence	Ν	Ν	Υ	Ν	Ν	Y	Ν	Υ
	8b	Type of randomization; details of any restriction (such as blocking and block size)	Ν	Ν	Y	Ν	Ν	Y	Ν	Y
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
	11b	If relevant, description of the similarity of interventions	N	N	N	N	N	N	N	N
Statistical methods	12a	Statistical methods used to compare groups for primary and	Y	Y	Y	Y	Y	Y	Y	Y
		secondary outcomes								
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Results										
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	N	Ν	N	Ν	Ν	Ν	N	Ν
	13b	For each group, losses and exclusions after randomization, together with reasons	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Recruitment	14a	Dates defining the periods of recruitment and follow-up	N	N	N	N	N	Ν	N	Ν
	14b	Why the trial ended or was stopped	N	N	N	N	N	Ν	N	Ν
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Y	Υ	Y	Y	Y	Y	Y	Y
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned	Y	Y	Y	Y	Y	Y	Y	Y
Outcomes and estimation	17a	groups For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% CI)	N	Ν	Ν	Ν	Ν	Ν	N	Ν
connation	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Discussion										
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	Ν	N	Ν	Ν	Ν	Ν	N	Ν
Interpretation	22	Interpretation consistent with results, balancing benefits, and harms, and considering other relevant evidence	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Other information										
Registration	23	Registration number and name of trial registry	Ν	N	N	N	Ν	Ν	Ν	Ν
Protocol	24	Where the full trial protocol can be accessed, if available	Ν	N	N	N	Ν	Ν	Ν	Ν
Funding	25	Sources of funding and other support (such as supply of drugs),	N	Ν	Ν	N	Ν	Ν	N	Ν
	and advant 1	role of funders		NI sector d		1				

CONSORT, consolidated standards of reporting trials; RCTs, randomized controlled trials; Y, adequately reported; N, not adequately reported

Table S2 Reporting quality of RCTs based on STRICOM

Item	Detail	Guo 2010	Guo 2011	Luo 2008	Pan 2015	Wang 2015	Xia 2014	Xu 2009	Zhang 2014
Moxibustion rationale	1a) Type of moxibustion (direct moxibustion, indirect moxibustion, heat-sensitive moxibustion, moxa burner moxibustion, natural moxibustion)	Y	Y	Y	Y	Y	Y	Y	Y
	1b) Reasoning for treatment provided, based on historical context, literature sources, and/ or consensus methods, with references where appropriate	Y	Y	Y	Y	Y	Y	Y	Y
	1c) Extent to which treatment was varied	N	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Details of moxibustion	2a) Materials used for moxibustion (moxa floss, moxa cone, moxa stick, herbal patches, and their sizes and manufacturers)	Ν	Ν	Y	Ν	Y	Y	Ν	N
	2b) Names of acupoints (or location if no standard name) for moxibustion (uni/bilateral)	Y	Y	Y	Y	Y	Y	Y	Y
	2c) Number of moxibustion units and/or moxibustion time per point (mean and range where relevant)	Y	Y	Y	Y	Y	Y	Y	Y
	2d) Procedure and technique for moxibustion (direct/indirect, warming/sparrow-pecking technique, warming needle, moxa box, heat- sensitive moxibustion)	Y	Y	Y	Ν	Y	Y	Y	Ν
	2e) Responses sought (warm feeling, skin reddening, burning pain, heat-sensitization phenomenon)	Y	Υ	Υ	Ν	Y	Y	Y	Ν
	2f) Patient posture and treatment environment	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Treatment regimen	3) Number, frequency, and duration of treatment sessions	Υ	Υ	Υ	Y	Y	Y	Y	Y
Other components of treatment	4a) Details of other interventions administered to the moxibustion group (acupuncture, cupping, herbs, exercises, lifestyle advice)	Ν	Ν	Y	Y	Ν	Y	Y	Y
	4b) Setting and context of treatment protocol, and information and explanation to patients	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Treatment provider background	5) Description of treatment provider (qualification or professional affiliation, years in moxibustion practice and other relevant experience for professional, or any special training in advance for layman)	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
Control or comparator interventions	6a) Rationale for the control or comparator in the context of the research question, with sources that justify this choice	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν
	6b) Precise description of the control or comparator. If another form of moxibustion or moxibustion-like control is used, provide details as for Items 1–3 above.	Ν	Ν	Y	Y	Ν	Y	Y	Y
Precaution measures	7) Precise description of the precaution measures, if any	Ν	Ν	Ν	Ν	Ν	Ν	Ν	Ν

STRICTOM, standards for reporting interventions in clinical trials of moxibustion; RCTs, randomized controlled trials; Y, adequately reported; N, not adequately reported.