Non-needle acupoint stimulation for prevention of nausea and vomiting after breast surgery
A meta-analysis

Ran Sun, BN^ab, Wei Dai, BN^ab, Yang Liu, MD^c, Changli Liu, BN^ab, Yongning Liu, BN^ab, Ying Gong, MN^ab,d, Xiaohong Sun, MN^al, Tieying Shi, MN^h, *, Mingzhi Song, MD, PhD^f,g,.*

Abstract
Background: Breast disease has been a global serious health problem, among women. Surgery is the main treatment for the patients suffering from breast disease. Postoperative nausea and vomiting are still disturbing. Acupoint stimulation, an effective treatment of traditional Chinese medicine, has been used to reduce postoperative nausea and vomiting. Recently, non-needle acupoint stimulation becomes a new intervention. Though several clinical trials have been done, there is still no final conclusion on the efficacy. This Meta-Analysis aims at evaluating the efficacy of non-needle acupoint stimulation for prevention of nausea and vomiting after breast surgery.

Methods: Systematic searches were conducted in PubMed, Embase, Cochrane, and Wanfang Med Online databases for studies. The review period covered from the inception of databases to December 31, 2017. The outcome measures of interest were frequency of nausea, frequency of vomiting, frequency of PONV, verbal rating scale of nausea, and use of rescue antiemetic. Data extraction and risks of bias evaluation were accomplished by 2 independent reviewers using the Cochrane Collaboration Review Manager software (RevMan 5.3.5).

Results: Fourteen randomized controlled trials with a total of 1009 female participants in the non-needle acupoint stimulation group and control group met the inclusion criteria. Although the therapeutically effect on vomiting within postoperative 2 hours was not obvious, non-needle acupoint stimulation still had an important role in reducing nausea and vomiting within postoperative 48 hours. According to Jadad scale, there was moderate quality evidence for the pooled analysis results in this study. In addition, stimulating acupoint by wristband acupressure was more likely to cause adverse reactions.

Conclusion: Non-needle acupoint stimulation can be used for female patients undergoing breast surgery to reduce postoperative nausea and vomiting. Into consideration, we recommend transcutaneous acupoint electrical stimulation on PC6 from 30 minutes before induction of anesthesia to the end of surgery for application. This non-pharmaceutical approach may be promising to promote the recovery of patients after breast surgery.

Abbreviations: LI11 = Quchi, LI4 = Hegu, PC6 = Naiguan, PC8 = Laogong, PONV = postoperative nausea and vomiting, RCT = randomized controlled trial, SJ5 = Waiguan, ST36 = Zusanli, TCM = traditional Chinese medicine.

Keywords: acupoint, breast, meta-analysis, nausea, non-needling stimulation, PONV, vomiting

1. Introduction
Due to advances in diagnostic techniques, diagnosis of breast disease is getting easier. As the main part of this disease, breast cancer is one of the most common causes of death among women. From that, breast disease has been a global serious health problem. Surgery seems to be the only alternative for the patients suffering from most of breast cancers, some kinds of benign breast diseases, and breast reconstruction. Although the curative effect of breast surgery is improving deeply, postoperative complications are still disturbing.

Among the postoperative complications, nausea and vomiting are important ones. Currently, the term “postoperative nausea and vomiting (PONV)” is often defined as nausea or vomiting within 24 hours after surgery. It has an incidence of 20% to 30% after anesthesia. Current thinking suggests that four primary risk predictors including female gender, history of motion sickness, nonsmoking, and the use of postoperative opioids are related to the PONV. Method and duration of anesthesia, and medications used during the surgical procedures are also known be related to PONV. Due to the gender specificity, breast surgery is often followed by a high incidence of PONV. Some
The search strategy for each database is available in Figure 1.

studies and reviews were manually searched for other articles. For all relevant studies, and the reference lists of all these included posed. In addition, experts in this field were consulted to search for other articles. These included studies were contacted for further information. The forms were merged into a single extraction form. Persistent descriptions of withdrawals and dropouts were considered to assess the included studies. These 2 individual forms were used to evaluate the trials: low risk of bias (all the items were measured outcomes. Additionally, the methodological quality of the studies included in this meta-analysis was evaluated using the Jadad scale. Perfect randomization, proper blinding, and adequate descriptions of withdrawals and dropouts were considered to assess the included studies. These 2 individual forms were discussed by all the reviewers until a consensus was reached, and these forms were merged into a single extraction form. Persistent disagreements were settled by. When necessary, the authors of these included studies were contacted for further information. Disagreements were resolved by a third reviewer (Mingzhi Song). When necessary, missing data or further information was sought from the primary authors via email if necessary.

2.2. Inclusion criteria

The studies which involved electrical stimulation or acupressure as a therapeutic intervention for preventing postoperative nausea and vomiting after breast surgery were included. All included studies should meet the following criteria:

(1) studies that had a randomized controlled trial (RCT) design and data collected after the surgery;
(2) electrical stimulation or acupressure was the primary intervention in the treatment group;
(3) sham and/or active control procedure was performed;
(4) primary outcomes included frequency of nausea, frequency of vomiting, frequency of PONV, verbal rating scale (VRS) of nausea, use of rescue antiemetic.

Exclusion criteria were as below:

(1) RCTs including other patients besides who underwent breast surgery;
(2) RCTs using antiemetic, laser acupuncture, traditional acupuncture and massage as controls;
(3) RCTs using traditional acupuncture as the primary interventions in the treatment group;
(4) trials which failed to offer proper data to extract.

2.3. Data extraction

Two reviewers (Wei Dai, Changli Liu) independently evaluated and extracted data from all included studies using a standardized extraction form especially created for this meta-analysis (Table 1). The form contained information of author, country, participants, the methodological aspects of the study, interventions, and measured outcomes. Additionally, the methodological quality of the studies included in this meta-analysis was evaluated using the Jadad scale. Perfect randomization, proper blinding, and adequate descriptions of withdrawals and dropouts were considered to assess the included studies. These 2 individual forms were discussed by all the reviewers until a consensus was reached, and these forms were merged into a single extraction form. Persistent disagreements were settled by. When necessary, the authors of these included studies were contacted for further information. Disagreements were resolved by a third reviewer (Mingzhi Song). When necessary, missing data or further information was sought from the primary authors via email if necessary.

2.3.1. Assessment for risk of bias. Risk of bias assessment of the included RCTs was independently fulfilled by 2 reviewers (Wei Dai, Changli Liu) using the Cochrane criteria. Discrepancies were resolved by discussion. Risk of bias of the following domains were assessed random sequence generation (selection bias), allocation concealment (selection bias), binding of participants and personnel (performance bias), binding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other potential sources of bias. Here, due to the characteristic of acupoint stimulation RCTs, other bias was defined as whether the study introduced the detailed operation method. Three levels were used to evaluate the trials: low risk of bias (all the items were in low risk of bias), high risk of bias (at least 1 item was in high risk of bias) and unclear risk of bias (at least 1 item was in unclear risk of bias). For examples, as for “low risk” of bias for the domain of random sequence generation, the investigators should describe a random component in the sequence generation process such as referring to a random number table; using a computer random number generator or coin tossing.
2.4. Statistical analysis

Meta-analysis was performed by using Review Manager V5.3. Continuous data were presented as mean difference (MD) and its 95% confidence intervals (CI). Heterogeneity was examined using the $I^2$ test, where $I^2$ values of 50% or more were considered to be indicative of a substantial level of heterogeneity. Random effects model was employed to present MD. Based on different outcome measures, if significant heterogeneity between studies was detected, the subgroup analysis would be conducted to investigate possible causes from clinical perspectives. Regarding dichotomous data, results were presented as RRs with 95% CIs, using random-effects model.

3. Results

3.1. Literature search

The process of literature search was shown in Figure 1. A total of 199 potential trials were identified via the primary search strategy. After duplicates remove, 63 studies remained. Twenty-four potentially relevant studies were evaluated for eligibility. Then, 10 studies with unavailable data were excluded. Finally, Fourteen RCTs were included in the current meta-analysis.

3.2. Study characteristics

The characteristics of the 14 studies that met the inclusion criteria were shown in Table 1. This analysis included a total of 1009 female patients. And the sample size ranged from 50 to 112. And 10 included studies were conducted in China, 1 in Spain, 1 in the United States, 1 in South Korea and 1 in Denmark.

Two patterns of non-needle acupoint stimulation were included in these studies: electrical stimulation (N=12 trials) and acupressure (N=2 trials). The most frequently used acupoint points were PC6 (N=14 trials), LI4 (N=5 trials), ST36 (N=4 trials), LI11 (N=2 trials) and SJ5 (N=1 trial). Moreover, seven trials adopted bilateral acupoints stimulation and others performed the unilateral acupoints stimulation. Participants received acupoints stimulation more than 30 minutes.
Table 1
Characteristics of the included studies.

| Authors            | Study design | Country     | Participants | Surgery method | Treatment | Control condition | Intervention method | Intervention time | Measure | Outcome measurement                          | Jadad score |
|--------------------|--------------|-------------|--------------|----------------|-----------|--------------------|---------------------|-------------------|---------|---------------------------------------------|-------------|
| Alcaraz et al 2014 | RCT          | Spain       | 102 Patients | Elective breast surgery | Acupressure | A cotton ball in PC6 acupoint | Stiper puncture in PC6 acupoint | 30 min before anaesthesia | PONV    | Statistically significant reduction of PONV after acupuncture stimulation | 2           |
| Gan et al 2004     | RCT          | The United States | 50 Patients | Major breast surgery | Electrical stimulation | Placement of electrodes without stimulation | HANS electrode in bilaterally PC6 acupoints | 30–60 min from induction of anesthesia to the end of surgery | VRS of nausea in PO2H; vomiting in PO24H; URA in PO24H | Statistically significant reduction of VRS of nausea in PO2H and of URA in PO24H after acupuncture stimulation | 4           |
| Gu et al 2009      | RCT          | China       | 59 Patients  | Modified radical mastectomy | Electrical stimulation | Routine nursing care | HANS electrode in PC6 acupoint | 30 min before surgery | PONV; VRS of nausea in PO2H; nausea in PO6H, PO12H, PO24H, PO48H; vomiting in PO6H, PO12H, PO24H, PO48H and vomiting in PO24H | Statistically significant reduction of PONV, nausea in PO6H, PO12H, PO24H, PO48H and vomiting in PO24H after acupuncture stimulation | 3           |
| Hu et al 2014      | RCT          | China       | 60 Patients  | Radical mastectomy | Electrical stimulation | Placement of electrodes without stimulation | Hwato electrode in bilaterally PC6, ST36 and L4 acupoints | 30 min before surgery | PONV | Statistically significant reduction of PONV after acupuncture stimulation | 2           |
| Kim et al 2004     | RCT          | South Korea | 66 Patients  | Minor breast surgery | Electrical stimulation | Placement of device without stimulation | ReliefBand device in the PC6 acupoint | 10 min before the end of surgery and lasting for 24 h | PONV; nausea in PO6H; nausea in PO24H; vomiting in PO6H; vomiting in PO24H; URA in PO24H | Statistically significant reduction of PONV, nausea in PO6H, PO24H and vomiting in PO24H after acupuncture stimulation | 2           |
| Lin et al 2015     | RCT          | China       | 60 Patients  | Segmental mastectomy | Electrical stimulation and auricular acupoints stimulation | Electrode in the PC6 and LI11 acupoints; magnetic paste in auricular acupoints | 20 min before surgery and lasting to the end of the surgery | PONV | PONV was not significantly different between groups | 2           |
| Liu et al 2011     | RCT          | China       | 86 Patients  | Modified radical mastectomy | Electrical stimulation | Electrical stimulation in sham acupoint | HANS electrode in PC6 acupoint | 30 min before surgery | Vomiting in PO24H; URA in PO24H | Statistically significant reduction of vomiting in PO24H and URA in PO24H after acupuncture stimulation | 2           |

(continued)
### Table 1 (continued)

| Authors | Study design | Country | Participants | Surgery method | Treatment | Control condition | Intervention method | Intervention time | Measure | Outcome measurement | Jadad score |
|---------|--------------|---------|--------------|----------------|-----------|-------------------|--------------------|-------------------|---------|---------------------|-------------|
| Majholm and Moller, 2011[21] | RCT | Denmark | 112 Patients | Breast surgery with or without axillary clearance | Acupressure | Acupressure stimulation in sham acupoint | Vital-Band wristband in PC6 acupoint | Before induction of anesthesia and lasting to PO24H | Nausea in PO24H; vomiting in PO24H; nausea in recovery room; vomiting in recovery; URA in PO24H | Nausea in PO24H, vomiting in PO24H, nausea in recovery room, vomiting in recovery and URA in PO24H were not significantly different between groups | 5 |
| Pan et al 2014[22] | RCT | China | 106 Patients | Breast surgery | Electrical stimulation | Routine nursing care | HANS electrode in bilaterally PC6 and LI11 acupoints | From the arrival of operation room to the end of surgery | Nausea in PO24H; vomiting in PO24H; nausea in recovery room; vomiting in recovery | Nausea in PO24H, nausea in PO48H; vomiting in PO24H and vomiting in PO48H after acupoint stimulation | Statistically significant reduction of nausea in PO24H, nausea in PO48H, vomiting in PO24H and vomiting in PO48H after acupoint stimulation | 2 |
| Wang et al 2017[23] | RCT | China | 68 Patients | Modified radical mastectomy | Electrical stimulation | Placement of electrodes without stimulation | HANS electrode in bilaterally PC6, L4 and ST36 acupoints | 30 min before induction of anesthesia | PO/NV | Statistically significant reduction of PO/NV after acupoint stimulation | 3 |
| Yu et al 2010[24] | RCT | China | 60 Patients | Radical mastectomy | Electrical stimulation | Routine nursing care | HANS electrode in PC6, SJ5, L4 and PC6 acupoints of the affected side | 30 min before induction of anesthesia | PO/NV | Statistically significant reduction of PO/NV after acupoint stimulation | 2 |
| Yu et al 2012[25] | RCT | China | 60 Patients | Modified radical mastectomy | Electrical stimulation | Electrical stimulation | HANS electrode in bilaterally PC6 acupoints | 30 min before induction of anesthesia | VRS of nausea in PO2H | VRS of nausea in PO2H was not significantly different between groups | 2 |
| Zhang et al 2014[26] | RCT | China | 59 Patients | Cosmetic breast surgery | Electrical stimulation | Placement of electrodes without stimulation | Hwato electrode in bilaterally L4, PC6 and ST36 acupoints | 30 min before induction of anesthesia | Nausea in recovery room | Statistically significant reduction of nausea in recovery room after acupoint stimulation | 4 |
| Zhou et al 2017[27] | RCT | China | 60 Patients | Modified radical mastectomy | Electrical stimulation | Routine nursing care | Electrode in bilaterally PC6, L4 and ST36 acupoints | 30 min before induction of anesthesia and lasting to the end of surgery | Nausea in PO6H; nausea in PO24H; nausea in PO48H; vomiting in PO6H; vomiting in PO24H; vomiting in PO48H | Statistically significant reduction of nausea in PO6H and vomiting in PO24H and vomiting in PO48H after acupoint stimulation | 2 |

G1 = the non-needle acupoint stimulation group, G2 = the control group, RCT = randomized controlled trial, URA = use of rescue antiemetic, Y = years old.
All the trials began the intervention before surgery and most of the intervention stopped at the end of surgery.

Methods of control groups consisted placement of sham stimulation (N=6 trials), stimulation in sham acupoint (N=3 trials), routine nursing care (N=4 trials) and auricular acupoints stimulation (N=1 trial).

Nausea and vomiting were measured by frequency of PONV, frequency of nausea (PO6H, PO12H, PO24H, and PO48H), frequency of vomiting (PO6H, PO12H, PO24H, and PO48H), frequency of nausea in recovery room, frequency of vomiting in recovery room, VRS and use of rescue antiemetic.

Furthermore, in these studies, all the included participants underwent general anesthesia.

### 3.3. Risk of bias assessment

Figure 2 summarized the risk of bias in the included studies. Randomization was performed in all 14 RCTs. Four studies adopted random number table.\cite{17,24,26,27} Two studies used opaque envelopes.\cite{15,21} One study performed the random number generator.\cite{15} One used SPSS software to generate random numbers.\cite{22} The randomization methods of other trials could not be obtained from the articles. Three studies introduced allocation concealment.\cite{15,21,26} Due to the inaccessibility of the trial protocol, reporting bias was generally “unclear” in the included RCTs. Only 2 trail protocols can be retrieved with the register numbers.\cite{21,26} One trial\cite{21} was considered as having a low risk of reporting bias while another\cite{26} was elected as “high risk”. There were only 4 trials\cite{15,21,23,26} performed a double-blinded method, because of the characteristics of acupoint stimulation. Two trials\cite{16,21} reported 23 dropouts, and only 1 of them provided no details on its dropout. Two trials\cite{20,22,27} were considered as having an unclear risk of other bias because of the lack of detailed description on non-needle acupoint stimulation.

### 3.4. Meta-analysis outcome

Based on various outcome measures after non-needle acupoint stimulation and control of the included studies, different pooled data of 14 RCTs were used in meta-analysis, respectively. The effect estimates of non-needle acupoint stimulation were shown in the forestplots (Figs. 3–6).

### 3.5. PONV

Half of the included studies measured and recorded the results of PONV after non-needle acupoint stimulation. Seven trials (N=475)\cite{14,16,19,23,24} reported that non-needle acupoint stimulation might more effectively reduce PONV, compared with the control (RR: 0.56, 95% CI: 0.43–0.72, N=475, and $I^2 = 0\%$; Fig. 3).

### 3.6. Nausea

#### 3.6.1. Nausea within PO6H

Nausea within PO6H in non-needle acupoint stimulation groups was compared with that in the control groups. Data from 3 studies\cite{16,18,27} indicated that nausea during this period (N=185) had an evidence of significant difference (RR: 0.46, 95% CI: 0.29–0.72, N=185, and $I^2 = 0\%$; Fig. 4A). This result indicated that non-needle acupoint stimulation could reduce nausea within PO6H compared with that in the control group.

#### 3.6.2. Nausea within PO12H

There was a significant difference about the results of nausea within PO12H. The combination of these 3 trials\cite{16,27} revealed that non-needle acupoint stimulation might more favorably reduce nausea within PO12H (RR: 0.40, 95% CI: 0.22–0.73, N=119, and $I^2 = 0\%$; Fig. 4B).

#### 3.6.3. Nausea within PO24H

The analysis of data obtained from five studies\cite{16,18,21,22,27} indicated heterogeneity with respect to nausea within PO24H ($P<.05$, $I^2=49\%$). The
decreasing change in non-needle acupoint stimulation group was statistically significant (RR: 0.61, 95% CI: 0.42–0.88, N=399, and $I^2=49\%$; Fig. 4C). In this result, there were 2 kinds of non-needle acupoint stimulation, but only 1 trial performed acupressure. So, when the trial by Majholm\(^{[21]}\) was excluded, the heterogeneity decreased to 0% (RR: 0.52, 95% CI: 0.39–0.70, N=291, and $I^2=0\%$; Fig. 4C). The remained trials revealed that, compared with control intervention, transcutaneous electrical acupoint stimulation could reduce vomiting within PO6H compared with that in the control group.

3.7.2. Vomiting within PO12H. There were 7 trials\(^{[15,16,18,20,22,27]}\) focus on results of vomiting within PO24H after non-needle acupoint stimulation. The combination of these data had an evidence of significant difference and revealed that non-needle acupoint stimulation might more favorably reduce vomiting within PO24H (RR: 0.60, 95% CI: 0.44–0.81, N = 537, and $I^2=0\%$; Fig. 5C).

3.7.3. Vomiting within PO48H. There were 3 studies\(^{[16,22,27]}\) measured nausea within PO48H of the participants (N=226) after non-needle acupoint stimulation. There was a significant difference in nausea within PO48H (RR: 0.56, 95% CI: 0.39–0.83, N=225, and $I^2=0\%$; Fig. 4D). This result indicated that nausea within PO48H could be improved by non-needle acupoint stimulation.

3.6.4. Nausea within PO48H. Three of the included studies\(^{[16,22,27]}\) measured nausea within PO48H of the participants (N=226) after non-needle acupoint stimulation. There was a significant difference in nausea within PO48H (RR: 0.56, 95% CI: 0.39–0.83, N=225, and $I^2=0\%$; Fig. 4D). This result indicated that nausea within PO48H could be improved by non-needle acupoint stimulation.

3.6.5. Nausea in the recovery room. Two studies\(^{[21,26]}\) were pooled and analyzed for the results of nausea in the recovery room. There was not a significant difference of nausea between non-needle acupoint stimulation and the control intervention in the recovery room (RR: 0.57, 95% CI: 0.30–1.05, N=176, $I^2=0\%$, $P>0.05$; Fig. 4E).

3.6.6. VRS of nausea within PO2H. Three studies\(^{[15,16,25]}\) measured nausea by using VRS in PO2H. With no statistical significance, this result revealed that non-needle acupoint stimulation could not relieve nausea within PO2H (MD:–0.47, 95% CI: –0.97–0.03, N=169, and $I^2=0\%$, $P>0.05$; Fig. 4F).

3.7. Vomiting

3.7.1. Vomiting within PO6H. There were 3 studies\(^{[16,18,27]}\) recorded vomiting within PO6H after non-needle acupoint stimulation. Data obtained from these studies revealed that vomiting in PO6H (N=186) had no statistical significance ($P>0.05$). This result indicated that non-needle acupoint stimulation could not reduce vomiting within PO6H compared with that in the control group (RR: 0.48, 95% CI: 0.23–1.02, N=185, and $I^2=0\%$; Fig. 5A).

3.7.2. Vomiting within PO12H. The analysis of data obtained from 2 studies\(^{[18,27]}\) indicated low significant heterogeneity and no statistical significance with respect to vomiting within PO12H ($P>0.05$, $I^2=22\%$). There was no evidence of significant difference in vomiting within PO12H (RR: 0.35, 95% CI: 0.10–1.2, N=119; Fig. 5B).

3.7.3. Vomiting within PO24H. There were 7 trials\(^{[15,16,18,20,22,27]}\) focus on results of vomiting within PO24H after non-needle acupoint stimulation. The combination of these data had an evidence of significant difference and revealed that non-needle acupoint stimulation might more favorably reduce vomiting within PO24H (RR: 0.60, 95% CI: 0.44–0.81, N = 537, and $I^2=0\%$; Fig. 5C).

3.7.4. Vomiting within PO48H. Three studies\(^{[16,22,27]}\) were pooled and analyzed for the results of vomiting within PO48H. Data from these studies had a negligible statistically heterogeneity ($P<0.05$, $I^2=3\%$). There was a significant difference of vomiting between non-needle acupoint stimulation and the control intervention during postoperative 48 hours (RR: 0.57, 95% CI: 0.35–0.92, N=225; Fig. 5D). This result indicates that non-needle acupoint stimulation might improve vomiting within PO48H.

3.7.5. Vomiting in the recovery room. Two of the included studies\(^{[21,26]}\) recorded vomiting of the participants (N=175) in the recovery room. The results of non-needle acupoint stimulation groups were compared with that of the control groups (Fig. 5E). There was no evidence of significant difference in vomiting in PO12H (RR: 0.35, 95% CI: 0.10–1.2, N=120, $I^2=0\%$, $P>0.05$; Fig. 5E).

3.7.6. Use of rescue antiemetic. The analysis of data obtained from 5 studies\(^{[14,15,16,20,21]}\) indicated a statistical significance with respect to use of rescue antiemetic within PO24H. This result showed that non-needle acupoint stimulation had a positive effect on reducing use of rescue antiemetic within PO24H compared with that in the control group (RR: 0.60, 95% CI: 0.44–0.83, N=112, and $I^2=0\%$; Fig. 6).

3.8. Adverse events

Only 2 study reported adverse events in the intervention or control group. Majholm and Møller reported 77 patients with wrist and hand side effects such as redness, swelling, tenderness, and paresthesias that were caused by the wristbands.\(^{[21]}\)

4. Discussion

Despite the fact that the curative effect of antiemetic on PONV has been widely proved, the avoidless side-effect remains a
Figure 4. The forest plots indicate the differences in nausea within PO6H (A), nausea within PO12H (B), nausea within PO24H (C), nausea within PO48H (D), and nausea in the recovery room (E).
Figure 5. The forest plots indicate the differences in vomiting within PO6H (A), nausea within PO12H (B), vomiting within PO24H (C), vomiting within PO48H (D), VRS of nausea within PO2H (E), and nausea in the recovery room (F).

Figure 6. The forest plot indicates the difference of use of rescue antiemetic between the non-needle acupoint stimulation group and control group.
challenges to both surgeons and nurses.\textsuperscript{1,26} There are reports that the female patients undergoing different kinds of breast surgery have a stronger tendency to suffer from PONV.\textsuperscript{15} Faced with these problems, various methods from clinical to nursing aspects such as surgery methods changing from mastectomy to modified radical mastectomy and from usual care to comfortable nursing have been applied to minimize the incidence of nausea and vomiting after breast surgery. However, the safe and effective method still remains unknown.

Acupoint stimulation is a complex, ritualistic somatosensory intervention with multiple components. Acupuncture is an original and important method of acupoint stimulation. Along with the development of TCM, more and more researchers apply acupoint stimulation to settle complications after treatment. Because of the particularity of acupuncture, reliance on skilled acupuncturist becomes the crucial part of treatment as well as limits the dissemination and generalization. The problem has been resolved, since instrumented replacements of acupuncture like transcutaneous electrical acupoint stimulation and acupressure are widely used to reduce postoperative complications. Particularly, studies about nausea and vomiting with satisfactory curative effects can often be found.\textsuperscript{17–20}

According to TCM constitutional theory, most of patients undergoing breast surgery have Qi-stagnation constitution or Qi-deficiency constitution.\textsuperscript{18} And patients with PONV often have Qi-deficiency constitution. By stimulating acupoints, meridian and collaterals could be activated to tonify and promote Qi. Neiguan, for example, is an important acupoint of pericardium meridian, which has an effect on regulating Qi and decreasing inverse. Additionally, stimulating Laogong, Waiquan, Zusanli, Hegu or Quchi could also be used for reducing PONV by activating different meridians. Therefore, theoretically, acupoint stimulation may prevent nausea and vomiting after breast surgery. In response to this, some clinical researches have been done to explore practical effects.\textsuperscript{14–27} Unfortunately, conclusions from these researches are not the same. Comprehensive summary and analysis become more urgent.

Through rigorous reviewing and screening, we finally collected 14 trials to complete a meta-analysis to explore the result whether acupoint stimulation could have effect on reducing PONV after the breast surgery or not. In this review, unclear risk of bias was found in most of the included trials. Description of blind method and allocation concealment were the main reason that was prone to prevent the analysis of a subjective outcome. Jadad scale was applied to assess all selected trials, a high-quality study should have the Jadad score equal to or more than 3.\textsuperscript{13} All of included studies had the Jadad score no less than 2. There were nine trials with Jadad score 2. Combining particularity of acupoint stimulation and elaborate evaluation, reviewers found that design and implementation of these trials were reasonable and reliable. Therefore, these trials with Jadad score 2 were also included. These enrolling criteria allowed us a moderate quality analysis.

Methods of evaluating nausea and vomiting mainly include frequency, VRS of nausea, and use of rescue antiemetic. Here, the included outcomes were within PO48H. According to the results of analysis, nausea could be reduced by acupoint stimulation in the early phase after breast surgery (0–12H). However, acupoint stimulation had no reducing effect on vomiting at the same time. Nausea was often treated as the early symptom of vomiting. From the data of included studies, the frequency of vomiting in the early phase was less than other phases. This reasonably explained why pooled analysis did not support the effectiveness of acupoint stimulation for reducing vomiting. PO24H was thought to be the medium phase in this study. Frequency of PONV, frequency of nausea, and frequency of vomiting were selected to assess the curative effect of acupoint stimulation in the early and medium phases (0–24H). Analysis results kept consistency showing that acupoint stimulation was able to markedly reduce the occurrence of nausea and vomiting. In this period, frequency of nausea and vomiting increased. Although there was the difference of included patients, those research results about other kinds of surgery still supported our viewpoint.\textsuperscript{13,9} Analyzing the outcome of nausea within PO24H, we only found heterogeneity appearing in this result. Then, according to the classification of non-needle acupoint stimulation, a subgroup analysis was completed and showed no heterogeneity. Between electrical stimulation and acupressure, there may be some differences such as operation, curative effect and so on. This explained the reason of the existence of heterogeneity. Within PO48H, the possibility of nausea and vomiting continues to increase for postoperative patients. The pooled analysis of 2 outcomes including nausea and vomiting suggested the effect of non-needle acupoint stimulation on reducing nausea and vomiting after breast surgery continue until PO48H. In addition, adverse events were reported in only 1 included study, which adopted wristbands to stimulating acupoint. However, these commercialized wristbands caused redness, swelling, tenderness and paresthesias. The occurrence of adverse events was related to tight wearing.

In terms of the choice of non-needle acupoint stimulation, electrical stimulation was more popular. The most common acupoint is PC6 that was selected in all the included studies. This was in line with trends in research that often recommended PC6 as the acupoint to prevent nausea and vomiting. Acupoint selection could be either bilateral or unilateral. Meanwhile, other acupoints also could be chose to play a synergistic role of reducing nausea and vomiting. Working time was generally specified as from 30 minutes before induction of anaesthesia to the end of surgery. When electrical stimulation was selected, working electric current was different among various instruments. Without the need of professional acupuncturist, non-needle acupoint stimulation has been gradually popularized in clinical nursing practice and revealed the potential of replacing anesthetic. Moreover, there was an inevitable question that the use of acupressure is often limited to wristband structures that cause uncomfortable or tight feelings.\textsuperscript{140} The presentation of adverse events may lead to reduce the usage of acupoint stimulation by wristband. Therefore, transcutaneous electrical acupoint stimulation seems safer than acupressure by wristband acupressure.

Most of studies that were included in this review had unclear risk of bias, recruited a small number of patients, and provided sparse data on most of our pre-established outcomes of interest. So, the pooling results in these meta-analyses were affected. Heterogeneity existed in the aspects of type of surgery, duration of surgery and anesthesia. From the viewpoint of gastrointestinal stimulation and nervous stimulation, laparoscopic abdominal surgery, gynecological surgery, and procedures involving the ear, nose and throat were easier to induce PONV.\textsuperscript{41} However, the difference of increasing PONV among different breast surgeries could not be ignored. Duration of surgery always had effect on incidence of PONV.\textsuperscript{42} Here, due to the selection of different breast surgery, the duration of surgery varied greatly from study to study. Anesthetic agents were also related to PONV. The use of anesthetic inhalation agents like nitrous oxide has long been associated with an increase in the risk of PONV.\textsuperscript{41} On the
contrary, total intravenous anesthetic using propofol has been found to reduce PONV.\[41\] Therefore, heterogeneity in anesthetic agents was obvious in the included studies. Furthermore, there were only 2 studies about acupressure. Others selected electroacupuncture as the therapeutic method for PONV. For reducing PONV of breast surgery, the different between acupressure and electroacupuncture was no conclusion. But heterogeneity in acupuncture as the therapeutic method for PONV. For reducing nausea and vomiting, the duration of surgery and use of anesthetic drug. Furthermore, there were only consistent measurements and more standard data records would help to more accurately confirm the final conclusion.

5. Conclusion
The results of this meta-analysis of fourteen relatively studies showed that non-needle acupoint stimulation was an effective method for reducing nausea and vomiting of female patients after breast surgery. Because of the limited number and quality of included studies, this conclusion could not be considered a conclusive statement. As one of the most commonly used non-pharmacological therapy, acupoint stimulation was especially suitable for solving PONV by nurses. It could be recommended in patients undergoing breast surgery with moderate-high risk for PONV or drugs contraindications. The routine operation was application of transcutaneous acupoint electrical stimulation on PC6 from 30 minutes before induction of anesthesia to the end of surgery. The comparison among various methods and different stimulating acupoints will be a meaningful topic for future studies. Although the quantity of Chinese studies about acupoint stimulation mounted up, more well-designed studies should be carried out.

Author contributions
Conceived and designed this meta-analysis: STY, SMZ and SR. Performed this meta-analysis: SR, DW and LCL. Analyzed the data: SMZ and SR. Contributed to software analysis and review of the paper: SR, DW, LCL, LYN, XY, SXH, STY and SMZ. Wrote the paper: SR and SMZ. Revised the paper: LY

References
[1] Hartmann LC, Sellers TA, Frost MH, et al. Benign breast disease and the risk of breast cancer. N Engl J Med 2003;351:229–37.
[2] Harbeck N, Guent M. Breast cancer. Lancet 2017;389:1134–50.
[3] Candiotti KA, Birnbach DJ, Lubarsky DA, et al. The impact of pharmacogenomics on postoperative nausea and vomiting: do CYP2D6 allele copy number and polymorphisms affect the success or failure of ondansetron prophylaxis? Anesthesiology 2005;102:543–9.
[4] Aplet CC, Heidrich PM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. Br J Anaesth 2012;109:742–53.
[5] Enqvist B, Björklund C, Engman M, et al. Preoperative hypnotic reduces postoperative vomiting after surgery of the breast: A prospective, randomized and blinded study. Acta Anaesthesiol Scand 1997;41:1028–32.
[6] Oddby-Muhbeck E, Jakobsson J, Andersson L, et al. Postoperative nausea and vomiting in a comparison between intravenous and inhalation anesthesia in breast surgery. Acta Anaesthesiol Scand 1994;38:52–6.
[7] Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014;118:85–113.
[8] Maskowski C. A review of the incidence, causes, consequences and management of gastrointestinal effects associated with postoperative opioid administration. J Perianesthes Nurs 2009;24:222–8.
[9] Janicki PK, Sugino S. Genetic factors associated with pharmacotherapy and background sensitivity to postoperative and chemotherapy-induced nausea and vomiting. Exp Brain Res 2014;232:6613–25.
[10] Sun et al. Medicine (2019) 98:10 www.md-journal.com
[11] Cho HK, Park JK, Jeong YM, et al. Can Perioperative acupuncture reduce the pain and vomiting experienced after tonsillectomy? A meta-analysis. Laryngoscope 2016;126:608–15.
[12] Quinlan-Woodward J, Gode A, Dusek JA, et al. Assessing the impact of acupuncture on pain, nausea, anxiety, and coping in women undergoing a mastectomy. Oncol Nurs Forum 2016;43:725–32.
[13] El-Deeb AM, Ahmedy MS. Effect of acupuncture on nausea and/or vomiting during and after cesarean section in comparison with ondansetron. J Anesth 2011;25:698–703.
[14] Alcaraz R, Monerris MM, Jiménez-Capel Y, et al. Effectiveness and safety of continuous stimulation without needles with STIPER™ puncture in the prophylaxis of postoperative nausea and vomiting in elective breast surgery: 1AP7–6. Eur J Anaesthesiol 2014;31:23.
[15] Gan TJ, Jiao KR, Zenn M. A randomized controlled comparison of electro-acupoint-stimulation and ondansetron versus placebo for the prevention of postoperative nausea and vomiting. Anesth Analg 2004;99:1070–5.
[16] Gu J, Wang G, Li M. Clinical observation of HANS for the prevention of postoperative nausea and vomiting after modified radical mastectomy. Heliyon J Med 2009;36:604–6.
[17] Hu X, Xie Y, Lu Z, et al. Application of transcutaneous electrical acupoint stimulation for analgesia in patients with breast cancer radical mastectomy. Med J Chin 2014;16:13–8.
[18] Kim SI, Yoo IS, Park HN, et al. Transcutaneous electrical stimulation of the P6 acupoint reduces postoperative nausea after minor breast surgery. Korean J Anesthesiol 2004;6:834–9.
[19] Lin M, Xiong X, Wei W. Effect of auricular point combination with transcutaneous electrical acupoint stimulation on prevention of postoperative nausea and vomiting in patients undergoing partial breast resection. J Pract Med 2015;31:1858–60.
[20] Liu Y, Yu H, Wang B, et al. Effect of percutaneous acupoint electrical stimulation on nausea and vomiting in female breast cancer patients after operation. Chin J Trad Med Sci Technol 2011;18:67–8.
[21] Majhol B, Møller AM. Acupuncture at acupoint P6 for prevention of postoperative nausea and vomiting a randomised clinical trial. Eur J Anaesthesiol 2011;28:412–9.
[22] Pan F, Geng H, He B, et al. Preventive and therapeutic effects of different acupoints and stimulating methods on nausea and vomiting after breast surgery. J New Chin Med 2014;46:169–71.
[23] Wang Z, Zeng F, Qian B. Effects of transcutaneous electrical acupoint stimulation on postoperative recovery quality after breast cancer surgery. Med J West China 2017;29:1233–6.
[24] Yu JM, Qu PS, Fan H, et al. Observation on the analgesic effect of transcutaneous electrical acupoint stimulation for breast radical carcinoma operation. Zhen Ci Yan Jiu 2010;35:83–6.
[25] Yu H, Qi L, Huang W, et al. Effects of transcutaneous electrical Neiguan acupoint stimulation on intraoperative heart rate and postoperative nausea and vomiting and pain in patients with breast cancer treated by imitation radical mastectomy. Pract Oncol J 2012;26:324–35.
[26] Zhang Q, Qiao Z, Wang H, et al. The effect of pre-treatment with transcutaneous electrical acupoint stimulation on the quality of recovery after ambulatory breast surgery. Anaeasthesia 2014;69:832–9.
[27] Zhou W, Hu L, Ye J, et al. Effect of percutaneous acupoint electrical stimulation on adverse reactions after modified radical mastectomy for breast cancer. Chin J Rural Med Pharm 2017;24:27–8.
[28] Zhou W, Benharash P. Effects and mechanisms of acupuncture based on the principle of meridians. J Acupuncture Meridian Stud 2014;7:190–3.
[29] Lv JQ, Feng RZ, Li N. P6 acupoint stimulation for prevention of postoperative nausea and vomiting in patients undergoing craniotomy: study protocol for a randomized controlled trial. Trials 2013;14:143.
[30] Chung YC, Tsou MY, Chen HH, et al. Integrative acupuncture stimulation to alleviate postoperative pain and morphine-related side effects: a sham-controlled study. Int J Nurs Stud 2014;51:370–8.
[31] 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;36:450–5.
[32] Kwon JH, Shin Y, Juon HS. Effects of Nei-Guan (P6) acupressure wristband on nausea, vomiting, and retching in women after thyroidectomy. Cancer Nurs 2016;39:61–6.
[33] Moher D, Liberati A, Tetzlaff J, et al. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151:264–9.
[34] Jadad AR, Moore RA, Caroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–2.
[35] Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011. Available from www.cochrane-handbook.org.
[36] Goodin S, Cunningham R. 5-HT(3)-receptor antagonists for the treatment of nausea and vomiting: a reappraisal of their side-effect profile. Oncologist 2002;7:424–36.
[37] Yang XY, Xiao J, Chen YH, et al. Dexamethasone alone vs in combination with transcutaneous electrical acupoint stimulation or tropisetron for prevention of postoperative nausea and vomiting in gynaecological patients undergoing laparoscopic surgery. Br J Anaesth 2015;115:883–9.
[38] He B, Ma Q, Pan F. Distribution of TCM constitution in patients with postoperative nausea and vomiting after mastectomy. Guangdong Med J 2017;38:1758–60.
[39] Bao T. Commentary on the Cochrane review of stimulation of the wrist acupuncture point p6 for preventing postoperative nausea and vomiting. Explore (NY) 2011;7:263–4.
[40] Cooke M, Rapchuk I, Doi SA, et al. Wrist acupressure for post-operative nausea and vomiting (WrAP): a pilot study. Complement Ther Med 2015;23:372–80.
[41] Matthews C. A review of nausea and vomiting in the anaesthetic and post anaesthetic environment. J Perioper Pract 2017;27:224–7.
[42] Chatterjee A, Rudra A, Sengupta S. Current concepts in the management of postoperative nausea and vomiting. Anesthesiol Res Pract 2011;74:1–0.