1. Introduction

Cervical cancer (CC) is one of the most common female malignancies and is also one of the leading causes of mortality in females worldwide.\(^1\)–\(^3\) The previous study reported that there were 527,600 new CC cases and 265,700 deaths in females worldwide in 2012.\(^4\) In China, there were about 98,900 new CC cases in 2015. It accounted for 18.7% of the global incidence of CC among the female population.\(^5\) Several risk factors can result in CC, such as many sexual partners, early sexual activity, other sexually transmitted infections, a weak immune system, and smoking.\(^6\)–\(^8\)

Currently available managements mainly include chemotherapy, radiotherapy, and surgery,\(^9\)–\(^13\) especially for chemotherapy. Thousands of clinical trials have reported that chemotherapy has achieved very satisfied efficacy.\(^14\)–\(^16\) However, it also accompanies lots of severe adverse events (AEs), such as nausea and vomiting, fatigue, loss of appetite, pain, diarrhea, and so on.\(^17\)–\(^19\) If these AEs cannot be treated fairly and timely, it may affect CC cure by reducing the dosage of chemotherapy, or even quit the chemotherapy. Thus, alternative interventions with fewer adverse reactions are urgently needed to treat those conditions caused by chemotherapy.

Fortunately, numerous clinical trials have reported that electrical stimulation (ES) can be used to treat AEs caused by chemotherapy effectively and safely.\(^20\)–\(^23\) However, up to date, no systematic review has systematically investigated the effectiveness and safety of ES for AEs result from chemotherapy in patients with CC. Therefore, in this systematic review, we aim to assess the effectiveness and safety of ES for AEs caused by chemotherapy in patients with CC.

2. Methods and analysis

2.1. Study registration

The reports of this systematic review protocol have followed the Preferred Reporting Items for Systematic Reviews and Meta-
2.2. Eligibility criteria

2.2.1. Types of studies. All randomized controlled trials (RCTs) comparing the effectiveness of ES on AEs caused by chemotherapy in patients with CC will be included, regardless the grades of AEs and the length of treatment period. Any other studies of non-RCTs, quasi-RCTs, case-control study, case reports, case series, review, comment, animal studies will all not be included.

2.2.2. Types of participants. CC patients with any following AEs caused by chemotherapy will be included regardless of sex, age, and race. It includes fatigue, nausea and vomiting, pain, and diarrhea. However, patients will be excluded if they have all these disorders before the chemotherapy or result from any other conditions, except the chemotherpay.

2.2.3. Types of interventions. In the experimental group, any types of ES, including electrical muscle stimulation, Russian ES, neuromuscular ES, functional ES, transcutaneous electrical nerve stimulation, and electroacupuncture regardless of dosage, treatment period will all be considered to include. If the study includes the ES plus other therapies, it will not be considered. Patients of the control group will be treated with any other interventions, but not any forms of ES.

2.2.4. Types of outcomes

2.2.4.1. Primary outcome. Fatigue: Fatigue severity, measured by The Multidimensional Fatigue Symptom Inventory-Short Form, Functional Assessment of Chronic Illness Therapy-Fatigue Scale, or the Brief Fatigue Index, or other relevant tools.

Nausea or vomiting: Frequency of nausea and vomiting.

Pain: Pain intensity, as measured by Visual Analog Scale, or Numeric Rating Scale, or any other relevant scales.

Diarrhea: Frequency of diarrhea, stool consistency.

2.2.4.2. Secondary outcomes. Secondary outcomes include quality of life, as measured by the 36-Item Short Form Survey. In addition, adverse reactions are also evaluated.

2.3. Search methods for the identification of studies

2.3.1. Search strategy. We will systematically retrieve the literature sources of PUBMED, PsycINFO, Scopus, OpenGrey, Cochrane Central Register of Controlled Trials, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Web of Science, Allied and Complementary Medicine Database, and Chinese Biomedical Literature Database from the inception to the date of study search ran. In addition, we will also retrieve the websites of clinical trials registry and reference lists provided in relevant studies and reviews. We have presented the search strategy sample for the Cochrane Central Register of Controlled Trials in Table 1. Any other databases and sources will also be retrieved by using the similar search strategy.

Table 1

| Number | Search terms                                      |
|--------|--------------------------------------------------|
| 1      | Mesh descriptor: (uterine cervical neoplasms) explode all trees |
| 2      | Mesh descriptor: (neoplasms) explode all trees    |
| 3      | (cervical cancer) or (uterine) or (cervical) or (neoplasms) or (carcinom) or (dysplas) or (intraepithelial neoplas) | ti, ab, kw |
| 4      | Or 1–3                                           |
| 5      | Mesh descriptor: (drug therapy) explode all trees |
| 6      | Mesh descriptor: (antineoplastic agents) explode all trees |
| 7      | Mesh descriptor: (antineoplastic combined chemotherapy protocols) explode all trees |
| 8      | (chemotherapy) or (drug) or (therapy) or (treatment) or (intervention) or (antineoplastic) or (agents) or (pharmacotherapy) | ti, ab, kw |
| 9      | Or 5–8                                          |
| 10     | (adverse event) explode all trees                |
| 11     | Mesh descriptor: (fatigue) explode all trees      |
| 12     | Mesh descriptor: (nausea) explode all trees       |
| 13     | Mesh descriptor: (vomiting) explode all trees     |
| 14     | Mesh descriptor: (pain) explode all trees         |
| 15     | Mesh descriptor: (diarrhea) explode all trees     |
| 16     | (fatigue) or (asthenia) or (asthenic) or (asthenia) or (exhaustion) or (exhausted) or (loss of energy) or (loss of vitality) or (weak) or (weakness) or (nausea) or (vomiting) or (emesis) or (pain) or (diarrhea) | ti, ab, kw |
| 17     | Or 10–16                                        |
| 18     | MeSH descriptor: (electric stimulation) explode all trees |
| 19     | MeSH descriptor: (transcranial direct current stimulation) explode all trees |
| 20     | MeSH descriptor: (transcutaneous electric nerve stimulation) explode all trees |
| 21     | MeSH descriptor: (electric stimulation therapy) explode all trees |
| 22     | MeSH descriptor: (electroacupuncture) explode all trees |
| 23     | (electrical stimulation) or (electric stimulation) or (electrical stimulation, therapeutic) or (electrotherapy) or (electrotherapy) or (electrical stimulation, transcutaneous) or (transcutaneous electric stimulation) or (transcutaneous electrical stimulation) or (transcutaneous nerve stimulation) or (transcutaneous electric stimulation) or (TENS) (Russian) or (stimulation) or (TENS) or (PENS) or (stimulation, transcutaneous electrical) or (stimulation, transcutaneous) or (stimulation, electrical) or (stimulations, electrical) or (stimulation, electric) or (stimulations, electric) or (stimulation therapy, electrical) or (stimulation therapy, electrical) or (percutaneous electric nerve stimulation) or (nerve stimulation, transcutaneous) or (electroacupuncture) or (electroacupuncture) | ti, ab, kw |
| 24     | Or 18–23                                        |
| 25     | MeSH descriptor: (randomized controlled trials) explode all trees |
| 26     | (random) or (allocation) or (random allocation) or (placebo) or (single blind) or (double blind) or (randomized control trial) or (RCT) | ti, ab, kw |
| 27     | Or 25–26                                        |
| 28     | 4 and 9 and 17 and 24 and 27                     |

CENTRAL = Cochrane Central Register of Controlled Trials.
2.3.2. **Study selection.** Two reviewers will independently select the potential studies based on the predefined eligibility criteria. All the study selection process will be performed according to the PRISMA flowchart, and is presented in Figure 1. Any disagreements will be solved by consulting a third reviewer through discussion.

2.3.3. **Data collection.** After selection, all the related data will be extracted from the included studies by using predefined data extraction forms. Two independent reviewers will carry out the data extraction. Any divergences of data extraction will be settled down by a third reviewer invited through discussion. The forms consist of the following information.

- **General information:** title, first author, publication year, country, eligibility criteria, and patient characteristics.
- **Study methods:** sample size, randomization, concealment, blinding, and any other potential risk of bias.
- **Intervention details:** dosage, frequency, duration.
- **Outcomes:** primary, secondary, and safety outcome measurements.

2.3.4. **Dealing with essential missing information.** Any essential missing information, including missing data, will be inquired by contracting original authors to request. We will pool the available data only if the missing data cannot be achieved.

2.4. **Risk of bias assessment**

In this study, we will apply Cochrane risk of bias tool to assess the methodology quality for each included study. All the procedures will be performed by 2 independent reviewers. Disagreements between 2 reviewers will be resolved by a third review through discussion.
2.5. Data synthesis and analysis

RevMan 5.3 software will be used to pool and to analyze the data. Continuous data will be pooled and presented as mean difference with 95% confidence intervals (CIs). Dichotomous data will be pooled and presented as risk ratio with 95% CIs. Heterogeneity will be detected by using the Chi-square test and $I^2$ values. The reasonable heterogeneity will be considered if $I^2 \leq 50\%$, and pooled will be pooled by using a fixed-effect model. The significant heterogeneity will be considered if $I^2 > 50\%$, and data will be pooled by using a random-effect model. Under such situation, subgroup analysis will be conducted. If there is still significant heterogeneity after the subgroup analysis, we will not pool the data, and carry out the meta-analysis. Instead, we will just report results as narrative description.

2.6. Additional analysis

2.6.1. Subgroup analysis. Subgroup analysis will be carried out if the heterogeneity is substantial. It will be conducted according to different locations, study quality, treatment types, treatment duration, and outcome tools.

2.6.2. Sensitivity analysis. Sensitivity analysis will be carried out to ensure the robustness and stability of pooled results data by removing low-quality trials.

2.6.3. Reporting bias. If sufficient eligible studies are included, the potential reporting bias will be identified by funnel plots. Additionally, Egger regression test will also be performed to check the asymmetry of funnel plots.

3. Discussion

To our best knowledge, although lots of clinical trials regarding the effectiveness of ES on AEs caused by chemotherapy in patients with CC were conducted, no systematic review specifically focused on the ES for AEs caused by chemotherapy in patients with CC. Therefore, the purpose of this study is to evaluate the effectiveness of ES on different AEs resulted from chemotherapy on CC. The results of this study will provide most present evidence on the effectiveness of ES for the treatment of AEs caused by chemotherapy in patients with CC. Its findings may also provide helpful evidence for the clinical practice, and researchers for further study.

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