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Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol of a systematic review and meta-analysis

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Keywords:	acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, systematic review, meta-analysis

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Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol of a systematic review and meta-analysis

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Jing Liu¹, Hong-Jia Zhao¹ #

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Abstract

Introduction: Cervical spondylotic radiculopathy (CSR) is the most common pattern of cervical spondylosis, which is a serious and common degenerative disease. Both acupotomy and acupuncture have been widely used clinically to treat CSR in China with satisfied efficacy. However, there is no systematic review comparing the effectiveness of these two therapies. The aim of this study is to compare the therapeutic efficacy and safety between acupotomy and acupuncture for CSR patients to provide evidence for clinical practice.

Methods and analysis: The following electronic databases will be searched: Web of Science, PubMed, Embase, Cochrane Library, China Knowledge Network Database (CNKI), China Biomedical Literature Database (CBM), Wanfang Database and Chinese Scientific Journal Database (VIP). The randomized controlled trials of acupotomy versus acupuncture with/without additional treatment for CSR will be searched in the databases from their inception to December 2018 by 2 researchers independently. The total effective rate and curative rate will be assessed as the primary outcomes. Visual analog scale and symptom score will be assessed as the secondary outcome. The Review Manager 5.3 will be used for meta-analysis and the evidence level will be assessed by using the method for Grading of Recommendations Assessment, Development, and Evaluation (GRADE). Continuous outcomes will be presented as the weighted mean difference (WMD) or standardized mean difference (SMD) with 95% confidence interval (CI), while dichotomous data will be expressed as relative risk (RR) with 95% CI. If the included studies have existing heterogeneity

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4 ($P<0.05$), a random-effects model will be used. Otherwise, we will calculate using a
5 fixed effects model.
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7 **Results:** This systematic review and meta-analysis will use high-quality
8 evidence-based medicine to compare the efficacy and safety between acupotomy and
9 acupuncture in CSR.
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11

12 **Conclusion:** The result will provide clear evidence to determine whether acupotomy
13 therapy is an effective and safe intervention for patients with CSR.
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17 **Strengths and limitations of this study**

- 18 • This systematic review will comprehensively compare the therapeutic efficacy
19 and safety between acupotomy and acupuncture for cervical spondylotic
20 radiculopathy.
- 21 • The study screening, data extraction and quality assessment will be performed by
22 two independent reviewers.
- 23 • Different types of acupuncture and some of the reviewed trials with small sample
24 sizes may cause considerable heterogeneity in this review. High- quality trials might
25 be deficient to generate convincing conclusions.
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38 **Abbreviations:** CSR = Cervical spondylotic radiculopathy, CBM = China
39 Biomedical Literature Database, CNKI = China National Knowledge Infrastructure,
40 VIP = China Science and Technology Journal Database, RCTs = randomized
41 controlled trials, VAS = Visual analog scale, GRADE = Grading of
42 Recommendations Assessment, Development, and Evaluation, WMD = weighted
43 mean difference, SMD = standardized mean difference, CI = confidence interval, RR
44 = relative risk, PRISMA-P = Preferred Reporting Items for Systematic Reviews and
45 Meta-analyses Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,
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56 **Keywords:** acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol,
57 systematic review, meta-analysis
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1. Introduction

Cervical spondylotic radiculopathy (CSR) is the most common pattern of cervical spondylosis, which is a serious and common degenerative disease in both middle aged and elderly populations. CSR, accounting for about 60 to 70 % of all cervical spondylosis, is also the common and frequently-occurring disease in clinic^[1]. Due to social technology advances, lifestyle changes and the increase in staff members, the incidence of CSR tends to increase and the onset age of the patient gets younger year by year, which has seriously affected the patients' physical health and quality of life.

Many therapeutic interventions have been applied for the treatment of CSR, including nonsteroidal anti-inflammatory drugs (NSAIDs)^[2], epidural steroid injections^[3], acupuncture^[4], physical therapy^[5], and exercises^[6, 7]. In clinical practice, acupotomy has also been widely used to treat cervical spondylosis, lumbar disc herniation, knee osteoarthritis and other diseases in China with satisfied efficacy, because of its effectiveness and low risk of complications^[8-12].

Acupotomy, also named needle-knife, originates from the "nine classical of needles" in Huang Di Nei Jing (*Huangdi's Internal Classic*) and was developed in China in 1976 by Zhu Hanzhang^[13]. Acupotomy therapy is considered a minimally invasive surgery that uses traditional Chinese medicine and combines Chinese acupuncture therapy and modern surgical principles^[14]. In the treatment of CSR, the role of acupotomy is to remove attached tissues, recover the dynamic function of soft tissues, relieve nerve pressure, and promote Qi-blood circulation to ameliorate pain and numbness symptoms with a flat-head bladed needle^[10, 15].

Acupotomy has the characteristics of both acupuncture and microinvasive operation. Therefore, both acupotomy and acupuncture are commonly used in treating similar conditions, especially CSR. However, there is no systematic review comparing the effectiveness of these two therapies in patients with CSR. It is worthy to critically review the evidence of the comparison of these two therapies to inform clinical practice. Herein, the aim of this study is to compare the therapeutic efficacy and

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4 safety between acupotomy and acupuncture on CSR to provide evidence for clinical
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6 practice.
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9 10 **2. Methods**

11 **2.1. Design and registration of the review**

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13 This systematic review and meta-analysis protocol was registered in PROSPERO
14 (CRD42019117348) at <https://www.crd.york.ac.uk/PROSPERO/#myprospero> and
15 developed following the guideline of Preferred Reporting Items for Systematic
16 Reviews and Meta-analyses Protocols (PRISMA-P) 2015 [16].
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19 **2.2. Inclusion criteria for study selection**

20 **2.2.1. Type of study.**

21
22 We will estimate the research literature according to the criteria of the review
23 objectives and participants, interventions, comparisons, outcomes (PICO).
24 Randomized controlled trials (RCTs), comparing acupotomy against any form of
25 acupuncture with/without additional treatment, will be included in this systematic
26 review. Moreover, blinding will not be considered because of the characteristics of
27 acupuncture and acupotomy treatment. Additionally, the language of the publications
28 will be limited to Chinese and English.
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31 **2.2.2. Types of participants.**

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33 Patients of any gender or age or race or nationality with CSR received acupotomy or
34 acupuncture therapy with/without additional treatment.
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- 37 1. In line with diagnostic criteria of CSR.
- 38 2. Participants who have not undergone an invasive intervention.
- 39 3. No restriction on age.

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41 The exclusion criteria were shown as follows: (1) Ruplicated studies; (2) No definite
42 diagnostic criteria of CSR; (3) Wrong interventions: these studies were excluded
43 which used open surgery or acupotomy was manipulated in both groups; (4) Reviews
44 or theory studies; (5) Animal experiments.
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47 **2.2.3. Types of interventions.**

48 **Experimental interventions**

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4 The treatment group will be treated with acupotomy (with/without additional
5 treatment). No restrictions are imposed on times of treatment, frequency of treatment,
6 and length of treatment period.
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9 **Comparator interventions**

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11 The treatment with several types of acupuncture (with/without same additional
12 treatment) will be included in this review as acupuncture, manual acupuncture,
13 auricular acupuncture, scalp acupuncture, fire needling, warm needling and
14 electro-acupuncture etc.
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19 **2.2.4. Types of outcome measures.**

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21 The primary outcome measurements will be total effective rate and curative rate. The
22 secondary outcome measures will include visual analog scale (VAS) and symptom
23 score.
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27 **2.3. Data sources**

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29 The main sources of information that will be obtained in this study include electronic
30 resource databases, trial registries, retroactive references, and different types of grey
31 literature.
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35 The following electronic databases will be searched: Web of Science, PubMed,
36 Embase, Cochrane Library, China Knowledge Network Database (CNKI), China
37 Biomedical Literature Database (CBM), Wanfang Database and Chinese Scientific
38 Journal Database (VIP). Reference lists of the relevant literature and systematic
39 reviews, as well as the tables of contents related to acupotomy versus acupuncture on
40 CSR will also be searched. RCTs of acupotomy versus acupuncture with/without
41 additional treatment for CSR patients will be searched in the databases from their
42 inception to December 2018 by two researchers independently
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50 **2.4. Search strategy**

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52 The strategy will be created according to the Cochrane handbook guidelines. The
53 established search strategy for PubMed was displayed, as following:
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56 **Mesh term #1:** ((acupotomy) OR (acupotome) OR (needle knife) OR (needle
57 scalpel)): ti, ab, kw
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60 **Mesh term #2:** ((acupuncture) OR (manual acupuncture) OR (auricular acupuncture)

OR (scalp acupuncture) OR (fire needling) OR (warm needling) OR (electro-acupuncture)): ti, ab, kw

Mesh term #3: ((cervical radiculopathy) OR (cervical spondylotic radiculopathy) OR (cervical spondylopathy) OR (cervical spondylosis) OR (neck pain) OR (neck syndrome)): ti, ab, kw

Mesh term #4: ((clinical trials) OR (random control trials))

#1 AND #2 AND #3 AND #4

The equivalent search words will be used in the Chinese databases.

2.5. Data collection and analysis

2.5.1. Selection of studies.

The researchers will import the retrieved literature into an EndNote library and eliminate duplicate data. Two review authors (Renpan Zhang and Anyang Lin) selected studies for eligibility and checked against the inclusion criteria independently. Any disagreement will be resolved by consensus or consultation with a third independent researcher (Hongjia Zhao). The selection process is illustrated in a PRISMA flow diagram (**Figure. 1**).

2.5.2. Data extraction and management.

Two review authors (Jing Liu and Zhongbiao Xiu) will independently use a standardized form for extracting data of the included articles. The following data were extracted: general information (e.g., title, authors, year and published country), details of study (e.g., design, inclusion and exclusion criteria, blinding, randomization and sample size), participant characteristics (e.g., age and number of subjects), description of interventions, types of outcomes assessed, and other detailed information. If necessary, we will contact the corresponding authors of trials as much as possible for further information.

2.5.3. Assessment of risk of bias and reporting of study quality.

The Cochrane Collaboration's tool will be applied to evaluate the quality and risk of bias in ultimate included studies by two authors (Renpan Zhang and Anyang Lin) independently[17]. The risk of bias will include random sequence generation, allocation concealment, blinding, completeness of outcome data, selective outcome

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4 reporting, and other bias. The assessments for each item will be graded as low risk,
5 unclear risk, and high risk. If there is any disagreement take place, the arbiter
6 (Hongjia Zhao) will do the final judge.
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8 9 **2.5.4. Measures of treatment effect.**

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11 Continuous outcomes will be presented as the mean difference (MD) for analysis,
12 while dichotomous data will be expressed as relative risk (RR), both of them will be
13 with 95% confidence intervals (CI)[18]. When the same outcome is measured in
14 different ways, the standardized mean difference (SMD) with 95%CI will be selected
15 to express the size of the intervention effect.
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18 19 **2.5.5. Dealing with missing data.**

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21 We will attempt to contact authors of included studies for missing or incomplete data
22 by E-mail. However, If the missing data cannot be obtained, the study will be
23 excluded from the analysis.
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26 27 **2.5.6. Assessment of heterogeneity.**

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29 Statistical heterogeneity will be detected by the I^2 statistic and χ^2 test. $P < 0.1$ of χ^2
30 test or $I^2 > 50\%$ indicates the possibility of statistical heterogeneity among the studies.
31 If the included studies have existing heterogeneity, a random-effect model will be
32 used. Otherwise, we will calculate using a fixed-effect model.
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35 36 **2.5.7. Assessment of reporting bias.**

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38 If more than 10 studies are included, visual asymmetry on the funnel plots will be
39 used to assess the potential reporting biases. In addition, we will test asymmetry using
40 the Harbord modified test for dichotomous outcomes and Egger test for continuous
41 outcomes.
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44 45 **2.5.8. Data synthesis.**

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47 The Review Manager 5.3 will be employed for meta-analysis. When statistical
48 heterogeneity is low among the results, the fixed-effects model will be used for the
49 meta-analysis. However, there is considerable heterogeneity, the random-effects
50 model will be performed to analyse the pooled effect estimates.
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53 54 **2.5.9. Subgroup analysis.**

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56 If there is significant heterogeneity in the included trials, we will conduct a subgroup
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analysis based on the acupotomy or acupuncture interventions with/without additional treatment, types of acupuncture (acupuncture, manual acupuncture, and electro-acupuncture etc) and different outcomes.

2.5.10. Sensitivity analysis.

A sensitivity analysis will be conducted to identify whether the review conclusions are robust according to the following criteria: missing data, sample size, heterogeneity qualities, and statistical model.

2.5.11. Grading the quality of evidence.

The evidence level will be assessed by using the method for Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and classified into four possible ratings: very low, low, moderate, or high.

2.5.12. Patient and Public Involvement

Patients and or public were not involved because no primary data are collected.

3. Discussion

The main symptoms of CSR include neck and shoulder pain, radicular pain or numbness in the upper extremities, weakening of grip strength, and sensory disturbances. Acupotomy, containing the characteristics of both acupuncture and microinvasive operation, have been widely used clinically to treat CSR by peeling synechia, removing attached tissue, and relieve nerve pressure. Currently, there are limited evidence to determine whether acupotomy and acupuncture has similar effect on relieving pain and improving other symptoms of CSR. Therefore, the comparisons of therapeutic efficacy and safety will be made between acupotomy and acupuncture with/without same additional treatment is given to both groups. This systematic review and meta-analysis will provide high-quality evidence-based medicine to determine whether acupotomy therapy is an effective and safe intervention for patients with CSR.

Author contributions

Bin Chen and Hongjia Zhao designed the systematic review. The article was drafted

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4 by Bin Chen and Cai Zhang. Renpan Zhang, Anyang Lin, Jing Liu and Zhongbiao
5 Xiu will independently screen the potential studies, extract the data, assess the risk of
6 bias and finish the data synthesis. Hongjia Zhao will arbitrate any disagreement and
7 ensure that no errors occur during the review. All review authors critically reviewed,
8 revised, and approved the subsequent and final version of the protocol.
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14
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16 NO.81804175 and 81873315) and Fujian Provincial Department of Education
17 Applied Discipline -- Clinical Medicine "Double First Class" Construction Project.
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21 **Competing interests**

22
23 None declared.
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29 **Conceptualization:** Ben Chen, Cai Zhang.

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31 **Data curation:** Ben Chen, Renpan Zhang.

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33 **Formal analysis:** Ben Chen, Renpan Zhang.

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35 **Investigation:** Anyang Lin, Zhongbiao Xiu, Jing Liu.

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37 **Methodology:** Ben Chen, Hongjia Zhao.

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39 **Project administration:** Hongjia Zhao.

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41 **Software:** Anyang Lin, Zhongbiao Xiu.

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43 **Supervision:** Hongjia Zhao, Ben Chen.

44
45 **Validation:** Hongjia Zhao, Jing Liu.

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47 **Visualization:** Ben Chen.

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49 **Writing – original draft:** Ben Chen, Cai Zhang.

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51 **Writing – review & editing:** Hongjia Zhao.
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53

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Figure Legends

Figure 1. PRISMA flow diagram of study process

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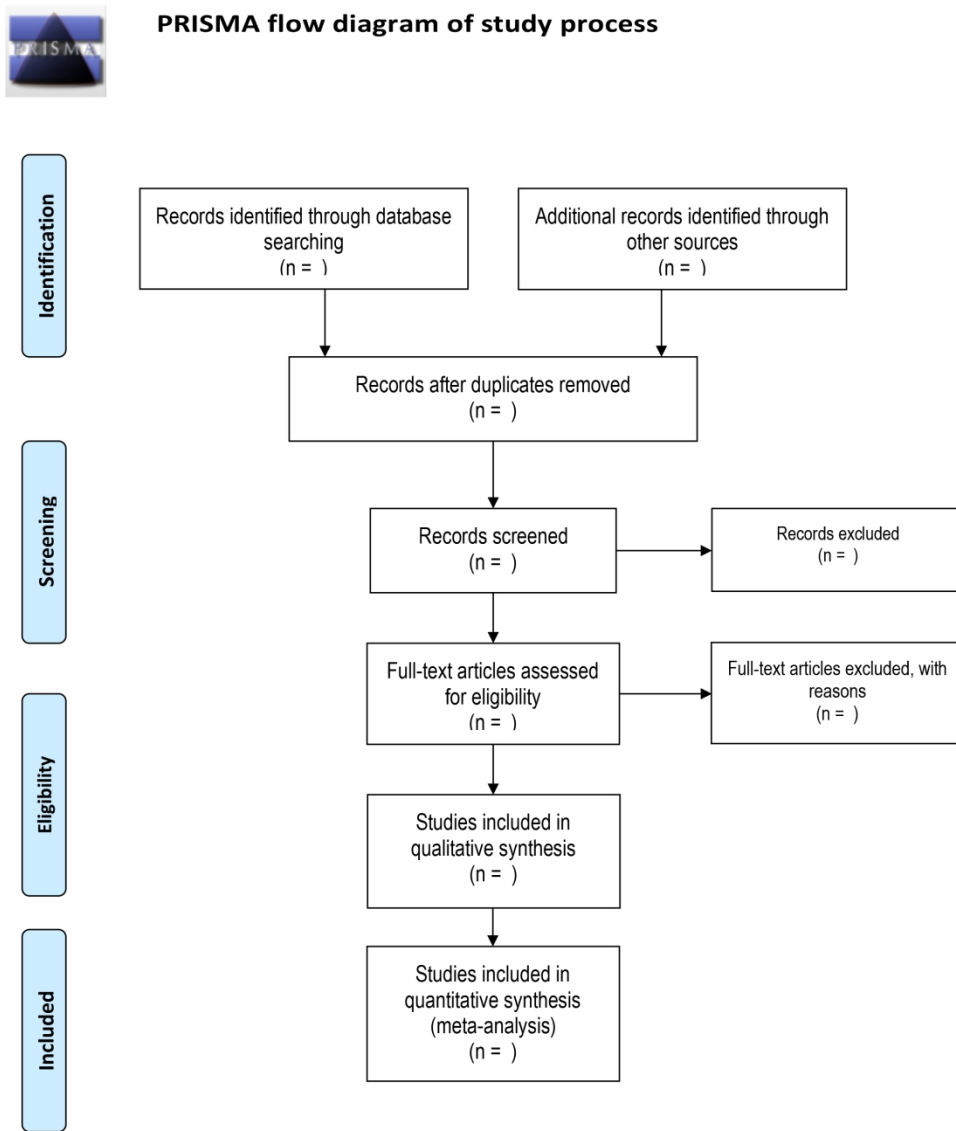


Figure 1. PRISMA flow diagram of study process

188x225mm (300 x 300 DPI)

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Secondary Subject Heading:	Rehabilitation medicine
Keywords:	acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, systematic review, meta-analysis

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4 **Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol**
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6 **of a systematic review and meta-analysis**

7 Bin Chen¹, Cai Zhang², Ren-Pan Zhang^{1,2}, An-Yang Lin^{1,2}, Zhong-Biao Xiu¹,
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16 Province, China.)

17
18
19 **Abstract**

20
21 **Introduction:** Cervical spondylotic radiculopathy (CSR) is the most common pattern
22 of cervical spondylosis, which is a serious and common degenerative disease. Both
23 acupotomy and acupuncture have been widely used clinically to treat CSR in China
24 with satisfied efficacy. However, there is no systematic review comparing the
25 effectiveness of these two therapies. The aim of this study is to compare the
26 therapeutic efficacy and safety between acupotomy and acupuncture for CSR patients
27 to provide evidence for clinical practice.

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34 **Methods and analysis:** The following electronic databases will be searched: Web of
35 Science, PubMed, Embase, Cochrane Library, China National Knowledge
36 Infrastructure (CNKI), China Biology Medicine disc (CBM), Wanfang Database and
37 Chinese Scientific Journal Database (VIP). The randomized controlled trials of
38 acupotomy versus acupuncture with/without additional treatment for CSR will be
39 searched in the databases from their inception to December 2018 by 2 researchers
40 independently. Visual analog scale and symptom score will be assessed as the primary
41 outcomes. The total effective rate, curative rate, adverse events, and amount of rescue
42 medication used will be assessed as the secondary outcomes. The Review Manager
43 5.3 will be used for meta-analysis and the evidence level will be assessed by using the
44 method for Grading of Recommendations Assessment, Development, and Evaluation
45 (GRADE). Continuous outcomes will be presented as the weighted mean difference
46 (WMD) or standardized mean difference (SMD) with 95% confidence interval (CI),
47 while dichotomous data will be expressed as relative risk (RR) with 95% CI. If the
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3 included studies have existing heterogeneity ($P<0.05$), a random-effects model will be
4 used. Otherwise, we will calculate using a fixed effects model.
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7 **Ethics and dissemination:** The ethical approval is not required because no primary
8 data are collected. This review will be published in a peer-reviewed journal and will
9 be presented at an international academic conference for dissemination. Our results
10 will provide clear evidence to determine whether acupotomy therapy is an effective
11 and safe intervention for patients with CSR, and thus will be beneficial to patients,
12 practitioners, and policymakers.
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21 **PROSPERO registration number:** CRD42019117348.
22

23 24 25 **Strengths and limitations of this study**

- 26 • This systematic review will comprehensively compare the therapeutic efficacy
27 and safety between acupotomy and acupuncture for cervical spondylotic
28 radiculopathy.
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- 30 • The study screening, data extraction, and quality assessment will be performed by
31 two independent reviewers.
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- 33 • Different types of acupuncture and some of the reviewed trials with small sample
34 sizes may cause considerable heterogeneity in this review. High- quality trials might
35 be deficient to generate convincing conclusions.
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44 **Abbreviations:** CSR = Cervical spondylotic radiculopathy, CBM = China Biology
45 Medicine disc, CNKI = China National Knowledge Infrastructure, VIP = China
46 Science and Technology Journal Database, RCTs = randomized controlled trials,
47 VAS = Visual analog scale, GRADE = Grading of Recommendations Assessment,
48 Development, and Evaluation, WMD = weighted mean difference, SMD =
49 standardized mean difference, CI = confidence interval, RR = relative risk,
50 PRISMA-P = Preferred Reporting Items for Systematic Reviews and Meta-analyses
51 Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,
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4 **Keywords:** acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol,
5 systematic review, meta-analysis
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1. Introduction

Cervical spondylotic radiculopathy (CSR) is defined as neck pain in a radicular pattern in one or both upper extremities related to compression and/or irritation of one or more cervical nerve roots. The most common level of nerve root compression is C7, followed by C6. CSR, accounting for about 60 to 70 % of all cervical spondylosis, is the common and frequently-occurring disease in both middle-aged and elderly populations^[1]. It has been reported that up to 80% of cervical spondylosis patients always complained of neck pain, which will become more and more serious over time. Due to social technology advances, lifestyle changes and the increase in staff members, the incidence of CSR tends to increase and the onset age of the patient gets younger year by year, which has seriously affected the patients' physical health and quality of life.

Management of CSR can be surgical or conservative. Conservative management is the initial treatment of choice for most patients, because surgery may be associated with adverse events and recurrence. Currently, many therapeutic interventions have been applied for the treatment of CSR, including nonsteroidal anti-inflammatory drugs (NSAIDs) ^[2], epidural steroid injections ^[3], acupuncture ^[4], physical therapy ^[5], and exercises ^[6, 7]. The main purpose of these treatments is to relieve pain, improve function, and enhance the quality of life. In clinical practice, acupotomy has also been widely used to treat cervical spondylosis, lumbar disc herniation, knee osteoarthritis and other diseases in China with satisfied efficacy, because of its effectiveness and low risk of complications ^[8-12].

Acupotomy, also named needle-knife, originates from the "nine classical of needles" in Huang Di Nei Jing (*Huangdi's Internal Classic*) and was developed in China in 1976 by Zhu Hanzhang ^[13]. It is a new-style bladed needle that composed of a thick flat-head and a cylindrical body, which is suitable for alleviating the adhesion of a lesion. Acupotomy therapy is considered as a minimally invasive surgery of traditional Chinese medicine, combining Chinese acupuncture therapy and modern surgical principles ^[14]. In the treatment of CSR, the role of acupotomy is to remove

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4 attached tissues, recover the dynamic function of soft tissues, relieve nerve pressure,
5 and promote Qi-blood circulation to ameliorate pain and numbness symptoms [10, 15].
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7 Acupotomy has many benefits because it converts open surgery to closed surgery,
8 thus reducing risk, time, and cost. This method only produces a small scar that will
9 fade with time [11].
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14 Acupotomy has the characteristics of both acupuncture and microinvasive operation.
15 Both acupotomy and acupuncture have been widely used clinically to treat CSR in
16 China with satisfied efficacy. However, there is no systematic review comparing the
17 effectiveness of these two therapies in patients with CSR. It is worthy to critically
18 review the evidence of the comparison of these two therapies to inform clinical
19 practice. Herein, the aim of this study is to compare the therapeutic efficacy and
20 safety between acupotomy and acupuncture on CSR to provide evidence for clinical
21 practice.
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32 **2. Methods**

33 **2.1. Study registration**

34 This systematic review and meta-analysis protocol was registered in PROSPERO
35 (CRD42019117348) at <https://www.crd.york.ac.uk/PROSPERO/#myprospero>.
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39 **2.2. Inclusion criteria for study selection**

40 **2.2.1. Type of study.**

41 We will estimate the research literature according to the criteria of the review
42 objectives and participants, interventions, comparisons, outcomes (PICO).
43 Randomized controlled trials (RCTs), comparing acupotomy against any form of
44 acupuncture with/without additional treatment, will be included in this systematic
45 review. We will include such studies if the expression “randomization” is mentioned.
46 However, we will grade these studies as high in the “risk of bias assessment” if the
47 detailed description on the randomization process is not provided. Furthermore, if an
48 incorrect randomization method such as coin toss was used, the study will not be
49 included. Moreover, blinding will not be considered because of the characteristics of
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3 acupuncture and acupotomy treatment. Additionally, the language of the publications
4 will be limited to Chinese and English.
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7 **2.2.2. Types of participants.**

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9 Patients of any gender or age or race or nationality with CSR received acupotomy or
10 acupuncture therapy with/without additional treatment.
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- 12 1. In line with the diagnostic criteria of CSR.
- 13 2. Participants who have not undergone an invasive intervention.
- 14 3. No restriction on age.

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16 The exclusion criteria were shown as follows: (1) Replicated studies; (2) No definite
17 diagnostic criteria of CSR; (3) Wrong interventions: these studies were excluded
18 which used open surgery or acupotomy was manipulated in both groups; (4) Reviews
19 or theory studies; (5) Animal experiments.
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22 **2.2.3. Types of interventions.**

23 **Experimental interventions**

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25 The treatment group will be treated with acupotomy (with/without additional
26 treatment). No restrictions are imposed on times of treatment, frequency of treatment,
27 and length of treatment period.
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29 **Comparator interventions**

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31 The treatment with several types of acupuncture (with/without same additional
32 treatment) will be included in this review as acupuncture, manual acupuncture,
33 auricular acupuncture, scalp acupuncture, fire needling, warm needling, and
34 electro-acupuncture, etc.
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37 The procedure of acupuncture and acupotomy should be reported in full compliance
38 with the standardized reporting methods such as the Standard of the Basic
39 Manipulations of Acupotomy (ZJ/T D001-2014) and Standards for Reporting
40 Interventions in Controlled Trials of Acupuncture (STRICTA).
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43 **2.2.4. Types of outcome measures.**

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45 Changes in visual analog scale (VAS) and symptom score will be evaluated as
46 primary outcomes. The total effective rate and the curative rate will be evaluated as
47 secondary outcomes. The secondary outcome measures are as follows:
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4 (1) Total effective rate and curative rate

5 The total effective rate and curative rate are non-validated outcome measures that are
6 processed secondarily according to certain evaluation criteria such as clinical
7 symptom improvement or the improvement rates of other quantified outcomes. In the
8 assessment of the total effective rate, participants are generally classified as “cured”,
9 “markedly improved”, “improved”, or “non-responder” after treatment. The total
10 effective rate is calculated consistently using the following formula:
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$$17 \quad \text{Total effective rate} = N_1 + N_2 + N_3 / N$$

$$18 \quad \text{Curative rate} = N_1 / N$$

19 where N1, N2, N3, and N are the number of patients who are cured, markedly
20 improved, improved, and who comprise the sample size, respectively.
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23 (2) The incidence of adverse events.

24 (3) The amount of rescue medication required.

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29 **2.3. Data sources**

30 The main sources of information to be obtained in this study include electronic
31 resource databases, trial registries, retroactive references, and different types of grey
32 literature.
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36 Electronics searches:

37 The following electronic databases will be searched: Web of Science, PubMed,
38 Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China
39 Biology Medicine disc (CBM), Wanfang Database and Chinese Scientific Journal
40 Database (VIP). In addition, “gray literature” such as conference proceedings and
41 theses will be allowed. Reference lists of the relevant literature and systematic
42 reviews, as well as the tables of contents related to acupotomy versus acupuncture on
43 CSR, will also be searched. RCTs of acupotomy versus acupuncture with/without
44 additional treatment for CSR patients will be searched in the databases from their
45 inception to December 2018 by two researchers independently.
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55 Searching for other resources:

56 Ambiguous literature will be investigated manually to avoid missing eligible trials.
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58 Reference lists of identified publications will also be manually searched. In addition,
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4 the following journals published in Chinese will be searched as a supplement:
5 *Chinese Acupuncture and Moxibustion* (1981–December 2018), *Acupuncture*
6 *Research* (1976–December 2018), *World Journal of Acupuncture-moxibustion*
7 (1991–December 2018), *Journal of Clinical Acupuncture and Moxibustion*
8 (1985–December 2018), *Shanghai Journal of Acupuncture and Moxibustion*
9 (1982–December 2018) and *Journal of Traditional Chinese Medicine*
10 (1960–December 2018).

17 **2.4. Search strategy**

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19 The strategy will be created according to the Cochrane handbook guidelines. The
20 established search strategy for PubMed was displayed, as follows:
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23 **Mesh term #1:** ((acupotomy) OR (acupotome) OR (needle knife) OR (needle scalpel)
24 OR (acupotomy) OR (miniscalpel acupuncture) OR (miniscalpel needle) OR
25 (stiletto needle) OR (sword like needle) OR (Xiaozhendao)): ti, ab, kw
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28 **Mesh term #2:** ((acupuncture) OR (manual acupuncture) OR (auricular acupuncture)
29 OR (scalp acupuncture) OR (fire needling) OR (warm needling) OR
30 (electro-acupuncture)): ti, ab, kw
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33 **Mesh term #3:** ((cervical radiculopathy) OR (cervical spondylotic radiculopathy) OR
34 (cervical spondylopathy) OR (cervical spondylosis) OR (neck pain) OR (neck
35 syndrome): ti, ab, kw
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38 **Mesh term #4:** ((clinical trials) OR (random control trials))
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41 **#1 AND #2 AND #3 AND #4**
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44 The equivalent search words will be used in Chinese databases.
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46 **2.5. Data collection and analysis**

47 **2.5.1. Selection of studies.**

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49 The researchers will import the retrieved literature into an EndNote library and
50 eliminate duplicate data. Two review authors (Renpan Zhang and Anyang Lin)
51 selected studies for eligibility and checked against the inclusion criteria independently.
52 Any disagreement will be resolved by consensus or consultation with a third
53 independent researcher (Hongjia Zhao). The selection process is illustrated in a
54 PRISMA flow diagram (**Figure. 1**).
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2.5.2. Data extraction and management.

Two review authors (Jing Liu and Zhongbiao Xiu) will independently use a standardized form for extracting data of the included articles. The following data were extracted: general information (e.g., title, authors, year and published country), details of study (e.g., design, inclusion and exclusion criteria, blinding, randomization and sample size), participant characteristics (e.g., age and number of subjects), description of interventions, types of outcomes assessed, adverse events, and other detailed information. If necessary, we will contact the corresponding authors of trials as much as possible for further information.

2.5.3. Assessment of risk of bias and reporting of study quality.

The Cochrane risk of bias tool will be applied to evaluate the quality and risk of bias in the ultimately included studies by two authors (Renpan Zhang and Anyang Lin) independently^[16-17]. Risk of bias assessment categories will include the following: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants; (4) blinding of outcome assessors; (5) completeness of outcome data; (6) selective outcome reporting; and (7) other biases. The assessments for each item will be graded as low risk, unclear risk, and high risk to evaluate several risks of bias that can occur in RCTs. In the case of other sources of bias, it was evaluated as “low” if the characteristics of participants in each group were reported to be statistically homogeneous at baseline, but was otherwise rated “high”. The results were presented as a risk of bias graph and risk of bias summary using the Cochrane Collaboration’s software program Review Manager (RevMan) version 5.3 for Windows (Copenhagen, The Nordic Cochrane Centre, the Cochrane Collaboration, 2012). If there is any disagreement take place, the arbiter (Hongjia Zhao) will do the final judge.

2.5.4. Measures of treatment effect.

Continuous outcomes will be presented as the mean difference (MD) for analysis, while dichotomous data will be expressed as relative risk (RR), both of them will be with 95% confidence intervals (CI)^[18]. When the same outcome is measured in different ways, the standardized mean difference (SMD) with 95%CI will be selected to express the size of the intervention effect.

2.5.5. Dealing with missing data.

We will attempt to contact authors of included studies for missing or incomplete data by E-mail. However, If the missing data cannot be obtained, the study will be excluded from the analysis.

2.5.6. Assessment of heterogeneity.

Statistical heterogeneity will be detected by the I^2 statistic and χ^2 test. $P < 0.1$ of χ^2 test or $I^2 > 50\%$ indicates the possibility of statistical heterogeneity among the studies. If the included studies have existing heterogeneity, a random-effect model will be used. Otherwise, we will use a fixed-effect model for calculation.

2.5.7. Assessment of reporting bias.

If more than 10 studies are included, visual asymmetry on the funnel plots will be used to assess the potential reporting biases. In addition, we will test asymmetry using the Harbord modified test for dichotomous outcomes and Egger test for continuous outcomes.

2.5.8. Data synthesis.

The Review Manager 5.3 will be employed for meta-analysis. When statistical heterogeneity is low among the results, the fixed-effects model will be used for the meta-analysis. However, there is considerable heterogeneity, the random-effects model will be performed to analyze the pooled effect estimates.

2.5.9. Subgroup analysis.

If there is significant heterogeneity in the included trials, we will conduct a subgroup analysis based on the acupotomy or acupuncture interventions with/without additional treatment, types of acupuncture (acupuncture, manual acupuncture, and electro-acupuncture, etc.) and different outcomes.

2.5.10. Sensitivity analysis.

A sensitivity analysis will be conducted to identify whether the review conclusions are robust according to the following criteria: missing data, sample size, heterogeneity qualities, and statistical model.

2.5.11. Grading the quality of evidence.

The evidence level will be assessed by using the method for Grading of

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4 Recommendations Assessment, Development, and Evaluation (GRADE) and
5 classified into four possible ratings: very low, low, moderate, or high.

6 7 **2.5.12. Patient and Public Involvement**

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9 Patients and or public were not involved because no primary data are collected.

10 11 12 13 **3. Discussion**

14
15 The main symptoms of CSR include neck and shoulder pain, radicular pain or
16 numbness in the upper extremities, weakening of grip strength, and sensory
17 disturbances. Acupotomy, containing the characteristics of both acupuncture and
18 micro-invasive operation, have been widely used clinically to treat CSR by peeling
19 synechia, removing attached tissue, and relieve nerve pressure. Currently, there is
20 limited evidence to determine whether acupotomy and acupuncture have a similar
21 effect on relieving pain and improving other symptoms of CSR. Therefore, the
22 comparisons of therapeutic efficacy and safety will be made between acupotomy and
23 acupuncture with/without the same additional treatment is given to both groups. This
24 systematic review and meta-analysis will provide high-quality evidence-based
25 medicine to determine whether acupotomy therapy is an effective and safe
26 intervention for patients with CSR.
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41 **Contributors**

42 Bin Chen and Hongjia Zhao designed the systematic review. The article was drafted
43 by Bin Chen and Cai Zhang. Renpan Zhang, Anyang Lin, Jing Liu, and Zhongbiao
44 Xiu will independently screen the potential studies, extract the data, assess the risk of
45 bias and finish the data synthesis. Hongjia Zhao will arbitrate any disagreement and
46 ensure that no errors occur during the review. All review authors critically reviewed,
47 revised, and approved the subsequent and final version of the protocol.
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3 Applied Discipline -- Clinical Medicine "Double First Class" Construction Project.
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7 **Competing interests**

8 None declared.
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13 **Patient consent**

14 Not required.
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Figure Legends

Figure 1. PRISMA flow diagram of study process

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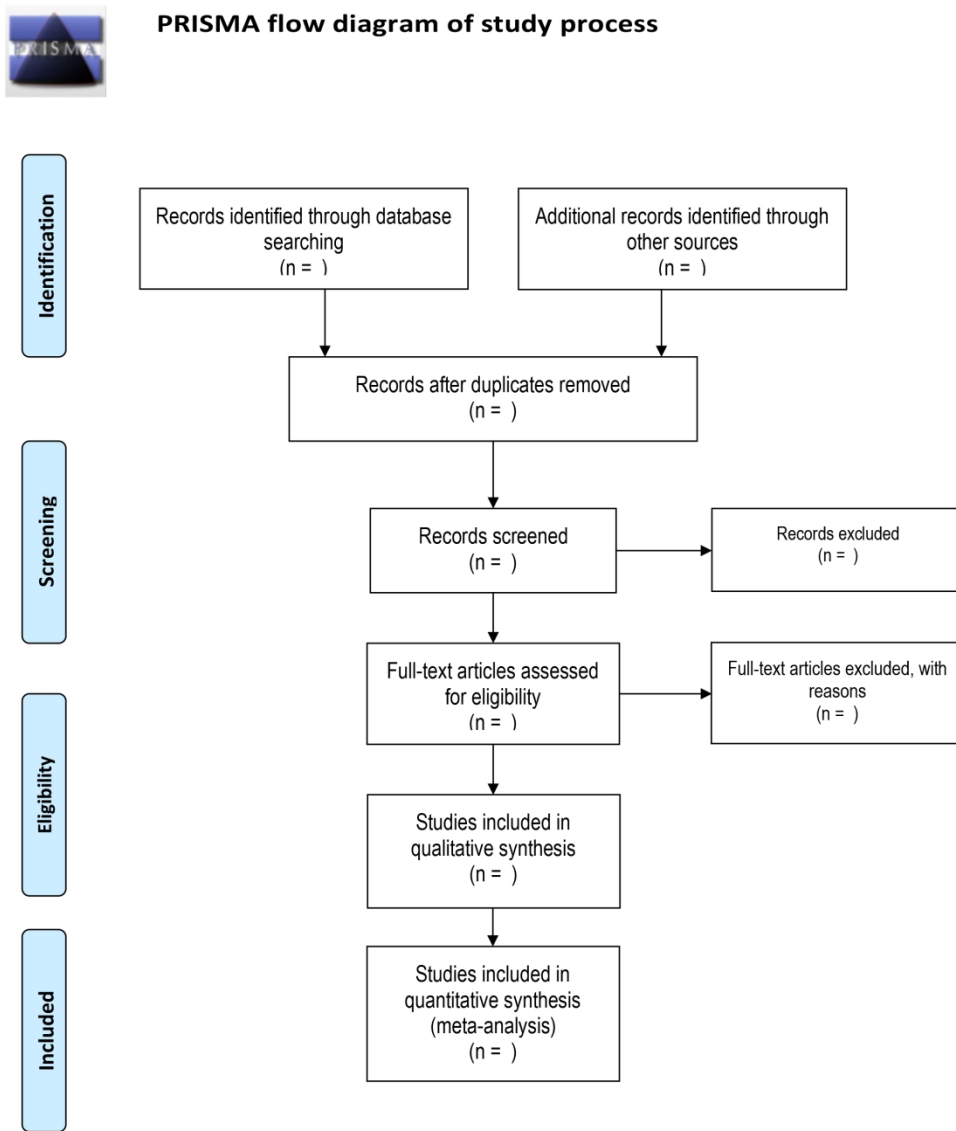


Figure 1. PRISMA flow diagram of study process

188x225mm (300 x 300 DPI)

BMJ Open

Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol of a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-029052.R2
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Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, systematic review, meta-analysis

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4 **Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol**
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6 **of a systematic review and meta-analysis**

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16 Province, China.)

17
18
19 **Abstract**

20
21 **Introduction:** Cervical spondylotic radiculopathy (CSR) is the most common pattern
22 of cervical spondylosis, which is a serious and common degenerative disease. Both
23 acupotomy and acupuncture have been widely used clinically to treat CSR in China
24 with satisfied efficacy. However, there is no systematic review comparing the
25 effectiveness of these two therapies. The aim of this study is to compare the
26 therapeutic efficacy and safety between acupotomy and acupuncture for CSR patients
27 to provide evidence for clinical practice.

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34 **Methods and analysis:** The following electronic databases will be searched: Web of
35 Science, PubMed, Embase, Cochrane Library, China National Knowledge
36 Infrastructure (CNKI), China Biology Medicine disc (CBM), Wanfang Database and
37 Chinese Scientific Journal Database (VIP). The randomized controlled trials of
38 acupotomy versus acupuncture with/without additional treatment for CSR will be
39 searched in the databases from their inception to December 2018 by 2 researchers
40 independently. Visual analog scale, symptom score and neck disability index (NDI)
41 will be assessed as the primary outcomes. The total effective rate, curative rate,
42 adverse events, and amount of rescue medication used will be assessed as the
43 secondary outcomes. The Review Manager 5.3 will be used for meta-analysis and the
44 evidence level will be assessed by using the method for Grading of Recommendations
45 Assessment, Development, and Evaluation (GRADE). Continuous outcomes will be
46 presented as the weighted mean difference (WMD) or standardized mean difference
47 (SMD) with 95% confidence interval (CI), while dichotomous data will be expressed
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4 as relative risk (RR) with 95% CI. If the included studies have existing heterogeneity
5 ($P<0.05$), a random-effects model will be used. Otherwise, we will calculate using a
6 fixed effects model.
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9 **Ethics and dissemination:** The ethical approval is not required because no primary
10 data are collected. This review will be published in a peer-reviewed journal and will
11 be presented at an international academic conference for dissemination.
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17 **PROSPERO registration number:** CRD42019117348.
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19 20 21 **Strengths and limitations of this study**

- 22
23 • This systematic review will comprehensively compare the therapeutic efficacy
24 and safety between acupotomy and acupuncture for cervical spondylotic
25 radiculopathy.
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- 27 • The study screening, data extraction, and quality assessment will be performed by
28 two independent reviewers.
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- 30 • Different types of acupuncture and some of the reviewed trials with small sample
31 sizes may cause considerable heterogeneity in this review. High- quality trials might
32 be deficient to generate convincing conclusions.
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41 **Abbreviations:** CSR = Cervical spondylotic radiculopathy, CBM = China Biology
42 Medicine disc, CNKI = China National Knowledge Infrastructure, VIP = China
43 Science and Technology Journal Database, RCTs = randomized controlled trials,
44 VAS = Visual analog scale, GRADE = Grading of Recommendations Assessment,
45 Development, and Evaluation, WMD = weighted mean difference, SMD =
46 standardized mean difference, CI = confidence interval, RR = relative risk,
47 PRISMA-P = Preferred Reporting Items for Systematic Reviews and Meta-analyses
48 Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,
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58 **Keywords:** acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol,
59 systematic review, meta-analysis
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1. Introduction

Cervical spondylotic radiculopathy (CSR) is defined as neck pain in a radicular pattern in one or both upper extremities related to compression and/or irritation of one or more cervical nerve roots. The most common level of nerve root compression is C7, followed by C6. CSR, accounting for about 60 to 70 % of all cervical spondylosis, is the common and frequently-occurring disease in both middle-aged and elderly populations^[1]. It has been reported that up to 80% of cervical spondylosis patients always complained of neck pain, which will become more and more serious over time. Due to social technology advances, lifestyle changes and the increase in staff members, the incidence of CSR tends to increase and the onset age of the patient gets younger year by year, which has seriously affected the patients' physical health and quality of life.

Management of CSR can be surgical or conservative. Conservative management is the initial treatment of choice for most patients, because surgery may be associated with adverse events and recurrence. Currently, many therapeutic interventions have been applied for the treatment of CSR, including nonsteroidal anti-inflammatory drugs (NSAIDs) ^[2], epidural steroid injections ^[3], acupuncture ^[4], physical therapy ^[5], and exercises ^[6, 7]. The main purpose of these treatments is to relieve pain, improve function, and enhance the quality of life. In clinical practice, acupotomy has also been widely used to treat cervical spondylosis, lumbar disc herniation, knee osteoarthritis and other diseases in China with satisfied efficacy, because of its effectiveness and low risk of complications ^[8-12].

Acupotomy, also named needle-knife, originates from the "nine classical of needles" in Huang Di Nei Jing (*Huangdi's Internal Classic*) and was developed in China in 1976 by Zhu Hanzhang ^[13]. It is a new-style bladed needle that composed of a thick flat-head and a cylindrical body, which is suitable for alleviating the adhesion of a lesion. Acupotomy therapy is considered as a minimally invasive surgery of traditional Chinese medicine, combining Chinese acupuncture therapy and modern surgical principles ^[14]. In the treatment of CSR, the role of acupotomy is to remove

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4 attached tissues, recover the dynamic function of soft tissues, relieve nerve pressure,
5 and promote Qi-blood circulation to ameliorate pain and numbness symptoms [10, 15].
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7 Acupotomy has many benefits because it converts open surgery to closed surgery,
8 thus reducing risk, time, and cost. This method only produces a small scar that will
9 fade with time [11].
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14 Acupotomy has the characteristics of both acupuncture and microinvasive operation.
15 Both acupotomy and acupuncture have been widely used clinically to treat CSR in
16 China with satisfied efficacy. However, there is no systematic review comparing the
17 effectiveness of these two therapies in patients with CSR. It is worthy to critically
18 review the evidence of the comparison of these two therapies to inform clinical
19 practice. Herein, the aim of this study is to compare the therapeutic efficacy and
20 safety between acupotomy and acupuncture on CSR to provide evidence for clinical
21 practice.
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32 **2. Methods**

33 **2.1. Study registration**

34 This systematic review and meta-analysis protocol was registered in PROSPERO
35 (CRD42019117348) at <https://www.crd.york.ac.uk/PROSPERO/#myprospero>.
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39 **2.2. Inclusion criteria for study selection**

40 **2.2.1. Type of study.**

41 We will estimate the research literature according to the criteria of the review
42 objectives and participants, interventions, comparisons, outcomes (PICO).
43 Randomized controlled trials (RCTs), comparing acupotomy against any form of
44 acupuncture with/without additional treatment, will be included in this systematic
45 review. We will include such studies if the expression “randomization” is mentioned.
46 However, we will grade these studies as high in the “risk of bias assessment” if the
47 detailed description on the randomization process is not provided. Furthermore, if an
48 incorrect randomization method such as coin toss was used, the study will not be
49 included. Moreover, blinding will not be considered because of the characteristics of
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4 acupuncture and acupotomy treatment. Additionally, the language of the publications
5 will be limited to Chinese and English.
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7 **2.2.2. Types of participants.**

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9 Patients of any gender or age or race or nationality with CSR received acupotomy or
10 acupuncture therapy with/without additional treatment.
11

- 12 1. In line with the diagnostic criteria of CSR.
- 13 2. Participants who have not undergone an invasive intervention.
- 14 3. No restriction on age.

15
16 The exclusion criteria were shown as follows: (1) Replicated studies; (2) No definite
17 diagnostic criteria of CSR; (3) Wrong interventions: these studies were excluded
18 which used open surgery or acupotomy was manipulated in both groups; (4) Reviews
19 or theory studies; (5) Animal experiments.
20

21 **2.2.3. Types of interventions.**

22 **Experimental interventions**

23 The treatment group will be treated with acupotomy (with/without additional
24 treatment). No restrictions are imposed on times of treatment, frequency of treatment,
25 and length of treatment period.
26

27 **Comparator interventions**

28 The treatment with several types of acupuncture (with/without same additional
29 treatment) will be included in this review as acupuncture, manual acupuncture,
30 auricular acupuncture, scalp acupuncture, fire needling, warm needling, and
31 electro-acupuncture, etc.
32

33 The procedure of acupuncture and acupotomy should be reported in full compliance
34 with the standardized reporting methods such as the Standard of the Basic
35 Manipulations of Acupotomy (ZJ/T D001-2014) and Standards for Reporting
36 Interventions in Controlled Trials of Acupuncture (STRICTA).
37

38 **2.2.4. Types of outcome measures.**

39 Changes in visual analog scale (VAS), symptom score and neck disability index (NDI)
40 will be evaluated as primary outcomes. The total effective rate and the curative rate
41 will be evaluated as secondary outcomes. The secondary outcome measures are as
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4 follows:

5 (1) Total effective rate and curative rate

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7 The total effective rate and curative rate are non-validated outcome measures that are
8 processed secondarily according to certain evaluation criteria such as clinical
9 symptom improvement or the improvement rates of other quantified outcomes. In the
10 assessment of the total effective rate, participants are generally classified as “cured”,
11 “markedly improved”, “improved”, or “non-responder” after treatment. The total
12 effective rate is calculated consistently using the following formula:
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$$19 \quad \textit{Total effective rate} = N_1 + N_2 + N_3 / N$$

$$20 \quad \textit{Curative rate} = N_1 / N$$

21
22 where N1, N2, N3, and N are the number of patients who are cured, markedly
23 improved, improved, and who comprise the sample size, respectively.
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26 (2) The incidence of adverse events.

27 (3) The amount of rescue medication required.

28 29 30 31 **2.3. Data sources**

32 The main sources of information to be obtained in this study include electronic
33 resource databases, trial registries, retroactive references, and different types of grey
34 literature.
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38 Electronics searches:

39 The following electronic databases will be searched: Web of Science, PubMed,
40 Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China
41 Biology Medicine disc (CBM), Wanfang Database and Chinese Scientific Journal
42 Database (VIP). In addition, “gray literature” such as conference proceedings and
43 theses will be allowed. Reference lists of the relevant literature and systematic
44 reviews, as well as the tables of contents related to acupotomy versus acupuncture on
45 CSR, will also be searched. RCTs of acupotomy versus acupuncture with/without
46 additional treatment for CSR patients will be searched in the databases from their
47 inception to December 2018 by two researchers independently.
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58 Searching for other resources:

59 Ambiguous literature will be investigated manually to avoid missing eligible trials.
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Reference lists of identified publications will also be manually searched. In addition, the following journals published in Chinese will be searched as a supplement: *Chinese Acupuncture and Moxibustion* (1981–December 2018), *Acupuncture Research* (1976–December 2018), *World Journal of Acupuncture-moxibustion* (1991–December 2018), *Journal of Clinical Acupuncture and Moxibustion* (1985–December 2018), *Shanghai Journal of Acupuncture and Moxibustion* (1982–December 2018) and *Journal of Traditional Chinese Medicine* (1960–December 2018).

2.4. Search strategy

The strategy will be created according to the Cochrane handbook guidelines. The established search strategy for PubMed was displayed, as follows:

Mesh term #1: ((acupotomy) OR (acupotome) OR (needle knife) OR (needle scalpel) OR (acupotomology) OR (miniscalpel acupuncture) OR (miniscalpel needle) OR (stiletto needle) OR (sword like needle) OR (Xiaozhendao)): ti, ab, kw

Mesh term #2: ((acupuncture) OR (manual acupuncture) OR (auricular acupuncture) OR (scalp acupuncture) OR (fire needling) OR (warm needling) OR (electro-acupuncture)): ti, ab, kw

Mesh term #3: ((cervical radiculopathy) OR (cervical spondylotic radiculopathy) OR (cervical spondylopathy) OR (cervical spondylosis) OR (neck pain) OR (neck syndrome)): ti, ab, kw

Mesh term #4: ((clinical trials) OR (random control trials))

#1 AND #2 AND #3 AND #4

The equivalent search words will be used in Chinese databases.

2.5. Data collection and analysis

2.5.1. Selection of studies.

The researchers will import the retrieved literature into an EndNote library and eliminate duplicate data. Two review authors (Renpan Zhang and Anyang Lin) selected studies for eligibility and checked against the inclusion criteria independently. Any disagreement will be resolved by consensus or consultation with a third independent researcher (Hongjia Zhao). The selection process is illustrated in a

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4 PRISMA flow diagram (**Figure. 1**).

5 6 **2.5.2. Data extraction and management.**

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8 Two review authors (Jing Liu and Zhongbiao Xiu) will independently use a
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10 standardized form for extracting data of the included articles. The following data were
11
12 extracted: general information (e.g., title, authors, year and published country), details
13
14 of study (e.g., design, inclusion and exclusion criteria, blinding, randomization and
15
16 sample size), participant characteristics (e.g., age and number of subjects), description
17
18 of interventions, types of outcomes assessed, adverse events, and other detailed
19
20 information. If necessary, we will contact the corresponding authors of trials as much
21
22 as possible for further information.

23 24 **2.5.3. Assessment of risk of bias and reporting of study quality.**

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26 The Cochrane risk of bias tool will be applied to evaluate the quality and risk of bias
27
28 in the ultimately included studies by two authors (Renpan Zhang and Anyang Lin)
29
30 independently [16-17]. Risk of bias assessment categories will include the following: (1)
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32 random sequence generation; (2) allocation concealment; (3) blinding of participants;
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34 (4) blinding of outcome assessors; (5) completeness of outcome data; (6) selective
35
36 outcome reporting; and (7) other biases. The assessments for each item will be graded
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38 as low risk, unclear risk, and high risk to evaluate several risks of bias that can occur
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40 in RCTs. In the case of other sources of bias, it was evaluated as “low” if the
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42 characteristics of participants in each group were reported to be statistically
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44 homogeneous at baseline, but was otherwise rated “high”. The results were presented
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46 as a risk of bias graph and risk of bias summary using the Cochrane Collaboration’s
47
48 software program Review Manager (RevMan) version 5.3 for Windows (Copenhagen,
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50 The Nordic Cochrane Centre, the Cochrane Collaboration, 2012). If there is any
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52 disagreement take place, the arbiter (Hongjia Zhao) will do the final judge.

53 54 **2.5.4. Measures of treatment effect.**

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56 Continuous outcomes will be presented as the mean difference (MD) for analysis,
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58 while dichotomous data will be expressed as relative risk (RR), both of them will be
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60 with 95% confidence intervals (CI) [18]. When the same outcome is measured in
different ways, the standardized mean difference (SMD) with 95%CI will be selected

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4 to express the size of the intervention effect.

5 6 **2.5.5. Dealing with missing data.**

7 We will attempt to contact authors of included studies for missing or incomplete data
8 by E-mail. However, If the missing data cannot be obtained, the study will be
9 excluded from the analysis.
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12 13 **2.5.6. Assessment of heterogeneity.**

14 Statistical heterogeneity will be detected by the I^2 statistic and χ^2 test. $P < 0.1$ of χ^2
15 test or $I^2 > 50\%$ indicates the possibility of statistical heterogeneity among the studies.
16 If the included studies have existing heterogeneity, a random-effect model will be
17 used. Otherwise, we will use a fixed-effect model for calculation.
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20 21 **2.5.7. Assessment of reporting bias.**

22 If more than 10 studies are included, visual asymmetry on the funnel plots will be
23 used to assess the potential reporting biases. In addition, we will test asymmetry using
24 the Harbord modified test for dichotomous outcomes and Egger test for continuous
25 outcomes.
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28 29 **2.5.8. Data synthesis.**

30 The Review Manager 5.3 will be employed for meta-analysis. When statistical
31 heterogeneity is low among the results, the fixed-effects model will be used for the
32 meta-analysis. However, there is considerable heterogeneity, the random-effects
33 model will be performed to analyze the pooled effect estimates.
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36 37 **2.5.9. Subgroup analysis.**

38 If there is significant heterogeneity in the included trials, we will conduct a subgroup
39 analysis based on the acupotomy or acupuncture interventions with/without additional
40 treatment, types of acupuncture (acupuncture, manual acupuncture, and
41 electro-acupuncture, etc.) and different outcomes.
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44 45 **2.5.10. Sensitivity analysis.**

46 A sensitivity analysis will be conducted to identify whether the review conclusions
47 are robust according to the following criteria: missing data, sample size, heterogeneity
48 qualities, and statistical model.
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51 52 **2.5.11. Grading the quality of evidence.**

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4 The evidence level will be assessed by using the method for Grading of
5 Recommendations Assessment, Development, and Evaluation (GRADE) and
6 classified into four possible ratings: very low, low, moderate, or high.
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9 10 **2.5.12. Patient and Public Involvement**

11 Patients and or public were not involved because no primary data are collected.
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15 **Ethics and dissemination:** The ethical approval will not be needed because no
16 primary data are collected. Our results will provide clear evidence to determine
17 whether acupotomy therapy is an effective and safe intervention for patients with
18 CSR, and thus will be beneficial to patients, practitioners, and policymakers. This
19 review will be published in a peer-reviewed journal and will be presented at an
20 international academic conference for dissemination.
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29 **3. Discussion**

30 The main symptoms of CSR include neck and shoulder pain, radicular pain or
31 numbness in the upper extremities, weakening of grip strength, and sensory
32 disturbances. Acupotomy, containing the characteristics of both acupuncture and
33 micro-invasive operation, have been widely used clinically to treat CSR by peeling
34 synechia, removing attached tissue, and relieve nerve pressure. Currently, there is
35 limited evidence to determine whether acupotomy and acupuncture have a similar
36 effect on relieving pain and improving other symptoms of CSR. Therefore, the
37 comparisons of therapeutic efficacy and safety will be made between acupotomy and
38 acupuncture with/without the same additional treatment is given to both groups. This
39 systematic review and meta-analysis will provide high-quality evidence-based
40 medicine to determine whether acupotomy therapy is an effective and safe
41 intervention for patients with CSR.
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56 **Contributors**

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58 Bin Chen and Hongjia Zhao designed the systematic review. The article was drafted
59 by Bin Chen and Cai Zhang. Renpan Zhang, Anyang Lin, Jing Liu, and Zhongbiao
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4 Xiu will independently screen the potential studies, extract the data, assess the risk of
5 bias and finish the data synthesis. Hongjia Zhao will arbitrate any disagreement and
6 ensure that no errors occur during the review. All review authors critically reviewed,
7 revised, and approved the subsequent and final version of the protocol.
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14
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23 **Competing interests**

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25 None declared.
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29 **Patient consent**

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31 Not required.
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Figure Legends

Figure 1. PRISMA flow diagram of study process

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PRISMA flow diagram of study process

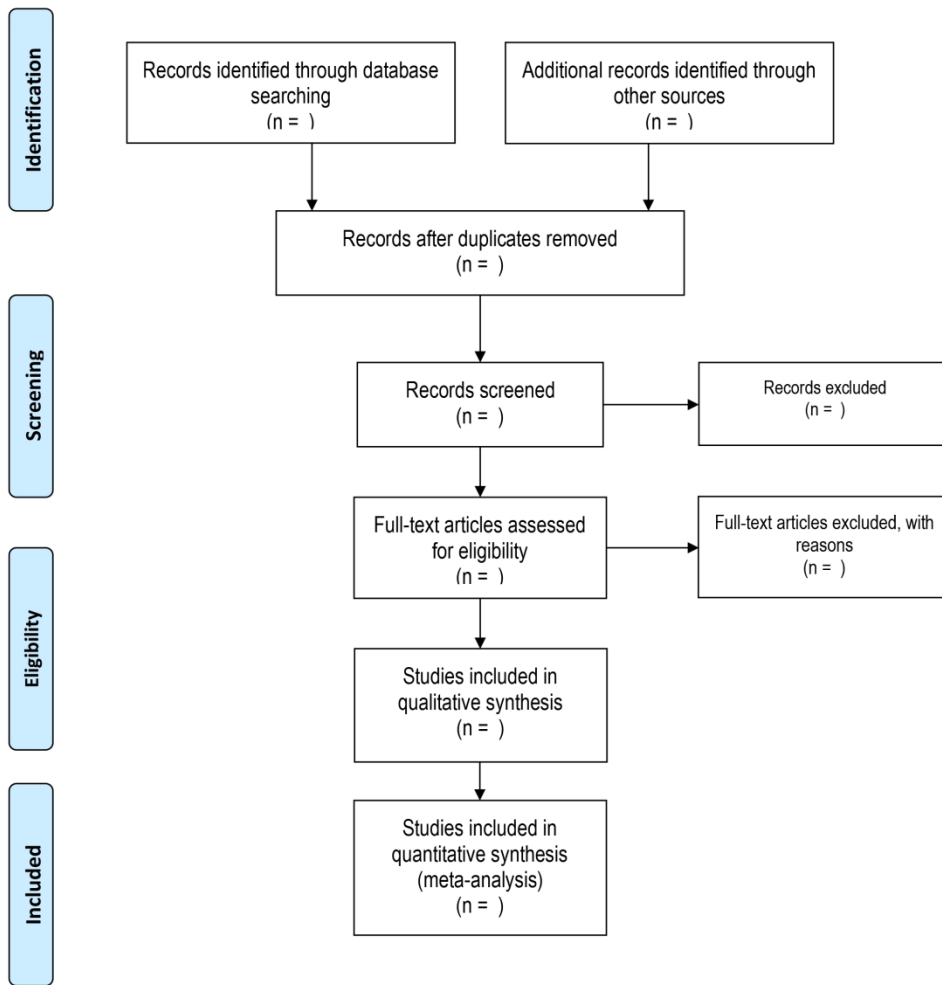


Figure 1. PRISMA flow diagram of study process

188x225mm (300 x 300 DPI)