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

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

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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 rearchers 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

(P<0.05), a random-effects model will be used. Otherwise, we will calculate using a fixed effects model.

Results: This systematic review and meta-analysis will use high-quality evidence-based medicine to compare the efficacy and safety between acupotomy and acupuncture in CSR.

Conclusion: The result will provide clear evidence to determine whether acupotomy therapy is an effective and safe intervention for patients with CSR.

Strengths and limitations of this study

- This systematic review will comprehensively compare the therapeutic efficacy and safety between acupotomy and acupuncture for cervical spondylotic radiculopathy.
- The study screening, data extraction and quality assessment will be performed by two independent reviewers.
- Different types of acupuncture and some of the reviewed trials with small sample sizes may cause considerable heterogeneity in this review. High- quality trials might be deficient to generate convincing conclusions.

Abbreviations: CSR = Cervical spondylotic radiculopathy, CBM = China Biomedical Literature Database, CNKI = China National Knowledge Infrastructure, VIP = China Science and Technology Journal Database, RCTs = randomized controlled trials, VAS = Visual analog scale, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, WMD = weighted mean difference, SMD = standardized mean difference, CI = confidence interval, RR = relative risk, PRISMA-P = Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,

Keywords: acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, 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

safety between acupotomy and acupuncture on CSR to provide evidence for clinical practice.

2. Methods

2.1. Design and registration of the review

This systematic review and meta-analysis protocol was registered in PROSPERO (CRD42019117348) at https://www.crd.york.ac.uk/PROSPERO/#myprospero and developed following the guideline of Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P) 2015 [16].

2.2. Inclusion criteria for study selection

2.2.1. Type of study.

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

2.2.2. Types of participants.

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

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

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

2.2.3. Types of interventions.

Experimental interventions

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

Comparator interventions

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

2.2.4. Types of outcome measures.

The primary outcome measurements will be total effective rate and curative rate. The secondary outcome measures will include visual analog scale (VAS) and symptom score.

2.3. Data sources

The main sources of information that will be obtained in this study include electronic resource databases, trial registries, retroactive references, and different types of grey literature.

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). Reference lists of the relevant literature and systematic reviews, as well as the tables of contents related to acupotomy versus acupuncture on CSR will also be searched. RCTs of acupotomy versus acupuncture with/without additional treatment for CSR patients will be searched in the databases from their inception to December 2018 by two rearchers independently

2.4. Search strategy

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

Mesh term #1: ((acupotomy) OR (acupotome) OR (needle knife) OR (needle scalpel)): 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 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

reporting, and other bias. The assessments for each item will be graded as low risk, unclear risk, and high risk. 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 calculate using a fixed-effect model.

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 analyse 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 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

by Bin Chen and Cai Zhang. Renpan Zhang, Anyang Lin, Jing Liu and Zhongbiao Xiu will independently screen the potential studies, extract the data, assess the risk of bias and finish the data synthesis. Hongjia Zhao will arbitrate any disagreement and ensure that no errors occur during the review. All review authors critically reviewed, revised, and approved the subsequent and final version of the protocol.

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Competing interests

None declared.

Conceptualization: Ben Chen, Cai Zhang.

Data curation: Ben Chen, Renpan Zhang.

Formal analysis: Ben Chen, Renpan Zhang.

Investigation: Anyang Lin, Zhongbiao Xiu, Jing Liu.

Methodology: Ben Chen, Hongjia Zhao.

Project administration: Hongjia Zhao.

Software: Anyang Lin, Zhongbiao Xiu.

Supervision: Hongjia Zhao, Ben Chen.

Validation: Hongjia Zhao, Jing Liu.

Visualization: Ben Chen.

Writing – original draft: Ben Chen, Cai Zhang.

Writing – review & editing: Hongjia Zhao.

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Figure Legends

Figure 1. PRISMA flow diagram of study process

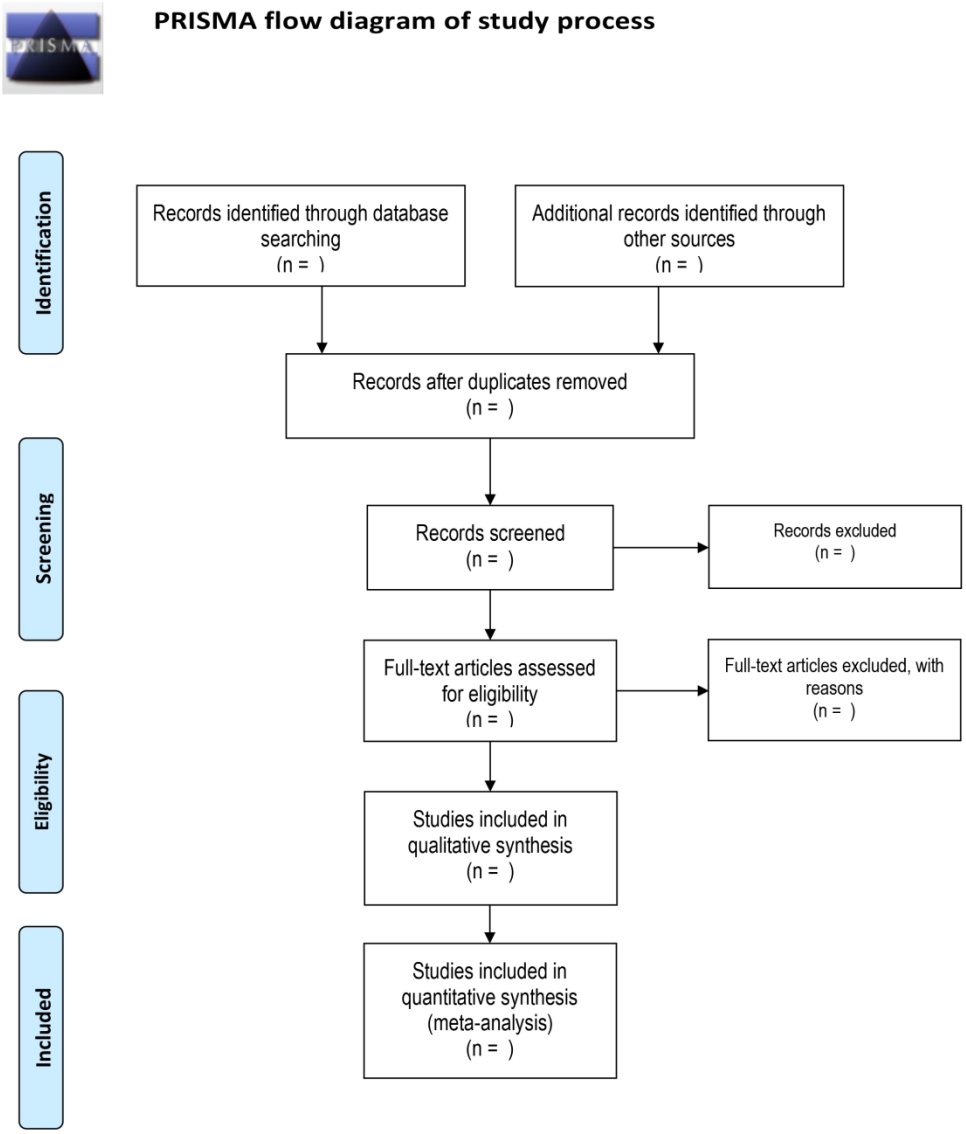

Figure 1. PRISMA flow diagram of study process

188x225mm (300 x 300 DPI)

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Primary Subject Heading:	Complementary medicine
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Acupotomy versus acupuncture for cervical spondylotic radiculopathy: protocol of a systematic review and meta-analysis

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(1. Department of Rehabilitation, The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine, Fuzhou 350004, Fujian Province, China. 2. Fujian University of Traditional Chinese Medicine, Fuzhou 350122, Fujian Province, China.)

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 National Knowledge Infrastructure (CNKI), China Biology Medicine disc (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. Visual analog scale and symptom score will be assessed as the primary outcomes. The total effective rate, curative rate, adverse events, and amount of rescue medication used will be assessed as the secondary outcomes. 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 (P<0.05), a random-effects model will be used. Otherwise, we will calculate using a fixed effects model.

Ethics and dissemination: The ethical approval is not required because no primary data are collected. This review will be published in a peer-reviewed journal and will be presented at an international academic conference for dissemination. Our results will provide clear evidence to determine whether acupotomy therapy is an effective and safe intervention for patients with CSR, and thus will be beneficial to patients, practitioners, and policymakers.

PROSPERO registration number: CRD42019117348.

Strengths and limitations of this study

- This systematic review will comprehensively compare the therapeutic efficacy and safety between acupotomy and acupuncture for cervical spondylotic radiculopathy.
- The study screening, data extraction, and quality assessment will be performed by two independent reviewers.
- Different types of acupuncture and some of the reviewed trials with small sample sizes may cause considerable heterogeneity in this review. High- quality trials might be deficient to generate convincing conclusions.

Abbreviations: CSR = Cervical spondylotic radiculopathy, CBM = China Biology Medicine disc, CNKI = China National Knowledge Infrastructure, VIP = China Science and Technology Journal Database, RCTs = randomized controlled trials, VAS = Visual analog scale, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, WMD = weighted mean difference, SMD = standardized mean difference, CI = confidence interval, RR = relative risk, PRISMA-P = Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,

Keywords: acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, 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

attached tissues, recover the dynamic function of soft tissues, relieve nerve pressure, and promote Qi-blood circulation to ameliorate pain and numbness symptoms [10, 15]. Acupotomy has many benefits because it converts open surgery to closed surgery, thus reducing risk, time, and cost. This method only produces a small scar that will fade with time [11].

Acupotomy has the characteristics of both acupuncture and microinvasive operation. 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 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 safety between acupotomy and acupuncture on CSR to provide evidence for clinical practice.

2. Methods

2.1. Study registration

This systematic review and meta-analysis protocol was registered in PROSPERO (CRD42019117348) at https://www.crd.york.ac.uk/PROSPERO/#myprospero.

2.2. Inclusion criteria for study selection

2.2.1. Type of study.

We will estimate the research literature according to the criteria of the review objectives and participants, interventions, comparisons, outcomes (PICO). Randomized controlled trials (RCTs), comparing acupotomy against any form of acupuncture with/without additional treatment, will be included in this systematic review. We will include such studies if the expression “randomization” is mentioned. However, we will grade these studies as high in the “risk of bias assessment” if the detailed description on the randomization process is not provided. Furthermore, if an incorrect randomization method such as coin toss was used, the study will not be included. Moreover, blinding will not be considered because of the characteristics of

acupuncture and acupotomy treatment. Additionally, the language of the publications will be limited to Chinese and English.

2.2.2. Types of participants.

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

1. In line with the diagnostic criteria of CSR.

2. Participants who have not undergone an invasive intervention.

3. No restriction on age.

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

2.2.3. Types of interventions.

Experimental interventions

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

Comparator interventions

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

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

2.2.4. Types of outcome measures.

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

(1) Total effective rate and curative rate

The total effective rate and curative rate are non-validated outcome measures that are processed secondarily according to certain evaluation criteria such as clinical symptom improvement or the improvement rates of other quantified outcomes. In the assessment of the total effective rate, participants are generally classified as "cured", "markedly improved", "improved", or "non-responder" after treatment. The total effective rate is calculated consistently using the following formula:

$$\textit{Total effective rate} = N_1 + N_2 + N_3 / N$$

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

where N1, N2, N3, and N are the number of patients who are cured, markedly improved, improved, and who comprise the sample size, respectively.

(2) The incidence of adverse events.

(3) The amount of rescue medication required.

2.3. Data sources

The main sources of information to be obtained in this study include electronic resource databases, trial registries, retroactive references, and different types of grey literature.

Electronics searches:

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

Searching for other resources:

Ambiguous literature will be investigated manually to avoid missing eligible trials. 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).

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

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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.

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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 micro-invasive operation, have been widely used clinically to treat CSR by peeling synechia, removing attached tissue, and relieve nerve pressure. Currently, there is limited evidence to determine whether acupotomy and acupuncture have a 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 the 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.

Contributors

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

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Applied Discipline -- Clinical Medicine "Double First Class" Construction Project.

Competing interests

None declared.

Patient consent

Not required.

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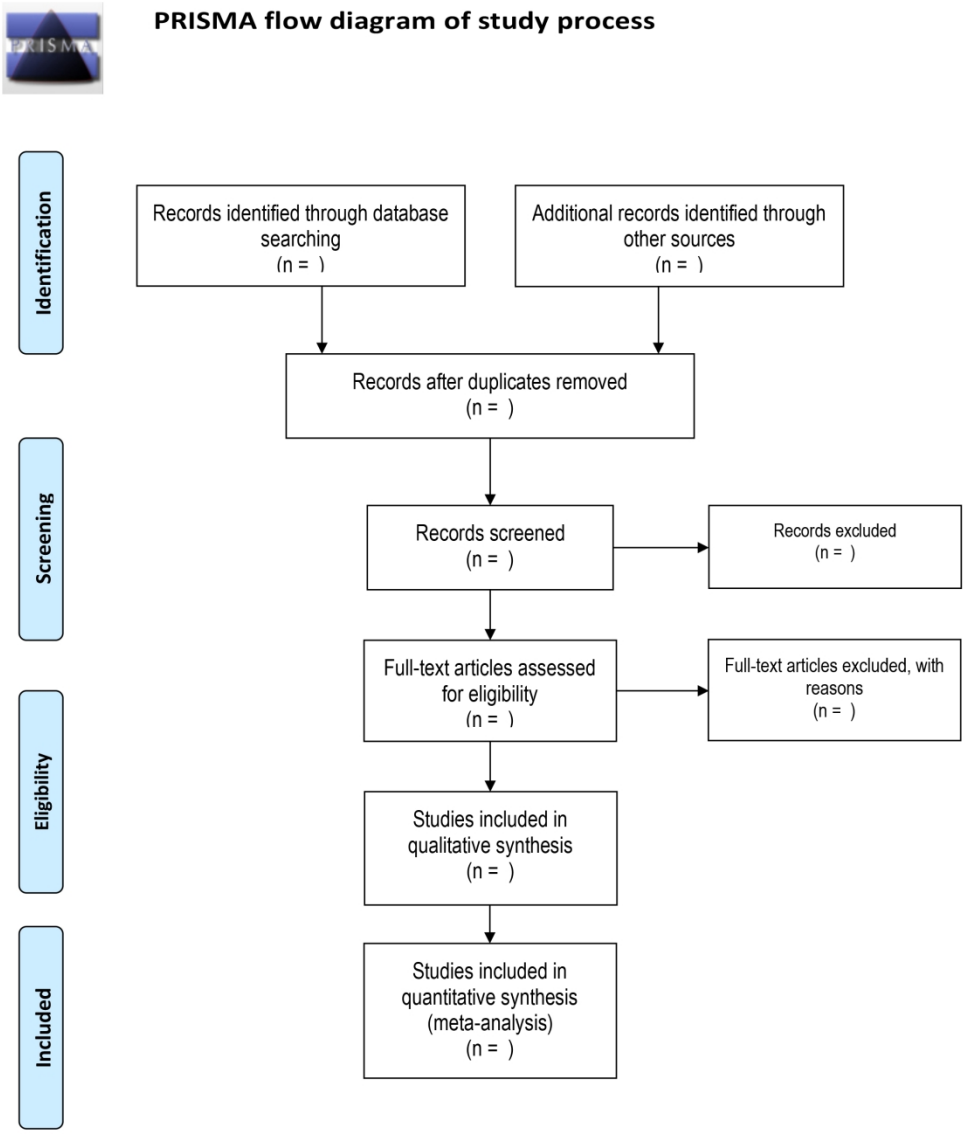
Figure Legends

Figure 1. PRISMA flow diagram of study process



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188x225mm (300 x 300 DPI)

BMJ Open

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

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Complete List of Authors:	Chen, Bin; The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine, Department of Rehabilitation Zhang, Cai; Fujian University of Traditional Chinese Medicine Zhang, Ren-pan ; Fujian University of Traditional Chinese Medicine Lin, An-yang; Fujian University of Traditional Chinese Medicine Xiu, Zhong-biao; The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine Liu, Jing; The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine Zhao, Hong-jia ; The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, systematic review, meta-analysis

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

Bin Chen[1], Cai Zhang[2], Ren-Pan Zhang[1,2], An-Yang Lin[1,2], Zhong-Biao Xiu[1], Jing Liu[1], Hong-Jia Zhao[1 #]

(1. Department of Rehabilitation, The Affiliated People's Hospital of Fujian University of Traditional Chinese Medicine, Fuzhou 350004, Fujian Province, China. 2. Fujian University of Traditional Chinese Medicine, Fuzhou 350122, Fujian Province, China.)

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 National Knowledge Infrastructure (CNKI), China Biology Medicine disc (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. Visual analog scale, symptom score and neck disability index (NDI) will be assessed as the primary outcomes. The total effective rate, curative rate, adverse events, and amount of rescue medication used will be assessed as the secondary outcomes. 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 (P<0.05), a random-effects model will be used. Otherwise, we will calculate using a fixed effects model.

Ethics and dissemination: The ethical approval is not required because no primary data are collected. This review will be published in a peer-reviewed journal and will be presented at an international academic conference for dissemination.

PROSPERO registration number: CRD42019117348.

Strengths and limitations of this study

- This systematic review will comprehensively compare the therapeutic efficacy and safety between acupotomy and acupuncture for cervical spondylotic radiculopathy.
- The study screening, data extraction, and quality assessment will be performed by two independent reviewers.
- Different types of acupuncture and some of the reviewed trials with small sample sizes may cause considerable heterogeneity in this review. High- quality trials might be deficient to generate convincing conclusions.

Abbreviations: CSR = Cervical spondylotic radiculopathy, CBM = China Biology Medicine disc, CNKI = China National Knowledge Infrastructure, VIP = China Science and Technology Journal Database, RCTs = randomized controlled trials, VAS = Visual analog scale, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, WMD = weighted mean difference, SMD = standardized mean difference, CI = confidence interval, RR = relative risk, PRISMA-P = Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols, NSAIDs = nonsteroidal anti-inflammatory drugs,

Keywords: acupotomy, acupuncture, cervical spondylotic radiculopathy, protocol, 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

attached tissues, recover the dynamic function of soft tissues, relieve nerve pressure, and promote Qi-blood circulation to ameliorate pain and numbness symptoms [10, 15]. Acupotomy has many benefits because it converts open surgery to closed surgery, thus reducing risk, time, and cost. This method only produces a small scar that will fade with time [11].

Acupotomy has the characteristics of both acupuncture and microinvasive operation. 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 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 safety between acupotomy and acupuncture on CSR to provide evidence for clinical practice.

2. Methods

2.1. Study registration

This systematic review and meta-analysis protocol was registered in PROSPERO (CRD42019117348) at https://www.crd.york.ac.uk/PROSPERO/#myprospero.

2.2. Inclusion criteria for study selection

2.2.1. Type of study.

We will estimate the research literature according to the criteria of the review objectives and participants, interventions, comparisons, outcomes (PICO). Randomized controlled trials (RCTs), comparing acupotomy against any form of acupuncture with/without additional treatment, will be included in this systematic review. We will include such studies if the expression “randomization” is mentioned. However, we will grade these studies as high in the “risk of bias assessment” if the detailed description on the randomization process is not provided. Furthermore, if an incorrect randomization method such as coin toss was used, the study will not be included. Moreover, blinding will not be considered because of the characteristics of

acupuncture and acupotomy treatment. Additionally, the language of the publications will be limited to Chinese and English.

2.2.2. Types of participants.

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

1. In line with the diagnostic criteria of CSR.

2. Participants who have not undergone an invasive intervention.

3. No restriction on age.

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

2.2.3. Types of interventions.

Experimental interventions

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

Comparator interventions

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

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

2.2.4. Types of outcome measures.

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

follows:

(1) Total effective rate and curative rate

The total effective rate and curative rate are non-validated outcome measures that are processed secondarily according to certain evaluation criteria such as clinical symptom improvement or the improvement rates of other quantified outcomes. In the assessment of the total effective rate, participants are generally classified as “cured”, “markedly improved”, “improved”, or “non-responder” after treatment. The total effective rate is calculated consistently using the following formula:

$$\textit{Total effective rate} = N_1 + N_2 + N_3 / N$$

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

where N1, N2, N3, and N are the number of patients who are cured, markedly improved, improved, and who comprise the sample size, respectively.

(2) The incidence of adverse events.

(3) The amount of rescue medication required.

2.3. Data sources

The main sources of information to be obtained in this study include electronic resource databases, trial registries, retroactive references, and different types of grey literature.

Electronics searches:

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

Searching for other resources:

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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).

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Contributors

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Competing interests

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Patient consent

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Figure Legends

Figure 1. PRISMA flow diagram of study process

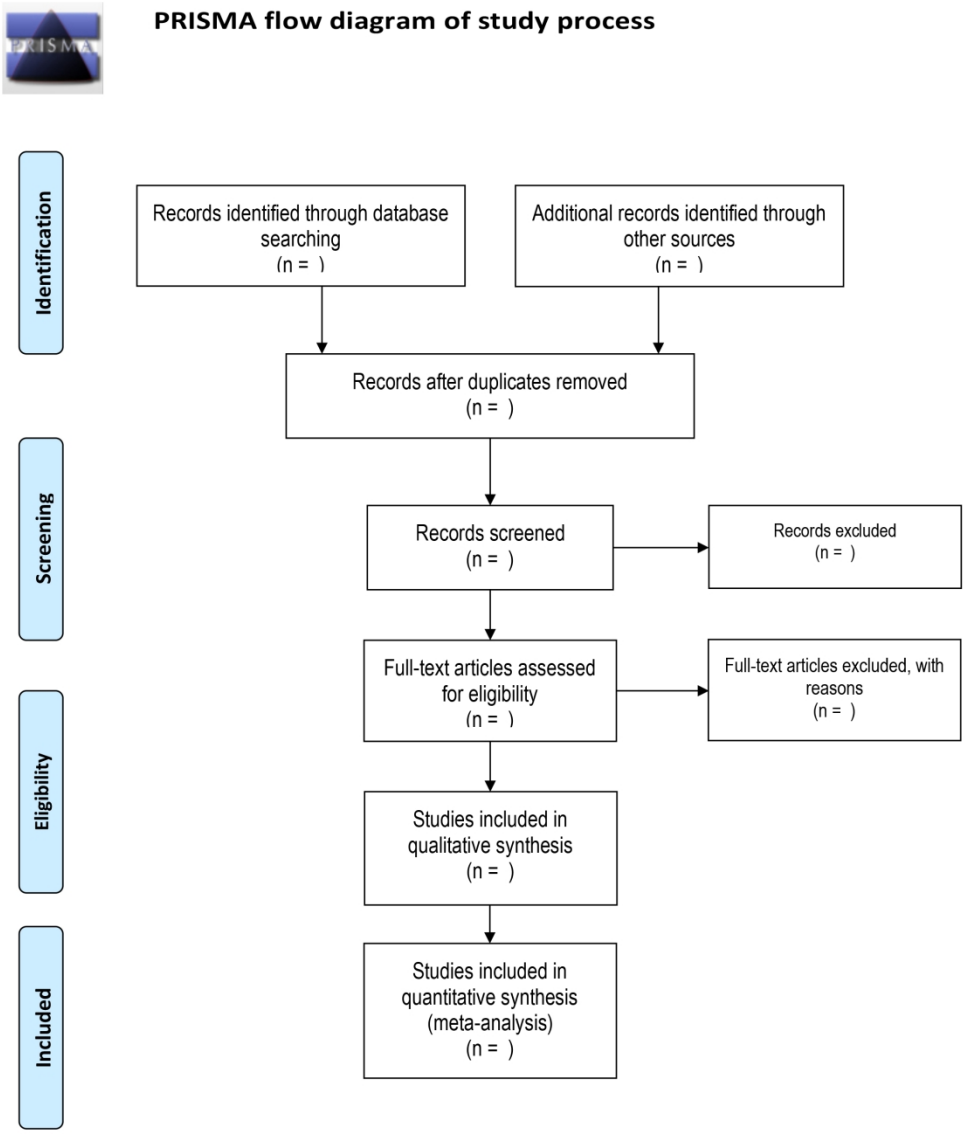

Figure 1. PRISMA flow diagram of study process

188x225mm (300 x 300 DPI)