

# The effect of exercise on cervical radiculopathy

## A systematic review and meta-analysis

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### Abstract

**Background:** Cervical radiculopathy (CR), which is most often stems from degenerative disease in the cervical spine, has increasingly become a common and frequently occurring disease in clinic due to the popularity of electronic products, such as computers and cell phones. Some studies have shown that exercise or exercise combined with other treatments can effectively decrease pain and improve functional status. The objective was to analyze the effects of exercise for treating patients with CR.

**Methods:** Seven databases were searched from inception to December 2018. Randomized controlled trials involving exercise alone or exercise combined with conventional treatment were enrolled. Data were pooled after trials quality assessment for meta-analysis. Outcomes were pain (visual analog scale [VAS]), quality of life (12-short form health survey, 36-short form health survey), and physical function assessed by neck disability index (NDI).

**Results:** Ten studies involving 871 participants with CR were included. Meta-analysis revealed that compared with control group, there was a reduction in VAS (standardized mean difference = -0.89; 95% confidence interval [CI]: -1.34 to -0.44;  $Z=3.89$ ;  $P<.001$ ). There was also an improvement of NDI (mean difference = -3.60; 95% CI: -6.27 to -0.94;  $Z=2.65$ ;  $P=.008$ ). Additionally, although the results of subgroup analyses were changed due to the paucity of the quantity and quality of the included studies. The pooled results were verified to be stable by sensitivity analyses. Besides, the grading of recommendations assessment, development, and evaluation level of evidence is low for each outcome.

**Conclusion:** Exercise alone or exercise plus other treatment may be helpful to patients with CR. However, exercise option should be carefully considered for each patient with CR in accordance with their different situations. Large-scale studies using proper methodology are recommended.

**Abbreviations:** CI = confidence interval, CR = cervical radiculopathy, GRADE = the grading of recommendations assessment, development, and evaluation, MD = mean difference, NDI = neck disability index, PROSPERO = international database of prospectively registered systematic reviews, RCTs = randomized controlled trials, SF-12 = 12-short form health survey, SF-36 = 36-short form health survey, SMD = standardized mean difference, VAS = visual analog scale.

**Keywords:** cervical radiculopathy, exercise, meta-analysis, neck disability index (NDI), visual analog scale (VAS)

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## 1. Introduction

Cervical radiculopathy (CR), which is a normal result of degenerative changes such as cervical disc herniation and bone hyperplasia, is characterized by neck pain and radiating pain from the neck to the shoulder.<sup>[1]</sup> And significant functional limitations and disabilities are common presenting complaints for people suffering from CR, with a peak at 50 to 54 years of age, because of structurally and functionally causing neural inflammation, edema, hypoxia, ischemia, and so on.<sup>[2,3]</sup> A study from the US military found an incidence of 1.79 per 1000 person-years.<sup>[4]</sup> At present, treatment for CR includes surgical and nonsurgical approaches.<sup>[5]</sup> However, the surgical treatment of CR is still controversial as a result of many complications after operation involving adjacent segment degeneration, loss in intervertebral disc height, and so on.<sup>[6]</sup> Conservative measures, including manual therapy, exercise, traction, cervical collar, and nonsteroidal antiinflammatory drugs, can relieve pain, improve neurologic function for CR patients.<sup>[2,3,7]</sup> However, none of the commonly recommended nonsurgical therapies for CR has been examined in randomized, placebo-controlled trials.<sup>[3,8]</sup>

In addition, lots of studies have shown that exercise or exercise combined with other treatments can effectively decrease pain, improve functional status and quality of life in patients with CR.<sup>[9,10,11]</sup> However, the studies evaluating physical exercise for patients with CR are of various quality, and the number of patients in the trials is small. Moreover, the guidelines for exercise therapy for CR have not given clear recommendations.<sup>[12–15]</sup> Hence, high-level quality evidence directly comparing exercise and no exercise intervention is urgently needed to help clinical decision-making for clinicians. After careful search, there are no published meta-analyses investing if the use of exercise actually improve clinical outcomes. So this systematic review and meta-analysis were to evaluate the existing literature about exercise therapy treating for CR to determine the strength of evidence.

## 2. Materials and methods

All analysis results of this study were based on previously published literature and therefore did not require ethical approval or patient consent. The protocol of this systematic review and meta-analysis has been published on the international database of prospectively registered systematic reviews (PROSPERO), which the registration number is CRD42019121886.

### 2.1. Literature research

The search strategies recommended by the Cochrane Back Review Group for the identification of randomized controlled trials (RCTs) were used.<sup>[16]</sup> The documents were searched using multiple online databases at home and abroad including Pubmed, Embase, Web of Science, the Cochrane Library, Chinese National Knowledge Infrastructure Database, Wanfang database, and VIP database from their start to December 2018. There were no restrictions on the date of the studies or any language, publication type, and status. The key terms used were “cervical radiculopathy,” “cervical spondylotic radiculopathy,” “nerve-root type cervical spondylosis,” “neck and arm pain,” “neck pain with radiculopathy,” “neck disorder with radiculopathy,” “exercise,” “physical activity,” “motion,” “fitness.” Different search strategies were used for Chinese and foreign language databases. Furthermore, a manual retrieval of previously published systematic reviews concerning the exercise therapy for CR was performed.

### 2.2. Inclusion criteria

The documents retrieved were selected by 2 independent reviewers to assess eligibility, and any disagreements were resolved in discussion or adjudicated by a third reviewer. Literature was reviewed to examine whether each study met the following criteria:

- (1) the type of publication must be a RCT;
- (2) participants must be patients with CR;
- (3) the intervention in the treatment group was exercise (without restriction for control group).

When multiple time points are reported in a study or in multiple articles of the same study, the longest follow-up period for treatment was considered in our article. And if overlapping groups of participants are reported in different studies, literature with high quality or large sample size is selected as the subjects. Full texts of all references were available.

### 2.3. Exclusion criteria

The excluded studies with the following reasons:

- (1) the studies did not meet the above criteria;
- (2) both the treatment group and the control group included exercise therapy;
- (3) the studies were conducted in the form of letters, abstracts, reviews, or comments;
- (4) the studies could not extract relevant data;
- (5) the CR patients were treated with surgery.

### 2.4. Data extraction

The following data were independently extracted by 2 authors: the name of first author, year of publication, study type, country, number of patients under exercise treatment and control group, sample size, age, gender of patients, disease course, the details of control interventions, follow-up duration, outcome, and intervention period. If the relevant data had not been reported, the authors may be contacted by email or in other means to try to obtain the missing contents.

### 2.5. Quality assessment

Assessing the risk of bias of RCTs in this review used the Cochrane Collaboration Risk of Bias Tool. And risk of bias was assessed according to the Cochrane Handbook.<sup>[16]</sup> For each included study, each type of bias was categorized as high, low, or unclear and entered into the risk of bias table. Two reviewers independently assessed the risk of bias of the included studies. Any discrepancies were resolved by consensus, including input from a third party if required.

### 2.6. Outcome measures

The 3 most recommended outcome indicators – visual analog scale (VAS), neck disability index (NDI), 36-short form health survey (SF-36) (or 12-short form health survey [SF-12]) in the guidelines on CR issued by the North American Spinal Association were selected as outcome indicators. VAS was the main outcome measure, and the secondary outcome measures were NDI and SF-36 (or SF-12).

## 2.7. Data synthesis and statistical analysis

The outcomes of interest include dichotomous data and continuous variables, dichotomous data were presented as the relative risk and mean difference (MD) was used to express the continuous variables. Meanwhile, standardized mean difference (SMD) was chosen if clinical outcome was the same but measured using different methods, evaluation criterion or the baselines of the studies are inconsistent in the different trials. The 95% confidence interval (CI) was computed. Heterogeneity across studies was quantified by the  $I^2$  statistic. An  $I^2 > 50\%$  was considered to represent the possibility of statistical heterogeneity, and the random-effects model was used in this meta-analysis. Otherwise, no obvious heterogeneity ( $I^2 < 50\%$ ) was considered to have occurred in the included studies, and the fixed-effects model was used. The forest plot for each parameter was constructed to illustrate the weight ratio of each incorporated study. Each article one by one was excluded to evaluate the sensitivity of the meta-analysis, and to compare the differences in the combined effects before and after. If the pooled results are reversed after exclusion, the results of this meta-analysis may be unstable. All statistical analyses were carried out using the RevMan5.3 software, and the significance threshold was a 2-sided  $P < .05$ . According to Cochrane Handbook 5.3, if inclusion studies include a study with multiple intervention groups, the recommended method in most situations is to combine all relevant experimental intervention groups of the study into a single group and to combine all relevant control intervention groups into a single control group. And the formulates of continuous variables for combining groups are displayed in Supplemental Table 1, <http://links.lww.com/MD/D327>. For dichotomous outcomes, both the sample sizes and the numbers of people with events can be summed across groups.

## 2.8. Grading the quality of evidence

The grading of recommendations assessment, development, and evaluation (GRADE) method was used to evaluate the quality of meta-analysis. Levels of quality of evidence were defined as high, moderate, low, and very low. All operations are on this page: <https://gradepro.org/>.

## 3. Results

### 3.1. Literature search and study sample characteristics

Supplemental Figure 1, <http://links.lww.com/MD/D327> summarizes our search for eligible studies.

A total of 3786 references were identified using the outlined literature search strategy. Among them, 1738 references were duplicated. According to the inclusion and exclusion criteria, 1858 articles were excluded after reading the titles and abstracts. Then, after a careful review of the full text, 180 references were excluded. Lastly, 10 RCTs were included in the systematic review and meta-analysis.

The characteristics of the included trials are summarized in Table 1. Two trials<sup>[17,18]</sup> were published in English, the others<sup>[19–26]</sup> in Chinese. Two studies<sup>[18,26]</sup> were RCTs with 3 parallel arms and the rest were trials with 2 parallel arms. In this meta-analysis, a total of 871 participants with CR were involved (424 and 447 in the treatment and control group, respectively). The trial sample size ranged from 41 to 192 participants. The intervention period is

reported between 10 days to 2 months. There was no baseline imbalance in demographic characteristics or results between the study groups. Two trials<sup>[17,18]</sup> reported details of sample size calculations.

### 3.2. Risk of bias

Figure 1 indicated the graph of methodological quality of articles. In the included studies, 6 trials showed methods of randomization using a random number table,<sup>[19,23,26]</sup> computer random method,<sup>[18,25]</sup> or the roll of a dice.<sup>[17]</sup> The remaining 4 trials<sup>[20–22,24]</sup> indicated “randomly allocating,” the detailed method used to generate the randomization sequence was not revealed. Two studies showed allocation concealment.<sup>[17,18]</sup> And the other studies did not report it clearly. All trials did not mention whether or not to use the blind method. Only 1 trial<sup>[18]</sup> reported participant losses. Selective reporting was difficult to assess, and trial protocols were unavailable.

### 3.3. Meta-analysis results

**3.3.1. VAS.** The VAS is shown in Figure 2, the results of the 9 trials<sup>[16–25]</sup> were included in the study, a random-effects model was used for statistical analysis due to the significant heterogeneity ( $I^2 = 87\%$ ). The results showed that there were a significant differences in improving VAS in favor of the exercise treatment ( $n = 751$ ; SMD =  $-0.89$ ; 95% CI:  $-1.34$  to  $-0.44$ ;  $Z = 3.89$ ;  $P < .001$ ).

**3.3.2. NDI.** Five trials,<sup>[18,21,24–26]</sup> involving a total of 514 patients, reported NDI as an outcome in the groups, and these trials exhibited significant heterogeneity ( $I^2 = 95\%$ ), as shown in Figure 3. And accordingly, a random-effects model was used for meta-analysis. The result of 5 trials revealed that patients treated by exercise had a statistically significant decrease in NDI (MD =  $-3.60$ ; 95% CI:  $-6.27$  to  $-0.94$ ;  $Z = 2.65$ ;  $P = .008$ ).

**3.3.3. SF-36 (SF-12).** As shown in Table 2, none of 10 studies reported SF-36 or SF-12. And no trial paid attention to quality of life for the participants.

**3.3.4. Publication bias.** The funnel plots were used to assess the publication bias. The funnel shape of the plot was not completely symmetrical, indicating a potential publication bias (Fig. 4).

**3.3.5. GRADE level of evidence.** The GRADE level of evidence is low for each outcome. As shown in Table 2, the main reasons for a reducing level were high heterogeneity and possible publication bias.

**3.3.6. Sensitivity analysis.** By removing single studies, the sensitivity analyses showed no noticeable changes in the statistical significance of all outcomes, which indicating all effects were stable.

**3.3.7. Subgroup analysis.** To investigate the specific factors influencing the outcomes of this study, subgroup analyses were performed on time to intervention, sample size, publication language, publication year, randomized methods. As shown in Tables 3 and 4, publication language may be the source of heterogeneity in this study. And the factors for its high heterogeneity may include time to intervention, publication language, publication year.

**Table 1**  
Basic characteristics of the included trials.

Study ID	Sample size E/C(M/F)	Age, yr E/C	Course of disease	Intervention		Time to intervention	Follow-up	Outcome measures
				Experiment group	Control group			
Diab 2011 Egypt	48 (27/21)/48 (23/25)	46.3±2.05/45.9±2.11	9±1.3/7±2.6, mo	A exercise program + ultrasound and infrared radiation	Ultrasound and infrared radiation	10 wk	6 mo	VAS
Kuljper 2009 Netherlands	E: 70 (34/36) C1: 69 (38/31) C2: 66 (32/34)	E: 46.7±10.9 C1: 47±9.1 C2: 47.7±10.6	E: 3±2.1 C1: 3.3±2.3 C2: 3.2±2, wk 16.9±7.3/17.2±6.2, d	Program of the cervical exercise	C1: Cervical collar C2: Wait and see policy	6 wk	6 mo	VAS; NDI
Cai 2015 China	30 (16/14)/30 (17/13)	50.8±8/49.9±8	10±12.1/8.2±6.9, mo	Baduanjin exercise + conventional therapy	Conventional therapy	3 wk	15.5 mo	VAS
Wu 2014 China	30 (12/18)/30 (17/13)	47.5±13.9/51.6±10.8	10±12.1/8.2±6.9, mo	Exercise + Loxoprofen sodium tablets + cervical traction	Loxoprofen sodium tablets + cervical traction	8 wk	-	VAS
Liu 2016 China	21 (9/12)/21 (7/14)	23.05±2.92/23.33±1.71	1.3±0.5/1.21±0.51, yr	Exercise + massage	Massage	4 wk	-	VAS; NDI
Hong 2016 China	22 (12/10)/19 (10/9)	48.4±6.69/50.21±6.89	Mean: 15.5 d/mean: 17.5 d	Exercise + conventional therapy	Conventional therapy	15 d	-	VAS
Chen 2017 China	50 (27/23)/50 (21/29)	40.2±16.1/41±12.5	14.67±6.62/16.88±7.52, mo	Exercise + massage + acupuncture	Massage + acupuncture	14 d	-	VAS; NDI
Fang 2018 China	60/30	-	-	E1: Exercise + 3-edged needle E2: Exercise	Three-edged needle	10 d	-	VAS; NDI
Zhao 2016 China	35 (16/19)/35 (17/18)	46.95±1.05/48.07±2.13	4.3±7.3/3.9±7.52, yr	Exercise + massage + acupuncture	Massage + acupuncture	2 mo	3 yr	VAS; NDI
Li 2015 China	60 (28/32)/60 (33/27)	41.69±1.87/43.2±1.73	2.28±1.63/2.33±1.53, yr	Exercise + conventional therapy	Conventional therapy	3 wk	-	NDI

C = control group, E = experiment group, M/F = male/female.

## 4. Discussion

More and more attention has been paid to the non-drug therapy of CR. Exercise often used in conjunction with other therapies, is one of the most important intervention methods.<sup>[27]</sup> This systematic review and meta-analysis found that exercise can significantly improve the VAS and NDI when comparing other methods without exercise in all included trials for quantitative synthesis. The beneficial evidence was validated by sensitivity analysis, which demonstrated the results of meta-analysis are robustness.

Some evidence exists on the mechanisms of exercise in giving symptom relief for CR patients. As for pain relief, many studies have been shown exercise can promote analgesia in a variety of chronic musculoskeletal conditions such as low back pain, myofascial pain, and so on.<sup>[28–31]</sup> Lima et al<sup>[29]</sup> found that exercise can reverse the hyperalgesia for injury animals, and prevents the development of the hyperalgesia in both neuropathic pain and muscle pain, which may be related to reduced N-Methyl-D-aspartate receptor phosphorylation, suggesting reduced central facilitation. Stolzman et al<sup>[32]</sup> also found exercise may activate conditioned pain modulation descending inhibitory pathways resulting in subsequent pain relief. Therefore, this study concludes that exercise may be effective in relieving pain in CR patients through the above ways, but the explanations provided in the literature are largely hypothetical. In addition, our systematic review and meta-analysis can also significantly improve NDI, is that representation of cervical spine function. Lima et al<sup>[29]</sup> demonstrated that improvement of cervical function achieved by restoring the normal muscle balance through strengthening the muscles and stretching the tight muscles. Besides, scapular strengthening and deep neck flexor exercises have provided some benefit in NDI described by Cleland et al<sup>[33]</sup> Then, in terms of SF-12 or SF-36, which is an important index of quality of life. But none of the eligible literature reported this. Therefore, future studies with larger sample sizes and high-level evidence should investigate to detect change in patient status about quality of life in patients with CR.

In this systematic review and meta-analysis, subgroup analysis was performed due to the statistically significant heterogeneity of these 2 indicators. The overall pooled data revealed a difference in favor of exercise for VAS (Fig. 2). But in subgroup analyses, the results changed. For studies from Chinese, exercise contributed to VAS with significant differences, whereas no significant differences were detected in studies from English countries. Moreover, subgroup analysis was also conducted based on NDI, as shown in Table 4, the results were changed by several factors including time to intervention, publication language, and publication year. For the above results, it is supposed that this may be related to the small number of studies included in this outcome indicator – NDI. So, additional well-designed and large-scale RCTs are needed to confirm clearly this finding. Thus, the exercise option should be carefully considered for each patient with CR in accordance with their different situations. And according to funnel plots, publication bias may also be the cause of the results with significant heterogeneity. However, although the results of subgroup analysis have changed in some aspects, sensitivity analysis shows that the results of this meta-analysis are robust.

To the best of our knowledge, several previous meta-analyses have reported on exercise for treating neck pain or neck disorders,<sup>[34–38]</sup> but there is no meta-analysis on the treatment of CR by exercise at present. As the first systematic review of



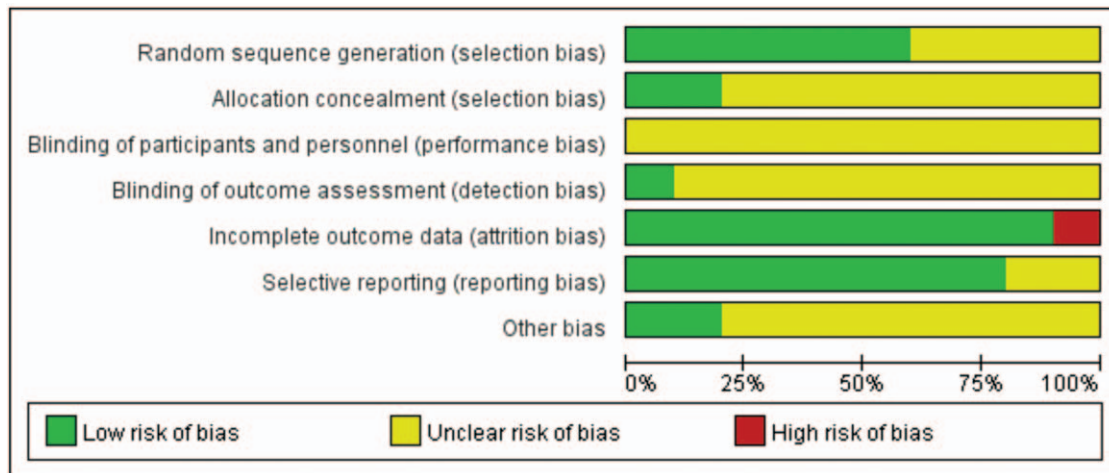


Figure 1. Risk of bias graph.

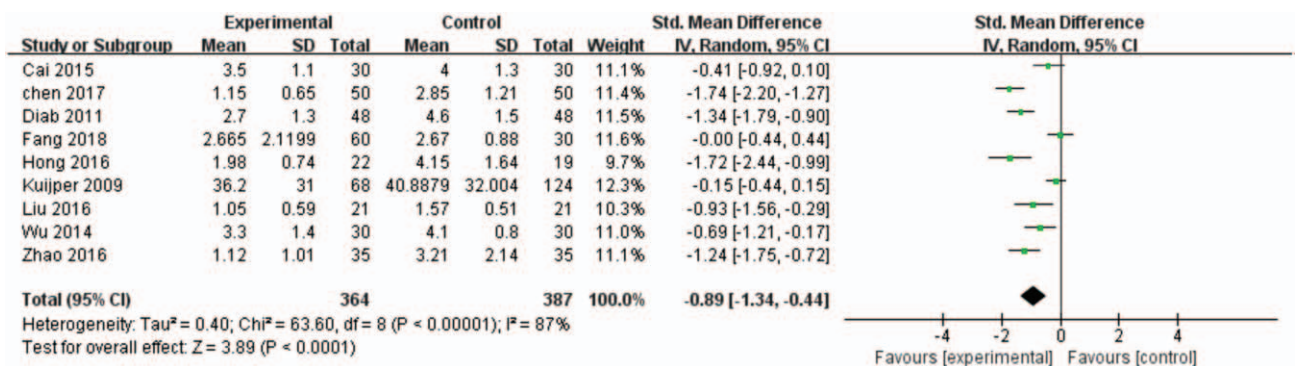


Figure 2. VAS comparison. VAS=visual analog scale.

exercise as an intervention measure for CR, the latest and high-level evidence-based results are obtained by synthesizing the results of multiple studies, although the GRADE level of evidence is low for 2 outcomes due to high heterogeneity and possible publication bias. Furthermore, the protocol of this study was registered on PROSPERO, which is more in line with PRISMA reporting guidelines. And a registered protocol may improve the transparency and quality of this meta-analysis. Furthermore, the level of evidence is given by performing the GRADE approach. Thus, the conclusions of this study can easily be used by clinicians.

Our systematic review also has some limitations. First, the included studies in this meta-analysis were performed in different

patient groups, different exercise program, different follow-up period, and different outcome evaluators. So the risk of introducing potential heterogeneity is present. Thus, sensitivity and subgroup analysis were performed regarding all results. Second, because exercise could not be blinded for doctors and patients, this may lead to unavoidable performance bias. Third, the exercise treatment often consists of various interventions and is typically also combined with drugs and other treatments which make it difficult to determine the effects of a single intervention. Hence, more rigorously designed and measured, randomized double-blind, placebo-controlled trials that conform to the CONSORT 2010 statement are needed to verify the current conclusions.

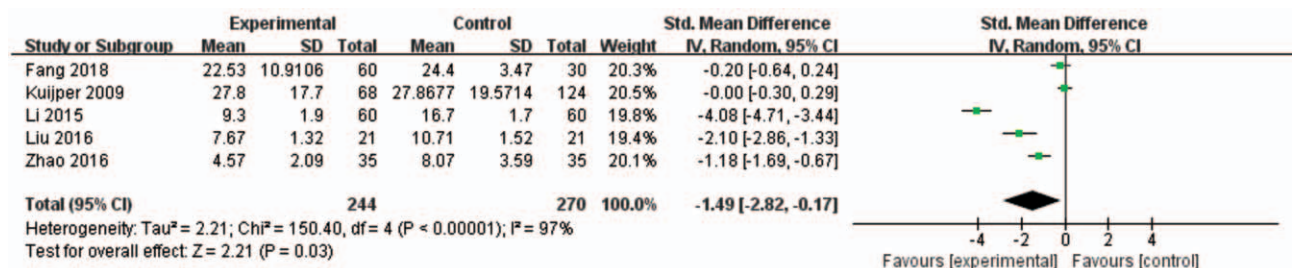


Figure 3. NDI comparison. NDI=neck disability index.

**Table 2**  
Summary of the evidence for each outcome.

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[exercise group]	[control group]	Relative (95% CI)	Absolute (95% CI)	
9	Randomized trials	Not serious	Not serious	Not serious	Serious <sup>a</sup>	Publication bias strongly suspected <sup>†</sup>	364	387	–	SMD 0.89 SD lower (1.34 lower to 0.44 lower)	□ □ □ □ LOW
5	Randomized trials	Not serious	Not serious	Not serious	Serious <sup>a</sup>	Publication bias strongly suspected <sup>†</sup>	244	270	–	SMD 1.49 SD lower (2.82 lower to 0.17 lower)	□ □ □ □ LOW

CI = confidence interval, SD = standard deviation.

<sup>a</sup>Statistical heterogeneity.

<sup>†</sup>Potential publication bias.

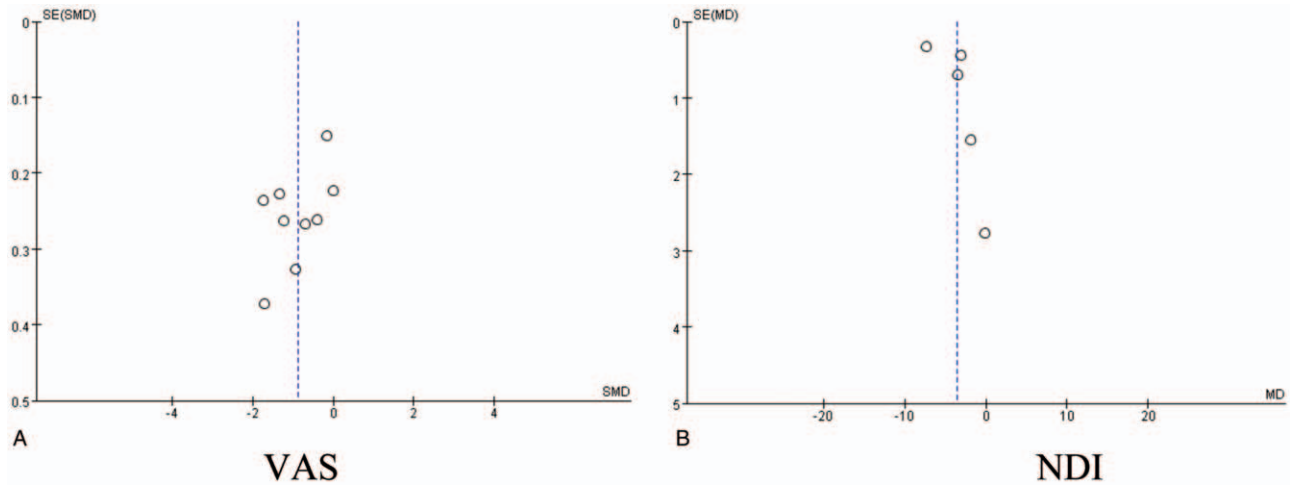


Figure 4. Funnel plot of the trials that compared treatment group with control group (VAS, NDI). NDI=neck disability index, VAS=visual analog scale.

**Table 3**  
Subgroup analysis based on VAS.

Group	No. of studies	No. of patients	RR	95% CI	Z	P (effect)
Time to intervention ≥4 wk	5	460	–0.85	[–1.38, –0.33]	3.17	.002
<4 wk	4	291	–0.95	[–1.86, –0.04]	2.05	.04
Sample size ≥70	5	548	–0.88	[–1.58, –0.19]	2.50	.01
<70	4	203	–0.89	[–1.39, –0.39]	3.47	.0005
Publication language English	2	288	–0.73	[–1.90, 0.44]	1.23	.22
Chinese	7	463	–0.94	[–1.46, –0.43]	3.60	.0003
Publication year ≥2016 (Published in the last 3 yr)	5	343	–1.11	[–1.81, –0.41]	3.09	.002
<2016 (Published before 3 yr)	4	408	–0.64	[–1.19, –0.08]	2.25	.02
Randomized methods Explicitly mentioned	5	518	–0.97	[–1.62, –0.32]	2.91	.004
Not explicitly mentioned	4	233	–0.79	[–1.48, –0.11]	2.28	.02

CI = confidence interval, RR = relative risk, VAS = visual analog scale.

**Table 4**  
Subgroup analysis based on NDI.

Group	No. of studies	No. of patients	RR	95% CI	Z	P (effect)
Time to intervention ≥4 wk	3	304	–3.11	[–3.84, –2.39]	8.44	<.00001
<4 wk	2	210	–4.84	[–10.25, 0.56]	1.76	.08
Sample size ≥70	4	472	–3.73	[–6.95, –0.19]	2.50	.02
<70	1	42	–3.04	[–3.90, –2.18]	6.92	<.00001
Publication language English	1	192	–0.07	[–5.51, 5.37]	0.02	.98
Chinese	4	322	–4.09	[–6.91, –1.27]	2.85	.004
Publication year ≥2016 (Published in the last 3 yr)	3	202	–3.10	[–3.81, –2.39]	8.56	<.00001
<2016 (published before 3 yr)	2	312	–4.25	[–11.36, 2.86]	1.17	.24
Randomized methods Explicitly mentioned	3	382	–4.35	[–7.93, –0.77]	2.38	.02
Not explicitly mentioned	2	132	–2.95	[–3.78, –2.12]	6.99	<.00001

CI = confidence interval, NDI = neck disability index, RR = relative risk.

## 5. Conclusions

Including exercise therapy is effective in the management of CR, which can relieve pain and improve cervical function. However, the conclusions of this study should be treating with caution. More high-quality RCTs are required to provide stronger evidence.

## Author contributions

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