Systematic Review and Meta-Analysis

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What is the superior surgical strategy for bi-level cervical spondylosis-anterior cervical disc replacement or anterior cervical decompression and fusion?

A meta-analysis from 11 studies

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Abstract

Background: Nowadays, anterior cervical artificial disc replacement (ACDR) has achieved favorable outcomes in treatment for patients with single-level cervical spondylosis. However, It is still controversial that whether or not it will become a potent therapeutic alternation in treating 2 contiguous levels cervical spondylosis compared with anterior cervical decompression and fusion (ACDF). Therefore, we conducted a systematic review and meta-analysis to compare the efficacy and safety of ACDR and ACDF in patients with 2 contiguous levels cervical spondylosis.

Methods: According to the computer-based online search, PubMed, Embase, Web of Science, and Cochrane Library for articles published before July 1, 2017 were searched. The following outcome measures were extracted: neck disability index (NDI), visual analog scale (VAS) neck, VAS arm, Short Form (SF)-12 mental component summary (MCS), SF-12 physical component summary (PCS), overall clinical success (OCS), patient satisfaction (PS), device-related adverse event (DRAE), subsequent surgical intervention (SSI), neurological deterioration (ND), and adjacent segment degeneration (ASD). Methodological quality was evaluated independently by 2 reviewers using the Furlan for randomized controlled trial (RCT) and MINORS scale for clinical controlled trials (CCT). The chi-squared test and Higgin I^2 test were used to evaluate the heterogeneity. A $P < .10$ for the chi-squared test or I^2 values exceeding 50% indicated substantial heterogeneity and a random-effect model was applied; otherwise, a fixed-effect model was used. All quantitative data were analyzed by the Review Manager 5.2 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Results: Nine RCTs and 2 CCT studies containing 2715 patients were included for this meta-analysis. The pooled analysis indicated that the ACDR group is superior to ACDF in NDI, VAS neck, PCS score, OCS, PS, DRAE, ASD, and SSI. However, the pooled results indicate that there was no significant difference in the ND, VAS arm and in MCS score.

Conclusions: The present meta-analysis suggests that for bi-level cervical spondylosis, ACDR appears to provide superior clinical effectiveness and safety effects than ACDF. In the future, more high-quality RCTs are warranted to enhance this conclusion.

Abbreviations: ACDF = anterior cervical decompression and fusion, ACDR = anterior cervical artificial disc replacement, ASD = adjacent segment degeneration, CCT = clinical controlled trial, CI = confidence interval, DRAE = device-related adverse event, MCS = mental component summary, ND = neurological deterioration, NDI = neck disability index, OCS = overall clinical success, PCS =

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Xing Yu contributed to the design of the study. He Zhao and Li-Jun Duan were responsible for data collection, data analysis, and drafting the manuscript. Yu-Shan Gao, Yong-Dong Yang, Ding-Yan Zhao, and Xiang-Sheng Tang contributed to analyzing the data with regard to its potential clinical significance. Yang Xiong, Zhen-Guo Hu, and Chuan-Hong Li conceived the meta-analysis and participated in its design and coordination. Xing Yu, He Zhao, and Li-Jun Duan screened titles and abstracts of eligible citations and determined if they met the inclusion criteria to this meta-analysis. All authors read and approved the final manuscript. All those who contributed to this meta-analysis meet the criteria for authorship and have been listed as authors.

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physical component summary, PS = patient satisfaction, RCT = randomized controlled trial, RR = risk ratio, SF-12 = Short Form 12, SMD = standard mean difference, SSI = subsequent surgical intervention, VAS = visual analog scale.

Keywords: anterior cervical artificial disc replacement, anterior cervical decompression and fusion, bi-level cervical spondylosis, follow-up, meta-analysis

1. Introduction

According to a recent public health report, the Global Burden of Disease Study, neck pain is the main cause of movement disorders, with current estimates of 349 million people affected worldwide.[1] This large number of patients will continue to increase further. A previous review of the literature, described neck pain as a chronic condition associated with intervertebral disc degeneration.[2,3] Current conservative treatment includes use of nonsteroidal anti-inflammatory drugs at earlier stages, but invasive interventions are standard treatments at later stages.[4]

Since the 1950s, anterior cervical decompression and fusion (ACDF) has been regarded as the "gold standard" of surgical therapy for symptomatic cervical myelopathy or radiculopathy, achieving neural decompression, segmental stabilization, and favorable results in clinical follow-up.[5–7] However, ACDF is associated with pseudarthrosis formation, limitation of index level, and accelerated adjacent segment degeneration (ASD).[8,9] Thus, anterior cervical artificial disc replacement (ACDR) represents a new, relative segmental motion-preserving procedure for cervical spondylosis. Compared with ACDF, ACDR can restore the interspace height of cervical vertebra, preserve the index/adjacent level, and also theoretically prevent ASD.[10,11] Each procedure has its own characteristic features, and most studies have compared single-level ACDR with ACDF, but the safety and efficacy of bi-level procedure remains controversial. To provide a high level of evidence for decision making by clinicians and patients, we performed a meta-analysis to compare outcomes after bi-level ACDR with those of bi-level ACDF, to evaluate which procedure yields more favorable patients.

2. Materials and methods

2.1. Search strategy

To search all of the relevant literature, we systematically searched literature published in the database (PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials). Search terms were subjected to the following: "anterior cervical artificial disc replacement," "cervical total disc replacement," "cervical artificial disc," "disc arthroplasty," ACDR, CTDA, CDA, "anterior cervical decompression and fusion," "anterior interbody fusion," ACDF, "2 level," "two level," "bi-level," "double level" with various combinations of the operators "AND," "NOT," and "OR." There were restriction of study design was controlled trial published between January 1, 2000 and July 1, 2017. Restriction of languages was English. References cited in the relevant articles were also reviewed (see in Supplement 1, http://links.lww.com/MD/C171).

2.2. Inclusion criteria

All studies on treatment of bi-level cervical spondylosis were reviewed. The criteria for inclusion of an article were ACDR compared with ACDF for treatment of 2-level cervical spondylosis; patients were 18 years old or greater; patients were diagnosed (computed tomography, magnetic resonance imaging, or plain radiographs) with symptomatic cervical degenerative disc disease in bi-level between C-1 to C-7; unresponsive to nonoperative: conservative treatment for at least 6 weeks or presence of progressive symptoms or signs of nerve root/spinal cord compression; physically and mentally able and willing to comply the protocol; and studies with follow-up more than 12 months (Table 1).

Table 1

Quality assessment of included RCT studies by using the Furlan scores.

Criteria	Cheng et al	Jawahar et al	Grob et al	Coric et al	Davis et al	Radcliff et al	Jackson and Johnson	Gornet et al	Lanman et al
(A) 1. Was the method of randomization adequate?	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
(B) 2. Was the treatment allocation concealed?	Unclear	Yes	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Unclear
(C) Was knowledge of the allocated interventions adequately prevented during the study?									
3. Was the patient blinded to the intervention?	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
4. Was the care provider blinded to the intervention?	Unclear	No	Unclear	Unclear	No	No	Unclear	Yes	No
5. Was the outcome assessor blinded to the intervention?	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	No	No
(D) Were incomplete outcome data adequately addressed?									
6. Was the drop-out rate described and acceptable?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Were all randomized participants analyzed in the group to which they were allocated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
(E) 8. Are reports of the study free of suggestion of selective outcome reporting?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
(F) Other sources of potential bias									
9. Were the groups similar at baseline regarding the most important prognostic indicators?	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes
10. Were cointerventions avoided or similar?	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes
11. Was the compliance acceptable in all groups?	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes
12. Was the timing of the outcome assessment similar in all group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Scores	7	10	8	6	10	10	6	10	7

RCTs = randomized controlled trials.

Table 2

Inclusion and exclusion criteria for article selection.

	Inclusion criteria	Exclusion criteria
Patients	18 years old or older	<18 years old
Type of condition	ACDR compared with ACDF for treatment of 2-level cervical spondylosis	Not ACDR and ACDF treating bi-level cervical spondylosis
	Patients were 18 years old or greater	<18 years old
	Patients were diagnosed (CT, MRI, or plain radiographs) with symptomatic cervical degenerative disc disease in bi-level between C-1 to C-7	Single- or multilevel cervical spondylosis
	Unresponsive to nonoperative: conservative treatment for at least 6 wk or presence of progressive symptoms or signs of nerve root/spinal cord compression	The outcomes were graphic without numerical values
	Physically and mentally able and willing to comply the protocol	Neoplastic etiology, infection, traumatic fracture, Paget disease, osteomalacia, osteoporosis, active systemic infection of surgical site or history, rheumatoid arthritis, other autoimmune disease or any other metabolic bone disease
	Studies with follow-up more than 12 mo	Metal sensitivity or mental diseases
		Studies with follow-up <12 mo
		Case report, review article, meta-analysis, the same data had been published previously
		Basic medical research (cell or animal experiment)
Treatment	Bi-levels ACDR vs. ACDF	Not included ACDR vs. ACDF
Publication data	Published between January 2000 and July 2017	Published before 2000
Language	English	Non-English
Design	Not limited	—

ACDF = anterior cervical decompression and fusion, ACDR = anterior cervical artificial disc replacement, CT = computed tomography, MRI = magnetic resonance imaging.

2.3. Exclusion criteria

Patients were excluded if they were associated with: not ACDR and ACDF treating bi-level cervical spondylosis; <18 years old; single- or multilevel cervical spondylosis; the outcomes were graphic without numerical values; neoplastic etiology, infection, traumatic fracture, Paget disease, osteomalacia, osteoporosis, active systemic infection of surgical site or history, rheumatoid arthritis, other autoimmune disease or any other metabolic bone disease; metal sensitivity or mental diseases; studies with follow-up <12 months; case report, review article, meta-analysis, the same data had been published previously; and basic medical research (cell or animal experiment) (Table 2).

2.4. Data extraction

The following data were extracted by 2 authors independently using a purpose-designed form: first author and year, study design, region, details, intervention, follow-up (months), and outcomes. Disagreement between the 2 reviewers was arbitrated by the third reviewer. If any disagreements existed, a third author was consulted to discussion until consensus was reached. The outcome including at least one of the following outcomes (Table 2):

1. NDI (neck disability index)
2. VAS (visual analog scale) neck
3. VAS arm
4. SF-12 (Short Form 12) MCS (mental component summary)
5. SF-12 (Short Form 12) PCS (physical component summary)
6. OCS (overall clinical success)
7. PS (patient satisfaction)
8. DRAE (device-related adverse event)
9. SSI (subsequent surgical intervention)
10. ND (neurological deterioration)
11. ASD (adjacent segment degeneration)

2.5. Quality assessment

The quality of the studies was independently assessed by the 2 authors according to The checklist by Furlan et al[12,13] was used to evaluate the methodological quality of randomized controlled trials (RCTs). Evaluation of clinical controlled studies was performed with the MINORS scale. Every study was assessed by 2 independent researchers and judgment of every item. Any disagreement with respect to eligibility during the extraction was discussed and resolved.

2.6. Statistical analysis

The risk ratio (RR) and the corresponding 95% confidence interval (CI) were assessed for the dichotomous outcomes, and the standardized mean difference (SMD) and 95% CI were assessed for the continuous outcomes. The chi-squared test and Higgin I^2 test were used to evaluate the heterogeneity. A P value <.10 for the chi-squared test or I^2 values exceeding 50% indicated substantial heterogeneity. A fixed-effect model was used if significantly statistical heterogeneity was absent; otherwise, a random-effect model was applied. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting 1 study in turn when necessary. Owing to the limited number (11) of included studies, publication bias was not assessed. $P < .05$ in 2-tailed tests was considered statistically significant. A meta-analysis was performed on the extracted data with RevMan 5.0 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

3. Results

3.1. Search results

Flow chart for inclusion of studies is shown in Fig. 1. The literature search initially yielded 325 relevant trials from PubMed

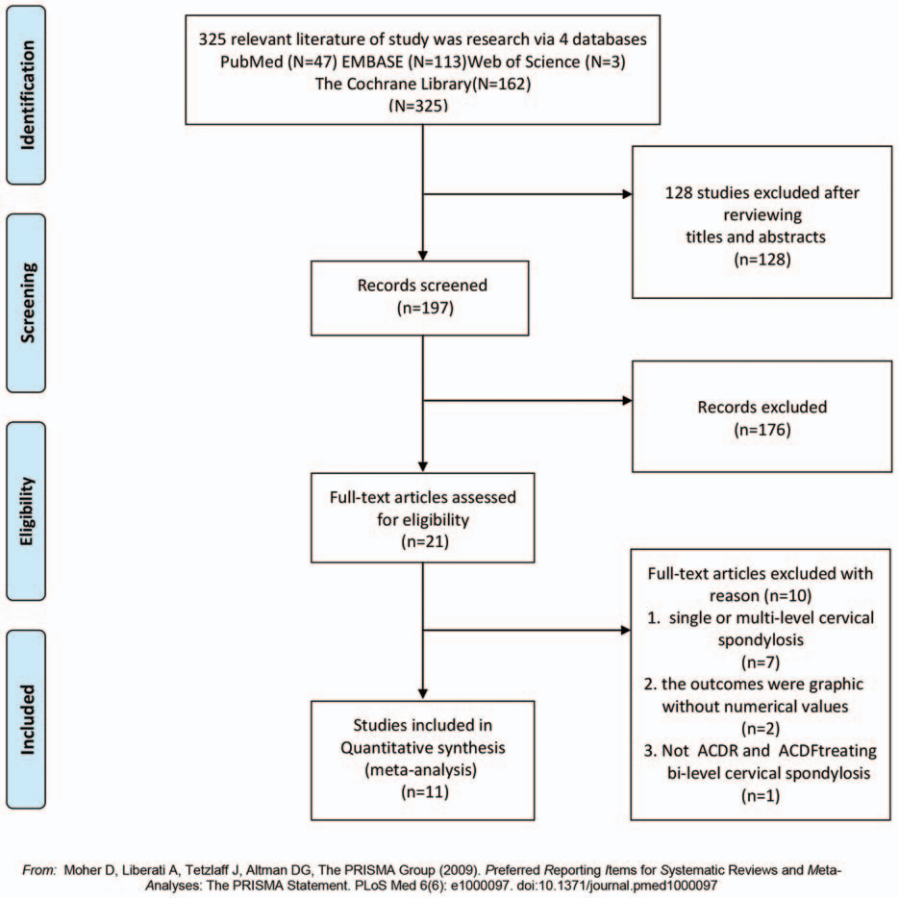

Figure 1. Flow chart for inclusion of studies.

(N=47), Embase (N=113), Web of Science (N=3), and The Cochrane Library (N=162). After we reviewed the titles and abstracts of all trials, 128 trials were excluded. We continued to refine and exclude the 197 studies, 21 potentially studies were obtained, then 10 studies were excluded due to fail to meet criteria. Finally, 9 RCTs and 2 clinical controlled trials (CCTs) containing 2715 patients were included for this meta-analysis. We recorded the characteristics of the 11 included trials, as well as the details of the clinical outcome measurement (Table 3).

3.2. Quality assessment

The Furlan scores in 9 RCTs were in the range from 6 to 10 of 12 (Table 1). Seven RCTs were scored 7 or higher, and 2 RCTs were scored lower than 7, suggesting overall high quality of studies. The MINORS scale of studies in both studies was 17 and 18 and judged as good quality (Table 4). They were considered high methodological quality.

3.3. Clinical effectiveness

Seven studies provided NDI score. There was significant difference in the NDI score between 2 groups. The overall effect showed that the ACDR group had statistically higher NDI scores improvement than the ACDF group (SMD=0.41 [0.29, 0.52], $P<.00001$, Fig. 2). Similarly, 7 studies with pooled results indicated that the ACDR group had statistically higher VAS scores in neck pain improvement than the ACDF group. VAS neck pain (SMD=0.69 [0.34, 1.04], $P=.0001$, Fig. 3). However, there is no significant difference between 2 groups in VAS arm pain (SMD=0.36 [−0.01, 0.73], $P=.06$, Fig. 3). Two studies and 3 studies provided SF-12 MCS and PCS score, respectively. The pooled results indicate that there was no significant difference in the MCS score between 2 groups (SMD=0.13 [−0.08, 0.34], $P=.21$, Fig. 4). The pooled PCS score showed significant difference between the ACDR and ACDF group (SMD=0.38 [0.22, 0.53], $P<.00001$, Fig. 4). There were 6 studies provided OCS, the pooled result showed that ACDR group is superior to ACDF group (SMD=1.49 [1.20, 1.85], $P=.0003$, Fig. 5). PS was also reported in 5 studies, the overall effect showed that ACDR group had statistically higher rate improvement than the ACDF group (SMD=1.06 [1.03, 1.09], $P=.0003$, Fig. 6), and 2 studies reported that one who experienced operation would also recommend their treatment to friends (SMD=1.12 [1.05, 1.19], $P=.0002$, Fig. 6).

3.4. Clinical safety

Six studies reported DRAE. Patients in the ACDR group had statistically significant lower incidence of DRAE (RR=0.59 [0.48, 0.73], $P<.0001$, Fig. 7). There was significantly more SSI rate extracted in 7 studies in the ACDF group than in the ACDR group (RR=0.29 [0.21, 0.39], $P<.00001$, Fig. 8). However, ND rate also indicates that there was no statistically significant

Table 3

Characteristics of included studies.

First author and year	Study design	Region	Details	Intervention	Follow-up, mo	Outcomes
Kim et al[14] 2009	Prospective cohort study	South Korea	n = 40	Prosthetic type	ACDR:	1.2
			ACDR: 12	ACDR: Bryan Cervical Artificial Disc Prosthesis (Medtronic Sofamor Danek, Memphis, TN)	18 (13–37)	
			ACDF: 28	ACDF: Blackstone cage (Blackstone Medical Inc)	ACDF:	
			Mean age	Solis cage (Stryker Spine)	21 (14–38)	
			ACDR: 46.9 y (30–58)	ABC plate (Aesculap)		
			ACDF: 52.7 y (30–78)	Atlantis plate (Medtronic, Sofamor Danek)		
			Gender	Types of cervical spondylosis		
			ACDR: 8 males, 4 females	ACDR: radiculopathy (n = 10) Myelopathy (n = 2)		
			ACDF: 17 males, 11 females	ACDF: radiculopathy (n = 24) Myelopathy (n = 4)		
			Follow-up rate	Index level		
				ACDR: C4–C5–C6 (n = 4), C5–C6–C7 (n = 8)		
				ACDF: C4–C5–C6 (n = 13), C5–C6–C7 (n = 15)		
Cheng et al[15] 2009	Prospective randomized controlled trial	China	n = 65	Prosthetic type	24	1.2.3.4.5
			ACDR: 31	ACDR: Bryan Cervical Disc (Medtronic Sofamor Danek)		
			ACDF: 34	ACDF: ACDF with an iliac crest autograft and plate		
			Mean age	Types of cervical spondylosis		
			ACDR: 45 y	All patients with radiculopathy or myelopathy		
			ACDF: 47 y	Index level		
			Gender	From C3 to C7		
			ACDR: 16 males, 15 females			
			ACDF: 17 male, 17 females			
			Follow-up rate			
			95.4%			
Jawahar et al[16]	Prospective randomized controlled	USA	n = 22	Prosthetic type	37 (24–49)	1.2.6
2010	FDA IDE trials		ACDR: 16	ACDR: Kineflex-C (SpinalMotion Inc., Mountain View, CA), Mobi-C (LDR spine, Austin, TX)		
			ACDF: 6	Advent Cervical Disc (Blackstone Inc., Parsippany, NJ)		
			Mean age	ACDF: ACDF with cortical bone allograft		
			ACDR: 45 y	Types of cervical spondylosis		
			ACDF: 47 y	All patients with radiculopathy or myelopathy		
			Gender	Index level		
			ACDR: 6 males, 10 females	From C3 to C7		
			ACDF: 2 males, 4 females			
			Follow-up rate: not described			
Grob et al[17] 2010	Randomized controlled trials	Switzerland	n = 266	Prosthetic type	24	7.8.9
			ACDR: 58	ACDR: Bryan Cervical Disc (Medtronic Sofamor Danek)		
			ACDF: 208	Prestige II (Medronic Sofamor Danek)		
			Mean age	Discover (dePuy)		
			ACDR: 45.8 ± 7.9	Prodisc-C (Synthes-Spine)		
			ACDF: 56.1 ± 10.8	ACDF: ACDF with autologous bone, allogenic bone, autogenic + allogenic, autogenic + bone substitute, other/no fusion material,		
			Gender	other anterior stabilization, interbody cage (Harms titanium cage [dePuy] or PEEK [Medtronic] cage), plates, cage + plates		
			ACDR: 27 males, 31 females	Types of cervical spondylosis		
			ACDF: 105 males, 103 females	Degenerative cervical spinal disease		
			Follow-up rate: 95%	Index level		
				Not described		
Hou et al[18] 2014	Cohort study	China	n = 120	Prosthetic type	ACDR:	1.2
			ACDR: 32	ACDR: discover artificial cervical disc (DePuy Spine, Raynham, MA)	24.2 (13–27)	
			ACDF: 88	ACDF: ACDF with autogenous bone, different types of anterior cervical plates, standalone cages	ACDF:	
			Mean age		23.3 (12–27)	
			ACDR: 46.3 y (30–69)	Types of cervical spondylosis		
			ACDF: 51.2 y (29–77)	All patients with radiculopathy or myelopathy		
			Gender	Index level		
			ACDR: 20 males, 12 females	ACDR: C3/C4–C5/C6 (n = 1), C4/C5–C5/C6 (n = 12)		
			ACDF: 38 males, 50 females	C5/C6–C6/C7 (n = 19)		
			Follow-up rate: 92.8%	ACDF: C4/C5–C5/C6 (n = 40), C5/C6–C6/C7 (n = 48)		

(*continued*)

Table 3

(continued).

First author and year	Study design	Region	Details	Intervention	Follow-up, mo	Outcomes
Coric et al[19] 2015	Prospective randomized controlled	USA	n = 330	Prosthetic type	60	6.9
	FDA IDE trials		ACDR: 225 ACDF: 105 Mean age: not described Gender: not described Follow-up rate: 90.8%	ACDR: Mobi-C cervical artificial disc ACDF: ACDF Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level: not described		
Davis et al[20] 2015	Prospective randomized controlled	USA	n = 330	Prosthetic type	48	1.2.3.4.5
	FDA IDE trials		ACDR: 225 ACDF: 105 Mean age ACDR: 45.3 ± 8.1 y ACDF: 46.2 ± 8.0 y Gender ACDR: 113 males, 112 females ACDF: 45 males, 60 females Follow-up rate: 86.5%	ACDR: Mobi-C cervical artificial disc (LDR Medical; Troyes, France) ACDF: ACDF with corticocancellous allograft + anterior cervical plate Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level ACDR: C3–C7 ACDF: C3–C7		6.7.8.9.10
Radcliff et al[21] 2016	Prospective randomized controlled	USA	n = 330	Prosthetic type	60	1.2.3.5.6
	FDA IDE trials		ACDR: 225 ACDF: 105 Mean age ACDR: 45.3 ± 8.10 y (27–67) ACDF: 46.2 ± 7.99 y (27–66) Gender ACDR: 113 males, 112 females ACDF: 45 males, 60 females Follow-up rate: 89.4%	ACDR: Mobi-C cervical artificial disc (LDR Medical) ACDF: ACDF with corticocancellous allograft+ anterior cervical plate Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level ACDR: C3–C7 ACDF: C3–C7		7.8.9.10
Jackson and Johnson[22] 2016	Prospective randomized controlled trials	USA	n = 330	Prosthetic type: not described	84	2.8.9.10
			ACDR: 225 ACDF: 105 Mean age: not described Gender: not described Follow-up rate: not described	Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level: not described		
Gornet et al[23] 2017	Prospective randomized controlled	USA	n = 397	Prosthetic type	24	1.6.7.8.9
	FDA IDE trials		ACDR: 209 ACDF: 188 Mean age ACDR: 47.1 ± 8.3 y ACDF: 47.3 ± 7.7 y Gender ACDR: 92 males, 117 females ACDF: 90 males, 98 females Follow-up rate: 90.4%	ACDR: Prestige LP (Medtronic Inc.) ACDF: ACDF with cortical ring allograft, Atlantis anterior cervical plate (Medtronic Inc.) as part of ACDF Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level ACDR: C3–C7 ACDF: C3–C7		
Lanman et al[24] 2017	Prospective randomized controlled	USA	n = 397	Prosthetic type	84	6.7.8.9.10
	FDA IDE trials		ACDR: 209 ACDF: 188 Mean age ACDR: 47.1 ± 8.3 y (22.0–75.0) ACDF: 47.3 ± 7.7 y (25.0–69.0) Gender ACDR: 92 males, 117 females ACDF: 90 males, 98 females Follow-up rate: 70.5%	ACDR: Prestige LP (Medtronic Inc.) ACDF: ACDF with cortical ring allograft, Atlantis cervical plate system (Medtronic Inc.) Types of cervical spondylosis Symptomatic cervical degenerative disc disease Index level ACDR: C3 to C7 ACDF: C3 to C7		

1. NDI (neck disability index); 2. VAS (visual analog scale) neck; 3. VAS arm; 4. SF-12 (Short Form 12) MCS (mental component summary); 5. SF-12 (Short Form 12) PCS (physical component summary); 6. OCS (overall clinical success); 7. PS (patient satisfaction); 8. DRAE (device-related adverse event); 9. SSI (subsequent surgical intervention); 10. ND (neurological deterioration); 11. ASD (adjacent segment degeneration).

ACDF = anterior cervical decompression and fusion, ACDR = anterior cervical artificial disc replacement.

Table 4

Methodological quality of the CCT studies by using MINORS scale.

Quality items	Kim et al	Hou et al
A clearly stated aim	2	2
Inclusion of consecutive patients	2	2
Prospective data collection	0	0
Endpoints appropriate to the aim of the study	2	2
Unbiased assessment of the study endpoint	1	1
A follow-up period appropriate to the aims of study	1	2
<5% loss to follow-up	2	1
Prospective calculation of the sample size	0	0
An adequate control group	1	2
Contemporary groups	2	2
Baseline equivalence of groups	2	2
Adequate statistical analyses	2	2
Total score	17	18

CCT = clinical controlled trial.

between 2 groups (RR = 0.61 [0.36, 1.01], $P = .06$, Fig. 9). In addition, 2 studies showed that there were also significantly more superior and inferior ASD rate in the ACDF group compared with ACDR (RR = 0.40 [0.35, 0.46], $P < .00001$, Fig. 10).

3.5. Sensitivity analysis

The sensitivity analysis was conducted to discover whether the lack of each study will change the pooled OR and SMD completely. After removing each, no original pooled results were significantly changed. It proves that the overall meta-analysis results were reliable.

4. Discussion

Through analysis of level 1 evidence from 9 prospective randomized well-controlled clinical trials and 2 high-quality cohort studies, it was demonstrated that ACDR is superior to ACDF. Both effectiveness and safety parameters were examined by using RevMan 5.3 software. Previously used indicators, including the NDI, VAS neck and arm pain, SF-12 MCS and PCS, OCS, and PS revealed that improvement with ACDR shown an advantage over ACDF. However, ND rate was not statistically different between the 2 groups. More recently used indicators, including device-related AE, subsequent surgical intervention (SSI), and ASD rate demonstrated a lower incidence rate for ACDR than for ACDF. Although a meta-analysis and an RCT offer level 1 evidence, a meta-analysis allows for pooling of results to obtain a quantitative and statistically significant

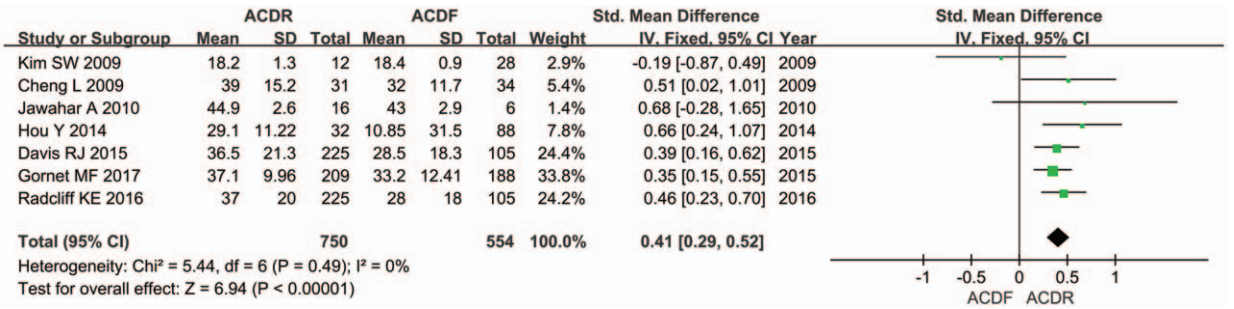

Figure 2. The standardized mean difference estimate for the neck disability index score.

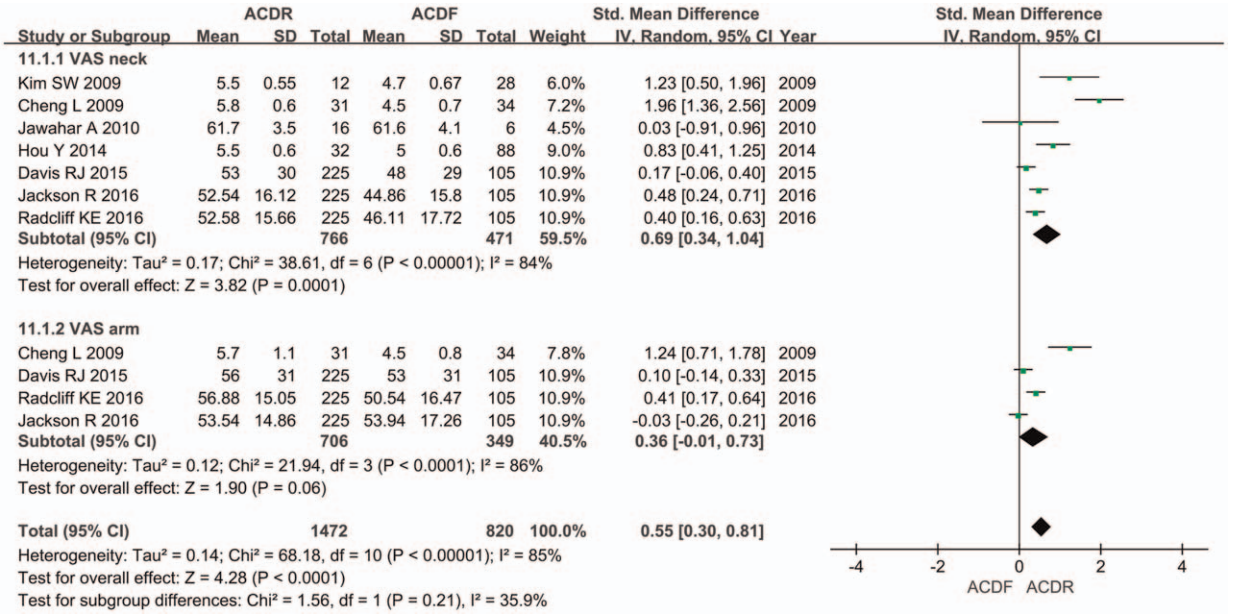

Figure 3. The standardized mean difference estimate for the visual analog scale neck and arm pain.

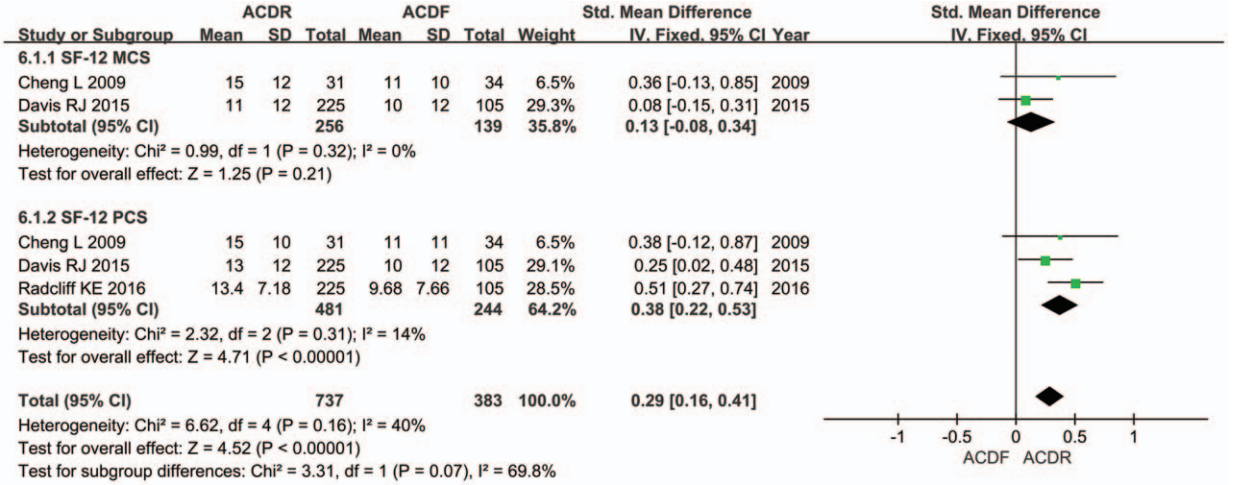

Figure 4. The standardized mean difference estimate for the Short Form 12 mental component summary and physical component summary.

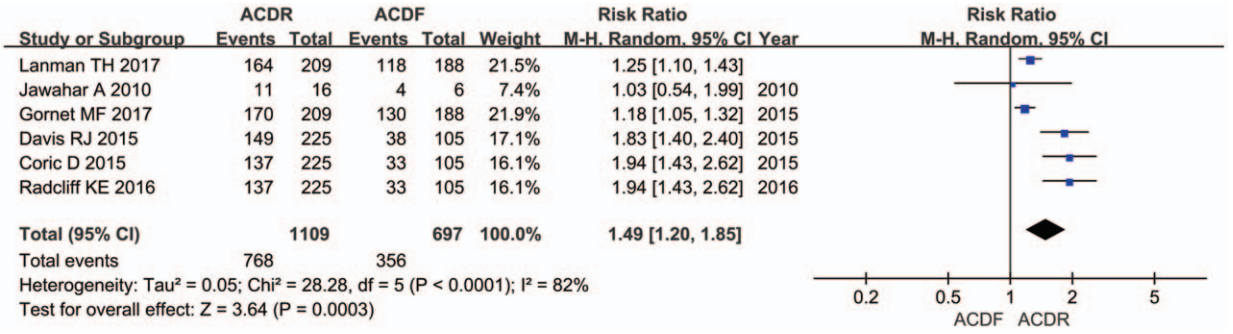

Figure 5. The risk ratio estimate for the clinical overall success rate.

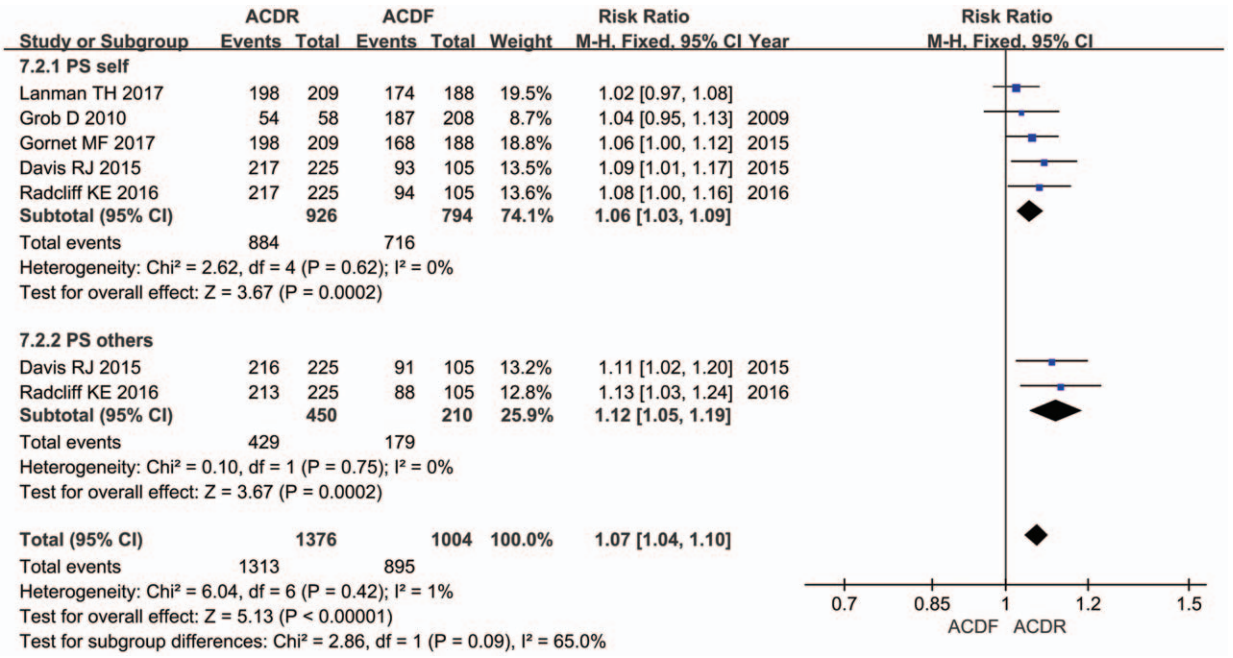

Figure 6. The risk ratio estimate for the patient satisfaction rate.

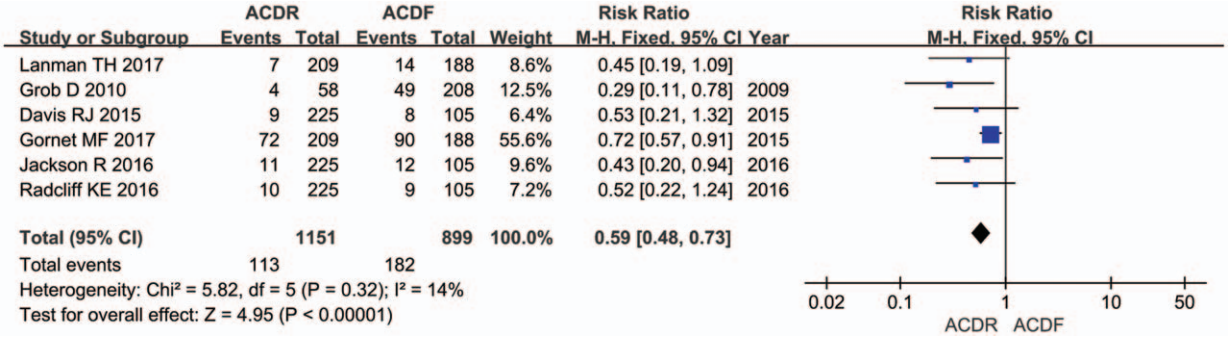

Figure 7. The risk ratio estimate for the device-related adverse events rate.

estimate of treatment effects and the ability to draw more convincing conclusions.

Patient treated with ACDR showed greater NDI improvement than those treated with ACDF in follow-up. This result is consistent with single- or multilevel cervical treatment.[24–26] We surmise that neck vertebrae can sustain a more favorable physical structure after an ACDR procedure compared with ACDF. The VAS score data for neck and arm pain, and the SF-12, for clinical effectiveness assessment, were also analyzed. The overall effect on neck pain showed that ACDR has favorable outcomes, possibly as a result of preservation of mobility and restoration of the neck muscles. However, some previous studies reported that there was no difference in clinical outcome between 2 types of operation in midterm follow-up.[27] We speculate that the discrepancy was due to different standards for inclusion criteria and statistical methods. Similarly, although VAS neck pain improvement with ACDR was superior to that with ACDF, we performed subgroup analysis and found that there was no difference between the 2 groups in VAS arm pain. Unlike neck pain, we know that improvement in arm pain after surgical treatment depends on the degree of nerve root decompression that is vital guarantee for surgical effectiveness, which may else interpret why there is no statistical difference in neurological success. To determine whether different prostheses result in different outcomes between the 2 surgeries strategy, we conducted subgroup analysis. The result showed that ACDR is as effective as ACDF. Different from previous reports,[24,26] on the SF-12 PCS, ACDR is showed more positive results than ACDF. Interestingly, SF-12 MCS showed no statistical difference.

Whether ACDR or ACDF could reduce the incidence rate of ASD has remained controversial.[28] Based on current understanding, ACDR cannot completely prevent the occurrence of ASD, but it can alleviate ASD by maintaining the mobility of the

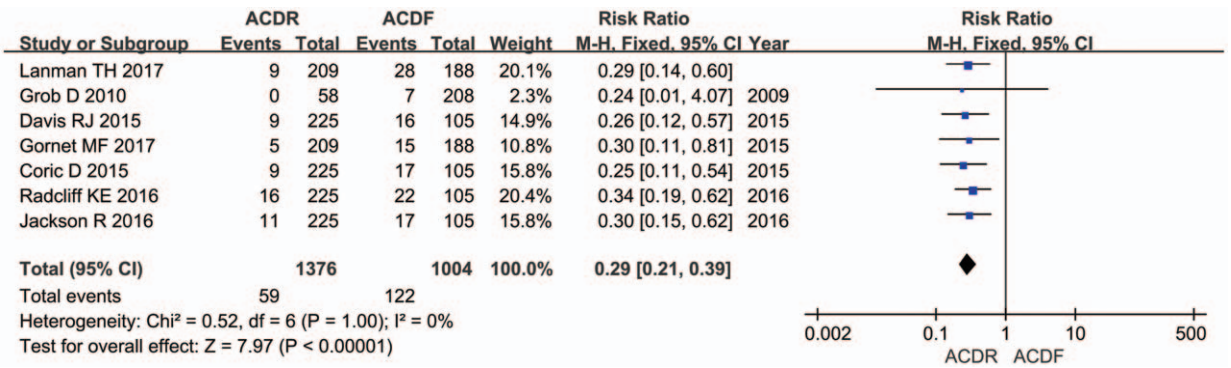

Figure 8. The risk ratio estimate for the subsequent surgical intervention.

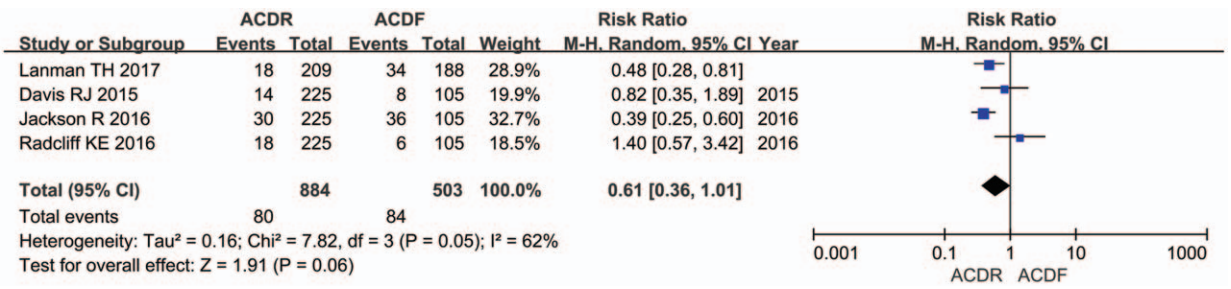

Figure 9. The risk ratio estimate for the neurological deterioration.

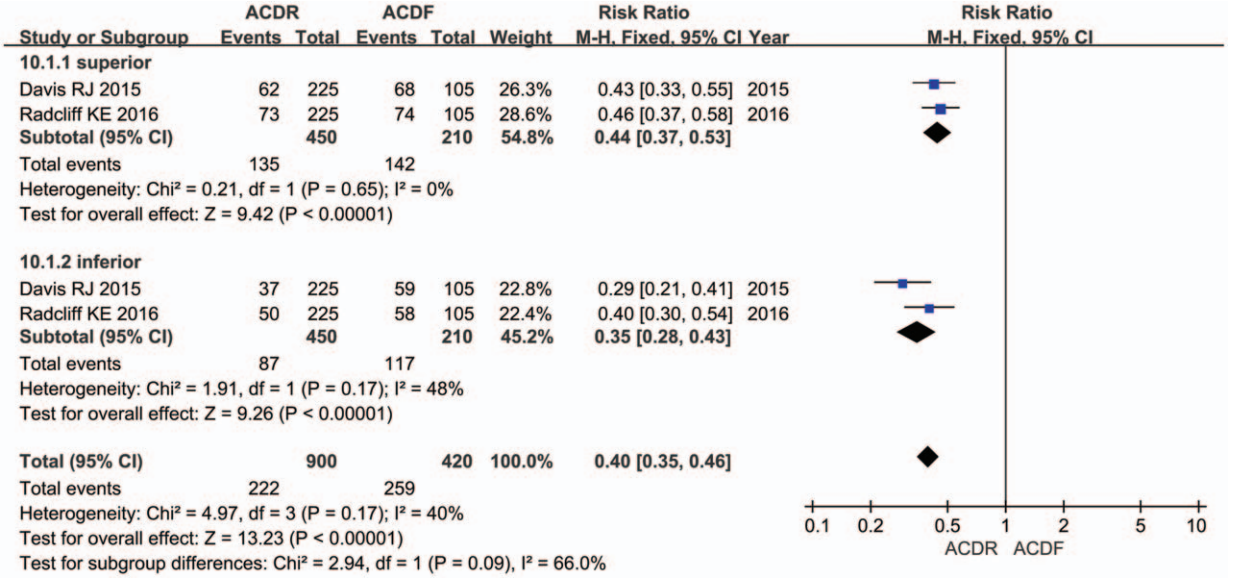

Figure 10. The risk ratio estimate for the adjacent-segment disc degeneration rate.

index level and relieving the intradiscal pressure in adjacent segment discs. On the one hand, Goffin et al[29] reported that the intradiscal pressure in the adjacent segment in 2-level ACDR was clearly lower than that for ACDF, causing lower degeneration rate in adjacent levels. However, other spine surgeon found that multifusion induces ASD more extensively. Hilibrand[30] reported that ASD outcomes in multilevel ACDF were inferior to those with single-level ACDF, the possible explanation is the fusion of degenerated or potentially degenerated segments during the operation. Conversely, in contrast to the doctrine of biomechanics, other authors believe that natural degeneration is the main cause of ASD.[31] Although this is somewhat reasonable, some still believe that the physiological environment of the neck will inevitably be changed after surgery, apart from genetic predisposition,[32] compared with ACDR, which preserves mobility, and flexibility, and is closer to a normal anatomic state, a fusion procedure changes the mechanical environment and adds to compensatory movement of the adjacent level, with both factors exacerbating ASD. Therefore, we speculate that there are 2 reasons for the high ASD rate in ACDF. First, the 2 pathological changes mentioned above lead to higher intradiscal pressure compared with that in ACDR, thus stimulating abundant inflammatory mediators in the adjacent disc. Second, the dominant inflammatory cytokines, such as interleukin-1β and tumor necrosis factor-α,[33,34] contribute significantly to ASD. Together, the main causes of ASD are based on natural degeneration and surgical intervention. Although ACDR has advantages over ACDF with regard to ASD development, the greater significance maintaining the range of motion and restoring neck function. Another focus of attention is the apparent correlation between reoperation rate and ASD.[35] In our study, we observed that SSI rate occurs more often with ACDF than ACDR. However, not all ASD requires reoperation, and vice versa. In addition, the author encounters a notable case in clinical, in which vertebrae between 2 prostheses developed a compression fracture resulting from excessive physiological load. Interestingly, no database search found a similar case report or study.

There are several limitations and merits of this study. First, only 11 studies were included in this study, the full text was available for 9, and the others were articles from conference proceeding. This may lead to bias due to missing data. Second, although our electronic and manual search encompassed a range of databases, we only included articles published in English, it may lead language bias. At last, some of RCTs with incomplete data may decrease the quality of evidence and strength of analysis. Although, limitations in this research, there were some merits existed. First, our up-to-date article retrieval yielded 11 eligible studies including 9 RCTs (evidence of level 1) and 2 CCTs (evidence of level 2), it provided more high-level literature from origin and generated more credible results by evidence-based medicine analysis. Moreover, 5 multicenter RCTs under the guidance of FDA out of 9 RCTs may further reinforce the quality of the evidence. Finally, more high-quality RCTs with large sample size are required to investigate the efficiency of ACDR compared with ACDF.

5. Conclusion

Although there was no significant difference between ACDR and ACDF in ND, VAS arm MCS score, most effective indices such as NDI, VAS neck, PCS score, PS, OCS, is superior to ACDR than ACDF. In addition, safety indices of ACDR including DRAE, ASD, and SSI were better than ACDF. In all, ACDR appears to be more effective and safety than ACDF; however, more well-designed studies with large samples are needed to provide further evidence for the effect and reliability of ACDR compared with ACDF in the treatment of cervical spondylosis.

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