

Anterior cervical discectomy and fusion without plate (ACDFWP) versus anterior cervical disc arthroplasty (ACDA) for cervical spondylosis: A meta-analysis and literature review

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SUMMARY This meta-analysis compared the clinical outcomes between two alternative surgeries for patients with cervical spondylosis, namely anterior cervical discectomy and fusion (ACDF) without plate (ACDFWP) vs. anterior cervical disc arthroplasty (ACDA). We searched databases, including PubMed, EMBASE, Cochrane Library, Google Scholar, and Web of Science (firstly available-2019). A standard meta-analysis was performed with the included studies. A Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was used for the evaluation of the study quality of nonrandomized-controlled trials (nRCTs), while a Risk of Bias (RoB) battery was used for randomized controlled trials (RCTs). Eight studies involving 640 patients were included. No significant difference was found in the indices of Neck Disability Index (NDI) score, Visual Analog Score (VAS), Japanese Orthopaedic Association (JOA) score, operative time, blood loss, Swallowing Quality of Life Score (SWAL-QL), and complications. Cervical alignment was significantly better in the ACDFWP than in ACDA (mean difference (MD) = -0.67, 95% confidence interval (CI) [-1.11, -0.23], $P = 0.003$, $I^2 = 20\%$). Although the alternative ACDFWP was slightly superior in terms of the index of cervical alignment, the limited research on this subject present insufficient evidence. Further well-designed studies are warranted in the future.

Keywords cervical spondylosis, anterior cervical discectomy and fusion without plate, anterior cervical disc arthroplasty, cervical alignment, meta-analysis

1. Introduction

Cervical spondylosis is a common disease characterized by progressive degeneration in the cervical spine and is regarded as a natural process of aging. The main symptoms of cervical spondylosis are neck pain and neck stiffness. Recently, an increasing number of young people are experiencing cervical spondylosis. It has been a public health concern related to remarkable disease burden. Since the 1950s, anterior cervical discectomy and fusion (ACDF) with plate has been regarded as the gold standard of therapy for cervical spondylosis (1-3). Although it has been well documented regarding its satisfactory efficacy, some complications, such as dysphagia (4), hoarseness

(2), and adjacent segment disease (ASD) (3) are also reported. Some authors believe that these complications are caused by the influence of anterior vertebral plate fixation (4). Kepler *et al.* found that the fusion itself may contribute to more pressure between the adjacent segmental discs (5). Moreover, ASD might also result from the progression of cervical degeneration (6,7). Thus, the conventional ACDF with plate has limitations, and the adverse events cannot be ignored. To prevent these adverse events, alternative surgeries, such as ACDF without plate (ACDFWP) and anterior cervical disc arthroplasty (ACDA) were developed against cervical spondylosis (Figure 1).

Currently, many studies have reported a comparison of the clinical outcomes of conventional ACDF (with

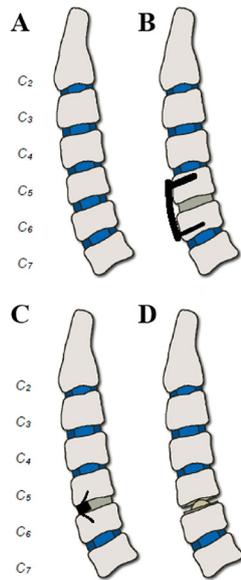


Figure 1. Schematic diagram of the surgeries for cervical spondylosis. **A.** Schematic diagram of the cervical spine. **B.** Conventional anterior cervical discectomy and fusion (ACDF) with plate. **C.** Anterior cervical discectomy and fusion without plate (ACDFWP). **D.** Anterior cervical disc arthroplasty (ACDA). Most of previous studies compared ACDF with plate and ACDA (B vs.D), in the present study we compared ACDFWP vs. ACDA (C vs. D).

plate) and alternative ACDFWP. Recently, Cheung *et al.* found that ACDFWP provides better clinical outcomes than conventional ACDF (with plate) (8). Other studies have also compared the clinical outcomes between conventional ACDF (with plate) and ACDA. Latka *et al.* reported that compared to conventional ACDF (with plate), ACDA significantly lowered the probability of ASD development at the 60-month follow-up. (9). And Maharaj *et al.* compared ACDA and ACDF (including with and without plate). They found that ACDA has superiority in terms of reoperation rate and reduction in neurological deficits (10). However, to our knowledge, no meta-analyses have compared the clinical outcomes between alternative surgeries, ACDFWP and ACDA. Thus, in order to provide a complete chain of evidence to enable the selection of an appropriate surgical technique for cervical spondylosis treatment by the clinicians, we designed this study to compare the clinical outcomes of the alternative ACDFWP and ACDA (Figure 1), strictly as per the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (11).

2. Materials and Methods

2.1. Literature search strategy

English-language search of databases, including PubMed, EMBASE, Cochrane Library, Google Scholar, and Web of Science was performed with the keywords of "cervical spondylosis" AND "anterior cervical"

AND "arthroplasty" AND "discectomy and fusion" OR "replacement". Studies from firstly available-2021 were included.

As per the inclusion criteria, (i) studies that compared the clinical outcomes between ACDA and ACDFWP in patients with cervical spondylosis, (ii) studies where complete data were available, (iii) randomized controlled trials (RCTs) and nonrandomized-controlled trials (nRCTs), and (iv) studies wherein at least one of the following assessments for clinical outcomes were reported: Neck Disability Index (NDI) score, Visual Analog Score (VAS), Japanese Orthopaedic Association (JOA) score, cervical alignment (The overall sagittal alignment of the cervical spine was calculated by the Cobb angle between the C2 and C7 vertebrae on the lateral radiograph), operative time, blood loss, complications, and Swallowing Quality of Life Score (SWAL-QL), were included. Furthermore, (i) non-English studies, (ii) review papers, (iii) meta-analyses, (iv) case reports and serious case reports, as well as (v) letters were excluded.

2.2. Data extraction

Three authors (JP, SL, XL) performed the literature search, read the title and abstract, and then screened the studies as per the inclusion/exclusion criteria. Subsequently, a senior scientist (TA) cross-checked and confirmed the quality of the included literature. Three authors (JP, SL, HS) extracted information (information of enrolled patients, therapy, experimental design, and outcome assessments) from the final selection of studies. We classified the assessments into two groups. One group contained indices that directly evaluated the clinical outcomes, including the NDI, VAS, JOA and cervical alignment; another group contained the other factors associated with the surgeries, including operative time, blood loss, complications, and SWAL-QL. We discussed the data every day to reach consensus. Finally, all the data were checked by third-party authors (DZ, RZ, MH, PL) before submission for the meta-analysis.

2.3. Statistical analyses

We designed and performed this study strictly as per the PRISMA guidelines (11). We employed a RevMan 5.3 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) for the meta-analysis. The odds ratio (OR) and the corresponding 95% confidence interval (CI) were calculated for the dichotomous outcomes. The mean difference (MD), and the 95% CI were calculated for the continuous data. During the homogeneity test, when $p \geq 0.1$ and $I^2 \leq 50\%$, the studies were considered to be homogeneous, which were analyzed with a fixed-effect model; when

$p < 0.1$ and $I^2 > 50\%$, the studies were regarded to be heterogeneous, which were analyzed with a random-effects model. Subgroups analyses were performed for considering the subgroups in some groups, such as VAS (neck and arm), cervical alignment (whole and local) and complications (ASD is regarded as the most important adverse event).

2.4. Assessment of study quality of the included studies

Three authors (SL, JP and RX) performed quality assessment for the study. A Risk of Bias (RoB) in Non-randomized Studies of Interventions (ROBINS-I) tool (12) was employed to assess the study quality of nRCTs. A RoB battery developed by the Cochrane Collaboration was used for the RCTs (13).

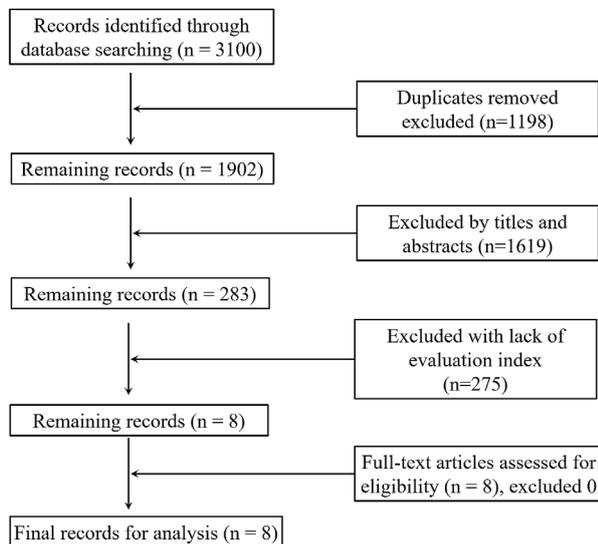


Figure 2. Flow chart of the searching strategy and selection of literature reports.

3. Results

3.1. Literature searching results

Total 3100 studies were identified in the first search. First, duplicate studies (1,198) and those with an inappropriate title and abstract (1,619) were excluded. Thereafter, the remaining 283 studies were read and selected within which 275 items were excluded. Finally, 8 studies were included and submitted for the meta-analysis (Figure 2). The characteristics of the included studies are listed in Table 1.

3.2. Assessments of the study quality

Figure 3 shows the results of the assessments of study quality using a RoB tool (for RCTs) and a ROBINS-I tool (for nRCTs). Overall, three RCTs had low RoB. Only one study (Qizhi *et al.* 2016) had a high risk of blinding, and one study had a high risk of other bias (Donk *et al.* 2017b). The study quality of the included RCTs was satisfactory (Figure 3A). However, the study quality of the included nRCTs was weaker. The study by Park *et al.* 2008 had a serious RoB and that by Vorsic *et al.* 2010 had a critical RoB. Confounding bias was involved in 2 studies (14,15). One study had missing data (14). Overall, two studies were of low quality (14,15), and other 3 studies were identified as having moderate study quality (Figure 3B). We could not evaluate the publication bias because only 3 RCTs and 5 nRCTs were included in this study.

3.3. Assessments of the postoperative clinical efficacy achieved with the ACDFWP and ACDA.

Figure 3 shows the results of the assessments of study quality using a RoB tool (for RCTs) and a ROBINS-I

Table 1. Characteristics of the included studies

Included Trials	Study Design	Sample size	Average age (\bar{y})	Gender (M/F)	Level	Implants
Park <i>et al.</i> 2008	R	ACDA: 21	45	11/10	1	Mobi-C Solis
		ACDFWP: 32	47	20/12		
Vorsic <i>et al.</i> 2010	P	ACDA: 40	48.1	13/27	1/2	ProDisc-C ChronOS
		ACDFWP: 40	51.3	12/28		
Park <i>et al.</i> 2012	R	ACDA: 22	39.9	19/3	1	ProDisc-C Solis
		ACDFWP: 21	44.3	11/10		
Qizhi <i>et al.</i> 2016	RCT	ACDA: 14	46.79	9/5	2	Discover Zore-P
		ACDFWP: 16	48.13	11/5		
Shi <i>et al.</i> 2016a	R	ACDA: 60	46.5	24/36	1	Discover Zore-P
		ACDFWP: 68	47.4	33/35		
Shi <i>et al.</i> 2016b	P	ACDA: 55	48.9 \pm 7.0	30/25	1	Discover Zore-P
		ACDFWP: 57	50.6 \pm 7.2	37/20		
Donk <i>et al.</i> 2017a	RCT	ACDA: 50	44.1 \pm 6.4	24/26	1	Bryan Brantigan
		ACDFWP: 47	43.1 \pm 7.5	25/22		
Donk <i>et al.</i> 2017b	RCT	ACDA: 50	53.6 \pm 6.9	24/26	1	Bryan Brantigan
		ACDFWP: 47	52.2 \pm 8.1	25/22		

ACDA: anterior cervical disc arthroplasty; ACDFWP: anterior cervical discectomy and fusion without plate; R: Retrospective; P: Prospective; RCT: Randomized controlled study.

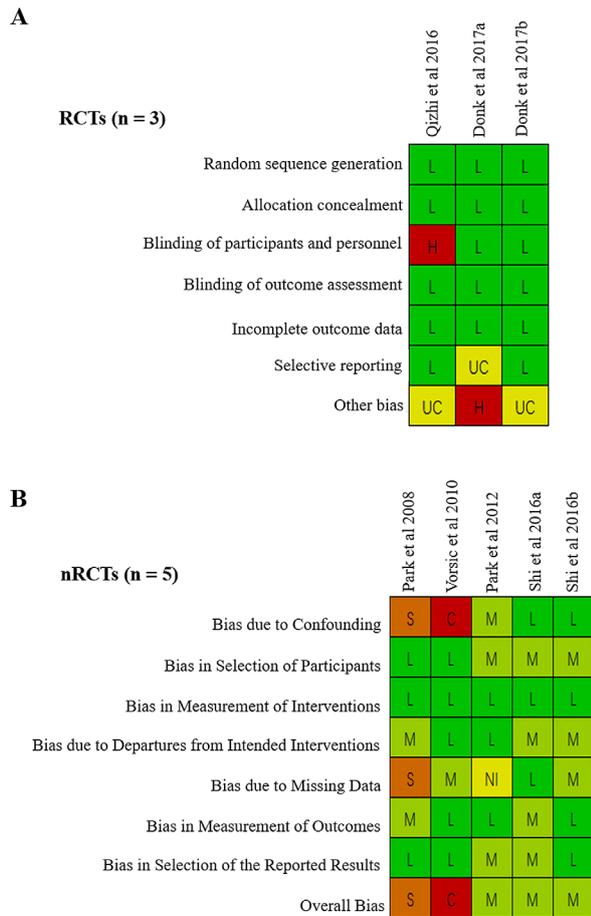


Figure 3. Quality assessment of the involved literatures with a RoB tool for RCTs (A) and a ROBINS-I tool for nRCTs (B). L = Low, UC = Unclear, H = High, M = Moderate, S = Serious, C = Critical, NI = No information.

tool (for nRCTs). Overall, three RCTs had low RoB. Only one study (Qizhi *et al.* 2016) had a high risk of blinding, and one study a had high risk of other bias (Donk *et al.* 2017b). The study quality of the included RCTs was satisfactory (Figure 3A). However, the study quality of the included nRCTs was weaker. The study by Park *et al.* 2008 had a serious RoB and that by Vorsic *et al.* 2010 had a critical RoB. Confounding bias was involved in 2 studies (14,15). One study had missing data (14). Overall, two studies were of low quality (14,15), and other 3 studies were identified as having moderate study quality (Figure 3B). We could not evaluate the publication bias because only 3 RCTs and 5 nRCTs were included in this study.

3.3.1. NDI

From among the studies that have reported postoperative NDI scores, one study (14) was excluded owing to lack of data on standard deviation of NDI. The remaining five studies (15-19) reported the postoperative NDI for 378 patients. No significant difference was observed in the NDI scores of the ACDFWP and ACDA (MD = 0.15,

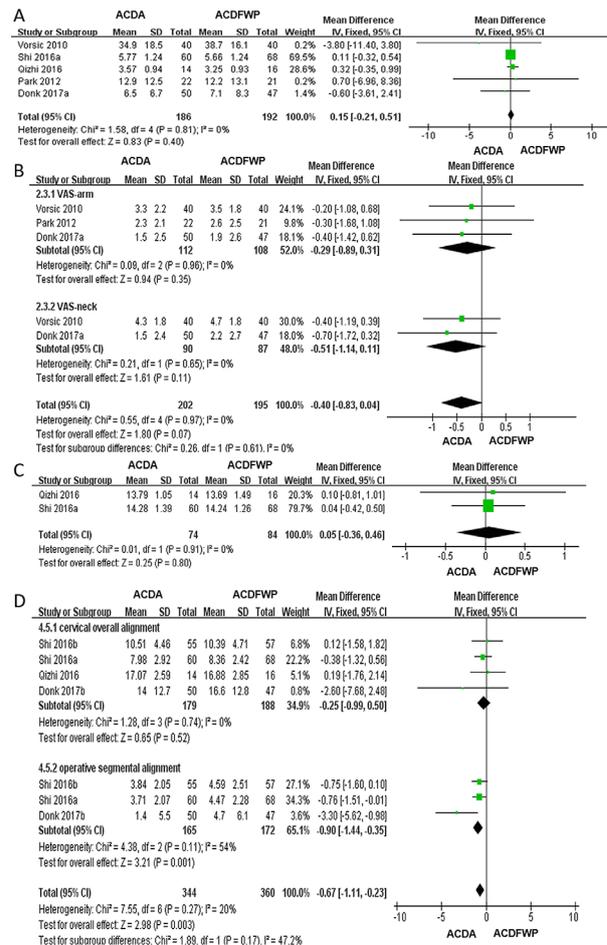


Figure 4. Meta-analysis for the clinical assessments of ACDA and ACDFWP. A. Forest plot for the scores of NDI. B. Forest plot for the scores of VAS. C. Forest plot for the scores of JOA. D. Forest plot for the scores of cervical alignment.

95% CI [-0.21, 0.51], P = 0.40, I² = 0%) (Figure 4A).

3.3.2. VAS

Four studies (14-16,19) reported the postoperative VAS scores, within one study (14) was withdrawn for analysis because they did not report the standard deviation. The remaining three studies suggested non-significant differences in the VAS scores of the two groups (MD = -0.40, 95% CI [-0.83, 0.04], P = 0.07, I² = 0%). We also introduced subgroups analysis and found no difference between the subgroups (Figure 4B).

3.3.3. JOA

Two studies reported the postoperative JOA scores (17,18), with 158 patients being enrolled. The pooled analysis showed no significant difference in the postoperative JOA scores of the ACDFWP and ACDA (MD = 0.05, 95% CI [-0.36, 0.46], P = 0.80, I² = 0%) (Figure 4C).

3.3.4. Cervical alignment

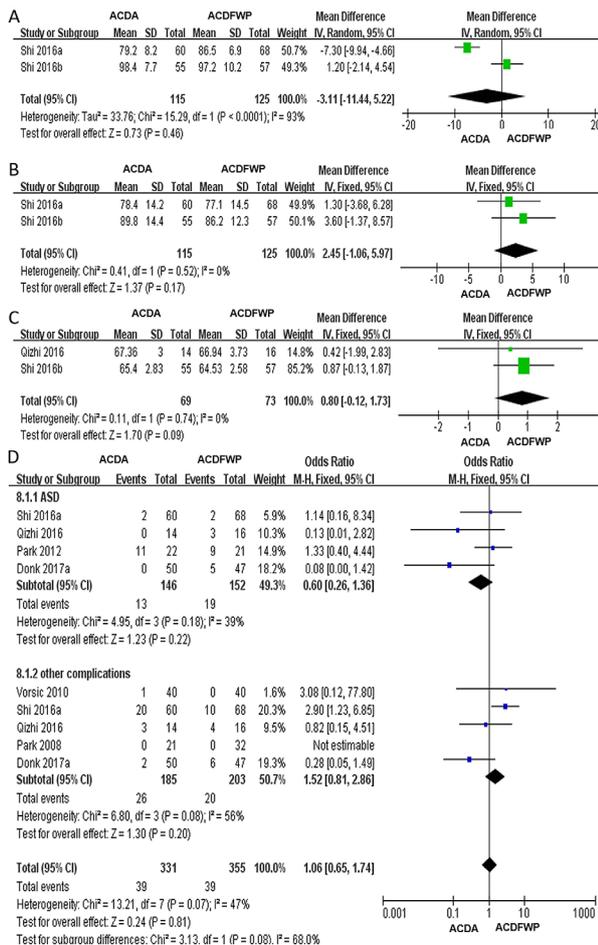


Figure 5. Meta-analyses of the other outcome indices of ACDA and ACDFWP. A. Forest plot for the operative time. **B.** Forest plot for the scores of blood loss. **C.** Forest plot for the scores of SWAL-QL. **D.** Forest plot for the scores of complications.

Six studies (14,16-18,20,21) reported the cervical alignment, while two (14,16) were excluded because they did not report the standard deviation. We conducted subgroups analyses to decrease the potential heterogeneity, and no significant differences were observed between the subgroups. Overall, the remaining four studies indicated that the cervical alignment was better in the ACDFWP (vs. ACDA, MD = -0.67, 95% CI [-1.11, -0.23], $P = 0.003$, $I^2 = 20\%$) (Figure 4D).

The assessment of postoperative clinical efficacy showed that the ACDFWP exhibited better efficacy only in the cervical alignment. No other significant difference was found in the other 3 indices.

3.4. Assessments of other clinical factors

3.4.1. Operation time

Four studies reported the operation time; two studies (14,16) were excluded owing to lack of data on standard deviation. Analysis of the remaining two studies (18,20) that included 240 patients found no difference between the ACDFWP and ACDA (MD = -3.11, 95% CI [-11.44,

5.22], $P = 0.46$, $I^2 = 93\%$) (Figure 5A).

3.4.2. Blood loss

Two studies reported blood loss (18,20). Total 240 patients were enrolled. However, no significant difference was identified between the ACDFWP and ACDA (MD = 2.45, 95% CI [-1.06, 5.97], $P = 0.17$, $I^2 = 0\%$) (Figure 5B).

3.4.3. Swallowing Quality of Life Score

SWAL-QL was reported in two studies (17,20) that involved 142 patients enrolled. No significant difference was found in the SWAL-QL of the two groups (MD = 0.80, 95% CI [-0.12, 1.73], $P = 0.09$, $I^2 = 0\%$) (Figure 5C).

3.4.4. Complications

Complications were reported in 6 studies (14-19) that involved 431 patients enrolled. No significant difference was observed in the complications between the two groups (MD = 1.06, 95% CI [0.65, 1.74], $P = 0.81$, $I^2 = 47\%$) (Figure 5D). Particularly, with regard to the frequency of occurrence of ASD, there were 19 cases in the ACDFWP and 13 cases in the ACDA, no significant difference was found between two groups ($Z = 1.23$, $P = 0.22$) (Figure 5D).

No significant difference was found in the other clinical-related indices.

4. Discussion

The present study compared the efficacy and other factors associated with the clinical outcome of ACDFWP and ACDA. To our knowledge, this is the first meta-analysis to compare these two alternative surgeries. We found that the ACDFWP seems had better efficacy in terms of cervical alignment than that ACDA. No significant difference was found in the other indices. Our results suggest a slight superiority of ACDFWP. These findings might contribute to the selection of surgery type in patients with cervical spondylosis. However, the relatively small number of included studies lowered the evidence level.

In the present study, 8 studies (3 RCTs and 5 nRCTs, 640 patients enrolled) were evaluated. Although 3 RCTs were included, the quality of the included RCTs were satisfactory, and the quality of the included nRCTs was moderate (Figure 3). Evidence-based comparison of the studies has limited worthiness.

With respect to the comparisons of clinical efficacy, the indices of NDI (MD = 0.15, 95% CI [-0.21, 0.51], $P = 0.40$, $I^2 = 0\%$), VAS (MD = -0.40, 95% CI [-0.83, 0.04], $P = 0.07$, $I^2 = 0\%$), and JOA (MD = 0.05, 95% CI [-0.36, 0.46], $P = 0.80$, $I^2 = 0\%$) showed the same

tendency. The homogeneity of the involved studies was high. We did not find any difference between the two surgeries. However, the results of the cervical alignment (MD = -0.67, 95% CI [-1.11, -0.23], $P = 0.003$, $I^2 = 20\%$) indicated better efficacy of ACDFWP (Figure 4). Under the support of cage, ACDF could achieve good operative alignment recovery.

With regard to the indices of other factors, we found no difference between the operation time [MD = -3.11, 95% CI (-11.44, 5.22), $P = 0.46$, $I^2 = 93\%$], blood loss [MD = 2.45, 95% CI (-1.06, 5.97), $P = 0.17$, $I^2 = 0\%$], SWAL-QL [MD = 0.80, 95% CI (-0.12, 1.73), $P = 0.09$, $I^2 = 0\%$], and complications [MD = 1.06, 95% CI (0.65, 1.74), $P = 0.81$, $I^2 = 47\%$]. There was no difference in the operation time and blood loss, postoperative QOL, and complications. ASD is the most important complication that must be considered while selecting the surgery. The aim of developing these alternative surgeries was to reduce the risk of complications, particularly, the onset of ASD because placing the anterior plate during the conventional ACDF is risky (22,23). It was reported that the incidence of ASD in ACDFWP was significantly lower than that in conventional ACDF (24). ACDA is another alternative surgery that is believed to lower the incidence of ASD onset. Previous evidence shows that ACDA contributes to maintain the motion at the involved segments and had a lower reoperation rate than those in conventional ACDF (1,25-27); a current study proved the long-term efficacy of ACDA in reducing the risk of ASD (9). However, our study found no difference between the ACDFWP and ACDA ($X^2 = 4.95$, $P = 0.18$, $I^2 = 39\%$) (Figure 5).

However, conventional ACDF (with plate), alternative ACDFWP, and ACDA, all the existing surgeries have their specific advantages and disadvantages. *i*) Conventional ACDF vs. alternative ACDF: Although alternative ACDF achieved low onset of ASD, the conventional ACDF (with plate), as the gold standard therapy for cervical spondylosis, also has its merits. Current two studies indicated that conventional ACDF is good for ensuring greater restoration of alignment in the operative segment (21,28). A long-term follow-up study found that the operative segmental alignment gradually decreased, and the overall alignment increased with time (21). *ii*) Conventional ACDF vs. ACDA: In addition to the low risk of ASD, ACDA has good efficacy. According to the results of several meta-analyses (29,30), the efficacy and safety of ACDA were superior to those of conventional ACDF. After a long-term follow-up, Ma *et al.* reported that ACDA was superior to conventional ACDF in terms of VAS and the overall success rate (30). Zhao *et al.* found that ACDA achieved a higher SF-36, a larger range of movement, a higher rate of neurological improvement, a lower VAS, a lower NDI, and a lower reoperation rate than conventional ACDF (29). Other studies have also indicated that ACDA was slightly better than the conventional ACDF in terms of the VAS score

(15,16,19) and SWAL-QL (17,20). However, ACDA also has its disadvantages. Tian *et al.* reported that ACDA might contribute to promote the progression of heterotopic ossification, especially for patients who had been preoperatively developed (31). Latka *et al.* reported that ACDA involved a longer operation time and more blood loss than the conventional ACDF. A longer traction on the structures of the soft neck is a major disadvantage of ACDA (9). *iii*) Alternative ACDF vs. ACDA (the present study): We found that only the alternative ACDF exhibited a slight benefit in the cervical alignment as compared to ACDA. No significant difference was found in the other indices between alternative ACDF and ACDA. In sum, both the conventional and alternative surgeries have their strengths and weaknesses. Based on the evidence available today, they cannot replace each other. The appropriate surgery should be seriously selected according to the individual pathophysiological state of each patient.

There are certain limitations of this study, as follows: *i*) The small number of included studies; only 3 RCTs were included; only studies published in English were included. Two studies by the same authors were included, namely Shi 2016a (20) and Shi 2016b (18), and Donk 2017a (19) and Donk 2017b (21). Although we have investigated the studies and excluded the possibility of overlap of patients, but the data sources were too narrow, which lowered the reliability of the evidence. *ii*) The study quality of some the included studies was low. *iii*) The heterogeneity of some items (operation time, complications) was high, lowering the level of evidence. *iv*) Long-term observation was not performed in all included literatures, which is required on the study of ASD. More rigorous studies with long-term follow-up are expected to compare the alternative ACDF and ACDA, particularly for the onset of ASD.

5. Conclusions

In this study, we compared the clinical outcomes between the alternative ACDFWP and ACDA. We found that the ACDFWP exhibited slightly better cervical alignment than ACDA. No significant difference was found in the other items, including NDI, VAS, JOA, operation time, blood loss, SWAL-QL, and complications. These findings may contribute to the selection of the appropriate surgery for patients with cervical spondylosis. However, limited studies exist; thus, the evidence level is low. Larger, better-planned studies are required in the future.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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