Review Article Comparison of three operative techniques in multilevel cervical spondylotic myelopathy: a meta-analysis

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Abstract: Background: Three operative techniques: anterior cervical discectomy and fusion (ACDF), anterior cervical corpectomy and fusion (ACCF) and Hybrid Surgery (HS), corpectomy combined with discectomy, are used to treat multilevel cervical spondylotic myelopathy (CSM). However, which one is the best treatment for multilevel CSM remains considerable controversy. Objective: A meta-analysis was performed to compare the clinical, radiographic and surgical outcomes among three surgical methods in the treatment for multilevel CSM. Methods: An extensive search of literature was performed in Pubmed/MEDLINE, Embase, the Cochrane library, CNKI and WANFANG databases on three operative techniques treating multilevel CSM from Jan. 2010 to Jan. 2017. The following variables were extracted: length of hospital stay, blood loss, operation time, Japanese Orthopedic Association scores (JOA), neck disability index score (NDI), fusion rate, Cobb angles of C2-C7, dysphagia, hoarseness, C5 palsy, infection, cerebral fluid leakage, epidural hematoma, graft subsidence, graft dislodgment and total complications. Data analysis was conducted with RevMan 5.3 and STATA 12.0. Results: A total of 12 studies with 1468 patients were included in our study. The results showed that there were significant differences among three methods in blood loss and total complications (all p<0.05). ACDF were better in the angle of C2-C7 at the final follow-up (p<0.00001), C5 plasy (p = 0.02), fusion rate (p = 0.04) and graft subsidence (p = 0.004) than ACCF. In term of angle of C2-C7 at final followup (p<0.00001), operation time (p = 0.003), fusion rate (p = 0.02) and hospital stay (p<0.00001), HS was better than ACCF. Conclusions: Based on our meta-analysis, except for blood loss and total complications, ACDF and hybrid surgery are effective choices for the treatment of multilevel CSM and ACCF is the last option.

Keywords: Anterior cervical discectomy and fusion, anterior cervical corpectomy and fusion, hybrid surgery, multilevel cervical spondylotic myelopathy, clinical efficacy, complications

Introduction

Cervical spondylotic myelopathy (CSM), a common progressive spinal cord disorder, strongly impacts quality of life and even results in disability for the elder [1-3]. CSM is usually caused by narrowing of cervical spinal canal due to degenerative and congenital changes [3-6]. It is controversial over optimal surgical treatment for CSM, especially for multilevel cervical spondylotic myelopathy (mCSM) [1-4, 5-9]. Recently anterior approaches were widely used, including ACDF [10-12], ACCF [11-15] and HS. ACDF treating CSM was firstly introduced by Smith, Robinson [16] and Cloward [17], anterior procedure has become the most widely applied for surgical choice [18]. Among anterior approaches, ACDF can decompress anterior spinal cord, preserve the stability of the spinal column [19, 20]; however, ACDF may have a high risk of incomplete decompression, limited visual exposure, and injury to the cord [21-25]. ACCF also provides extensive decompression and serves as a source for autografting [26-33]. Unfortunately, ACCF is a difficult procedure to perform and also has a high incidence of complications, such as injuring the spinal cord or nerve roots, excessive bleeding, graft displacement [34-38]. Hybrid surgery, corpectomy combined with discectomy, provides a good option for nerve tissue decompression and spinal reconstruction while reducing complications [39, 40].

Previous meta-analysis [41-44] mainly focused on the comparison between ACDF and ACCF or Hybrid surgery, combining cervical disc arthroplasty with fusion. However, comparisons of 3 operative techniques still remain controversial. The purpose of this article is to compare clinical outcomes, radiographic outcomes and surgical outcomes among 3 operative techniques, ACDF, ACCF and HS, in the treatment for mCSM.

Materials and methods

Ethics statement

There was no need to seek informed consent from patients, because this meta-analysis based on the published data.

Search strategy

An extensive search of literature was performed in PubMed, Embase, the Cochrane library, CNKI and WANFANG databases. The following key words were used for search: "anterior cervical discectomy and fusion", "anterior cervical corpectomy and fusion", "hybrid surgery", "corpectomy combined with discectomy", "multilevel cervical spondylotic myelopathy" from Jan. 2010 to Jan. 2017, with various combinations of the operators "AND" and "OR". Language was restricted to Chinese and English.

Inclusion criteria

Studies were included if they met the following criteria: (1) randomized or non-randomized controlled study; (2) age \geq 18 years old; (3) studies on comparison between ACDF and ACCF, ACDF and HS, HS and ACCF or among 3 methods, including ACDF, ACCF and HS for treatment of CSM; (4) three or four levels cervical spondylotic myelopathy; (5) follow-up more than 1 year.

Exclusion criteria

Studies were excluded if they met the following criteria: (1) dealt only with ACDF, ACCF or HS alone for treatment of CSM; (2) had an average follow-up time less than 1 year; (3) had repeated data; (4) did not report outcomes of interest; (5) in vitro human cadaveric biomechanical studies; (6) earlier trial, reviews, and case-reports (7) have ossification of posterior longitudinal ligament.

Selection of studies

Two reviewers independently reviewed all subjects, abstracts and the full text of articles.

Then the eligible trials were selected according to the inclusion criteria. When consensus could not be reached, a third reviewer was consulted to resolve the disagreement.

Data extraction and management

Two reviewers extracted data independently. The data extracted including the following categories: study ID, study design, study location, total patients, follow-up, mean age, gender, clinical outcomes including length of hospital stay, preoperative and at the final follow-up JOA and NDI; radiographic outcomes including preoperative and at the final follow-up Cobb angles of C2-C7, fusion rate, graft subsidence, graft dislodgment and surgical outcomes including blood loss, operation time, dysphagia, hoarseness, C5 palsy, infection, cerebral fluid leakage, epidural hematoma and total complications.

Statistical analysis

Data analysis was performed with RevMan 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) and STATA 12.0 (Stata Corporation, College Station, TX, USA). Odds ratio (OR) was used as a summary statistic to analyze dichotomous variables, and the standardized mean difference (SMD) was used to analyze continuous variables. Both were reported with 95% confidence intervals (CI), and a P value of 0.05 was used as the level of statistical significance. Assessment for statistical heterogeneity was calculated using the I² tests, which described the proportion of the total variation in meta-analysis assessments from 0% to 100%. The random effects model was used for the analysis when an obvious heterogeneity was observed among the included studies (I²>50%). The fixed-effects model was used when there was no significant heterogeneity between the included studies (l²≤50%) [45, 46].

Test for risk of publication bias

We performed a visual inspection of the funnel plot for publication bias. The funnel plot should be asymmetric when there was publication bias and symmetric in the case of no publication bias. We performed Egger and Begg tests to measure the funnel plot asymmetry by using a significance level of P<0.05. The trim and fill computation was used to estimate the effect of publication bias.



Results

Search results

We had searched 199 English studies in MEDLINE, EMBASE and 79 Chinese studies in WANFANG and CNKI. Of these, 122 English articles and 36 Chinese duplicates were removed, 47 English articles and 28 Chinese articles were excluded due to unrelated studies. 24 English articles and 9 Chinese article were excluded due to eligibility criteria. As a result, a total of 12 studies were identified for this meta-analysis. The literature search procedure was shown in **Figure 1**.

Baseline characteristics and quality assessment

A total of 12 studies containing 1468 patients with mCSM were included in our study. Of these studies, 4 studies compared 3 operative techniques, 4 studies compared ACDF with ACCF and 4 studies compared ACCF with HS. Baseline characteristics of included articles were shown in **Table 1**. All included studies were retrospective studies, we assessed the quality of each study by using the Newcastle Ottawa Quality Assessment Scale (NOQAS). This scale were applied to allocate a maximum of nine points for the quality of selection, comparability, exposure, and outcomes for study participants. Of these studies, ten studies scored 8 points and two studies scored 7 points. Hence, the quality of each study was relatively high (Table 2).

Clinical outcomes

JOA score: There was no significant difference in preoperative and final follow-up JOA between ACDF and ACCF [47-53] [P = 0.29, SMD = 0.13 (-0.11, 0.37); heterogeneity: P = 0.63, $l^2 = 0\%$, Fixed-effect model, **Figure 2**; P = 0.62, SMD = 0.06 (-0.18, 0.30); het-0.23, $l^2 = 26\%$ Fixed-effect

erogeneity: P=0.23, $I^2 = 26\%$, Fixed-effect model, Figure 3].

NDI score: There was no significant difference in preoperative and final follow-up NDI between ACDF and ACCF [47, 48, 52] and between HS and ACCF [47, 48] [P = 0.38, SMD = 0.28 (-0.35, 0.91); heterogeneity: P = 0.59, I² = 0%, fixedeffect model, **Figure 4**; P = 0.36, SMD = -0.49 (-1.54, 0.56); heterogeneity: P = 0.07, I² = 61%, random-effect model, **Figure 5**; P = 0.23, SMD = 0.41 (-0.26, 1.07); heterogeneity: P = 0.67, I²= 0%, fixed-effect model, **Figure 4**; P = 0.40, SMD = 0.79 (-1.07, 2.65); heterogeneity: P = 0.009, I² = 85%, random-effect model, **Figure 5**].

Hospital stay: There was no significant difference in hospital stay between ACDF and ACCF [49, 52] [P = 0.40, SMD = -3.40 (-11.31, 4.51); heterogeneity: P = 0.00004, l^2 = 92%, random-effect model, **Figure 6**], but significant difference between HS and ACCF [55, 57] [P<0.00001, SMD = 2.51 (1.57, 3.44); heterogeneity: P = 0.82, l^2 = 0%, fixed-effect model, **Figure 6**].

First author	Year	Country	No. participants			Study Type	Mean Age, years (Range)			Gender (M/F)			Follow-up, month (mean)		
			ACDF	ACCF	HS	Study Type	ACDF	ACCF	HS	ACDF	ACCF	HS	ACDF	ACCF	HS
Yang Liu [47]	2012	China	69	39	72	Retrospective study	46.1 ± 6.8	47.8 ± 6.4	46.9 ± 7.1	39/30	26/13	44/28	26.8	26.4	25.6
Yang Liu [48]	2012	China	103	87	96	Retrospective study	53.48 ± 8.50	53.68 ± 7.80	54.36 ± 7.82	57/46	51/36	58/38	24	24	24
Kyung-Jin Song [49]	2012	Korea	25	15		Retrospective study	50.3 ± 7.5	54.1 ± 9.8		19/6	11/4		87.3 ± 21.7	94.3 ± 25.3	
Qiushui Lin [50]	2012	China	57	63		Retrospective study	58.74 ± 9.7	57.90 ± 10		38/19	43/20		24	24	
Qunfeng Guo [51]	2011	China	43	24	53	Retrospective study	52.7 ± 9.4	55.2 ± 10.1	53.4 ± 9.5	24/19	13/11	35/18	37.7 ± 7.2	37.3 ± 7.3	37.3 ± 7.0
Zhonghai Li [52]	2016	China	31	39		Retrospective study	54.9 ± 8.1	56.8 ± 8.6		21/10	28/11		35.2 ± 7.1	39.1 ± 7.5	
Qi Min [53]	2012	China	124	94	109	Retrospective study	53.48 ± 8.5	54.36 ± 7.82	53.68 ± 7.8	69/55	51/43	61/48	24	24	24
Hou Shubin [54]	2014	China	27	38		Retrospective study	50.43 ± 6.5	52.31 ± 7.32		20/7	25/13		24	24	
Gong Chen [55]	2011	China		18	18	Retrospective study		53.41 ± 3.45	52.53 ± 2.42		11/7	10/8		23.12 ± 11.2	25.36 ± 10.5
Zhong Bin [56]	2010	China		21	18	Retrospective study		35-68	38-62		8/13	8/10		21	21
Cui Guopeng [57]	2016	China		65	65	Retrospective study		48.24 ± 6.71	48.17 ± 6.17		21/44	24/41		25.61 ± 7.2	25.68 ± 7.24
Wu Liang [58]	2014	China		22	29	Retrospective study		53.26 ± 2.43	54.16 ± 2.88		15/7	18/11		15.8	15.8
Total			479	529	460										

Table 1. Characteristics of included studies

Study	Soloction	Comparability	Exposuro	Total
Study	Selection	comparability	Lxposure	score
Yang Liu [47]	3	2	3	8
Yang Liu [48]	3	2	3	8
Kyung-Jin Song [49]	3	2	3	8
Qiushui Lin [50]	2	2	3	7
Qunfeng Guo [51]	3	2	3	8
Zhonghai Li [52]	3	2	3	8
Qi Min [53]	2	2	3	7
Hou Shubin [54]	3	3	2	8
Gong Chen [55]	3	2	3	8
Zhong Bin [56]	3	2	3	8
Cui Guopeng [57]	3	2	3	8
Wu Liang [58]	3	2	3	8

Table 2. The quality assessment according to the New-castle Ottawa Quality Assessment Scale (NOQAS) of eachstudy

Radiographic outcomes

The angle of C2-C7: There was no difference in preoperative C2-C7 between ACDF and ACCF [47, 52, 54] and between ACCF and HS [47, 51] [P = 0.33, SMD = -0.42 (-1.27, 0.43); heterogeneity: P = 0.67, $I^2 = 0\%$, fixed-effect model, Figure 7; P = 0.41, SMD = -1.34 (-4.50, 1.83); heterogeneity: P = 0.83, $I^2 = 0\%$, fixed-effect model, Figure 7], but significant difference in final follow-up C2-C7 [P<0.00001, SMD = 4.76 (3.48, 6.03); heterogeneity: P = 0.17, I² = 43%, fixed-effect model, Figure 8; P<0.00001, SMD = -6.87 (-9.70, -4.04); heterogeneity: P = 0.69, I² = 0%, fixed-effect model, Figure 8]. Two studies [47, 51] reported these variables between ACDF and HS and there is no difference [P = 0.15, SMD = -5.75 (-13.51, 2.01); heterogeneity: P = 0.007, $I^2 = 86\%$, random-effect model, Figure 7; P = 0.62, SMD = -0.98 (-4.85, 2.90); heterogeneity: P = 0.08, $I^2 = 68\%$, randomeffect model, Figure 8].

Fusion rate: There was significant difference in fusion rate between ACDF and ACCF [47, 49, 51, 52, 54] [P = 0.04, OR = 2.54 95% CI (1.05, 6.11); heterogeneity: P = 0.29, I² = 20%, fixed-effect model, **Figure 9**] and between HS and ACCF [47, 51, 55, 56] [P = 0.02, OR = 0.28 95% CI (0.09, 0.81); heterogeneity: P = 0.90, I² = 0%, fixed-effect model, **Figure 9**]. But different results presented between ACDF and HS [47, 51]. [P = 0.78, OR = 1.66 95% CI (0.05, 54.51); heterogeneity: P = 0.11, I² = 61%, random-effect model, **Figure 9**].

Graft subsidence: There was significant difference in graft subsidence between ACDF and ACCF [47, 49-51] [P = 0.004, OR = 0.11 95% CI (0.02, 0.48); heterogeneity: P = 0.94, I² = 0%, fixed-effect model, **Figure 10**]. However, there was no significant difference in graft subsidence between ACDF and HS [47, 51] [P = 0.09, OR = 0.16 95% CI (0.02, 1.30); heterogeneity: P = 0.58, I² = 0%, fixed-effect model, **Figure 10**] and between ACCF and HS [47, 51] [P = 0.19, OR = 2.24 95% CI (0.68, 7.45); heterogeneity: P = 0.30, I² = 8%, fixed-effect model, **Figure 10**].

Graft dislodgment: There was no significant difference in graft dislodgment between ACDF and ACCF [47, 50, 52] [P = 0.27, OR = 0.46 95% CI (0.12, 1.83); heterogeneity: P = 0.45, $I^2 = 0\%$, Fixed-

effect model, **Figure 11**] and between HS and ACCF [47, 56, 57] [P = 0.10, OR = 2.38 95% CI (0.85, 6.67); heterogeneity: P = 0.89, I² = 0%, fixed-effect model, **Figure 11**].

Surgical outcomes

Blood loss: There was significant difference in blood loss between ACDF and ACCF [47, 50-52, 54] [P<0.00001, SMD = -53.12 (-64.61, -41.64); heterogeneity: P = 0.29, I² = 20%, fixed-effect model, **Figure 12**], between ACDF and HS [47, 51] [P<0.00001, SMD = -30.29 (-45.06, -15.52); heterogeneity: P = 0.38, I² = 0%, fixed-effect model, **Figure 12**] and between HS and ACCF [47, 53, 55-57] [P<0.00001, SMD = 40.83 (33.05, 48.60); heterogeneity: P = 0.62, I² = 0%, fixed-effect model, **Figure 12**].

Operation time: There was no significant difference in operation time between ACDF and ACCF [47, 49-52, 54] [P = 0.40, SMD = -8.99 (-29.76, 11.79); heterogeneity: P<0.00001, I² = 93%, random-effect model, **Figure 13**] and between ACDF and HS [47, 51] [P = 0.82, SMD = 2.63 (-19.62, 24.87); heterogeneity: P = 0.0002, I² = 93%, random-effect model, **Figure 13**]. But the different results showed between HS and ACCF [47, 51, 55-58] [P = 0.003, SMD = 17.37 (5.81, 28.93); heterogeneity: P<0.00001, I² = 89%, random-effect model, **Figure 13**].

Total complications: There was significant difference in number of total complications

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Figure 2. The standardized mean difference (SMD) estimate preoperative JOA score in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 3. Forest plot showing at the final follow-up JOA score in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 4. The standardized mean difference (SMD) estimate preoperative NDI score in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

between ACDF and ACCF [47, 48, 50-54] [P = 0.0009, OR = 0.56 95% CI (0.40, 0.79); heterogeneity: P = 0.29, I² = 18%, fixed-effect model, **Figure 14**], between ACDF and HS [47, 48, 51, 53] [P = 0.04, OR = 0.66 95% CI (0.44, 0.98); heterogeneity: P = 0.37, I² = 4%, fixed-effect model, **Figure 14**] and between ACCF and HS [47, 48, 51, 53, 56] [P = 0.04, OR = 1.47 95% CI (1.01, 2.13); heterogeneity: P = 0.48, I² = 0%, fixed-effect model, **Figure 14**].

C5 plasy: There was significant difference in C5 plasy between ACDF and ACCF [47, 48, 50-53] [P = 0.02, OR = 0.42 95% CI (0.21, 0.86); heterogeneity: P = 0.52, $I^2 = 0\%$, fixed-effect model, **Figure 15**]. But different results showed between ACDF and HS [47, 48, 51, 53] [P = 0.09, OR = 0.48 95% CI (0.21, 1.11); heterogeneity: P = 0.85, $I^2 = 0\%$, fixed-effect model, **Figure 15**] and between ACCF and HS [47, 48, 51, 53] [P = 0.22, OR = 1.54 95% CI (0.78, 51, 53] [P = 0.22, OR = 1.54 95% CI (0.78, 51, 53] [P = 0.22, OR = 1.54 95% CI (0.78, 51, 53] [P = 0.22, OR = 1.54 95\% CI (0.78, 51, 53] [P = 0.22, OR = 1.54 95\% CI (0.78, 51, 53] [P = 0.22, OR = 0.25\% CI (0.78, 51, 53] [P = 0.22, OR = 0.25\% CI (0.78, 51, 53] [P = 0.22, OR = 0.25\% CI (0.78, 51, 53] [P = 0.22, OR = 0.25\% CI (0.78, 51, 53] [P = 0.25\% CI (0.78\%)] [P = 0.25\%)] [P = 0.25\%) [P = 0.25\%)] [P = 0.25\% CI (0.78\%)] [P = 0.25\%) [P = 0.25\%)] [P = 0.

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Figure 5. The standardized mean difference (SMD) estimate at the final follow-up NDI score in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 6. The standardized mean difference (SMD) estimate Hospital stay in two groups. Cl = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 7. The standardized mean difference (SMD) estimate preoperative the angle of C2-C7 in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 8. The standardized mean difference (SMD) estimate at the final follow-up the angle of C2-C7 in two groups. CI = confidence interval.



Figure 9. Forest plot showing Fusion rate in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

3.04); heterogeneity: P = 0.67, $I^2 = 0\%$, fixed-effect model, **Figure 15**].

Infection: There was no significant difference in infection between ACDF and ACCF [47, 48, 53, 54] [P = 0.12, OR = 0.28 95% CI (0.06, 1.39); heterogeneity: P = 0.98, $I^2 = 0\%$, fixed-effect model, **Figure 16**], between ACDF and HS [47, 48, 53] [P = 0.14, OR = 0.25 95% CI (0.04,

1.55); heterogeneity: P = 0.95, $I^2 = 0\%$, fixedeffect model, **Figure 16**] and between ACCF and HS [47, 48, 53] [P = 0.97, OR = 0.98 95% CI (0.22, 4.38); heterogeneity: P = 0.82, $I^2 = 0\%$, fixed-effect model, **Figure 16**].

Cerebral fluid leakage: There was no significant difference in cerebral fluid leakage between ACDF and ACCF [47, 48, 50-54] [P = 0.29, OR =



Figure 10. Forest plot showing Graft subsidence in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 11. Forest plot showing Graft dislodgment in two groups. Cl = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

1.67 95% CI (0.65, 4.29); heterogeneity: P = 0.81, $I^2 = 0\%$, fixed-effect model, **Figure 17**], between ACDF and HS [47, 48, 51, 53] [P = 0.24, OR = 2.16 95% CI (0.59, 7.89); heterogeneity: P = 0.66, $I^2 = 0\%$, fixed-effect model, **Figure 17**] and between ACCF and HS [48, 51, 53] [P = 0.43, OR = 1.84 95% CI (0.40, 8.37); heterogeneity: P = 0.46, $I^2 = 0\%$, fixed-effect model, **Figure 17**].

Hoarseness: There was no significant difference in hoarseness between ACDF and ACCF [47-50, 52-54] [P = 0.71, OR = 0.88 95% Cl

(0.45, 1.73); heterogeneity: P = 1.00, $I^2 = 0\%$, fixed-effect model, **Figure 18**], between ACDF and HS [47, 48, 53] [P = 0.45, OR = 1.42 95% CI (0.57, 3.53); heterogeneity: P = 0.98, $I^2 = 0\%$, fixed-effect model, **Figure 18**] and between ACCF and HS [47, 48, 53] [P = 0.46, OR = 1.44 95% CI (0.55, 3.81); heterogeneity: P = 0.91, $I^2 = 0\%$, fixed-effect model, **Figure 18**].

Dysphagia: There was no significant difference in dysphagia between ACDF and ACCF [47-50, 52-54] [P = 0.83, OR = 1.06 95% CI (0.63, 1.78); heterogeneity: P = 0.91, I² = 0%, fixed-



Figure 12. The standardized mean difference (SMD) estimate Blood loss in two groups. Cl = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 13. The standardized mean difference (SMD) Operation time in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

effect model, **Figure 19**], between ACDF and HS [47, 48, 53] [P = 0.45, OR = 1.27 95% CI

(0.68, 2.37); heterogeneity: P = 0.96, $I^2 = 0\%$, fixed-effect model, **Figure 19**] and between



Figure 14. Forest plot showing Number of total complications in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 15. Forest plot showing C5 plasy in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

ACDF and HS [47, 48, 53] [P = 0.96, OR = 0.98 95% CI (0.48, 2.02); heterogeneity: P = 0.52, I² = 0%, fixed-effect model, **Figure 19**]. *Epidural hematoma:* There was no significant difference in epidural hematoma between ACDF and ACCF [47, 50-52] [P = 0.22, OR =



Figure 16. Forest plot showing Infection in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 17. Forest plot showing Cerebral fluid leakage in two groups. Cl = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

0.41 95% CI (0.10, 1.69); heterogeneity: P = 0.95, $I^2 = 0\%$, fixed-effect model, **Figure 20**], between ACDF and HS [47, 51] [P = 0.90, OR = 1.14 95% CI (0.15, 8.34); heterogeneity: P = 0.37, $I^2 = 0\%$, fixed-effect model, **Figure 20**] and between ACDF and HS [47, 51] [P = 0.24, OR = 3.49 95% CI (0.44, 27.50); heterogen

eity: P = 0.67, $I^2 = 0\%$, fixed-effect model, **Figure 20**].

Publication bias: After a detection of publication bias by STATA 12.0, but there was no publication bias found for all included studies (all p<0.05).

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Figure 18. Forest plot showing Hoarseness in two groups. Cl = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.



Figure 19. Forest plot showing Dysphagia in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

Discussion

The surgical treatment for CSM had a history of more than half a century. Up to now, regarding

single-level CSM, the surgical option has been reached a consensus. However, as for multilevel CSM (mCSM), the option of surgical approach remains debated [23, 52-55]. The



Figure 20. Forest plot showing Epidural hematoma in two groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

common operative option included anterior, posterior and combined anteroposterior approaches. In the 1960s, posterior approaches including laminectomy and laminoplasty were widely used in the treatment of mCSM [24-26, 58, 59]. But recently the anterior approaches were extensively applied for surgical treatment of mCSM, which could directly decompress spinal cord and nerve root due to discs herniation or ossification [3-7, 60]. Everything has doubleedged sword. Complications of anterior approach, such as graft migration, collapse or displacement, hoarseness, dysphagia, C5 palsy, cerebral fluid leakage and infection, are difficult to avoid and worth our attention [61, 62].

Recently, Liu et al. [47] reported the comparisons of 3 reconstructive techniques in the treatment for mCSM. In term of clinical outcomes, radiological parameters, and complications incidence, Liu believed that compared with ACDF and ACCF, hybrid surgery (1-level corpectomy plus 1-level discectomy) was the best alternative . Shamji et al. [63] reviewed studies on the same topic, but concluded that all three operative approaches are effective strategies for the anterior surgical option of multilevel CSM. However, which surgery is the best option in the treatment of multilevel CSM remains unclear. Wen et al. [43] and Han et al. [44] performed a meta-analysis on comparisons of surgical treatments for mCSM between ACDF and ACCF. And they had the same conclusion that both ACDF and ACCF were effective option in treatment for mCSM. Zhang *et al.* [41] reported a meta-analysis on comparisons of surgical treatments for mCSM between HS and ACDF and found that HS provided equivalent outcomes and functional recovery for cervical disc diseases, and significantly better preservation of C2-C7 than ACDF at 2-year follow up. Liu *et al.* [42] concluded that both HS technique and ACCF could receive good results for mCSM. Nevertheless, above mentioned meta-analysis studies have few variables or old included studies and no meta-analysis performed on comparisons of 3 operative techniques for treating mCSM.

In this meta-analysis, we carried on strict eligibility criteria. Although no RCT studies were included in our study, all included studies had high quality according to NOQAS and the baseline variables were similar. Thus, we considered included reports suitable for meta-analysis. We assessed clinical outcomes (length of hospital stay, JOA and NDI), radiographic outcomes (Cobb angles of C2-C7, fusion rate, graft subsidence and graft dislodgment) and surgical outcomes (blood loss, operation time, dysphagia, hoarseness, C5 palsy, infection, cerebral fluid leakage, epidural hematoma and total complications) in the meta-analysis. The pooled results showed that there were significant differences among three methods in blood loss and total complications (all p<0.05). ACDF were

better in the angle of C2-C7 (p<0.00001), C5 plasy (p = 0.02), fusion rate (p = 0.04) and graft subsidence (p = 0.004) at final follow-up than these of ACCF. In term of angle of C2-C7 at final follow-up (p<0.00001), operation time (p = 0.003), fusion rate (p = 0.02) and hospital stay (p<0.00001), HS was better than ACCF.

In our meta-analysis of preoperative and final follow-up JOA and NDI, scores were similar among three groups. However, compared to preoperative JOA and NDI, three groups demonstrated a significant increasedJOA and decreased NDI at final follow-up, indicating three operative techniques could effectively decompress spinal cord by directly removing anterior pathogenic structures and clinical outcomes were similar in long term among three groups. However, in length of hospital stay, HS was less than ACCF. There was significant heterogeneity in the length of hospital stay between HS and ACCF (heterogeneity: $I^2 = 92\%$), which could not be explained by our predefined subgroup analysis. Therefore, the quality of evidence for this outcome was low.

Regarding radiographic outcomes, we found that three groups were similar in preoperative C2-C7, but C2-C7 was significantly increased at final follow-up. However, the increase in ACDF or HS was better than that in ACCF, which was the same with results of Liu [42]. Both ACDF and HS could provide more points of distraction and fixation except for the graft and interbody space shaping than these of ACCF. Besides, both ACDF and HS can also restore alignment by pulling the involved vertebral bodies toward the lordotic ventral plate [22-28, 64-66]. Besides, ACCF grafts may straighten cervical spinal column between remaining vertebral bodies and have fewer force fulcrum leading to imbalanced force distribution [36-42]. Fusion rate in ACDF or HS were higher than these in ACCF and ACDF had more satisfactory results in graft subsidence than ACCF. Obviously, both ACDF and HS were able to offer more fixation points to hold the construct rigidly in place: however, compared to ACDF and HS, ACCF provided less points of fixation causing more graftrelated problems occur. Wen [43] and Han [44] showed that fusion rates between ACDF and ACCF were not significantly different, which was opposite to our result. But our results wer the same with that of Liu [42]. Considering some flaws above mentioned in previous meta-analysis [43, 44], we regarded the fusion rate was better in ACDF and HS.

We selected blood loss, operation time and complication-related outcomes to evaluate surgical outcomes and found that ACDF was less in blood loss and total complications than ACCF or HS and HS was less than ACCF, which were the same with previous studies [42-44]. ACDF was less in C5 plasy than that in ACCF. C5 palsy is considered as an important complication after cervical decompression surgery, Sakaura et al. [67] reported the average incidence is 4.6 % (range from 0 to 30 %), but pathogenesis of C5 palsy remains unclear still now, multilevel corpectomy may lead to significant drift of spinal cord away ventral side. There were similar rates of dysphagia and hoarseness between two groups. Dysphagia and hoarseness are common complications after multilevel anterior cervical surgery [68], which may be caused by trachea and esophagus traction [69]. As for operation time, HS was less than ACCF, but ACDF and ACCF was similar. There was significant heterogeneity in operation time between ACDF and ACCF (heterogeneity: $I^2 = 93\%$), which can not be explained by our predefined subgroup analysis. Therefore, the quality of evidence for this outcome is low.

There are several limitations of this study. First, there is no RCT comparing the outcomes among three techniques, thus we need RCT to further study; Second, the statistical power could be improved in the future by including more studies. Due to the small number of included studies, some parameters could not be analyzed by subgroups to avoid a high heterogeneity which may exert instability on the consistency of the outcomes. Third, follow-up of all included article is up to 1 year, which is not enough to observe the long-term recovery and complications. Fourth, the searching strategy is restricted to articles published in the English and Chinese languages. Articles with potentially high-quality data that are published in other languages is not included because of anticipated difficulties in obtaining accurate medical translations.

In summary, our meta-analysis showed that ACDF or HS are better choices than ACCF in the treatment for multilevel CSM considering radiographic outcomes and surgical outcomes. Except for blood loss and total complications, ACDF and HS have similar satisfactory efficacy for treating multilevel CSM. In the future, more studies with high methodological quality and long-term follow-up periods are needed to evaluate the two procedures for multilevel CSM treatment.

Disclosure of conflict of interest

None.

Abbreviations

ACDF, anterior cervical discectomy and fusion; ACCF, anterior cervical corpectomy and fusion; HS, Hybrid Surgery; CSM, cervical spondylotic myelopathy; mCSM, multilevel cervical spondylotic myelopathy; JOA, Japanese Orthopedic Association scores; NDI, neck disability index score; OR, Odd ratio; SMD, standardized mean difference; CI, confidence intervals.

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