



Comparison between 3-level and 4level anterior cervical discectomy and fusion in the treatment of cervical spondylotic myelopathy: A meta-analysis

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ABSTRACT

Objective: Our objective is to estimate the clinical effectiveness of 3-level and 4-level anterior cervical discectomy and fusion (ACDF) in the management of cervical spondylotic myelopathy (CSM).

Methods: We conducted a thorough search in English databases. We gathered the data on surgical variables and complications to contrast the clinical effectiveness between 3-level and 4-level. We utilized RevMan 5.3 and STATA 12.0 to analyze the data.

Results: Finally, eight studies met inclusion criteria of this study. Our findings indicated that operation time [p for heterogeneity = 0.23, $I^2 = 32\%$, $p < 0.00001$, OR = -24.93, 95%CI (-32.39,-17.49)], blood loss [p for heterogeneity = 0.33, $I^2 = 10\%$, $p < 0.00001$, OR = -60.87, 95%CI (-85.43,-36.32)] and the total number of complications [p for heterogeneity = 0.36, $I^2 = 0\%$, $p = 0.004$, OR = 0.37, 95%CI (0.18,0.72)] in 3-level ACDF were significantly less than in 4-level ACDF. No marked difference was found in hospital stay, revision rate, fusion rate, the number of readmissions, infection, hematoma, or pseudarthrosis between 3-level and 4-level ACDF.

Conclusions: It is easy to understand that performing 4-level needs more operation time and blood loss. No obvious discrepancy was found with regard to the subgroups of complications between the two procedures, yet 4-level procedures had a more number of complications.

1. Introduction

Anterior cervical discectomy and fusion (ACDF) has been extensively applied due to clinical efficacy for treating cervical spondylotic myelopathy (CSM) since it was first reported in 1958 [1–5]. ACDF could not only adequately relieve neurological symptoms but also reconstruct cervical lordosis [6–9]. However, the complications of ACDF, such as pseudarthrosis, C5 palsy, and hematoma, are troublesome for spinal surgeons [10–14]. A growing number of studies have reported comparable clinical improvement and a low rate of complications in single- and two-level ACDF [15,16]. Nevertheless, a few articles studied 3-level or even 4-level ACDF due to the

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relatively lower rate of multilevel cervical spondylotic myelopathy [17–24]. The surgical relevant information of multilevel ACDF remain unclear, therefore, our objective is to contrast these information between 3-level and 4-level.

2. Methods

2.1. Search strategy

We searched for English databases, including PubMed, Embase, and Cochrane Library, up to Jan 2023 by the keywords: “anterior cervical discectomy and fusion”, “cervical spondylotic myelopathy”, “3-level ACDF”, and “4-level ACDF”. We searched all studies.

2.2. Eligibility criteria

Inclusion criteria: (1) ≥ 18 years old; (2) studies focusing on 3-level vs 4-level ACDF. Exclusion criteria: (1) not original articles; (2) repetitive data; (3) patients with tumors, infection, or inflammation; or (5) have previous cervical operation.

2.3. Data extraction and outcome measures

Table 1 showed described characteristic of study. Two author extracted the data. We used the funnel plot for assessing publication bias. When it is asymmetric implying publishing bias, whereas it is symmetric indicating no publishing bias, which needs Egger and Begg tests by the trim and fill method. Sensitivity analysis was not done in this study because of the low heterogeneity of each component.

2.4. Statistical analysis

Odd ratios (OR) and 95 % confidence intervals (CI) were used to assess continuous variables. P -value < 0.05 was the significance threshold. Heterogeneity of outcomes was evaluated by Chi squared test with (p value < 0.10) and the I^2 ($> 50\%$) determines using random-effects or fixed-effects models. We utilized Review Manager (version 5.3, The Cochrane Collaboration, Oxford, UK) and STATA 12.0 (Stata Corporation, College Station, TX, USA) to analyze the data.

3. Results

3.1. Study identification and selection

Forty-five English articles were found. Twenty-four one were deleted because of repetition, and ten articles were removed due to titles and abstracts. Three papers were eliminated after the remaining 11 articles were retrieved for inclusion criteria (Fig. 1). Finally, the current meta-analysis consisting of eight publications satisfied the inclusion criteria.

3.2. Baseline characteristics and quality assessment

Table 1 showed the characteristics of included studies that were published before Jan 2023. Because all the retrospective studies, Newcastle Ottawa Quality Assessment Scale with a maximum of nine points was utilized to assess them. Five studies gained eight points and others received seven, implying good quality. (Table 2).

3.3. Operation time

Three articles [17–19] assessed operation time in 3-level and 4-level ACDF. There was low heterogeneity in operation time ($p = 0.23$, $I^2 = 32\%$, Fig. 2). Operation time was significantly shorter in 3-level than in 4-level [$p < 0.00001$, OR = -24.93 , 95 % CI

Table 1
Characteristics of included studies.

First author	Year	Country	No. of participants		Study type
			3-level	4-level	
Kim [17]	2019	USA	54	51	retrospective
McClure [18]	2020	USA	47	19	retrospective
Mesfin [19]	2020	USA	44	20	retrospective
Canseco [20]	2021	USA	97	22	retrospective
De la Garza-Ramos [21]	2016	USA	71	26	retrospective
Mullins [22]	2018	Germany	246	36	retrospective
Lee [23]	2019	China	12	4	retrospective
Wewel [24]	2018	USA	56	16	retrospective

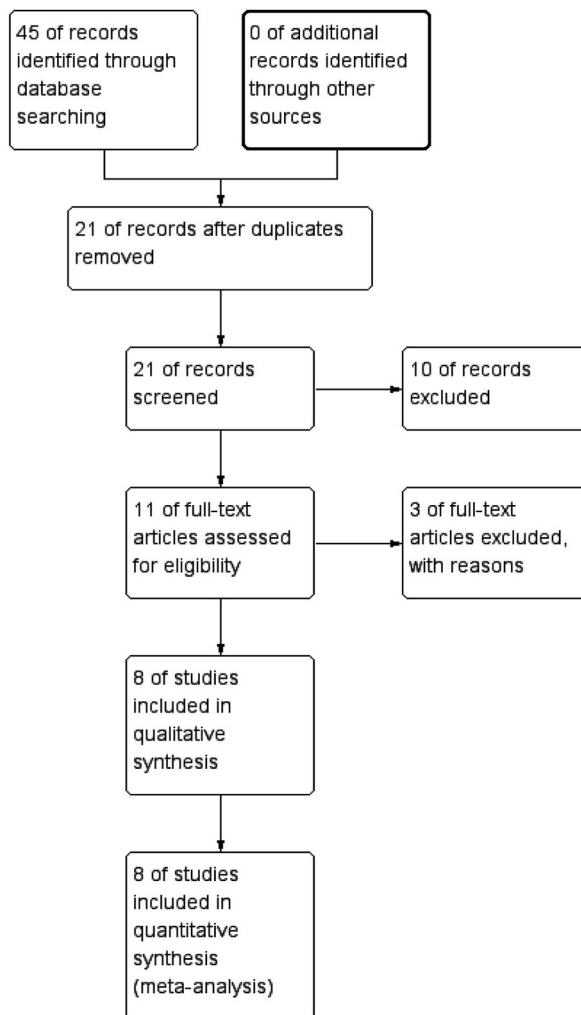


Fig. 1. Flow diagram of study selection.

Table 2

The quality assessment according to the Newcastle Ottawa Quality Assessment Scale (NOQAS) of each study.

Study	Selection	Comparability	Exposure	Total score
Kim [17]	2	3	3	8
McClure [18]	2	3	3	8
Mesfin [19]	2	3	2	7
Canseco [20]	2	3	2	7
De la Garza-Ramos [21]	3	2	3	8
Mullins [22]	3	2	3	8
Lee [23]	3	3	2	8
Wewel [24]	3	2	2	7

(−32.38, −17.49), Fig. 2].

3.4. Blood loss

Three articles [18,20,21] assessed blood loss in two groups. There was low heterogeneity in blood loss ($p = 0.33, I^2 = 10\%$, Fig. 3). Blood loss was significantly less in 3-level than in 4-level ($p < 0.00001, OR = -60.87, 95\%CI (-85.43,-36.32)$, Fig. 3).

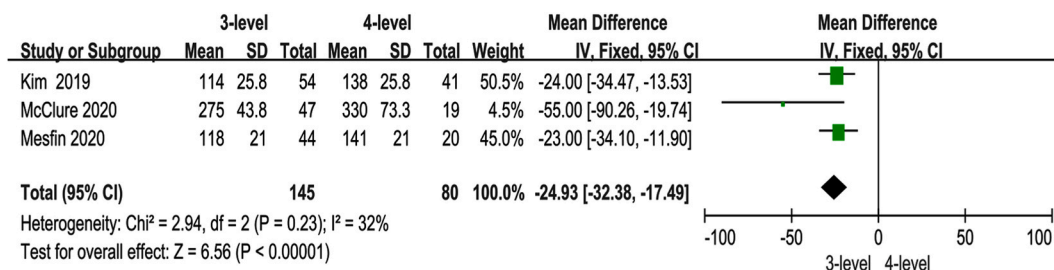


Fig. 2. Forest plot showing operation time in 2 groups. CI = confidence interval, df = degrees of freedom.

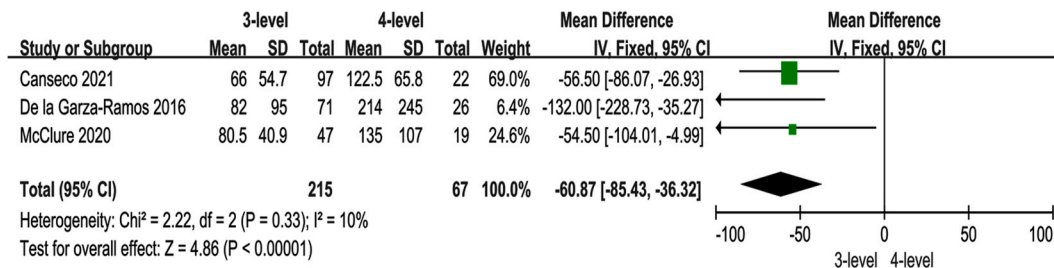


Fig. 3. Forest plot showing blood loss in 2 groups. CI = confidence interval, df = degrees of freedom.

3.5. Hospital stay

Five studies [17–21] reported hospital stays in two groups. There was low heterogeneity in hospital stays ($p = 0.20$, $I^2 = 33\%$, Fig. 4). We found no significant difference in hospital stay ($p = 0.25$, $\text{OR} = -0.17$, $95\% \text{CI} (-0.46, 0.12)$, Fig. 4).

3.6. Total complications

Two studies [21,22] reported the total complications in two groups. There was low heterogeneity in the total complications ($p = 0.36$, $I^2 = 0\%$, Fig. 5). The total complications were significantly less in 3-level than in 4-level ($p = 0.004$, $\text{OR} = -0.37$, $95\% \text{CI} (0.18, 0.72)$, Fig. 5).

3.7. Infection

Three studies [17,19,21] reported infections in two groups. There was low heterogeneity ($p = 0.92$, $I^2 = 0\%$, Fig. 6). No significant difference was found regarding infections ($p = 0.36$, $\text{OR} = 0.40$, $95\% \text{CI} [0.05, 2.92]$, Fig. 6).

3.8. Fusion rate

Two studies [20,23] have reported the fusion rate in two groups. Low heterogeneity was found regarding fusion rate ($p = 0.95$, $I^2 = 0\%$, Fig. 7). No significant difference was found regarding fusion rate ($p = 0.89$, $\text{OR} = 0.94$, $95\% \text{CI} [0.37, 2.36]$, Fig. 7).

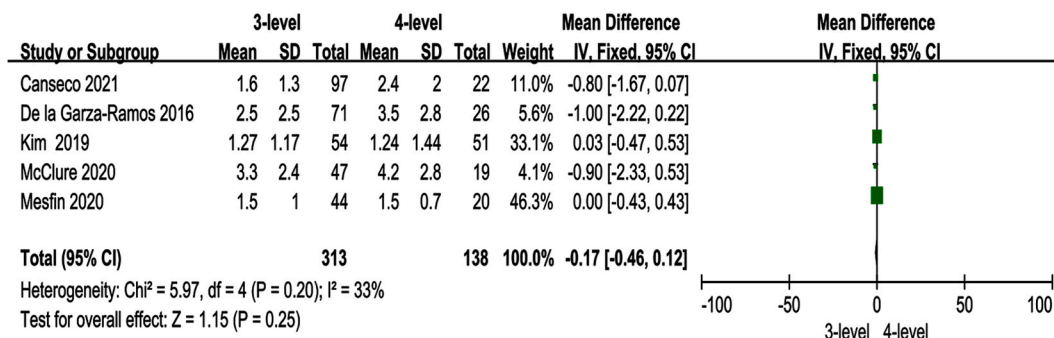


Fig. 4. Forest plot showing hospital stay in 2 groups. CI = confidence interval, df = degrees of freedom.

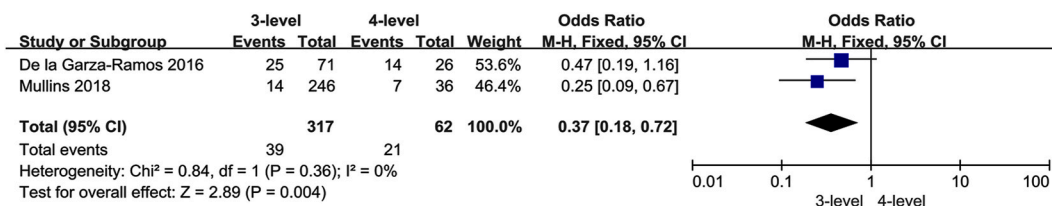


Fig. 5. Forest plot showing the total number of complications and subgroups of complications in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

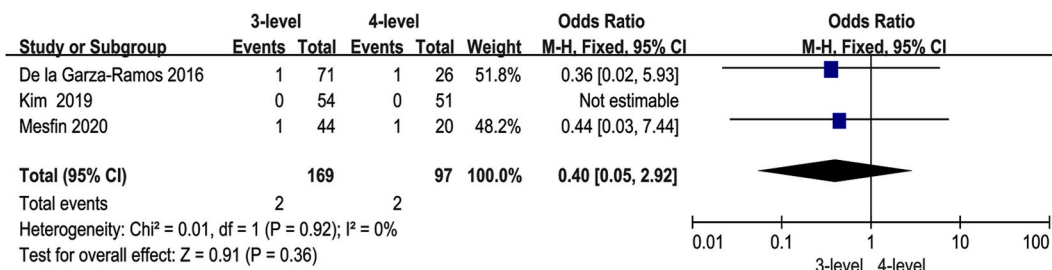


Fig. 6. Forest plot showing infection in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

3.9. Hematoma

Two studies [17,22] have reported hematoma in two groups. There was low heterogeneity ($p = 0.46, I^2 = 0\%$, Fig. 8) and we found no obvious discrepancy regarding hematoma ($p = 0.28, OR = 0.43, 95\% CI [0.09, 1.98]$, Fig. 8).

3.10. Pseudarthrosis

Two studies [21,24] reported pseudarthrosis in two groups. There was low heterogeneity ($p = 0.54, I^2 = 0\%$, Fig. 9) and we found no obvious discrepancy regarding pseudarthrosis ($p = 0.11, OR = 0.48, 95\% CI [0.20, 1.17]$, Fig. 9).

3.11. Revision surgery

Five studies [17,18,20,21,24] reported revision surgery in two groups. There was low heterogeneity ($p = 0.39, I^2 = 0\%$, Fig. 10) and we found no obvious discrepancy regarding revision surgery ($p = 0.94, OR = 1.03, 95\% CI [0.50, 2.10]$, Fig. 10).

3.12. Readmission

Two studies [19,20] reported the readmission in two groups. There was low heterogeneity ($p = 0.75, I^2 = 0\%$, Fig. 11). We found no obvious discrepancy regarding readmission ($p = 0.13, OR = 0.32, 95\% CI [0.07, 1.39]$, Fig. 11).

3.13. Publication bias

All included studies did not have publication bias (all $P > 0.05$) after detection by STATA 12.0.

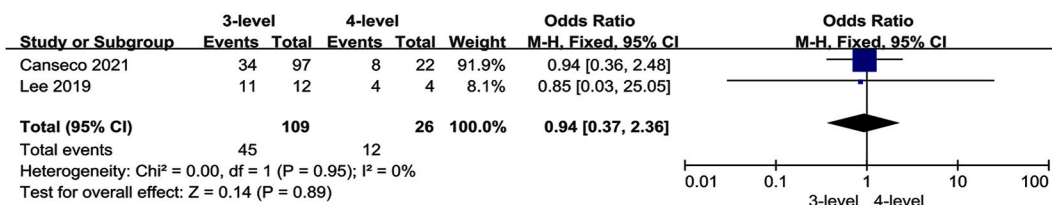


Fig. 7. Forest plot showing fusion rate in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

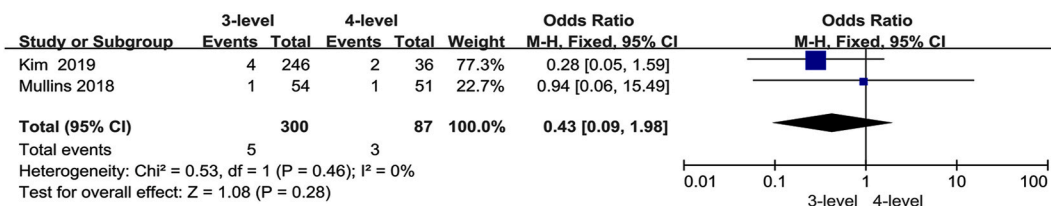


Fig. 8. Forest plot showing hematoma in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel–Haenszel.

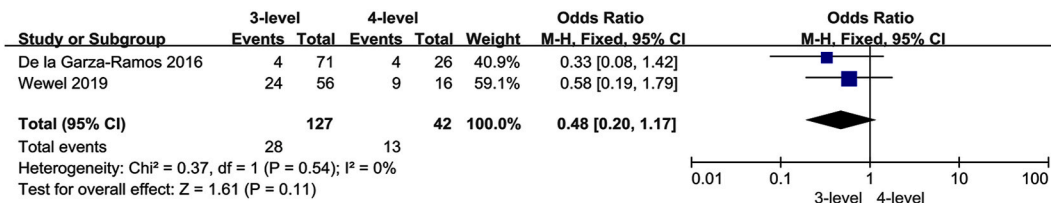


Fig. 9. Forest plot showing pseudoarthrosis in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel–Haenszel.

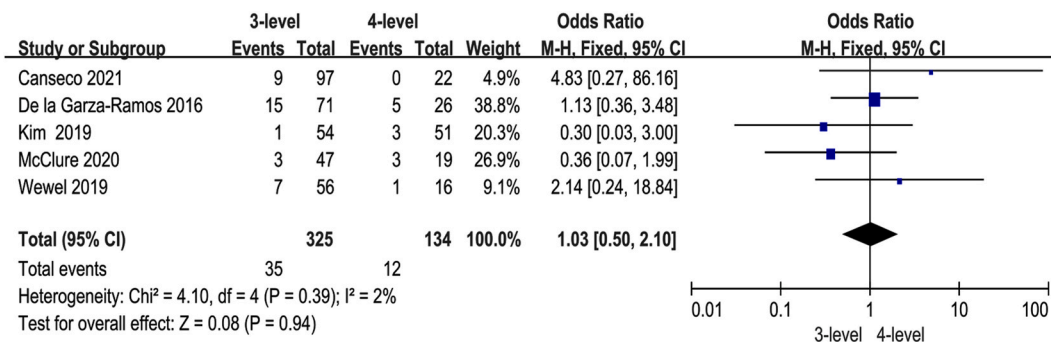


Fig. 10. Forest plot showing revision surgery in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel–Haenszel.

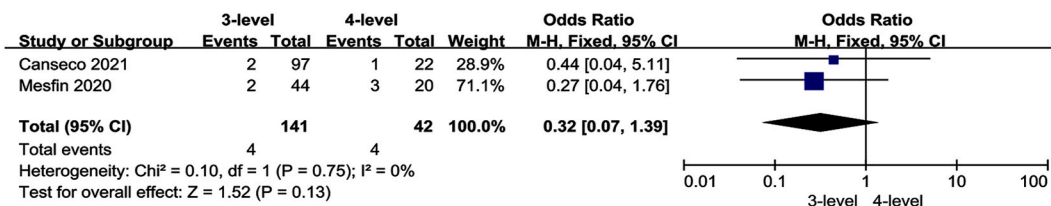


Fig. 11. Forest plot showing readmission in 2 groups. CI = confidence interval, df = degrees of freedom, M-H = Mantel–Haenszel.

4. Discussion

Recently, ACDF was a commonly operative procedure in the management of CSM. Although it can effectively relieve nerve compression [41], it also cause some intractable complications, such as hoarseness and dysphagia. While ACDF procedures have been well proven to improve symptoms in less than 3-level CSM [25], there remains controversy over the clinical efficacy and complications of 3-level or 4-level ACDF due to limited research. McClure [18] found that both two techniques were good options for CSM in terms of fusion rate. Canseco [20] demonstrated similar results in clinical outcomes between 3-level and 4-level, while De la Garza-Ramos [21] suggested a 4-level ACDF with a markedly increase in perioperative morbidity and worsened outcomes in comparison with a 3-level ACDF. Therefore, our objective was to assess the surgical relevant information between the two procedure. To our knowledge, this meta-analysis is the first regarding this comparison. Our results indicated that operation time, blood loss, and overall complications in 3-level were dramatically less than in 4-level. No obvious difference was found in hospital stay, revision rate, fusion rate, the number of readmissions, infection, hematoma, or pseudarthrosis in two groups.

The length of the operation and the amount of blood loss were also crucial criteria in determining surgical trauma. As predicted, operative duration and blood loss in 4-level were substantially higher than in 3-level due to longer surgical time and dissection,

implying that surgical trauma was greater in the 4-level group. Theoretically, we extrapolated that surgical trauma might be a significant component in explaining why the 4-level had more complications than the 3-level. Prior articles [17–21] suggested the hospital stay in 4-level was slightly longer than in 3-level, but no obvious difference was found, which was the same as our results. It implied that 4-level was similar to 3-level in rapidly reaching the standard of discharge.

Concerns about the fusion rate drew many authors to any spinal fusion procedure. According to previous studies [26–29], the fusion rate of ACDF varied by 40%-nearly 100 %, which was mainly affected by two main factors: fusion criteria and follow-up time. Follow-up time is a crucial factor that can explain the diversity of fusion rates as reported by prior research. A recent study demonstrated that fusion rate was closely related to follow-up time [30]. Canseco [20] reported the overall fusion rate of 3-level and 4-level were 79.1 % and 53.3 %, respectively, while Lee [23] found a similar fusion rate between 3- and 4-level ACDF. In our meta-analysis, we also discovered similar results in fusion rates in two groups. Although there was a difference in the method of evaluating the fusion in our included studies [20,23], our results showed low heterogeneity ($I^2 = 0\%$), implying the high quality of our included studies. Pseudarthrosis, ranging from 0 % to 50 %, was another important complication after multilevel ACDF. Wewel [24] indicated the incidence of pseudarthrosis was higher in 4-level (56 %) compared with 3-level (42 %), while there was no obvious difference in the study of De la Garza-Ramos [21], which was consistent with our findings. Additionally, we also assessed the rate of revision surgery, which was usually caused by pseudarthrosis and non-fusion, and discovered no difference between the two groups. Furthermore, Mesfin [19] reported that the readmission rate after 4-level was more than three times that of 3-level. Canseco [20] obtained similar results in terms of readmission rate, which was consistent with our findings.

In terms of the total number of complications, De la Garza-Ramos [21] found a statistical difference regarding complications in two groups (14.1 % in 3-level vs 38.5 % in 4-level). Whereas, the rate of overall complications in the study of Kim [17] was 42.6 % and 39.2 % in 3- and 4-level ACDF, respectively, suggesting that one more level of ACDF did not cause a marked discrepancy. Mullins [22] obtained similar results, which were in line with Kim [17]. In the current study, complications in 4-level ACDF were found to be significantly higher in comparison with 3-level ACDF. It is well understood that more surgical time and blood loss may be associated with worsening outcomes. Notably, no obvious discrepancy was found in the subgroups of complications, yet the total complications in 4-level were statistically higher than in 3-level. It may be related to the partial complications included in our study because of a few studies focusing on this topic.

There are some limitations. First, no RCT article was found regarding this topic. It was needed in the further study. Second, because of a few included studies, some complications, such as dysphagia and C5 palsy, could not be analyzed. Additionally, a few included studies limit subgroups analyses can't be performed. Third, we only search for English articles.

In conclusion, operative duration and blood loss in 3-level ACDF were fewer than in 4-level ACDF. We found similar results in the subgroup of complications, yet the total complications in the 4-level was more than in the 3-level. More studies were needed in future research.

Ethics approval and consent to participate

Before data collection, this study obtained permission to proceed by our hospital's Institutional Review Board. As a meta-analysis study, informed consent procedures are not necessary.

Consent for publication

No applicable.

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Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

CRedit authorship contribution statement

Tao Wang: Writing – original draft. **Yubin Long:** Methodology. **Junfei Guo:** Validation, Supervision. **Zhiyong Hou:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

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No Applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e21595>.

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