Efficacy and safety of anterior controllable antidisplacement and fusion surgical therapy for cervical ossification of the posterior longitudinal ligament: a systematic review and meta-analysis

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Background: There are many treatment options for ossification of the posterior longitudinal ligament (OPLL), such as laminectomy, open-door laminoplasty, anterior cervical corpectomy with fusion and anterior controllable antidisplacement and fusion (ACAF). But the treatment of ACAF for OPLL remains controversial. This study aimed to evaluate the efficacy and safety of ACAF for cervical OPLL.

Methods: The databases were searched of PubMed, Embase and the Cochrane, Chinese National Knowledge Infrastructure, Chongqing VIP Database and Wanfang Database through December 2021 for randomized controlled trials (RCTs) and retrospective studies. Mantel-Haenszel χ^2 test and the I^2 statistic were used in this meta-analysis. Newcastle-Ottawa Scale (NOS) and Cochrane risk of bias tool were used for quality assessment.

Results: Ten studies involving 709 patients were included in this meta-analysis with moderate to high quality. The results demonstrated that ACAF was more beneficial on cervical OPLL compared with other surgeries. The pooled results of this meta-analysis showed: Japanese Orthopedic Association (JOA) score [mean difference (MD) =0.88, 95% CI: 0.53–1.24, P<0.00001], JOA recovery rate (MD =9.79%, 95% CI: 6.26–13.32, P<0.00001), Visual Analogue Scale (VAS) score (MD =−0.85, 95% CI: −1.16 to −0.55, P<0.00001), Cobb angle (MD =8.68°, 95% CI: 6.95°–10.41°, P<0.00001), operation time (MD =50.96 min, 95% CI: 5.39–96.53, P=0.03), blood loss (MD =−69.40 mL, 95% CI: −175.14 to 36.34, P=0.20) and Neck Disability Index (NDI) score (MD =−1.89, 95% CI: −3.92 to 0.14, P=0.07). Adverse events associated with ACAF can be significantly reduced [odds ratio (OR) =0.43, 95% CI: 0.28–0.66, P=0.0001].

Discussion: ACAF is effective and safe in the treatment of cervical OPLL compared with other surgeries. What's more, ACAF has fewer complications than other surgeries. However, because of the small sample of included studies, further studies are needed to verify if ACAF is better than other surgical treatments.

Keywords: Meta-analysis; anterior controllable antidisplacement and fusion (ACAF); ossification of the posterior longitudinal ligament (OPLL); effect

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Introduction

Ossification of the posterior longitudinal ligament (OPLL) refers to chronic ossification of the spinal ligament, which is characterized by chronic compression and damage to the spinal cord (1,2). In Japan, the incidence of OPLL among patients with spinal disorders is 1.9% to 4.3% (3,4). Insufficient sleep, excessive sleep, obesity and diabetes are major causes of OPLL, leading to narrowing of the spinal canal and spinal cord compression (5,6). Then, OPLL leads to spinal canal stenosis, spinal cord injury and certain motion disorders of hands and feet, which seriously affect the quality of life of the patients (7).

Anterior decompression and posterior decompression are the conventional treatments for cervical OPLL. However, those technologies remain controversial and should be treated with caution because of their shortcomings (8,9). The conventional anterior approach allows direct decompression by removing the ossified ligament and reconstruction of the stability by a solid spinal fusion (10,11). But it has many surgical complications such as graft failure hoarseness, cerebrospinal fluid (CSF) leakage and C5 nerve root paralysis, etc. (12). The conventional anterior approach is also affected by the degree of spinal canal stenosis (13). On the other hand, the posterior approach (laminoplasty and laminectomy) is popular in clinical practice. However, the incidence of progressive ossification and kyphotic deformity increases in the long-term follow-up (14,15). Besides, its clinical effect on patients with straight or kyphotic cervical curvature is not satisfactory (16).

Anterior controllable antidisplacement and fusion (ACAF), a novel anterior approach surgery, was firstly reported by Sun *et al.* for the treatment of OPLL with myelopathy (17), which can achieve anterior direct decompression without cutting the posterior longitudinal ligament, especially for OPLL with dural ossification. It can isolate and actively transport the cervical OPLL ventrally to restore the space of the spinal canal and thus achieve direct decompression of the neural elements with their location unchanged (18). Some studies reported ACAF had longer operation time than laminoplasty, and the Neck Disability Index (NDI) score and Cobb angle were no significant differences (19). However, Sun *et al.* reported in Cobb angle and Japanese Orthopedic Association (JOA) score ACAF was better than laminoplasty (20).

Although numerous studies have evaluated the effect of ACAF and those studies found that excellent postoperative outcomes can be achieved with the use of ACAF, the treatment of ACAF for OPLL remains controversial (6). Hence, we performed a systematic review and meta-analysis to assess the existing evidence for the effectiveness of ACAF in the treatment of cervical OPLL compared with other normal surgeries. We present the following article in accordance with the PRISMA reporting checklist (available at https://jxym.amegroups.com/article/view/10.21037/jxym-21-44/rc) (21).

Methods

Literature retrieval strategy

The following electronic databases such as PubMed, Embase and the Cochrane, Chinese National Knowledge Infrastructure, Chongqing VIP Database and Wanfang Database were searched up to December 2021. All randomized controlled trials (RCTs) and retrospective studies comparing ACAF for the treatment of cervical OPLL were collected. The retrieval method adopts the combination of subject words and free words, and English retrieval words and Chinese versions include: ((Anterior controllable antidisplacement [Title/Abstract] AND fusion[Title/Abstract]) OR (ACAF[Title/Abstract])) AND (((((Posterior Longitudinal Ligament Ossification[Title/Abstract]) OR (Posterior Longitudinal Ligament Calcification[Title/Abstract])) OR (Calcification of Posterior Longitudinal Ligament[Title/Abstract])) OR (OPLL[Title/Abstract])) OR ("Ossification of Posterior Longitudinal Ligament"[Mesh])); in addition, the references of the included literature were reviewed to extract the relevant studies.

Inclusion and exclusion criteria

We describe the inclusion of studies by using Population, Intervention, Comparison, Outcomes and Study (PICOS) criteria (22).

Inclusion criteria

Studies were eligible for inclusion if they met the following criteria: (I) P: Patients were diagnosed with cervical myelopathy due to OPLL and prepared for surgery; (II) I: ACAF was used for patients with OPLL; (III) C: Others' surgical treatment for OPLL; (IV) O: Outcomes including JOA score, JOA recovery rate, Visual Analogue Scale (VAS) score, NDI score, blood loss, operation time and complications; (V) S: RCTs and retrospective studies.

Exclusion criteria

Studies were ineligible if they met the following criteria: (I) studies aren't published in Chinese or English; (II) studies cannot extract data; (III) poor quality and repeated reports; (IV) other interventions or drugs were used; (V) animal studies, biomechanical studies, duplicate publications of one trial, case report, letter, revision, technology note, commentaries, reviews, withdrawn trails and meta-analysis.

Data extraction

Two researchers (J Hu and J Yan) independently read the full text of potential literature that met the inclusion and exclusion criteria. The data were extracted as follows: basic information on the sample included in the study (year of publication, total number of participants, authors, age, gender, interventions and outcomes, etc.); study design type (cross-sectional, prospective, and retrospective study), study duration, and study observation indicators, etc. When information was missing, we attempted to contact the primary author via email to seek clarification or exclude the study.

Risk of bias assessment and grading quality of evidence assessment

The risk of bias in the included studies was evaluated using the Cochrane risk of bias tool for RCTs. Newcastle-Ottawa Scale (NOS) for retrospective studies, the studies scored ≥7 were considered to be high quality articles. Bias assessments were carried by 2 researchers (T Li AND F Wang) independently. Any unresolved disagreements between reviewers were resolved through discussion or by evaluation by a third reviewer (X Liu).

Statistical analysis

The Revman 5.4 software package was used for this meta-analysis. The dichotomous outcomes were reported by OR with 95% CI and we report continuous outcomes for MD with 95% CI. Heterogeneity test was performed on the included study results by chi-square test. If $P \geq 0.1$ and $I^2 \leq 50\%$, it indicated that there was no homogeneity among the research results, and a fixed effect model was used. If $P<0.1$ or $I^2>50\%$, then, heterogeneity existed among studies, and a random effect model was used. We also performed a sensitivity analysis to identify the resource of the heterogeneity, by eliminating the included literature one by one. Publication bias was assessed by the funnel plot.

Results

Search result

The initial search yielded 217 records, from which we excluded 91 due to duplication. After examination of the titles and abstracts, 13 potentially eligible studies were assessed for inclusion criteria. After application of the inclusion criteria, 7 trials (19,20,23-27) published in English, 2 trails (28,29) published in Chinese and 1 thesis (30) published in Chinese were included in this meta-analysis. *Figure 1* displays the selection algorithm, the numbers of included and excluded studies. All titles, abstracts, and text were dually and independently reviewed by the authors based on the inclusion and exclusion criteria to minimize bias.

Study characteristic

Of those included studies, 1 was RCT (19) and 9 were retrospective studies (20,23-30) included 709 patients in this meta-analysis. Among those included studies, 7 trails (19,20,23,27-30) used laminoplasty as a control, while 2 trails (24,25) utilize ACCF and one used skip corpectomy and fusion (SCF) (26). The follow-up time in the studies ranged from 9.68 to 28.5 months. The main basic characteristics of the included literature are shown in *Table 1*.

The bias risk assessment results of the included studies

Retrospective studies conducted NOS to evaluate the risk of bias. The included retrospective studies met most of the quality assessment criteria, and all these studies were scaled as a total score >6. The detail of information can be seen in *Table 2*. RCT is evaluated by the Cochrane risk of bias tool. The quality assessment of included studies was shown in *Figure 2* for details.

Meta-analysis results

JOA score

A total of 10 studies (19,20,23-30) reported the JOA scores. There exists significant heterogeneity of studies ($P<0.0001$, $I^2=74\%$). Random effects model was performed. Pooled results showed that patients treated with ACAF were superior to those who were treated with other treatments

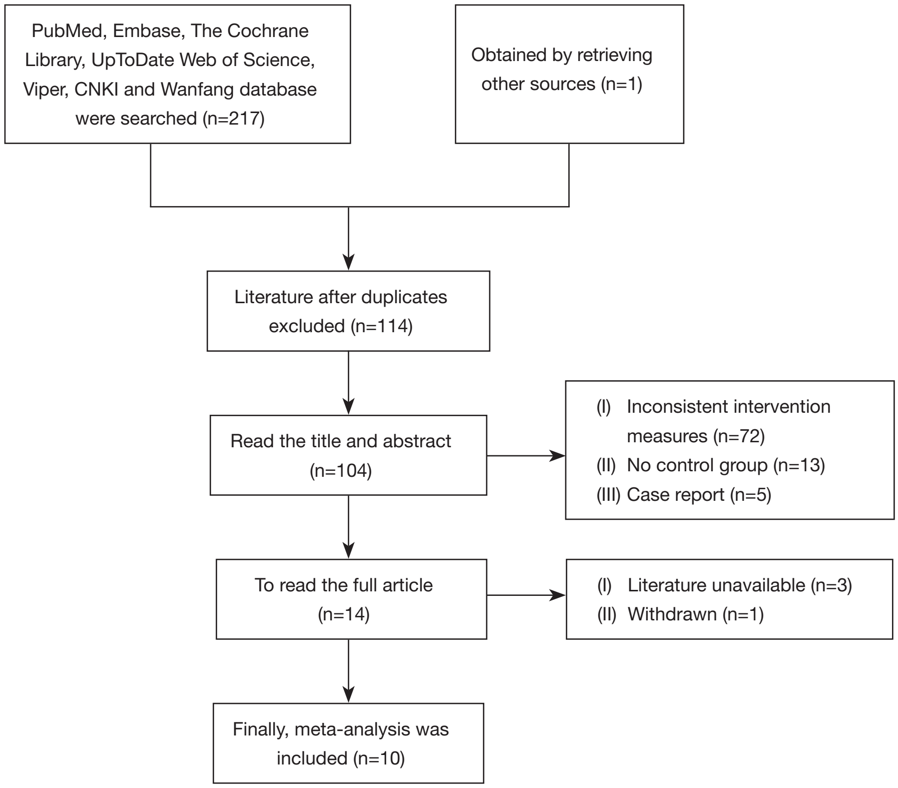

Figure 1 Flow diagram.

Table 1 Characteristics of studies included in the meta-analysis

First author	Year	Study type	Age (I/C)	Number of persons (I/C)	Intervention group	Controlled group	Follow-up time (I/C)
Sun	2020	Retrospective	58.18/58.06	38/33	ACAF	Laminectomy	12/12
Yang	2019	Retrospective	58.0/58.7	28/31	ACAF	ACCF	N/N
Chen	2020	Prospective	54.6/57.2	39/38	ACAF	Laminoplasty	18.6/18.6
Sun	2019	Retrospective	57.2/58.1	42/38	ACAF	Laminoplasty	18.2/17.7
Yang	2018	Retrospective	58.6/58.4	34/36	ACAF	ACCF	10.1/12.4
Zhang	2019	Retrospective	53.3/49.8	32/30	ACAF	SCF	19.8/18.6
Wang	2019	Retrospective	60.22/58.74	32/31	ACAF	Open-door laminoplasty	16.59/17.35
Luo	2020	Retrospective	59.7/57.8	42/36	ACAF	Open-door laminoplasty	21.7
Wang	2019	Retrospective	NA	45/49	ACAF	Laminectomy	9.68
Kong	2021	Retrospective	60.7/57.6	21/32	ACAF	Laminoplasty	26.7/28.5

I/C, Intervention/Control; ACAF, anterior controllable antedisplacement and fusion; ACCF, anterior cervical corpectomy with fusion; SCF, skip corpectomy and fusion; NA, not available.

Table 2 Results of quality assessment using Newcastle-Ottawa scale for retrospective studies

Study selection	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Quality score
Yang, 2018	1	1	1	1	1	1	1	1	8
Sun, 2020	1	1	1	1	1	1	1	1	8
Yang, 2019	1	1	1	1	1	1	1	0	7
Sun, 2019	1	1	1	1	1	1	1	1	8
Zhang, 2019	1	1	1	1	1	1	1	1	8
Wang, 2019	1	1	0	1	1	1	1	1	7
Luo, 2020	1	1	1	1	1	1	1	1	7
Wang, 2019	1	1	1	1	1	1	1	1	8
Kong, 2021	1	1	1	1	1	1	1	1	8

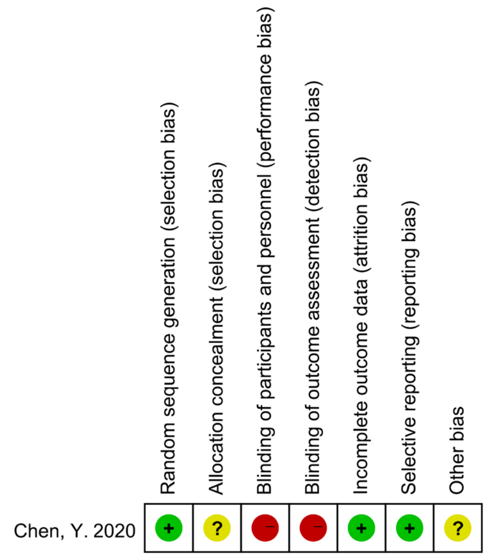

Figure 2 Results of quality assessment using Cochrane risk of bias tool for RCTs. RCT, randomized controlled trial.

(MD =0.88; 95% CI: 0.53–1.24; P<0.00001, *Figure 3*). What's more, we also found patients treated with ACAF were not superior to other treatments (MD =0.60; 95% CI: −0.05 to 1.25; P=0.07, *Figure 3*), when we only included prospective studies.

Operation time

A total of 7 studies (19,24-27,29,30) reported the operation time. There exists significant heterogeneity in pooled results (P<0.00001, I^2=98%). Random effects model was performed. Pooled results showed that there's a statistical association between patients treated with ACAF and those who were treated with other treatments (MD =50.96 min, 95% CI: 5.39–96.53 min, P=0.03, *Figure 4*). What's more, we also found both prospective and retrospective studies of ACAF had a longer operation time than other treatments (*Figure 4*).

Bleeding loss

A total of 7 studies (19,24-27,29,30) reported bleeding loss. There exists significant heterogeneity (P<0.00001, I^2=99%). Random effects model was performed. The pooled results showed no statistical significance between patients treated with ACAF and those who were treated with other treatments (MD =−69.40 mL, 95% CI: −175.14 to 36.34 mL, P=0.20; *Figure 5*). What's more, we also found patients treated with ACAF had less bleeding loss to other treatments (MD =−45.90 mL; 95% CI: −58.43 to

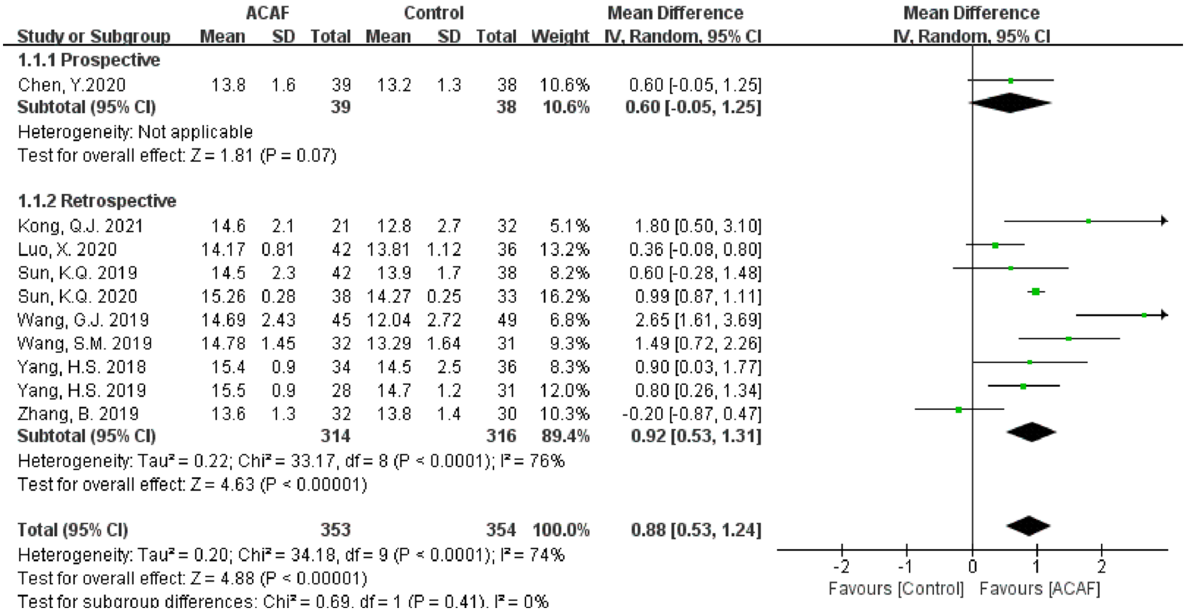

Figure 3 Forest plot showing JOA score under the random-effects model. JOA, Japanese Orthopedic Association; ACAF, anterior controllable antedisplacement and fusion.

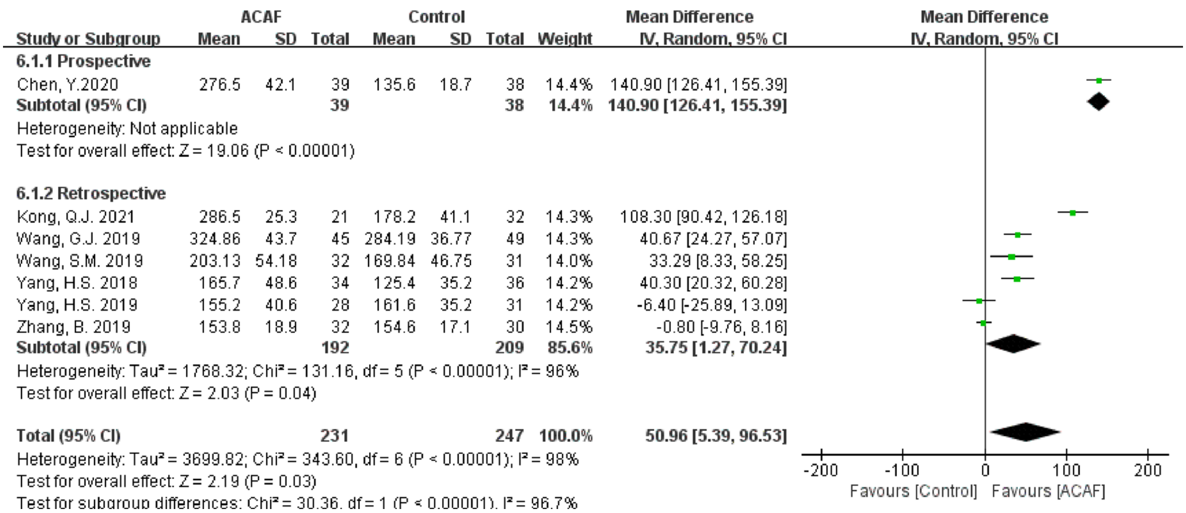

Figure 4 Forest plot showing operation time under the random-effects model. ACAF, anterior controllable antedisplacement and fusion.

−33.37 mL; P<0.00001, *Figure 5*), when we only included prospective studies.

JOA recovery rate

A total of 9 studies (19,20,23-28,30) reported the JOA recovery rate. There exists significant heterogeneity (P=0.0004, I^2=72%). Random effects model was performed. Pooled results showed that patients treated with ACAF were superior to those who were treated with other treatments (MD =9.79, 95% CI: 6.26–13.32, P<0.00001; *Figure 6*), and we performed a sensitivity analysis to explore the potential source of heterogeneity. By eliminating the included literature one by one, we found Zhang *et al.* (26) had high heterogeneity, and the heterogeneity was reduced from 74% to 49%. What's more, we also found both prospective and retrospective studies of ACAF had a higher JOA recovery

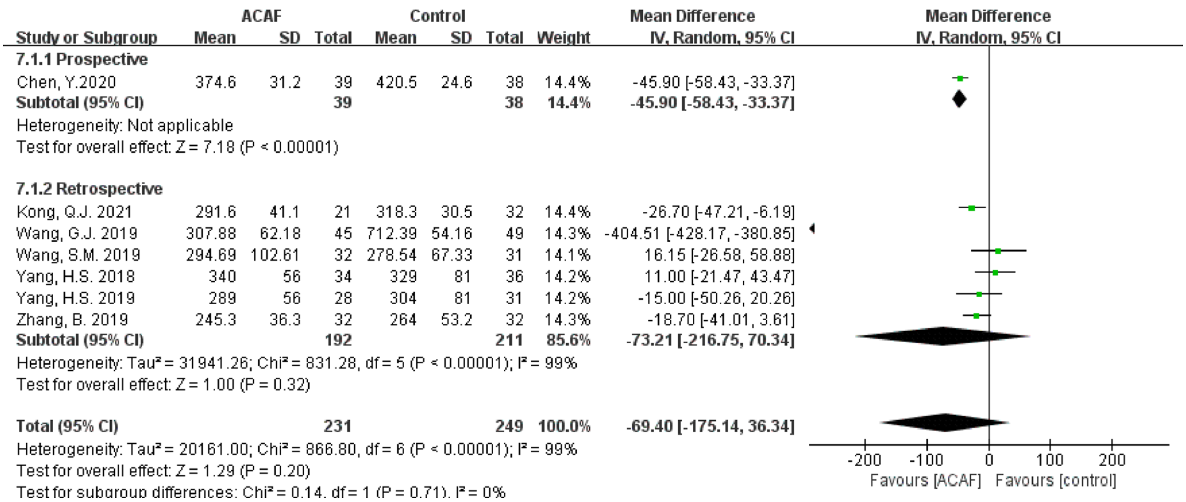

Figure 5 Forest plot showing bleeding loss under the random-effects model. ACAF, anterior controllable antedisplacement and fusion.

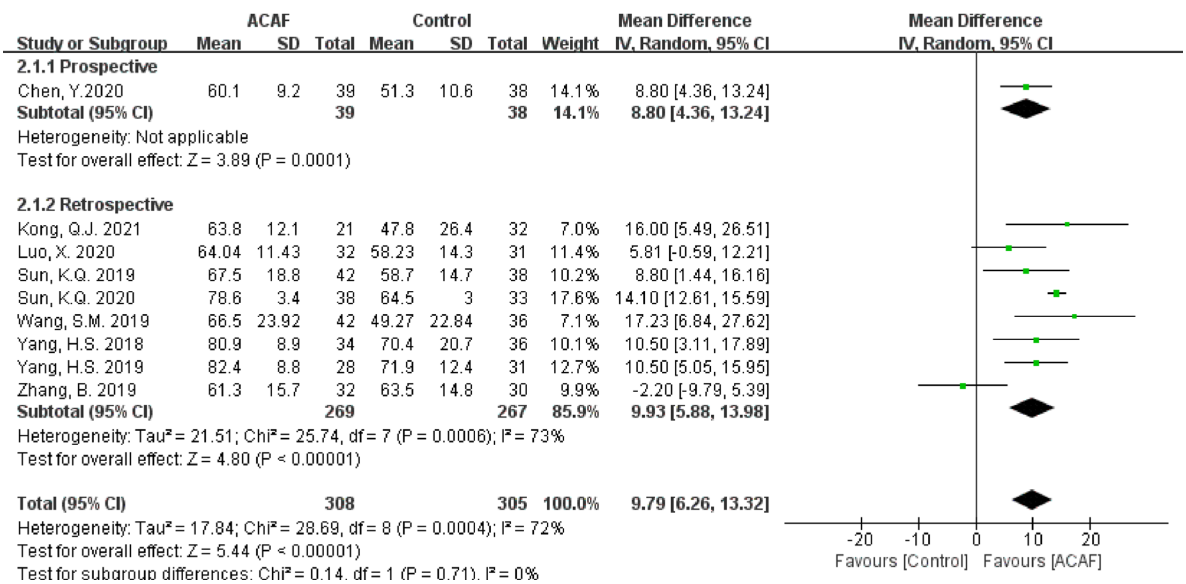

Figure 6 Forest plot showing JOA recover rate under the random-effects model. JOA, Japanese Orthopedic Association; ACAF, anterior controllable antedisplacement and fusion.

rate than other treatments (*Figure 6*).

VAS

A total of 3 studies (19,29,30) reported the VAS score. No significant heterogeneity was found (P=0.22, I^2=34%). A fixed-effects model was performed. Pooled results showed that patients treated with ACAF were superior to those who were treated with other treatments (MD =−0.85, 95% CI: −1.16 to −0.55, P<0.00001; *Figure 7*).

Cobb angle

A total of 6 studies (19,20,26-29) reported Cobb angle. There exists significant heterogeneity (P<0.00001, I^2=95%). Random effects model was performed. Pooled results showed that patients treated with ACAF were superior to those who were treated with other treatments (MD =8.68°, 95% CI: 6.95°–10.41°, P<0.00001; *Figure 8*). What's more, we also found both prospective and retrospective studies of ACAF had higher Cobb angle than other treatments (*Figure 8*).

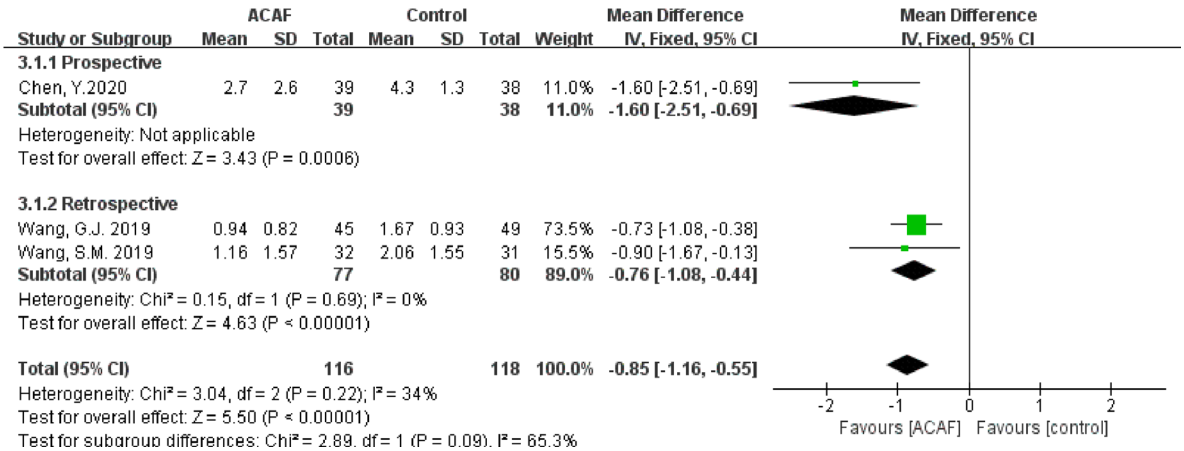

Figure 7 Forest plot showing VAS score under the fixed-effects model. VAS, Visual Analogue Scale; ACAF, anterior controllable antedisplacement and fusion.

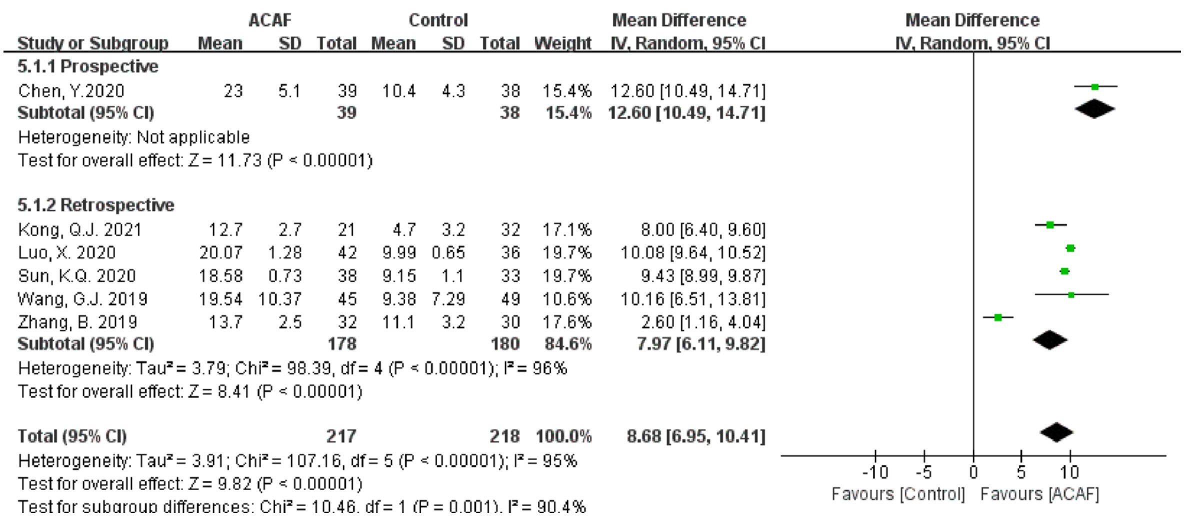

Figure 8 Forest plot showing Cobb angle under the random-effects model. ACAF, anterior controllable antedisplacement and fusion.

NID score

A total of 2 studies (19,26) reported the NID score. There exists significant heterogeneity (P=0.03, I^2=95%). Pooled results showed no statistical significance between the two groups (MD =–1.89, 95% CI: –3.92 to 0.14, P=0.07; *Figure 9*).

Publication bias

The Egger test's (*Figure 10*) results of the evaluation indicate the study exist a possibility of publication bias (P=0.004).

Safety

Ten studies (19,20,23-30) reported the incidence of all adverse events in included studies. The results demonstrated that there was a statistical difference between the two groups (OR =0.43; 95% CI: 0.28 to 0.66; P=0.0001, *Figure 11*). No significant heterogeneity (I^2=15%, P=0.31, *Figure 11*) was found, suggesting that patients who underwent ACAF was safer than those who underwent other treatments. *Table 3* showed the pooled results of adverse events from included studies.

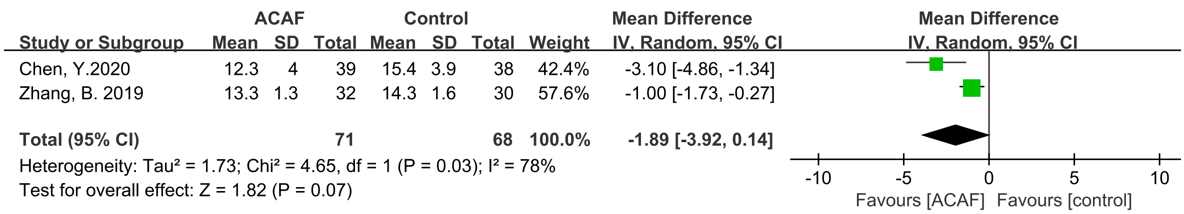

Figure 9 Forest plot showing NDI score under the random-effects model. NDI, Neck Disability Index; ACAF, anterior controllable antedisplacement and fusion.

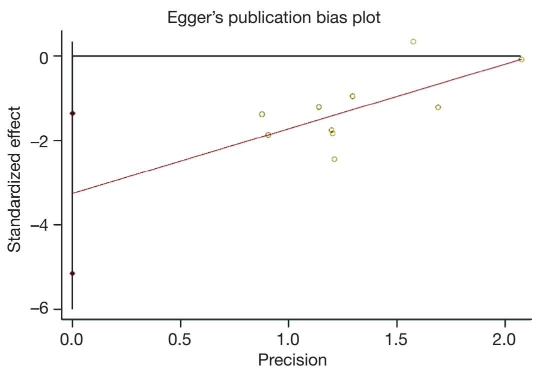

Figure 10 Egger test showing the publication bias.

Discussion

According to the present meta-analysis, ACAF appeared to be safe and effective for patients with cervical OPLL. It is applicable to restore the space of the spinal canal and direct decompression of the neural elements. ACAF was superior to other treatments in promoting the successful completion of surgery. Furthermore, relatively lower incidences of adverse events were observed in the patients treated with ACAF compared with those who were treated with other treatments.

The sufficient release of the compression of the cord is the key point in the treatment of compressive cervical myelopathy. There has been great controversy over the choice of surgical approach for this kind of disease. Conventional anterior surgery has been widely used in the surgical treatment of cervical spinal degenerative diseases, and ossified ligament can be directly removed by the anterior approach. However, the technical difficulties and risks limited its' application (9,31). In addition, the difficulties associated with the anterior approach lie not only in the decompression process, but also in reconstruction of the multilevel OPLL. What's more, patients with a higher occupying ratio usually have longer vertebral level involvement. The surgery of longer cervical anterior decompression and stabilization can be extremely associated with surgery-related complications (32). The risks of excessive hemorrhage, iatrogenic damage to neural tissue, CSF leakage, and hardware failure are common complications (33,34). The posterior surgery takes less time and the posterior anatomical structure is relatively simple, but the effect of delaying the progress of ossification is not satisfactory and the treatment effect is not ideal (35,36). ACAF, as a novel surgical technique, removes the vertebrae with ossification masses to release the compression of the spinal cord, reconstruct the volume of spinal canal, restore the intervertebral height and reduce complications (24,37,38). Both ACAF surgery and other surgeries can restore cervical disc height and lordosis. However, cervical lordosis can be corrected easily by ACAF, which may due to the multiple distraction points of distraction and fixation in addition to the graft and interbody space (39). Cervical lordosis was better treated than other treatments, and the NDI scores and JOA scores were more satisfactory at the final follow-up, which indicates that ACAF is an effective surgical technique that can achieve satisfactory clinical outcomes in the treatment of cervical OPLL. In the procedure of ACAF, the ossified mass was not resected like ACCF. Instead, as a novel anterior approach, ACAF can restore the spinal canal to its normal morphology easily, which we consider is significant for the sufficient expansion of the cord. Secondly, for patients with dura ossification, the dura may also be elevated due to the adhesion to OPLL after ACAF, which facilitated to decrease the pressure of CSF leakage on the cord. In its procedure, it doesn't need to handle the adhesion of the dura and OPLL or ossified dura (40), which markedly decreases technical demanding and incidence of complications. As a result, ACAF may provide better cost-effectiveness for the cervical OPLL patients compared with other surgeries.

Cobb angle (C2-C7) correlates with clinical outcomes.

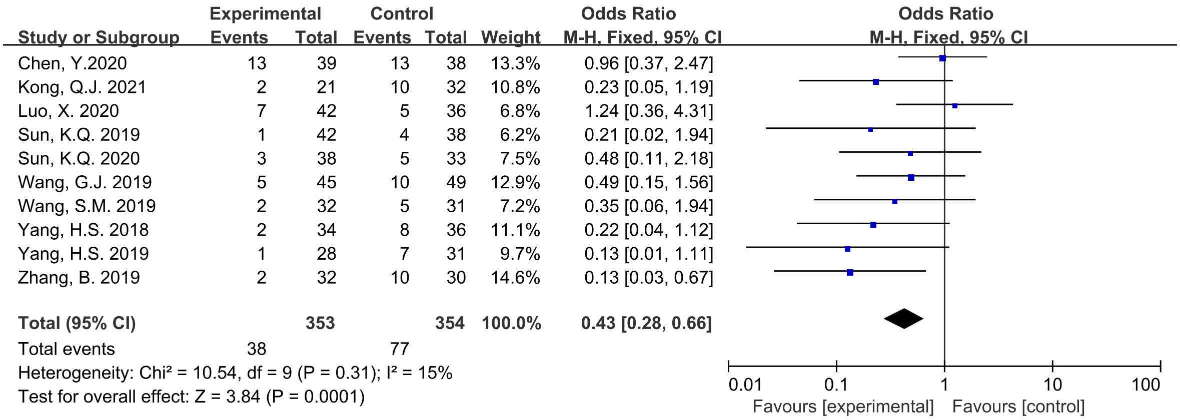

Figure 11 Forest plot showing Total adverse events under the fixed-effects model.

Table 3 Adverse events

Stratification	No. of studies	No. of patients	Pooled OR	95% CI of pooled OR	P value	Heterogeneity I^2 (%)
Total adverse events	10	707	0.43	0.28–0.66	0.0001	15
Dysphagia	6	467	3.25	1.34–7.92	0.009	13
Hoarseness	2	139	2.50	0.47–13.26	0.28	0
Axial pain	4	286	0.16	0.05–0.52	0.002	0
C5 palsy	7	484	0.32	0.14–0.73	0.007	0
CSF leakage	9	627	0.39	0.19–0.81	0.01	0

OR, odd ratio; CI, confidence interval; CSF, cerebrospinal fluid.

Fujimori *et al.* reported that neurological function can be strongly influenced by local cord angle and the expansion of the spinal cord (32). Kim *et al.* (41) reported that Cobb angle is related to patients who underwent surgeries that acquired satisfactory restoration of cervical lordosis; whereas for patients who underwent laminoplasty, the Cobb angle decreased at the final follow-up. Sun *et al.* (20) reckoned that the worsening of Cobb angle after posterior laminectomy may also contribute to the lower improvement rate of JOA score. In our systematic review and meta-analysis, among patients treated with ACAF, the results of Cobb angle were significantly better than those who were treated with laminoplasty, ACCF and SCF at the final follow-up.

Considering safety, our study found that patients who received the ACAF had a lower incidence of adverse events than the others treated by laminoplasty, ACCF and SCF. Among reported adverse events, C5 palsy is a common complication related to adversely affects outcomes and prognosis (42). C5 nerve is vulnerable to bearing maximized tension because of the location of C5 nerve and the migration of the spinal cord after surgery (43,44). Extremely wide and asymmetric decompression (45), wider laminectomy (46) and open-door laminoplasty (47) may increase the risk of C5 palsy by some published studies due to the tethering effect induced by excessive shift of the spinal cord after surgery or nerve root traction. In another review, the incidence of neurologic deficit after ACCF ranged from 1.4% to 21.4%, with an overall incidence of 8.4% (48). ACAF maximally preserves the posterior cervical structures while limiting posterior displacement of the spinal cord, so the complications undergo ACAF treatment are significantly lower than the other treated by laminoplasty, ACCF and SCF. Moreover, a previous study reported the incidence of CSF leakage after anterior decompression for OPLL ranged from 4% to 32% (49). Chen *et al.* also reported that ACCF for OPLL with a mean incidence of CSF leakage of 8.3% (50). Although CSF leakage normally did not affect neurological improvement, it led to a long hospital stay, prolonged recovery duration, high economic cost, higher infection probability, and increased the chance of revision surgery (51-53). Furthermore, the CSF leakage was easily controlled after ACAF and ACAF can achieve a lower incidence of CSF leakage. What's more, although there was a higher incidence of dysphagia in our pooled results due to multilevel anterior cervical exposure and long-time traction of esophagus in ACAF, these complications were gradually relieved without special treatments in the follow-up period in included studies.

This study has some limitations: (I) some pooled results from included studies were strongly subjective, which may influence the results due to the different experiences of doctors; (II) most of the included studies were retrospective studies, which mostly affected the pooled results; (III) all the included studies were conducted in Chinese populations; (IV) the majority of patients who had cervical OPLL were multilevel. Therefore, physicians around the world should interpret our results with caution when applying them in clinical practice.

Conclusions

In the present meta-analysis, ACAF, a new surgical technique, is associated with significantly more satisfactory outcomes at final follow-up and a lower risk of adverse events. Therefore, ACAF may be a good option for patients with severe and multi-segmental cervical OPLL and we recommend when treating cervical OPLL. Considering ACAF also has its own limitations, therefore, large sample, double-blind and multi-center RCTs are needed to verify our conclusion.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://jxym.amegroups.com/article/view/10.21037/jxym-21-44/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jxym.amegroups.com/article/view/10.21037/jxym-21-44/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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