Comparison of Clinical and Radiologic Outcomes Between Self-Locking Stand-Alone Cage and Cage with Anterior Plate for Multilevel Anterior Cervical Discectomy and Fusion: A Meta-Analysis

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OBJECTIVE: **This meta-analysis was conducted to evaluate the therapeutic effects in clinical and radiologic outcomes of a self-locking stand-alone cage (SSC) and cage-with-plate (CP) for multilevel anterior cervical discectomy and fusion (ACDF).**

METHODS: **A systematic search was performed for all comparative studies reported up to August 2018. Operative time, hospital stay, intraoperative blood loss, Japanese Orthopedic Association score, Neck Disability Index (NDI), cervical and segmental Cobb angle, intervertebral height, fusion rate, incidence of subsidence, dysphagia, and adjacent segment degeneration were analyzed with the RevMan 5.3.3 software.**

RESULTS: **A total of 15 studies were included. There was no difference regarding preoperative or postoperative Japanese Orthopedic Association score, Neck Disability Index, segmental Cobb angle and intervertebral height, preoperative cervical Cobb angle, fusion rate, incidence of subsidence, and adjacent segment degeneration between the SSC and CP group ($P > 0.05$). However, the SSC group had shorter operative time (mean difference [MD], −11.35; 95% confidence interval [CI], −16.24 to −3.66) and hospital stay (MD, −0.64; 95% CI, −1.21 to −0.06), less intraoperative blood loss (MD, −13.22; 95% CI, −19.03 to −7.41) and postoperative cervical Cobb angle (MD, −0.70; 95% CI, −1.35 to −0.06), and lower incidence of dysphagia significantly (odds ratio, −0.57; 95% CI, 0.40−0.82) ($P < 0.05$).**

CONCLUSIONS: **ACDF with SSC and CP in multilevel cervical spondylosis achieved similar clinical relief. Although CP maintained better cervical lordosis, SSC contributed to less surgical pain and fewer complications. ACDF with SSC is safe and efficient in treating multilevel cervical spondylosis.**

INTRODUCTION

Anterior cervical discectomy and fusion (ACDF) is still considered a safe and effective procedure after the failure of conservative therapy for cervical spondylotic disease, especially for single-level cervical degenerative disease.[1] This procedure allows direct decompression of neural structures, restoration of intervertebral space height, and stabilization of the cervical segments at the operative level.[2] The success of the procedure relies on the development of a solid intervertebral arthrodesis.[3] The use of iliac bone graft in ACDF for fusion has been largely superseded by polyetheretherketone cages because of the complications associated with donor site pain, hematoma, infection, and graft collapse.[4,5] Traditionally, an anterior plate is

Key words
- ACDF
- Anterior cervical decompression and fusion
- Anterior plate
- Meta-analysis
- Multilevel cervical spondylosis
- Self-locking stand-alone cage

Abbreviations and Acronyms
ACDF: Anterior cervical discectomy and fusion
ASD: Adjacent segment degeneration
CI: Confidence interval
CP: Cage-with-plate
JOA: Japanese Orthopedic Association
MCDDD: Multilevel cervical degenerative disc disease
MD: Mean difference
NDI: Neck Disability Index
OR: Odds ratio
RCT: Randomized controlled trial
SSC: Self-locking stand-alone cage

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applied to enhance cervical stability, increase fusion rate, prevent cage dislocation, and improve cervical lordotic alignment.[6] However, multilevel ACDF with a plate would lead to other complications. The incidence of graft complications in multilevel ACDF is higher than in single-level ACDF, and the rate of good fusion declines as the level increases.[7] The anterior approach with a long titanium plate needs wider surgical exposure, which was probably associated with potential disadvantages and complications, such as loosening of screws, trachea-esophageal injury, postoperative dysphagia, or neurovascular structural injuries.[8,9]

The self-locking stand-alone cage (SSC), a new kind of cervical interbody device, has been gradually applied for multilevel cervical degenerative disc disease (MCDDD) in clinic. It is designed with self-locking anchoring clips or screws impacted through the cage into the vertebral bodies of the adjacent segments accomplished with a zero profile plate or not.[10] The application of this device can avoid implant contact with the anterior soft tissue, limit the risk of cage migration, increase the rigidity of the fusion construct, and provide adequate stability. It is convenient for procedure and it has been reported that SSC reduces the potential risk of the drawbacks and complications associated with traditional anterior cervical long plates.[11,12]

Many clinical studies have tried to compare the clinical and radiologic outcomes between SSC and cage-with-plate (CP) fixation in treating patients with MCDDD. Most studies reported similar satisfactory clinical outcomes for patients receiving SSC compared with the patients receiving CP, but there still exist controversies, such as incidence of dysphagia, cage subsidence, and sagittal alignment restoration.[13-15] Although some previous meta-analyses have been reported, there is lack of research on the clinical and radiologic outcomes of SSC compared with CP in patients with MCDDD. This article is the first meta-analysis to compare clinical and radiographic results in patients using the SSC implant with CP fixation in treating MCDDD, and it is expected to provide evidence for clinicians to make clinical decisions.

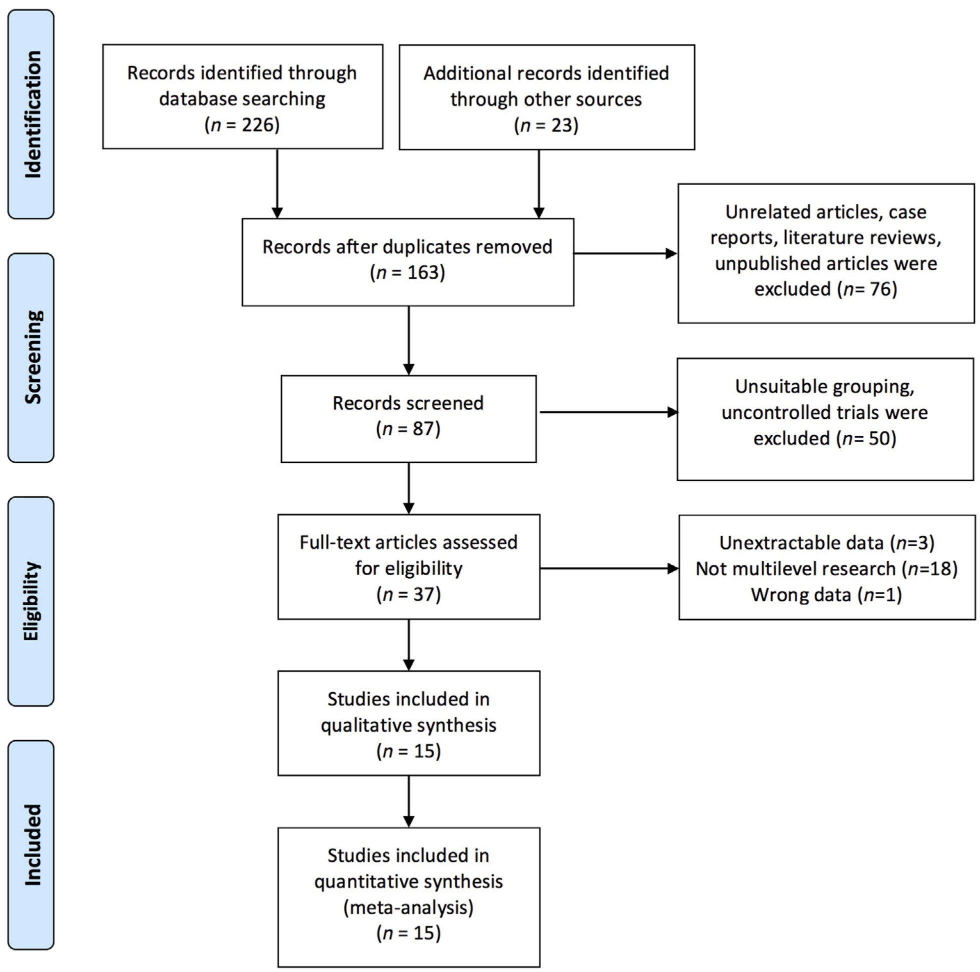

Figure 1. Flow diagram of study selection.

Table 1. Characteristics of the 15 Studies Included in this Meta-Analysis

				Sample Size (n)		Mean Age (years)		Male/ Female (n)		Follow-Up (Months)		
Study	**Country**	**Design**	**Type of Self-Locking Cage**	**SSC**	**CP**	**SSC**	**CP**	**SSC**	**CP**	**SSC**	**CP**	**Level**
Yuqiao et al., 2016[14]	China	R	ROI-C	28	26	54.1 ± 8.8	54.7 ± 12.1	18/10	15/11	28.8 ± 9.7	29.6 ± 8.3	3
Shenghua et al., 2018[19]	China	P	Zero-P	52	52	55.4 ± 12.4	59.5 ± 12.6	28/24	27/25	NR	NR	2, 3, 4
Yuanyuan et al., 2015[18]	China	P	Zero-P	37	32	48.9 ± 4.0	49.5 ± 4.2	21/16	20/12	40.6 ± 9.2	43.5 ± 10.4	2
Yu et al., 2016[13]	China	P	Zero-P	34	38	56.9 ± 5.9	56.2 ± 5.7	21/13	25/13	36	36	3
Yijie et al., 2016[15]	China	R	ROI-C	28	32	56.6 ± 9.7	57.5 ± 9.5	10/18	12/20	23.3 ± 6.9	24.2 ± 6.4	3, 4
Yi et al., 2016[20]	China	R	Zero-P	60	63	47.9 ± 8.84	48.03 ± 8.46	24/36	28/35	NR	NR	2
Yuanyuan et al., 2017[21]	China	R	Zero-P	33	38	49.3 ± 3.7	48.8 ± 3.9	18/15	21/17	30.2 ± 5	31.5 ± 4.5	3
Sheng et al., 2015[22]	China	R	Zero-P	18	20	56.7 ± 3.9	56.2 ± 4.8	11/7	12/8	30.1 ± 2.8	30.5 ± 3.4	3
Qi et al., 2013[23]	China	R	Zero-P	40	48	43.4	43.5	23/17	26/22	18.1	18.6	2
				26	35	44.1	45.2	14/12	18/17	19.0	19.5	3
Dong-Ju et al., 2016[24]	Korea	R	Zero-P	31	32	53.29 ± 7.55	54.18 ± 9.87	22/9	29/3	12.77 ± 7.85	13.62 ± 9.21	2
Lili et al., 2012[9]	China	R	Zero-P	24	28	55.26 ± 8.98	56.36 ± 7.97	17/7	21/7	14.6	14.6	3, 4
Haisong et al., 2015[25]	China	R	Zero-P	9	10	NR	NR	NR	NR	NR	NR	2
				8	7							3
Xingping and Wujun, 2016[26]	China	R	Zero-P	21	20	53.8 ± 8.7	55.7 ± 9.2	12/9	8/10	NR	NR	2
Jian et al., 2018[27]	China	R	ROI-C	18	14	NR	NR	NR	NR	NR	NR	2
				13	12							3
Zhiwen et al., 2015[12]	China	R	ROI-C	16	15	NR	NR	NR	NR	NR	NR	2

SSC, self-locking stand-alone group; CP, cage-with-plate group; R, retrospective study; P, prospective study; NR, not referred.

METHODS

This research was conducted under the guidelines from the Review Manager handbook from the Cochrane Collaboration and was performed on the basis of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[16]

Search Strategy

A systematic search of the literature was conducted in the Cochrane Library, Web of Science (all databases), Embase.com, Medline (OvidSP), PubMed, Wanfang data, and China National Knowledge Infrastructure (CNKI). More effort was made on Google Scholar for additional references. The search was designed and executed by an experienced doctor. The keywords used for searches included "cervical," "cervical spine," "anterior cervical discectomy and fusion," "ACDF," "anterior cervical fusion," "interbody fusion," "zero-profile," "zero-p," "ROI-C," "anchored fusion", "anchored spacer device," "low profile," "stand-alone," "self-locking," and "cage with plate," with various combinations of the operators "AND" and "OR" during the literature retrieval. The restriction of study design was controlled trials published updated at August 1, 2018. Language was restricted to Chinese and English.

Inclusion and Exclusion Criteria

Two independent reviewers (F.W. and D.Z.) performed the selection procedure. All subjects, abstracts, and the full text of articles were reviewed. Studies were included if they met the following criteria: 1) randomized or nonrandomized controlled study; 2) included patients diagnosed with cervical spondylosis or cervical degenerative diseases who received multilevel (≥2 segments) ACDF procedure; 3) studies involving comparison between SSC and CP plate fixation for multilevel ACDF; 4) patients were followed up for >12 months; and 5) patients were aged ≥18 years. Studies were excluded if they: 1) were noncontrolled; 2) combined anterior and posterior surgery; 3) had a history of cervical surgery; 4) meeting abstracts, review articles, editorial comments, letters, technical reports, case reports, biomechanical studies, or animal experiments; 5) duplicate publications; 6) data were not expressed as mean ± standard deviation; and 7) articles for which full text was not available. When the 2 reviewers had disagreements, D.Z. joined in discussion until consensus was achieved.

Data Extraction

Two independent reviewers collected information from each study included individually. Items involved in comparisons include operative time, blood loss, hospital stay, preoperative

Table 2. Methodological Quality Assessment of Studies Included in the Meta-Analysis Based on Newcastle-Ottawa Scale

	Yuqiao et al., 2016[14]	Shenghua et al., 2018[19]	Yuanyuan et al., 2015[18]	Yu et al., 2016[13]	Yijie et al., 2016[15]	Yi et al., 2016[20]	Yuanyuan et al., 2016[21]	Sheng et al., 2015[22]	Qi et al., 2013[23]	Dong-Ju et al., 2016[24]	Lili et al., 2012[9]	Hasisong et al., 2015[25]	Xingping and Wujun, 2016[26]	Jian et al., 2018[21]	Zhiwei et al., 2014[12]
Selection															
Representativeness of the exposed cohort	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Selection of the nonexposed cohort	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ascertainment of exposure	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Demonstration that outcome of interest was not present at start of study	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Comparability															
Study controls for age of gender	1	1	1	1	1	1	1	1	0	1	1	0	1	0	0
Study controls for any additional factor	1	1	1	0	1	1	0	1	1	0	0	0	1	1	1
Outcome															
Assessment of outcome	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Was follow-up long enough for outcomes to occur	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Adequacy of follow-up of cohorts	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total	9	9	9	8	9	9	8	9	8	8	8	7	9	8	8

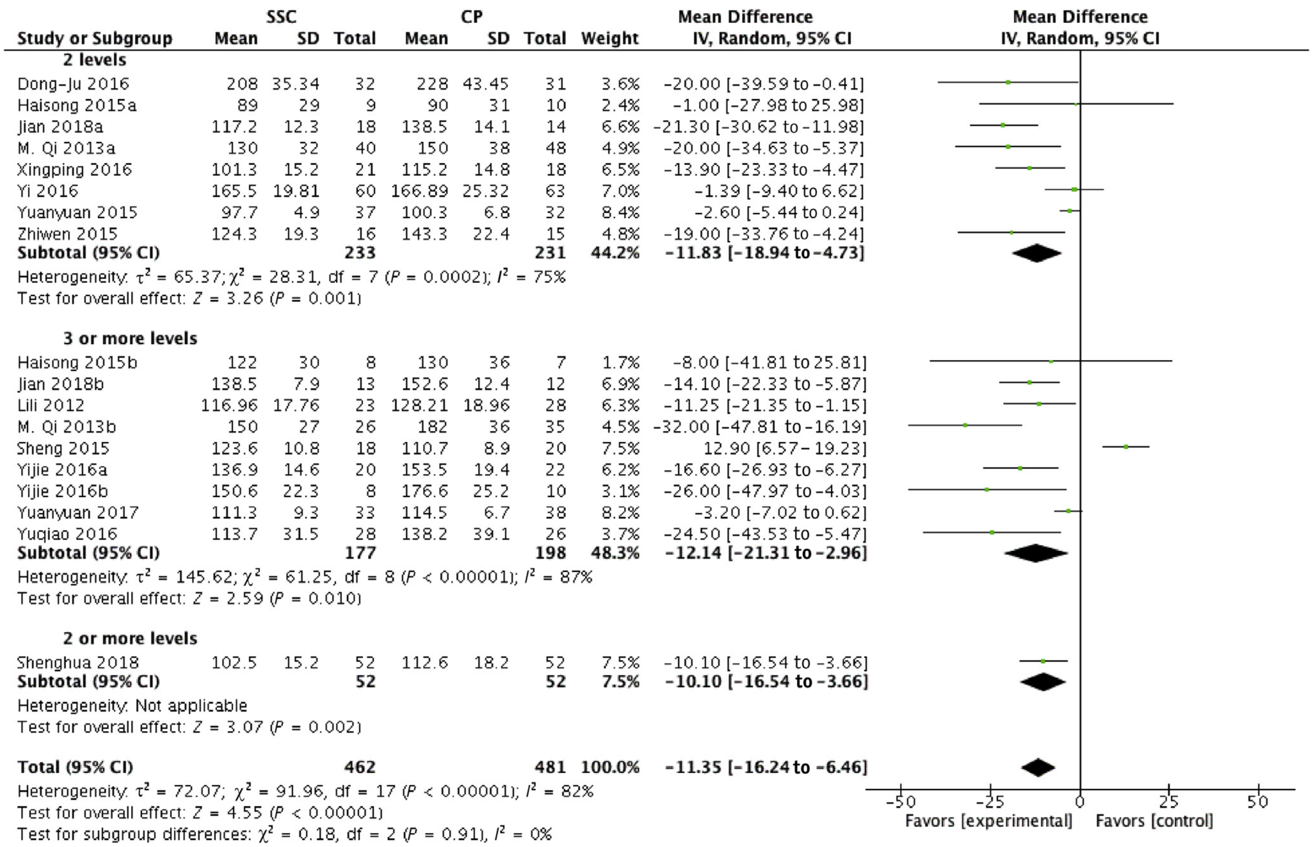

Figure 2. Comparison of operative time with subgroups. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

and postoperative Japanese Orthopedic Association (JOA) score, preoperative and postoperative Neck Disability Index (NDI), preoperative and postoperative cervical Cobb angle (measured as the angle between the inferior end plate of the C2 vertebra and the inferior end plate of the C7 vertebra), preoperative and postoperative segmental Cobb angle (measured as the angle formed by the superior end plate of upper vertebra and the inferior end plate of lower vertebra), incidence of subsidence, adjacent segment degeneration (ASD) and dysphagia, and fusion rate. Besides these data, the basic characteristics were recorded: 1) first author; 2) publication year; 3) study design; 4) sample size; 5) types of internal fixation; 6) number of surgical segments; 7) country; and 8) length of follow-up. If the data were available in figures rather than raw data, the software GetData Graph Digitizer (version 2.25) was used to obtain the data from graphs.

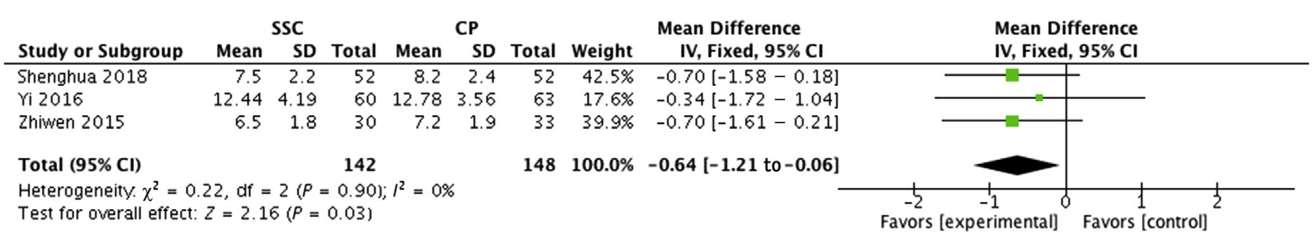

Figure 3. Comparison of hospital stay. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

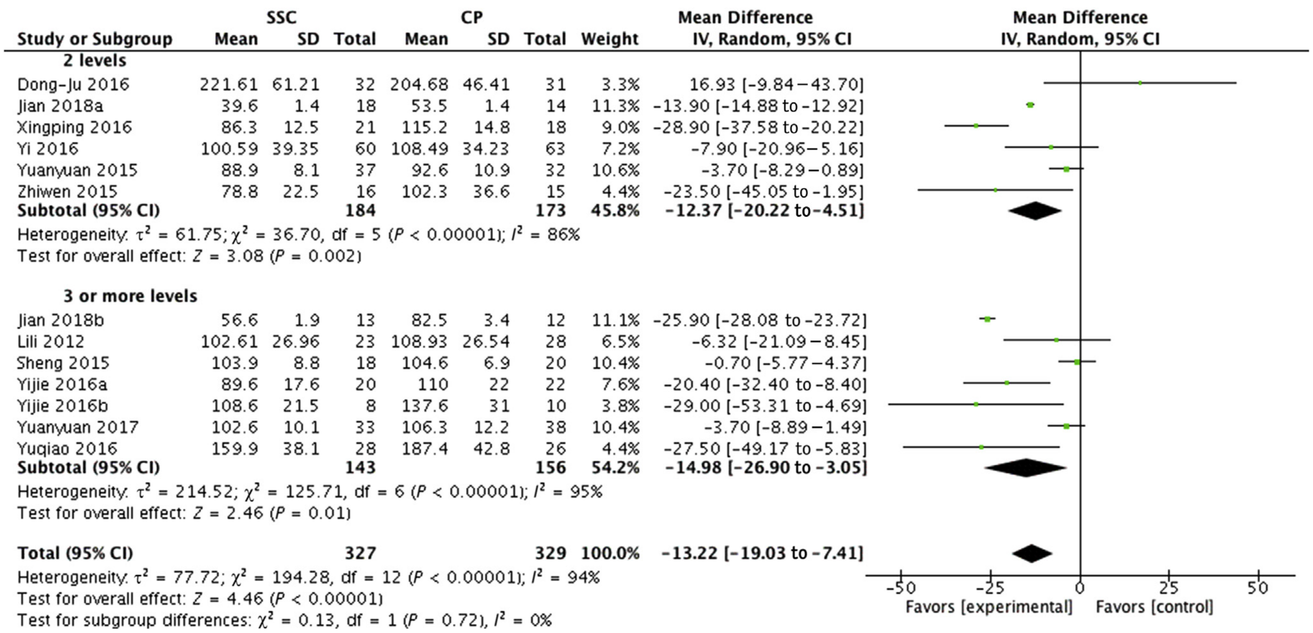

Figure 4. Comparison of intraoperative blood loss. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

Quality Assessment

Two authors assessed the methodological quality of each study independently. The quality of retrospective and prospective studies was assessed using the Newcastle-Ottawa Scale.[17] It was evaluated by examining 3 items (selection, comparability, and exposure), with higher scores representing studies of higher quality. The quality of each study was graded as either level 1 (0–5) or level 2 (6–9), and the randomized controlled trials (RCTs) were evaluated in accordance with the Cochrane Handbook.

Statistical Analysis

This meta-analysis was performed using Review Manager software (version 5.3.3, Cochrane Collaboration). Mean difference (MD) and 95% confidence interval (CI) were assessed for continuous data (operative time, blood loss, hospital stay, JOA score, NDI, and Cobb angle). Risk ratio and 95% CI were used for dichotomous data (incidence of subsidence, ASD and dysphagia, and fusion rate). It was considered statistically significant when the P value was <0.05. Heterogeneity was assessed using the I^2 statistic of a χ^2 test result ranging from 0% to 100%. When I^2 was $>50\%$,

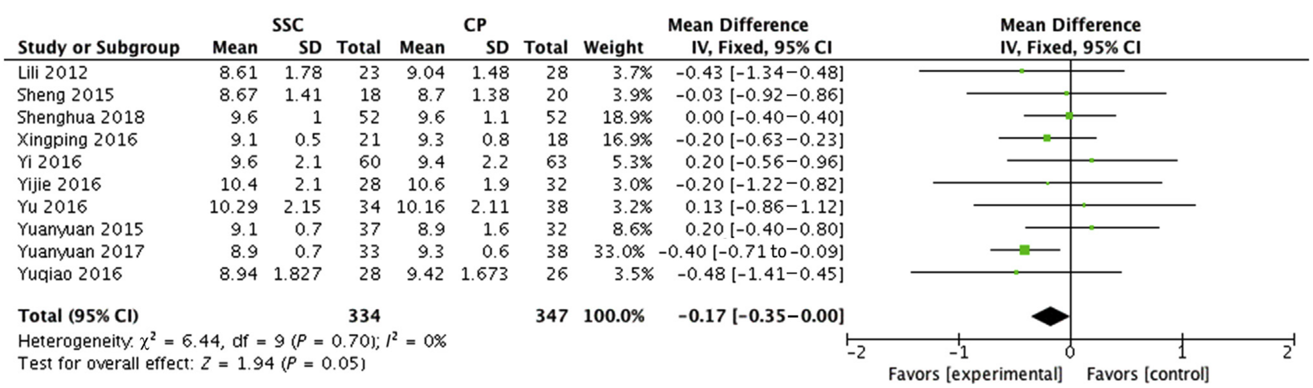

Figure 5. Comparison of preoperative Japanese Orthopedic Association score. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

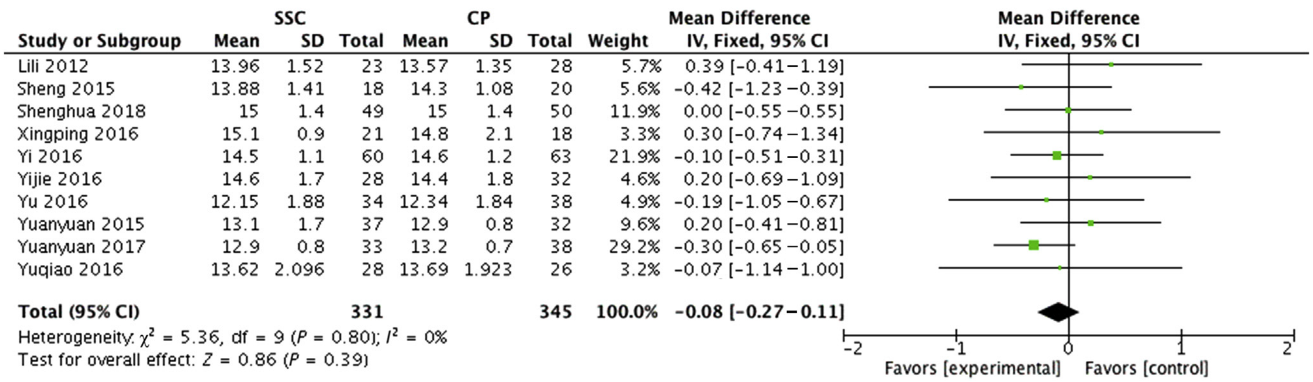

Figure 6. Comparison of postoperative Japanese Orthopedic Association score. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

heterogeneity was assumed to be significantly obvious and random-effects modeling was applied. Fixed-effects modeling was applied when I^2 was <50%.

RESULTS

Literature Results and Bias Assessment

A total of 249 studies were identified according to the search strategy initially. A total of 212 studies were excluded because of duplicates, unrelated studies, case reports, revision surgeries, hybrid surgeries, artificial disc surgeries, and reviews. After a detailed and comprehensive evaluation, 22 of the remaining 37 articles were subsequently excluded for the following reasons: unavailable data or single-level ACDF operation researches. Fifteen studies were included for meta-analysis and all are retrospective or prospective studies[9,12-15,18-27] (Figure 1). The included studies were reported between 2012 and 2018 and included 1018 patients (SSC group, 496 patients; CP group, 522 patients). The basic characteristics and preoperative and postoperative evaluation data are summarized in Table 1. The self-locking cages used in these articles were ROI-C (LDR, France) and Zero-p (DePuy Synthes, USA).

Assessment of Study Quality

Two independent investigators evaluated each study with Newcastle-Ottawa Scale assessment. No RCTs were included in this meta-analysis. Three of 13 studies were prospective, whereas the other 10 studies were retrospective. All the major baseline characteristics of patients in each study were similar. Seven studies scored 9 points, 7 studies scored 8 points, and 1 study scored 7 points, which indicated that all the studies were of a relatively high-quality (Table 2).

Operative Time

Thirteen studies were selected to compare the operative time between the SSC and CP group with a total of 943 patients (SSC group, 462; CP group, 481). The random-effects model was

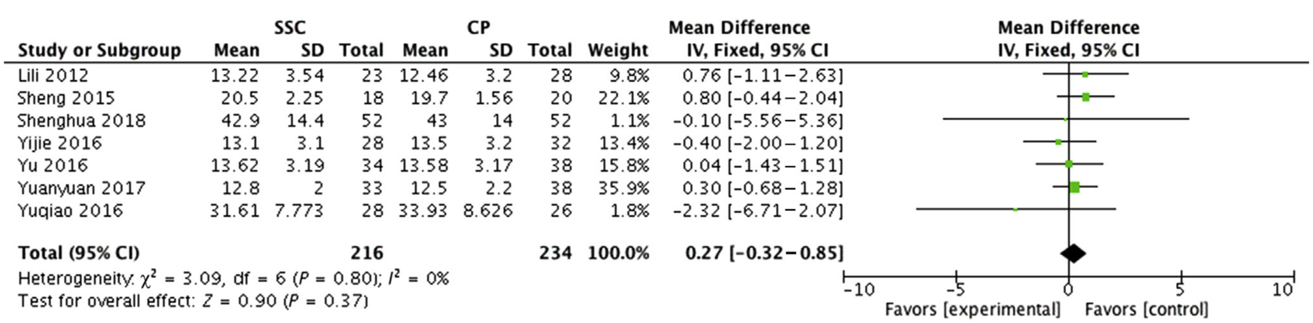

Figure 7. Comparison of preoperative Neck Disability Index. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

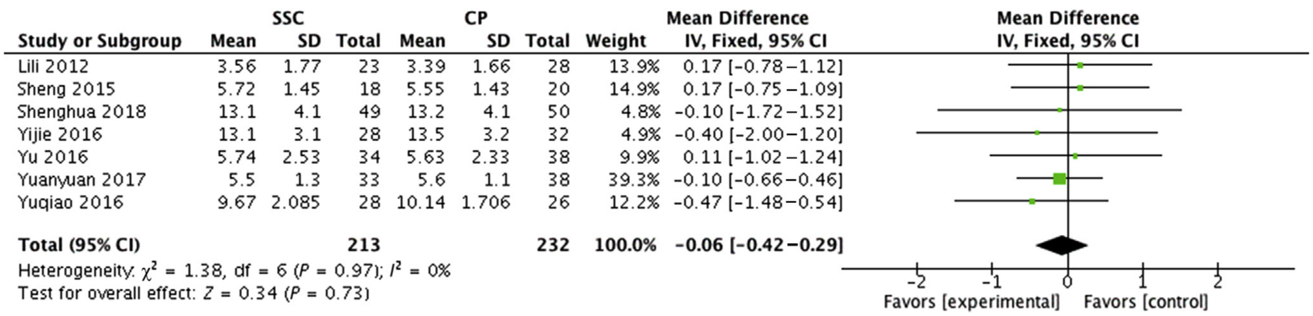

Figure 8. Comparison of postoperative Neck Disability Index. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

applied with high overall heterogeneity ($I^2 = 82\%$). The result suggested that the self-locking technique has a significantly shorter operative time than has the CP fixation technique in 2 levels (MD, −11.83; 95% CI, −18.94 to −4.73; $P = 0.001$), ≥3 levels (MD, −12.14; 95% CI, −21.31 to −2.96; $P = 0.010$), and ≥2 levels. The subgroup heterogeneity ($I^2 = 0\%$) contributed nothing to the overall heterogeneity (Figure 2).

Hospital Stay

Three studies reported the hospital stay between SSC and CP group with a total of 290 patients (SSC group, 142; CP group, 148). The fixed-effects model was applied without heterogeneity ($I^2 = 0\%$). The result (MD, −0.64; 95% CI, −1.21 to −0.06; $P = 0.03$) showed patients with SSC had a shorter hospital stay (Figure 3).

Blood Loss

Ten studies compared the intraoperative blood loss between the SSC and CP group with a total of 656 patients (SSC group, 327; CP group, 329). The random-effects model was applied, with high heterogeneity in the 2-level subgroup ($I^2 = 86\%$) and ≥3-level group ($I^2 = 95\%$). The result in the 2-level group (MD, −12.37; 95% CI, −20.22 to −4.51; $P = 0.002$) and ≥3 levels group (MD, −14.98; 95% CI, −26.90 to −3.05; $P = 0.01$) suggested that the SSC had a significantly reduced intraoperative blood loss compared with CP fixation, no matter how many levels there were. The cause of high heterogeneity was not associated with number of levels without subgroup heterogeneity ($I^2 = 0\%$) (Figure 4).

JOA Score

Six hundred and eighty-one patients in 9 studies reported preoperative and postoperative JOA scores (SSC group, 334; CP group, 347). The fixed-effects model was applied without heterogeneity ($I^2 = 0\%$). There was no difference in preoperative and postoperative JOA scores between SSC group and CP without heterogeneity ($I^2 = 0\%$) (Figures 5 and 6).

NDI

Seven studies reported preoperative and postoperative NDI, which involved 450 patients (SSC group, 213; CP group, 232). Five patients were lost to follow-up. There was no significant difference in preoperative and postoperative NDI without heterogeneity ($I^2 = 0\%$) (Figures 7 and 8).

Segmental Cobb Angle

Five studies analyzed preoperative and postoperative segmental Cobb angle, which involved 295 patients (SSC group, 148; CP group, 147). There was no significant difference in preoperative segmental Cobb angle (MD, −0.42; 95% CI, −1.54 to 0.70; $P = 0.46$) without

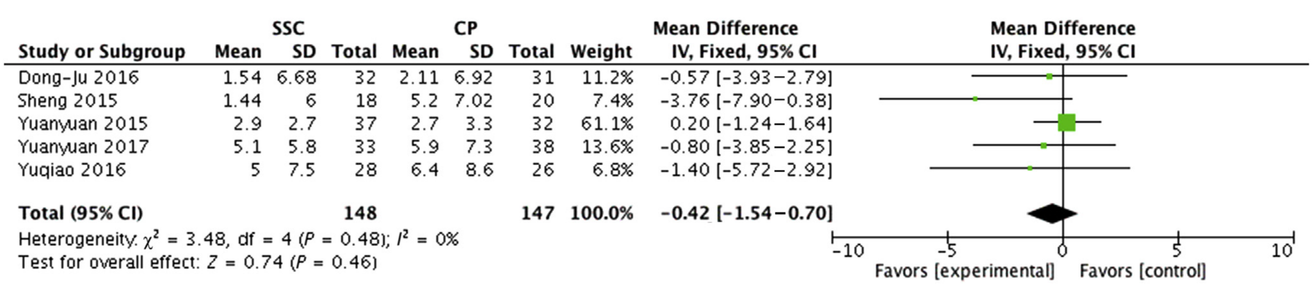

Figure 9. Comparison of preoperative segmental Cobb angle. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

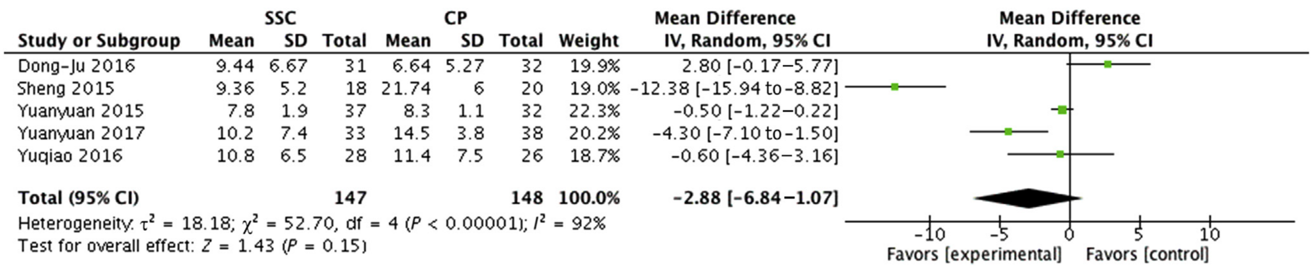

Figure 10. Comparison of postoperative segmental Cobb angle. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

heterogeneity ($I^2 = 0\%$). There was no significant difference in postoperative segmental Cobb angle (MD, −2.88; 95% CI, −6.84 to 1.07; P = 0.15) with high heterogeneity ($I^2 = 92\%$) (Figures 9 and 10).

Cervical Cobb Angle (C2-C7)

The preoperative and postoperative cervical Cobb angle was analyzed in 10 studies, which involved 731 patients (SSC group, 351; CP group, 380). There was no difference in cervical Cobb angle (MD, −0.14; 95% CI, −0.65 to 0.37; P = 0.59) between the SSC group and CP group before surgery without heterogeneity ($I^2 = 0\%$) and when a fixed-effects model was applied, whereas postoperative cervical Cobb angle in the SSC group was significantly smaller than in the CP group (MD, −0.70; 95% CI, −1.35 to −0.06; P = 0.03) with median heterogeneity ($I^2 = 56\%$) (Figures 11 and 12).

Intervertebral Height

Three studies consisting of 618 fused segments reported preoperative and postoperative intervertebral height (SSC group, 302; CP group, 316). There was no significant difference in preoperative intervertebral height (MD, 0.01; 95% CI, −0.04 to 0.07; P = 0.65) without heterogeneity ($I^2 = 0\%$). There was no significant difference in postoperative intervertebral height (MD, 0.11; 95% CI, −0.15 to 0.37; P = 0.41) as well, but the heterogeneity was median ($I^2 = 81\%$) (Figures 13 and 14).

Fusion Rate

Seven studies reported fusion rate at the end of follow-up, which involved 454 patients (SSC group, 223; CP group, 231). There was no difference (odds ratio [OR], 1.07; 95% CI, 0.52−2.21; P = 0.86) in fusion rate between the SSC group and CP group without heterogeneity ($I^2 = 0\%$) (Figure 15).

Incidence of Dysphagia

Eleven studies reported incidence of dysphagia during the period of follow-up, which involved 751 patients (SSC group, 363; CP group, 378). The fixed-effects model was applied and the comparison showed that the incidence of dysphagia (OR, 0.57; 95% CI, 0.40−0.82; P = 0.002) was significantly lower in the SSC group than in the CP group without heterogeneity ($I^2 = 0\%$) (Figure 16).

Incidence of Subsidence

Three studies reported data on subsidence occurrence, which involved 339 patients (SSC group, 169; CP group, 170). The

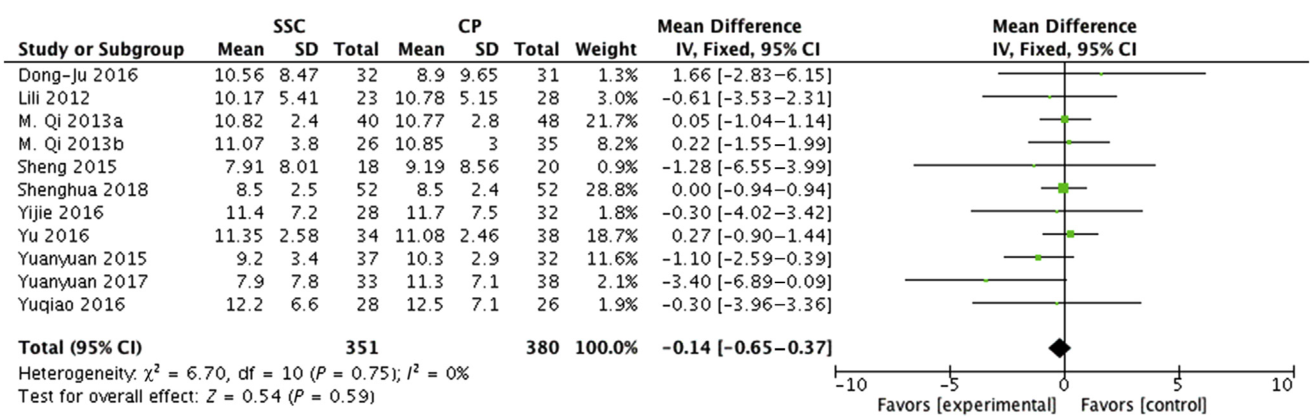

Figure 11. Comparison of preoperative cervical Cobb angle. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

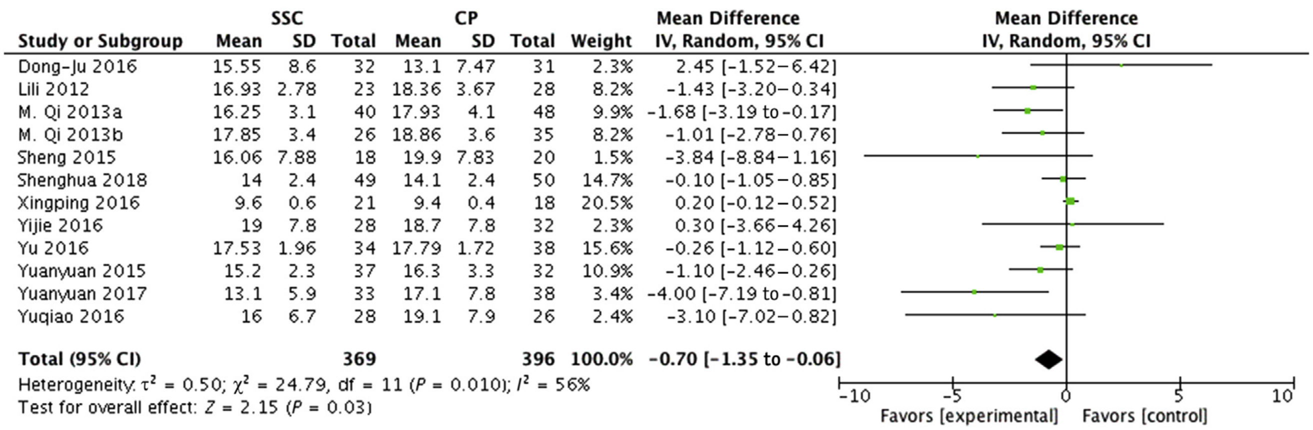

Figure 12. Comparison of postoperative cervical Cobb angle. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

random-effects model was applied and the comparison showed that there was no difference in the incidence of subsidence (OR, 2.57; 95% CI, 0.57−11.56; P = 0.22) between the CP group and SSC group with median heterogeneity (I^2 = 69%) (**Figure 17**).

Incidence of ASD

Four studies reported incidence of ASD at the end of follow-up, which involved 272 patients (SSC group, 132; CP group, 140). The fixed-effects model was applied and the comparison showed that there was no difference in the incidence of ASD (OR, 0.45; 95% CI, 0.20−0.99; P = 0.05) between the CP group and SSC group without (I^2 = 0%) (**Figure 18**).

DISCUSSION

During the past decades, ACDF has been widely accepted as a gold-standard surgery for single-level symptomatic cervical disc degenerative disease, with satisfactory clinical outcomes.[28] However, MCDDD involves ≥2 levels of the cervical spine with complicated pathologic conditions and the surgical decision remains controversial.[29,30] Multilevel ACDF or posterior approaches could be viable alternatives. Because of surgical trauma, axial pain, loss of lordosis, or C5 root palsy in posterior approaches, multilevel ACDF is gradually becoming accepted as the first choice.[31] ACDF can decompress the anterior spinal cord directly, preserve the stability of the spinal column, and maintain satisfactory cervical spine sagittal alignment. However, long fixation with an anterior plate may also be associated with potential disadvantages and complications, such as soft tissue damage, high incidence of dysphagia, loss of the cervical motion, ASD, and hoarseness.[32,33]

To prevent these adverse events and provide immediate stability, as is the case with the plate, SSC has been applied in the clinic and can be independently applied without a traditional plate. Initial clinical reports on the use of these devices for ACDF showed satisfactory clinical and radiologic results in single-level cervical degenerative disease.[34] Furthermore, several relevant clinical studies have indicated that multilevel ACDF can also achieve encouraging clinical outcomes.[13-15] However, the evidence regarding whether SSC is superior to an anterior plate is insufficient. It is still a subject of debate whether the SSC can offer similar clinical outcomes and additional stabilization to CP with lower incidence of complications in treating multilevel ACDF. Therefore, we performed a meta-analysis and evaluated SSC and CP, comparing the clinical outcomes and radiologic outcomes.

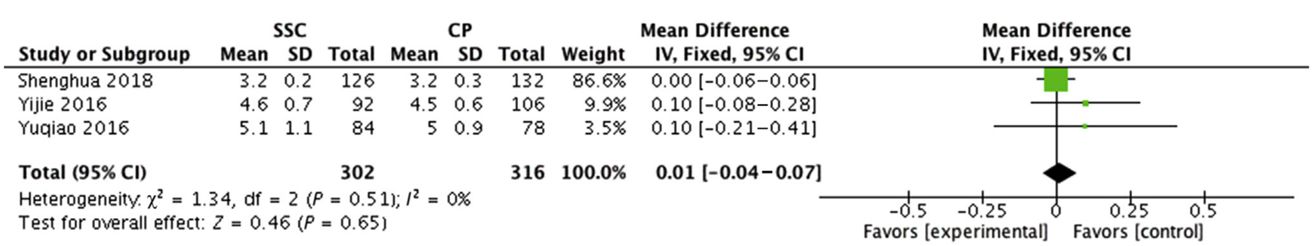

Figure 13. Comparison of preoperative intervertebral height. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

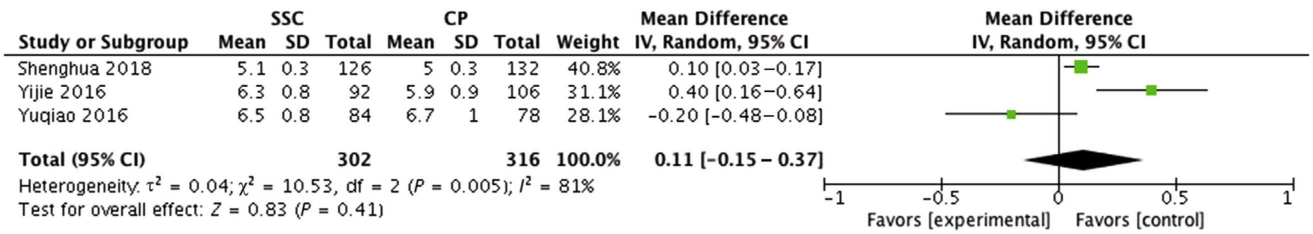

Figure 14. Comparison of postoperative intervertebral height. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; IV, inverse variance; SD, standard deviation; SSC, self-locking stand-alone cage.

Clinical Outcomes

Regarding assessment of clinical effectiveness, preoperative and final follow-up JOA score and NDI were similar in the 2 groups, and both procedures promoted JOA and NDI scores at last follow-up. There was a significant increase of JOA scores and decrease of NDI scores at final follow-up compared with preoperative baseline. This result indicated that both SSC and CP provided equal symptom relief and neurofunctional recovery. A possible explanation is that, despite different types of cage and fixation, both procedures decompressed the spinal cord directly by removing the anterior pathogenic compressions such as the soft disc herniation and small osteophyte of the posteior of the vertebra.

Dysphagia is a relatively common postoperative complication after anterior cervical surgery, with a reported incidence of between 2% and 67%.[35,36] In our meta-analysis, we analyzed the incidence of postoperative dysphagia during follow-up. Patients with CP had higher incidence of dysphagia than did those who received SSC. The plate was placed anterior to the vertebral body and posterior to the esophagus, which contributes considerably to the high incidence of dysphagia. Recently, some studies have reported that the risk factors related to an anterior plate include hematoma, vocal cord paralysis, adhesion formation, esophageal injury, and soft tissue swelling.[37,38] On the other hand, SSC does not cause irritation to the esophagus, which may decrease the risk of postoperative dysphagia.

Blood loss, operative time, and length of hospital stay were also involved in clinical outcomes. Based on this meta-analysis, the SSC group was associated with significantly shorter operative times and length of hospital stay and less intraoperative blood loss for MCDDD. The result is reasonable because the procedure is simpler with SSC and less soft tissue is destroyed. We believe that patients with SSC would receive less exposure to X-rays, although no studies have focused on this. Other complication-related outcomes including C5 palsy, hoarseness, infection, cerebral fluid leakage, and epidural hematoma were seldom or never reported in all studies. This finding might indicate that both SSC and CP surgeries are relatively safe.

No definite conclusions can be drawn regarding the superiority of 1 procedure over the other in functional outcomes. Because of the limited sample of studies and absence of RCTs in the present analysis, further studies are needed to determine the validity of these findings.

Radiologic Outcomes

Successful treatment with ACDF depends on adequate decompression and solid fusion.[39] Biomechanical studies have already shown that SSC can provide equal biomechanical stability to the CP in 1-level or 2-level ACDF but less stiffness of cervical spine in multilevel ACDF.[40] However, a high fusion rate can also be

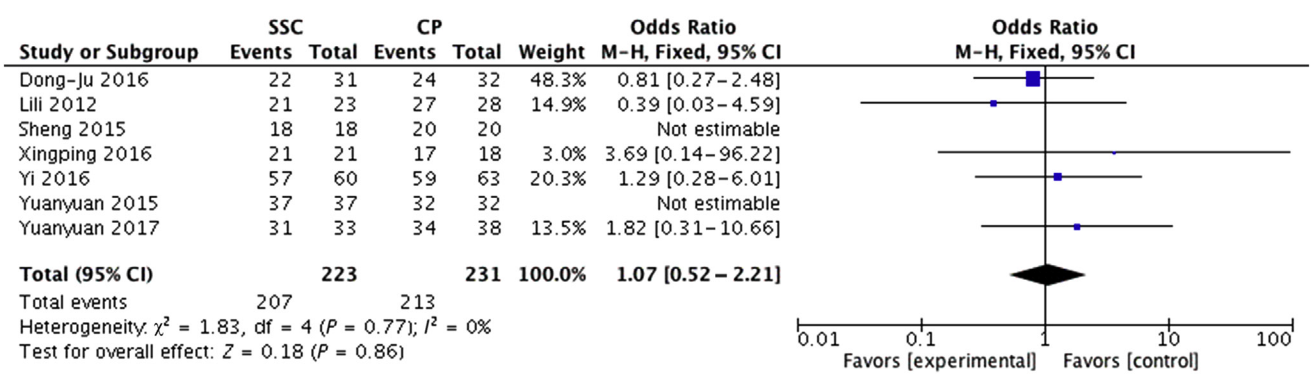

Figure 15. Comparison of fusion rate at final follow-up. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; M-H, Mantel-Haenszel; SD, standard deviation; SSC, self-locking stand-alone cage.

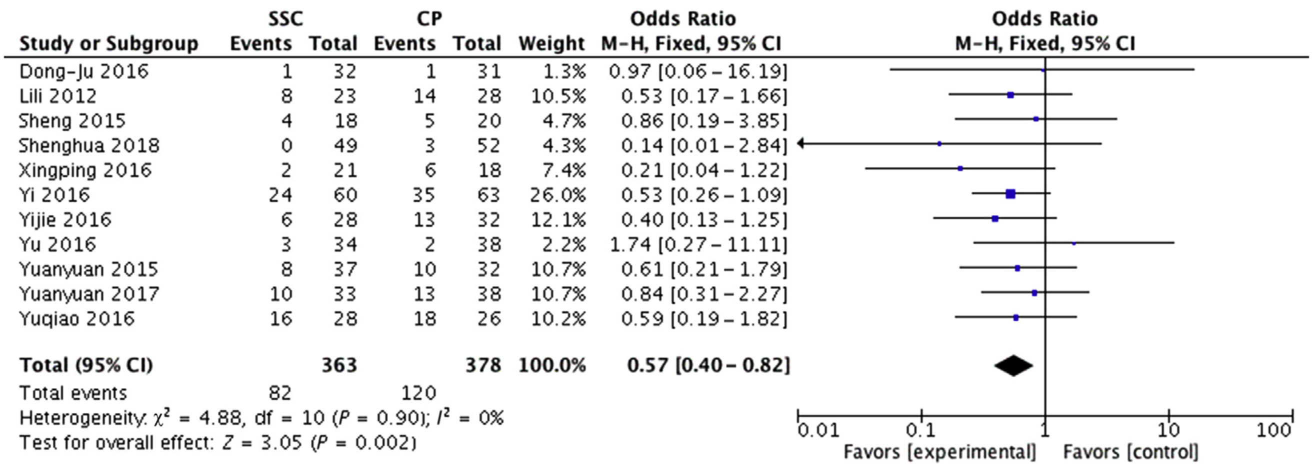

Figure 16. Comparison of incidence of dysphagia during follow-up. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; M-H, Mantel-Haenszel; SD, standard deviation; SSC, self-locking stand-alone cage.

achieved under treatment with SSC for single-level or multilevel ACDF in some clinical research and several studies have reported similar fusion rates to those of a plate.[13,41]

Our study is the first systematic review and meta-analysis comparing outcomes between the 2 ACDF procedures for MCDDD. The results show that ACDF using SSC can achieve a similar fusion rate to the polyetheretherketone cage and plate system in multilevel ACDF. Surgical techniques, including complete removal of the cartilage end plate and optimal preparation of the fusion bed, also contribute to the satisfactory fusion rate.

The incidence of subsidence after ACDF has been reported from 5.4% to 55.6% depending on surgical methods.[42,43] Recent data have suggested that subsidence happens within the first 3 months after surgery, because the formation of bone fusion at 3 months after surgery may restrain the further progress of subsidence.[44] Several systematic reviews have been published, but the conclusions have not been the same. One of the limitations is that these studies did not consider the influence of number of levels. Based on this limitation, it is not difficult to understand some contrary findings in previous research. Duan et al.[45] and Liu et al.[46] reported independently that SSC was associated with higher incidence of subsidence compared with CP. The 2 meta-analyses included just 1 multilevel study, whereas the others were single level. We included all the studies focused on multilevel ACDF, and the result showed that SSC did not cause a higher rate of subsidence. This finding indicates that number of levels is one of the relevant factors of subsidence,[47-49] other relevant factors include damage of the end plate, overdistraction of the fusion segment, oversized cages during surgery, and low bone mineral density of patients.

If the cage subsides, intervertebral foraminal height and the cervical alignment would fail to restore, which may influence the clinical outcomes. The incidence of cage subsidence and its consequences reported in the literature were different.[50-52] In this meta-analysis, we found that the SSC group had a similar subsidence rate to the plate group, with no statistically significant difference.

Normal cervical lordotic alignment is one of the most important factors related to good motion and function of the cervical spine, as well as being responsible for changes in the biomechanics of the whole spine.[53,54] Sagittal malalignment after ACDF may cause postoperative axial pain, adjacent level degeneration, and

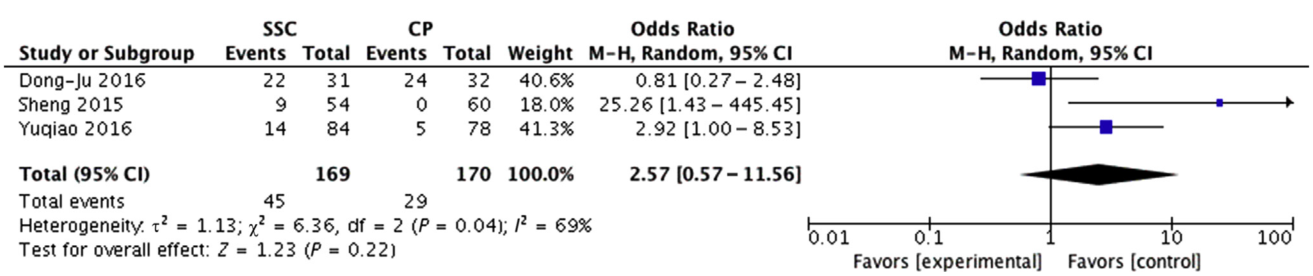

Figure 17. Comparison of incidence of subsistence during follow-up. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; M-H, Mantel-Haenszel; SD, standard deviation; SSC, self-locking stand-alone cage.

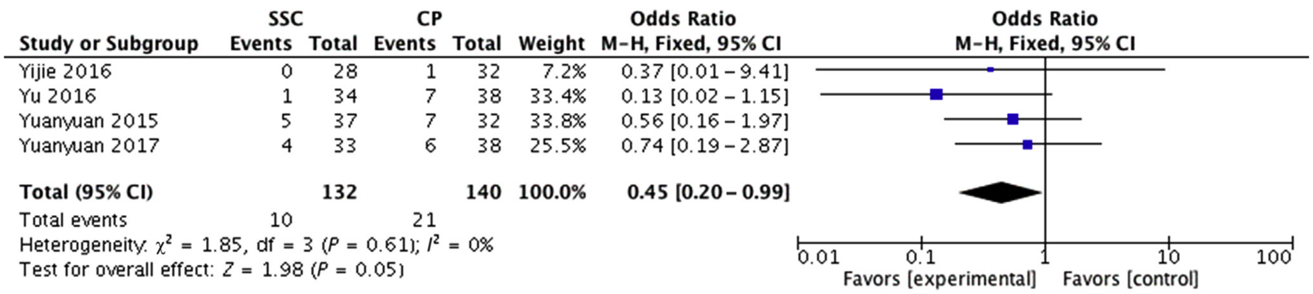

Figure 18. Comparison of incidence of adjacent segment degeneration during follow-up. CI, confidence interval; CP, cage-with-plate; df, degree of freedom; M-H, Mantel-Haenszel; SD, standard deviation; SSC, self-locking stand-alone cage.

worsening of neurologic deficits, which is believed to influence functional recovery. It is widely accepted that restoration and preservation of cervical lordosis is a main goal of surgical treatment in multilevel ACDF.[55] The plate curve helps to preserve global cervical lordosis and the fusion segment angle, preventing cage subsidence during the process of fusion.[56] However, the ability to restore and preserve the cervical lordosis between SSC and CP were not accordant; one study reported loss of cervical lordosis and fused segment angle using SSC, whereas another study reported that there was no difference.[14,15] In our meta-analysis of radiographic outcomes, we found that preoperative and final follow-up C2-7 Cobb angle and fused segment angle in the SSC group and CP group were similar. C2-7 Cobb angle and fused segment angle at final follow-up were significantly increased in the 2 groups.

The precise cause of ASD is still not known even although it has been reported that increased rigidity of adjacent segment and abnormal sagittal balance after ACDF promotes ASD.[57] The incidence of ASD was reported to be higher in the patients undergoing CP because of an increased fixation force generated in the adjacent intervertebral discs with the plate used.[58]

Most surgeons believed that SSC prevented ASD in consideration of the less restriction of range of motion. However, no study reported that SSC surgery could reduce the incidence of ASD more than CP surgery. Our meta-analysis showed that there was no statistically significant difference in ASD incidence between the SSC and CP groups. Nevertheless, all patients need close observation in a longer follow-up.

Limitations

This study was restricted by a few limitations. First, none of the studies included in the meta-analysis were RCTs. Second, it may be insufficient to reflect the changes of radiologic outcomes, because there is no comparison of other cervical alignment parameters, such as C2-7 sagittal vertical axis, T1 slope, or T1 inlet angle, which could affect the clinical outcomes more comprehensively. Third, the follow-up of all included articles is on average 43.5 ± 10.42 months, which is not enough to observe long-term recovery and complications. Fourth, the variability in the indications for surgery and the surgical technologies used at the different treatment centers may confound the results of the meta-analysis. The searching strategy was restricted to articles published in English and Chinese. The limitation of publication bias should be recognized in this study.

CONCLUSIONS

Available evidence indicates that SSC procedures are significantly associated with less blood loss, shorter operative time and length of hospital stay, and lower incidence of postoperative dysphagia compared with CP procedures, which could provide equivalent outcomes and functional recovery for MCDDD. Overall, no significant differences in postoperative subsidence, cervical lordosis, and fusion rate were found. We expect more well-designed studies with large samples of patients and long-term follow-up in the future.

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Author contributions: D.Zha. and D.Zhu conceived the project. J.Z. and Y.Y. designed the search strategy and inclusion and exclusion criteria. C.L. and F.W. performed the systematic search. F.W. and D.Zhu selected the studies. J.Z. and C.L. extracted the data. D.Zha. analyzed the data. D.Zha. and D.Zhu wrote the manuscript. B.L. revised the manuscript.

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