Comparison of zero-profile anchored spacer versus plate-cage construct in treatment of cervical spondylosis with regard to clinical outcomes and incidence of major complications: a meta-analysis

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Purpose: Meta-analysis was conducted to evaluate whether zero-profile anchored spacer (Zero-P) could reduce complication rates, while maintaining similar clinical outcomes compared to plate-cage construct (PCC) in the treatment of cervical spondylosis.

Methods: All prospective and retrospective comparative studies published up to May 2015 that compared the clinical outcomes of Zero-P versus PCC in the treatment of cervical spondylosis were acquired by a comprehensive search in PubMed and EMBASE. Exclusion criteria were non-English studies, noncomparative studies, hybrid surgeries, revision surgeries, and surgeries with less than a 12-month follow-up period. The main end points including Japanese Orthopedic Association (JOA) and Neck Disability Index (NDI) scores, cervical lordosis, fusion rate, subsidence, and dysphagia were analyzed. All studies were analyzed with the RevMan 5.2.0 software. Publication biases of main results were examined using Stata 12.0.

Results: A total of 12 studies were included in the meta-analysis. No statistical difference was observed with regard to preoperative or postoperative JOA and NDI scores, cervical lordosis, and fusion rate. The Zero-P group had a higher subsidence rate than the PCC group ($P < 0.05$, risk difference = 0.13, 95% confidence interval [CI] 0.00–0.26). However, the Zero-P group had a significantly lower postoperative dysphagia rate than the PCC group within the first 2 weeks ($P < 0.05$, odds ratio [OR] = 0.64, 95% CI 0.45–0.91), at the 6th month [$P < 0.05$, OR = 0.20, 95% CI 0.04–0.90], and at the final follow-up time [$P < 0.05$, OR = 0.13, 95% CI 0.04–0.45].

Conclusion: Our meta-analysis suggested that surgical treatments of single or multiple levels of cervical spondylosis using Zero-P and PCC were similar in terms of JOA score, NDI score, cervical lordosis, and fusion rate. Although the Zero-P group had a higher subsidence rate than the PCC group, Zero-P had a lower postoperative dysphagia rate and might have a lower adjacent-level ossification rate.

Keywords: cervical spondylosis, anterior cervical decompression and fusion, integrated interbody device, dysphagia, meta-analysis, subsidence, adjacent-level ossification

Introduction

Age-related cervical degeneration is evident in over 50% of the middle-aged population and is the most common cause of neural dysfunction.¹ Although the majority of cases are asymptomatic, changes such as disc herniation, osteophyte formation, and hypertrophied ligaments may compress the cervical neuraxis to result in neck pain, radiculopathy, or myelopathy.² Conservative treatment is initially recommended for patients who do not have a significant neurological deficit; surgery is indicated for

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patients with moderate-to-severe myelopathy, or patients with unremitting and progressive symptoms that have failed nonoperative treatment.³

Since the first anterior cervical decompression and fusion (ACDF) was introduced in 1958,⁴ the procedure has become the gold-standard operation for single or multiple levels of degenerative cervical spondylosis.^{5,6} Traditionally, iliac bone graft was used; however, cervical cages were introduced to avoid donor-site complications such as hematoma, infection, and pain. Anterior plate is commonly added in order to reduce the incidence of pseudarthrosis and enhance construct stability. Although current anterior plates are thinner than earlier designs, there are still some potential plate-related complications such as dysphagia and adjacent-level ossification (ALO).⁷⁻¹¹

To avoid these complications, stand-alone cages had been advocated by some surgeons. Nevertheless, cage dislocation, subsidence, nonunion, and sagittal malalignment of stand-alone cages are still of great concern.^{12,13} Zero-profile anchored spacer (Zero-P) is likely to provide immediate stability and prevent plate-related complications by virtue of the advantages of stand-alone cage and anchoring screws fixation. Nowadays, Zero-P devices are developed from different companies with different designs.

Some studies have tried to investigate the differences between Zero-P and plate-cage construct (PCC) on the clinical outcomes and complication rates in the treatment of cervical spondylosis. Most of these studies agreed that the Zero-P group had similar clinical outcomes and fusion rate compared to the PCC group, but no consensus on complication rates, especially dysphagia, has been reached.¹⁴⁻²⁵ It is unknown whether the differences in the literature have been mostly due to the limitation of sample size or genuine heterogeneity. In this study, we sought to conduct a systematic review and meta-analysis from published studies to evaluate whether Zero-P could reduce the complication rates, while maintaining fusion rate and clinical outcomes similar to or even better than that of PCC.

Methods

Search strategy

The primary source of the reviewed studies was PubMed and EMBASE. The search included literature exclusively in English published up to May 27, 2015. The following search terms were used: 1) anchored cage OR anchored spacer; 2) zero-profile OR integrated plate OR self-locking stand-alone; 3) cervical; 2) and 3). Reference lists of all included studies were scanned to identify additional potentially relevant studies. Two reviewers independently screened the

titles and abstracts of identified papers, and full text copies of all potentially relevant studies were obtained.

Inclusion criteria

Studies were included if they met the following criteria: 1) study design: prospective or retrospective comparative study; 2) patients with cervical spondylosis, including neck pain, radiculopathy, or myelopathy, who had one-to-four levels operation; excluding patients with tumor, trauma, infection, previous surgery, revision surgery, and hybrid surgery; 3) purpose of interventions: to compare clinical outcome differences between Zero-P and PCC; 4) outcome measurements: clinical evaluations including Japanese Orthopedic Association (JOA) and Neck Disability Index (NDI); radiological evaluations including cervical lordosis, fusion rate, and subsidence; complications including dysphagia; 5) more than 12-month mean follow-up term; 6) English studies. Studies that did not meet the above criteria were excluded from selection.

Data extraction

The following information was extracted from each study:

- 1) study ID; 2) study design; 3) study location; 4) etiology; 5) number of cases; 6) length of follow-up; 7) number of surgical levels; 8) preoperative and postoperative JOA scores; 9) preoperative and postoperative NDI scores; 10) fusion rate; 11) subsidence; 12) dysphagia; 13) other complications.

Data analysis

Statistical analysis was conducted using the Review Manager software (RevMan Version 5.2; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). Heterogeneity was tested using the chi-square test and quantified by calculating the I^2 statistic, in which $P < 0.05$ and $I^2 > 50\%$ was considered statistically significant. For the pooled effects, weighted mean difference (WMD) was calculated for continuous variables according to the consistency of measurement units, and odds ratio (OR) was calculated for dichotomous variables. Continuous variables are presented as mean differences and 95% confidence intervals (CIs), whereas dichotomous variables are presented as ORs and 95% CI. Random-effects or fixed-effects models were used depending on the heterogeneity of the studies included. Publication bias was tested using a funnel plot.

Results

Characteristics of studies

A total of 376 papers were identified by screening the titles and abstracts; 339 papers were excluded due to duplicates,

irrelevant studies, case reports, revision surgeries, hybrid surgeries, non-English studies, and reviews. The remaining 37 papers underwent a detailed and comprehensive evaluation (Figure 1). Biomechanics studies, noncomparative studies, and studies with less than 12-month follow-up were excluded. Twelve studies were finally included in this meta-analysis.^{14–25} Information of all the studies was listed (Table 1).

Quality assessment

Two investigators evaluated each study and extracted data independently, and any controversies were resolved via discussion. The major baseline characteristics of participants in each study were similar. Newcastle–Ottawa scale was used to assess the quality of included studies. Of the studies, one scored 9 points, ten scored 8 points, and one scored 7 points; it indicated that all the studies were of a relatively high-quality (Table 1).

Preoperative JOA score

The preoperative JOA scores were analyzed in seven studies. Statistical data of one study were unavailable. Six studies and 350 cases were involved including 162 cases of Zero-P

and 188 cases of PCC. There was no significant difference in the preoperative JOA score between Zero-P group and PCC groups ($P>0.05$, WMD -0.23 [$-0.57, 0.11$]; Figure 2). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.19$).

Postoperative JOA score

The postoperative JOA scores of the final follow-up time were analyzed in seven studies. Statistical data of one study were unavailable. Six studies and 350 cases were involved including 162 cases of Zero-P and 188 cases of PCC. There was no significant difference in the postoperative JOA score between Zero-P and PCC groups ($P>0.05$, WMD 0.07 [$-0.24, 0.38$]; Figure 2). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.66$).

Preoperative NDI score

The preoperative NDI scores were analyzed in four studies. Statistical data of one study were unavailable. Three studies and 152 cases were involved including 71 cases of Zero-P and 81 cases of PCC. There was no significant difference in the preoperative NDI score between Zero-P and PCC groups ($P>0.05$, WMD 0.76 [$-0.27, 1.79$]; Figure 2). The χ^2 test

Figure 1 Flow chart of study selection.

Table 1 Characteristics and quality assessment of included studies

References	Design	Country	Number of cases		Etiology	Levels of operation	The mean follow-up term (months) ^a		Newcastle-Ottawa scale
			Zero-P	PCC			Zero-P	PCC	
Lee et al ¹⁴	Nonrandomized retrospective comparative	Korea	23	18	Neck pain, radiculopathy	One	12.57±2.09	28.89±20.24	7
Shi et al ¹⁵	Nonrandomized retrospective comparative	People's Republic of China	18	20	Myelopathy	Three	30.5±3.4	30.1±2.8	8
Wang et al ¹⁶	Nonrandomized retrospective comparative	People's Republic of China	30	33	Myelopathy, radiculopathy	One or two	24.1±7.8	23.8±8.2	8
Nemoto et al ¹⁷	Randomized prospective controlled	Japan	24	22	Radiculopathy	One	24 ^b	24 ^b	8
Vanek et al ¹⁸	Nonrandomized prospective controlled	Czech Republic	44	33	Radiculopathy	One or two	24 ^b	24 ^b	8
Yang et al ¹⁹	Nonrandomized retrospective comparative	People's Republic of China	23	28	Myelopathy	Three or four	14.6 ^c	14.6 ^c	8
Yang et al ²⁰	Nonrandomized retrospective comparative	People's Republic of China	30	32	Cervical spondylosis	One, two, and three	30.6 ^c	33.1 ^c	8
Wang et al ²¹	Nonrandomized retrospective comparative	People's Republic of China	22	25	Myelopathy	One	33.59±5.52	33.16±5.97	8
Li et al ²²	Randomized prospective controlled	People's Republic of China	23	23	Radiculopathy, myelopathy	One	24 ^b	24 ^b	9
Qi et al ²³	Nonrandomized retrospective comparative	People's Republic of China	83	107	Radiculopathy, myelopathy, myeloradiculopathy	One, two, and three	18.6±4.2	19.3±4.1	8
Miao et al ²⁴	Nonrandomized prospective controlled	People's Republic of China	39	50	Cervical spondylosis	One, two, and three	16.9 ^c	16.9 ^c	8
Hofstetter et al ²⁵	Nonrandomized retrospective comparative	USA	35	35	Cervical spondylosis	One, two, and three	13.0±1.6	14.8±2.1	8

Notes: ^aData are represented as mean ± standard deviation unless otherwise indicated. ^bNo standard deviation. ^cOnly mean values were reported.

Abbreviations: Zero-P, zero-profile anchored spacer; PCC, plate-cage construct.

Figure 2 Forest plot (fixed-effects model) illustrating the preoperative JOA score (2.1), the postoperative JOA score (2.2), the preoperative NDI score (2.3), the postoperative NDI score (2.4), and the preoperative cervical lordosis (2.5), postoperative cervical lordosis (2.6) in comparison between Zero-P and PCC groups.

Abbreviations: CI, confidence interval; IV, independent variable; JOA, Japanese Orthopedic Association; NDI, Neck Disability Index; PCC, plate-cage construct; Zero-P, zero-profile anchored spacer.

indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.15$).

Postoperative NDI score

The postoperative NDI scores at the 3rd month were analyzed in four studies. Statistical data of one study were unavailable. Three studies and 152 cases were involved including 71 cases of Zero-P and 81 cases of PCC. There was no significant difference in the postoperative NDI score between Zero-P and PCC group ($P>0.05$, WMD 0.07 [−0.63, 0.76]; Figure 2). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.85$).

Preoperative cervical lordosis

Preoperative cervical lordosis was analyzed in seven studies. Statistical data of two studies were unavailable. Five studies and 290 cases were involved including 139 cases of Zero-P and 151 cases of PCC. There was no significant difference in preoperative cervical lordosis between Zero-P and PCC groups ($P>0.05$, WMD 1.07 [−0.34, 2.49]; Figure 2). Moderate heterogeneity existed between these studies ($I^2=58\%$, $P=0.14$).

Postoperative cervical lordosis

Postoperative cervical lordosis at the 12th month was analyzed in four studies, in which 239 cases were involved including 116 cases of Zero-P and 123 cases of PCC. There was no significant difference in postoperative cervical lordosis between Zero-P and PCC group ($P>0.05$, WMD 0.79 [−0.65, 2.22]; Figure 2). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.28$).

Fusion rate

Five studies provided a postoperative (final follow-up) fusion rate. Here, 412 cases were involved including 189 cases of Zero-P and 223 cases of PCC. Fusion rates in Zero-P group were 100% in Shi et al,¹⁵ 100% in Wang et al,¹⁶ 100% in

Yang et al,¹⁹ 100% in Qi et al²³ and 95.2% in Hofstetter et al.²⁵ In comparison, fusion rates in the PCC group were 100% in Shi et al,¹⁵ 100% in Wang et al,¹⁶ 100% in Yang et al,¹⁹ 100% in Qi et al²³ and 96% in Hofstetter et al.²⁵ A cross-study analysis was calculated to measure the homogeneity of outcomes. P -values of each study with the other four studies were analyzed in Zero-P and PCC group, and P -values were all >0.05 except for the study of Hofstetter et al.²⁵ However, the sample number of this study was small and fusion rates of all five studies were similar. All data for five studies were involved in the final statistical analysis, where no significant difference was found in fusion rate between Zero-P and PCC groups ($P=0.468$).

Subsidence

Subsidence was analyzed in three studies. Here, 125 cases were involved including 65 cases of Zero-P and 60 cases of PCC. The Zero-P group had a significantly higher subsidence rate than the PCC group ($P<0.05$, risk difference =0.13, 95% CI 0.00–0.26; Figure 3). Mild heterogeneity existed between these studies ($I^2=28\%$, $P=0.04$).

Postoperative dysphagia rate within the first 2 weeks

Postoperative dysphagia rates within the first 2 weeks were analyzed in nine studies. Statistical data of one study were unavailable. Eight studies and 582 cases were involved including 279 cases of Zero-P and 303 cases of PCC. The Zero-P group had a significantly lower dysphagia rate than the PCC group ($P<0.05$, OR=0.64, 95% CI 0.45–0.91; Figure 4). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.01$).

Postoperative dysphagia rate at the 6th month

Four studies reported postoperative dysphagia rates at the 6th month. Here, 377 cases were involved including 167 cases of Zero-P and 210 cases of PCC. The dysphagia rate

Figure 3 Forest plot (fixed-effects model) illustrating the subsidence rate of meta-analysis in comparison between Zero-P and PCC groups.

Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; PCC, plate-cage construct; Zero-P, zero-profile anchored spacer.

Figure 4 Forest plot (fixed-effects model) illustrating the postoperative dysphagia rate within the first 2 weeks (4.1), at the 6th month (4.2), and at the final follow-up time (4.3) of meta-analysis in comparison between Zero-P and PCC groups.

Abbreviations: CI, confidence interval; M-H, Mantel-Haenszel; PCC, plate-cage construct; Zero-P, zero-profile anchored spacer.

was significantly lower in the Zero-P group compared to the PCC group ($P<0.05$, OR =0.20, 95% CI 0.04–0.90; Figure 4). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.04$).

Postoperative dysphagia rate at the final follow-up time

Postoperative dysphagia rates at the final follow-up time were analyzed in seven studies, 566 cases were involved including 266 cases of Zero-P and 300 cases of PCC. The Zero-P group had a significantly lower dysphagia rate than the PCC group ($P<0.05$, OR =0.13, 95% CI 0.04–0.45; Figure 4). The χ^2 test indicated no statistical evidence of heterogeneity ($I^2=0\%$, $P=0.001$).

Publication bias

The Stata 12.0 software (StataCorp LP, College Station, TX, USA) was used to examine the publication bias of the main results. All funnel plots were largely symmetric including preoperative and postoperative JOA and NDI, cervical lordosis, subsidence, and postoperative dysphagia rate within the first 2 weeks (Figure 5). These results indicated that publication bias might not play a vital role in the observed effects and the conclusions were reliable.

Discussion

ACDF is considered the standard operation for cervical spondylosis when nonoperative treatment fails. The outcomes of ACDF depend on direct decompression, stability of fused

Figure 5 Funnel plot analysis of studies on the preoperative JOA score (A), the postoperative JOA score (B), the preoperative NDI score (C), the postoperative NDI score (D), the preoperative cervical lordosis (E), the postoperative cervical lordosis (F), postoperative dysphagia rate within the first 2 weeks (G), at the 6th month (H), and at the final follow-up time (I), and the subsidence rate (J) that shows publication bias.

Abbreviations: JOA, Japanese Orthopedic Association; MD, mean difference; NDI, Neck Disability Index; OR, odds ratio; SE, standard error; RD, risk difference.

segment, restoration of cervical lordosis, and avoidance of complications. To achieve these objectives, a series of cages and plates were designed. Zero-P was approved by the US Food and Drug Administration in 2008. It utilizes an integrated, anchor design to avoid protrusion in front of the vertebral body, which is likely to provide immediate stability and prevent plate-related complications. Biomechanical studies reported that Zero-P provided a similar stability to PCC in one-level ACDF,²⁶ although it might not provide adequate segmental stability in multilevel ACDF,^{27,28} the encouraging clinical outcomes were reported in one or multiple levels ACDF surgery.¹⁴⁻²⁵ However, conflicting results existed in different studies with regard to complications, especially dysphagia. To verify the conclusion of clinical outcomes

based on the latest high-quality studies for strong evidence, we systematically compared Zero-P with PCC in terms of clinical outcomes and incidence of major complications in the treatment of one- or multiple-level cervical spondylosis.

In our meta-analysis, there were no statistically significant differences in preoperative or postoperative JOA and NDI scores between Zero-P and PCC groups. Visual Analog Scale (VAS) scores were also reported in four studies, but only one study provided the detailed data of arm or neck VAS score. No statistically significant differences were reported in preoperative or postoperative VAS scores between Zero-P and PCC groups in these studies. All these available evidence indicated that the clinic evaluations of both Zero-P and PCC groups were similar.

Fusion is a basic goal of ACDF. The nonunion rate after ACDF can vary based on the number of levels fused, the type of allograft used, and the surgical technique. Fraser and Hartl reported an increased rate of nonunion for stand-alone cage surgery in comparison with PCC surgery in a meta-analysis.²⁹ The nonunion rate increased from 7.9% for one-level, 21.1% for two-level, to 35% for three-level stand-alone cage surgery. In comparison, a significantly lower nonunion rate (2.9% one-level, 4.1% two-level, and 17.5% three-level) was detected when an additional plate was used. Symptomatic pseudarthrosis needs a revision surgery. Although it might not provide adequate segmental stability like PCC in multilevel ACDF, Zero-P was more stable than stand-alone cage not only in one but also in two or three levels.^{27,28} In this meta-analysis, we found a relatively high-fusion rate in both Zero-P and PCC groups and no statistically significant difference was observed between them. These results indicated that the Zero-P held the equivalent capability for solid fusion to that of PCC.

The occurrence of cage subsidence might be related to various factors including size, position, and contact surface ratio of a cage as well as bone density and applied distraction during surgery.¹⁷ Hida et al reported a 7% of subsidence rate in the stand-alone cage.³⁰ Although clinical outcomes of the patients affected by the cage subsidence were controversial, the secondary kyphosis of subsidence may be regarded as a risk factor contributing to the progression of degenerative changes in adjacent segments.¹⁷ Subsidence rate after ACDF varied from 5.4% to 55.6% depending on the surgical method.^{31–35} The reported subsidence rates of Zero-P were not accordant, one study reported that it was higher than that of PCC,¹⁵ while another study reported that it was similar.¹⁷ In this meta-analysis, we found that the Zero-P group had a higher subsidence rate than the PCC group, however, no statistically significant difference was found in cervical lordosis.

Dysphagia is a common complication of ACDF. The incidence of dysphagia was between 2% and 67%.^{7–10} In the majority of cases, dysphagia resolves within the first 3 months; however, in 12.5%–35.1% of patients, dysphagia persists for more than 3 months.⁸ Postoperative soft tissue swelling, hematoma at the operative site, esophageal injury, and adhesion formation around implanted cervical plates may be possible reasons for dysphagia.⁷ Dysphagia was also related to the thickness of the anterior plate at the fusion level.³⁶ In this meta-analysis, we analyzed postoperative dysphagia rates at three different time points including within the first 2 weeks, at the 6th month and at the final

follow-up time. The Zero-P group had statistically significant lower postoperative dysphagia rate than the PCC group at all three time points.

ALO was considered as another plate-related complication. Park et al reported a positive association between the plate-to-disc distance and ALO following anterior cervical plate procedures.¹¹ The incidence of ALO was significantly increased when the distance was below 5 mm. Two included studies reported that Zero-P surgery could reduce the incidence of ALO than PCC surgery.^{17,20} However, an obvious limitation was that the follow-up terms of both studies were not sufficient. Mean follow-up terms of both studies were <33 months, and no other studies reported ALO. Longer follow-up term and more related studies are needed for stronger evidence in future.

Temporary postoperative hoarseness was reported in both Zero-P and PCC groups. All other complications including hematoma, dual tear, screw loosening, dislocation, and infection had been seldom or not reported in all these studies. It might indicate that both Zero-P and PCC surgeries are relatively safe.

However, there are some limitations to this meta-analysis. First, all the included publications are English language, thus a potential language bias maybe exist in this meta-analysis. Second, the sample size is not large enough to find the possible existing evidence, more included studies are needed. Third, there was a variable length of follow-up between the studies, which is important for evaluating good surgery results. Lastly, clinical heterogeneity might be caused by the various indications for surgery and the surgical technologies used at the different treatment centers. In summary, our meta-analysis suggested that, in the treatment of cervical spondylosis, the Zero-P group had a higher subsidence rate and lower postoperative dysphagia rate when it maintained the similar clinical outcomes compared to the PCC group. We believe that Zero-P implant is a viable alternative to ACDF in patients with cervical spondylosis, especially when it is applied in one-level ACDF surgery. However, longer follow-up term and more randomized prospective studies especially on multilevel Zero-P surgery are needed.

Conclusion

In this meta-analysis, we systematically compared Zero-P with PCC with regard to clinical outcomes and incidence of major complications in the treatment of one or multiple levels of cervical spondylosis. No statistical difference was observed in JOA score, NDI score, cervical lordosis, and fusion rate between Zero-P and PCC groups. Although the

Zero-P group had a higher subsidence rate than the PCC group, Zero-P had a lower postoperative dysphagia rate and might have a lower ALO rate. However, the evaluation criteria of fusion in the studies were not accordant, which might result in a deviated outcome. Larger-scale and higher-quality studies with longer follow-up terms are needed to provide more reliable evidence for future evaluation.

Disclosure

The authors report no conflicts of interest in this work.

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