Clinical improvement, fusion rate, and incidence of major complications of anterior cervical discectomy and fusion using a zero-profile implant versus a standard interposition graft with anterior plating regard to: a meta-analysis

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Abstract

Purpose A meta-analysis was conducted to determine whether the use of a zero-profile (Z-P) implant could reduce the complication rate of anterior cervical discectomy and fusion (ACDF), while maintaining similar clinical results to that of standard interposition graft with anterior plating (A-P).

Methods A Medline search was performed to identify relevant studies. Statistical analyses were conducted to calculate the relative risk (RR) and 95% confidence intervals (CI) of dichotomous variables, while the weighted mean difference (WMD) was used to compare continuous variables according to the consistency of measurement units. Results Nine articles met our inclusion criteria. There were no significant differences in surgical duration between the Z-P and A-P groups; however, intraoperative blood loss was less in the Z-P group than in the A-P group ($p=0.0008$). Moreover, there was no significance difference in the Japanese Orthopedic Association (JOA) score or the incidence of adjacent segment disease (ASD) between the two groups. But, the degree of cervical lordosis was greater in the A-P group than in the Z-P group ($p<0.00001$). More importantly, the Z-P group had a lower rate of dysphagia at 2 weeks after surgery and at the end of the follow-up period (RR=0.34; $p=0.0005$ and RR=0.12; $p=0.0001$, respectively). Conclusions Both Z-P and A-P implants are safe and efficacious for use in ACDF procedures in terms of JOA scores, while the ASD rate was similar between groups. However, the Z-P device is easier to insert, results in less blood loss, and a decreased incidence of postoperative dysphagia.
Introduction

Anterior cervical disectomy and fusion (ACDF) techniques are the gold standard for treatment of cervical degenerative disk disease when conservative therapy fails. Currently, the anterior locking plate (A-P) with a stand-alone cage is the standard procedure for ACDF, in which the plates used to stabilize the cervical spine form a rigid fixation implant that decreases the risk of non-union. However, these plates may be insufficient to maintain lordosis of the cervical spine, particularly in multilevel cases [1-3]. Moreover, the use of an A-P device may cause other complications, such as screw or plate dislodgement, soft-tissue injury, and dysphagia, and may also significantly increase the incidence of adjacent level degeneration (ASD) [4-6]. In order to reduce the potential complications of A-P with a stand-alone cage, the zero-profile (Z-P) implant was introduced as a simple procedure that does not require as much exposure as an A-P. Moreover, the use of a Z-P implant can lower the incidence of dysphagia and ASD [7, 8]. However, no consensus on the use of a Z-P implant has been reached, as various studies have yielded conflicting results [3, 5-16]. Whether these differences in the findings of these previous studies are mostly due to limited sample size or genuine heterogeneity remains unknown. In order to solve this dispute of the two ACDF procedures, we performed a meta-analysis to compare clinical and radiographical outcomes as well as complications in the treatment of cervical spine disease between a Z-P implant versus standard interposition graft with A-P.

Patients and methods

Literature search strategy

We searched the MEDLINE database (http://www.ncbi.nlm.nih.gov/pubmed/) for articles published up to April 25, 2015, using the key words “cervical” and “zero profile” or “Zero-P.” In addition, we manually searched the reference lists of the retrieved articles that met our inclusion criteria. In studies where there were overlapping patients, of which criteria included the study period, hospitalization, and treatment information, we retained only the largest cohort to avoid the duplication of information. In cases where a particular study did not publish all demographics, efforts were made to contact the authors to obtain any missing data.

Inclusion/exclusion criteria

Two authors (Yi Zuo and Jing Zhou) reviewed the full texts. The inclusion criteria for this study were as follows: (1) all patients with cervical spine disease who underwent an anterior fusion procedure; (2) studies involving two cervical fusion groups (a Z-P implant vs. an A-P device); and (3) follow-up period of ≥12 months. The following articles were excluded: (1) articles written in languages other than English; (2) non-spine-related studies, reports with no clinical data, biomechanical cadaveric studies, and studies that lacked a control group; (3) studies that did not meet the inclusion criteria; (4) articles considered as duplicate publications; and (5) articles for which the full text was not available.
Study quality assessment
The quality of the included studies was independently assessed by two of the co-authors according to the Newcastle-Ottawa Scale (NOS). The NOS scores ranged from 0 to 9, with a score ≥ 6 indicating good quality.

Statistical analysis
Statistical analyses were conducted to calculate the relative risk (RR) and 95% confidence interval (CI) of dichotomous variables. The weighted mean difference (WMD) was used for comparisons of continuous variables according to the consistency of measurement units. Random effect or fixed effect models were applied according to the heterogeneity of the included studies. A RR of > 1.0 suggests poor outcomes for the Z-P group relative to the A-P group. Heterogeneity among studies was determined using the Q test and I² measure of inconsistency to assess the degree of heterogeneity. A probability (p) value of <0.05 and I² value of >50% were considered statistically significant. A funnel plot was created to explore the possibility of publication bias. All analyses were performed using Review Manager 5.2 software (http://tech.cochrane.org/revman).

Results
Characteristics of the included studies
A total of 31 articles were initially identified, but 19 were excluded after reviewing the titles and abstracts, which included unrelated studies, studies with a follow-up period of less than one year, imaging studies, studies focused on non-human subjects, and studies that did not describe surgical procedures. Three additional studies were excluded after reviewing the full text, thus a total of nine publications were further analyzed (Fig. 1) [3, 8-15]. The included studies were conducted in China [8-10, 13-15], the US [3], and South Korea [11, 12] (Table 1). Five studies included Japanese Orthopedic Association (JOA) scores [8, 10, 11, 14, 15]. Four studies described the surgical duration and amount of blood loss [3, 10, 11, 15]. Three studies included information regarding cervical lordosis [8, 13, 15]. Four studies mentioned the rate of dysphagia 2 weeks after surgery and six supplied the dysphagia rate at the end of the follow-up period [11, 12, 14, 15]. Four studies included the incidence of ASD (Table 2) [3, 9, 14, 15]. The quality assessment results are shown in Table 1.

Assessment of surgical parameters
Four studies described the surgical duration and amount of blood loss [3, 10, 11, 15]. As shown in Fig. 2, the Z-P group included 116 patients, while the A-P group included 127. There was no significant difference in the surgical duration between the Z-P and A-P groups (WMD = -8.63; 95% CI = -22.48–5.22; p = 0.22). However, there was a significant difference in the amount of the blood loss between the Z-P and A-P groups (WMD = -33.32; 95% CI = -52.75 to -13.89; p = 0.0008).

Assessment of JOA
Five studies included JOA scores at 12 months after surgery (Fig. 3A). The fixed-effects model was applied to compare the JOA scores between the two groups (heterogeneity, I² = 0%). There was no significant difference in JOA
scores between groups Z-P and A-P (WMD = 0.18; 95% CI = -0.11–0.47; \( p = 0.22 \)) was a significant difference in the degree of cervical lordosis between groups Z-P and A-P (WMD = -2.25; 95% CI = -3.67 to -1.43; \( p < 0.00001 \)).

### Assessment of cervical lordosis

Three studies compared the degree of cervical lordosis between groups Z-P and A-P (Fig. 3B). There was a significant difference in the degree of cervical lordosis between groups Z-P and A-P (WMD = -2.25; 95% CI = -3.67 to -1.43; \( p < 0.00001 \)).

### Assessment of ASD

Four studies included the incidence of ASD at 12 months after surgery. As shown in Fig. 3C, (WMD = 0.68; 95% CI = 0.28–1.65; \( p = 0.40 \)).

![Figure 1](image1.png)  
**Figure 1** | Three additional studies were excluded after reviewing the full text, thus a total of nine publications were further analyzed.

![Figure 2](image2.png)  
**Figure 2** | Assessment of surgical parameters in this research were measured.
Rate of dysphagia within 2 weeks after surgery and at the end of the follow-up period

Four studies evaluated the rate of dysphagia within 2 weeks after surgery (Fig. 3D). There was a significant difference in the rate of dysphagia within 2 weeks after surgery between groups Z-P and A-P (RR = 0.34; 95% CI = 0.19–0.62; p = 0.0005). We also compared the dysphagia score between the two groups at the end of the follow-up period and found that the incidence in group Z-P was significantly lower than that in group A-P (RR = 0.12; 95% CI = 0.04–0.34; p = 0.0001) (Fig. 3E).

Figure 3 | Assessment of JOA scores at 12 months after surgery was measured.

Publication bias and sensitivity analysis

The funnel plot showed that there was no significant publication bias among the included studies (Fig. 4).
Discussion

We selected nine comparative studies of Z-P versus A-P to assess which is the optimal surgical procedure for cervical degenerative disk disease. Although there was no randomized controlled trial (RCT) included in this meta-analysis, our findings revealed that there was moderate quality evidence indicating that Z-P implant conveyed the advantages of reduced blood loss, improved or maintained cervical lordosis, and reduced incidence of dysphagia, as compared to use of an A-P devise. Low-quality evidence indicated that there was no significant difference between the two procedures regarding surgical duration, JOA score, or ASD rate.

Surgical duration and intraoperative blood loss are important factors to assess surgical trauma. Our meta-analysis data showed that the surgical duration was similar between groups Z-P and A-P; however, the amount of intraoperative blood loss was significantly less in the Z-P group (WMD = -33.32; 95% CI = -52.75 to -13.89; p = 0.0008). In regards to the considerable variation in methodologies and surgical techniques both between and within the studies, the use of a Z-P implant actually did not require more exposure than the use of an A-P implant, as only exposure of the target disc was necessary to complete the fixation procedure, which might explain the reduced amount of blood loss.

The JOA score is one of the most important factors to evaluate nerve function after cervical spine surgery. We found that the therapeutic efficacy in terms of the JOA score was similar between the two groups. However, one might expect that with an appropriate diagnosis and adequate decompression, similar JOA scores would be achieved with the two different fixation devises. However, it seemed that the outcomes of the A-P group were superior to those of the Z-P group in terms of maintenance of cervical physiological lordosis. A possible reason for this result is that the A-P implant provides multiple points of distraction and the vertebral body is pulled toward the ventral plate, which can more easily restore lordosis [16]. Although, postoperative global alinement was accumulated by placement of multiple convex Z-P spacers in the cervical spine, patients who received a Z-P implant seem to lose physiological lordosis somewhat within the 1-year follow-up period [17].

The occurrence of complications can severely impact intraoperative safety and treatment outcome. Cervical ASD is a degenerative condition at levels adjacent to the fused segments, which involves osteophyte formation, disc degeneration, spinal canal stenosis, and segmental instability [18]. However, the underlying mechanisms leading to these complications remain unclear. The Z-P implant was designed to prevent contact with adjacent levels and avoid interference with adjacent segments after implantation [17]. However, our pooled data demonstrated similar rates of ASD between the two ACDF procedures. A possible explanation for this observation may be that the two ACDF procedures both involve fusion implants, which impedes movement at the target segment. Dysphagia is an-
other well-known postoperative complication related to the anterior cervical plate following ACDF. The rate of dysphagia (> 3 months) has been estimated to range from 12.5% to 35.1% [19]. We found that the incidence of dysphagia in the A-P group was significantly higher than in the Z-P group at 2 weeks after surgery and at the end of the follow-up period (RR = 0.34; 95% CI = 0.19–0.62; p = 0.0005 and RR = 0.12; 95% CI = 0.04, 0.34; p = 0.0001, respectively). The mechanism may due to the placement of the anterior cervical locking plate directly posterior to the esophagus, which may impinge or irritate the esophagus [20]. Moreover, other possible suspected mechanisms for postoperative dysphagia in the A-P group included soft tissue edema, esophageal injury, postoperative hematoma, and adhesive formation around the implant. However, the use of a Z-P implant can overcome the shortcomings of A-P in regards to lowering the rate of dysphagia [3].

There were several limitations to this study that should be addressed. First, the number of included articles was somewhat limited. Second, different types of grafts, cages, and plates were used, which may have affected the accuracy of the conclusions. Third, the fusion rate data was insufficient to pool, thus a well-designed and long-term follow-up prospective RCT should be performed in the future.

In conclusion, the Z-P and A-P implants are both safe and effective ACDF procedures in terms of clinic results, and also have similar ASD rates. However, the Z-P device is more easily inserted with less blood loss and decreased incidence of postoperative dysphagia, thus the surgeon should select the most appropriate device for the individual patient.

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Competing interests none.

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