# Multilevel anterior cervical discectomy and fusion using zero-profile anchored cages: a minimum 5-year follow-up study

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**Research Article**

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## Abstract

***Background*** To evaluate the mid-term results of anterior cervical discectomy and fusion (ACDF) using zero-profile anchored cages for the treatment of multilevel degenerative cervical spondylosis.

***Methods*** Thirty-four patients aged 54.1±6.0 years (range, 41–64 years) who underwent 3- or 4-level ACDF with zero-profile anchored cages for degenerative cervical spondylosis in a single institute between 2014 and 2016 were included. Clinical outcomes were assessed using the visual analogue scale (VAS), modified Japanese Orthopaedic Association (mJOA) scores, and Neck Disability Index (NDI) preoperatively and postoperatively at the 1-, 2-, and 5-year follow-ups. Radiological outcomes including fusion rate, disc height (DH), subsidence, fused segment angle (FSA), and cervical lordosis (CL) were also assessed at the same intervals.

***Results*** The mean follow-up time was 68 months. All patients had significant recovery of neurological function. Compared with the preoperative scores, the postoperative VAS, JOA, and NDI scores were improved at each time point ($p$<0.05). The FSA and CL were improved at each follow-up time point after the operation($p$<0.05). All surgical segments were fused and there was 32 cage subsidence (30.2%) observed at the 5-year follow-up. The differences in VAS, JOA scores, NDI, fused segment angle, and cervical lordosis between the 5-year and the 2-year follow-up were not statistically significant($p$>0.05). The loss of lordosis was not related to symptoms.

***Conclusions*** ACDF using zero-profile anchored cages for multilevel cervical spondylopathy achieved satisfactory mid-term outcomes. Cage subsidence and loss of cervical lordosis mainly occurred duringthe first two years but remained stable afterward and were not related to symptoms.

## Background

Anterior cervical discectomy and fusion (ACDF) is increasingly used in multilevel degenerative cervical spine disorders. The anterior plate has been extensively used in ACDF to promote fusion, enhance fixation rigidity, improve sagittal alignment, and prevent graft subsidence[1]. However, the profile of the anterior cervical plate can lead to prolonged operation time and increased incidence of complications such as postoperative dysphagia, especially in multilevel diseases[2]. Therefore, a zero-profile implant was developed to overcome these setbacks and has been confirmed to be superior to the traditional cage-plate in their preliminary practice[2, 3]. It is well known that successful treatment with ACDF relies on adequate decompression and solid fusion rates with a low complication rate. However, the fusion rate was reported to decrease as the number of levels increased [4]. Hilibrand et al.[5] also reported that multilevel ACDF had a higher nonunion rate. In a meta-analysis by Liu et al.[6], this technique was associated with a higher rate of subsidence, although this risk did not lead to a clinical difference in disability or pain scores. In recent years, some researchers proposed that the biomechanical stability of self-locking stand-alone cages is not as great as cage-with-plate fixation in mid-term follow-up although their fusion rates are comparable[7]. Tsalimas et al.[8] found that one of the risk factors for dysphagia after ACDF is multilevel surgery. In a previous short-term follow-up study, the post-operative cage subsidence cervical lordosis, and the fused segment angle were relatively higher in multilevel ACDF using anchored cages than cages and plates[9]. However, there was a paucity of mid- to long-term results of these zero-profile cages in multilevel cases. In this study, we retrospectively reviewed a series of cervical spondylotic disorders treated with 3- or 4-level ACDF using zero-profile anchored cages that were followed for at least 5 years to investigate the correlation between their clinical results and radiological outcomes.

# Method

## Patient population and indications

This study was approved by The Ethics Committee of The Second Xiangya Hospital of Central South University (No. S043). Informed consent was obtained upon the final follow-up by written consent. From January 2014 to January 2016, our surgical team completed a total of 646 cervical spine surgeries. Among them, 34 patients, aged 54.1 ± 8.8 years (range, 41–64 years), with 20 male and 14 female, were finally analyzed. Patients were divided into 2 cohorts according to surgical levels which consisted of 30 patients of three levels and 4 patients of four levels (Table 1). The average operated levels per patient were 3.1. The process of case selection is shown in Fig. 1. The patient demographics are shown in Table 2. Preoperative X-ray, CT, and MRI were completed for each patient. The inclusion criteria were as follows: (1) cervical myelopathy or radiculopathy presented with a corresponding history and physical examination; and (2) three- or four-disc level compression on neurological structure visible on MRI. The exclusion criteria were: (1) developmental cervical spinal stenosis(DCSS); (2) ossification of the posterior longitudinal ligament of the cervical spine(OPLL); and (3) a history of cervical spinal surgery[10].

Table 1
The operated levels of the patients.

| **Operated levels** | **Number of patients** |
|---|---|
| 3 levels | 30 |
| *C3-6* | 18 |
| *C4-7* | 12 |
| 4 levels | 4 |
| *C3-7* | 3 |
| *C4-T1* | 1 |

Table 2
Demographic data of patients

| Patient No. | Sex | Age | Co-morbidities | Smoke or not | Patient No. | Sex | Age | Co-morbidities | Smoke or not |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Male | 41 | None | NOT | 18 | Male | 57 | Diabetes mellitus | Smoke |
| 2 | Male | 44 | None | NOT | 19 | Female | 53 | None | NOT |
| 3 | Male | 53 | Hypertension | NOT | 20 | Female | 59 | Diabetes mellitus | NOT |
| 4 | Male | 58 | Hypertension | Smoke | 21 | Female | 55 | None | NOT |
| 5 | Male | 59 | None | NOT | 22 | Male | 53 | None | NOT |
| 6 | Female | 44 | None | NOT | 23 | Male | 52 | None | Smoke |
| 7 | Male | 47 | None | NOT | 24 | Female | 51 | None | NOT |
| 8 | Male | 51 | None | NOT | 25 | Female | 49 | None | NOT |
| 9 | Male | 61 | None | Smoke | 26 | Female | 62 | Diabetes mellitus, Hypertension | NOT |
| 10 | Male | 57 | None | NOT | 27 | Female | 61 | None | NOT |
| 11 | Female | 51 | Hypertension | NOT | 28 | Male | 59 | None | NOT |
| 12 | Male | 59 | None | Smoke | 29 | Female | 44 | None | Smoke |
| 13 | Male | 48 | None | NOT | 30 | Male | 49 | None | NOT |
| 14 | Female | 57 | Diabetes mellitus | NOT | 31 | Female | 54 | None | NOT |
| 15 | Female | 63 | Diabetes mellitus | NOT | 32 | Male | 58 | Hypertension | NOT |
| 16 | Male | 61 | Hypertension | NOT | 33 | Female | 49 | None | NOT |
| 17 | Male | 58 | Hypertension | NOT | 34 | Male | 64 | Hypertension, Coronary artery disease | NOT |

# Surgical procedure

Neuroelectrophysiological monitoring, including evoked potential monitoring and electromyography monitoring, was used in every surgery. Under general anaesthesia, horizontal incisions were used, and all surgical procedures were performed by the same senior surgeon (Kuang) using a standard Smith-Robinson approach[11]. In the early 10 cases, we adopted a double transverse incision (one above and one below, about 4–6 cm each). As experiences accumulated, we realized that the skin of the neck and the platysma muscles were relaxed which can be mobilized. The surgical area of ACDFs was performed level by level and can be easily exposed without much stress on the esophagus. Therefore, all the following patients were treated with a single transverse incision (about 8–10 cm). The disc and cartilaginous disc endplates were carefully removed, and care was taken to avoid excessive damage to the bony endplate. The posterior osteophytes were removed by curettes and Kerrison rongeurs. After complete decompression of the spinal cord and nerve roots, the ideal sizes of the cages (ROI-C® or ROI-MC$^+$®, LDR, France) were selected by radiographic-assisted trials. The width of the cage was determined by the distance between the two Luschka's joints, and the height of the cage was determined by different trials under radiography when trails are tightly fitted in the disc space without over distraction of the disc space or facet joints. Porous bioceramic artificial bone (Dragonbio®, Hubei, China) was used to fill in the cage in all patients[9]. After the insertion of cages, the self-retaining anchoring clips were inserted along the axis of the disc through the implant holder and then through the cage into the vertebrae. The ACDFs were performed level by level. Usually, the most prominent segment of compression was operated first, followed by the lower and then the upper segment. The wound was closed with absorbable undyed sutures (SXMD2B406, Johnsons & Johnsons, Shanghai, China), and a 15mm diameter of Silicone drain (Ande®, Shandong, China) was left post-operatively, which was usually removed when drainage was less than 30 ml per day. Patients were recommended to wear a neck brace for 4–6 weeks.

# Outcome assessment

# Clinical outcomes

The clinical outcomes, including the visual analogue scale (VAS), modified Japanese Orthopaedic Association (mJOA) scores, and Neck Disability Index (NDI), were assessed by two independent residents (Wang and Chen). Data were collected before surgery, 2 weeks, 3 months, 6 months after surgery, and 1, 2, and 5 years after surgery. As this study was designed to evaluate mid to long-term results, statistical analysis was performed only on data from preoperatively, 2 weeks, 1, 2, and 5 years postoperatively. Disagreements were resolved, and a consensus was reached through discussion with another independent expert (Lü).

# Radiological outcomes

The radiological outcome was assessed by two independent residents (Pan and Yuan). The interspinous motion (ISM) $< 1$mm and superjacent interspinous motion $\geq 4$mm confirm the fusion diagnosis on the 150% mag magnified flexion and extension radiographs[12, 13](Fig. 2). Pseudarthrosis rate is defined as the number of pseudarthrosis present divided by the total surgical segment. The disc height was defined as the mean value of the anterior disc height (ADH) and the posterior disc height (PDH). Subsidence was defined as the loss of the disc height more than 3 mm compared to two weeks after surgery[14]. The fused segment angle was defined as the angle formed by the upper endplate of the superior vertebral body and the lower endplate of the inferior vertebral body in a neutral position. Cervical lordosis (CL) was defined as the angle formed by the upper-end plate of C2 and the lower-end plate of C7 in a neutral position[9]. Discordant opinions about fusion and subsidence were resolved by discussion with another independent expert (Li), and a consensus was reached.

# Statistical analysis

The intraclass correlation coefficient (ICC) value was calculated to evaluate the intraobserver discrepancy when judging cervical lordosis, fused segment angle, and disc height, with a higher value indicating better reliability. In our study, the intra- and interobserver variability was evaluated by the intraclass correlation coefficient (ICC) based on the Shrout and Fleiss criteria for reliability testing (poor, ICC $< 0.40$; fair to good, ICC 0.40 to 0.75;

excellent, ICC > 0.75)[15]. Preoperatively and at each follow-up, outcomes were compared using the paired sample t-test. A *p*-value of < 0.05 was considered statistically significant.

# Results

## Clinical outcome assessments

The mean follow-up time was 68 months, with a female-to-male ratio of 0.7:1. No instances of perioperative cerebral fluid leakage, wound infection, or haematoma were reported in any patient. VAS score for neck pain decreased from a preoperative mean value of 7.8 ± 2.9 to 3.6 ± 1.9 after surgery ($p < 0.05$) and 1.6 ± 2.3 at 5-year follow-up($p < 0.05$). The mean arm pain VAS score reduced from 6.9 ± 2.9 before surgery to 2.9 ± 1.3 at post-operative evaluation($p < 0.05$) and 1.9 ± 1.4 at 5-year follow-up($p < 0.05$). The mean NDI score reduced from 33.62 ± 8.14 before surgery to 12.16 ± 6.33 at post-operative evaluation($p < 0.05$) and 8.25 ± 1.67 at 5-year follow-up($p < 0.05$), and the mean mJOA score increased from 10.3 ± 3.6 before surgery to 13.5 ± 2.4 at post-operative evaluation($p < 0.05$) and 14.5 ± 2.2 at 5-year follow-up($p < 0.05$). Compared with the preoperative values, the postoperative VAS, JOA, and NDI scores were improved at each time point. However, the differences in VAS scores, JOA scores, and NDI scores between the 5-year and 2-year follow-ups were not statistically significant ($P > 0.05$).

## Radiological outcomes

All surgical segments were fused through radiographs obtained at a 5-year follow-up. The mean change in cervical lordosis between 5 and 2 years was 0.9°±0.5°, which was much smaller than the 5.9°±2.9° between 2 years and immediately after surgery ($p < 0.05$). The mean change in the fused segment angle between 5 and 2 years was 0.7°±0.5°, which was smaller than the 5.5° ±3.1° between 2 years and immediately after surgery ($p < 0.05$). The mean change in the fused segment angle between 5 and 2 years was 0.7°±0.5°, which was smaller than the 5.5° ±3.1° between 2 years and immediately after surgery ($p < 0.05$). The mean change in disc height between 5 and 2 years was 1.2 ± 1.1 mm, which was smaller than the 5.1 ± 3.9 mm between 2 years and immediately after surgery ($p < 0.05$) (Fig. 3). The results showed that the intraobserver ICCs for CL, FSAs, and DH were 0.990, 0.982 and 0.984, respectively, while the interobserver ICCs were 0.976, 0.963, and 0.968, respectively. The difference in CL loss between the cases with and without pseudarthrosis, and cases with and without subsidence were statistically significant. ($p < 0.05$) (Table 3).

Table 3
The relationship between CL loss and radiological complications

| N = 34 | | | CL loss | *p*-value |
|---|---|---|---|---|
| Pseudarthrosis | with | 26 | 7.7 ± 1.4 | < 0.05 |
| | without | 8 | 12.0 ± 3.0 | |
| Subsidence | with | 13 | 10.6 ± 3.2 | < 0.05 |
| | without | 21 | 7.6 ± 1.2 | |

## Complications

Twelve patients complained of mild dysphagia within 24 hours of surgery. All 12 patients were treated with atomized inhalation for 2 weeks. Five patients recovered at 2 weeks and five at 3 months after surgery. The rest 2 patients had symptoms relieved at 6 months follow-up. Three patients developed mild hoarseness after surgery, which gradually improved after two weeks of atomization and disappeared entirely four weeks after surgery. A 59-year-old female patient who underwent three-level ACDF using anchored cages at C4-7 levels had C6/7 cage migration and clip loosening at 1-year follow-up. However, the ISM of C4/5, C5/6, and C6/7 was 0.5mm, 3.8mm, and 0.6mm, indicating that C4/5 and C6/7 have been fused (less than 1mm). The patient had no symptoms. The cage at C5/6 was found displaced at five years follow-ups without causing any discomfort, but the interspinous motion of C5/6 was less than 1mm (0.1mm), indicating that it has been fused (Fig. 4). In another patient, a 52-year-old female patient who underwent three-level ACDF using anchored cages at C4-7 levels had a clip breakage without displacement at C4/5 at the 3-year follow-up (Fig. 5). However, fusion was already achieved at this level, and her preoperative symptoms were improved at the moment so no treatment was given. Other postoperative complications such as cerebrospinal fluid leakage, wound infection, hematoma, and so on were not encountered (Table 4).

Table 4
Complications of the patients

| Complications | P.O | 2w P.O | 3m P.O | 6m P.O | 1y P.O | 2y P.O | 5y P.O |
|---|---|---|---|---|---|---|---|
| Dysphagia | 12 | 7 | 2 | 0 | 0 | 0 | 0 |
| CSF leakage | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Wound infection | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hematoma | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hoarseness | 3 | 3 | 0 | 0 | 0 | 0 | 0 |
| Re-operation | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Subsidence(levels) | 0/106 | 0/106 | 15/106 | 25/106 | 30/106 | 32/106 | 32/106 |
| Pseudarthrosis(levels) | / | / | 51/106 | 35/106 | 18/106 | 4/106 | 0/106 |
| Loss of lordosis(°) | / | / | / | / | 2.7 | 5.9 | 6.7 |
| Cage migration | 0 | 0 | 0 | 0 | 1 | 2 | 2 |
| Anchored clip breakage | 0 | 0 | 0 | 0 | 0 | 1 | 1 |

*CSF leakage* Cerebrospinal fluid leakage, *P.O* Immediately post-operatively, *2w P.O* 2 weeks post-operatively, *3m P.O* 3 months post-operatively, *6m P.O* 6 months post-operatively, *1y P.O* 1 years post-operatively, *2y P.O* 2 years post-operatively, *5y P.O* 5 years post-operatively

# Discussion

ACDF has been one of the standard treatments for cervical spondylopathy since it was first described in the 1950s[16, 17]. For multilevel lesions, although many prefer the posterior approach to achieve broader indirect decompression[18], the anterior approach has the characteristic of direct decompression of the neurological structures, less interference with posterior muscles, and hence less surgical trauma[19–22]. As experience with the anterior cervical plate has accumulated, the advantages of an enhanced fusion rate, better cervical spine realignment, and lordosis maintenance have been proven[23]. However, complications of dysphagia and tracheoesophageal lesions, which increase with the number of fusion levels[24, 25], are a concern[26, 27]. The zero-profile anchored cage, which integrates the stand-alone cage and the fixating screws or clips, has been developed to reduce the above complications and shorten the time of operation in multisegment disorder. Several studies have confirmed that these cages effectively avoid the complications of plates with similar surgical efficacy[22, 28]. However, few studies have reported mid- to long-term results.

Fusion

The reconstructed multiaxial CT scan has the best interobserver reliability of predicting pseudoarthrosis[29], so CT scans are used to evaluate for extragraft bone bridging (ExGBB) given its superior diagnostic qualities[13]. However, the evaluation of fusion status is either vague or subjective sometimes, as there are no specific parameters. And it is limited to findings derived from a static moment in time[13]. It fails to assess the dynamic changes during motion, which makes some cases of pseudoarthrosis seen only with movement. Song et al.[30] showed that using ISM ≥ 1 mm as the cutoff for detection of anterior cervical pseudarthrosis on radiographs magnified 150% and made with a superjacent interspinous motion of ≥ 4 mm yielded accuracies comparable with those of CT. In our study, we also found that patients who appeared to be fused on CT did not meet the ISM fusion standard(Fig. 6). In addition, some patients refused to take CT scans due to the high cost and time. To ensure the consistency of evaluation standards we use the ISM criterion to evaluate pseudarthrosis instead of CT.

A systematic review reported the results of ACDF using different kinds of implants[31]. The bone fusion rate was 88.6% in 5738 patients treated with a stand-alone cage (without a screw-plate or integrating fixation system), and the fusion rate was 91.4% in 3971 patients treated with a screw-plate system. Nevertheless, the highest fusion rate was 96.6% in 499 patients treated with a zero-profile anchored cage. The fusion rate of our 5-year follow-up study was 100%, which also proved that the zero-profile anchored cage achieved a satisfactory fusion effect. The zero-profile anchored cage we used was a cage with two anchoring clips. These unique structures offer a fixation mechanism that is similar to the function of a plate and screws[32]. Scholz et al.[33] found that the anchored spacer provided similar biomechanical stability to that of the established anterior fusion technique using an anterior plate and cage. In our study, we also found an excellent fusion rate with good stability. The self-locking clips ensure excellent primary stability of the implant and promote early fusion. Furthermore, the elastic modulus of the anchored cage is similar to that of bone, which theoretically helps to decrease the stress shielding effect and increase bony fusion. The anatomical shape of the anchored cage allows a wide grafting space and close contact between the endplate bone and the implant. In addition, this satisfactory fusion rate may be related to surgical techniques that include optimal preparation of the fusion bed and proper disc space distraction. Although clip fractures have occurred in these cases, they may collapse the intervertebral space, and fracture clips can limit the effect to some extent, resulting in a lack of apparent early instability. Similarly, despite the presence of cases of cage migration, the full clip can still have a limited effect; therefore, they ultimately achieve stable fusion.

The fusion rate at the 1-year follow-up of our series was 85.8%, with the extension of follow-up time, the fusion rate gradually increased to 100%. Our finding was consistent with the previous studies. Sun et al.[34] performed a 5-year 3-level ACDF study and found 81 surgical levels were completely fused at the 5-year follow-up, but six levels remained unfused in the first year after surgery. In a similar three-year study[35], the fusion rates at 1, 2, and 3 years after surgery were 77.9%, 94.1%, and 100%, respectively. In another study[36] involving 78 patients who also used the spinous processes criteria to assess fusion rate, all surgical levels were fused within the first year. Although the researcher claimed that the peak number of new fusion levels was 3–6 months postoperative, it also indicated that the overall fusion rate increased over time. The speed of fusion may relate to age[37], smoking[37], osteoporosis[38], diabetes,[39] drinking[39] and other factors. Indeed, of the 18 levels of pseudarthrosis (14 patients) at 1-year follow-up, 6 patients had been smoking for more than 20 years with at least one pack per day. At the 2-year follow-up, a total of 4 levels of pseudarthrosis (4 patients) were found, and 3 of them were long-term smokers. There were 3 out of the 5 diabetic patients had pseudarthrosis at 1-year follow-up, and two of them still had pseudarthrosis at 2-year follow-up. A total of one patient was both a chronic smoker and a diabetic. Unfortunately, It was not until the fifth year of follow-up that the patient achieved fusion at all surgical levels.

Subsidence

Subsidence is an adverse event after ACDF. Many studies have shown that cage subsidence is the main complication in ACDF with stand-alone cages regardless of the composite material[40–46]. In a systematic review comprising 4784 patients using single- and multilevel cages, the mean subsidence rate was 21.1%, ranging from 0 to 83%[47]. The subsidence of the cage causes loss of intervertebral disc height, which may result in the narrowing of the foramen, nerve root compression, and pseudarthrosis due to cervical instability[47]. Our previous study[9] indicated that subsidence occurs mainly in the early postoperative period. In this study, the subsidence rate was 14.3%. However, there was no new subsidence during 2 to 5 years of follow-up, which indicated that it occurred early after surgery. This was consistent with a prospective study conducted by Igarashi et al.[48] Most subsidence occurred in the first month after surgery, probably due to the great pressure applied to the interior endplate when patients got out of bed in the initial days following surgery [48]. Cho et al.[49] compared Zero-P (zero-profile cage with integrated screws) with a stand-alone cage without integrating a fixation system. In this comparison, the subsidence of the Zero-P was lower, which seems logical since the screws force the cage to be placed in the anterior cortical plane, and the screws themselves are placed cortically.

The endplate may be another factor affecting subsidence. Lowe et al.[50] performed compression tests on vertebral bodies under an intact endplate, partial and complete resection of the endplate, and compared the failure load of each group. They showed that the ultimate compressive strength of intact endplate vertebral bodies was significantly higher than that of vertebral bodies with endplate resection. The injury of the endplate of the vertebral body significantly increased the incidence of the deposition and displacement of the interbody fusion device. Therefore, the endplate should be handled gently to prevent injury to reduce the occurrence of the deposition of the interbody fusion device[51]. In our study, all of the surgeries were performed by the same surgeon with similar endplate preparation. However, the insertion of anchored clips through the cage we used would destroy the endplate to a certain extent, making it one of the factors leading to the inevitable subsidence.

The height and size of the cage are both related to subsidence. Truumees et al.[52] reported that higher distractive and compressive forces were recorded with larger grafts. Yamagata et al.[53] found that a cage height of 6.5 or 7.5 mm had a higher risk of cage subsidence than a height of 4.5 or 5.5 mm. This finding can be explained by the larger amount of stress on the vertebral endplates, which presumably results in subsidence. Yang et al.[54] found that the use of 14 mm anteroposterior diameter cages led to a significantly lower risk of subsidence than using 12 mm diameter cages. This is because the cage with a larger surface area reduces the pressure per unit area of the endplate, thus reducing the risk of subsidence. Combined with our study, we recommend minimizing overdistraction during surgery and using the widest cage to minimize the risk of subsidence.

Alignment

Loss of cervical lordosis after surgery is one of the major disadvantages of using a zero-profile anchored cage. Pereira et al.[55] reported that the use of multiple independent PEEK cages in the treatment of multilevel cervical spondylotic myelopathy achieved good intermediate results. A meta-analysis demonstrated that the cage-plate technique resulted in significantly greater cervical lordosis than the stand-alone cage technique[56]. Many degenerative patients have wedge-shaped vertebrae with a lower anterior wall and a higher posterior wall. Given the zero-profile cage with the same height from the front to back, the cervical lordosis could not be recovered or maintained without additional reduction force by the screw-plate system. In our study, the loss of cervical curvature occurred mainly in the early postoperative period. In our last 2-year follow-up study[9], the maintenance of cervical curvature in the early period after surgery was not ideal, and concerns have been raised to determine the association between the loss of curvature and symptoms. This study proved that the curvature tends to be stable after fusion. The clinical outcomes of all patients were maintained during the 5-year follow-up, indicating that the loss of cervical curvature to a certain distance was unrelated to postoperative symptoms. In our follow-up case, the largest change was from 22.5° immediately after surgery to 3.8° at the 5-year follow-up, but the patient's postoperative symptoms continued to improve. Nevertheless, we failed to determine a definite threshold due to the small sample size of our study. This finding was consistent with the study of Spanos et al.[57], who included single- or consecutive two-level ACDF with a PEEK interbody cage and reported that the slight increase in cervical lordosis after ACDF was lost at the 12-month follow-up but had no correlation with the pain or function of the subjects. The study of Godlewski et al.[58] also demonstrated that the greatest changes in lordosis and disc space height after ACDF were noted immediately after surgery but reduced over time, and this change was not correlated with clinical outcomes. Song et al.[59] compared the PEEK stand-alone cage group with the cage-plate group in 1- and 2-level ACDF. At approximately three years of follow-up, they found that the cage-plate group had a better sagittal alignment, a higher fusion rate, and lower cage subsidence. However, there were no significant differences in clinical outcomes between the two groups. They explained that the clinical sequelae resulting from loss of cervical lordosis may take years to develop and thus may not show up in these relatively short follow-ups. Meng et al.[60] reported a 3-level ACDF and hybrid cervical surgery study with a 5-year follow-up. They also found that there was no correlation between cervical balance and clinical outcomes. This result is also consistent with the results of this study, subsidence and cervical lordosis have no correlation with clinical outcomes.

Hoarseness and dysphagia

Voice hoarseness and dysphagia were prevalent postoperative complaints following ACDF surgery. Rates of immediate postoperative dysphagia after ACDF ranged from 1.7–67%[61], In multiple series, the rates of symptomatic postoperative recurrent laryngeal nerve palsies (RLNP) ranged from 0.9%-8.3%[62–65]. Gowd et al.[61] claim that swallowing dysfunction correlated with advanced age, a prior history of such dysfunction, longer surgical procedures, and a trend toward increased dysphagia with multilevel surgery attributed to greater soft tissue swelling/retraction injury. Tsalimas et al.[8] found that female sex, smoking, surgical approach, use of rhBMP-2, and multilevel surgery were risk factors for dysphagia after ACDF.

In our series, mild post-operative dysphagia was reported by 35.3% of patients at early postoperative follow-up. However, it improved over time and disappeared within six months after surgery (Table 3). It suggests that the onset of dysphagia in multilevel cases could be related more likely to the surgical procedure and soft-tissue swelling. For hoarseness, the primary mechanism of injury is through direct compression or traction of the RLN rather than accidental resection. The endotracheal tube cuff, when inflated, has been reported to exert direct compression forces that can induce nerve ischemia. Gowd et al. put forward that it is likely that there is an additive effect of retractor placement and increased endotracheal cuff pressure that results in voice hoarseness. Furthermore, increased BMI may increase intraoperative pressure and subsequently add to postoperative symptoms. These apparent findings may suggest that attention be paid to each of these contributions during surgery to minimize postoperative hoarseness[61].

Limitations

There were limitations of the study. This was a single-center, retrospective study with a relatively small number of patients. Confounding factors, such as patients' bone mineral density, history of medication, and other risk factors for bone fusion, were not fully excluded. Further prospective randomized multi-center studies with long-term follow-up are needed to investigate the correlation between clinical and radiological findings.

# Conclusion

ACDF using a zero-profile anchored cage achieved satisfactory clinical and radiological outcomes at the 5-year follow-up. Despite the persistent loss of disc height and cervical lordosis within 2 years post-operatively, the loss ceased from then on and was not correlated with the clinical results. However, as one of the most prominent radiological complications, the long-term effect of loss of cervical lordosis still needs investigation.

# Declarations


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### Ethical Approval

This study was approved by The Ethics Committee of The Second Xiangya Hospital of Central South University. Written informed consent to participate in the study was obtained from each participant.

### Consent to Publication

Not applicable.

### Competing interests

The authors have no conflict of interest

### Authors' contributions

KL and HHY contributed to the design of the study and wrote the manuscript. WXX, CZJ, PCY, and YH were responsible for data collection and supervision of the study. LGH and LYC performed statistical analysis. All authors read and approved the final manuscript.

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### Availability of data and materials

The results/data/figures in this manuscript have not been published elsewhere. nor are they under consideration by another publisher. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

**All information or images have been processed so that could not lead to the identification of a study participant**

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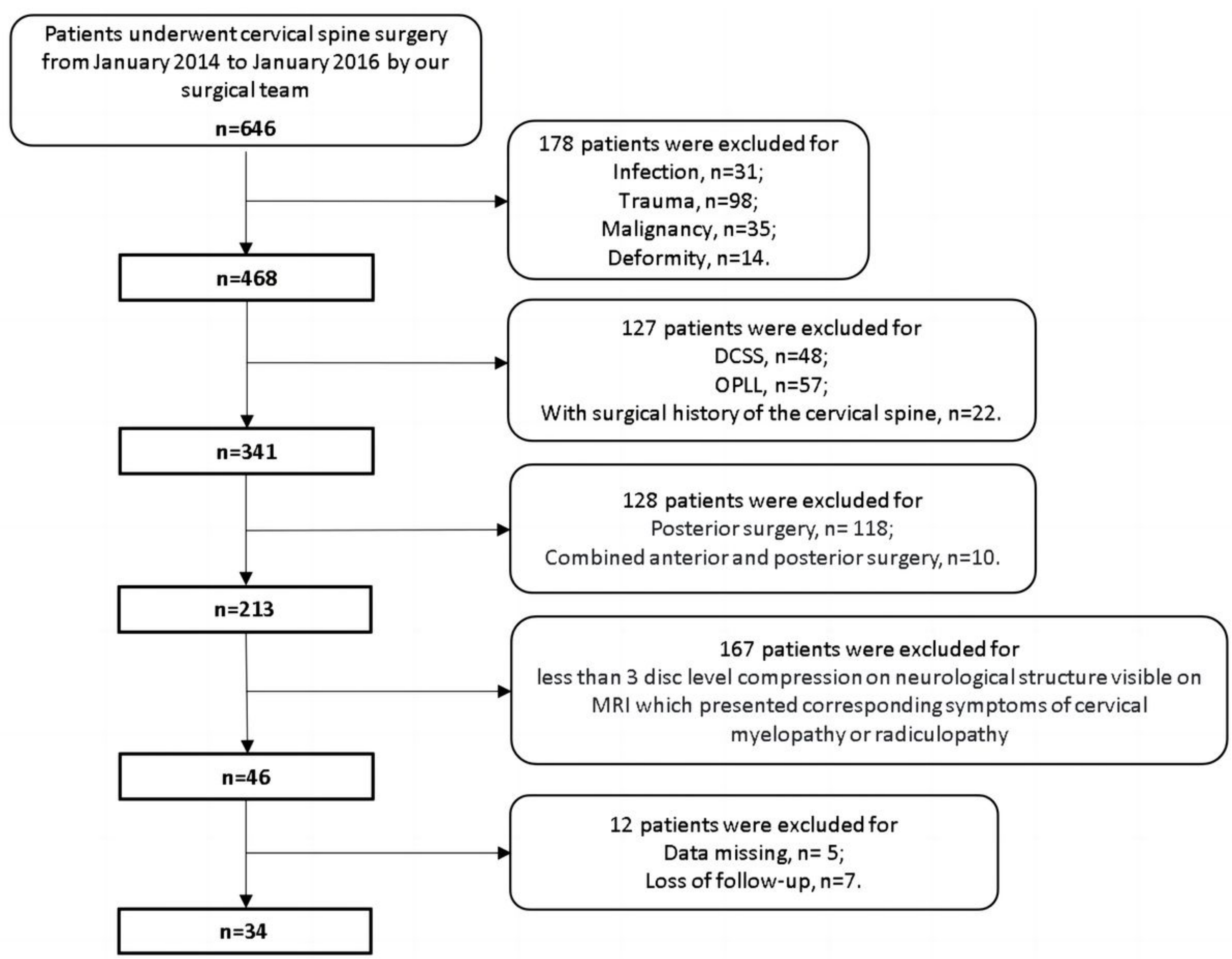
# Figures




## Figure 1

A flow chart of case selection of the study

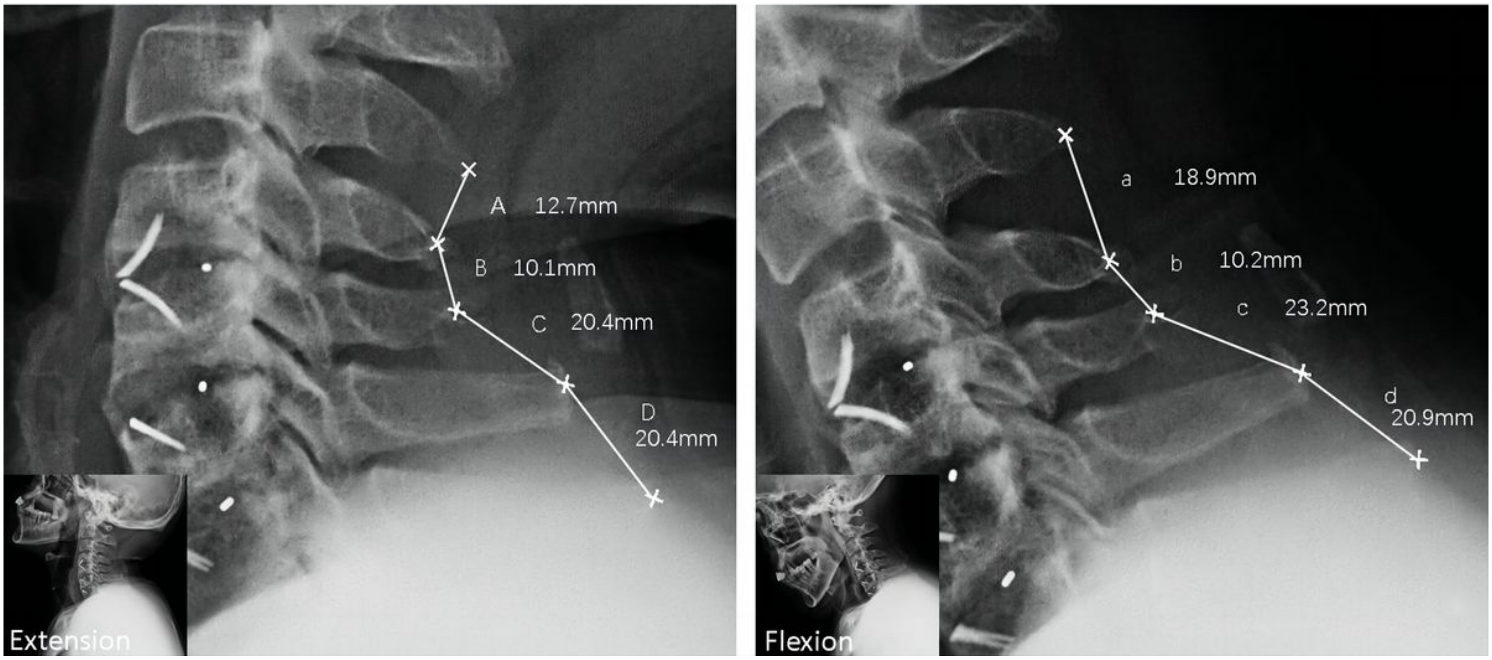



**Figure 2**

Measurement of interspinous movement (ISM) at superjacent level (C3-4) and operated levels (C4-7) on the 150% magnified flexion and extension radiographs. The superjacent ISM at C3-4 (A and a) was 6.2 mm, which indicated adequate dynamic motion ( ≥ 4 mm). ISM at C4-5 (B and b) and C6-7 (D and d) were 0.1 mm and 0.5mm, which were consistent with the definition of fusion ( < 1 mm). ISM at C5-6 (C and c) was 2.8 mm, which indicated pseudoarthrosis ( ≥ 1 mm).

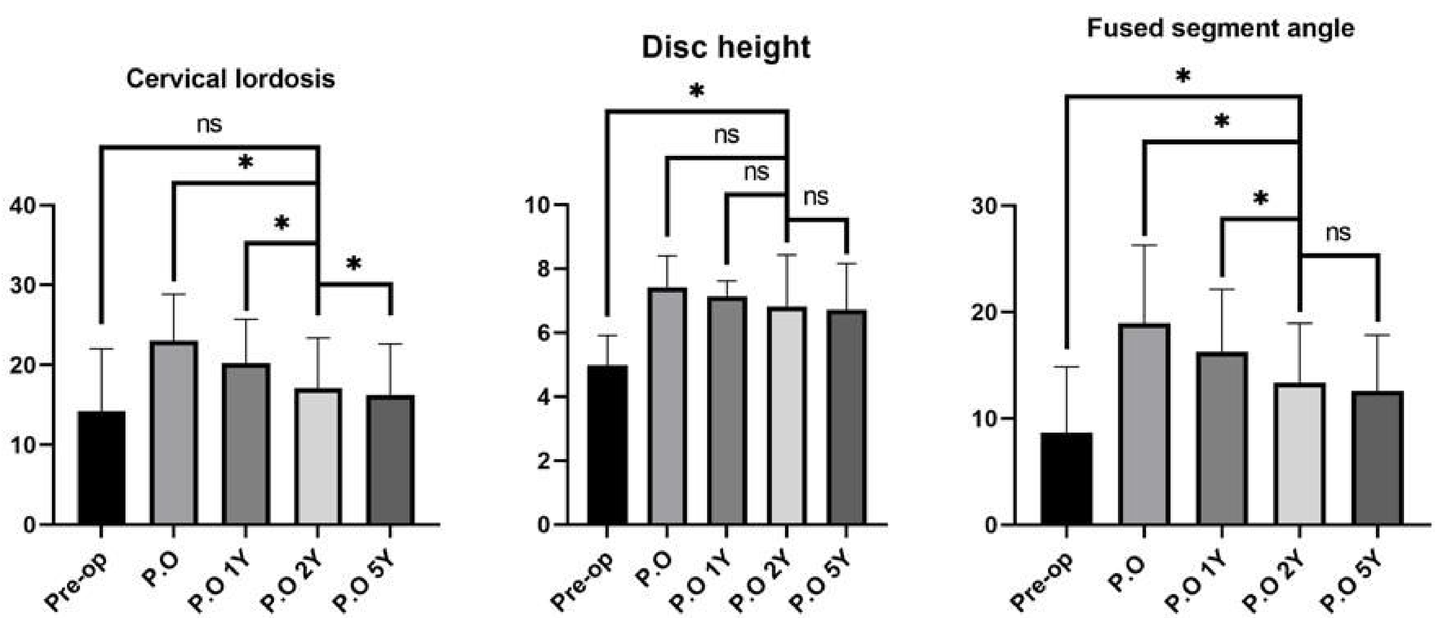



**Figure 3**

The radiological outcomes. a Cervical lordosis at each time point b Fused segment angle at each time point; c Disc height at each time point. Asterisk statistically significant compared between the two time points($p < 0.05$). NS, not statistically significant; Pre-op, pre-operation; P.O, post-operation; 1Y P.O, 1 year post-operatively; 2Y P.O, 2 year post-operatively; 5Y P.O, 5 year post-operatively.

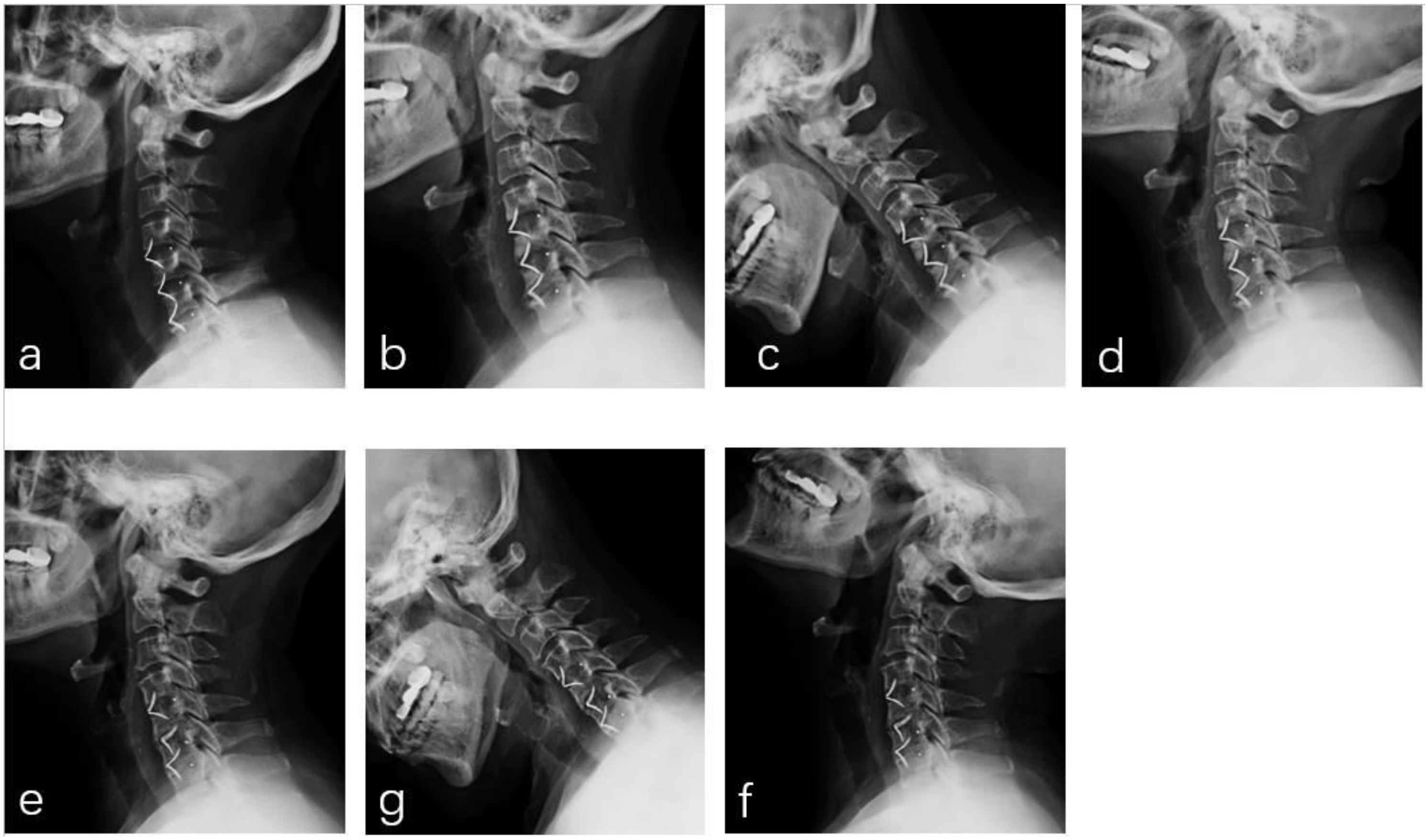



**Figure 4**

A 59-year-old female patient who underwent three-level ACDF using stand-alone cages at C4/5, C5/6, and C6/7 levels. a The post-operative lateral radiograph of the cervical spine; b The lateral radiograph of the cervical spine at 1 year after operation, the cage at C6/7 was displaced c and d The flexion-extension lateral radiograph of the cervical spine at 1 year after operation. The ISM of C4/5, C5/6 and C6/7 was 0.5mm, 3.8mm and 0.6mm, indicating C4/5 and C6/7 have been fused (< 1 mm) and C5/6 have not ( $\geq$ 1 mm) e The lateral radiograph of the cervical spine at 5 years after operation, the cage at C5/6 and C6/7 was displaced; f and g The flexion-extension lateral radiograph of the cervical spine at 5 year after operation showed the ISM of C4/5, C5/6 and C6/7 was 0.4mm, 0.1mm and 0mm, indicating that they were all fused.

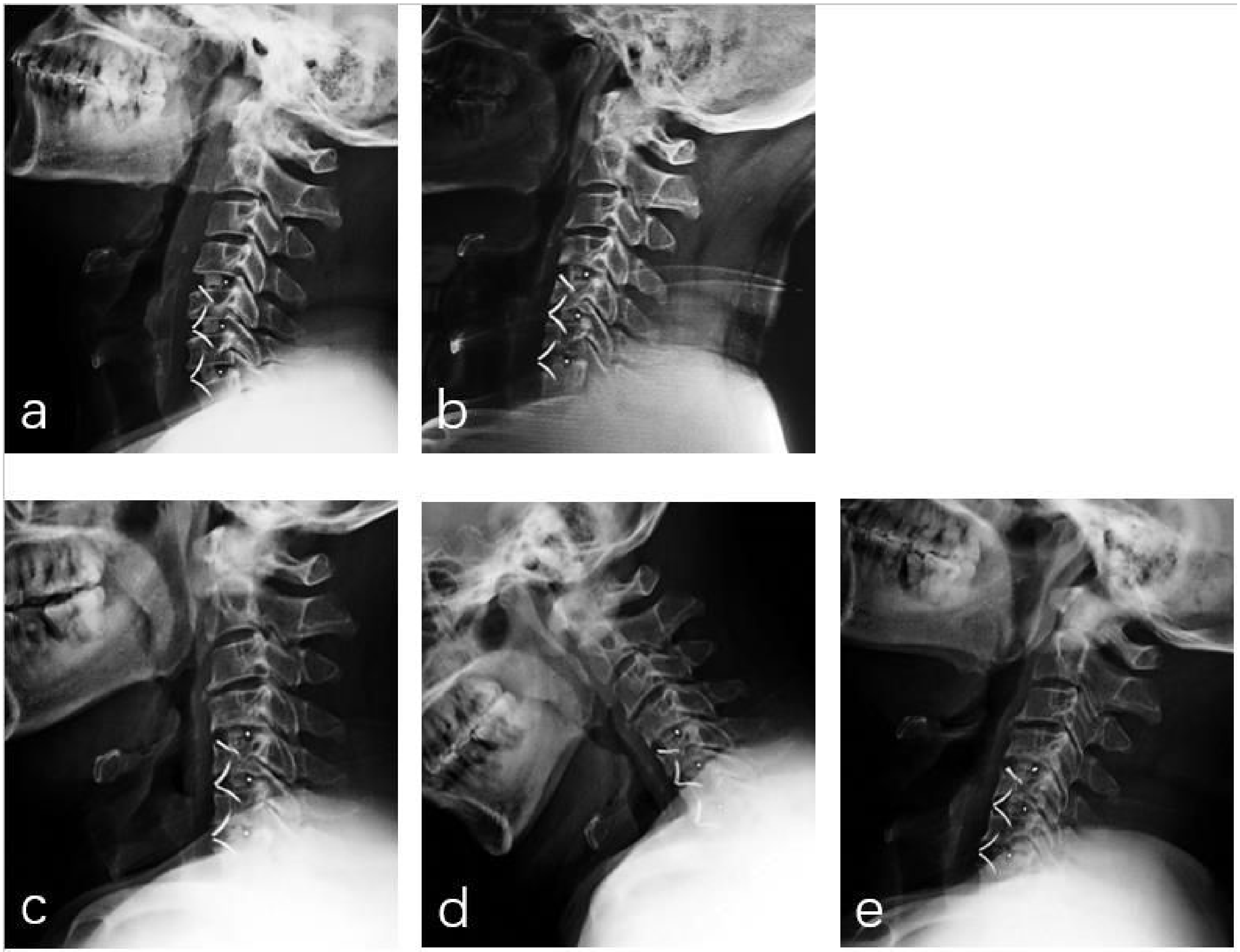



**Figure 5**

A 52-year-old female patient who underwent three-level ACDF using stand-alone cages at C4/5, C5/6, and C6/7 levels. a The post-operative lateral radiograph of the cervical spine; b The lateral radiograph of the cervical spine at 3 year after operation, clip fractures was found on the cage of C4/5; c, d, and e The lateral, flexion-extension radiograph of the cervical spine at 5 year after operation showed the interspinous motion of C4/5 was less than 1mm (0.5mm), indicating that it has been fused.

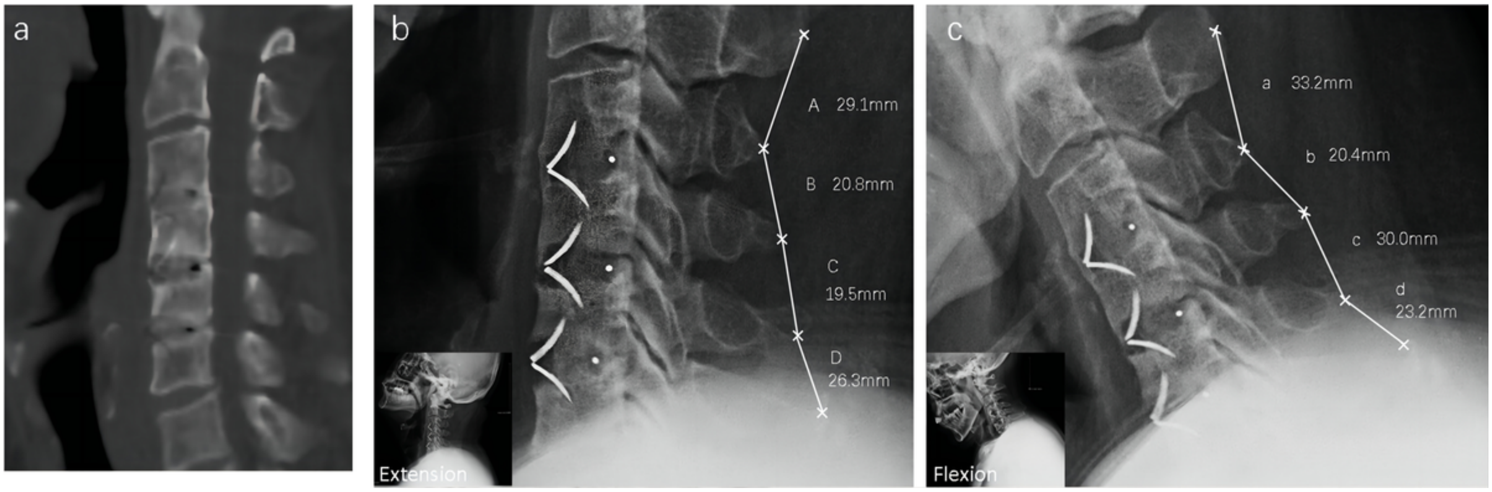



**Figure 6**

A 63-year-old male patient who underwent three-level ACDF using stand-alone cages at C3/4, C4/5, and C5/6 levels. a One-year postoperative CT scan; b and c One-year postoperative X-ray. In the patient's CT review one year after surgery, it was found that C3/4 had fused, and C5/6 seemed to have fused, but the X-ray showed that the ISM for C3/4 and C5/6 was 0.4mm and 2.9mm, respectively, indicating that C3/4 met the ISM fusion standard, while C5/6 did not.

# Supplementary Files

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