# Multilevel Anterior Cervical Diskectomy and Fusion with Zero-Profile Devices: Analysis of Safety and Feasibility, with Focus on Sagittal Alignment and Impact on Clinical Outcome: Single-Institution Experience and Review of Literature

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BACKGROUND: **In multilevel degenerative conditions posterior approaches are often preferred, but anterior approaches provide comparable clinical results and better alignment. Anterior plating entails higher rates of soft tissue injuries and dysphagia, particularly in multilevel cases.**

**This study evaluates efficacy and safety of zero-profile devices in 3- and 4-level anterior cervical diskectomy and fusion, analyzing patients' clinical and radiologic long-term outcomes.**

METHODS: **We prospectively enrolled 24 patients with cervical spondylotic myeloradiculopathy who underwent 3- and 4-level anterior cervical diskectomy and fusion with the zero-profile device. Mean follow-up was 39 months (range 24—72). Nurick grading was used for myelopathy, Neck Disability Index and Visual Analog Scale scores for arm and neck pain, and Short Form 36 survey for physical and mental health status. Postoperative radiograph and computed tomography were obtained after surgery, at 6 and 12 months, and at last follow-up to assess fusion rate and complications. Cervical alignment was measured by Cobb angle. Incidence of postoperative dysphagia was monitored according to Bazaz dysphagia index.**

RESULTS: **On last computed tomography scan, fusion was present in 49% of spaces (40 of 82). Mean neck and arm pain visual analog scale decreased from 6.7—1.6 ($P < 0.01$) and 5.9—0.9 ($P < 0.01$), respectively. Improvements in the Short Form 36 survey and Neck Disability Index were documented ($P < 0.01$). Lordosis was restored in all patients. Five of 24 patients complained of mild dysphagia (20.8%): in three (12.5%) short-term dysphagia and in two (8.3%) medium-term dysphagia. No long-term dysphagia (≥6 months) was observed.**

CONCLUSION: **Anterior cervical diskectomy and fusion with a zero-profile device is effective and safe for 3- and 4-level cervical spondylotic myeloradiculopathy. It allows to restore cervical lordosis and achieve long-term satisfactory clinical outcome.**

## INTRODUCTION

Anterior cervical diskectomy and fusion (ACDF) is still considered a safe and effective option in the surgical treatment of single- and double-level cervical degenerative disk disease not suitable for disk arthroplasty.[1,2] Conversely, the best surgical strategy (i.e., anterior vs. posterior approach) in 3- or 4-level cases is not established and controversy remains.

Posterior approaches are usually performed to address multilevel neural compression, but their use is limited because of postoperative complications and loss of lordosis, particularly in noninstrumented procedures (i.e., laminectomy or laminotomy).[3]

Multilevel ACDF could be a viable alternative; indeed, a direct control of the anterior cervical column provides adequate neural decompression and allows maintenance or satisfactory restoration of cervical spine sagittal alignment.[3,4]

**Key words**
- ACDF
- Cage
- Cervical spondylosis
- Lordosis
- Plate
- Sagittal alignment
- Zero-profile

**Abbreviations and Acronyms**
**ACDF**: Anterior cervical diskectomy and fusion
**CSM**: Cervical spondylotic myeloradiculopathy
**CT**: Computed tomography
**NDI**: Neck Disability Index
**PLL**: Posterior longitudinal ligament
**SD**: Standard deviation
**VA**: Variable angle
**VAS**: Visual analog scale

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Up to now, 3- and 4-level ACDF has not reached large consensus because a wide surgical exposure, with consequent visceral retraction, is required and long-segment anterior plating is often necessary if stand-alone interbody cages are implanted. Anterior plates in multilevel ACDF aim to increase fusion rates,[5-7] reduce instrument failures,[8] and prevent the development of late kyphotic deformities, as the plate allows to maintain or improve cervical lordotic alignment.[8,9]

However, anterior plating may also be associated with potential disadvantages and complications. Although modern anterior plates are low profile and soft tissue dissection, as well as microsurgery, allows adequate surgical exposure in multilevel cases without excessive retraction, the incidence of postoperative dysphagia after anterior plating, albeit transient, is still high.[10,11]

Integrated zero-profile cage-plate devices have been introduced in cervical spine surgery over the past years[12-16] with the aim to reduce morbidity associated with traditional anterior cervical plates, while maintaining the benefits of both intervertebral cages and plating.

The "Zero-P" cage-plate (DePuy Synthes, West Chester, Pennsylvania, USA) and its further evolution named "Zero-P VA" (variable angle) have been introduced to the market (Figure 1). Initial clinical reports on the use of these devices for ACDF showed satisfactory clinical and radiologic results in single- and double-level CSM.[2,13,17]

This prospective study focuses on the use of Zero-P and Zero-P VA devices in multilevel (i.e., 3- and 4-level) ACDF. Clinical and radiologic data of 24 patients were collected at long-term follow-up. Radiologic analysis focused on the comparison among preoperative, postoperative, and follow-up cervical sagittal alignment and investigated the correlation between clinical parameters and cervical sagittal alignement. Fusion rate and incidence and course of postoperative dysphagia were also analyzed.

## MATERIALS AND METHODS

### Patients

Between 2009 and 2013, we prospectively included 24 patients (14 male) who underwent 3- or 4-level ACDF with Zero-P devices (DePuy Synthes). Mean age was 58.4 (range 41—77), with a standard deviation of 10.6 years.

All patients suffered from symptomatic cervical spondylotic myeloradiculopathy (CSM), unresponsive to conservative treatment, involving 3 or 4 levels between C3—C4 and C6—C7. Clinical indications included radiculopathy, with or without neck pain, pyramidal signs (e.g., hyperreflexia, positive Babinski and/or Hoffmann signs, spasticity), gait, and urinary disturbances (Table 1). Patients with obvious signs of ossification of the posterior longitudinal ligament were considered not suitable for multilevel anterior approach and were treated with monolevel or multilevel somatectomies.

Fourteen patients (58.3%), with a mean age of 55.9 years, underwent 3-level surgery, whereas the remaining 10 patients (41.7%), with mean age of 61.7 years, underwent 4-level surgery. One patient included in the 3-level group was treated combining Zero-P devices with stand-alone cage: 1 stand-alone cage at C3—C4 and 2 Zero-P devices at C4—C5 and C5—C6.

Eighty-two cages were implanted in 24 patients. In 16 patients (66.7%, those operated before February 2013), the first type of cage-plate Zero-P device (i.e., the one with 4 screws) was used; in the remaining 8 patients (33.3%) the new Zero-P VA device was implanted (device with only 2 screws).

The C3—C4 level was treated in 18 patients (75%); C4—C5 and C5—C6 levels, respectively, were operated in all patients (100%) and C6—C7 level in 16 patients (66.7%).

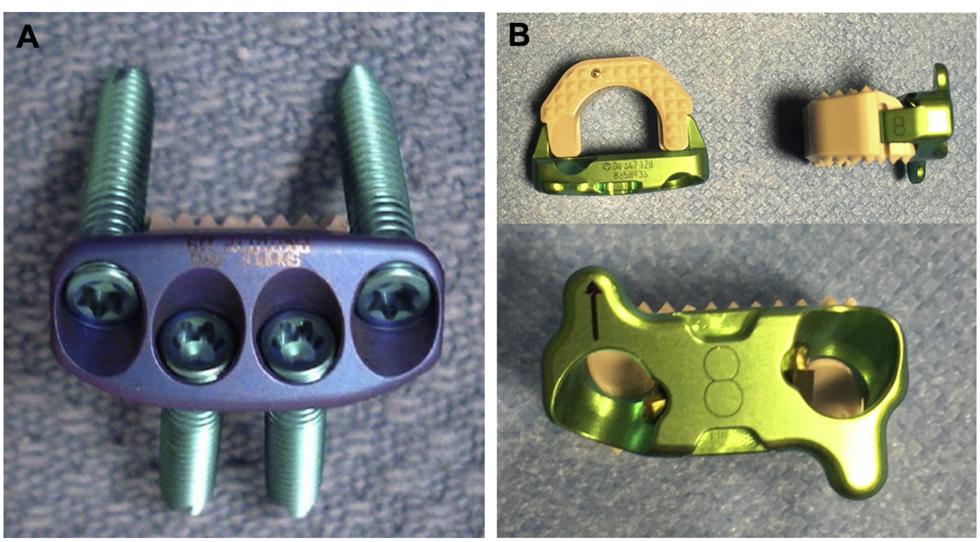


**Figure 1.** (**A**) Zero-P device. (**B**) Zero-P VA device.

**Table 1.** Summary of Demographic and Clinical Data

| | 3-Level Patients | 4-Level Patients | Total |
|---|---|---|---|
| Number of patients | 14 | 10 | 24 |
| Mean age (range) | 55.9 (41–68) | 61.7 (53–77) | 58.4 (41–77) |
| Sex | 7 males/ 7 females | 7 males/ 3 females | 14 males/ 10 females |
| Myelopathy signs | 6 | 9 | 15 |
| Radicular signs | 13 | 10 | 23 |
| Gait impairment | 5 | 6 | 11 |
| Urinary impairment | 6 | 6 | 12 |

### Zero-P Devices

The stand-alone, Zero-P cage-plate is a zero-profile, radiolucent, polyether ether ketone cage integrated with an anterior titanium plate containing 4 or 2 holes (in the most recent VA version) with screw treads. The first version of the Zero-P device has the 2 medial holes for inferiorly directed screws, whereas the lateral ones are designed to insert cranial screws. The new Zero-P VA has an anterior plate with only 2 holes for cranial and caudal screws, respectively (see **Figure 1**). Moreover, the new system has some peculiar features making screw insertion easier. Indeed, the VA insertion slots in both the medial-lateral direction (15–29 degrees) and cranial-caudal direction (27–44 degrees) allow for adjusting the screw trajectories within the vertebral body without modifying the cage position. VA screws are designed to prevent graft expulsion and are allowed to toggle postoperatively within vertebral bodies, which may potentially prevent load shielding of the graft in the event of graft subsidence. Yet the plate of Zero-P VA has a secure lock for the screw, which allows for auditory, tactile, and visual locking confirmation; contralateral safety stops have been designed to reduce the risk of overinsertion and to align with the interior surface of the vertebral bodies; finally, 2 different sizes of the device, a standard (13.6 mm) and a large size (16.6 mm), have been produced to expand its versatility. Both Zero-P systems have 3 different end plate configurations: parallel shaped, convex shaped, and lordotic shaped. According to manufacturer instruction, the Zero-P device contains a polyether ether ketone body with tantalum markers useful for controlling position during insertion. Screws that are 12, 14, or 16 mm in length are available, according to individual vertebral anatomy, and can be inserted using straight or angled perforators, together with drills and angled screw holders with torque limitation. In particular, angled instruments are designed to facilitate the screw insertion at the most cranial or caudal levels (i.e., C2–C3, C3–C4, or C6–C7).

### Clinical Evaluation

Clinical status was recorded preoperatively, postoperatively (30 days after surgery) and at last follow-up visit. The latter was made in 2015, six years after the starting patients' enrollment. Neck and radicular arm pain were evaluated on a visual analogue scale (VAS). Functional outcome and health status were assessed using the Neck Disability Index (NDI) and the Short Form 36 (SF36) survey. Nurick scale was also used to grade severity of myelopathy. Dysphagia-related symptoms were considered as none (no episodes of swallowing problems), mild (rare episodes of dysphagia), moderate (occasional swallowing difficulty with specific food), and severe (frequent difficult swallowing with majority of food) according to the Bazaz et al[10] grading system.

### Radiologic Evaluation

Preoperative radiologic evaluation included standard anteroposterior, lateral and flexion-extension radiographs, multiplanar reconstructed computed tomography (CT), and magnetic resonance. Postoperatively, plain radiographs (anteroposterior and lateral views) were obtained at each follow-up visit (6 and 12 months postoperatively and at last follow-up). CT scans were performed within 48 hours after surgery, as well as at last follow-up to assess fusion rate. According to Pitzen et al,[8] fusion was defined as absence of radiolucencies in the graft–end plate area, absence of bone sclerosis, and evidence of bridging trabecular bone within the fusion area. Postoperative MR scans were also collected to document neural decompression and verify the quality of images (i.e., absence of artefacts) in patients treated with the Zero-P devices. Alignment of the cervical spine was measured on lateral radiographs in neutral position preoperatively and at each follow-up appointment, assessing Cobb angle between C2 and C7 (given by the intersection of 2 straight lines, 1 parallel to the inferior end plate of C2 and the other to the superior endplate of C7, respectively). Negative values indicate lordosis, while positive ones indicate kyphosis.

### Surgical Procedure

All patients underwent a standard, right-sided, anterior approach to the cervical spine according to the Smith-Robinson technique. Identification of disk space midline for cage positioning was performed according to the technique that we previously described.[18] Following microsurgical diskectomy, when indicated, we performed a wide spondilectomy using a high-speed drill with a 3- or 4-mm ball tip (cutting first and coarse diamond tip afterwards), in order to perform wide bony spur removal from the inferior posterior end plate of the cranial vertebra and the superior posterior end plate of the caudal vertebral body, respectively. This strategy allows resection, in a V shape, of both posterior end plates' edges and decompresses neural structures at multiple levels when compressing osteophytes are located just at the disk level or along the cranial and caudal one third of the vertebral body adjacent to the intervertebral disk and not behind the midportion of the vertebral body itself (**Figures 2** and **3**). This step is crucial to obtain a satisfactory neural decompression in multiple-level cases.

If necessary, the base of the uncinate processes was also drilled to achieve adequate foraminotomy and nerve root decompression. In spondylotic cases, after removing the compressing posterior osteophytes, the posterior longitudinal ligament (PLL) was thinned by diamond drill and fenestrated in order to explore the underlying epidural space and make sure that no compressing bony spurs had been left behind. In cases of combined pathologies (i.e., spondylosis at some levels and disk hernia at others), the PLL was opened even wider to make sure that the hernia had been completely removed and no further disk fragments were still compressing neural structures.

Trial spacers were used to determine the most suitable implant shape (convex vs. lordotic cage) and size before implanting the corresponding zero profile cage-plate device filled with bone graft (Actifuse ABX—Baxter, Deerfield, Illinois, USA in 16 cases, and DBX, DePuy Synthes in 8 cases). The cage's position was checked by intraoperative lateral fluoroscopy. After the device was correctly placed in the intervertebral space, harboring a wide contact surface with end plates, the locking screws (2 or 4, according to the specific Zero-P model used) were inserted in the cranial and caudal vertebral bodies through the preexisting holes in the anterior plate.

### Statistical Analysis

Clinical outcome parameters, as well as variation of Cobb angle for cervical lordosis, were analyzed. The paired Student's *t*-test was used, and a P value of $<0.01$ was considered statistically significant.

## RESULTS

### Postoperative Course and Complications

We did not observe major complications in our series. All patients received a standard dose of pain medication (ketorolac tromethamine 60 mg/day and paracetamol 3000 mg/day, on first and second postoperative days) and a satisfactory control of postoperative pain was achieved. Of 24 patients, 18 have routinely used analgesic drugs during the 3 months before surgery. All of them discontinued pain medications after surgery. All patients were able to independently walk the first day after surgery and a cervical collar was never used after surgery. Mean postoperative hospitalization was 3 days (range 2—4). Cervical soft tissue swelling occurred during the postoperative period in 2 patients, but it was not clinically relevant and successfully managed with steroids. Revision surgery was never necessary. According to Bazaz criteria,[10] the incidence of dysphagia was evaluated: 5 patients (20.8%) complained of mild dysphagia; 3 of them recovered within 2 months (short-term dysphagia), whereas the remaining 2 referred regression of symptoms after 6 months (midterm dysphagia). Neither long-term nor moderate or severe dysphagia was observed. Mean follow-up was 39 months (range 24—72) (Table 2).

### Clinical Outcome

VAS score for neck pain decreased from a preoperative mean value of 6.7 (standard deviation [SD] 2.9) to 2.6 (SD 1.9) after surgery and 1.6 (SD 2.3) at last follow-up. Mean arm pain VAS score reduced from 5.9 (SD 2.9), before surgery, to 1.9 (SD 1.3) and 0.9 (SD 1.4) at postoperative evaluation and last follow-up, respectively. The differences between preoperative and postoperative values were statistically significant ($P < 0.01$). Such improvement was maintained over time, and there were no statistically significant differences ($P > 0.01$) between postoperative and last follow-up clinical values (Table 3).

NDI changed from a preoperative mean value of 60.4% (SD21.4) to 24.4% (SD17.0) at last follow-up. Similarly, the SF36 survey, in its physical component increased from a mean of 28.1 (SD 5.7) before surgery to 42.2 (SD 10.2) at last follow-up; mental component varied from 32.2 (SD 7.2) to 48 (SD 10.3) at last follow-up. According to such values, both NDI and SF36 survey postoperative scores showed statistically significant differences ($P < 0.01$) when compared with preoperative values.

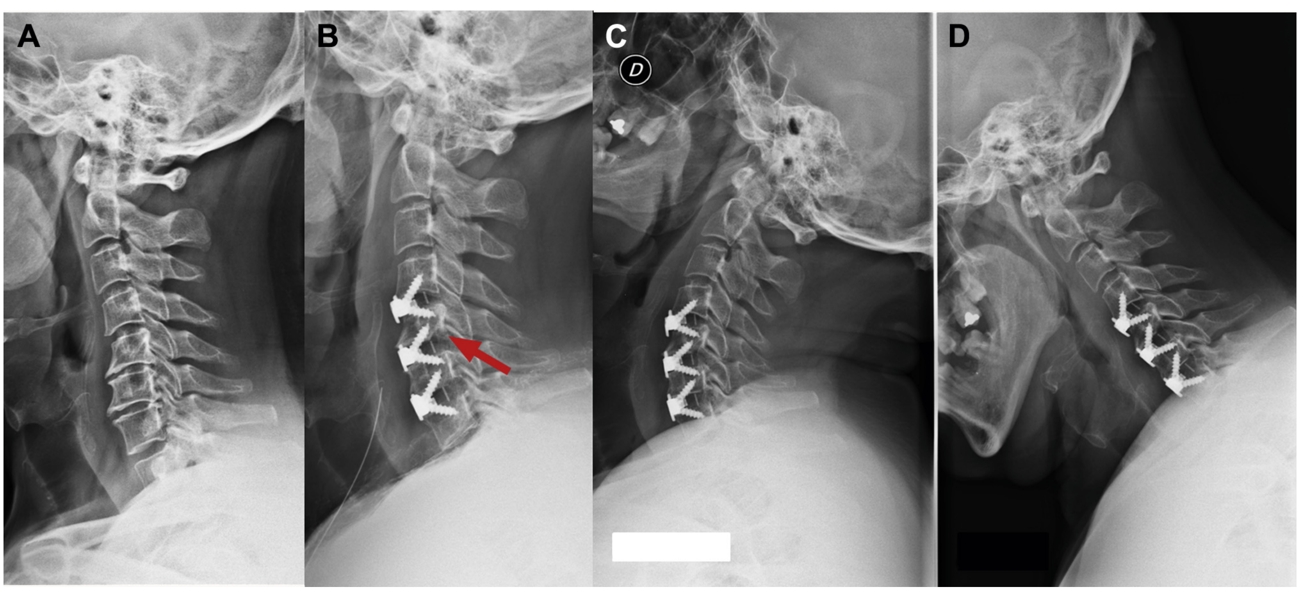


**Figure 2.** Correction of cervical spine alignment with zero-profile devices in 3-level anterior cervical diskectomy and fusion. Preoperative lateral radiographs showing kyphotic spine (**A**). Lordosis restoration is achieved after surgery (**B**), with preserved stability on extension (**C**) and flexion (**D**) views. *Red arrow* indicates the V-shaped bone removal in the vertebral bodies (i.e., the bone drilled off in the posterior area of the vertebral bodies).

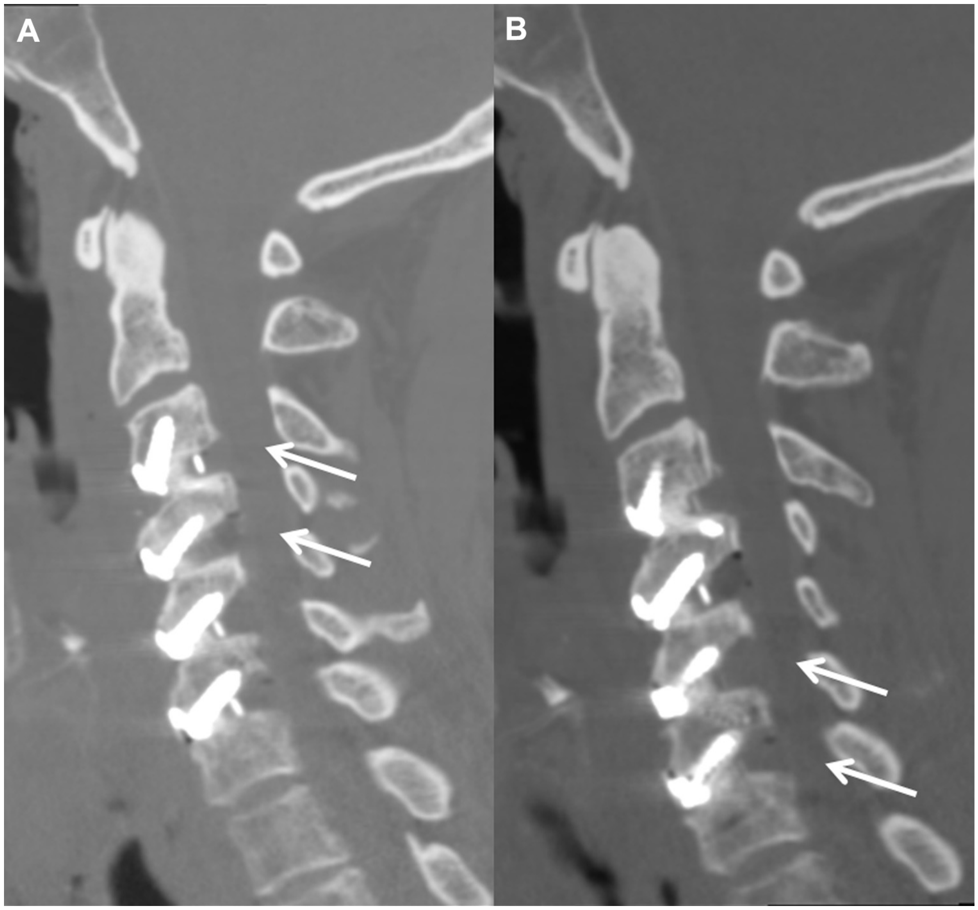


**Figure 3.** Sagittal reconstructed postoperative computed tomography scan showing wide posterior osteophytectomy at C3–C4, C4–C5 (**A**), C5–C6 and C6–C7 (**B**). Note the V-shaped bone removal allowing adequate neural decompression (*white arrows*).

According to the Nurick scale, myelopathy improved: scores changed from 2.7 (SD 1.1), preoperatively, to 0.5 (SD 0.9) at last follow-up. Such difference was statistically significant ($P < 0.01$) (Table 4).

**Table 2.** Incidence of Postoperative Dysphagia Evaluated After Surgery and Over Follow-Up Period*

| | Dysphagia Incidence | Short-Term Dysphagia (<2 months) | Medium-Term Dysphagia (3–6 months) | Long-Term Dysphagia (>6 months) |
|---|---|---|---|---|
| Number of patients | 5/24 | 3/24 | 2/24 | 0/24 |
| Percentage | 20.8% | 12.5% | 8.3% | 0% |

*Note the progressive reduction in incidence and absence of persistent dysphagia at long-term follow-up.

### Radiologic Follow-up

82 zero-profile devices were checked by radiographs at each follow-up appointment and CT scan at last follow-up visit. No device-related complications were encountered; implant failure, subsidence, cage-plate, and/or screw dislocation were never observed. Postoperative imaging did not demonstrate cage or screw malpositioning in any case. Early postoperative CT scan documented the removal of compressing posterior osteophytes and magnetic resonance imaging confirmed neural decompression. The latter was defined as the presence of continuous cerebrospinal fluid signal around the spinal cord on axial and sagittal magnetic resonance T2 sequences. Interestingly, Zero-P devices (both the standard and variable angle ones) did not cause significant image artefacts on magnetic resonance images and allowed reliable evaluation of neural structures both on sagittal and axial views. Multiplanar CT scans, obtained at last follow-up, documented a complete fusion in 43 of 88 (49%) intervertebral spaces according to Pitzen's criteria. Hence in 22 of 24 patients (91.7%) at least 1 intervertebral space was fused

**Table 3.** Changes in Visual Analog Scale (VAS) Score During Follow-up*

| | Preoperative | Early Postoperative | ($P$ < 0.01) | Early Postoperative | Last Follow-Up | ($P$ < 0.01) |
|---|---|---|---|---|---|---|
| VAS (neck) mean, DS | 6.7 ± 2.9 | 2.6 ± 1.9 | Yes (ss) | 2.6 ± 1.9 | 1.6 ± 2.3 | No (nss) |
| VAS (arm) mean, DS | 5.9 ± 2.9 | 1.9 ± 1.3 | Yes (ss) | 1.9 ± 1.3 | 0.9 ± 1.4 | No (nss) |

ss, statistically significant; nss, not statistically significant.
*Student's *t*-test confirms statistically significant values comparing preoperative and early postoperative scores. Comparison between early postoperative and last follow-up scores is not statistically significant.

(Figures 4 and 5). Among 43 fused levels, 28 were fused with standard 4-screw Zero-P cages, whereas 15 levels were fused with Zero-P VA.

Neither early postoperative nor last follow-up CT scans demonstrated vertebral body fractures; indeed, both Zero-P models, the one with 4 screws and the most recent VA one with 2 screws, were never associated with damage of the vertebral body above or below in multilevel cases.

Analysis of sagittal alignment was performed on lateral radiographs, preoperatively, postoperatively, and at last follow-up, respectively, using the Cobb angle method. The cervical Cobb angle was given by the intersection of 2 straight lines, 1 parallel to the inferior end plate of C2 and the other to the superior end plate of C7, respectively, and conventionally defined as a negative value when a lordotic curve was present and a positive one in case of kyphosis. It varied from a mean preoperative value of −11.9 degrees (SD 10.7 degrees) to −18.2 degrees (SD 4.1 degrees) postoperatively. The mean Cobb angle was −14.9 degrees (SD 5.5 degrees) at last follow-up. The differences between sagittal angles comparing preoperative, postoperative, and last follow-up values were statistically significant ($P < 0.01$) (Table 5). Slight reduction in lordosis was observed at last follow-up, but the difference with early postoperative values was not statistically significant ($P > 0.01$) (see Table 5 and Figures 2 and 4).

Eighteen of 24 (75%) patients, preoperatively, had a lordotic curvature, 3 had patients (12.5%) a straight cervical spine, and 3 were in kyphosis. On early postoperative evaluation (i.e., within 3 days after surgery), all patients showed lordotic alignment and this was maintained at last follow-up evaluation.

Such data confirm the maintenance of lordosis in patients with 3- and 4-level disease at last radiologic follow-up.

## DISCUSSION

In multilevel ACDF (≥2 levels), anterior cervical plating is commonly used to reduce instrumentation failure (i.e., cage or graft extrusion), increase fusion rate, and maintain adequate sagittal lordosis.[3,5,6] However, the purported benefits related to multilevel anterior plating are counterbalanced by serious and well-known complications. Among these, dysphagia has been reported as the most frequent one.[10,11,19-22] The occurrence of oesophageal fistulas due to anterior plating is less frequent, despite it being a serious event that may complicate early or late postoperative stages.[23,24] Another important disadvantage of anterior plating is linked to the correct placement of the plate. This should adapt to, and maintain, the sagittal contour of the cervical spine, having a wide and flat contact surface with vertebral bodies' anterior surface. Hence accurate anterior osteophytectomy is essential to smoothen the vertebral bodies' anterior surface and achieve satisfactory positioning of the plate.[8] Anterior plating has also been advocated as a possible risk factor favoring adjacent segment disease in cases of incorrect positioning or displacement.[8] Dynamic plates were used to reduce mechanical stress on screws and prevent their pull-out; however, further observations on the use of such devices demonstrated a higher incidence of loss of segmental lordosis than that observed with rigid plates.[25]

Recent studies on short and medium-term follow-up in patients treated with zero-profile devices have shown a reduction of the above disadvantages associated with anterior plating.[26] In 2013 Qi et al[27] compared the clinical and radiologic results of 2 cohorts of patients treated for CSM at 1, 2, or 3 levels with the Zero-P device and cage plus anterior plate, respectively. They observed similar results in both groups, except for the incidence of early postoperative dysphagia, which was lower in the Zero-P group. Similar results were reported by further comparative studies[13,14,16,28,29]: Yang et al[29] described a statistically significant lower incidence of adjacent segment disease in patient treated with zero-profile systems. In our previous study on Zero-P implants, we also pointed out the main advantages of such devices, reported our initial experience in treating multilevel cases,[2] and hypothesized the possible role of zero-profile devices as a reliable alternative to cage and anterior plating or to posterior approaches in the management of multilevel (i.e., >2 levels) cervical degenerative disease. However, our observations on 3- and 4-level cases were limited because of the small number of patients enrolled and the short-term follow-up.[2]

We have continued to treat patients with multilevel disease (see Figures 2, 4–6) as we consider multilevel ACDF with these zero-profile devices as a feasible and effective alternative to either multilevel ACDF with cages and standard anterior plating or posterior surgery. Indeed, the gold standard surgical technique for multilevel cervical spondylosis has not been defined yet, and several surgical options are still debated.[30-32] Many surgeons prefer posterior approaches for multilevel cases with a preserved

**Table 4.** Changes in Clinical Parameters During Follow-Up

| | Preoperative | Last Follow-Up | ($P$ < 0.01) |
|---|---|---|---|
| Nurick | 2.7 ± 1.1 | 0.5 ± 0.9 | Yes (ss) |
| NDI | 60.4 ± 21.4% | 24.4 ± 17% | Yes (ss) |
| SF36 (physical) | 28.1 ± 5.7 | 42.2 ± 10.2 | Yes (ss) |
| SF36 (mental) | 32.2 ± 7.2 | 48 ± 10.3 | Yes (ss) |

NDI, Neck Disability Index; SF36, 36-item Short Form survey; ss, statistically significant.

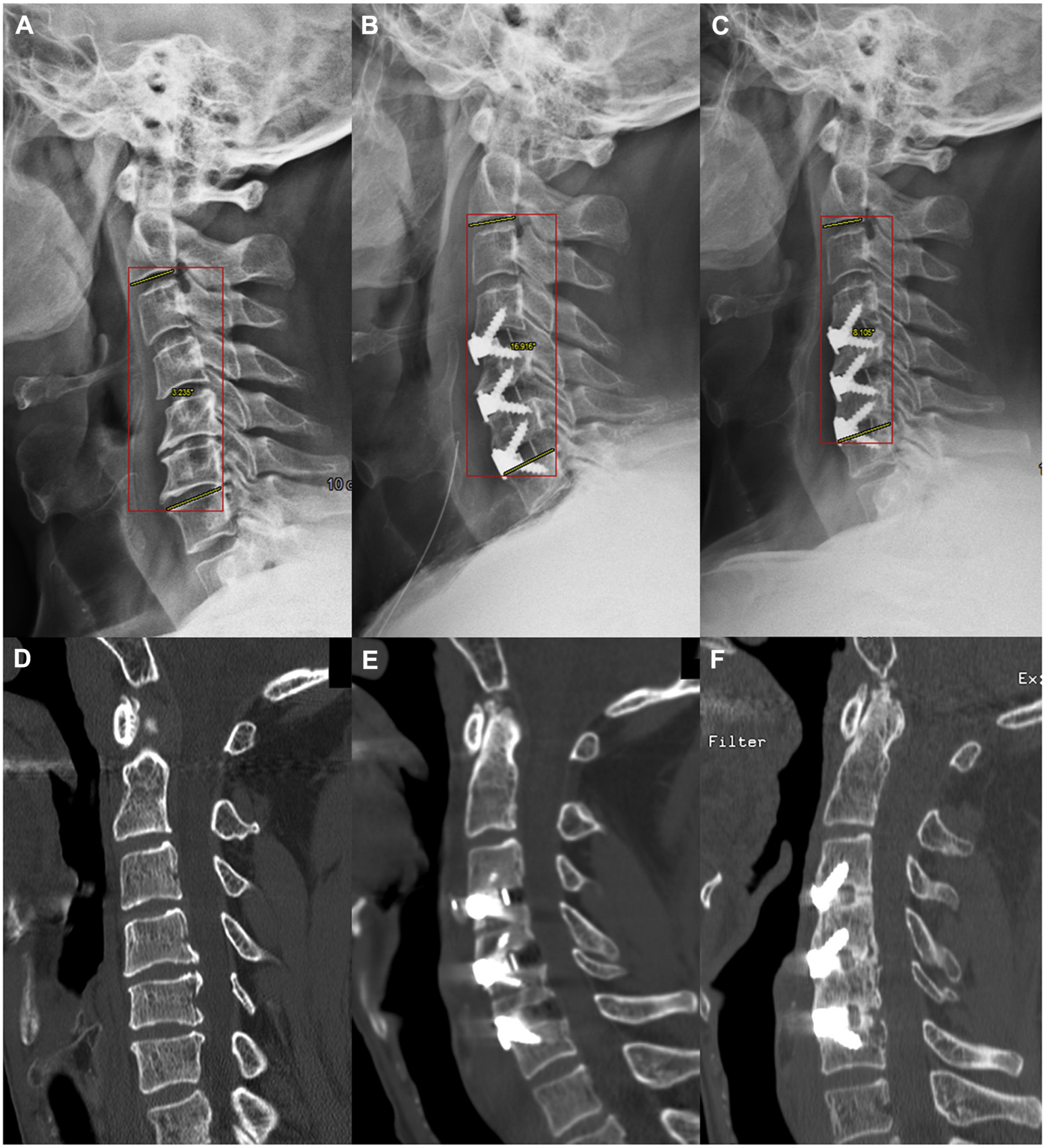


**Figure 4.** Comparison between preoperative (**A**), early postoperative (**B**), and last follow-up (**C**) lateral radiographs documents the changes in sagittal alignment measured according to Cobb's method. Evaluation of preoperative and postoperative sagittal reconstructed computed tomography (CT) scans documents the extent of posterior osteophytectomy (**B**, **C**, **E**). Last follow-up CT scan shows complete fusion at C4—C5 and incomplete fusion at C3—C4 and C5—C6 levels (**F**) in a 58-year-old nonsmoker.

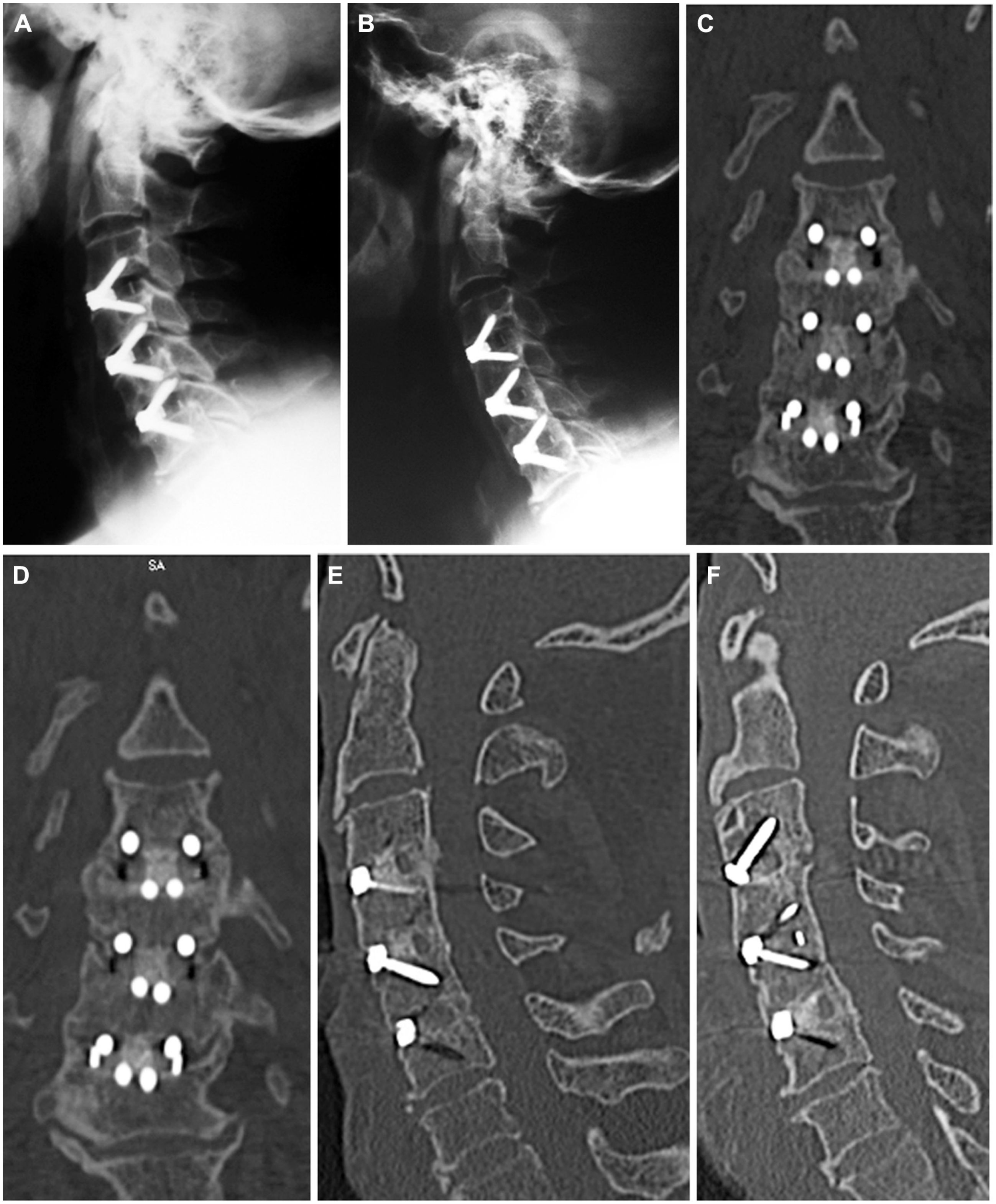


**Figure 5.** Early postoperative (**A**) and 2-year follow-up (**B**) radiographs showing a 3-level surgery with Zero-P device. Coronal (**C**, **D**) and sagittal (**E**, **F**) computed tomography scan confirming solid interbody fusion at 2-year follow-up.

**Table 5.** Sagittal Alignment Evaluation and Comparison*

| | Preoperative | Early Postoperative | ($P < 0.01$) | Early Postoperative | Last Follow-Up | ($P < 0.01$) |
|---|---|---|---|---|---|---|
| Cobb angle mean, DS | −11.9 ± 10.7 | −18.2 ± 4.1 | Yes (ss) | −18.2 ± 4.1° | 14.9 ± 5.5 | No (nss) |
| Lordotic spine | 75% | 100% | — | — | 100% | — |
| Straight spine | 12.5% | 0% | — | — | 0% | — |
| Kyphotic spine | 12.5% | 0% | — | — | 0% | — |

ss, statistically significant; nss, not statistically significant.

*Student's *t*-test confirms statistically significant values comparing preoperative and early postoperative scores. Comparison between early postoperative and last follow-up scores is not statistically significant.

lordosis.[33,34] Nevertheless, the choice to use anterior approaches is becoming more popular, albeit they have been reported to be associated with a high rate of postoperative complications.[35,36] A recent meta-analysis focused on the best approach for multilevel CSM, analyzing the data reported by 17 studies.[37] The authors concluded that anterior approaches are associated with a higher risk of postoperative complications, but they were not able to define the optimal surgical option, as no sufficient or high-quality data were found in the existing literature. Interestingly, no studies on zero-profile devices for multilevel CSM were included in this meta-analysis. Similar results were obtained by Luo et al., who performed another meta-analysis on 10 articles on the same topic.[38] No studies included in these 2 meta-analyses correlated clinical outcome with cervical sagittal alignment.

In our series we did not encounter any device-related complication. Most importantly, no vertebral body fractures secondary to multiple screws (i.e., 4 or 2) inserted in the same vertebral body were detected by early or late CT scans (**Figures 4** and **5**).

A previous review on multilevel CSM also investigated the fusion rate in multilevel ACDF and compared it with the one observed in multilevel corpectomy and fusion procedures.[39] The nonunion rate in 3-level approaches was much higher than that observed in 2-level cases, regardless of which procedure (i.e., diskectomy vs. corpectomy) had been performed; 4-level ACDF procedures were not present as a surgical option in that review. The authors hypothesized that the high number of fusion surfaces involved may be responsible for nonunion in 3-level ACDF.[39] In our series, we analyzed the fusion rate at each level by CT scan and found that nearly half (49%) of the intervertebral spaces were fused at last follow-up. Such value, probably linked to the high number of bony surfaces in each patient, is similar to that reported by Jiang et al[32] for 3-level ACDF, albeit our series also includes 10 cases of 4-level ACDF (**Figure 6**). Interestingly, the lack of complete fusion in all treated levels did not correlate with unsatisfactory clinical outcome. Indeed, all patients reported a statistically significant improvement of clinical parameters: neck and arm pain, myelopathy-related symptoms, as well as quality of life. Such improvement was also maintained at last follow-up assessment. Assessment of fusion was made on last follow-up CT scan. In the present series patients with the shortest follow-up underwent CT scan at 2 years after surgery; however, most of the patients included in the study had a CT scan at 3 or more years after surgery.

The standard short-lasting postoperative analgesic protocol with NSAID (ketorolac) is unlikely to have influenced the fusion rate in our series. Moreover, patients included in the study did not take pain medications routinely over follow-up visits. Therefore fusion rates should not be biased by the use of analgesics.

We did not observe differences in fusion rate related to the different types of Zero-P cages (standard type with 4 screws vs. VA with 2 screws). The radiologic outcome demonstrated similar results between the 2 different cages, in terms of fusion rate and biomechanical stability. According to our experience, the differences between the 2 types of Zero-P devices, in degenerative disease cases, are limited to the surgical technique.

One of our most relevant findings during the follow-up period is related to changes in sagittal alignment comparing preoperative, early postoperative, and follow-up radiologic evaluation (see **Table 5**). We always found restoration of cervical lordosis, even in patients harboring preoperative kyphosis (see **Figure 4**). Such data are in keeping with Wang's et al[16] findings, who reported both a significant improvement of neck and arm pain at 12 months' mean follow-up, as well as a concomitant statistically significant increase of cervical lordosis in 52 patients treated with Zero-P at 1 or 2 levels. Similarly, Njoku et al[15] evaluated the clinical and radiologic medium-term follow-up data in 41 patients treated with Zero-P for CSM, describing a concurrent improvement of both clinical outcome and cervical sagittal alignment in 1-, 2-, or 3-level patients. However, only 4 patients treated at 3 levels were included in their series.[15]

Loss of cervical lordosis is known to cause invalidating neck pain and disability, also being responsible for changes of whole spine's biomechanics.[40,41] Despite restoration of lordosis in a kyphotic cervical spine being a main goal of surgical treatment, there is no consensus about the optimal value of lordosis to achieve. Moreover, correlation between clinical outcome and cervical sagittal alignment has not been thoroughly investigated. Few studies based on small cohorts of patients have reported nonconclusive results.[15,16] Hence only scant and even less clear data have been published on the clinical impact of lordosis restoration in multilevel ACDF. Our results document a positive correlation between sagittal alignment and clinical outcome (**Tables 4** and **5**), including in cases without complete intervertebral fusion. Therefore we hypothesize that clinical outcome following cervical multilevel ACDF may be influenced more by correction of the spinal curvature than complete fusion. Indeed, in the present series all patients showed maintenance or restoration of sagittal lordosis at long-term follow-up; as no patients presented a kyphotic or straight cervical spine at follow-up


**Figure 6.** Sagittal, T2-weighted magnetic resonance imaging scan (**A**, **B**) showing 4-level degenerative disk disease causing neural compression leading to myeloradiculopathy. Postoperative radiograph (**C**) demonstrating anterior cervical diskectomy and fusion at 4 levels with zero-profile devices.

evaluation, it is not possible to correlate their reported improved clinical and functional outcome with sagittal malalignment. In our series, restoration of an adequate cervical alignment was achieved through extensive posterior osteophytectomy, thinning or opening of the posterior longitudinal ligament, and accurate choice of cages' sizes and shapes. In particular, wide posterior osteophytectomy was carried out using proper oblique angulation of the microscope and high-speed drill equipped with 3.0 or 4.0 round cutting and coarse diamond burs. Such technique provides adequate neural decompression at multiple levels (see **Figures 2—4**), creating a V-shaped open space with larger surface on the dura and a thoroughly decompressed spinal cord. Indeed, extensive bony removal around the posterior edges of the vertebral body is not a contraindication to implant of Zero-P devices, as the cage-plate is sited in the anterior two thirds of vertebral body and maintained in place by both screws and retaining teethes on the superior and inferior cage's surfaces.

At 6 years' maximum follow-up, we did not experience cases of adjacent segment disease or cage migration or instrument failure, regardless of the cage (Zero-P or Zero-P VA) used. Such findings reinforce the previously published results on Zero-P devices[2,13-16,26-29] and further demonstrate the safety and effectiveness of such devices even in multilevel cases at long-term follow-up. The latter observations led to the conclusions that Zero-P can be used in multilevel cervical degenerative conditions and are at least as safe and effective as standard multilevel ACDF with interbody cages and anterior plating. Conversely, the latter procedure has been associated with higher risk of instrumentation failure, particularly in multilevel cases.[35-37]

Dysphagia has been advocated as an important drawback of anterior approaches for multilevel disease.[22,35,42] Previously reported experiences with zero-profile devices documented a lower incidence of dysphagia than with multilevel anterior plating.[2,13-16,26-29] In our series, mild postoperative dysphagia was reported by 20.8% of patients at early postoperative follow-up; however, it improved over time and disappeared within 6 months after surgery (see **Table 2**). Such results suggest that the onset of dysphagia in multilevel cases could be related more likely to the surgical procedure and soft tissue swelling rather than to implants. Yet transient dysphagia was successfully treated with medical therapy, without negatively influencing patients' quality of life, as demonstrated by clinical results.

We are aware that the main limitation in the present study is the small number of patients; however, the relevance of our clinical and radiologic results is supported by their statistical significance.

## CONCLUSIONS

Although the best surgical option for multilevel CSM is still debated, anterior approaches with zero-profile devices seem to be feasible, safe, and effective even for 3- and 4-level ACDF. They allow adequate neural decompression and lordosis restoration, with positive impact on clinical outcome. Our results demonstrate several advantages: low complication rate, low incidence of dysphagia, absence of device-related failure, and persistent favorable outcome at long-term follow-up. Despite these limitations, our data suggest a clear correlation between restoration of cervical lordosis and clinical outcome in patients suffering from 3- and 4-level CSM.

## REFERENCES


1. Klineberg E. Cervical spondylotic myelopathy: a review of the evidence. *Orthop Clin North Am*. 2010; 41:193-202.
2. Barbagallo GM, Romano D, Certo F, Milone P, Albanese V. Zero-P: a new zero-profile cage-plate device for single and multilevel ACDF. A single Institution series with four years maximum follow-up and review of the literature on zero-profile devices. *Eur Spine J*. 2013;22(suppl 6): 868-878.
3. Lin D, Zhai W, Lian K, Kang L, Ding Z. Anterior versus posterior approach for four-level cervical spondylotic myelopathy. *Orthopedics*. 2013;36: 1431-1436.
4. Seng C, Tow BP, Siddiqui MA, Srivastava A, Wang L, Yew AK, et al. Surgically treated cervical myelopathy: a functional outcome comparison study between multilevel anterior cervical decompression fusion with instrumentation and posterior laminoplasty. *Spine J*. 2013; 13:723-731.
5. Fraser JF, Hartl R. Anterior approaches to fusion of the cervical spine: a metaanalysis of fusion rates. *J Neurosurg Spine*. 2007;6:298-303.
6. Kaiser MG, Haid RW Jr, Subach BR, Barnes B, Rodts GE Jr. Anterior cervical plating enhances arthrodesis after discectomy and fusion with cortical allograft. *Neurosurgery*. 2002;50:229-238.
7. Song KJ, Taghavi CE, Lee KB, Song JH, Eun JP. The efficacy of plate construct augmentation versus cage alone in anterior cervical fusion. *Spine (Phila Pa 1976)*. 2009;34:2886-2892.
8. Pitzen TR, Chrobok J, Stulik J, Ruffing S, Drumm J, Sova L, et al. Implant complications, fusion, loss of lordosis, and outcome after anterior cervical plating with dynamic or rigid plates: two year result of a multicentric, randomized, controlled study. *Spine (Phila Pa 1976)*. 2009;34: 641-646.
9. Kim SW, Limson MA, Kim SB, Arbatin JJ, Chang KY, Park MS, et al. Comparison of radiographic changes after ACDF versus Bryan disc arthroplasty in single and bi-level cases. *Eur Spine J*. 2009;18:218-231.
10. Bazaz R, Lee MJ, Yoo JU. Incidence of dysphagia after anterior cervical spine surgery: a prospective study. *Spine (Phila Pa 1976)*. 2002;27:2453-2458.
11. Lee MJ, Bazaz R, Furey CG, Yoo J. Influence of anterior cervical plate design on dysphagia: a 2-year prospective longitudinal follow-up study. *J Spinal Disord Tech*. 2005;18:406-409.
12. Goel A. Alternative tricortical methods of screw implantation for anterior cervical plate fixation: a preliminary report. *J Clin Neurosci*. 2000;7: 134-136.
13. Chen Y, Chen H, Cao P, Yuan W. Anterior cervical interbody fusion with the Zero-P spacer: mid-term results of two-level fusion. *Eur Spine J*. 2015;24: 1666-1672.
14. Miao J, Shen Y, Kuang Y, Yang L, Wang X, Chen Y, et al. Early follow-up outcomes of a new zero-profile implant used in anterior cervical discectomy and fusion. *J Spinal Disord Tech*. 2013;26: E193-E197.
15. Njoku I Jr, Alimi M, Leng LZ, Shin BJ, James AR, Bhangoo S, et al. Anterior cervical discectomy and fusion with a zero-profile integrated plate and spacer device: a clinical and radiological study: clinical article. *J Neurosurg Spine*. 2014;21:529-537.
16. Wang C, Zhang Y, Yuan W. Early clinical outcomes and radiographic features after treatment of cervical degenerative disc disease with the new zero-profile implant: a one-year follow-up retrospective study. *J Spinal Disord Tech*. 2016;29: E73-E79.
17. Cho HJ, Hur JW, Lee JB, Han JS, Cho TH, Park JY. Cervical stand-alone polyetheretherketone cage versus zero-profile anchored spacer in single-level anterior cervical discectomy and fusion: minimum 2-year assessment of radiographic and clinical outcome. *J Korean Neurosurg Soc*. 2015;58:119-124.
18. Barbagallo GM, Corbino LA, Papavero L, Fritzsche E, Albanese V. Anatomic midline marking during cervical arthroplasty with ProDisc-C: an alternative, simple, and reliable method: technical note. *J Spinal Disord Tech*. 2009;22: 610-614.
19. Fountas KN, Kapsalaki EZ, Nikolakakos LG, Smisson HF, Johnston KW, Grigorian AA, et al. Anterior cervical discectomy and fusion associated complications. *Spine (Phila Pa 1976)*. 2007;32: 2310-2317.
20. Fehlings MG, Ibrahim A, Tetreault L, Albanese V, Alvarado M, Arnold P, et al. A global perspective on the outcomes of surgical decompression in patients with cervical spondylotic myelopathy: results from the prospective multicenter AOSpine International study on 479 patients. *Spine (Phila Pa 1976)*. 2015;40:1322-1328.
21. Tetreault L, Tan G, Kopjar B, Côté P, Arnold P, Nugaeva N, et al. Clinical and surgical predictors of complications following surgery for the treatment of cervical spondylotic myelopathy: results from the multicenter, prospective AOSpine International study of 479 Patients. *Neurosurgery*. 2016; 79:33-44.
22. Tetreault L, Nagoshi N, Nakashima H, Arnold PM, Barbagallo G, Kopjar B, et al. Risk factors and clinical outcomes of dysphagia after anterior cervical surgery in patients with degenerative cervical myelopathy: results from the AOSpine International and North America Studies. *Neurosurgery*. 2016;63(suppl 1):190.
23. Kuo YC, Levine MS. Erosion of anterior cervical plate into pharynx with pharyngotracheal fistula. *Dysphagia*. 2010;25:334-337.
24. Sansur CA, Early S, Reibel J, Arlet V. Pharyngocutaneous fistula after anterior cervical spine surgery. *Eur Spine J*. 2009;18:586-591.
25. Lawrence BD, Patel AA, Guss A, Ryan Spiker W, Brodke DS. Malaligned dynamic anterior cervical plate: a biomechanical analysis of effectiveness. *Spine (Phila Pa 1976)*. 2014;39:2057-2061.
26. Yang Y, Ma L, Liu H, Xu M. A meta-analysis of the incidence of patient-reported dysphagia after anterior cervical decompression and fusion with the zero-profile implant system. *Dysphagia*. 2016; 31:134-145.
27. Qi M, Chen H, Liu Y, Zhang Y, Liang L, Yuan W. The use of a zero-profile device compared with an anterior plate and cage in the treatment of patients with symptomatic cervical spondylosis: a preliminary clinical investigation. *Bone Joint J*. 2013;95:543-547.
28. Li Y, Hao D, He B, Wang X, Yan L. The efficiency of zero-profile implant in anterior cervical discectomy fusion: a prospective controlled long-term follow-up study. *J Spinal Disord Tech*. 2013; 28:398-403.
29. Yang H, Chen D, Wang X, Yang L, He H, Yuan W. Zero-profile integrated plate and spacer device reduces rate of adjacent-level ossification development and dysphagia compared to ACDF with plating and cage system. *Arch Orthop Trauma Surg*. 2015;135:781-787.
30. Stewart TJ, Schlenk RP, Benzel EC. Multiple level discectomy and fusion. *Neurosurgery*. 2007; 60(supp1 1):S143-S148.
31. Lin Q, Zhou X, Wang X, Cao P, Tsai N, Yuan W. A comparison of anterior cervical discectomy and corpectomy in patients with multilevel cervical

spondylotic myelopathy. *Eur Spine J*. 2012;21: 474-481.

32. Guo Q, Bi X, Ni B, Lu X, Chen J, Yang J, et al. Outcomes of three anterior decompression and fusion techniques in the treatment of three-level cervical spondylosis. *Eur Spine J*. 2011;20: 1539-1544.

33. Lawrence BD, Jacobs WB, Norvell DC, Hermsmeyer JT, Chapman JR, Brodke DS. Anterior versus posterior approach for treatment of cervical spondylotic myelopathy: a systematic review. *Spine (Phila Pa 1976)*. 2013;38(suppl 1): 173-182.

34. Liu X, Min S, Zhang H, Zhou Z, Wang H, Jin A. Anterior corpectomy versus posterior laminoplasty for multilevel cervical myelopathy: a systematic review and meta-analysis. *Eur Spine J*. 2014;23: 362-372.

35. Barbagallo G, Certo F, Albanese V, Visocchi M. The impact of complications following cervical spine surgery: a systematic review. *J Neurosurg Sci*. 2014;58(suppl 1):55-64.

36. Veeravagu A, Cole T, Jiang B, Ratliff JK. Revision rates and complication incidence in single- and multilevel anterior cervical discectomy and fusion procedures: an administrative database study. *Spine J*. 2014;14:1125-1131.

37. Sun Y, Li L, Zhao J, Gu R. Comparison between anterior approaches and posterior approaches for the treatment of multilevel cervical spondylotic myelopathy: a meta-analysis. *Clin Neurol Neurosurg*. 2015;134:28-36.

38. Luo J, Cao K, Huang S, Li L, Yu T, Cao C, et al. Comparison of anterior approach versus posterior approach for the treatment of multilevel cervical spondylotic myelopathy. *Eur Spine J*. 2015;24: 1621-1630.

39. Jiang SD, Jiang LS, Dai LY. Anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion for multilevel cervical spondylosis: a systematic review. *Arch Orthop Trauma Surg*. 2012;132:155-161.

40. Hardacker JW, Shuford RF, Capicotto PN, Pryor PW. Radiographic standing cervical segmental alignment in adult volunteers without neck symptoms. *Spine (Phila Pa 1976)*. 1997;22: 1472-1480.

41. McAviney J, Schulz D, Bock R, Harrison DE, Holland B. Determining the relationship between cervical lordosis and neck complaints. *J Manipulative Physiol Ther*. 2005;28:187-193.

42. Cho SK, Lu Y, Lee DH. Dysphagia following anterior cervical spinal surgery: a systematic review. *Bone Joint J*. 2013;95-B:868-873.

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