


CLINICAL ARTICLE

Preoperative Cervical Cobb Angle Is a Risk Factor for Postoperative Axial Neck Pain after Anterior Cervical Discectomy and Fusion with Zero-Profile Interbody

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Objectives: Anterior cervical discectomy and fusion (ACDF) with zero-profile interbody has a lower incidence of complications in treating cervical spondylotic myelopathy (CSM). However, postoperative axial neck pain is still commonly occurred, and the factors affecting which is not known. Here, we retrospectively analyze the risk factors for postoperative axial pain after performing ACDF with zero-profile implant in single-level CSM.

Methods: Patients who suffered from single-level CSM and who received ACDF with zero-profile implant between 2018 January to 2020 December were reviewed. Of 180 single-level CSM patients, 144 patients who passed the inclusion criteria were enrolled. Patients were divided into two groups according to the severity of postoperative axial pain as measured by postoperative neck visual analogue scale (nVAS). Clinical parameters including age, sex, smoking history, symptom duration, body mass index (BMI), the Japanese Orthopaedic Association (JOA) scores, as well as radiological parameters were obtained pre- and post-operatively, and the data were compared between two groups. Pearson's chi-square tests and Mann-Whitney U tests were implemented to identify statistically significant differences between subgroups for categorical and continuous data, respectively; otherwise, the data were tested with Student's t-test. Risk factors were identified using logistic regression.

Results: Of the patients (97.8%) achieved satisfied neurological recovery, and 88.2% of the patients achieved fusion at 1-year follow-up. 33% of the patients (48 patients out of 144) had sustained postoperative axial pain after the surgery. Comparison of different severity groups exhibited no significant differences in terms of the possible risk factors ($P > 0.05$) except for pre- and post-operative C2–C7 Cobb angles (6.33 ± 6.53 vs. 11.88 ± 7.41 , $P < 0.05$; 13.49 ± 5.31 vs. 16.64 ± 7.34 , $P < 0.05$). Furthermore, correlation analysis showed that the preoperative C2–C7 Cobb angle is significantly correlated with the severity of the postoperative axial pain ($R^2 = 0.83$, $P < 0.01$). In addition, logistic regression analysis demonstrated that the preoperative C2–C7 Cobb angle is an independent predictor of postoperative axial pain ($P < 0.01$, OR = 0.53). Further receiver operating characteristic (ROC) analysis displayed an area under the curve (AUC) of 0.78 ($P < 0.01$) for preoperative C2–C7 Cobb angle, and the optimal cutoff was 8.4° (sensitivity 0.77, specificity 0.65).

Conclusion: The pre-operative C2–C7 Cobb angle is a risk factor for severe postoperative axial pain after anterior cervical discectomy and fusion with zero-profile interbody, and we should be cautious when poor preoperative C2–C7 Cobb angle is found in myelopathy patients planning to use zero-profile interbody to treat such patients.

Key words: Axial pain; Cervical alignment; Risk factor; Zero-profile interbody

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Introduction

Cervical spondylotic myelopathy (CSM) is a neurologic disease that results in neurologic dysfunction and deformity of the cervical spine.¹ The most widely used approach to treat CSM is anterior cervical discectomy and fusion (ACDF), and has been proved to be satisfying in most cases, but the incidence of postoperative complications including dysphagia, hematoma, axial pain and adjacent segment degeneration (ASD) is still high and cannot be neglected.^{2,3} To minimize the complications, various improvements were made. The zero-profile (Zero-P) integrated interbody system can reduce the risk of instrument failure and postoperative dysphagia compared to traditional plate and cage system, which significantly increased the clinical outcome of ACDF treated CSM patients.⁴ However, recent studies showed that postoperative axial pain is still a prominent complication that plagues many treated patients.^{5,6}

Defined as the neck pain spreading from the nuchal to the shoulder or periscapular regions, axial pain is diagnosed only after excluding the possibilities of diseases related with other systems.⁷ There are literatures report that axial pain can occur in up to 35.4% of the patients who received ACDF surgery and interbody implementation.⁸ The reasons of which, and the factors that affect the phenomenon are not clearly stated, and few studies involved single-level ACDF with zero-profile interbody patients who suffered from post-operative axial pain.⁹ Previous studies have shown that post-operative axial pain after ACDF surgical treatment is associated with hyper-distraction of the cervical vertebrae,¹⁰ however, the conclusion is controversial since other studies showed that there is no direct relationship between over-distraction and postoperative axial pain.^{11,12} There are other reports showing that preoperative cervical curvature is an important factor that influences the clinical outcomes after ACDF surgeries, and some scholars believe that excessive cervical curvature change may contribute to postoperative axial pain.¹³ Due to the uncertainty and controversy on postoperative axial pain after ACDF with zero-profile implants, we aimed to: (i) identify the potential risk factors of post-operative axial pain after ACDF with zero-profile implant in single-level CSM patient; (ii) clarify the correlation between postoperative axial pain and disc height change in this study, and (iii) provide evidence in preventing ACDF-related post-operative axial pain, and increase the clinical outcome of ACDF-treated CSM patients (Figs 1–3).

Methods

Ethics Approval and Consent to Participate

The study procedures were approved by the Shanghai Changzheng Hospital Institutional Review Board (IRB number. 2018SL036), and were performed in accordance with the ethical protocol. Informed consent was obtained from each patient enrolled.

Patient Information and Grouping Method

We initially collected data from 180 consecutive patients who underwent ACDF using zero-profile (Zero-P) spacer

between 2018 to the 2020 at our institute prospectively. Inclusion criteria were as follows: (i) male or female patient who is over 30 years of age; (ii) the diagnosis of single-level CSM was confirmed by typical clinical presentation and cervical magnetic resonance imaging (MRI) demonstrating spinal cord compression; and (iii) patients who underwent ACDF surgery using a Zero-P spacer.

Patients were analyzed for the following exclusion criteria: (i) acute spinal cord injuries; (ii) severe cervical kyphosis; (iii) previous cervical surgeries; (iv) lumbar or thoracic diseases; and (v) history of rheumatoid arthritis, cerebral palsy, cerebral infarction, traumatic spine diseases, tumors or other systematic diseases.

Finally, of the 180 patients enrolled, 144 patients have met the criteria and were included for further study. All patients were followed-up for at least 1 year, and the mean time of follow-up was 15.19 months (from 12 to 18 months).

For analyzing the factors that correlate with postoperative axial pain, participants that passed the inclusion criteria were divided into two groups based on the postoperative visual analogue scale of neck pain (nVAS) score. Patients

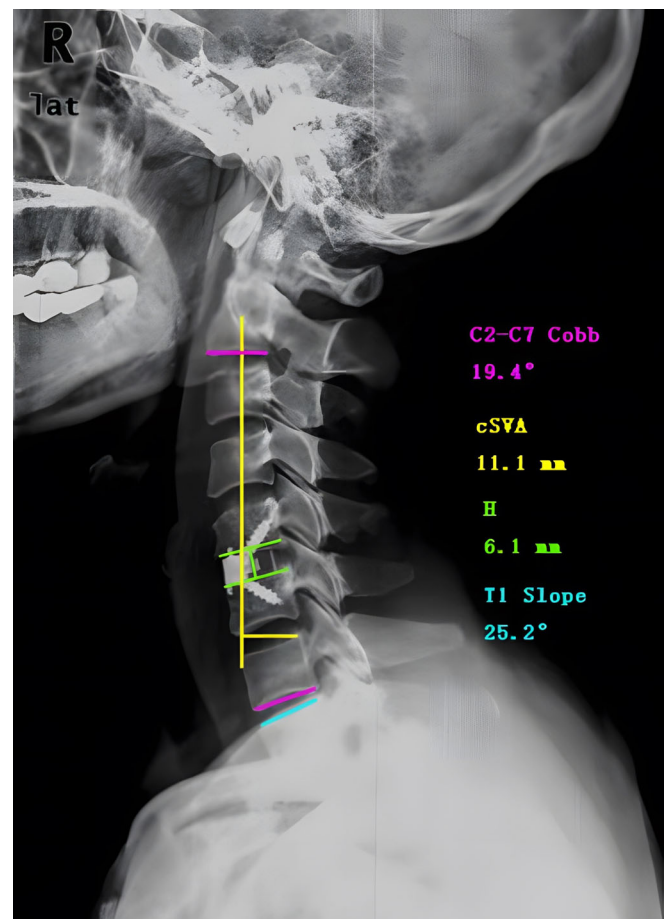


Fig. 1 Parameters defining cervical sagittal alignment and analysis example for radiological parameters

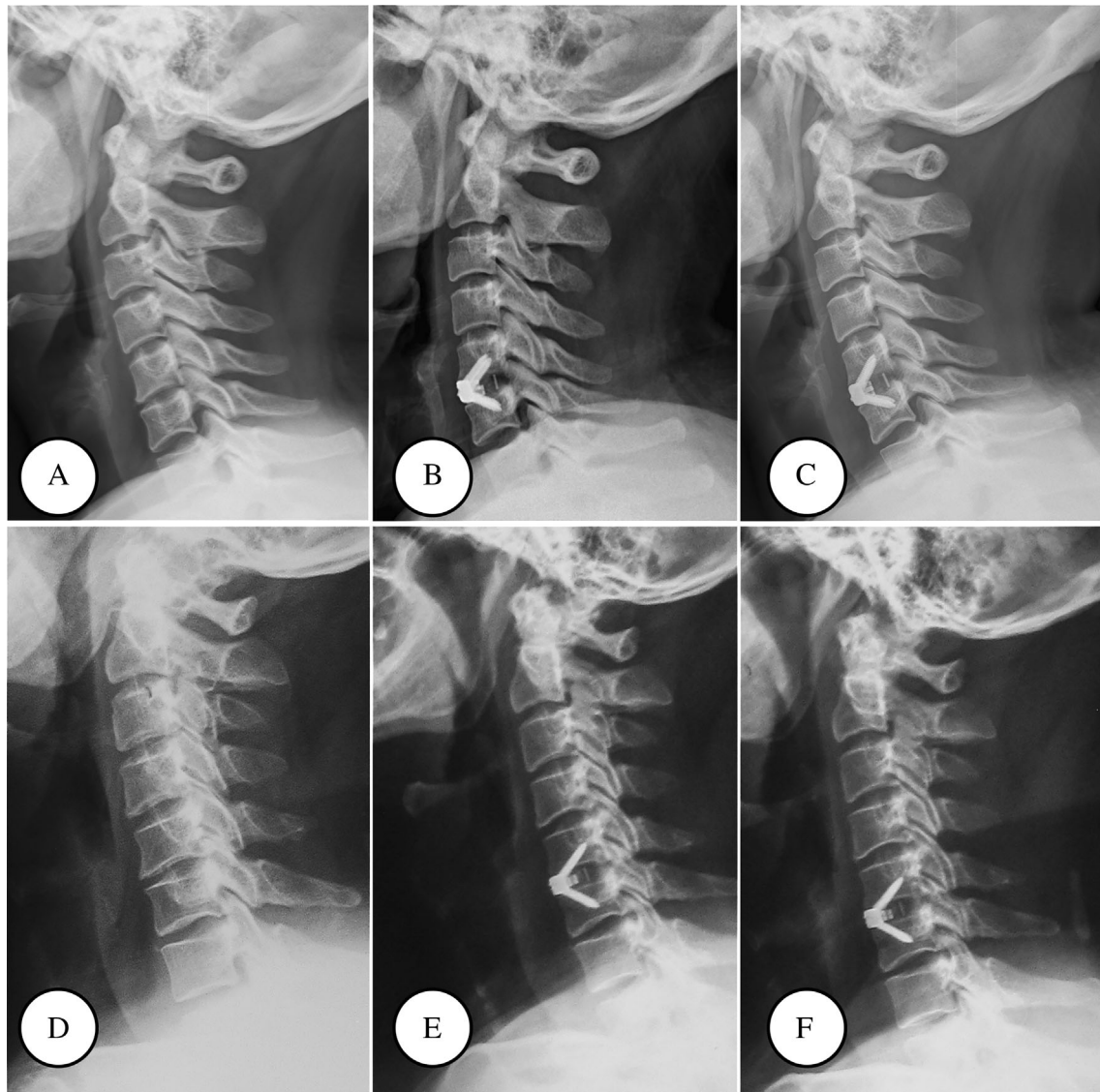


Fig. 2 Presentation of typical case. (A–C) A 45-years-old female CSM patient received C5/6 segment fusion with zero-profile implant. The preoperative Cobb angle was 12.4° lordosis (A), and after the surgery the alignment changed to 20.1° (B), and 16.8° at one-year follow-up (C). This patient recovered well and did not suffer from postoperative axial pain. (D–F) Another 52-year-old male CSM patient who received C5/6 segment fusion with zero-profile implant. The preoperative Cobb angle was 4.5° lordosis (D), and after the surgery the alignment changed to 5.4° (E), and 4.8° at one-year follow-up (F). This patient had severe axial pain (nVAS = 8) after the surgery and recovered to mild axial pain after one-year (nVAS = 3)

with nVAS ≥ 4 were considered as moderate to severe axial pain, and less than 4 were considered mild or no axial pain.

Surgical Method

An experienced professor was responsible for performing all ACDF procedures in our orthopedic spine department following the standard Smith-Robinson anterior approach as previously described.⁶ Subsequent to general anesthesia, the patients were placed in supine position. Intraoperative radiography was used to confirm the surgical level, and the disc, osteophytes and part of the posterior longitudinal ligament

were removed and resected to ensure thorough decompression. During which, a Casper distractor were used to provide sufficient decompression space for the operator. A suitable size of Zero-P spacer was chosen according to the height of adjacent normal intervertebral space. Following the operation, the patients were requested to wear a Philadelphia collar for at least 2 weeks, and discharged at 3 days after the surgery.

Clinical Parameters

General Parameters included age, sex, BMI, symptom duration was recorded for each patient.

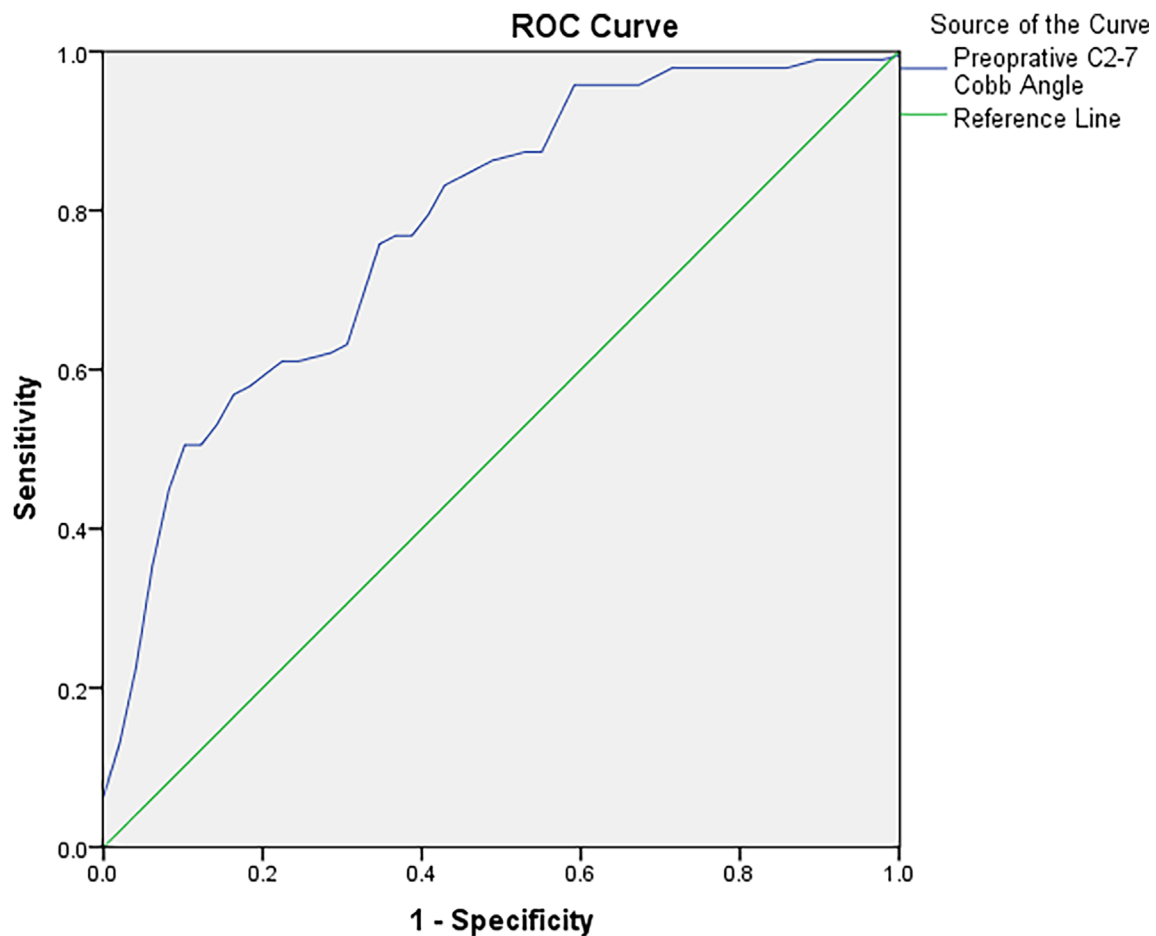


Fig. 3 Receiver operating characteristics (ROC) Curve of preoperative C2–C7 Cobb angle for moderate to severe postoperative axial pain

Neurological Function Assessment

The neurological function was assessed with the Japanese Orthopaedic Association (JOA) scoring system, and both the pre- and post-operative JOA scores were recorded for each patient. Two independent clinical research assistants, who were not involved in the study and blinded to all clinical information, performed the assessments, and the average values of both observers were used in the present study.

Neck Pain Assessment

The degree of axial pain was analyzed with the nVAS, and an nVAS ≥ 4 was considered to have moderate axial pain, nVAS ≥ 7 was considered to have severe axial pain according to previous report.¹⁴ Postoperative axial pain was defined as sustained axial pain (axial pain that exist for more than 2 months past). The clinical parameters were recorded preoperatively, postoperatively, 3-month follow-up, 6-month follow-up and 1-year follow-up for each patient.

Complications

Postoperative cerebrospinal fluid (CSF) leakage, the event of axial neck pain, and C5 nerve root palsy or other complications were recorded.

Radiographical Outcomes

Before and after the surgery, all patients had their radiographic images taken on lateral, anteroposterior, and maximal flexion-extension lateral parts. Image J software (National Institutes of Health, Bethesda, MD, USA) was used to analyze all radiological measurements. The radiological parameters were recorded preoperatively, postoperatively, 3-month follow-up, 6-month follow-up and 1-year follow-up for each patient.

Cervical Lordosis and Postoperative Cobb Angle Change

Cobb angle was measured between the lower endplate of C₇ and the upper endplate of C₂. All pre- and post-operative C2–C₇ Cobb angles were recorded, and the Cobb angle change (Δ C2–C₇ Cobb Angle) after the surgery was calculated using postoperative – preoperative C2–C₇ Cobb angle.

C2–C7 SVA

C2–7 sagittal vertical axis (SVA) was calculated by measuring the horizontal distance between the posterosuperior corner of the C7 vertebral body and a plumb line drawn from the centroid of C2.

T1 Slope

The T1 slope was measured as the angle between a horizontal line and the superior end plate of T1.

Height of Intervertebral Disc Space

Lateral X-ray was implemented to measure the height of intervertebral disc space, and the postoperative disc height change ratio was calculated by (postoperative disc height – preoperative disc height)/preoperative disc height.

Statistical Analysis

SPSS version 21.0 for Windows (SPSS, Inc., Chicago, IL, USA). was used to collect and analyze the data obtained in this study. Means \pm standard deviations (SD) were implemented to describe continuous variables, while percentages were used to describe categorical variables. The Shapiro–Wilk test was performed to test the normality of continuous variables. When data failed the normality test, Pearson's chi-square tests and Mann–Whitney U tests were implemented to identify statistically significant differences between subgroups for categorical and continuous data, respectively; otherwise, the data were tested with Student's *t*-test. $P < 0.05$ was considered statistically significant. Logistic regression analysis with backward LR method was used to test for risk factors. The receiver operating characteristic (ROC) curve was also analyzed using SPSS to evaluate the significance of the differences in the area under the ROC curve (AUC). The Youden index was used to determine the cutoff value for the moderate to severe postoperative axial pain.

Results**General Information of the Patients**

One hundred forty-four patients passed the exclusion criteria and were followed-up regularly at least for 1 year. The clinical and demographic features of all participants were shown in Table 1. One hundred forty-one patients (97.8%) of patients achieved satisfied neurological recovery, while two patients had recurrent neurological symptoms due to pseudoarthrosis and one patient had severe adjacent segment degeneration. 88.2% (127 patients) of the patients achieved solid fusion at 1-year follow-up, and 33.3% of the patients enrolled have postoperative axial pain after surgery. No other prominent complications were found during the follow-up.

TABLE 1 The baseline data of the enrolled patients

Items	Mean \pm SD (n = 144 patients)
Age	49.04 \pm 10.03
Male/female	73/71
BMI	22.25 \pm 1.76
Symptom duration (month)	8.32 \pm 5.61
Smoking/nonsmoking	43/101
Preoperative C2–C7 SVA (mm)	16.79 \pm 9.17
Preoperative T1 slope (°)	15.47 \pm 7.40
Preoperative C2–C7 Cobb angle (°)	11.49 \pm 7.99
Postoperative C2–C7 Cobb angle (°)	10.32 \pm 7.89
Preoperative disc height (mm)	4.97 \pm 1.13
Postoperative disc height (mm)	6.33 \pm 1.29
Postoperative disc height change ratio	1.43 \pm 0.26
Preoperative JOA scores	10.59 \pm 1.42
Postoperative JOA scores	14.09 \pm 1.14
Preoperative nVAS	5.63 \pm 3.43
Postoperative nVAS	3.47 \pm 2.78

Note: Values are shown as mean \pm standard deviation or number. Postoperative parameters at 1-year follow-up were shown.; Abbreviations: BMI, body mass index, JOA, Japanese orthopedic association, postoperative disc height change ratio (postoperative disc height/preoperative disc height), nVAS, neck visual analog scale.; Postoperative parameters at 1-year follow-up were shown

Characteristics of Patients with Moderate to Severe Postoperative Axial Pain

To further analyse the factors that correlate with postoperative axial pain, participants were divided into two groups based on the postoperative nVAS score. No significant differences were observed for age, sex, BMI, smoking history, symptom duration, preoperative JOA scores, postoperative JOA scores, preoperative disc height, postoperative disc height, postoperative disc height change and postoperative C2–C7 Cobb angle change between the groups ($P > 0.05$). However, pre- and postoperative C2–C7 Cobb angles in the group of moderate to severe axial pain were significantly lower than those in the other group ($P < 0.05$). In addition, the BMI showed differences between the groups but is less significant ($P = 0.051$, Table 2).

Preoperative C2–C7 Cobb Angle Is a Risk Factor for Postoperative Axial Pain

Since the Cobb angle of moderate to severe axial pain group showed significant differences, we then analyzed the correlation of radiological parameters with axial pain nVAS values (Table 3). Results showed that only preoperative C2–C7 Cobb angle showed significant correlation with the severity of the postoperative axial pain degree ($R^2 = 0.827$, $P < 0.01$). We further confirmed the risk factors using logistic regression (Table 4). The results showed that preoperative C2–C7 Cobb angle, Postoperative disc height change, Postoperative C2–C7 Cobb angle, and BMI were associated with postoperative axial pain, while only preoperative C2–C7 Cobb angle showed significant risk correlated to moderate to severe postoperative axial pain. The area under ROC curves (AUC) between preoperative C2–C7 Cobb

TABLE 2 Characteristics of patients with postoperative axial pain

Items	Moderate to severe postoperative axial pain group (nVAS ≥ 4 , n = 48)	Mild postoperative axial pain group (nVAS < 4, n = 96)	t value	P value
Age	50.58 \pm 10.76	48.28 \pm 8.89	1.62	0.12
Male (female)	28 (20)	45 (51)	-	0.22
BMI	22.87 \pm 1.76	22.04 \pm 1.73	1.98	0.05
Symptom Duration (month)	4.92 \pm 4.63	5.71 \pm 4.85	1.48	0.16
Smoking (Nonsmoking)	15 (33)	28 (68)	-	0.19
Preoperative C2–C7 Cobb angle ($^{\circ}$)	6.33 \pm 6.53	11.88 \pm 7.41	3.61	<0.001 ^a
Postoperative C2–C7 Cobb angle ($^{\circ}$)	13.49 \pm 5.31	16.64 \pm 7.34	2.35	0.02 ^a
Postoperative Cobb angle change ($^{\circ}$)	5.87 \pm 5.43	5.75 \pm 5.82	0.36	0.87
Preoperative C2–C7 SVA (mm)	16.51 \pm 10.12	16.94 \pm 8.90	0.29	0.90
Preoperative T1 slope ($^{\circ}$)	13.13 \pm 3.07	16.85 \pm 8.79	1.35	0.19
Preoperative disc height (mm)	4.40 \pm 1.23	4.23 \pm 1.53	0.72	0.45
Postoperative disc height (mm)	5.47 \pm 1.28	6.25 \pm 1.41	1.62	0.12
Postoperative disc height change (mm)	1.40 \pm 0.53	1.56 \pm 0.47	1.05	0.28
Preoperative JOA scores	10.46 \pm 1.45	10.66 \pm 1.41	0.83	0.41
Postoperative JOA scores	14.05 \pm 1.23	14.11 \pm 1.09	0.48	0.74

Notes: Values are shown as mean \pm standard deviation or number.; ^a $P < 0.05$ was considered statistically significant. Postoperative parameters at 1-year follow-up were used for analysis.; Abbreviations: BMI, body mass index; JOA, Japanese orthopedic association, postoperative disc height change ratio (postoperative disc height/preoperative disc height); nVAS, neck visual analog scale.

TABLE 3 Correlation of postoperative axial pain with radiological factors

Items	Pearson correlation	R ²	P value
Preoperative C2–C7 Cobb angle	-0.735	0.827	<0.001 ^a
Postoperative C2–C7 Cobb angle	0.385	0.535	0.38
Postoperative Cobb angle change	0.435	0.514	0.17
Preoperative disc height	-0.175	0.257	0.60
Postoperative disc height	0.116	0.204	0.59
Postoperative disc height change	0.413	0.478	0.28
Preoperative C2–C7 SVA	0.368	0.382	0.41
Preoperative T1 slope	0.261	0.385	0.74

Notes: ^a $P < 0.05$ was considered statistically significant. Postoperative parameters at 1-year follow-up were used for analysis.

TABLE 4 Logistic regression analysis showing risk factors for moderate to severe postoperative axial pain

Items	Exp (B)	95%CI	P value
Preoperative C2–C7 Cobb angle	0.534	0.405–0.689	<0.001 ^a
Postoperative disc height change	1.255	0.260–6.044	0.052
Postoperative C2–C7 Cobb angle	0.924	0.534–2.641	0.063
BMI	0.806	0.636–1.021	0.074

Abbreviation: BMI, body mass index.; ^a Note: $P < 0.05$ was considered statistically significant.

angle and axial pain are shown in Table 5 (AUC = 0.78, $p < 0.01$). Based on the ROC curve, the preoperative C2–C7 Cobb angle corresponding to the optimal Youden index (0.42) was 8.4 $^{\circ}$ (sensitivity 0.77, specificity 0.65).

Discussion

Postoperative axial pain has become a common complication after ACDF in recent data, and our study showed that 33.3% of patients had moderate to severe postoperative axial pain. We found less preoperative C2–C7 Cobb Angle was a risk factor for axial pain.

Intervertebral Disc Height Change Is Not an Effective Indicator for Postoperative Axial Pain

Bai *et al.*¹¹ observed that postoperative axial pain will significantly become more prevalent if the surgical segment changed in its intervertebral height after ACDF by over 10%. However, in our study, intervertebral height changed much more than 10% and we did not observe severe axial pain correlated with postoperative disc height change. A similar result has been reported by Chang *et al.*,⁸ who evaluated the increase in intervertebral space by inserting a large graft material while performing ACDF to treat degenerative cervical disease. These authors claimed no correlation between intervertebral disc height change and the occurrence and severity of postoperative axial pain, which is consistent with our results.

The Relationship between Cervical Sagittal Balance Indexes and Postoperative Axial Pain

The cervical sagittal balance is a tool for surgical decision making as it is associated with quality of life, and it is assessed most commonly by the T1 slope, SVA and C2–C7

TABLE 5 Receiver operating characteristic

Items	Area	Standard deviation	p-value	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
Preoperative C2–C7 Cobb angle	0.782	0.40	<0.001 ^a	0.703	0.861

Note:^a $P < 0.05$ was considered statistically significant.

Cobb angles.¹⁵ Particularly, the C2–C7 Cobb angle is measured between the C2 and C7 endplates. The vertebral alignment, as well as numerous tissues around the cervical vertebrae play important roles in maintaining normal cervical curvature and function. After the surgery, the stability is important for patients to maintain cervical curvature and function, and when the cervical curvature is not maintained at a biomechanically stable state, pain and other symptoms may occur. However, how sagittal balance affects axial pain is not fully understood. Axial pain is a multifactorial problem involving muscular, bony, discogenic and ligamentous anatomy.¹⁶ Specifically, the hominids modified their profile with the cervical curvature they developed to keep a horizontal gaze.¹⁵ Also, the cervical extensor muscles maintain the balance of kyphotic and extensor forces to keep the lordosis of cervical spine. Dynamically, when the curvature of the cervical spine decreases, the cervical extensor muscles should exert with more force to maintain a horizontal gaze. This compensation mechanism that maintain horizontal gaze could lead to axial pain.¹⁷ Our results indicate that preoperative C2–C7 Cobb angle was significantly associated with axial pain after zero-profile interbody fusion. Since the curvature correction capacity of a single level ACDF is very limited, we believe that a poor preoperative cervical lordosis that cannot be corrected by a single-level ACDF may affect the biomechanical state of the cervical spine and thus cause sustained axial pain even after the surgery.

Facet Joint Pressure Change May Cause Postoperative Axial Pain

The facet joint belongs to synovial joint. The joint capsule is attached to the edge of articular cartilage.¹⁸ The loss of cervical curvature subjects the facet joints to more stretching force, and in an intense state which may irradiate the sensory nerves. A tissue or structure can generate pain only if it is innervated. The cervical facet joint capsule is rich in receptors that can sense the intensity of physiological stimulation, and can produce a painful sensation when overstretched.¹⁹ It is reported that uneven distraction of the facet joint is more likely to cause axial pain than an evenly over-distractioned facet joint.⁵ Thus, we believe that a poor lordosis with axial distraction using zero-profile implants may cause uneven joint distraction during the early months after the surgery, which may cause severe postoperative axial pain.

Pal and Routal²⁰ found that at the C2 endplate, the compressive force on the superior articular surfaces was transmitted to the inferior body surface and two inferior articular facets. As the cervical region has posterior curvature, the posterior columns become more capable to withstand the compressive force. Adams and Hutton²¹ found that, the facet joints are more resistant to intervertebral compressive forces when in the erect standing posture compared to the erect sitting posture. When the curvature of the cervical spine decreases, the anterior disc is under more pressure.²² Excess and chronic exposure to high mechanical load can harm the intervertebral disc and make it more prone to degeneration.²³ In terms of pathophysiology of discogenic pain, the degenerated disc demonstrates multiple correlated macro- and micro-scopic changes. First, microscopic damage stimulates cytokine secretion and immune cell migration, thereby creating a positive feedback system. Consequently, an increase in neutrophil numbers occur, and spinal nerve sensitization and nerve ingrowth also appears, leading to axial pain. Finally, physical irritation as a result of anatomical changes can bring deeper neural compression and more intense neuropathic pain.²⁴ Patients in our study did not have exacerbation or remission of the axial pain other than adjacent segmental degeneration of the surgical site. And we believe that taking nonsteroidal anti-inflammatory drugs, receiving physical therapy routinely and achieving a solid fusion will help to provide symptomatic relief.

Among various patient characteristics and baseline parameters tested, preoperative C2–C7 Cobb Angle was the predictor of postoperative axial pain. Indications for zero-profile implants should be carefully determined in myelopathy patients with less preoperative C2–C7 Cobb Angle.

Strengths and Limitations

This study has several strengths. First, this is the first study to investigate the relationship between preoperative cervical curvature and axial pain after zero-p interbody fusion. Second, this study uncovered the importance of preoperative C2–C7 Cobb angle as a postoperative axial pain indicator and risk factor that can be used in patients who are planning to treat CSM with ACDF with zero-profile implants.

However, our research also has limitations. First, the cohort size in this retrospective study is still small. Second, the period of follow-up was too short. Third to facilitate data collection, we included only patients who underwent single-

level surgery. Fourth this study is limited to zero-profile implants. There is no comparison of the incidence of axial pain after various surgical procedures. Whether single level traditional plate and cage system is more advantageous in maintaining cervical curvature than zero-profile implants are still inconclusive. However, we found the less preoperative C2–C7 Cobb Angle was a risk factor for axial pain. It would provide useful insights for ACDF practices and the management of postoperative patients.

Conclusions

Among various patient characteristics and baseline parameters tested, preoperative C2–C7 Cobb Angle was the predictor of postoperative axial pain. If the preoperative C2–C7 Cobb Angle was less than 8.4° , the possibility of having moderate to severe postoperative axial pain would be more likely. And there is no direct relationship between postoperative axial pain and disc height change. Indications for ACDF with zero-profile implants should be carefully determined in

myelopathy patients with less preoperative C2–C7 Cobb Angle.

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