

# Risk factors of cage subsidence after removal of localized heterotopic ossification by anterior cervical discectomy and fusion

## A retrospective multivariable analysis

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### Abstract

The purpose of the study was to identify risk factors of cage subsidence and evaluate surgical outcome by at least 12 months postoperative follow-up.

We retrospectively investigated 113 consecutive patients who underwent anterior surgery to relieve spine cord compression resulted from localized heterotopic ossification, from July, 2011 to February, 2016. We divided the patients into 2 groups: cage subsidence <2mm group and ≥2mm group. According to magnetic resonance imaging (MRI), the severity of increased signal intensity (ISI) was classified into grade 0, 1, and 2. Clinical outcome was assessed by the Japanese Orthopedic Association (JOA) scoring system. Logistic regression analysis and receiver-operating characteristic (ROC) curve were utilized for predicting risk factors of cage subsidence, and the recovery rate was evaluated by Kruskal–Wallis test or Mann–Whitney *U* test.

Logistic regression with cage subsidence as the dependent variable showed independent risks associated with a cervical sagittal malalignment (odds ratio [OR] 11.23, 95% confidence interval [CI] 3.595–35.064, *P* < .001), thoracic 1 (T1) slope angle (OR 1.59, 95% CI 1.259–1.945, *P* < .001), and excisional thickness (OR 2.38, 95% CI 1.163–4.888.0, *P* = .018). The cut-off values of T1 slope and excisional thickness were 19.65 angle and 3.7 mm, respectively. Patients with high occupying ratio (*P* = .001) and high ISI grade (*P* = .012) are more likely to occur lower recovery rate.

Patients with high T1 slope angle or preoperative kyphotic deformity should avoid excessive removal of endplate and vertebral body so as to reduce the occurrence of cage subsidence. Poor outcome was closely related to cervical sagittal malalignment and higher ISI grade.

**Abbreviations:** ACDF = anterior cervical discectomy and fusion, BMI = body mass index, CIs = confidence intervals, C-OPLL = cervical ossification of the posterior longitudinal ligament, CSA = cervical sagittal alignment, CSM = cervical spondylotic myelopathy, IH = intervertebral height, ISI = increased signal intensity, JOA = Japanese Orthopedic Association, MRI = magnetic resonance imaging, ORs = odds ratios, PEEK = poly-ether-ether-ketone, ROC curve = receiver-operating characteristic curve, SN = sensitivity, SP = specificity, SVA = sagittal vertical axial, T1 = thoracic 1.

**Keywords:** anterior cervical discectomy and fusion, cage subsidence, heterotopic ossification, kyphotic alignment, postoperative outcome

## 1. Introduction

Cervical ossification of the posterior longitudinal ligament (C-OPLL) has been recognized as 1 of the most important causes

which led to cervical spondylotic myelopathy (CSM).<sup>[1,2]</sup> However, it is rarely concerned that the spinal cord compression come from the posterior annulus fibrosus ossification and osteophyte of the posterior vertebral edge. Anterior approach has many advantages such as removing directly the lesions of compression of spinal cord so as to get sufficient decompression and acquire good outcome, especially as for the circumscribed-type C-OPLL.<sup>[1]</sup> Due to the narrow operating space and the location of the ossification, it is technically demanding to remove the localized heterotopic ossification by anterior cervical discectomy and fusion (ACDF).<sup>[3,4]</sup> It should be point out that this approach could cause some serious complications, such as intraoperative cerebrospinal fluid leakage, cervical 5 palsy, and postoperative dysphagia.<sup>[5]</sup> Although the removal of osseous endplate and vertebral body can enlarge intervertebral space for furthest removing heterotopic ossification, it also contributes to cage subsidence to a certain extent.

Some scholars have reported that cage subsidence results from some causes such as cage morphology, the position of cage and early intervertebral fusion rate, and the incidence of cage subsidence also exists differently.<sup>[6–8]</sup> Historically, few investigations have focused on the removal thickness of endplate and vertebral body, cervical sagittal alignment (CSA), and thoracic 1

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(T1) slope angle. In addition, there were some controversies about the relationship between postoperative poor outcome and the cage subsidence.<sup>[9–11]</sup> Although there are many factors that contribute to poor postoperative outcome, the cage subsidence still as 1 cause is concerned. Hence, we designed the present study to identify the risk factors of cage subsidence and analyze the cause of postoperative poor outcomes. Furthermore, this study analyzes the effects of cervical sagittal balance on postoperative outcome.

## 2. Material and methods

### 2.1. Ethical considerations

This study was approved by the Institutional Ethics Board of the Orthopedics Hospital of XingTai city, and informed consent was obtained from all individual participants included. The methods were carried out in accordance with the doctor–patient relationship regulations which strictly observed the STROBE statement.

### 2.2. Patients

The criteria for inclusion were the following: diagnosis of CSM caused by localized heterotopic ossification which include circumscribed-type C-OPLL, the posterior annulus fibrosus ossification, and osteophyte of the posterior vertebral edge; increased signal intensity (ISI) of the spinal cord on T2-weighted sagittal magnetic resonance imaging (T2-MRI) or obvious symptoms resulted from spinal cord compression; and patients underwent ACDF approach to remove heterotopic ossification. Some exclusion criterion included: there is a history of cervical surgery; with spinal tumors or other complex concomitant diseases; incomplete imaging data.

These patients had various symptoms before surgery, such as gait disturbance, urinary dysfunction, and sensory abnormality of the trunk or extremities. All the patients of this study had at least 12 months follow-up after surgery and obtained intervertebral fusion at final follow-up. We divided patients into 2 groups by the loss of intervertebral height (IH). The Japanese Orthopedic Association (JOA) score was used to evaluate neurological function at preoperative and the final follow-up. The surgical outcome was estimated by means of the recovery rate = (postoperative JOA score – preoperative JOA score) / (17 – preoperative JOA score) × 100%.

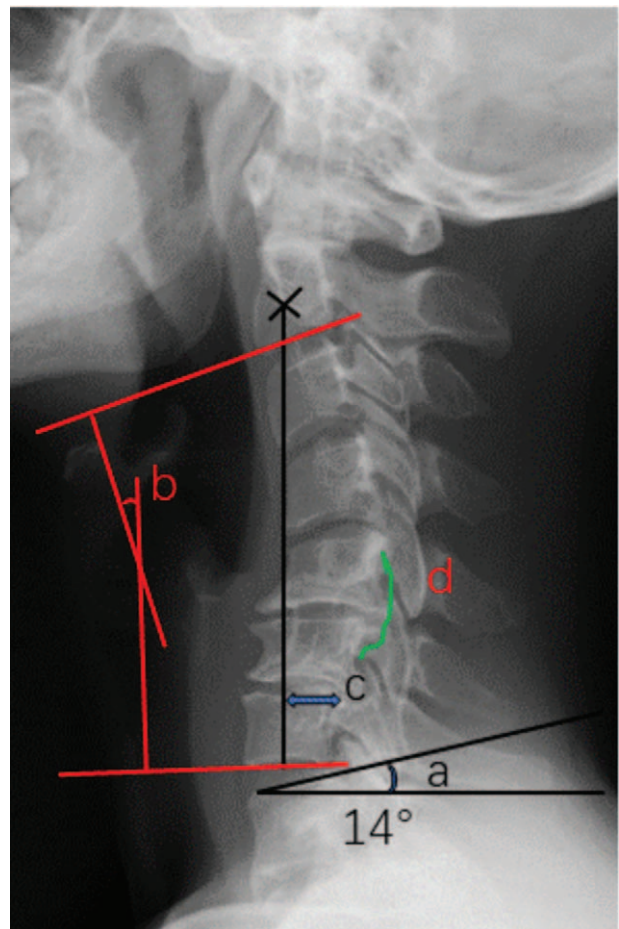
### 2.3. Surgical procedure

The surgical approach was determined by physical condition, degree of symptoms, and the location of compression spinal cord. All patients underwent no more than 3-segment ACDF approach. When the location of spinal cord compression occurred in posterior vertebral body or continuous ossification zone had more than 3 segments, anterior cervical corpectomy and fusion approach or posterior approach would be considerable. The patients under general anesthesia with supine position were placed on a surgical bed. We adopted a right transverse skin incision after the determination of surgical segments by body surface location. It reached the anterior edge of diseased level at medial side of sternocleidomastoid by blunt separation of the neck muscles. The assistant medially pulled the trachea and esophagus to the left side by a thyroid retractor. We released the

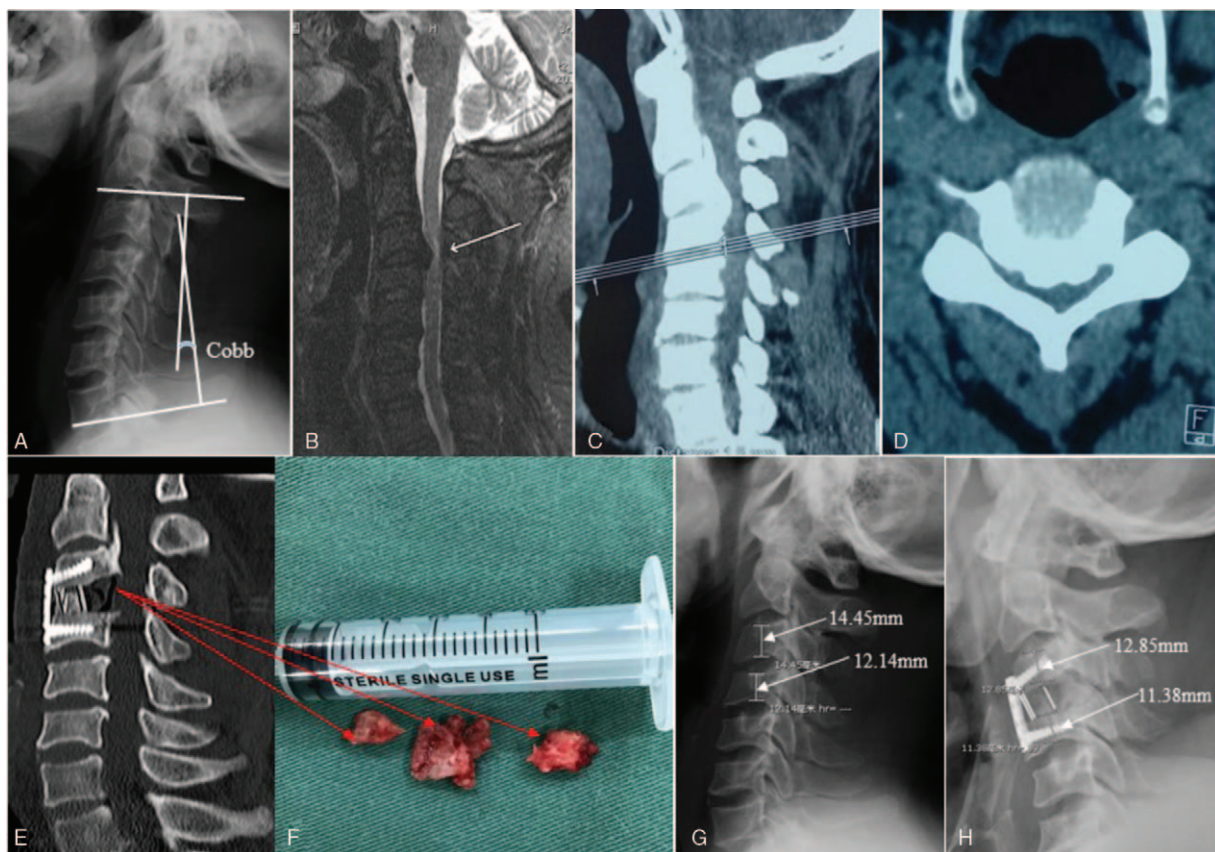
uncovertebral joint and removed part of the endplate (including cartilage and cortical bone) to expand intervertebral space for the decompression of spinal cord. An optimal poly-ether-ether-ketone (PEEK) cage with bone allograft was inserted into the disc space, and the anterior fixation with plate system. It has to be noticed that the rupture of venous plexus will increase intraoperative bleeding. All patients were restricted to bed only one or two days and told to use a cervical collar for 3 weeks after surgery.

### 2.4. Radiologic assessment

Patients' imaging data were evaluated on lateral radiographs and T2-weighted sagittal MRI. We defined the CSA as follows: positive, lordotic; negative, kyphotic; lordotic, more than +5°; straight, +5° to –5°; kyphotic, less than –5°. The C2–C7 Cobb was defined as the angle of intersection between lines parallel to the inferior end plates of C2 and C7. The C2–C7 sagittal vertical axial (SVA) was defined as the distance between the posterior superior corner of C7 and a plumb line of C2 centroid. T1 sagittal angle or T1 slope was defined as the angle between the superior endplate of T1 and a horizontal line on standing lateral radiograph (Fig. 1).<sup>[12]</sup> The cage significant subsidence was defined loss of the IH as more than 2 mm between postoperative



**Figure 1.** Radiographic measurements: (A) T1 slope; (B) C2–C7 Cobb angle; (C) C2–C7 SVA; (D) location of compression spinal cord. SVA = sagittal vertical axial.



**Figure 2.** Case 16: A patient was 57 years o;d, female, the compression spinal cord due to heterotopic ossification at C3-C4, MRI (B) and CT (C, D) before revision ACDF. We performed single-level ACDF to remove the lesion (E, F). The changes of upper and lower bodies before and after surgery (G, H). ACDF = anterior cervical discectomy and fusion, CT = computed tomography, MRI = magnetic resonance imaging.

and final follow-up. The patients underwent 2 or 3 segments anterior surgery, with at least 1-segment subsidence more than 2 mm assigned to the subsidence group. The excisional thickness was measured as the difference between upper and lower vertebral height of operative segment before and after surgery (Fig. 2G and H). The grade of ISI was classified as follows: grade 0, no ISI on T2-weighted MRI; grade 1, ISI on T2-weighted MRI limited to 1 disc level; grade 2, ISI on T2-weighted MRI beyond 1 disc level.<sup>[13]</sup> The T1S was classified into 2 groups: <20 degrees group and  $\geq 20$  degrees group.

### 2.5. Statistical analyses

In the data description, continuous variables were made using means and standard deviations (SDs), and categorical variables were described by frequencies and percentages. In univariate analysis, the factors of  $P$  value <.05 were brought into the multivariable logistic model. Multivariable logistic regression analysis was applied to control for potential confounding variables with the dependent variable of “poor outcome,” with adjusted odds ratios (ORs) within 95% confidence intervals (CIs). The continuous variables data among the risk factors were summarized by the specificity (SP), sensitivity (SN), area under the curve, and cut-off of risk factors and the receiver-operating characteristic (ROC) curves. The Youden index is defined as SN plus SP minus 1. The cut-off was defined as the maximum of

Youden index, which represented the best compromise between SN and SP. Kruskal–Wallis test or Mann–Whitney  $U$  test was used for comparative analysis of the variables of recovery rate, as appropriate. A  $P$  value <.05 was considered statistically significant. All data analyses were performed by SPSS software (Version 21.0, Chicago, IL), and the ROC were drawn by the GraphPad Prism 8.

## 3. Results

### 3.2. Participants

IN all, 113 patients with CSM resulted from heterotopic ossification, who underwent anterior decompression and fusion, were retrospectively reviewed from July, 2011 to February, 2016. In the present study, there were 54 males and 59 females (mean age 59.9 years), of which 65, 30, and 18 patients underwent single-level ACDF, 2-level ACDF, and 3-level ACDF, respectively.

### 3.3. Univariate and multivariable analyses

All patients were apportioned to 2 groups according to the degree of cage subsidence: <2 mm ( $n = 79$ ) and  $\geq 2$  mm ( $n = 34$ ; Table 1). By comparing the 2 groups, a statistically significant difference could also be found for excisional thickness ( $P < .001$ ), T1 slope ( $P < .001$ ), and CSA ( $P = .02$ ). There was no significant difference between the 2 groups with regard to age at surgery, sex, body

**Table 1****Comparison of patient characteristics between cage subsidence <2mm group and ≥2mm group.**

Variables	<2 mm (n = 79)	≥2 mm (n = 34)	P
Age at surgery, y	59.1 ± 8.3	61.6 ± 7.9	.134
Female, n (%)	40 (50.6%)	19 (55.9%)	.501
BMI (kg/m)	24.7 ± 3.4	25.4 ± 3.8	.315
Excisional thickness, mm	3.28 ± 0.71	3.89 ± 0.69	<.001
T1 slope	17.8 ± 3.4	21.0 ± 5.0	<.001
Involved levels, n (%)			.299
One	49 (62%)	16 (47.1%)	
Two	18 (22.8%)	12 (35.3%)	
Three	12 (15.2%)	6 (17.6%)	
JOA score			
Preoperative	8.87 ± 1.92	8.57 ± 1.67	.438
Final follow-up	14 (13.5, 15)*	13.5 (12.5, 14.5)*	.107
Recovery rate, %	62.1 ± 17.3	57.9 ± 14.5	.212
CSA, n (%)			.026
Lordotic	47 (59.5%)	16 (47.1%)	
Straight	25 (31.6%)	8 (23.5%)	
Kyphotic	7 (8.7%)	10 (29.4%)	
Smoking, n (%)			.384
Yes	14 (17.7%)	8 (23.5%)	
No	65 (82.3%)	26 (76.5%)	
Duration of symptoms, m	12 (18, 24)	18 (15, 30)	.175

BMI=body mass index, CSA=cervical sagittal alignment, JOA=Japanese Orthopaedic Association.

\*Significantly different at the final follow-up compare with preoperation ( $P < .05$ ).

mass index, number of involved segment, smoking, and duration of symptoms. (Table 1). The T1 slope (OR 1.59, 95% CI 1.259–1.945,  $P < .001$ ), excisional thickness (OR 2.38, 95% CI 1.163–4.888.0,  $P = .018$ ), and CSA (OR 11.23, 95% CI 3.595–35.064,  $P < .001$ ) were identified as the risk factors of the implant subsidence (Table 2).

### 3.4. ROC curves analysis

The cut-off values of T1 slope and excisional thickness were 19.65 angle and 3.7mm, respectively. It means that the implant would sink in all probability when the parameters achieve or approximate cut-off values (Table 3 and Fig. 3).

### 3.5. Clinical outcomes

In this study, compared with the preoperative JOA score, there was a statistically significant improvement after surgery in cage subsidence <2 mm group and ≥2 mm groups ( $P < .05$ ) (Table 1). The recovery rate of the 2 groups had no significant difference ( $62.1 \pm 17.3\%$  and  $57.9 \pm 14.5\%$ , respectively;  $P = .212$ ). In addition, we analyzed the reasons for recovery effect. There was a significant difference between kyphotic cohort and lordotic or straight cohort ( $P < .05$ ). The patients with the spinal cord

**Table 2****Multiple logistic regression analysis forecasted risk factors for the cage subsidence.**

Variable	OR (95% CI)	P
T1 slope	1.59 (1.295–1.945)	<.001
Excisional thickness	2.38 (1.163–4.888)	.018
CSA	11.23 (3.595–35.064)	<.001

CI=confidence interval, CSA=cervical sagittal alignment, OR=odds ratio.

**Table 3****Sensitivity, specificity, AUC, and cut-off of risk factors for predicting cage subsidence.**

Variable	SN	SP	AUC	Cut-off	P
T1 slope	0.676	0.734	0.692	19.65	.001
Excisional thickness	0.647	0.785	0.745	3.7	<.001

AUC=area under the curve, SN=sensitivity, SP=specificity.

compression beyond 1 disc level would have a significantly adverse outcome after ACDF approach ( $P < .001$ ). In addition, there was a nonsignificant relation between the JOA recovery rate and T1 slope by Mann–Whitney  $U$  test ( $P = .668$ ) (Table 4).

## 4. Discussion

Surgical treatment of CSM has 3 approaches including anterior, posterior, and combine anteroposterior. The posterior approach generates an indirect decompression resulting from the posterior shift of the spinal cord. The anterior approach is becoming more common due to the direct removal of the lesion, especially for patients with cervical sagittal kyphosis or circumscribed OPLL with a ≥50% canal occupying ratio.<sup>[14,15]</sup> However, to remove the heterotopic ossification as much as possible, removal of osseous endplate or vertebral body would be demanded. Cage subsidence seemed to be unavoidable in a majority of the cases after the removal of osseous endplate or vertebral body.<sup>[16]</sup> However, moderate removal of the endplate can promote early fusion.<sup>[7]</sup> In addition, Gercek et al<sup>[17]</sup> defined the titanium cage subsidence as the intervertebral change at least 3 mm after ACDF approach. Because of the obtuse contact face of PEEK cage in this study, we divided the patients into the mild group (<2 mm) and the severe group (≥2 mm).

There are many factors contributed to the cage subsidence. Firstly, some investigations have showed that older patients occurred implant subsidence.<sup>[8,16]</sup> It is commonly thought that the major causes of cage subsidence in older patients are bone density and cortical endplate decrease.<sup>[18]</sup> However, Bartels et al<sup>[19]</sup> deemed that advanced age was not an independent risk factor of cage subsidence after the ACDF approach. In our study, age was not included as a potential risk factor, owing to most patients without severe osteoporosis. Secondly, some investigators thought that it was advantageous to prevent cage subsidence if the contact area between bone surface and the cage was increased.<sup>[5]</sup> Nevertheless, the use of the end caps is controversial because it decreases the ratio of bone fusion while increasing the contact area.<sup>[16]</sup> In addition, Marino<sup>[20]</sup> found that the excisional thickness of endplate was significantly related to cage subsidence after posterior lumbar interbody fusion. By the multivariable logistic analysis, we corroborated the association between the excisional thickness of endplate and cage subsidence after anterior cervical surgery. Meanwhile, the cut-off value showed that excisional thickness over 3.7 mm was significantly associated with cage subsidence. On the contrary, previous studies reported that the early intervertebral fusion could prevent the implant subsidence after anterior surgery.<sup>[7,21]</sup>

Although various risk factors of cage subsidence have been reported in the previous studies, the loss of cervical sagittal malalignment remains a lack of a concern. Park et al<sup>[4]</sup> thought that graft subsidence was not correlated with cervical sagittal alignments before and after surgery. However, in our study, there

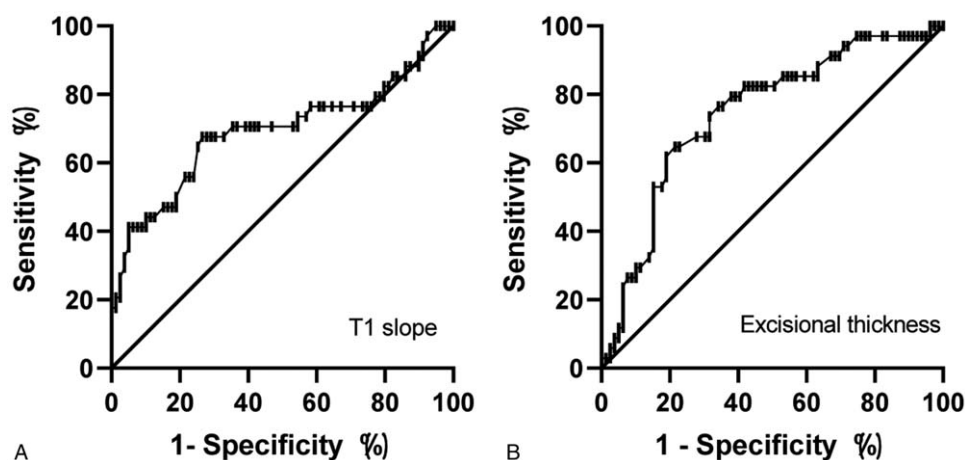


Figure 3. The T1 slope (A) and excisional thickness (B) were shown by the ROC, respectively. ROC=receiver-operating characteristic curve.

was a contrary consequence for this relationship. Although these results showed a significant statistical relation between the preoperative kyphotic alignment and postoperative cage subsidence, cage subsidence does not necessarily mean kyphosis after surgery. In fact, if the anterior portion of the implant is more subsidence than the posterior portion, the local kyphosis would occur. Nevertheless, one research reported that the implant subsidence usually occurred at the posterior upper endplates of the caudal bodies.<sup>[22]</sup> We thought the cause was the function of head gravity center. Historically, T1 slope angle was related to the cervical sagittal balance.<sup>[23]</sup> Therefore, the incidence of cage subsidence should be related to the T1 slope angle. Our study revealed that patients with T1 slope over 19.65° had a high incidence of cage subsidence after ACDF approach. We cannot determine who would obtain a sinking cage, but we could adopt appropriate technique during the surgery by avoiding excessive removal of the endplate and correcting abnormal cervical curvature.

Previous investigations showed that implant subsidence does not have a significant association with clinical outcome after anterior operation.<sup>[4,16,22]</sup> Our findings corroborated the conclusion of previous investigations. Furthermore, we found that the

CSA, C2-C7 SVA distance, and grade of ISI were significantly associated with postoperative outcome. Hence, the reconstruction of cervical alignment was 1 of the important preconditions for a good surgical outcome. In addition, Tang et al<sup>[24]</sup> deemed that patients with C2-C7 SVA value of approximately 40 mm had a significant association with postoperative poor outcome.

As with all studies, there were some weaknesses and limitations in the current study. Firstly, our investigation is a retrospective and single-center study. Secondly, the number of eligible patients was still not large. Only the sample of a large, multicenter, and randomized study can adequately forecast the risk factors of the cage subsidence. Thirdly, the follow-up term of involved patients were over 12 months after surgery, but a relationship could not be clearly established between long-term outcome and risk factors. Finally, JOA scores were calculated based on patients' subjective feelings, which inevitably lead to the deviation of outcomes. Although the selection of surgical procedures depended on spinal cord decompression needs, we cannot definitively conclude which is the best surgical procedure for patients with multistage spinal cord compression. In the future, some studies need to ascertain the relationship between adjacent-segment degeneration and cage subsidence after anterior surgery.

Table 4

Difference of the JOA recovery rate due to preoperative the factors.

Variables	Category	n	JOA recovery rate		P
			Median + interquartile range, %		
CSA	Lordotic	63	65 (55, 75)		.016*
	Straight	33	62 (51, 75)		
	Kyphotic	17	53 (43.5, 60.5) <sup>†</sup>		
C2-C7 SVA distance	<40 mm	94	64 (53.75, 75.25)		<.001 <sup>‡</sup>
	≥40 mm	19	36 (27, 56)		
Grade of ISI on MRI	G0 or G1	85	64 (53, 75.5)		.001 <sup>‡</sup>
	G2	28	57 (34.25, 64.75)		
T1S	<20 degrees	76	62 (50, 75.75)		.668 <sup>‡</sup>
	≥20 degrees	37	61 (52.5, 71)		

CSA=cervical sagittal alignment, ISI=increased signal intensity, JOA=Japanese Orthopaedic Association, MRI=magnetic resonance imaging, T1S=thoracic 1 slope.

\* Kruskal-Wallis test.

<sup>†</sup> Different from lordotic or straight ( $P<.05$ ).

<sup>‡</sup> Mann-Whitney  $U$  test.

## 5. Conclusions

Risk factors of cage subsidence included higher T1 slope, more excisional thickness, and inverted CSA. We suggest that patients with high T1 slope angle or preoperative kyphotic deformity should avoid excessive removal of endplate and vertebral body so as to reduce the occurrence of cage subsidence. Poor outcome had significant association with cervical kyphotic sagittal and higher ISI grade.

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**Methodology:** ShaoQing Li.

**Software:** ShaoQing Li.

**Supervision:** Yong Shen, Zhanyong Wu.

**Validation:** Hao Zhang, Zhanyong Wu.

**Visualization:** ShaoQing Li, Yong Shen, Zhanyong Wu.

**Writing – original draft:** ShaoQing Li.

**Writing – review & editing:** ShaoQing Li.

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