Risk factors of cage nonunion after anterior cervical discectomy and fusion

Bao Ren, MD\textsuperscript{a,b}, Wenshan Gao, MD\textsuperscript{b}, Jilong An, MD\textsuperscript{b}, Menghui Wu, MD\textsuperscript{a}, Yong Shen, MD\textsuperscript{a,*}

Abstract
The aim of our study was to explore risk factors of cage nonunion after anterior cervical discectomy and fusion (ACDF).

295 patients underwent ACDF in our hospital between Jan. 2014 and Jan. 2017. Of them, 277 patients suffered cage union (union group, UG) after 6-month follow-up and 18 did not (nonunion group, NG). We collected possible factors including gender, history of smoking, alcohol, hypertension, heart disease, diabetes, body mass index, diagnose, and preoperative visual analog scale -neck, visual analog scale-arm, neck disability index (NDI) and Japanese Orthorpaedic Association, surgical duration, blood loss, fusion levels, superior fusion segment, angle of C2–C7, range of motion for C2–C7, C2–C7 sagittal vertical axis and T1 slope. We performed univariable and multivariable analysis to compare data in 2 groups.

The rate of cage nonunion after ACDF was 6.1% (18 of 295) in our study. The outcome of univariable analysis showed that age (63.5 ± 10.1), angle of C2–C7 (18.0 ± 4.6), range of motion of C2–C7 (32.5 ± 7.7), C2–C7 sagittal vertical axis (17.9 ± 4.3) and T1 slope (22.1 ± 5.3) were higher in NG than these (59.4 ± 9.2, 16.2 ± 4.5, 30.2 ± 6.9, 16.1 ± 4.0, 20.9 ± 4.9) in UG. Additionally, patients with osteoporosis had markedly higher rate of cage nonunion after ACDF than those without. What’s more, the multivariable analysis implied the same results with univariable analysis.

Many factors could predict cage nonunion after ACDF. Cervical sagittal parameters play an important role in cage nonunion after ACDF. We hope that we can provide some guidance for spine surgeon before performing ACDF.

Abbreviations: ACDF = anterior cervical discectomy and fusion, ROM = range of motion, SVA = sagittal vertical axis.

Keywords: anterior cervical discectomy and fusion, cage, nonunion rate

1. Introduction
Cervical spondylotic disease, often caused by disc herniation or ossified ligament, is a common lesion, especially for the elderly. It may lower the quality of life, or even lead to disability for the patients.\textsuperscript{[1]} Anterior cervical discectomy and fusion (ACDF) has been the most widely used surgical choice in the treatment of degenerative cervical disc disease.\textsuperscript{[2–3]} Cage nonunion is a relatively low rate of complications, which has been reported varied by previous studies. Nevertheless, once it happens, it may cause serious consequences.\textsuperscript{[2–4]} Few study assessed risk factors for cage nonunion after this surgical procedure. The purpose of this study is to explore the possible risk factors for cage nonunion after ACDF. What’s more, we regard cervical sagittal parameters as predictors to explore risk factors of cage nonunion after ACDF.

2. Patients and methods
2.1. Ethics statement
The study was approved by the Institutional Review Board of our hospital before data collection and analysis. There was no need to obtain informed consent from patients since this was a retrospective study and all the data were collected and analyzed anonymously.

2.2. Patients
We collected data of 295 patients who underwent ACDF with polyetheretherketone cage from Jan. 2014 and Jan. 2017 in our hospital. At 6-month follow-up, 18 patients suffered cage nonunion, regarded as nonunion group and 277 patients had cage union, considered as union group. We defined cage nonunion as segmental range of motion (ROM) >2° and 2mm as cage subsidence on flexion-extension lateral views at 6-month follow-up.\textsuperscript{[4]} The inclusion criteria for study were as follows:
(1) diagnosed with cervical spondylotic disease before ACDF;
(2) underwent ACDF;
(3) cage nonunion can be seen by X-ray posteroanterior, lateral and dynamic lateral overflexional and overextensive views;
(4) more than 18 years old;

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\textsuperscript{a}Department of Spinal Surgery, The Third Hospital of Hebei Medical University, Shijiazhuang. \textsuperscript{b}Department of Orthopaedics, Affiliated Hospital of Hebei University, Baoding, China.

Correspondence: Yong Shen, Department of Spinal Surgery, The Third Hospital of Hebei Medical University, No. 139 Ziqiang Road, Shijiazhuang 050051, China (e-mail: hbsyjzsy777@163.com).

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2.3. Image assessment

X-ray posteroanterior, lateral and dynamic lateral overflexional and overextensive views were performed for all patients before ACDF. The following radiological variables include angle of C2 to C7 (C2–C7, the angle formed by the inferior endplates of C2 and C7 in lateral radiographs), C2 to C7 ROM (the sum of the C2–7 Cobb angle during flexion and extension lateral radiographs), C2–C7 sagittal vertical axis (SVA, distance from the posterosuperior corner of C7 and the vertical line from the center of the C2 body), T1 slope (the angle between a horizontal line and the superior endplate of T1 on lateral radiograph).

2.4. Clinical evaluation

Clinical evaluations included the pre-operative NDI, Japanese Orthopaedic Association, and visual analog scales for neck pain (VAS-neck) and arm pain (VAS-arm).

3. Methods

The methods were carried out in accordance with the approved guidelines. Two authors identified and collected all the data of patients according to inclusion criteria and exclusion criteria. In addition, two authors were responsible for data analysis. All measurement data were presented as the mean ± SD (standard deviation). When data satisfied criteria for normality and homogeneity of variance, statistical analysis between groups was performed using independent samples t-test. Otherwise, statistical analysis was performed using Mann-Whitney U test. For count data, chi-square test was used for data analysis. To identify the best predictors of cage nonunion after ACDF, univariable and multivariable analysis were computed. Statistical significance level was considered to be P < .05. All statistical analyses were carried out using SPSS, version 21.0 (SPSS Inc., Chicago, IL).

4. Results

Table 1 shows that there is no significant difference in gender, history of smoking, alcohol, hypertension, heart disease, diabetes, body mass index, diagnose (cervical spondylotic myelopathy, CSM or ossification of posterior longitudinal ligament, OPLL), and preoperative VAS-neck, VAS-arm, NDI and Japanese Orthopaedic Association between 2 groups. But, angle of C2–7 Cobb (18.0 ± 4.6), C2–C7 ROM (32.5 ± 7.7), C2–C7 SVA (17.9 ± 4.3) and T1 slope (22.1 ± 5.3) are higher in NG than these (16.2 ± 4.5, 30.2 ± 6.9,16.1 ± 4.0, 20.9 ± 4.9) in UG.

Table 2 summaries the multivariable analysis for cage nonunion after ACDF. Our results show that age [OR = 1.75, 95CI (1.22,2.28), P < .0001 =, osteoporosis [OR = 1.94, 95CI (1.44,2.51), p = 0.001], angle of C2–C7 [OR = 1.24, 95CI (1.21,1.129), P = .001], C2–C7 ROM [OR = 3.44, 95CI (1.09,6.75), P < .0001 =, C2–C7 SVA [OR = 1.20, 95CI (1.05,1.35), P = .001], and T1 slope [OR = 5.30, 95CI (2.20,9.10), P < .0001 = are independent predictors for cage nonunion after ACDF.

5. Discussion

ACDF is an optimal alternative to treat cervical spondylotic disease, which is able to promote instant stability, restoration of the neural foraminal height and interbody fusion. Previous studies reported that the rate of cage nonunion was less than 10% after ACDF. However, its risk factors are controversial. Yang et al. found that rate of nonunion was 0% and 35% after one-level fusion and two-level fusion, respectively, indicating a significantly higher rate of nonunion in two-level fusion. Nevertheless, Van Jonbergen et al. reported that number of segments was not a risk factor for cage nonunion after ACDF. As far as we know, few article regarded sagittal parameters as a vital indicator to assess risk factors for cage nonunion after ACDF. The purpose of our study is to find the best predictors of cage nonunion after ACDF.
work is to explore the difference of sagittal parameters in 2 groups. In our study, the rate of cage nonunion in our study is 6.1%, which is consistent with results of previous studies.\cite{4,5} Based on the univariable and multivariable analysis, the most important findings of this study are that high angle of C2–C7, C2–C7 ROM, C2–C7 SVA and T1 slope are positively associated with cage nonunion after ACDF. In addition, we also find that patients with advanced age and osteoporosis have a higher rate of cage nonunion following ACDF than those without.

Some literature demonstrated that advanced age and low bone mineral density were known risk factors for cage nonunion after ACDF. Our results are consistent with previous studies,\cite{2–3} showing 63.5 years of mean age in NG and 59.4 years in UG, and 11 of 18 (61.1%) patients with osteoporosis were in NG and 98 of 277 (35.4%) in UG (all $P < .05$). Additionally, no obvious difference is found on body mass index between 2 groups in present study, which is opposite with date of previous study.\cite{4} Yang\cite{6} demonstrated that patients with 2-level ACDF had significantly higher rate of nonunion in comparison with one-level. However, we find no statistical difference in 2 groups, which is the same with results of Van Jonbergen.\cite{7}

Recently, increasing reports paid attention on cervical sagittal parameters as elements to evaluate risk factors of cage nonunion after ACDF. Previous study\cite{11} indicated that there was a positive correlation between T1 slope and angle of C2–C7, C2–C7 ROM and C2–C7 SVA. As patients with high T1 slope companied with high C2–C7 angle, C2–C7 ROM and C2–C7 SVA, the cervical spine tends to fall forward, meaning that it could generate a large amount of shear force paralleled to the intervertebral space. It is well known that greater force that perpendicular to the intervertebral space is beneficial to cage union. Assumed that

### Table 3
Comparison of cervical sagittal parameters in union group (UG) and nonunion group (NG).

| Factors                  | nonunion (n=18) | union (n=277) | $P$-value |
|-------------------------|-----------------|---------------|-----------|
| C2–C7 angle (°)         | 18.0±4.6        | 16.2±4.5      | .001      |
| C2–C7 ROM (°)           | 32.5±7.7        | 30.2±6.9      | .001      |
| C2–C7 SVA (mm)          | 17.9±4.3        | 16.1±4.0      | .01       |
| T1 slope (°)            | 22.1±5.3        | 20.9±4.9      | .001      |

### Table 4
Factors may be associated with cage nonunion after surgery by multiple logistic regression analysis. (We just presented the significant risk factors.)

| Factors          | $P$-value | 95% CI     |
|------------------|-----------|------------|
| X1 = Age         | <.0001    | 1.75 (1.22,2.28) |
| X2 = Osteoporosis| .001      | 1.94 (1.44,2.51) |
| X3 = C2–C7 angle (°) | .001  | 1.24 (1.21,1.29) |
| X4 = C2–C7 ROM   | <.0001    | 3.44 (1.09,6.75) |
| X5 = C2–C7 SVA   | .001      | 1.20 (1.05,1.35) |
| X6 = T1 slope    | <.0001    | 5.30 (2.20,9.10) |

Cl = confidence interval, ROM = range of motion, SVA = sagittal vertical axis.
gravity is constant, if the shear force increases, the force that perpendicular to the intervertebral space would naturally decrease, as shown in Figure 1. Patwardhan[12] found that the subjacent segment mechanical burden became greater with increasing C2 to C7 angle or SVA. We assume that change of biomechanical force in section of cervical caused by high C2 to C7 angle or SVA after ACDF may be correlated with cage nonunion. Additionally, we try to explore whether the pre-surgical cervical curvature is an independent risk factor for cage nonunion after ACDF. However, we do not find positive correlation between pre-surgical cervical curvature and cage nonunion after ACDF.

Although this study provides several novel findings, it has some limitations. First, this is a retrospective and single-center study and low incidence of cage nonunion leads to a small sample size. Thus, a larger sample, prospective and multicenter study is needed; second, there were 2 surgeons performed ACDF in this series, but every surgeon was skillful and worked in spine surgery for more than 10 years. However, to the best of our knowledge, few studies reported the role of sagittal alignment in cage nonunion following ACDF.

In conclusion, many factors are found to be correlative with cage nonunion following ACDF by univariable and multivariable analysis. Our results also show that great T1 slope, as a vital predictor, is association with cage nonunion. This article could give some information for surgeons that patients with high T1 slope had relatively higher rate of cage nonunion after ACDF.

Author contributions
Methodology: Jilong An, Menghui Wu.
Writing – original draft: bao ren, Wenshan Gao.
Writing – review & editing: Yong Shen.

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