Factors predicting adjacent segment disease after anterior cervical discectomy and fusion treating cervical spondylotic myelopathy
A retrospective study with 5-year follow-up

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Abstract
The purpose of this study is to explore perioperative factors predicting symptomatic adjacent segment disease (ASD) after anterior cervical discectomy and fusion (ACDF) for patients with cervical spondylotic myelopathy (CSM) at 5-year follow-up.

This study included 356 patients who underwent ACDF for CSM from Jan.2011 to Jan.2013. Up to Jan. 2018, 39 patients suffered from ASD and 317 did not. Assessments include: age, sex, body mass index (BMI), diabetes, smoking, alcohol, duration of symptoms, preoperative Cobb angle of C2 to 7, T1 slope, C2 to 7 range of motion (C2–7 range of motion [ROM]), C2 to 7 sagittal vertical axis (C2–7 SVA), fusion level involved, superior fusion segment, high signal intensity on T2-WI, preoperative visual analogue scale (VAS), VAS-neck, VAS-Arm, Neck Disability Index (NDI) and Japanese Orthopaedic Association (JOA).

Factors were processed by univariate analysis and multivariate linear regression.

Data analyzed by univariate and multivariate analysis shows that age (68.9 years old), duration of symptoms (18.8 months), superior fusion segment, more fusion level involved (2.7), high signal intensity on T2-WI (17 of 39 patients), Cobb angle of C2 to C7 (18.7°), C2 to C7 SV (51.0 mm), T1 slope (28.4°), preoperative VAS-neck (5.2), VAS-Arm (5.6) and NDI (36.7) in ASD group are significantly higher than those in non-ASD group, however, preoperative JOA (8.2 vs 11.2, P < .001) has an opposite trend in 2 groups.

The rate of ASD after ACDF is 10.9% in 5-year follow up. Patients with cervical sagittal imbalance, advanced age and sever state of CSM, which have a positive relation with ASD before surgery should be paid attention for surgeons.

Abbreviations: ACDF = anterior cervical discectomy and fusion, ASD = adjacent segment disease, BMI = body mass index, CSM = cervical spondylotic myelopathy, JOA = Japanese Orthopaedic Association, MRI = magnetic resonance imaging, NDI = Neck Disability Index, ROM = range of motion, SVA = sagittal vertical axis, VAS = visual analogue scale.

Keywords: adjacent segment disease, anterior cervical discectomy and fusion, cervical spondylotic myelopathy

1. Introduction
Anterior cervical discectomy and fusion (ACDF) has been widely applied to treat cervical spondylotic myelopathy (CSM), which is a common degenerative disease in clinic. ACDF could remove anterior spinal cord compression and preserve the stability of the spinal column, but patients with ACDF may have a high risk of incomplete decompression, limited visual exposure and injury to the cord. Additionally, some literature reported that ACDF had a high incidence of adjacent segment disease (ASD), especially in treatment for multilevel CSM, or even revision surgery. Veeravagu reported that the rate of revision surgery due to ASD ranged from 2.1% to 9.13% for single level surgeries, and for multilevel surgeries, ranged from 4.4% to 10.7% at ACDF in 2-year follow-up.

A growing number of scholars focus on symptomatic ASD after ACDF, but few reports on perioperative factors predicting ASD after ACDF in long follow-ups. As far as we know, this is the first study to explore the perioperative variables including radiographic parameter predicting symptomatic ASD after ACDF in 5-year follow-up.

2. Materials and methods

2.1. Ethics statement
The study was approved by the Institutional Review Board of our hospital before data collection and analysis.

2.2. Patients
The study included 356 patients who were performed ACDF from Jan.2011 to Jan.2013 in our hospital. Up to Jan. 2018, 39
patients suffered from symptomatic ASD, and 317 did not. The inclusion criteria are as follow:

1. diagnosed with CSM before surgery;
2. had a surgical history of ACDF;
3. diagnosed with Symptomatic ASD in the final follow up;
4. more than 5-year follow up.

Exclusion criteria:

1. have spinal deformities;
2. have acute spinal trauma or tumour;
3. preoperation-kypotic deformity;
4. younger than 18 years old.

2.3. Surgical method

All patients who received ACDF were performed by 1 surgeon. After complete discectomy and osteophytectomy, we performed adequate decompression of cervical cord and inserted a cervical titanium cage including autologous into intervertebral space. Ambulation was allowed on the second day after surgery, whereas external immobilization of the cervical spine was kept for 2 months with a cervical collar.

2.4. Radiological assessment

Patients were checked by cervical lateral, extension and flexion radiographs. The following radiological variables include angle of C2 to C7 (C2–C7) (defined as the angle formed by the inferior endplates of C2 and C7 in lateral radiographs), C2 to C7 range of motion (ROM) (defined as the sum of the C2–7 Cobb angle during flexion and extension lateral radiographs), C2 to 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), as shown in Figures 1–3. Additionally, age, sex, body mass index (BMI), history of smoking, alcohol and diabetes, duration of symptoms, fusion level involved, superior fusion segment, high signal intensity on T2-WI, preoperative visual analogue scale (VAS)-neck, VAS-arm, Neuroradiology (Neuromuscular) (NDI), Japanese Orthopaedic Association (JOA) were also accessed in our study.

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, 2 authors were responsible for data analyses. All measurement data are presented as the mean ± standard deviation (SD) when data satisfied criteria for normality with P > .05. When data satisfied criteria for normality and homogeneity of variance, statistical analysis between groups was performed using independent samples t test. For count data, Chi-square test was used for data analysis. The Kolmogorov–Smirnoff test was used to verify the normal data distribution. Statistical significance levels were considered to be p < 0.05. All statistical analyses were carried out using SPSS, version 21.0 (SPSS Inc., Chicago, IL). To identify the best predictors of revision surgery, multiple linear regression models were computed.

3. Results

Table 1 shows that there is no significant difference in sex, BMI, history of smoking, alcohol, diabetes, superior fusion segment and C2 to C7 ROM between 2 groups. Age (68.9 ± 9.4), duration of symptoms (18.8 ± 3.7), fusion level involved (2.7 ± 1.1), superior fusion segment, Cobb angle of C2 to C7 (18.7 ± 5.3), C2 to C7 SVA (31.0 ± 7.1), T1 slope (28.4 ± 6.9), preoperative VAS-neck (5.2 ± 1.5), preoperative VAS-arm (5.6 ± 1.5) and preoperative NDI (36.7 ± 8.1) are markedly higher in ASD group than those (63.9 ± 7.9, 10.1 ± 2.3, 2.1 ± 1.0, 16.0 ± 4.3, 16.9 ± 4.4, 21.1 ± 6.3, 4.3 ± 1.2, 4.7 ± 1.2, 32.0 ± 10.6, all P < .05) in non-ASD group, however, the preoperative JOA (8.2 ± 1.9 vs 11.2 ± 2.2, P < .001) is significantly lower in ASD group than that in non-ASD group. There are 17 out of 39 (43.6%) patients with high signal intensity on T2-WI on cervical magnetic resonance imaging (MRI) before surgery in ASD group.

Table 2 summaries the multiple linear regression for ASD after ACDF. Our results show that age [OR = 0.68 95% CI (0.53–0.74), P = .004], duration of symptoms [OR = 0.36 95% CI (0.22–0.50), P < .0001 =, fusion level involved] [OR = 1.98 95% CI (1.32–2.64), P = .001], Cobb angle of C2–C7] [OR = 1.36 95% CI (0.82–1.80), P = .002], C2–C7 SVA [OR = 0.85 95% CI (0.61–0.85), P < .0001 =, T1 slope] [OR = 1.23 95% CI (1.01–1.88), P = .0001 =, preoperative VAS-neck] [OR = 0.64 95% CI (0.45–0.84), P < .0001 =, preoperative VAS-arm] [OR = 1.25 95% CI (0.88–1.62), P < .0001 =, NDI] [OR = 0.69 95% CI (0.45–0.94), P = .002], and JOA [OR = 1.89 95% CI (1.52–2.29), P < .0001] are independent predictors for ASD after ACDF.
4. Discussion

As for multilevel CSM, risk of complications and surgical revision must be considered when choosing operation plan. Veeravagu compared the rate of revision surgery due to ASD between single level and multilevel ACDF and found that the rate of cervical reoperations in the multilevel ACDF group was 10.68%, but for single level was 9.16%, implying that multilevel ACDF was more likely to cause ASD after ACDF. Meanwhile, his study showed that incidence of revision surgery due to ASD was 3.4% per year for the multilevel ACDF patients and 2.9% per year in the single-level. Satomi followed 33 patients receiving laminoplasty for 5 years and found that 6 presented recurrence of spinal canal stenosis and need revision surgery. Komura reported on revision surgery after failed cervical laminoplasty and regarded ACDF with fibular strut graft as an effective procedure for failed laminoplasty. Even though the number of ASD after cervical surgery is increasing, but few studies focus on factors predicting ASD after ACDF. As far as I am concerned, this is the first article to explore perioperative predictors including radiographic parameters for ASD after ACDF.

Our results show that the rate of ASD is 10.9% in 5 years follow-up and are analyzed by univariate and multivariate analysis showing that advanced age, longer duration of symptoms, more fusion level involved, superior fusion segment, Cobb angle of C2 to C7, C2 to C7 SVA, T1 slope, higher preoperative VAS-neck, VAS-arm and NDI scores, less preoperative JOA, high signal intensity on T2-WI on cervical MRI are perioperative predictor of ASD after ACDF.

| Factors                             | non-ASD group (n = 317) | ASD group (n = 39) | P     |
|-------------------------------------|-------------------------|-------------------|-------|
| Age (years)                         | 62.4 ± 8.1              | 68.9 ± 9.4        | <.001 |
| Sex (Male/Female)                   | 172/145                 | 22/17             | .799  |
| BMI, kg/m²                          | 25.7 ± 3.8              | 24.4 ± 2.8        | .064  |
| Smoking (Yes/No)                    | 133/184                 | 15/24             | .869  |
| alcohol use (Yes/No)                | 240/77                  | 30/9              | .413  |
| Diabetes (Yes/No)                   | 241/76                  | 25/14             | .106  |
| Duration of symptoms (months)       | 10.8 ± 2.2              | 18.8 ± 3.7        | <.001 |
| Fusion level involved               | 2.1 ± 1.0               | 2.7 ± 1.1         | <.001 |
| Superior fusion segment             |                         |                   |       |
| C2–C3                               | 30                      | 7                 |       |
| C3–C4                               | 42                      | 15                |       |
| C4–C5                               | 143                     | 7                 |       |
| C5–C6                               | 79                      | 5                 |       |
| C6–C7                               | 23                      | 5                 |       |
| C2–C7 (°)                           | 16.0 ± 4.3              | 18.7 ± 5.3        | <.001 |
| C2–C7 ROM                           | 30.6 ± 8.2              | 31.0 ± 8.5        | .825  |
| C2–C7 SVA, mm                       | 16.9 ± 4.4              | 31.0 ± 7.1        | <.001 |
| T1 slope                            | 21.1 ± 6.3              | 28.4 ± 6.9        | <.001 |
| High signal intensity on T2-WI (Yes/No) | 22/295               | 17/22             | <.001 |
| Preoperative VAS-neck               | 4.6 ± 1.2               | 5.2 ± 1.3         | .002  |
| Preoperative VAS-arm                | 4.6 ± 1.2               | 5.6 ± 1.5         | <.001 |
| Preoperative NDI                    | 30.0 ± 10.5             | 36.7 ± 8.1        | <.001 |
| Preoperative JOA                    | 10.5 ± 2.2              | 8.2 ± 1.9         | <.001 |

ASD = adjacent segment disease, BMI = body mass index, JOA = Japanese Orthopaedic Association, NDI = Neck Disability Index, ROM = range of motion, SVA = sagittal vertical axis, VAS = visual analogue scale.
Veeravagu[7] respectively compared single-level and multi-level ACDF in reoperation rate. In 2-years follow-up, revision rate due to ASD was 9.13% in the single-level ACDF, but multilevel had a markedly higher incidence of 10.7%. In our study, the rate of ASD after ACDF was 10.9% at 5-year follow-up. Additionally, patients receiving more than 3 level fusions were more likely to suffer from ASD in his study, which was similar to our results. In our study, compared to non-ASD group, more fusion level involved (2.2 ± 1.0 vs 2.7 ± 1.1) had a higher rate of ASD, implying that increasing number of levels fused was correlated with ASD after ACDF. Patwardhan[13] performed a biomechanical study and noted that increased intradiscal pressures in both superior and inferior adjacent segments with increasing level fusions. Undoubtedly, great pressure in adjacent segments could accelerate disc degeneration.

Lately, cervical sagittal balance plays a vital role in predicting clinical and functional outcomes after surgery. Generally, C2 to C7 SVA, defined as the distance from the posterosuperior corner of C7 and the vertical line from the center of the C2 body, was regarded as an important factor determining clinical outcomes after cervical surgeries. Cobb angles of C2 to C7 measured lordosis. T1 was also an important factor in cervical sagittal parameters which influencing degree of thoracic kyphosis. Sakai[15] found that, for patients suffering from CSM without cervical kyphosis, cervical sagittal imbalance and relatively larger age were the preoperative risk factors for kyphotic deformity after laminoplasty. Park[16] reported that sagittal balance after surgery may affect the development of adjacent segment pathology which need requiring surgery. Tang[17] demonstrated that postsurgical sagittal balance as measured by C2 to C7 SVA, correlated with postoperative Neck NDI and Short-Form 36 physical component summary (SF-36 PCS) scores for patients after cervical posterior surgery.

Roguski[18] performed a prospective study to explore whether postoperative cervical sagittal balance was an independent predictor of clinical outcome after surgery for CSM and indicated that both preoperative and postoperative cervical sagittal balance parameters could independently predict clinical outcomes after surgery for CSM. In our study, we explore the relationship between preoperative cervical sagittal parameters and symptomatic ASD after ACDF and find that there is cervical sagittal imbalance in ASD group, suggesting that cervical sagittal imbalance is correlated with ASD after ACDF at 5-year follow-up. Sakai[15] showed that preoperative high C2 to C7 SVA could predict kyphotic deformity and Kim[19] reported that high T1 slope was a predictive risk factor of kyphotic deformity. Patwardhan[13] tried to explore whether the presence of cervical sagittal imbalance was an independent risk factor for increasing the mechanical burden on adjacent discs and found that the subjacent segment mechanical burden became greater with increasing C2 to C7 angle or SVA, which could speed up ASD or even led to revision surgery.

Our results also present that advanced age is a vital predictor for symptomatic ASD, which is similar to Sakai.[15] Besides, 17 out of 39 (43.6%) patients with high signal intensity on T2-WI of cervical MRI before operation in this study. What is more, preoperative VAS-arm, VAS-neck, NDI, JOA, and longer duration of symptoms played an important role in predicting ASD, implying that sever pathogenic condition before surgery was more likely to suffer from ASD after ACDF.

Although this study provides several novel findings, it has some limitations. First, this paper is a retrospective study, prospective study needs to conduct; second, we just analyze perioperative predictors of ASD, other factors causing ASD should be analyzed in further study; third, for patients with sagittal imbalance, whether there is correction of the imbalance after decompression of the responsible level is the direction of further study. However, to the best of our knowledge, this is the first study reporting on perioperative predictors of ASD after ACDF in treatment for CSM.

In conclusion, the rate of adjacent segment degeneration after ACDF is 10.9% in 5-year follow-up. Our data shows that many factors are related with ASD after ACDF. We should talk to patients, especially for whom with cervical sagittal imbalance, advanced age and severe state of CSM about the possibility of ASD after surgery. All above should be considered during surgical planning.

Author contributions
Study conception and design by BR
Data collection by JPY and XHT, data analysis by WSG, and manuscript by WYD and YS.
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