

Risk factors associated with clinical adjacent segment pathology following multi-level cervical fusion surgery

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Abstract

Few clinical studies investigate risk factors associated with clinical adjacent segment pathology (CASP) following multi-level cervical fusion surgery. The aim is to record the incidence of postoperative CASP in patients after at least 2 years' follow-up and to identify possible risk factors that may be associated with the CASP after multi-level cervical surgery.

We retrospectively reviewed patients who underwent multi-level cervical surgery in our hospital from January 2004 to February 2016. All patients underwent more than 2 years' follow-up. The diagnosis of CASP is according to clinical symptoms as well as image findings. Potential risk factors were collected from demographic data and radiographic images.

A total of 301 patients after multi-level cervical surgery were analyzed. During follow-up, 28 patients (9.3%) were diagnosed as having CASP. Among these patients, 7 showed symptoms of CASP within 3 years after surgery, 6 showed symptoms between 3 and 5 years, 14 showed symptoms between 5 and 10 years, and the last one showed symptoms more than 10 years later. In the multivariate analysis, degeneration of adjacent segment (OR, 1.592; 95% CI, 1.113–2.277), decreased Cobb angle in fused vertebrae (OR, 2.113; 95% CI, 1.338–3.334) and decreased Cobb angle in cervical spine (OR, 1.896; 95% CI, 1.246–2.886) were correlated with the incidence of CASP during follow-up.

The incidence of CASP following multi-level cervical surgery was 9.3% with a mean of about 70 months' follow-up. Patients with preoperative degeneration of adjacent segment and postoperative imbalance of sagittal alignment have a higher risk of developing CASP after multi-level cervical surgery.

Abbreviations: ACDF = anterior cervical discectomy and fusion, AO = arbeitsgemeinschaft für osteosynthesefragen, ASP = adjacent segment pathology, BMI = body mass index, CASP = clinical adjacent segment pathology, CT = computed tomography, MRI = magnetic resonance imaging, OLF = ossification of ligamentum flavum, OPLL = ossification of posterior longitudinal ligament, PCLF = posterior cervical laminectomy and fusion, RASP = radiographic adjacent segment pathology, ROM = range of motion.

Keywords: adjacent segment pathology, cervical fusion, multi-level, risk factors

1. Introduction

In recent decades, the aging of society has developed rapidly. In the meantime, the number of patients with degenerative cervical disorders has risen sharply.^[1,2] For patients with multi-level

cervical disorders, anterior cervical discectomy and fusion (ACDF) or posterior cervical laminectomy and fusion (PCLF) has become standard treatment strategies after failure of conservative treatment.^[3,4] However, with the increased number of cervical surgery, some studies have shown that postoperative breakdown may occur at levels adjacent to the index surgery during follow-up. Postoperative adjacent segment pathology (ASP) has become the leading topic drawing clinical interest in spine surgery.^[5,6] With the development of imaging^[7,8] and the deepening of people's acquaintance with it, ASP has received more and more attentions.

ASP is a well-known illness involving both the cervical and lumbar spine. Arbeitsgemeinschaft für Osteosynthesefragen (AO) Spine has subdivided ASP into radiographic adjacent segment pathology (RASP) and clinical adjacent segment pathology (CASP). RASP refers to radiographic degeneration at adjacent segment without symptoms; CASP, in contrast, refers to not only degenerative changes at adjacent segment but also clinically related symptoms, such as radiculopathy, myelopathy, or features suggestive of instability.^[9]

Nowadays, the exact pathogenesis of CASP still remains a source of significant controversy. Scholars continue to debate whether it is an acceleration of degeneration caused by the biomechanical effects of prior fusion surgery, or just a natural age-related degenerative process.^[10–12] Besides, though risk factors for CASP have been investigated by previous studies, some controversy existed in certain predictive factors. For

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examples, the cervical alignment was not demonstrated to be a predictor of CASP in patients after single-level surgery.^[13] However, in a recent laboratory study, the cervical sagittal imbalance arising from regional and/or global spinal sagittal malalignment was considered to play a role in exacerbating CASP after multi-level anterior cervical arthrodesis.^[14] There is a possibility that the pathogenesis of CASP in patients after multiple-level surgery is different from that after single-level surgery. Though several clinical studies about CASP have been conducted in patients after single-level surgery, few clinical studies have been conducted in patients after multi-level surgery.

In the current study, we tried to fill some of these gaps in clinical research by analyzing patients who only underwent multi-level cervical surgery. The aim is to record the incidence of postoperative CASP in patients after more than 2 years' follow-up and to identify possible risk factors that may be associated with the CASP.

2. Methods

2.1. Patient population

We retrospectively reviewed patients who underwent multi-level cervical surgery in our hospital from January 2004 to February 2016. The inclusion criteria were adult patients with radiculopathy, myelopathy or myeloradiculopathy, which resulted from multi-level cervical degenerative disc disease, ossification of posterior longitudinal ligament (OPLL) or ossification of ligamentum flavum (OLF), and were confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) scan. Patients with tumor, infection, deformity, trauma or prior cervical spinal surgery were excluded. For patients with any non-fusion surgery, such as one- or two-side open door laminoplasty, laminectomy without fusion was also excluded. The ethics committee of the Third Hospital of Hebei Medical University approved this research and waived the informed consent because this was a retrospective observational study and all data were collected and analyzed anonymously.

2.2. Treatment and follow-up

Before surgery, antero-posterior, lateral, and flexion/extension lateral X-ray tests, CT and MRI scans were performed for patients. All patients underwent ACDF or PCLF procedures.^[3,4] A soft collar was used for 6 to 8 weeks postoperatively.

Routine X-ray tests were performed postoperatively at 6 weeks, 3-, 6- and 12 months, and then annually in erect position. Instability was considered to be present if more than 2 mm of slippage displacement was observed on extension-flexion radiographs. Patients who developed additional cervical radiculopathy or myelopathy symptoms, or features suggestive of instability during follow-up were advised to go back to our clinic at their earliest convenience, and physical examination as well as radiographic test, especially MRI scan, were performed to get the diagnosis of CASP.

The CASP is defined as newly developed symptoms of radiculopathy, myelopathy or myeloradiculopathy, which include features suggestive of instability, as well as compressive lesions of nerve root or spinal cord in the levels adjacent to the previous surgery in radiographic images.

2.3. Parameter evaluation

Basic characteristics of patients included age at surgery, gender, body mass index (BMI), smoking history, alcohol history,

diabetes mellitus, surgical approach, and number of levels fused. Postoperative radiographs at the 6-month follow-up were used to assess the following parameters, such as congenital stenosis, Cobb angle of fused vertebrae, Cobb angle of the cervical spine, range of motion (ROM) of C2-C7, and T1 slope. Preoperative and postoperative radiographs were used to calculate changes of Cobb angle in the fused vertebrae and in the whole cervical spine.

These parameters were evaluated as we described in our previous study.^[13] In brief, the Pavlov ratio was used to assess the spinal canal diameter at the C5 level, and its value was equal to antero-posterior diameter of the spinal canal divided by the antero-posterior diameter of the vertebral body. A Pavlov ratio less than 0.80 was regarded as the presence of congenital stenosis; The Cobb angle of fused vertebrae was determined by the superior endplate of cranial vertebral body and the inferior endplate of caudal vertebral body in the index level; The Cobb angle of cervical spine was formed by the inferior endplates of C2 and C7 in standing lateral radiographs; The ROM of C2-C7 was defined as the sum of the absolute value of C2-7 Cobb angle in flexion and extension lateral radiographs; The T1 slope was formed by the angle between the superior endplate of T1 and the horizontal line.

According to Hilibrand definitions,^[15] pre-existing degenerative changes of adjacent segments was evaluated according to preoperative radiographs and MRI. The existence of mild degeneration of adjacent segment was defined as a potential risk factor. Those who have moderate or severe degeneration of adjacent segment were not included in our study.

Two blinded observers assess the radiographic findings independently. For continuous variables, the mean values were used. For categorical variables, disagreements between the 2 observers were settled by discussion, and the third observer made the final decision if no consensus could be reached.

2.4. Data analysis

All statistical analysis was performed with the Statistical Package for Social Sciences software (version 17.0; SPSS Inc., Chicago, IL, USA). The difference between groups was determined by Fisher exact tests or independent-samples *t* tests. After univariate analysis, Variables that might be potentially associated with CASP ($P < .10$) entered into the multiple logistic regression analysis. Probability value less than .05 was considered to be statistically significant.

3. Results

A total of 301 patients after multi-level cervical spine surgery were analyzed in this study. Among these patients, 154 were male, and 147 were female. The mean age at the time of surgery was 56.7 ± 9.9 years. Two hundred fifty-three patients were diagnosed with cervical degenerative disc disease, 31 were diagnosed with OPLL, and 17 were diagnosed with OLF. Two hundred thirty-three patients underwent surgery by anterior approach, and the other 68 patients underwent surgery by posterior approach. The length of follow-up was 70.6 ± 10.4 months.

During follow-up, 28 patients were diagnosed with CASP and the incidence was 9.3%. Seventeen of them were at the cephalad adjacent level, and the other 11 were at the caudal level. Twenty-six of them happened in patients after 2-levels surgery, 2 in patients after 3-levels surgery, and no one happened in patients after 4-levels surgery. Among these patients, 7 showed symptoms

Table 1
Demographic data of patients with CASP after multilevel cervical surgery.

Variables	Values
Number of patients	28
Age at surgery (year)	57.5±11.6
Gender	
Male	12
Female	16
Levels fused	
2 levels	26
3 levels	2
4 levels	0
Approach	
Anterior approach	23
Posterior approach	5
Location of CASP	
Cephalad segment	17
Caudal segment	11
The presentation of symptoms	
Within 3 years	7
3–5 years	6
5–10 years	14
More than 10 years	1

CASP = clinical adjacent segment pathology.

of CASP within three years after surgery, 6 showed symptoms between 3 and 5 years, 14 showed symptoms between 5 and 10 years, and the other one showed symptoms more than 10 years later (Table 1). Twenty-three patients underwent conservative treatment and the symptoms resolved gradually. Only 5 patients required and underwent revision surgery.

In the univariate analyses of patients' basic data as well as radiographic data, we found that less fused levels, degeneration of adjacent segment, less Cobb angle of fused vertebrae, decreased Cobb angle in fused vertebrae and decreased Cobb angle in cervical spine were potential risk factors ($P < .10$), while age at surgery, gender, BMI, smoking or alcohol habit, diabetes mellitus, surgical approach, congenital stenosis, Cobb angle of cervical spine, postoperative ROM of C2–C7 or T1 slope were not (Table 2). In the further multivariate logistic regression, degeneration of adjacent segment (OR, 1.592; 95% CI, 1.113–2.277), decreased Cobb angle in fused vertebrae (OR, 2.113; 95% CI, 1.338–3.334) and decreased Cobb angle in cervical spine (OR, 1.896; 95% CI, 1.246–2.886) were correlated with the incidence of CASP during follow-up (Table 3).

4. Discussion

Identification of the predictive factors for development of CASP may help surgeons to identify patients at the greatest risk for it and to adjust their monitoring and follow-up decisions.^[16] Though factors associated with CASP after single-level surgery has been investigated, few clinical studies have investigated risk factors associated with CASP following multi-level cervical fusion surgery. In this study, we only reviewed patients after multi-level cervical surgery and revealed that the incidence of CASP was 9.3% with a mean of about 70 months' follow-up. The etiology of CASP is likely to be multifactorial. Patients with degeneration of adjacent segment, decreased Cobb angle in fused vertebrae and decreased Cobb angle in cervical spine have a higher risk to develop CASP after multi-level cervical surgery.

Table 2
The comparison of data in patients with and without CASP.

Characteristic	CASP patients (n=28)	None-CASP patients (n=273)	P value
Age at surgery (year)	57.5±11.6	56.6±9.3	0.634
Gender			
Male	12	142	0.429
Female	16	131	
BMI (kg/m ²)	25.4±2.3	25.8±2.1	0.342
Smoking			
Yes	7	71	0.908
No	21	202	
Alcohol			
Yes	9	92	0.868
No	19	181	
Diabetes mellitus			
Yes	5	26	0.186
No	23	247	
Approach			
Anterior	23	210	0.156
Posterior	5	63	
Levels fused			
2 levels	26	212	0.085
3 or more levels	2	61	
Congenital stenosis			
Yes	13	96	0.302
No	15	177	
Degeneration of adjacent segment			
Yes	18	98	0.004
No	10	175	
Cobb angle of fused vertebrae (degree)	2.4±1.9	3.6±2.1	0.054
Decreased Cobb angle in fused vertebrae			
Yes	13	57	0.004
No	15	216	
Cobb angle of cervical spine (degree)	10.4±7.1	12.2±6.5	0.168
Decreased Cobb angle in cervical spine			
Yes	16	72	0.002
No	12	201	
Postoperative ROM of C2–C7 (degree)	36.8±11.2	38.7±12.1	0.403
T1 slope (degree)	28.1±6.3	26.9±7.1	0.390

BMI = body mass index, CASP = clinical adjacent segment pathology, ROM = range of motion.

Table 3
Multivariate logistic regression analysis of predictive factors associated CASP following multi-level cervical surgery.

	P value	Odds ratio	95% CI
Less levels fused	.128	3.355	0.773–14.561
Degeneration of adjacent segment	.039	1.592	1.113–2.277
Cobb angle of fused vertebrae < 3 degree	.098	1.484	0.989–2.227
Decreased Cobb angle in fused vertebrae	.009	2.113	1.338–3.334
Decreased Cobb angle in cervical spine	.014	1.896	1.246–2.886

CASP = clinical adjacent segment pathology, CI = confidence interval.

Therefore, clinical suspicion and early diagnosis are necessary for these patients as they have a higher risk to have CASP.

The incidence of ASP after cervical surgery has been documented by previous studies, but corresponding information varies widely.^[17–20] In the study by Hilibrand et al, the authors estimated that more than a quarter of all patients would develop radiographic degeneration of spinal elements adjacent to the index surgery, and two-thirds of those would go on to require additional surgery.^[21] Eubanks et al reviewed 364 patients and

found that ASP occurred in up to 25% patients at 10 years after the index procedure.^[22] We think that the difference in incidence is mainly due to the inclusion of various samples, the different definition of ASP criteria and the diverse length of follow-up. In our previous study, we reviewed a series of patients after single-level cervical arthrodesis and found that 31 patients were diagnosed as CASP in 256 patients.^[13] The calculated incidence is 12.1%, which is higher than the current study with similar length of follow-up. We assumed that though patients after single-level surgery had a larger ROM in the cervical spine, there are more susceptible discs left in comparison with patients after multi-level surgeries. As a result, patients after single-level surgery had more chances to develop CASP.

Whether CASP results from disease progression or is just a fusion-associated phenomenon cannot be determined yet.^[10,11] Previous studies have shown that pre-existing disc degeneration is a predictor for the development of CASP. For example, Park et al counted the number of preoperative adjacent-segment degeneration in patients after anterior cervical surgery and found that the rate of degeneration was significantly higher in patients with adjacent-segment disease than those without (85% vs 52.2%). They concluded that adjacent-segment pathology may be associated with a natural history of disc degeneration rather than arthrodesis.^[23] Our result is consistent with their study. Though the exact pathogenesis cannot be determined, we assumed that the pre-existing degenerative disease may act as a triggering factor for CASP. Surgeons should be careful with the level selection before surgery, and it is important to scrutinize all levels and have a relatively low threshold for including fusion levels.

In the current study, decreased Cobb angle in fused vertebrae and in the cervical spine are two factors associated with postoperative CASP, which mean that the regain of sagittal alignment during surgery is necessary. The sagittal imbalance may play a role in increasing adjacent disc loading after multi-level cervical surgery. Patwardhan et al used a laboratory model incorporating cadaveric specimens to investigate the influence of cervical spine imbalance on the mechanics of the cervical spine and draw a similar conclusion.^[14] However, no prior clinical study has looked at the influence of cervical sagittal imbalance on adjacent segment biomechanics after multi-level cervical surgery. It seems that disruption of the normal cervical lordotic curve can not only cause undesirable symptoms such as neck pain and cord compression, but also increase the risk of CASP. When performing surgical fusion, it is necessary to be cognizant of the importance of sagittal alignment.^[24] For surgeons, attention should be paid to adequate plate or stick contouring, as well as appropriately sized bone grafts or interbody cages.

This study has several limitations. First of all, the incidence of CASP was low. Though we tried to collect a large number of patients, the sample size was relatively small. This may weaken the ability of our study in the assessment of risk factors. A further subgroup analysis of patients after ACDF and PCLF treatments would decrease the heterogeneity of this study and may show more valuable information. Besides, only limited numbers of predictive factors were investigated, and the involvement of other factors in the further study may show more information to us. Finally, as this is a retrospective study, the study design and potential for bias are the typical restrictions of our study. A prospective, multicenter study involving a larger population and more risk factors is required to confirm our results.

In summary, we found that the incidence of CASP following multi-level cervical surgery was 9.3% with a mean of about 70

months' follow-up. The etiology of CASP is likely to be multifactorial. Patients with degeneration of adjacent segment decreased Cobb angle in fused vertebrae and decreased Cobb angle in cervical spine have a higher risk to develop CASP after multi-level cervical surgery. Therefore, deliberate surgical plan and close follow-up are necessary for patients with these risk factors.

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