In-Depth Analysis on Influencing Factors of Adjacent Segment Degeneration After Cervical Fusion

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Background: To explore the related influencing factors of adjacent segment degeneration (ASD) after cervical disectomy and fusion (ACDF).

Material/Methods: A retrospective analysis of 263 patients who underwent ACDF was carried out. Cervical x-ray and magnetic resonance imaging (MRI) were required before operation, after operation, and at the last follow-up. General information and some radiographic parameters of all patients were measured and recorded. According to the imaging data, patients were put into one of two groups: non-ASD group and ASD group. The differences between the two groups were compared by t-test and \( \chi^2 \)-test, and the related influencing factors of ASD were analyzed by logistic regression.

Results: In all, 138 patients had imaging ASD. Comparing the age, the postoperative cervical arc chord distance (po-CACD), and the plate to disc distance (PDD) of the two groups, differences were statistically significant (p<0.05). The gender, the fusion segment number, the pre-CACD, the pre-and-po CACD, the preoperative cervical spinal canal ratio, and the upper and lower disc height (DH) showed no statistical difference between the two groups (p>0.05). The results of logistic regression analysis showed that there were significant correlations in the following characteristics: age, postoperative po-CACD, and the PDD (p<0.05). Of all these characteristics, the correlation of age was the highest (R=1.820).

Conclusions: Age, po-CACD, and PDD were risk factors for ASD after ACDF. The older the operation age, the worse the recovery was of postoperative physiological curvature of cervical spine, and a PDD < 5 mm was more likely to lead to ASD.

MeSH Keywords: Intervertebral Disc Degeneration • Spinal Fusion • Uterine Cervical Diseases

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Background

Cervical spondylosis is one of the common degenerative diseases in our country, which causes a series of neurological symptoms and spinal cord compression, and thus adversely affects people’s lives. Surgery is now one of the important methods for its treatment. In the 1950s, Smith and Robinson created anterior cervical disectomy and fusion (ACDF) for the treatment of cervical spondylosis [1]. And it is still in use today. Many studies have shown that ACDF can achieve good curative effect in the clinic setting [2–4]. In recent years, the incidence of cervical diseases in our country has been increasing, and as such, fusion surgery has gradually become one of the widely used surgical methods. Cervical fusion may cause some complications, and adjacent segment degeneration (ASD) is the most common middle- and long-term complications after surgery. In the past, a large number of studies reported on ASD [3,5,6], but there have been few studies that have reported on the factors affecting ASD, and there is still no clear and unified argument for cervical fusion. With the widespread use of ACDF, the incidence of ASD is also increasing, and some patients need to return to the hospital for reoperation [7,8]. Therefore, it is necessary to explore the relevant factors that influence ASD after cervical fusion.

Material and Methods

Our study was a retrospective analysis of the clinical data of patients with cervical disc herniation or cervical spondylosis who underwent anterior cervical disectomy and fusion (ACDF) in our hospital from August 2006 to June 2011. Inclusion criteria: the adjacent segment of the Kellgren degeneration grading [9] was grade 0–1 and the adjacent segment of Miyazaki intervertebral disc degeneration grading [10] was grade I–II. Exclusion criteria: postoperative recovery was not good, or the operation effect was poor; serious complication occurred after the operation; simultaneous anterior and posterior surgery; poor compliance, regular follow-up did not occur, and the follow-up materials were not sufficient. A total of 263 cases met the study criteria, including 141 males and 122 females, ages ranged from 30 to 71 years, with an average age of 50.35±6.91 years. The last follow-up time was about 5 to 8.5 years, with an average follow-up time of 67.53±10.52 months. There were 154 cases with single-level fusion: C3/4 had 12 cases, C4/5 had 36 cases, C5/6 had 67 cases, and C6/7 had 39 cases. There were 79 two-level fusion cases: C3/5 had 11 cases, C4/6 had 45 cases and C5/7 had 23 cases. There were 30 three-level fusion cases: C3/6 had 9 cases and C4/7 had 21 cases. According to the Kellgren degeneration grading of adjacent intervertebral disc on x-ray: grade 0 had 181 cases, 1 grade had 82 cases. According to the Miyazaki’ intervertebral disc degeneration grading of adjacent segment on MRI: grade I had 169 cases and grade II had 94 cases. The 263 patients were divided into an image ASD group and a non ASD group according to the re-examined films, inspection results of cervical vertebra, and ASD evaluation standards. The study was carried out under the required law, rules, and regulations. All patients signed informed consent when hospitalized. This study received permission from the Medical Ethics Committee of the Guangxi Zhuang Autonomous Region People’s Hospital.

Surgical approach

For all patients, we used an anterior approach to the cervical spine, as originally described by Robinson and Smith. The patient was anesthetized. Along the right side of the thyroid cartilage, a transverse incision of about 7 cm of skin was made at the front of the neck. Then the subcutaneous tissue and the platysma were cut open. Soft tissue was separated to both sides and the external jugular vein was isolated and ligated. Along the edge of the sternocleidomastoid muscle, a longitudinal incision of fascia was cut apart. The gap between the vascular sheath and the trachea, esophagus was separated with the finger until approaching the leading edge of the vertebral body and intervertebral disc. With a needle positioning, the C-arm x-ray machine was used to make sure that the position of the intervertebral disc would be removed. A fixed screw was placed in the center of the upper and lower vertebral body of the intervertebral disc, and around the ill intervertebral disc, the distractor was installed and used. The anterior longitudinal ligament and fiber ring were cut off with a knife. Nucleus pulposus was removed as far as possible. A curette for clearance of cartilage endplate was applied. The iliac bone particles were filled into appropriate interbody fusion cage. A small part of the iliac bone that was made of bone particles were filled into appropriate interbody fusion cage. The cage was implanted into the intervertebral space. The distractor was loosened to stabilize the bone graft. If it was a multi-segment fusion, the operation about other affected intervertebral disc was the same. The anterior cervical plate was set and drilled, the depth of the hole was measured, and the screws were installed respectively. The C-arm x-ray machine was used to make sure that the position of the steel plate system was correct, the internal fixation was locked and a drainage tube was placed with a layered suture.

Evaluation method of intervertebral disc degeneration

All the patients received re-examination of the aligning and lateral radiographs and MRI scanning of cervical vertebra. If the test showed Kellgren degeneration grading by x-ray in the adjacent segment was ≥ grade 2 (Figure 1A–1E) or the Miyazaki intervertebral disc degeneration grading was ≥ grade III (Figure 2A–2E), then it was called imaging ASD.
Preoperative and postoperative imaging data

The following parameters of the x-ray of the cervical vertebra were measured and recorded before surgery, at one week after surgery, and during the follow-up period.

1) Cervical spinal canal ratio before surgery represented the effect of the spinal canal size on ASD. The sagittal diameter of the vertebral canal and vertebral body of C4–C6 were both measured. The spinal canal ratio refers to the spinal canal sagittal diameter/sagittal diameter of the vertebral body; the mean value of the cervical canal ratio of C4–C6 [11] was considered the cervical spinal canal ratio (Figure 3A).

2) Cervical arc chord distance was measured to determine the cervical physiological curvature. A straight line through two points was made, from the upper edge of the odontoid process to the lower trailing edge of C7. A curve along the trailing edge of cervical vertebra and a transverse intersection vertical line between arc and line were made. The widest distance was considered the cervical arc chord distance [12].

The D-value was the difference between the preoperative and the postoperative cervical arc chord distance (Figure 3B, 3C)

3) Plate to disc distance (PDD) was measured at one week after surgery as the shortest distance from the head/tail of the steel plate to the head/tail of the vertebral body of the operation segment (Figure 3D).

4) Adjacent intervertebral disc height (DH) was measured at one week after surgery as the distance from the end of the fused segment to the end plate of the adjacent vertebral body (Figure 3E).

Statistical analysis

The clinical data were analyzed by statistical software SPSS17.0. The Kolmogorov-Smirnov test was used to detect the normal distribution of data, and mean ± standard deviation was used for measurement data. The single-factor analysis was used for comparing the difference between the two groups: using the t-test for measurement data, and the χ² test for count data. Logistic regression was used to analyze the relevancy;
the higher the R value, the higher the correlation. A value of \( p < 0.05 \) indicated that the difference was statistically significant.

**Results**

There were 138 cases (52.47%) of adjacent segment degeneration after fusion. There were 78 cases of single segment fusion: C3/4 had 4 cases, C4/5 had 15 cases, C5/6 had 37 cases, and C6/7 had 22 cases. There were 3 cases of two-level fusion: C3/5 had 5 cases, C4/6 had 25 cases and C5/7 had 13 cases. There were 17 cases of three-level fusion: C3/6 had 4 cases and C4/7 had 13 cases.

According to the Kellgren degeneration grading method on x-ray, grade 2 had 49 cases, grade 3 had 86 cases, and grade 4 had 3 cases. The patients were classified into a non-ASD group (125 cases) and an ASD group (138 cases) according to the grading of the adjacent segment degeneration after fusion. Comparison of preoperative degeneration grade composition between the ASD group (grade 0 had 94 cases and grade 1 had 44 cases) and the non-ASD group (grade 0 had 87 cases and grade 1 had 38 cases) found the difference was not statistically significant (\( p > 0.05 \)).

When we compared the age of patients and the postoperative cervical arc chord distance and the PDD of the two groups, the differences were statistically significant (\( p < 0.05 \)). For gender and fusion segment number and preoperative cervical arc chord distance, the difference between preoperative and postoperative arc chord distances, the upper/lower adjacent intervertebral disc height, and the preoperative cervical spinal canal ratio showed no statistical differences between the ASD group and the non-ASD group (\( p > 0.05 \)) (Table 1).

We assigned values to the statistically significant factors (Table 2). The results of logistic regression analysis showed that there was significant relevance between age, the postoperative cervical arc chord distance, the PDD, and the ASD after fusion (\( p < 0.05 \)). The relevance of age was the highest (\( R = 1.820 \)) (Table 3). The older operation age, the shorter the postoperative cervical arc chord distance, and PDD less than 5 mm were the related risk factors, among which age had the most significant effect on ASD.

**Discussion**

ASD has long been considered the most common middle- and long-term complication after cervical fusion; complications include adjacent intervertebral disc degeneration, vertebral ossification, narrowing of intervertebral space, and vertebral slip. Research [18,13] has shown that patients who had ACDF operations had a higher incidence of ASD than those who had posterior decompression and disc replacements. The imaging ASD could be seen in any of the nonfusion segments after anterior cervical decompression and fusion, while more significantly occurring in the adjacent segment [14]. In our study, the
The incidence of ASD was about 52.47% during the follow-up of 5 to 8.5 years. However, another study found the imaging ASD was about 92.1%, with clinical manifestation in about 19.2% of patients, and 6.8% patients had a reoperation in a 10 year follow-up study [5]. The incidence of ASD was found to be the highest after cervical internal fixation and fusion, which may be because it can induce the degeneration of adjacent intervertebral disc, and the different levels of cervical internal fixation and fusion may have different effects on the adjacent segment of cervical intervertebral disc [15].

Table 1. The general information of all patients.

| Factor                        | ASD group | Non ASD group |
|-------------------------------|-----------|---------------|
| Grade 0                       | 94        | 87            |
| Grade 1                       | 44        | 38            |
| Age (y)                       | 53.60±6.51| 47.31±5.95*   |
| Sex rat (male/female)         | 73/65     | 61/64         |
| Fusion number (case)          | 1         | 76            |
| Arc chord distance (mm)       |           |               |
| Preoperative                  | 9.55±3.33 | 9.89±3.42     |
| Postoperative                 | 5.65±2.45 | 7.84±3.14*    |
| Preoperative and postoperative reduction | 3.89±3.96 | 2.05±4.24 |
| Spinal canal ratio            | 0.87±0.12 | 0.84±0.11     |
| Adjacent intervertebral disc height (mm) |   |               |
| Lower                         | 5.50±1.24 | 5.68±1.25     |
| Upper                         | 5.39±1.12 | 5.56±1.17     |
| Plate to disc distance (case)* |             |               |
| Upper and lower PDD <5 mm    | 64        | 38            |
| Upper or lower PDD ≥5 mm     | 35        | 61            |
| Upper and lower PDD ≥5 mm    | 19        | 26            |

* Compared with No ASD group, P<0.05.

Table 2. Assigning values to each factor with statistical difference.

| Factor                        | Variable | Assignment description |
|-------------------------------|----------|------------------------|
| Age X1                        | <50.46=0; ≥50.46=1 | Average (47.31+53.60)/2=50.46 |
| The postoperative X2          | <6.75=0; ≥6.75=1 | Average(7.84+5.65)/2=6.75 |
| Cervical arc chord distance   | Upper and lower PDD <5 mm 0; Upper <5 mm and lower PDD ≥5 mm or Upper PDD ≥5 mm and lower PDD <5 mm 1; | Upper and lower PDD ≥5 mm 2 |
| PDD X3                        | ASD Y    | No=0; Yes=1           |
Table 3. The results about The Logistic regression analysis of the factors and the ASD.

|             | B     | SE    | Wald  | P      | OR     | 95% confidence interval |
|-------------|-------|-------|-------|--------|--------|-------------------------|
|             |       |       |       |        |        | Low value               |
| The age     | 0.599 | 0.260 | 5.314 | 0.021* | 1.820  | 1.094 - 3.028           |
| The postoperative cervical arc chord distance | -0.604 | 0.257 | 5.541 | 0.019* | 0.546  | 0.330 - 0.904           |
| The PDD     | -0.445 | 0.180 | 6.115 | 0.013* | 0.641  | 0.450 - 0.912           |
| Constant    | 0.479 | 0.243 | 3.886 | 0.049* | 1.614  |                         |

C4/C5, C5/C6, and C6/C7 have reported higher incidence of degenerative diseases in adjacent segment [2,16,17]. When the curvature of the fusion segments was abnormal, and the motion range of the upper and lower adjacent segments were increased in different degrees, the resultant the concentration of the pressure into the adjacent segment may accelerated the development of ASD [18]. Relevant biomechanics research has shown that the pressure of the adjacent segment joint and intervertebral disc increased more significantly than that of the normal spine and the load accelerates the development of ASD [19,20]. There are also a number of studies that reported the difference in the incidence of the ASD between fusion and nonfusion was not statistically significant (p>0.05) [21,22]. The fusion segment is generally considered as a whole fixed unit of motion after surgery, so the overall activity of the cervical spine decreases, but the stiffness increases. When the cervical spine does daily flexion and extension movement, the nonfusion segments need to compensate for the required degree of movement of the cervical spine. The compensation degree is the highest in the adjacent segment, and gradually decreases toward the two ends. Therefore, the load is concentrated in the adjacent segment, and the pressure of adjacent intervertebral disc and articular process is significant, thus accelerating the degeneration of the intervertebral disc and the wear of the articular process, resulting in ASD.

Most current studies suggest that the older the operation age, the greater the risk suffering from the ASD [15,23,24], and not only was there a greater likelihood of postoperative ASD but also the risk of the ASD increased. The natural age-related degeneration has more affects than the fusion itself on the development of ASD [25]. We used the t-test to compare the difference in age between the non ASD group and the ASD group, and found that it was statistically significant (p<0.01). By logistic regression analysis, we showed that the operation age was significantly correlated with the development of ASD (p<0.01), and compared with other factors, its absolute value of R was the largest in the regression. With the development of human bodies, bones are also affected by metabolism. As human beings grow older, the bone cells gradually age. ASD may thus also be the result of naturally degenerating bone as age increases even without the effects of fusion. Therefore, ASD cannot be ruled out as a natural part of the aging process. The cervical spine in the elderly may have a potential risk of degeneration, and the fusion stimulates the emergence of degeneration. Therefore, we believe that the older the operation age, the higher the risk of ASD. In our study, its correlation with ASD was the most significant influencing factor.

Gender is considered another independent influencing factor of ASD after ACDF. The few current studies have widely different conclusions. Lee et al. [26] found that men had a lower risk of ASD. However, Song et al. [6] found that the incidence of ASD in women was lower: 11 women (11.82%) and 22 men (14.76%) with ASD. The effect of gender difference mainly correlates with hormone levels in the body. Estrogen and androgen are involved in bone metabolism, and both affect bone development and shaping. So hormones may have an impact on the development of ASD. There have been a few studies on the effect of the gender on ASD, that when compared, we found that the prevalence of female ASD (27.27%) was higher than that of male ASD (21.28%), but the difference was not statistically significant (p>0.05).

At present, there were many studies that support the fusion segment number as one of the factors that affects ASD [2,5,27], suggesting that more fusion segments would promote the development of ASD. In the biomechanics research, Prasarn et al. [28] found that the range of motion of adjacent segments increased significantly on the double segments fusion. Wu XD et al. [29] found that more than three segments had a significant effect on the cervical range of motion. The reason could be that with the increasing of the number of fusion segments, the activity of the upper adjacent segment and the small joint pressure gradually increase, resulting in the acceleration of ASD. However, Lee et al. [26] believed that the risk of ASD after the fusion involving three or more vertebrae was smaller than that of single and double segment fusion. Some scholars pointed...
out that the possible reason was that the easily degenerative segments were fused and the development of ASD was hampered [17]. We agree with the point of view that the number of fusion segment is not the incentive to accelerate ASD [7]. Although, in our study, the incidence of ASD (53.57%) was slightly higher than that of two-level fusion (47.89%) and the latter was slightly higher than that of single-segment (42.65%) after the three-segment fusion surgery, however, there was no significant difference between the two group (p>0.05). In general, the more easily degenerative segments were C4–5, C5–6, and C6–7. We believe that when these segments were adjacent to the fusion segment after single-segment fusion, it could be more prone to degenerate or have a faster rate of degeneration than other segments. In our study when these segments are adjacent to the fusion segment after multi-segment fusion, activity of the adjacent segment increased, which could lead to the development of accelerated degeneration. But sometimes, the easily degenerative segments were fused in multi-segment fusion, which may cause the decreased rate in the ASD group to be slower than the single-segment fusion. Therefore, whether comparing single-segment or multi-segments fusion, we could not rule out the influence of easily degenerative segment distribution on the development of ASD, which needs more in-depth study.

Studies have demonstrated that the straight cervical physiological curvature or poor recovery of the curvature in the operation segment region may be the significant factor that result in the adjacent segment degeneration after fusion [15,30]. Posterior protrusion of the cervical spine that cannot be corrected could lead to a higher incidence of ASD [31]. Falsini et al. [32] also pointed out that maintaining appropriate postoperative sagittal position of cervical lordosis could prevent ASD after fusion. In our study, the preoperative cervical curvature and the D-value between the preoperative and the postoperative cervical arc chord distance, both had no significant effects on ASD (p>0.05). The possible reason is that if the postoperative cervical lordosis angle is too small or too large when the cervical needs to be maintained upright, flexible or for extended postures, gravity cannot be balanced to each segment from top to bottom, so the pressure on the intervertebral discs and facet joints is unevenly distributed the intervertebral discs under pressure are short of blood and water, and the facet joints wear out. When the cervical spine is in flexion and extension movement, the vertebral body, intervertebral disc, and facet joint need to bear a gradually increasing load.

Some scholars have pointed out that developmental spinal stenosis was one of the influencing factors for ASD [33,34]. Zhang et al. [35] found that the incidence of ASD in the developmental spinal stenosis group (66%) was significantly higher than in the absence of developmental cervical stenosis group (43%), and if the sagittal diameter of vertebral canal was less than 13 mm, the incidence of ASD increased. Song et al. [6] found that ASD was more likely to occur when the cervical canal ratio was less than 0.70; and the size of the spinal canal may affect the development of ASD. However, in our study, the mean diameter of the spinal canal in the ASD group was less than that in the non-ASD group, and there was no significant difference between the two groups (p>0.05), which showed that the size of the spinal canal was not a risk factor associated with ASD. The reason for this result may be related to the fact that posterior decompression and fixation were performed due to the narrowness of vertebral canal of the patient. However, patients with posterior surgery were not included in our study, which may have an impact on the results of our study related to the correlation between the size of the spinal canal and ASD.

Li et al. [36] suggested that a postoperative DH that is too big is one of the factors that could lead to the development of ASD. Ahn et al. [23] found that the height of the adjacent intervertebral disc in patients with postoperative ASD decreased significantly during the follow-up period. Balkovec et al. [37] suggested that the loss of disc height affected the surrounding microenvironment, which thus affected the activity of the adjacent segment. Therefore, the changes in the height of adjacent intervertebral space at one week after surgery may have a long-term effect on the adjacent segment. But, we founded that the height of the intervertebral space was not the factor that affect the development of ASD and it may only change with the development of ASD.

Anterior cervical fusion can be fixed internally with a steel plate depending on the condition. At present, there has been no unified agreement about accelerating the occurrence of ASD by internal fusion fixation and single fusion. Chung et al. [5] found that there was a statistically significant difference between patients with PPD ≥5 mm and PDD ≥5 mm in degenerative changes in the adjacent segment, and they clearly pointed out that PDD < 5 mm was a very important risk factor. Yang et al. [38] suggested that PDD >5 mm would not decrease the incidence of ASD, but could avoid the development of adjacent segment ossification. However, Zhao et al. [33] supported the conclusion that PDD did not affect the development of ASD. In our study, we could not separately evaluate the effects of the upper and lower PDD on the upper and lower adjacent segment, so the patients were divided into three groups according to the value of PDD. By the logistic regression analysis, the result showed that there was a significant correlation between PDD and ASD (p<0.01); and that PDD <5 mm was the influencing factor for ASD. We believed that the internal fixation, to a certain extent, would increase the overall stiffness of the cervical spine, especially when the cervical spine was in movement, the stress was excessively uneven, and the steel plate may protect the surgical segments. However, our
study suggests that the stress was transmitted to the intervertebral discs and facet joints of the adjacent segment, and the stress of the adjacent segments increased most obviously, which accelerated the process of ASD. Currently, there are still disputes about the influence of PDD on ASD. It is possible that the effect of upper PDD on the upper adjacent segment is larger than that of upper PDD on the lower adjacent segment, and the effect of lower PDD on the lower adjacent segment is larger than that of lower PDD on the upper adjacent segment. More research and thorough analysis are needed in this area.

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Conclusions

The results of our study showed that the age, the postoperative cervical arc, and the PDD were related risk factors of imaging ASD after cervical fusion. The older the operation age, the poorer the recovery of postoperative cervical lordosis; and a PDD <5 mm was more likely to lead to ASD. Therefore, age was closely related to ASD. When treating patients with fusion, the relevant risk factors should be taken into account as far as possible to avoid various risk factors that accelerate ASD.

Declaration of conflict of interest

None.

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