

Analysis of Risk Factors for Adjacent Segment Degeneration Occurring More than 5 Years after Fusion with Pedicle Screw Fixation for Degenerative Lumbar Spine

Jaewan Soh¹, Jae Chul Lee², Byung Joon Shin²

¹Department of Orthopaedic Surgery, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, Cheonan, Korea

²Department of Orthopaedic Surgery and Spine Center, Soonchunhyang University College of Medicine, Seoul, Korea

Study Design: A retrospective study.

Purpose: We investigated the risk factors in adjacent segment degeneration (ASD) after more than 5 years of follow-up of lumbar spinal fusion.

Overview of Literature: There are many concerns regarding ASD followed by lumbar spinal fusion. However, there is a great deal of dispute about the risk factors.

Methods: A total of 55 patients who were followed up for more than 5 years after lumbar fusion were observed. Gender, age, residence, fusion method, number of fusion segments and radiological measurements were analyzed. In the radiological measurement, disc height, lumbar lordotic angle (LLA), fusion segment lordotic angle and fusion segment lordotic angle per level (FSLA per level) were estimated. In preoperative MRI, Pfirrmann's classification was used. The clinical result was evaluated by the criteria of Kim and Kim. Statistical univariate analysis was performed with the chi-square test by using SPSS ver. 12.0. Multivariate logistic regression analysis was conducted with SAS ver. 9.

Results: There were 21 patients with adjacent segment degeneration. Further, there was little relationship between ASD and gender, age, residence, fusion method, number of fusion segments, degree of preoperative adjacent disc degeneration in MRI, or preoperative and postoperative LLA. However, the frequency of ASD was significantly low in cases where FSLA per level was $>15^\circ$ ($p=0.009$). There was no significant relationship between ASD and the clinical result.

Conclusions: In patients followed up for more than 5 years after lumbar spinal fusion, the most important factor in the prevention of ASD was the restoration of FSLA per level to $>15^\circ$.

Keywords: Lumbar; Adjacent segment degeneration; Fusion; Pedicle screw fixation

Introduction

When a structural deformation or nerve compression

is so severe that simple decompression alone does not produce satisfactory outcomes for degenerative lumbar disease, extensive decompression and lumbar vertebral

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Corresponding author: Byung Joon Shin

Department of Orthopaedic Surgery, Soonchunhyang University College of Medicine,
59 Daesagwan-ro, Yongsan-gu, Seoul 140-743, Korea

Tel: +82-2-709-9250, Fax: +82-2-794-9414, E-mail: schsbj@schmc.ac.kr

fusion to maintain stability are widely-conducted surgical treatments.

Although some fusion methods and fixation systems have been developed to achieve successful fusion in spinal surgery, a long-term follow-up after a strong fusion has revealed degenerative changes at the adjacent segments due to the loss of mobility of the fusion site and the mechanical load caused thereby [1,2]. Degenerative changes at the adjacent segments include segmental instability, spinal stenosis, intervertebral disc lesion, retro-spondylolisthesis and fracture [3-5]. These poor outcomes are known to follow the accelerated degenerative changes at the adjacent segments after fusion [2,6,7]. As these complications are observed during a long-term follow-up, a cautious application of the fusion itself as well as new alternatives have been suggested. Therefore, measures to reduce and treat degenerative changes after fusion are discussed, along with the increased interest in causative factors related to the prevention and treatment reported by many studies. Nevertheless, these are still controversial.

On the basis of previous studies, in order to determine its causative factors, we statistically analyzed the correlation between possible factors and the degenerative change in adjacent segments among patients with radiographic changes during middle- or long-term follow-up of over 5 years after fusion with pedicle screw. In addition, we investigated the correlation between a radiological degenerative change at the adjacent segments and the actual clinical symptoms in order to show whether the radiological change was an index of the actual abnormality. We define that the degenerative change in the adjacent segment with a radiographic change is 'adjacent segment degeneration', and the adjacent segment degeneration with clinical symptom is 'adjacent segment disease'.

Materials and Methods

1. Materials

The subjects of this study were 55 patients who had undergone pedicle screw fixation and spine fusion of three or fewer segments due to degenerative lumbar disease. The patients had been followed up for over 5 years. Their mean age at operation was 50.2 years (range, 34–67 years) and they consisted of 18 males and 37 females. Their mean follow-up period was 8 years and 6 months (range,

60–190 months). All of the surgery was performed by one orthopedic surgeon. The fusion methods were posterolateral fusion and posterior lumbar interbody fusion in 24 and 31 cases, respectively (Table 1).

2. Methods

The 55 subjects were retrospectively investigated with their medical records and radiological findings.

Criteria of degenerative change at adjacent segments: radiological degenerative change at the adjacent segments was considered to exist when anterior or posterior displacement of >3 mm was found on the X-ray of the sagittal plane of the closest upper segment and the closest lower segment at the last follow-up, when the height of the intervertebral disc relative to that of the upper interbody had declined by 20% and when a segmental motion instability of more than 15° was observed on the X-ray of the sagittal plane with flexion and extension.

1) Patient-related factors

Gender, age and lifestyle by residential area were analyzed as patient-related factors, which could have some influence. Age was examined by dividing the patients into two groups: ≥ 50 years and < 50 years of age (mean, 50 years). The effect of differences in lifestyle was examined by classifying residential areas into urban and rural categories.

2) Preoperative lumbar factors

Magnetic resonance imaging (MRI) was used to investigate whether there had been a degree of preoperative adjacent disc degeneration. Patients recording grade \geq III in the five-grade classification of Pfirrmann et al. [8] based on MRI were considered to have a degenerative change. In addition, the preoperative lumbar lordotic angle was measured by Cobb's angle made by the upper endplate of the first lumbar vertebra and the upper endplate of the sacrum. It was classified, with its mean value of 32° as a standard, into $\geq 32^\circ$ and $< 32^\circ$; moreover, its correlation with a degenerative change at the adjacent segments was assessed.

3) Surgery-related factors

As factors related to surgical treatment, fusion method (posterolateral fusion or posterior lumbar interbody fusion) and the number of fusion segments (one, two and three segments) were analyzed.

Table 1. Summarized data of 55 patients followed up for over 5 years after spinal fusion

No.	Age (yr)	Gender	Follow-up period (mo)	Residence	ASD	ASD in preop. MRI	Preop. lumbar lordotic angle (°)	Fusion method	No. of fusion segments	Postop. lumbar lordotic angle (°)	Fusion segment lordotic angle per level (°)	Clinical result	Revision surgery
1	63	F	153	Urban	N	N	30	PLF	1	32	22	U	Y
2	41	F	58	Urban	N	Y	38	PLIF	1	33	20	S	N
3	40	F	113	Rural	Y	N	24	PLF	2	18	15	S	N
4	56	M	134	Rural	Y	Y	42	PLF	2	52	15	S	N
5	59	F	60	Rural	N	N	46	PLIF	1	48	25	S	N
6	65	F	114	Rural	Y	Y	19	PLIF	2	30	11	U	Y
7	59	F	60	Rural	Y	Y	42	PLIF	1	50	19	S	N
8	55	F	72	Urban	N	Y	32	PLIF	1	54	32	S	N
9	47	F	121	Urban	N	N	41	PLF	2	38	24	S	N
10	57	F	68	Rural	N	N	32	PLF	2	38	12	S	N
11	44	F	101	Urban	N	Y	26	PLIF	1	48	17	S	N
12	65	F	98	Urban	N	Y	45	PLIF	3	54	12	S	N
13	61	F	74	Urban	N	N	64	PLIF	1	50	18	U	N
14	53	M	129	Urban	Y	Y	21	PLF	2	33	4	S	N
15	42	F	87	Urban	Y	N	30	PLIF	1	40	10	S	N
16	42	F	132	Urban	Y	N	32	PLF	1	32	5	S	N
17	38	F	120	Urban	N	N	33	PLIF	2	40	12	S	N
18	51	F	126	Urban	Y	Y	34	PLIF	1	42	30	S	N
19	37	F	91	Urban	N	Y	55	PLIF	1	43	16	S	N
20	47	F	126	Rural	Y	N	52	PLIF	1	53	12	S	N
21	59	F	89	Rural	N	N	14	PLF	1	39	25	U	N
22	56	F	57	Rural	N	Y	25	PLF	2	37	6	U	N
23	34	M	105	Urban	N	N	10	PLF	3	30	12	S	N
24	56	M	60	Urban	N	N	22	PLF	2	28	12	S	N
25	59	M	125	Urban	Y	N	18	PLF	2	30	10	S	N
26	36	F	84	Rural	N	Y	5	PLIF	2	23	10	U	N
27	56	M	75	Urban	Y	N	30	PLIF	1	45	10	S	N
28	62	F	60	Urban	Y	Y	17	PLIF	2	24	9	S	N

(Continued to the next page)

Table 1. Continued

No.	Age (yr)	Gender	Follow-up period (mo)	Residence	ASD	ASD in preop. MRI	Preop. lumbar lordotic angle (°)	Fusion method	No. of fusion segments	Postop. lumbar lordotic angle (°)	Fusion segment lordotic angle per level (°)	Clinical result	Revision surgery
29	53	F	190	Rural	N	N	50	PLF	2	55	18	S	N
30	56	F	90	Urban	N	Y	47	PLIF	1	58	25	S	N
31	67	F	116	Urban	N	Y	47	PLIF	2	50	19	S	N
32	46	M	121	Urban	N	Y	35	PLIF	1	44	18	S	N
33	61	F	132	Rural	N	Y	42	PLIF	1	58	17	S	N
34	38	M	109	Rural	Y	Y	38	PLIF	1	30	15	S	N
35	49	M	128	Urban	Y	Y	35	PLIF	1	32	14	U	Y
36	44	M	92	Urban	N	Y	53	PLIF	1	40	16	S	N
37	51	F	126	Urban	Y	N	35	PLF	2	30	8	S	N
38	58	F	126	Urban	Y	N	20	PLF	3	45	11	S	N
39	60	M	63	Rural	N	N	22	PLF	3	36	8	S	N
40	49	F	74	Rural	N	N	56	PLIF	1	54	18	S	N
41	62	F	72	Urban	N	Y	34	PLIF	2	38	15	S	N
42	62	F	126	Urban	N	Y	54	PLF	2	54	14	S	N
43	47	M	148	Urban	N	Y	34	PLF	2	37	6	U	N
44	58	M	74	Rural	N	Y	40	PLIF	1	56	13	U	N
45	44	F	106	Urban	N	N	32	PLIF	1	52	32	S	N
46	37	M	109	Urban	N	Y	24	PLIF	1	32	17	S	N
47	41	M	96	Urban	N	N	40	PLIF	1	45	20	S	N
48	53	F	77	Urban	Y	Y	18	PLIF	2	35	9	S	N
49	51	M	79	Urban	N	N	30	PLF	2	42	17	U	N
50	54	F	100	Rural	N	Y	32	PLIF	1	38	21	S	N
51	55	F	80	Rural	Y	N	23	PLF	2	41	6	U	N
52	64	M	129	Rural	Y	N	46	PLF	2	58	17	S	N
53	65	M	145	Urban	N	N	20	PLF	2	38	8	S	N
54	56	F	68	Rural	Y	Y	14	PLF	2	41	4	S	N
55	48	F	183	Urban	Y	Y	27	PLF	3	36	5	S	N

ASD, adjacent segment degeneration; preop., preoperative; MRI, magnetic resonance imaging; Postop., postoperative; N, no; PLF, posterolateral fusion; U, unsatisfactory; Y, yes; PLIF, posterior lumbar interbody fusion; S, satisfactory.

4) Postoperative radiological change-related factors

Measures from the radiological images taken just after surgery were evaluated as surgical outcomes. First, the postoperative lumbar lordotic angle was classified, with its mean value of 40° as a standard, into $\geq 40^\circ$ and $< 40^\circ$, and the meaning of each group was analyzed. Next, the fusion segment lordotic angle per level was calculated by dividing the lordotic angle of the fusion site or a Cobb's angle between the upper endplate of the fusion segment and the lower endplate of the fusion segment by the number of fused segments. It was also divided, with its mean of 15°, into $\geq 15^\circ$ and $< 15^\circ$, and its correlation with the degenerative change of adjacent segments was assessed.

5) Correlation between radiological degenerative change in adjacent segment and clinical symptoms

The relationship between degenerative change in the adjacent segments and clinical outcome was assessed. The clinical outcomes were divided into satisfactory (excellent, good) and unsatisfactory (fair, poor) on the basis of the assessment base of the criteria of Kim and Kim [9].

6) Statistical analysis

To verify the significance of each factor, a univariate analysis was performed with the chi-square test by using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). Multivariate logistic regression analysis including all factors was also performed with SAS ver. 9 (SAS Institute, Cary, NC, USA), and the odds ratio of the significant factors was calculated. The significance level was $p < 0.05$.

Results

1. Radiological degenerative change at adjacent segments

Degenerative change at the adjacent segments was observed in a total of 21 cases. The change occurred at the upper segments (14 of retrolisthesis, seven of decreased height of the intervertebral disc, seven of segmental motion instability, and one of spondylolisthesis) in 18 cases, at the lower segments (one of retrolisthesis, two of decreased height of the intervertebral disc and one of spondylolisthesis) in four cases, and there was one case that showed the change at both the upper and lower segments.

2. Analysis on causative factors

1) Patient-related factors

According to the analysis of patient-related factors, the subjects included 18 males and 37 females, and the postoperative degenerative change was found in seven males and 14 females; hence, there was no significant difference by gender ($p=0.940$). The age of the subjects was ≥ 50 years and < 50 years in 34 and 21 cases, respectively. The degenerative change did not show any significant difference by age as it was found in 14 out of the 34 cases with the age of ≥ 50 years and in seven out of the 21 aged < 50 years ($p=0.561$). The relationship between degenerative change and differences in residential area as lifestyle was examined. The change was observed in 12 of 35 residents of urban areas and nine of 20 resident in rural areas; there was no statistically significant correlation ($p=0.431$) (Table 2).

2) Preoperative lumbar factors

When the influence of the degree of preoperative adjacent disc degeneration was investigated by MRI, the degenerative change at the adjacent segments was found at the last follow-up in 11 out of 29 cases with and ten out of 26 without preoperative degenerative change; the difference was not statistically significant ($p=0.968$). In addition, the degenerative change was observed in eight and 13 among 27 and 28 cases with the preoperative lumbar lordotic angle of $\geq 32^\circ$ and $< 32^\circ$, respectively; hence, there was no significant difference ($p=0.200$) (Table 2).

3) Surgery-related factors

When the difference by the fusion method was investigated, the degenerative change was found in 11 and 10 out of 24 and 31 cases treated with posterolateral fusion and posterior lumbar interbody fusion, respectively, and the difference was not statistically significant ($p=0.304$). As for the number of fusion segments, one-segment fusion and two- and three-segment fusions were performed in 26 and 29 cases, respectively, and the degenerative change was observed in eight and 13, respectively. There was also no significant difference ($p=0.284$) (Table 2).

4) Postoperative radiological change-related factors

When the influence of the postoperative lumbar lordotic angle on the degenerative change at the adjacent segments was investigated, the change was found in ten and

Table 2. Univariate analysis of risk factors for adjacent segment degeneration

Risk factors	No. of patients	ASD	<i>p</i> -value
Patient-related factors			
Gender			0.940
Male	18	7	
Female	37	14	
Age (yr)			0.561
<50	21	7	
≥50	34	14	
Residence			0.431
Urban	35	12	
Rural	20	9	
Preoperative lumbar factors			
Preoperative ADD on MRI			0.986
Yes	29	11	
No	26	10	
Preoperative LLA			0.200
<32°	28	13	
≥32°	27	8	
Surgery-related factors			
Fusion method			0.304
PLF	24	11	
PLIF	31	10	
Nor of fusion segments			0.284
Single	26	8	
2 or 3	29	13	
Postoperative radiological-related factors			
Postoperative LLA			0.551
<40°	26	11	
≥40°	29	10	
FSLA per level			0.009
<15°	27	15	
≥15°	28	6	
Correlation between ASD and clinical symptom			
Clinical result			0.405
Satisfactory	44	18	
Unsatisfactory	11	3	

ASD, adjacent segment degeneration; ADD, adjacent disc degeneration; MRI, magnetic resonance imaging; LLA, lumbar lordotic angle; PLF, posterolateral fusion; PLIF, posterior lumbar interbody fusion; FSLA, fusion segment lordotic angle.

11 cases out of 29 and 26 with the angle $\geq 40^\circ$ and $< 40^\circ$, and the difference was not significant ($p=0.551$). In addition, the fusion segment lordotic angle per level recorded $\geq 15^\circ$ and $< 15^\circ$ in 28 and 27 cases, respectively, and the degenerative change was shown in six and 15 cases, respectively. Thus, their difference was statistically significant ($p=0.009$) (Table 2).

5) Correlation between radiological degenerative change of adjacent segments and clinical symptoms

For the correlation between the degenerative change of adjacent segments and clinical outcomes, the change was shown in 18 out of 44 cases with satisfactory clinical outcomes and three out of 11 with unsatisfactory outcomes. As there was no significant difference, the radiological change did not imply unsatisfactory clinical outcomes ($p=0.405$) (Table 2).

Among the 21 cases with change at the adjacent segments, three needed a revision surgery (14.3%, 5.5% out of the total subjects); two of these were surgically treated for spinal stenosis at the upper adjacent segments, and the other one was treated for segmental instability.

When the multivariate logistic regression analysis on risk factors was conducted—with independent variables as gender, age, residential area, fusion method, degree of preoperative adjacent disc degeneration on MRI, the number of fusion segments, and the lumbar lordotic angle and the fusion segment lordotic angle per level at the fusion site after the surgery—the fusion segment lordotic angle per level of $< 15^\circ$ increased the risk of degenerative change at the adjacent segments 4.666 times (range, 1.015–21.439 times) (Table 3).

Discussion

Decompression and lumbar vertebral fusion have been widely conducted as surgical treatment for lumbar degenerative change. Spinal fusion provoked a conflict between benefits secured just after the surgery and future problems. The complications of lumbar vertebral fusion, such as intervertebral disc degeneration at adjacent segments, instability, fatigue and fracture, were observed during middle- and long-term follow-up [3-5]. Although many researchers have pointed out the degenerative lesions at the adjacent segments occurring frequently after fusion as major causes of these late complications [2,6,7], their causes, frequencies and risk factors are still controversial.

Table 3. Multivariate logistic regression analysis including all risk factors

Risk factors	<i>p</i> -value	Odds ratio	95% CI	
			Upper	Lower
Gender	0.9712	1.026	0.257	4.088
Age	0.2131	3.284	0.508	21.241
Residence	0.3185	0.499	0.128	1.954
Fusion method	0.8535	0.821	0.101	6.680
Preoperative ADD on MRI	0.6413	0.707	0.164	3.039
Number of fusion segments	0.9026	0.878	0.109	7.097
Preoperative LLA (32°)	0.2962	2.162	0.509	9.182
Postoperative LLA (40°)	0.8032	0.827	0.185	3.693
FSLA per level (15°)	0.0478	4.666	1.015	21.439

CI, confidence interval; ADD, adjacent disc degeneration; MRI, magnetic resonance imaging; LLA, lumbar lordotic angle; FSLA, fusion segment lordotic angle.

It is the predominant view that the degenerative lesion at the adjacent segments can be part of normal aging, and that the reduced mobility and the mechanical load following lumbar fusion accelerates the degeneration [1-3,10,11]. This biomechanical change at the adjacent segments is affected by the range of fused segments and the sagittal angle, and stronger fixation of fused segments is known to be associated with a larger effect as more stress is put on the adjacent segments [12,13]. Cunningham et al. [14] reported that the pressure of the adjacent intervertebral disc became larger by 45% in their cadaveric study, and Lee and Langrana [15] found that the load at the adjacent segments was raised in their biomechanical study on lumbosacral fusion. For the influence of gender, Kumar et al. [16] and Ha et al. [17] showed no significant difference in the rate of the degenerative change by gender, while Etebar and Cahill [18] insisted that the rate of the change at the adjacent segments was higher in females after menopause. This study did not reveal any significant difference by gender.

Many researchers believe that older age leads to more change at the adjacent segments [10,18-21]. As reasons for that, Aota et al. [20] pointed out that it was more difficult for the spine to adapt to postoperative biomechanical change in the elderly, whereas Etebar and Cahill [18] reported that osteoporosis negatively affected the existing degenerative procedure. However, we found no significant correlation between age and the degenerative change at the adjacent segments. As for the effect of lifestyle, Gillet [22] and Cho et al. [23] reported that differences in lifestyle could influence the adjacent segments, and Ahn

et al. [24] reported that manual workers and residents in rural areas had around 47 times higher risk compared with those in urban areas. However, no significant correlation with residential area was observed in this study.

When the cases with preoperative instability or intervertebral disc degeneration at the adjacent segments were reviewed, Aota et al. [20] reported that instability deteriorated after the surgery in all cases with preoperative anterior displacement of ≥ 3 mm. Ha et al. [21] showed that preoperatively, more severe degenerative change in the adjacent joints was associated with more radiological change in the joints, and no degenerative change was observed for more than 5 years of follow-up in cases without preoperative degenerative change in the joints. However, this study did not show any direct correlation between preoperative adjacent disc degeneration on MRI and postoperative degenerative change at the adjacent segments.

Schlegel et al. [13] revealed that the change at the adjacent segments occurred early in the fusion when a device was used for fixation, and Rahm and Hall [2] insisted that posterior intervertebral body fusion increased the load over adjacent segments because the remaining mobility after bone fusion was excluded along with stronger initial fixation. However, Kim et al. [25] and Ha et al. [21] found no significant difference in the frequency of the degenerative change by the fixation system or fusion method. This study also showed that the correlation between the fusion method and degenerative change was not significant. Moreover, there was no significant difference in the degenerative change by the number of fusion segments.

Although Aota et al. [20] and Etebar and Cahill [18] insisted that the changes at the adjacent segments became larger due to more stress on the segments for multi-level fusion, Kettler et al. [26] and Ha et al. [17] reported that there was no correlation between the number of fusion segments and the change. This study also indicated no significant correlation between them.

For the change at the adjacent segments by the sagittal angle, reduced lordotic angle has been reported to promote the degenerative change early by leading to a concentrated load of segmental motion at the adjacent segments [27,28]. Herkowitz and Kurz [29], Cho et al. [23] and Ahn et al. [24] stated that it was critical to maintain the lumbar lordotic angle during follow-up after fusion, and decreased lordotic angle eventually stimulated the degenerative change at the adjacent segments. For the segmental sagittal angle, Ahn et al. [19] found that the decrease in the fusion segment lordotic angle by 10° was associated with 3.2 times the increase in the degenerative change. In this study, the degenerative change was observed more frequently in the cases where the fusion segment lordotic angle per level was <15° after the surgery.

The incidence rate of the degenerative change at the adjacent segments after lumbar vertebral fusion has been reported variously as between 19.4% and 40% [3,20,21,25]. When it was investigated whether the degenerative change provoked clinical symptoms, Booth et al. [6] reported that a radiological degenerative change was found in many cases in >5 years after lumbar vertebral fusion; however, there were almost no cases with this symptom; other previous studies also revealed no correlation between radiological change and clinical symptoms [2,18,23,30]. This study found that unsatisfactory outcomes were observed in only 11 among 21 cases with the degenerative change at the adjacent segments, and that the correlation between radiological change and surgical outcomes was not statistically significant. However, it was reported that if clinical symptoms were observed again along with the degenerative change at the adjacent segments, surgical treatments were necessary in 8% to 16.8% of cases [14,20,25]. This study also revealed that three (14.3%) out of the 21 cases needed surgical treatment.

Conclusions

During the long-term follow-up after pedicle screw fixation and fusion, gender, age, residential area, fusion

method, the number of fusion segments, and the degree of preoperative adjacent disc degeneration on MRI showed no significant relationship with the postoperative degenerative change at the adjacent segments; however, the correlation between the fusion segment lordotic angle per level and the postoperative degenerative change was significant. Therefore, efforts to restore the fusion segment lordotic angle per level to >15° are most important and are considered to be able to reduce the degenerative change at the adjacent segments.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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