

# Survival and Prognostic Analysis of Adjacent Segments after Spinal Fusion

Dong Ki Ahn, MD, Hoon Seok Park, MD, Dae Jung Choi, MD, Kwan Soo Kim, MD, Seung Jin Yang, MD

*Department of Orthopaedic Surgery, Seoul Sacred Heart General Hospital, Seoul, Korea*

**Background:** To examine the survival function and prognostic factors of the adjacent segments based on a second operation after thoracolumbar spinal fusion.

**Methods:** This retrospective study reviewed 3,188 patients (3,193 cases) who underwent a thoracolumbar spinal fusion at the author's hospital. Survival analysis was performed on the event of a second operation due to adjacent segment degeneration. The prognostic factors, such as the cause of the disease, surgical procedure, age, gender and number of fusion segments, were examined. Sagittal alignment and the location of the adjacent segment were measured in the second operation cases, and their association with the types of degeneration was investigated.

**Results:** One hundred seven patients, 112 cases (3.5%), underwent a second operation due to adjacent segment degeneration. The survival function was 97% and 94% at 5 and 10 years after surgery, respectively, showing a 0.6% linear reduction per year. The significant prognostic factors were old age, degenerative disease, multiple-level fusion and male. Among the second operation cases, the locations of the adjacent segments were the thoracolumbar junctional area and lumbosacral area in 11.6% and 88.4% of cases, respectively. Sagittal alignment was negative or neutral, positive and strongly positive in 47.3%, 38.9%, and 15.7%, respectively. Regarding the type of degeneration, spondylolisthesis or kyphosis, retrolisthesis, and neutral balance in the sagittal view was noted in 13.4%, 36.6%, and 50% of cases, respectively. There was a significant difference according to the location of the adjacent segment ( $p=0.000$ ) and sagittal alignment ( $p=0.041$ ).

**Conclusions:** The survival function of the adjacent segments was 94% at 10 years, which had decreased linearly by 0.6% per a year. The likelihood of a second operation was high in those with old age, degenerative disease, multiple-level fusion and male. There was a tendency for the type of degeneration to be spondylolisthesis or kyphosis in cases of the thoracolumbar junctional area and strongly positive sagittal alignment, but retrolisthesis in cases of the lumbosacral area and neutral or positive sagittal alignment.

**Keywords:** *Survival analysis, Prognosis, Spinal fusion, Adjacent segment*

Adjacent segment degeneration after spinal fusion has been examined extensively. Nevertheless, there is still some controversy regarding its incidence and risk factors. Given that degenerative changes occur over time, it is likely that

those who were considered as a control group at one point would end up requiring an operation on the adjacent segments at a later point. Therefore, it is difficult to design a comparative study or perform a long-term prospective study on adjacent segment degeneration after spinal fusion. In addition, there have been few retrospective studies including a long-term follow-up and large study population and considering the time factor.

This study estimated the survival functions of the adjacent segments after a second operation and an-

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Correspondence to: Hoon Seok Park, MD

Department of Orthopaedic Surgery, Seoul Sacred Heart General Hospital,  
40-12 Cheongnyangni-dong, Dongdaemun-gu, Seoul 130-010, Korea

Tel: +82-2-966-1616, Fax: +82-2-968-2394

E-mail: hoon0319@gmail.com

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alyzed the effect of the various prognostic factors on the survival functions in 3,193 cases who had undergone thoracolumbar spinal fusion between January 1994 and August 2007. In particular, this study evaluated measures to prevent and predict adjacent segment degeneration by assessing the location of the degenerative segments, sagittal alignment, and type of degeneration in cases, who had undergone a second operation due to degenerative changes in the adjacent segments. Although stratified sampling was not performed, an attempt was made to offset the limitation by conducting multivariate analysis, which considers the confounding effects of the variables. In addition, the type 2 errors were reduced by the sufficiently large sample size.

## METHODS

Of the patients who had undergone thoracolumbar spinal fusion performed by 6 spinal surgeons at our institution between January 1994 and August 2007, 3,188 patients (3,193 cases) who were available for follow-up were included in this study. The study was carried out by a retrospective review of the medical records and radiological data. The end of the follow-up examination was defined as the last visit at the outpatient clinic or the last phone contact. In cases of reoperated patients, the survival period was defined as the interval from thoracolumbar fusion to the second operation due to adjacent segment degeneration. A second operation due to adjacent segment degeneration was treated as an event, whereas patients with second operations caused by other reasons were regarded as censored data. A second surgery on the adjacent segments was carried out in cases showing adjacent segment degeneration on the radiographs and the neurological symptoms recurred. A symptom free period of at least 6 months was requested to exclude incomplete surgery.

In an analysis of the prognostic factors, all variables were transformed into dichotomous variables to increase the statistical power: age ( $\geq 61$  years old and  $< 61$  years old), disease (degenerative and others) (Table 1), surgical method (posterior lumbar interbody fusion using cages, which was expected to have the greatest impact on the adjacent segments due to initial strong fixation strength and others), and number of fused segments (single level and multiple levels). Herniation of the nucleus pulposus was classified as degenerative if it was combined with posterior facet joint degeneration or spinal stenosis, such as an enlargement of the ligament flavum, and as non-degenerative if posterior facet joint degeneration

was not present in the cases, such as giant herniation of nucleus pulposus requiring bilateral approaches. The location of the adjacent segments in cases requiring a second operation was categorized into thoracolumbar junctional (T12-L2) and lumbosacral areas. The lumbar lordosis angle was determined to be the angle between the superior endplate of L1 (or the inferior endplate of L1 if there was a deformation caused by compression fracture) and the superior endplate of S1. The sagittal alignment was measured on the standing lateral radiographs and classified as negative or neutral, positive, and strongly positive ( $\geq 20$  cm of anterior translation of the C7 plumb line relative to the posterior border of S1). Four cases without available standing radiographs were excluded for sagittal alignment analysis. The type of degeneration was divided into spondylolisthesis or kyphosis of the superior vertebral body, retrolisthesis of the upper vertebral body, and no change in sagittal alignment based on the sagittal plane radiographs.

Cox regression was performed to examine the prognostic factors. The Kaplan Meier method was used to construct the survival curves of all patients. The Breslow test was used to compare the survival functions in the subgroups. The differences in degenerative changes according to the location of the adjacent segments and sagittal alignment were evaluated using the likelihood ratio test

**Table 1.** Classification According to the Causes of the Disease

	Disease	No. of cases (%)
Degenerative group	Spinal stenosis	1,045 (32.7)
	Degenerative spondylolisthesis	562 (17.6)
	Spinal stenosis with HNP	204 (6.4)
	Spondylosis	32 (1.0)
	Degenerative scoliosis	12 (0.4)
	Adjacent segment degeneration	5 (0.2)
	Etc.	180 (5.6)
The other group	Spondylolytic spondylolisthesis	393 (12.3)
	Herniated nucleus pulposus	471 (14.8)
	Trauma	161 (5.0)
	Deformity	92 (2.8)
	Infection	27 (0.8)
	Tumor	9 (0.3)
Total		3,193

HNP: Herniated nucleus pulposus.

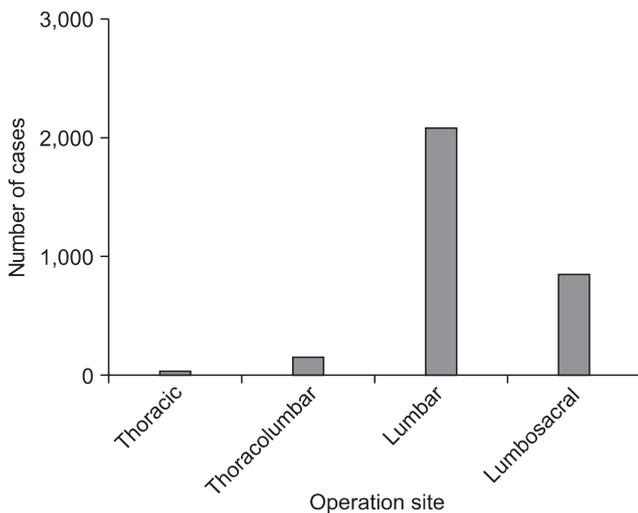
(LR test) for the trend. The confidence interval was set to 95%.

### RESULTS

The mean age of the patients was  $57 \pm 11$  years (males,  $55 \pm 13$  years; females,  $58 \pm 10$  years); 1,351 cases (42.3%) were < 61 years of age and 1,842 cases (57.7%) were  $\geq 61$  years of age. There were 1,043 (32.7%) males and 2,150 (67.3%) females. Degenerative and non-degenerative disease was noted in 2,040 (63.9%) and 1,153 (36.1%) cases, respectively (Table 1). Posterior interbody fusion using cages were carried out in 1,451 cases (45.4%) and other techniques were used in 1,742 cases (54.6%). Spinal

fusion at the initial surgery was performed in the thoracic spine in 13 cases (0.4%), thoracolumbar junctional area in 147 cases (4.6%), lumbar spine in 2,064 cases (64.6%), and lumbosacral spine in 969 cases (30.3%) (Fig. 1). The mean number of fused segments was  $1.6 \pm 0.89$ . There were 2,309 cases (72.3%) of single-level fusion and 884 cases of (27.7%) multi-level fusion.

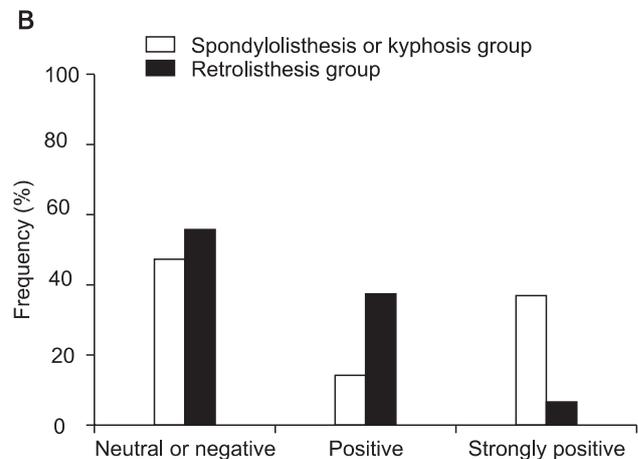
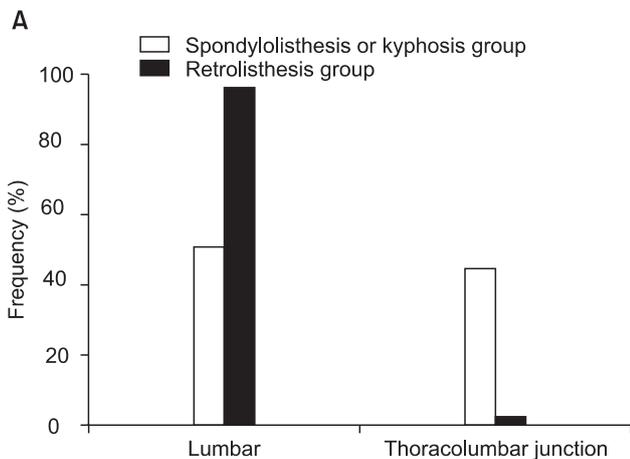
Of the 3,188 patients (3,193 cases), 107 patients (112 cases, 3.5%) underwent a second procedure for adjacent segment degeneration and an additional surgical treatment due to repeated adjacent segment degeneration was required in 5 of them. Degenerative changes were noted in the proximal segments, distal segments and both segments in 89 (79.5%), 21 (18.8%) and 2 (1.8%) cases, respectively. In the above-mentioned 5 patients, the changes were noted in the proximal segments. The second surgery was



**Fig. 1.** This graph shows the number of cases according to the surgical site.

**Table 2.** Distribution According to the Number of Previous Fusion Segments in Patients Who Underwent a Second Operation for Adjacent Segment Degeneration

No. of previous fusion segments	Distribution (%)
Single-level	1 (58.0)
Multiple-level	2 (31.3)
	3 (5.4)
	4 (3.6)
	5 (1.8)
	Total
Total	112



**Fig. 2.** (A) Comparison of the surgical segment between spondylolisthesis or kyphosis group and retrolisthesis group. (B) Comparison of the sagittal balance between the spondylolisthesis or kyphosis group and retrolisthesis group.

performed in the lumbosacral spine and thoracolumbar spine in 99 (88.4%), and 13 (11.6%) cases, respectively.

The mean lumbar lordosis angle in patients with a second surgery was  $31 \pm 15^\circ$ . The sagittal alignment was negative or neutral, positive and strongly positive in 49 (45.3%), 42 (38.9%), and 17 (15.7%) cases, respectively. Single-level and multi-level fusion was performed in 65 (58.0%), and 47 cases (42.0%), respectively (Table 2). The type of degeneration observed on the sagittal images was spondylolisthesis or kyphosis, retrolisthesis and neutral balance in 15 (13%), 41 (37%), and 56 (50%) cases, respectively.

In those cases with spondylolisthesis or kyphosis, the segments involved were the thoracolumbar junctional area and lumbar spine in 7 (46.7%), and 8 (53.3%) cases, respectively. The sagittal alignment was neutral, positive and strongly positive in 6 (46.2%), 2 (15.4%), and 5

(38.5%) cases, respectively. In cases with retrolisthesis, the segments involved were the lumbosacral and thoracolumbar junctional area in 40 (97.6%), and 1 case (2.4%), respectively. Their sagittal alignment was negative or neutral, positive and strongly positive in 22 (55.0%), 15 (37.5%), and 3 (7.5%) cases, respectively (Fig. 2). The LR test for the trend showed that the location of the adjacent segments ( $p = 0.000$ ) and sagittal alignment ( $p = 0.041$ ) had a significant association with the type of degeneration.

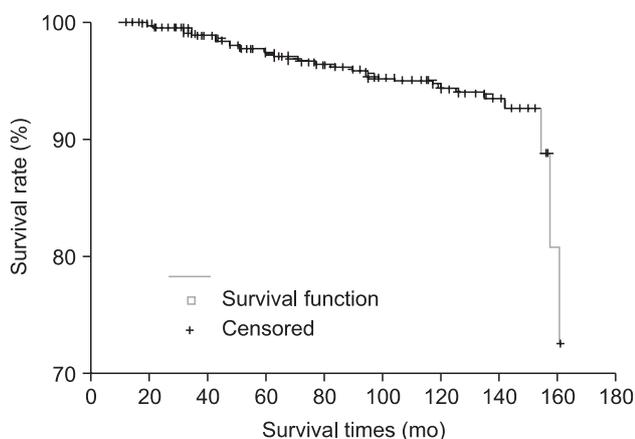
Regarding survival analysis using the Kaplan-Meier method, the 5- and 10-year survival rate of the adjacent segments was 97% and 94%, respectively. The survival curve was linear with the survival rate decreasing by approximately 0.6% each year (Fig. 3).

Prognostic factor analysis using Cox regression revealed age, degenerative disease, multi-level fusion, and gender to be associated with the risk of adjacent segment degeneration. Patients  $\geq 61$  years of age, had degenerative disease, and underwent multi-level fusion had a 3.9, 2.9, and 1.9 times higher risk of adjacent segment degeneration than their counterparts, respectively. Males were 1.8 times more likely to develop adjacent segment degeneration than females. Patients with all four risk factors were 6.6 times more predisposed to degeneration. The surgical methods did not appear to be related to the risk of adjacent segment degeneration (Table 3).

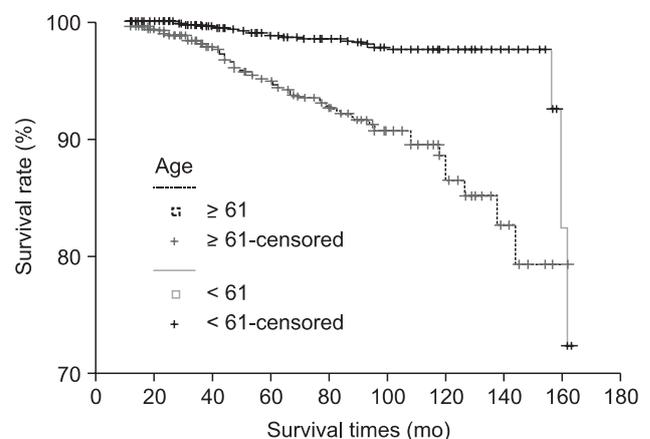
The 10-year survival rates of the adjacent segments in the patients classified according to the prognostic factors were as follows: 98% in the patients  $< 61$  years of age and 88% in the patients  $\geq 61$  years of age ( $p = 0.000$ ) (Fig. 4); 92% in those with degenerative diseases and 97% in those with non-degenerative diseases ( $p = 0.000$ ) (Fig.

**Table 3.** Result of Prognostic Factors Analysis by Cox Regression Model

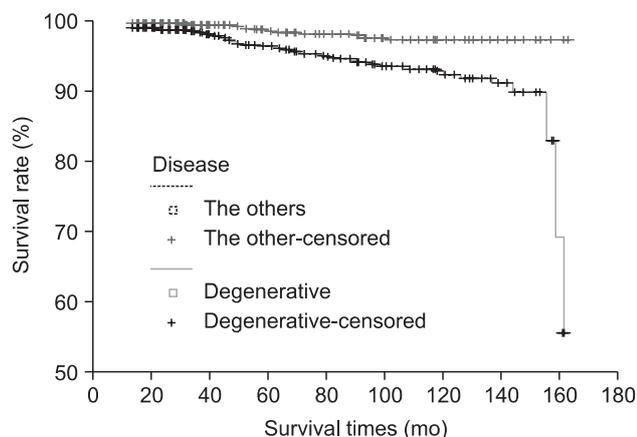
Prognostic factor	Odds ratio	p-value	95.0% Confidence interval	
			Lower	Upper
Old age (over 61 yr)	3.931	0.000	2.579	5.991
Male	1.758	0.004	1.196	2.586
Degenerative disease	2.943	0.000	1.716	5.045
Posterior lumbar interbody fusion	0.973	0.903	0.629	1.550
Multisegment fusion	1.932	0.001	1.315	2.84



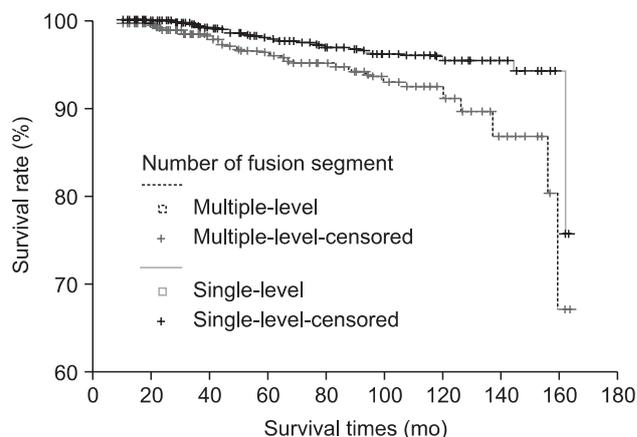
**Fig. 3.** This graph shows the survival function after thoracolumbar spinal fusion that reduced linearly. Overall survival function was approximately 97% at 60 months and approximately 94% at the 120 month follow-up.



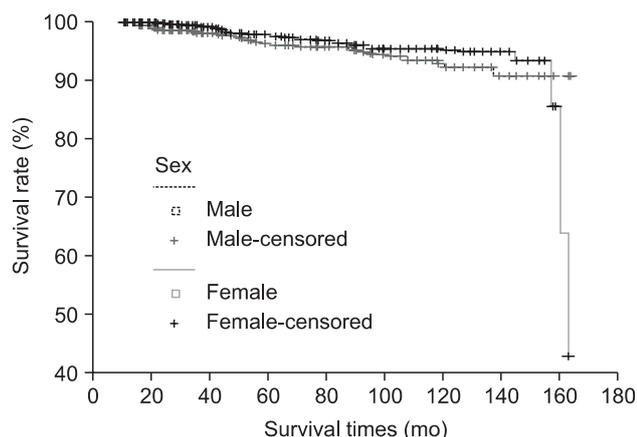
**Fig. 4.** Different survival function of the adjacent segment according to age. The 120 month survival function was 98% for  $< 61$  year-old age group and 88% for equal or above the 61 year-old age group ( $p = 0.000$ ).



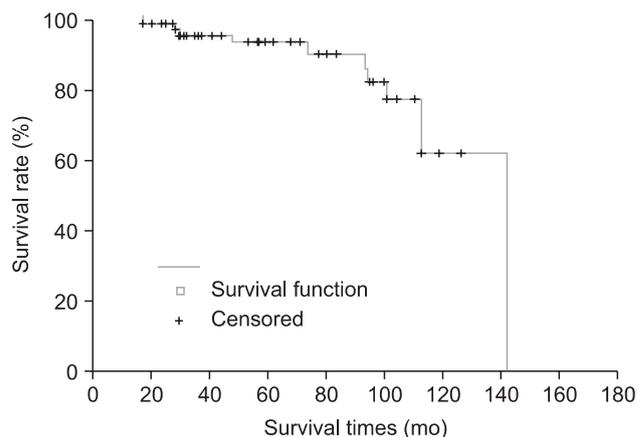
**Fig. 5.** Different survival function of the adjacent segment according to disease. The 120 month survival function was 92% for the degenerative disease group and 97% for the other group ( $p = 0.000$ ).



**Fig. 7.** Different survival function of the adjacent segment according to number of fusion segment. The 120 month survival function was 95% for the single-level fusion group and 91% for the above multiple-level fusion group ( $p = 0.012$ ).



**Fig. 6.** Different survival function of the adjacent segment according to gender. The 120 month survival function was 95% for women and 92% for men ( $p = 0.087$ ).



**Fig. 8.** Survival function of the adjacent segment in cases with all 4 negative prognostic factors. The 120 month survival function was 61%.

5); 95% in females and 92% in males ( $p = 0.087$ ) (Fig. 6); 95% in those who had undergone single-level fusion and 91% in those who undergone multiple-level fusion ( $p = 0.012$ ) (Fig. 7). The rate was 61% in patients with the four negative prognostic factors (Fig. 8).

## DISCUSSION

Thoracolumbar fusion is the standard procedure for the treatment of various spinal disorders. In addition, the improvement in fixation devices and increase in the number of successful treatment reports led to a sharp increase in the application of the technique.<sup>1,2</sup> However, many studies also reported that hypermobility at the adjacent segments

after fusion may accelerate the degenerative changes. Unfortunately, posterior dynamic stabilization aimed at maintaining the mobility of the spinal segments could not be an alternative to fusion in most cases.<sup>3</sup> Although it resulted in less hypermobility and degeneration at the adjacent segment in some studies,<sup>4,6</sup> the technique should be used with great care given that no long-term results have been published and other serious complications have been reported.<sup>7</sup> Numerous clinical and experimental studies have been carried out in the hope of predicting or preventing degenerative changes at the adjacent segments. However, it difficult to prove the impact of the risk factors identified under experimental conditions in clinical settings. Lee et al.<sup>8</sup> observed that the sagittal rotation of the

proximal adjacent segments increased by 37% after the fusion of one or two segments of the lumbar spine and concluded that hypermobility at the adjacent segments was one of the causes of degenerative changes. On the other hand, Axelsson et al.<sup>9)</sup> reported that adjacent segment hypermobility was not associated with degenerative changes, and Hoogendoorn et al.<sup>10)</sup> stated that adjacent segment hypermobility did not occur. Several studies have reported conflicting results. Degenerative changes, as the term itself suggests, are likely to increase with time. Accordingly, a study in which time is not addressed as a factor fails to reflect the reality. The design of a study on the risk factors of the adjacent segment degeneration published in 2005 was flawed. Two of the patients in the control group had to undergo surgery for degenerative changes after the study period, even though objective standards were applied for patient grouping.<sup>11)</sup> Although, the most desirable method is to design a prospective study using stratified sampling, it is practically impossible considering that a long-term observation period is needed for such studies. Therefore, the survival functions of the patients who had undergone spinal fusion using pedicle screw fixation were estimated between January 1994 and August 2007, and the prognostic factors that were analyzed using a multivariate Cox regression model accounted for the confounding effect between variables.

Although there were differences in the incidence of adjacent segment degeneration, most authors have reported that clinical symptoms occurred at a lower rate compared to radiological evidence of degeneration and concluded that they were not related to each other.<sup>5,12-19)</sup> However, their conclusion can be justified if radiological degenerative changes are demonstrated not to be a preceding stage of the clinical changes and either the extent of radiological changes or occurrence of clinical symptoms do not increase with time. In this study, only cases with symptoms for which a second surgery was indicated were used for survival analysis, and the survival rate decreased steadily by approximately 0.6% per year indicating that the clinical condition worsened with time. Although the changes in radiological degeneration were not analyzed, it is believed that the radiological degenerative changes were followed by the development of clinical symptoms given that the symptoms of adjacent segment increased proportionally with time.

The survival rate obtained in this study was better than that reported in any other study.<sup>14,20)</sup> This was attributed to conservative treatments being performed more aggressively because of the patients' and surgeons' aversion to second surgery and surgical treatment not being con-

sidered as an option in some patients due to old age, combined medical disorders, and the patient's financial situation. Therefore, the survival rate of the adjacent segments may have been lower if the study had included all patients who developed symptoms requiring a second surgery not those who had actually undergone a second operation.

It is still unclear if adjacent segment degeneration is a consequence of degenerative disease<sup>10,21)</sup> or results from biomechanical changes after spinal fusion.<sup>22)</sup> In this study, adjacent segment degeneration occurred at a higher rate in the patients who were old or had preexisting degenerative diseases, such as spinal stenosis or degenerative spondylolisthesis. Accordingly, the degeneration of the spine was related to the natural degenerative changes at the adjacent segments. However, considering that postoperative degeneration can also be identified in patients with non-degenerative disease, it is believed that biomechanical changes also have an impact on the degenerative changes after spinal fusion.

Patients with advanced age had a relatively poor prognosis. This was attributed to the difficulty in them becoming accustomed to the biomechanical changes,<sup>23)</sup> osteoporosis had a negative influence,<sup>13)</sup> and the degenerative changes had already begun.<sup>12)</sup>

With regard to the impact of gender, it was expected that the adjacent segment degeneration would be higher in females because degenerative diseases, such as spinal stenosis and degenerative spondylolisthesis, are far more prevalent in females. However, the survival rate was higher in females, even though the mean age was higher than that of males in this study. Harrop et al.<sup>5)</sup> also reported that second surgery due to adjacent segment degeneration was more common in males. A previous study reported that second surgery for adjacent segment degeneration was frequent in people engaged in labor intensive activities.<sup>11)</sup> Therefore, the poor prognosis in male patients may have been caused by their involvement in intensive activities after surgery.

The relationship between the number of the fused segments and adjacent segment degeneration is one of the issues of contention. Some authors reported that the increase in the number of fused segments did not result in a higher rate of degenerative changes at the adjacent segments.<sup>11,14)</sup> On the other hand, the risk of degeneration developing increased with increasing length of fusion,<sup>13,24-26)</sup> whereas there are studies showing opposite results.<sup>14)</sup> In this study, the cases were subdivided into one-level fusion and multi-level fusion cases, and that the risk of degeneration was higher in the latter group. An attempt was made to assess the risk according to the number of

the fused segments, but it was difficult to demonstrate statistical significance due to the large difference in the number of the cases between groups. The type II error increased when the cases were divided into those with one segment fusion, 2 segment fusion and  $\geq 3$  segment fusion for the same reason.

Authors have been divided regarding the correlation between the surgical method and adjacent segment degeneration. Some reported that posterior lumbar interbody fusion accelerated the adjacent segment degeneration because of the initial fixation strength and location of the fusion mass, which was located anterior to the posterior facet joint,<sup>17,27)</sup> whereas others disputed such a relationship.<sup>28)</sup> In this study, posterior lumbar interbody fusion had no effect on the prognosis. Compared to posterolateral fusion with pedicle screw fixation, fusion with an interbody cage and pedicle screw fixation would result in a higher intervertebral disc pressure at the adjacent segments due to the increased interbody pressure. However, the two techniques would not cause differences in tension of the interspinous ligament and pressure on the posterior facet joint. According to our observation, the adjacent segment degeneration on the sagittal views appeared to be associated more with a deficiency of the posterior facet joint and interspinous ligaments in cases, such as spondylolisthesis, kyphosis, or retrolisthesis of the superior vertebral body than with intervertebral subsidence. In addition, there was no correlation between the surgical methods and prognosis because the fixation strength of the metal bar located at the posterior side had more impact than the intervertebral cage. With regard to the relationship between the location of the adjacent segments and the type of degeneration, spondylolisthesis or kyphosis and retrolisthesis was more common in the thoracolumbar junctional area and lumbosacral area, respectively. Considering that the incidence of spondy-

lolisthesis or kyphosis increased with increasing positive sagittal alignment, the importance of changing the daily habits after surgery should not be taken lightly.

There are some factors expected to influence the prognosis, such as the preoperative condition of the adjacent segments, postoperative living behavior and muscle strength level. Unfortunately, these factors could not be accounted for in this study due to the limited data available.

The survival rate of the adjacent segments after second surgery decreased at a steady rate of 0.6% per year: it was 97% at the 5th year and 94% at the 10th year. The risk factors for surgery at the adjacent segments after fusion were advanced age, degenerative disease, multi-level fusion and male gender, whereas posterior lumbar interbody fusion had no impact.

Considering that the incidence of adjacent segment degeneration was higher in patients with advanced age or degenerative disease, the advancement of degenerative disease, let alone the mechanical impact of the fusion, appears to be one of the major causes of adjacent segment degeneration. Spondylolisthesis or kyphosis of the upper segment was more common in patients with degeneration at the thoracolumbar junctional area and strongly positive sagittal alignment, and retrolisthesis of the upper segment was more common in those with degeneration at the lumbosacral area and neutral or slightly positive sagittal alignment. Therefore, it is recommended that surgeons consider these types of adjacent segment degeneration when determining the level of fusion and guide their patients not to take postures or be involved in working conditions that could accelerate the degenerative process.

## CONFLICT OF INTEREST

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

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