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Risk-factor analysis of adjacent-segment pathology requiring surgery following anterior, posterior, fusion, and nonfusion cervical spine operations: Survivorship analysis of 1358 patients

Jae Chul Lee
Soonchunhyang University

Sang-Hun Lee
Kyung Hee University Hospital at Gangdong

Colleen Peters
Washington University School of Medicine in St. Louis

K. Daniel Riew
Washington University School of Medicine in St. Louis

Risk-Factor Analysis of Adjacent-Segment Pathology Requiring Surgery Following Anterior, Posterior, Fusion, and Nonfusion Cervical Spine Operations

Survivorship Analysis of 1358 Patients

Jae Chul Lee, MD, Sang-Hun Lee, MD, Colleen Peters, MA, and K. Daniel Riew, MD

Investigation performed at the Cervical Spine Service, Washington University Orthopedics, St. Louis, Missouri

Background: Adjacent-segment pathology is an important issue involving the cervical spine, but there have been few comprehensive studies of this problem. The purpose of the current study was to determine the risk factors for adjacent-segment pathology and to compare the survivorship of adjacent segments in patients who underwent cervical spine operations including arthrodesis and motion-sparing procedures.

Methods: This was a retrospective analysis of a consecutive series of 1358 patients with radiculopathy, myelopathy, or myeloradiculopathy who underwent cervical spine surgery performed by a single surgeon. We calculated the annual incidence of adjacent-segment pathology requiring surgery and, with use of Kaplan-Meier analysis, determined survivorship. Cox regression analysis was used to identify risk factors.

Results: The index surgical procedures included cervical arthrodesis (1095 patients; 1038 anterior, twenty-nine posterior, and twenty-eight combined anterior and posterior), posterior decompression (214 patients; 145 laminoplasty and sixty-nine foraminotomy), arthroplasty (thirty-two patients), and a combination of arthroplasty and anterior arthrodesis (seventeen patients). Secondary surgery on adjacent segments occurred at a relatively constant rate of 2.3% per year (95% confidence interval, 1.9 to 2.9). Kaplan-Meier analysis predicted that 21.9% of patients would need secondary surgery on adjacent segments by ten years postoperatively. Factors increasing the risk were smoking, female sex, and type of procedure. The posterior arthrodesis group (posterior-only or combined anterior and posterior arthrodesis) had a 7.5-times greater risk of adjacent-segment pathology requiring reoperation than posterior decompression, and a 3.0-times greater risk than the anterior arthrodesis group. However, when we compared the anterior cervical arthrodesis group, the arthroplasty group (arthroplasty or hybrid arthroplasty), and the posterior decompression group to each other, there were no significant differences. Age, neurological diagnosis, diabetes, and number of surgically treated segments were not significant risk factors.

Conclusions: Patients treated with posterior or combined anterior and posterior arthrodesis were far more likely to develop clinical adjacent-segment pathology requiring surgery than those treated with posterior decompression or anterior arthrodesis. Smokers and women had a higher chance of clinical adjacent-segment pathology after cervical spine surgery.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

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Cervical arthrodesis has been blamed for accelerating degenerative changes at adjacent spinal segments[1]. Many researchers believe that these changes may be related to increased mechanical stress and segmental motion[2,3]. However, others argue that the changes are part of the natural aging process of the cervical spine and point out the lack of

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definitive evidence that arthrodesis increases the incidence of adjacent-segment degeneration[4]. More recently, such degeneration has been termed clinical adjacent-segment pathology for those with clinical symptoms, and radiographic adjacent-segment pathology for those with only radiographic findings of degeneration at a level adjacent to a previous operation[5]. Several studies examining adjacent-segment pathology following motion-sparing cervical operations have demonstrated rates similar to those following arthrodesis[6-10].

To our knowledge, there has been no comprehensive study on the topic involving a large number of patients, as previous studies have been mostly limited to adjacent-segment pathology following anterior arthrodesis of the cervical spine or comparison of the rates of adjacent-segment pathology following arthroplasty and arthrodesis. The purpose of the current study was to determine the risk factors for adjacent-segment pathology requiring surgical treatment and to compare the survivorship curve among patients treated with various cervical spine operations including arthrodesis and motion-sparing procedures.

Materials and Methods

This study was approved by the institutional review board of our university. This was a retrospective study of a consecutive series of patients who underwent cervical spine surgery performed by the senior author (K.D.R.) for radiculopathy, myelopathy, or myeloradiculopathy between January 1999 and December 2010. Exclusion criteria were any prior cervical spine operation, fracture or dislocation, neoplasm, conversion of index laminoplasty or foraminotomy to cervical arthrodesis within the treated levels during follow-up, pseudarthrosis, implant-related reoperation, or inflammatory conditions such as rheumatoid arthritis and ankylosing spondylitis. Patients who required an adjacent-segment operation within twelve months of the index surgery were excluded because it was believed that the short duration was more likely due to an insufficient number of levels treated initially than to adjacent-segment pathology resulting from the index operation. The clinical features of these patients are summarized in a table in the Appendix. Two independent, experienced, academic spine surgeons (J.C.L. and S.-H.L.) reviewed the hospital records, office charts, and prospectively collected data, which included all pertinent imaging studies. For the patients who had not returned for at least one year of follow-up, mailed inquiries and telephone interviews were used to determine if a patient had had adjacent-level spinal surgery.

The primary indication for the cervical spine procedures performed among the study population was radiculopathy, myelopathy, or myeloradiculopathy that was unresponsive to a full trial of nonoperative treatments. Surgical intervention was performed at all of the segments responsible for patient symptoms and signs, and neural compressive lesions were identified on the imaging studies. Patients were examined regularly by the senior author during follow-up visits to the office. Patient symptoms and functional status were documented, and neurological status was determined through sensory, motor, and reflex testing, at every visit. Radiographs, including dynamic lateral views, were also obtained at each follow-up visit.

Adjacent segments were defined as one segment cephalad or caudad to the surgically treated segments. Recurrent radicular symptoms after the index operation were treated with nonoperative modalities, including nonsteroidal anti-inflammatory medications, oral corticosteroids, gabapentin or pregabalin, physical therapy, and perineural corticosteroid injections. If the radicular symptoms did not respond to a full trial of noninvasive treatment or patients had myelopathic symptoms, magnetic resonance imaging (MRI) and/or computed tomography (CT) were performed. Neural compression at adjacent segments was carefully identified on the imaging studies. Surgical intervention was performed only at the adjacent segments when the senior author determined that the imaging studies correlated with patient symptoms and signs. When the clinical examination and history were not adequate to identify the symptomatic level, it was confirmed by selective perineural injection. It is the senior author's practice to recommend such blocks on all non-contraindicated patients with painful radiculopathy unless they have a profound neurological deficit as their chief complaint. The indications for adjacent-segment surgery were basically the same as for the index surgery: radiculopathy, myelopathy, or myeloradiculopathy that did not respond to a full trial of nonoperative treatments associated with radiological correlation.

Statistical Analysis

The incidence and prevalence of surgery for adjacent-segment pathology were calculated by life-table method for each year, and Kaplan-Meier survivorship curves were constructed with a 95% confidence interval (CI). The annual incidence of operations for adjacent-segment pathology was defined as the percentage of the patients who had not had a second operation by the start of the given year and who then had an adjacent-segment operation during that year. The prevalence was defined as the percentage of the patients who underwent a secondary operation for adjacent-segment pathology during a given time period.

A Cox proportional-hazards model was used to determine the potential risk factors that contributed to the incidence of adjacent-segment pathology requiring surgery. Variables were age, sex, tobacco use, neurological diagnosis, diabetes, type of surgery, and number of surgically treated segments. Initially, Cox regression survivorship curves for each surgical method were determined. We then divided all procedures into four groups, according to the type of procedure: posterior decompression (laminoplasty or foraminotomy), anterior arthrodesis, arthroplasty (arthroplasty-only or hybrid arthroplasty, a combination of arthroplasty and arthrodesis), and posterior arthrodesis (posterior-only or combined anterior and posterior arthrodesis). Cox proportional-hazard analysis was performed for these four groups and with other previously described variables.

The level of significance was set at $p < 0.05$.

Source of Funding

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Results

A total of 1358 patients (729 men and 629 women) underwent cervical spine surgery for radiculopathy, myelopathy, or myeloradiculopathy. The mean age at the time of the index operation was fifty-one years (range, twenty to ninety-one years). Two hundred and forty-two patients had less than one year of follow-up. Fifty-eight of those patients responded to mail or phone inquiries, and therefore, a total of 184 patients were lost to follow-up less than one year postoperatively. The mean duration of follow-up was forty-eight months (range, twelve to 168 months). Twenty-five patients died, including five patients before one year postoperatively and twenty patients after one year. Two of the twenty patients had undergone revision surgery before their death, and the other twenty-three patients who died were classified as censored cases without event.

At the time of the index operation, 980 patients had a diagnosis of radiculopathy; seventy-eight patients, myelopathy; and 300 patients, myeloradiculopathy. The index surgical procedures included cervical arthrodesis (1095 patients; 1038 anterior, twenty-nine posterior, and twenty-eight combined anterior and posterior), posterior decompression (214 patients; 145 laminoplasty and sixty-nine foraminotomy), arthroplasty (thirty-two patients; twenty-nine single-level and three double-level), and a combination of arthroplasty and anterior cervical

TABLE I Incidence of Adjacent-Segment Pathology by Hazard Function*

	No. of Patients Entering Interval	No. of Patients Lost to Follow-up/Death	No. of Patients with Reoperation	Incidence (%)	95% CI (%)
Months					
0-12	1358	189	0	N/A†	N/A†
12-24	1169	228	22	2.2	1.8-2.6
24-36	919	239	16	2.2	1.8-2.6
36-48	664	128	18	3.1	2.5-3.9
48-60	518	95	7	1.5	1.2-1.9
60-72	416	94	4	1.1	0.9-1.5
72-84	318	73	6	2.1	1.6-2.8
84-96	239	60	6	3.0	2.1-4.1
96-108	173	46	10	7.2	4.8-11.0
108-120	117	33	2	2.0	1.3-3.1
Average annual incidence				2.3	1.9-2.9

*This table presents the annual incidence and ten-year average incidence of adjacent-segment pathology requiring reoperation within ten years after the index surgery. Three more events occurred in the eleventh, twelfth, and thirteen year, but they were truncated. The total number of patients who underwent reoperation for adjacent-segment pathology was ninety-four. †N/A = not applicable (adjacent-segment pathology was defined as new disease requiring surgery developed at a minimum of one year after the index cervical operation).

discectomy and fusion (ACDF) (seventeen patients; thirteen single-level arthroplasty and single-level ACDF, and four single-level arthroplasty and double-level ACDF).

Four hundred and six patients were treated at one level, 433 at two levels, 291 at three levels, 180 at four levels, thirty at five levels, thirteen at six levels, three at seven levels, and two at eight levels.

Four hundred and three (30%) of the patients were smokers, and nine hundred and fifty-five were not. One hundred and four (8%) of the patients were diabetic.

Incidence of Adjacent Pathology

Ninety-four patients required a reoperation for adjacent-segment pathology. Forty-one patients had treatment at the cephalad adjacent segment, thirty-two at the caudal adjacent segment, and twenty-one at both the cephalad and caudal adjacent segments. The incidence of reoperation for adjacent-segment pathology was relatively constant at an average of 2.3% per year (95% CI, 1.9% to 2.9%) (Table I).

Overall Survival of Adjacent Segments

Kaplan-Meier analysis predicted a 90.6% disease-free survival rate for adjacent segments (95% CI, 85.4% to 92.8%) at five years and 78.1% (95% CI, 72.7% to 83.5%) at ten years. In terms of the prevalence of adjacent-segment pathology, these results suggested that 9.4% (95% CI, 7.2% to 11.6%) of patients would need an additional operation within five years, and 21.9% (95% CI, 16.5% to 27.3%) by ten years (Fig. 1).

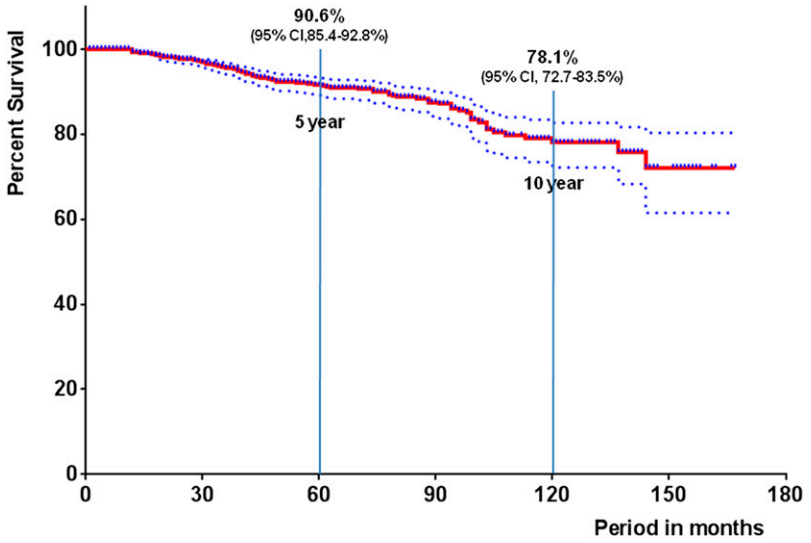

Fig. 1
Overall Kaplan-Meier survivorship curve for adjacent segments following cervical spine operations to treat cervical radiculopathy, myelopathy, or myeloradiculopathy.

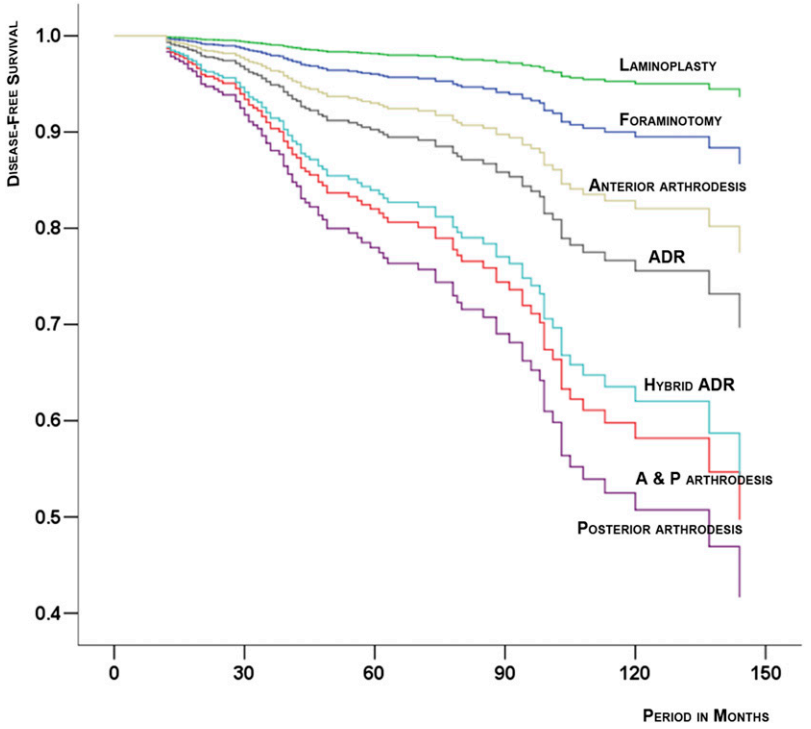

Fig. 2

Cox proportional-hazards regression survivorship curves for each type of cervical spine operation corrected by multiple variables. ADR = artificial disc replacement, and A & P = combined anterior and posterior.

Risk-Factor Analysis

Corrected survivorship curves for each operative procedure were determined with use of a Cox regression analysis with previously described variables (Fig. 2). We then grouped all procedures into four groups as previously described and performed the final Cox analysis for those four groups. The factors that significantly increased the risk of adjacent-segment pathology requiring reoperation were type of procedure, smoking, and female sex (Table II). In terms of procedure type, the posterior arthrodesis group (posterior or combined anterior and posterior arthrodesis) had a 7.51-times (95% CI, 2.00 to 28.19 times) greater risk of adjacent-segment pathology

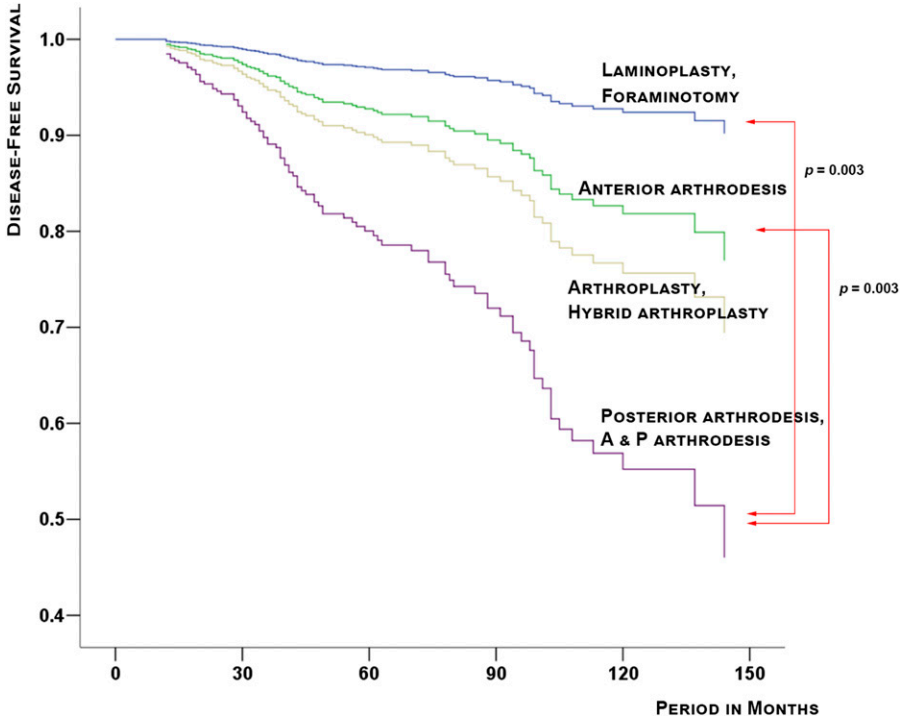

Fig. 3

Cox proportional-hazards regression survivorship curves with types of cervical spine operation as covariates. The operations were stratified into four groups: posterior decompression (laminoplasty or foraminotomy), anterior arthrodesis, arthroplasty or hybrid arthroplasty (combination of arthroplasty and arthrodesis), and posterior arthrodesis (posterior-only or combined anterior and posterior [A & P] arthrodesis).

TABLE II Cox Proportional Hazards for Risk of Adjacent-Segment Pathology Following Cervical Operations*

	No. of Patients N = 1358	ASP (*No. of Patients*) N = 94	P Value	Hazard Ratio	95% CI
Age			0.336		
≤60 year	1093	86		Reference group	
>60 year	265	8		0.68	0.31-1.49
Sex			0.029†		
M	729	36		Reference group	
F	629	58		1.61	1.05-2.46
Smoking			0.009†		
No	955	54		Reference group	
Yes	403	40		1.75	1.15-2.67
Diabetes			0.395		
No	1254	88		Reference group	
Yes	104	6		0.70	0.30-1.60
Neurological diagnosis			0.620		
Radiculopathy	980	79		Reference group	
Myelopathy	78	3	0.976	1.02	0.31-3.30
Myeloradiculopathy	300	12	0.332	0.71	0.36-1.41
Procedure			0.007†		
Laminoplasty or foraminotomy	214	3		Reference group	
Anterior arthrodesis	1038	78	0.122	2.53	0.78-8.23
ADR or hybrid ADR	49	4	0.130	3.53	0.69-18.10
Posterior or A & P arthrodesis	57	9	0.003†	7.51	2.00-28.19
Number of surgically treated segments			0.090		
1 or 2 segments	839	72		1.57	0.93-2.65
≥3 segments	519	22		Reference group	

ASP = adjacent-segment pathology, ADR = artificial disc replacement (arthroplasty), hybrid ADR = combination of single-level artificial disc replacement and neighboring-level anterior cervical arthrodesis, and A & P arthrodesis = combined anterior and posterior arthrodesis. †$P < 0.05$.

requiring reoperation than the posterior decompression group (laminoplasty or foraminotomy). However, the anterior cervical arthrodesis group and the arthroplasty group (arthroplasty or hybrid arthroplasty, a combination of arthroplasty and arthrodesis) did not differ significantly from the posterior decompression group (Fig. 3). Smoking increased the risk of reoperation by 1.75 times (95% CI, 1.15 to 2.67 times), and female sex by 1.61 times (95% CI, 1.05 to 2.46 times).

We found that the following were not significant risk factors: an age of greater than sixty years at the time of the index surgery (hazard ratio [HR], 0.68 [95% CI, 0.31 to 1.49]), neurological diagnosis (HR, 1.02 [95% CI, 0.31 to 3.30] for myelopathy and 0.71 [95% CI, 0.36 to 1.41] for myeloradiculopathy, with radiculopathy as the reference group), diabetes (HR, 0.70 [95% CI, 0.30 to 1.60]), and the number of surgically treated segments (HR, 1.57 [95% CI, 0.93 to 2.65] for one or two segments, with three or more segments as the reference group).

For further comparison of procedure types, we repeated the same analysis, using the same variables, but with anterior arthrodesis as a reference. The posterior arthrodesis group (posterior or combined anterior and posterior arthrodesis) had a 3.0-times (95% CI, 1.4 to 6.1 times) greater risk of adjacent-segment pathology requiring reoperation than the anterior arthrodesis group. However, the risk for the arthroplasty group (HR, 1.40 [95% CI, 0.44 to 4.46]) and posterior decompression group (HR, 0.40 [95% CI, 0.12 to 1.28]) was not significantly different from that of the anterior cervical arthrodesis group.

Discussion

It has been postulated that arthrodesis of the cervical spine causes stress transfer to adjacent spinal segments and may result in adjacent-segment pathology[1-3,11]. In the same context, many researchers believe that motion-sparing operations may result in a lower incidence of adjacent-segment pathology than arthrodesis. Unfortunately, the majority of the studies on the topic had small numbers or only analyzed the outcomes of anterior procedures and did not statistically control confounding variables with use of multivariate analyses. In the present study, we attempted to fill some of these gaps by determining the incidence and prevalence of

adjacent-segment pathology in a large group of patients who had undergone various cervical spine procedures, and we further performed multivariate Cox analysis. As insufficient or loss of follow-up is an inevitable problem in clinical research, we used Kaplan-Meier survivorship analysis to predict survival of adjacent segments, including among those who were lost to follow-up.

The reoperation rate at the adjacent segment varied with type of operative procedure. Patients treated with operative methods that included posterior arthrodesis experienced a higher risk of adjacent-segment pathology than those treated with posterior decompression or anterior arthrodesis. There were no significant differences in terms of the risk of adjacent-segment pathology among the following groups: posterior decompression, anterior arthrodesis, and arthroplasty.

The posterior arthrodesis group had a 7.5-times greater risk of reoperation for adjacent-segment pathology than the posterior decompression group, and 3.0-times greater risk than the anterior arthrodesis group. We are not aware of any previous studies that demonstrated that posterior arthrodesis had a higher incidence of adjacent-segment pathology than anterior arthrodesis. The possible explanations for this phenomenon are soft-tissue injury of ligaments, facet capsule, and muscle during posterior arthrodesis, or the rigidity of posterior instrumentation. Some basic studies may support these explanations. A study using finite element analysis demonstrated that disruption of posterior elements and the ligamentous complex can induce kyphosis on the surgically treated and adjacent levels[12]. Also, the authors of biomechanical studies involving cadaveric spines have reported increased stress on adjacent segments after posterior cervical laminectomy and instrumentation[13,14].

The current study showed that the procedure type with the lowest risk of adjacent-segment pathology was posterior decompression (laminoplasty and foraminotomy). In a comparative study involving MRI evaluation following laminoplasty and anterior arthrodesis, no change was found in the signal quality of the adjacent discs after laminoplasty, which was not the case following anterior cervical arthrodesis[15]. Clinically, it appears that the development of adjacent-segment pathology after laminoplasty may be rare, as there have been, to our knowledge, only two case reports in the literature[16,17]. Moreover, the current study found that the incidence of adjacent-segment pathology after foraminotomy is also low.

In our study, anterior arthrodesis had a relatively low incidence of adjacent-segment pathology compared with other operations. Survivorship of the adjacent segments following anterior arthrodesis was not significantly inferior to that of the laminoplasty and foraminotomy group, which had the best survivorship of adjacent segments. This is similar to the findings of other studies. In a prospective study comparing anterior arthrodesis to foraminotomy for cervical soft disc herniations, radiographic changes at the adjacent segments were observed in 41% of the anterior arthrodesis patients compared with 50% of the foraminotomy patients[18]. In another study observing 846 consecutively treated patients who underwent posterior laminoforaminotomy without arthrodesis, the annual incidence of adjacent-segment pathology requiring surgery was approximately 3%[19]. This is similar to the 2.7% annual incidence of symptomatic adjacent-segment pathology following anterior arthrodesis in the study by Hilibrand et al.[4]. The results of these three studies suggest that anterior arthrodesis and posterior decompression have similar rates of adjacent-segment pathology. One possible explanation is that the anterior approach minimizes disruption of supporting structures such as ligaments and muscles.

Smoking was a significant risk factor for adjacent-segment pathology in our study. Multiple studies have demonstrated that smoking increases the risk of degenerative disc disease and back pain in the spine[13,20,21]. In a study of 600 twin siblings, Battié et al. found that smokers had higher disc-degeneration scores than their nonsmoking twins[14]. In our study, smoking was an independent risk factor for adjacent-segment pathology with very high significance; we believe that smoking may accelerate disc degeneration after various spinal surgical procedures, increasing the incidence of adjacent-segment pathology.

In our study, female sex also was a risk factor for adjacent-segment pathology. In a radiographic follow-up study of cervical disc degeneration in 707 patients, cervical disc degeneration was found to progress at a faster rate in females than in males between ages forty and sixty years, whereas males had a faster degeneration rate between ages sixty and seventy-nine years[22]. The average ages of the male and female patients in our study were fifty-two and fifty-one years, with a standard deviation of twelve and eleven years, respectively. Most of the patients in our study were between ages forty and sixty years, suggesting a possible explanation for the increased risk in females.

Our study had several limitations. First, it was retrospective, although it was based on prospectively collected data. While a prospective study can alleviate any bias for selective recording, a prospective study with a large number of patients with long-term follow-up is practically very difficult. While we have such data from several FDA-IDE (U.S. Food and Drug Administration-Investigational Device Exemption) studies on disc arthroplasty compared with arthrodesis, such data gathering is not likely to be repeated for other types of cervical procedures. Second, radiographic analysis was not included in this study, as we were interested in reoperation rates and not radiographic adjacent-segment pathology.

On the basis of our results, we believe that patients can be instructed that posterior arthrodesis alone, or in combination with anterior arthrodesis, can increase the risk of adjacent-segment pathology. This is of practical importance for smokers with multilevel degenerative disease who undergo circumferential arthrodesis to improve fusion rates. Such patients may be at increased risk of adjacent-segment pathology not only from the posterior arthrodesis but also from smoking. If they are female, the risk may be further increased. We therefore carefully review these patients to determine if they can be treated with laminoplasty, foraminotomy, or arthroplasty instead of

undergoing combined anterior and posterior arthrodesis or posterior-only arthrodesis. While spine surgeons may already advise a patient who is a candidate of cervical arthrodesis to quit smoking, our study suggests that these patients should also be warned that, if he or she smokes, it may increase the risk of needing an adjacent-level reoperation. This was found to be true, even after motion-preserving operations. Finally, female patients should also be advised of the increased risk for reoperation.

In conclusion, this is the largest series, to our knowledge, to report on adjacent-segment pathology following both anterior and posterior cervical operations. Patients treated with posterior or combined anterior and posterior arthrodesis were far more likely to develop clinical adjacent-segment pathology requiring additional surgery than those treated with posterior decompression (laminoplasty or foraminotomy) or anterior arthrodesis. There was no difference in risk among anterior arthrodesis, arthroplasty, and posterior decompression procedures. Smokers and women were at a greater risk for reoperations for adjacent-segment pathology.

Appendix

eA A table summarizing the clinical features of the eleven patients who required adjacent-segment surgery before twelve months of follow-up is available with the online version of this article as a data supplement at jbjs.org. ■

Jae Chul Lee, MD
Department of Orthopedic Surgery,
Soonchunhyang University Seoul Hospital,
59 Daesagwan-ro,
Yongsan-gu, Seoul,
140-743, Republic of Korea

Sang-Hun Lee, MD
Department of Orthopedic Surgery,
Kyung Hee University Hospital at Gangdong,
#149 Sangil-dong,
Gangdong-gu, Seoul,
134-727, Republic of Korea

Colleen Peters, MA
K. Daniel Riew, MD
Department of Orthopedic Surgery,
Washington University School of Medicine,
660 South Euclid Avenue,
Campus Box 8233,
St. Louis, MO 63110

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