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The Influence of Comorbidities on Reoperations Following Primary Surgery of Lumbar Degenerative Diseases : A Nationwide Population-Based Retrospective Cohort Study from 2009–2016

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Objective : Spinal degeneration is a progressive disease, worsening over time. Lumbar degenerative disease (LDD) is a major spinal disease in elderly patients. Surgical treatment is considered for medically intractable patients with LDD and reoperation after primary surgery is not uncommon. The surgical outcome is occasionally unpredictable because of comorbidities. In the present study, the relationship between comorbidities and the incidence of reoperation for LDD over time was determined.

Methods : The claims data of the health insurance national database were used to identify a cohort of patients who underwent spinal surgery for LDD in 2009. The patients were followed up until 2016. Medical comorbidity was assessed according to the Charlson comorbidity index (CCI). Cox proportional hazard regression modeling was used to identify significant differences in sex, surgery, age, causative disease, and comorbidity.

Results : The study cohort included 78241 patients; 10328 patients (13.2%) underwent reoperation during the observation period. The reoperation rate was statistically higher (p<0.01) in males, patients 55–74 years and 65–74 years of age, and patients with decompression or discectomy. Significant association was found between increasing reoperation rate and CCI score (p<0.01). Based on multivariate analysis of comorbidities, the significantly higher reoperation rates were observed in patients with peripheral vascular disease, pulmonary lung disease, peptic ulcer, diabetes, and diabetes complications (p<0.01).

Conclusion : The study results indicate the reoperation rate for LDD is associated with patient comorbidities. The comorbidities identified in this study could be helpful in future LDD studies.

Key Words : National health insurance · Lumbar vertebrae · Degenerative disease · Surgery · Comorbidity.

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INTRODUCTION

Spinal degeneration is a progressive disease, worsening over time. Lumbar degenerative disease (LDD) is a major spinal disease in elderly patients. The rapid increase in the elderly population will inevitably produce an increase in medical expenses for LDD. The etiology of LDD is complex and the mechanism remains unclear. Many factors such as aging, spine injuries and diseases, mechanical stress, smoking, infection, trauma, and genetic factors are involved in the pathogenesis of LDD[6,22]. Surgical treatment is considered for medically intractable patients with LDD; however, the surgical outcome is occasionally unpredictable because of comorbidities[14]. Reoperation after primary surgery is not uncommon[6]. The need for reoperation has been reported and potentially increased costs and inferior outcomes are of concern among patients who require a revision.

Reportedly, 3.3% of patients in a previous study required reoperation every year after spinal operation for lumbar spinal stenosis with 50% occurring at adjacent levels[19]. Studies that identify predictors of reoperation for LDD are lacking due to the relatively low incidence of reoperation[10,14].

Therefore, investigating the risk factors involved in reoperation for LDD over time is important. In the present study, the relationship between comorbidities and the incidence of reoperation for LDD over time was determined.

MATERIALS AND METHODS

Data source

The research protocol was approved by the Institutional Review Board (IRB) of Soonchunhyang University Hospital (IRB number 2017-05-008) and performed in accordance with the Declaration of Helsinki. This was an anonymous observational study, thus the need for informed consent was waived.

Claims data from the Health Insurance Review and Assessment Service (HIRA; https://www.hira.or.kr) national database were used to identify a population of patients who received spinal treatments for LDD from 2007–2016. The claims data represent 46 million patients per year that account for 90% of the total population in South Korea[15]. The HIRA claim data are organized into five categories : 1) general information, 2) specific information regarding the health care provided, 3) diagnostic information, 4) outpatient prescription, and 5) health care provider information. The disease codes using the International Classification of Diseases, 10th version (ICD-10) were used.

Cohort group

The study cohort consisted of patients who were first diagnosed with LDD and received spinal surgery for LDD in 2009. To clarify the definition of new-onset, patients diagnosed with spinal surgery within the past 2 years (2007–2008) were excluded. In addition, patients who were diagnosed and received reoperation within 1 year were excluded. Reoperation was defined as repeated surgery performed in the lumbar spine, because we could not distinguish whether or not reoperation was performed on the same segment of the previous operation in this study. The patients were classified into three groups : spinal fusion group, discectomy group, and decompression group and the final number in the study cohort was 78241.

Comorbidities

The Charlson comorbidity index (CCI) has been a useful tool for health researchers to measure comorbid disease status or case mix in health care databases[21]. The comorbidities were defined as numerous clinical conditions based on review of hospital charts and the relevance in the prediction of 1-year mortality assessed. In the present study, medical comorbidity was assessed according to the ICD-10 of the CCI. The CCI value was calculated using 17 comorbidities. Each comorbidity is assigned a score (weight) when computing the weighted Charlson index. Diabetes with complications, hemiplegia, renal disease, and cancer are assigned a score of 2; metastatic cancer and severe liver disease are assigned a score of 3; and human immunodeficiency virus is assigned a score of 6; the remaining comorbidities are assigned a score of 1[21].

Statistical analyses

All statistical analyses in this study were performed using program R version 3.3.2 (www.r-project.org) and SAS Enterprise version 9.1.3 (SAS institute Inc., Cary, NC, USA). Survival analysis was used to compare the cumulative incidence of reoperations on patients and reoperation time was calculated as the number of years between the hospital admission day for the first surgery and second surgery. Censoring occurred when the patient reached the end of the follow-up period

without a second surgery, which included patients who died outside the hospital or died of other causes during the follow-up period. Cox proportional hazard regression modeling was used to identify significant differences in sex, surgery, age, causative disease, and comorbidity. The hazard plots and tests of the Schoenfeld residuals were performed to determine whether the proportional assumptions of the Cox regression model were violated. A hazard ratio (HR) and a 95% confidence interval (CI) were calculated, and a Kaplan-Meier plot was performed for visualization. A two-tailed p-value <0.05 was considered statistically significant.

Table 1. Descriptive summary of patient cohort

Category	Number of patients with reoperation	Total patient
Overall	10328 (100)	78241 (100)
Sex		
Male	5342 (51.7)	36504 (46.7)
Female	4986 (48.3)	41737 (53.3)
Age (years)		
<35	906 (8.8)	7479 (9.6)
35–44	1243 (12.0)	10046 (12.8)
45–54	2083 (20.2)	16570 (21.2)
55–64	2674 (25.9)	18359 (23.5)
65–74	2879 (27.9)	20374 (26.0)
≥75	543 (5.2)	5413 (6.9)
Diagnosis		
Spondylolisthesis	909 (8.8)	10036 (12.8)
Radiculopathy	139 (1.3)	1090 (1.4)
Low back pain	59 (0.6)	492 (0.6)
Lumbar stenosis	3831 (37.1)	28104 (35.9)
L-HIVD	5346 (51.8)	38228 (48.9)
Other	44 (0.4)	291 (0.4)
Surgery		
Spinal fusion	493 (4.8)	4597 (5.9)
Decompression	7441 (72.0)	54426 (69.5)
Diskectomy	2394 (23.2)	19218 (24.6)

Values are presented as number (%). L-HIVD : lumbar herniated intervertebral disc

RESULTS

Patient population

In 2009, 78241 patients underwent primary surgery for LDD; 46.7% were males and 53.3% were females. Among the patients, 26.0% were 65–77 years of age and 6.9% were 75 years of age or older. The percentage of patients who underwent spinal surgery for lumbar herniated intervertebral disc (L-HIVD) was 48.9%, for lumbar stenosis 35.9%, and for spondylolisthesis 12.8%. The surgical methods included decompression (69.5%), discectomy, (24.5%), and spinal fusion (5.9%; Table 1). The incidence of medical comorbidities was : pulmonary disease (22.3%), diabetes (20.3%), and peripheral vascular disease (17.6%; Table 2).

Reoperation in patients

Among the 78241 patients who were followed up for 8 years, 10328 underwent reoperation for LDD (Table 1). The reoperation rate for LDD was 13.2%. Cumulative probability curve of reoperation was the concave type, which has the greatest reoperation rate in early follow-up, decreasing over time (Fig. 1).

Table 2. Patient comorbidities

Comorbidity	Weight	Number of patients
Acute myocardial infarction	1	444 (0.6)
Congestive heart failure	1	90 (0.1)
Peripheral vascular disease	1	11404 (14.6)
Cerebrovascular disease	1	819 (1.1)
Dementia	1	385 (0.5)
Pulmonary disease	1	17427 (22.3)
Connective tissue disorder	1	448 (0.6)
Peptic ulcer	1	3030 (3.9)
Liver disease	1	798 (1.0)
Diabetes	1	15880 (20.3)
Diabetes complications	2	5396 (6.9)
Hemiplegia	2	156 (0.2)
Renal disease	2	167 (0.2)
Cancer	2	3187 (4.1)
Metastatic cancer	3	19 (0.02)
Severe liver disease	3	420 (0.5)
HIV	6	10 (0.01)

Values are presented as number (%). HIV : human immunodeficiency virus

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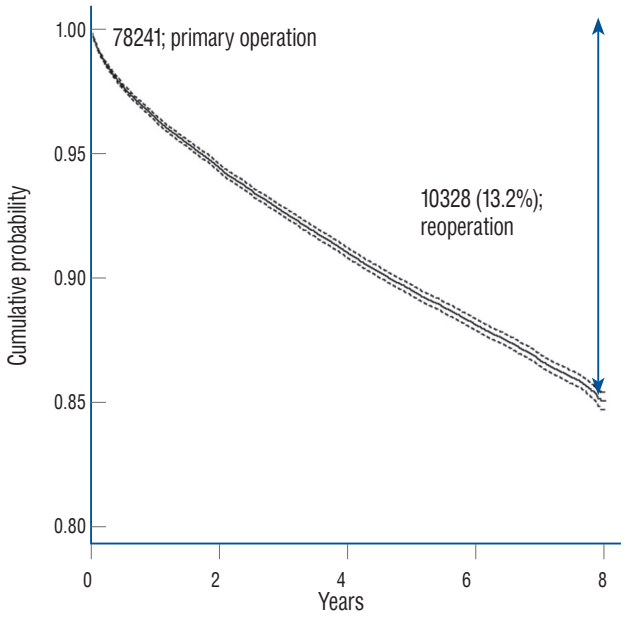

Fig. 1. Kaplan-Meier plot of 1.00 cumulative reoperation for lumbar degenerative disease.

The percentage of males and females was 51.7% and 48.3%, respectively. The reason for reoperation was L-HIVD (51.8%), lumbar stenosis (37.1%), and spondylolisthesis (8.8%). The surgical methods were decompression (72.0%), discectomy, (23.2%), and spinal fusion (4.8%; Table 1).

Demographic factors for reoperation

Based on multivariate Cox regression analysis with HR estimates and CIs, sex, age, causative disease, and surgical method showed significant differences for LDD reoperation rate (Table 3). The reoperation rate in male patients was statistically higher (p<0.01) than in female patients (HR, 1.32; 95% CI, 1.27–1.37). Patients 55–74 years and 65–74 years of age had statistically higher reoperation rates (p<0.01) than patients under 35 years of age (55–64 years : HR, 1.41; 95% CI, 1.30–1.52; 65–74 years : HR, 1.39; 95% CI, 1.28–1.50). Lumbar stenosis and L-HIVD showed higher reoperation rate (p<0.01) than spondylolisthesis (lumbar stenosis : HR, 1.50; 95% CI,

Table 3. Cox proportional HR of demographic factors for reoperation

	Univariate analysis				Multivariate analysis			
	HR	95% CI		*p*-value	HR	95% CI		*p*-value
		Lower	Upper			Lower	Upper	
Sex								
Female				References				
Male	1.28	1.23	1.33	<0.01	1.32	1.27	1.37	<0.01
Age (years)								
<35				References				
35–44	1.03	0.94	1.12	0.57	1.06	0.98	1.16	0.16
45–54	1.03	0.95	1.11	0.48	1.14	1.06	1.24	<0.01
55–64	1.203	1.12	1.30	<0.01	1.39	1.28	1.50	<0.01
65–74	1.209	1.12	1.30	<0.01	1.41	1.30	1.52	<0.01
≥75	0.92	0.82	1.02	0.11	1.08	0.97	1.20	0.17
Causative disease								
Spondylolisthesis				References				
Radiculopathy	1.47	1.23	1.76	<0.01	1.51	1.26	1.81	<0.01
Low back pain	1.37	1.06	1.79	0.02	1.39	1.06	1.80	0.02
Lumbar stenosis	1.56	1.45	1.68	<0.01	1.50	1.39	1.61	<0.01
L-HIVD	1.61	1.50	1.73	<0.01	1.63	1.52	1.76	<0.01
Other	1.75	1.29	2.37	<0.01	1.71	1.27	2.32	<0.01
Surgery								
Spinal fusion				References				
Decompression	1.30	1.19	1.43	<0.01	1.38	1.26	1.51	<0.01
Discectomy	1.19	1.08	1.31	<0.01	1.21	1.109	1.34	<0.01

HR : hazard ratio, CI : confidence interval, L-HIVD : lumbar herniated intervertebral disc

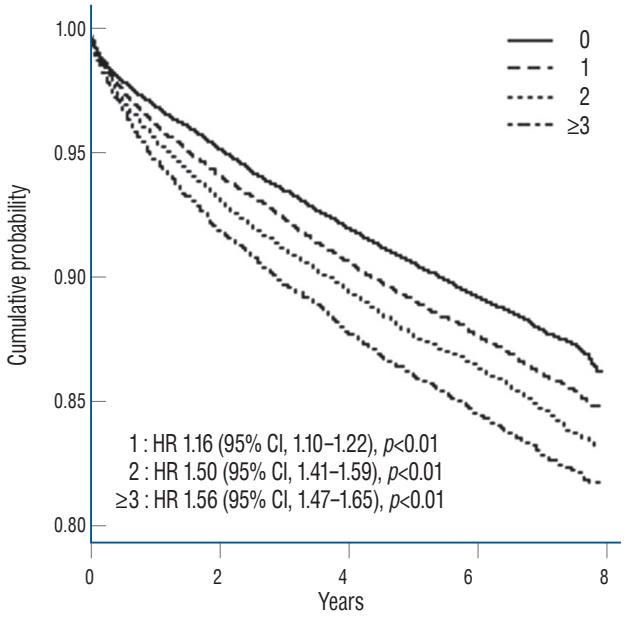

Fig. 2. Kaplan-Meier plot based on Charlson Comorbidity Index group for reoperation. HR : hazard ratio, CI : confidence interval.

1.40–1.61; L-HIVD : HR, 1.63; 95% CI, 1.52–1.76). Decompression and discectomy showed a higher reoperation rate (p<0.01) than fusion surgery (decompression : HR, 1.38; 95% CI, 1.26–1.51; discectomy : HR, 1.21; 95% CI, 1.10–1.33).

Comorbidities for reoperation

Based on univariate HR analysis, higher CCI score was associated with significantly higher reoperation rate (p<0.01; Fig. 2). Multivariate HR analysis of comorbidities indicated peripheral vascular disease (HR, 1.14; 95% CI, 1.08–1.20), pulmonary disease (HR, 1.20; 95% CI, 1.15–1.26), peptic ulcer (HR, 1.19; 95% CI, 1.09–1.31), diabetes (HR, 1.15; 95% CI, 1.10–1.21), and diabetes complications (HR, 1.17; 95% CI, 1.08–1.26), were associated with a significant increase in reoperation rate (p<0.01) (Table 4).

Table 4. Cox proportional HR of the comorbidities for reoperation

	Univariate analysis				Multiple analysis			
	HR	95% CI		*p*-value	HR	95% CI		*p*-value
		Lower	Upper			Lower	Upper	
Acute myocardial infarction	1.31	1.04	1.64	0.02	1.19	0.95	1.50	0.14
Congestive heart failure	0.75	0.39	1.44	0.38				
Peripheral vascular disease	1.19	1.13	1.25	<0.01	1.14	1.08	1.20	<0.01
Cerebrovascular disease	1.00	0.82	1.21	0.98				
Dementia	1.23	0.95	1.59	0.11				
Pulmonary disease	1.23	1.17	1.28	<0.01	1.20	1.15	1.26	<0.01
Connective tissue disorder	1.31	1.04	1.64	0.02	1.25	0.99	1.56	0.06
Peptic ulcer	1.23	1.12	1.35	<0.01	1.20	1.09	1.31	<0.01
Liver disease	1.13	0.94	1.35	0.20				
Diabetes	1.24	1.19	1.30	<0.01	1.15	1.10	1.21	<0.01
Diabetes complications	1.33	1.24	1.42	<0.01	1.17	1.08	1.26	<0.01
Hemiplegia	1.38	0.93	2.02	0.10				
Renal disease	0.87	0.56	1.37	0.54				
Cancer	1.12	1.02	1.22	0.02	1.06	0.97	1.17	0.22
Metastatic cancer	0.41	0.06	2.91	0.37				
Severe liver disease	1.03	0.79	1.33	0.85				
HIV	0.81	0.11	5.74	0.83				

HR : hazard ratio, CI : confidence interval, HIV : human immunodeficiency virus

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DISCUSSION

Reoperation for LDD

The reasons for LDD reoperation are surgery-related complications, worsening of surgical site, and adjacent segment degeneration (ASD). In previous studies, reoperation rates differed for each disease. The reported reoperation rates based on the disease were more than 20% in lumbar spondylolisthesis, 15–20% in lumbar stenosis, and less than 10% in lumbar disc herniation[10,12,14,19,20]. Generally, the reoperation rate was reportedly approximately 13% in patients with LDD over a 6-year period; reoperation rate for LDD was 13.2% over an 8-year period in the present study.

Risk factors for reoperation in LDD

The risk factors for various reoperations have been reported in previous studies and include preexisting spinal stenosis, diabetes, fusion of two or more levels, blood loss, non-fusion surgery, decompression alone, preoperative scoliotic wedging/listhesis, use of antidepressants, no neurogenic claudication, higher body mass index (BMI), greater disc height, sex (male), facet degeneration, ASD, and Pfirrmann grading for disc degeneration[5,6,10,12,14,20,24].

In the present study, the reoperation rate for LDD was 1.32 times higher in males than in females. Sato et al.[20] suggested that male sex was the greatest independent risk factor for adjacent segmental disease in reoperation for degenerative spondylolisthesis. However, this result was inconsistent in other studies. The effects of sex on higher reoperation rates for LDD is not clearly understood. Assumedly, life activities associated with men's occupations cause theoretically increasing the risk of reoperation.

Surgical methods were also associated with reoperation rate. In the present study, the rate of reoperation for LDD was 1.21 times higher in discectomy and 1.38 times higher in decompression than in fusion. In previous studies, the difference in reoperation rate between decompression alone and decompression with fusion for LDD was controversial[4,5,20]. Decompression and discectomy are likely to increase the reoperation at the surgical site, and decompression with fusion is expected to increase reoperation for ASD.

Aging is a main risk factor for intervertebral disc degeneration (IDD)[2]. In previous studies, age was not always statistically significant as a risk factor for reoperation after lumbar surgery[6,24]. The reason may be because the shorter the observation period, the less effect of age, and the longer the observation period, the greater the likelihood of reoperation due to deterioration of degenerative change.

Comorbidities for reoperation in LDD

The comorbidity measures showed a significant relationship with increased risk of reoperation after total hip replacement[11]. In a study on the association between reoperation and comorbidity in LDD, only diabetes was evaluated[14]. The present study showed there was a significant relationship with increased risk of reoperation based on increased CCI scores, indicating a higher comorbidity burden measured using the CCI is associated with increased reoperation rate for LDD.

Peripheral vascular disease

The present study results showed LDD reoperation increased 1.14 times in patients with peripheral vascular disease; research on this relationship has not previously been conducted. Dyslipidemia is a risk factor for the development of atherosclerosis and causes other atherosclerotic diseases. Zhang et al.[23], found dyslipidemia was positively correlated with the development of L-HIVD and IDD via atherosclerosis or inflammatory pathways. We hypothesize peripheral vascular disease associated with dyslipidemia, atherosclerosis, or inflammation pathways aggravate LDD and lead to an increase in reoperation rate.

Pulmonary disease

The study results showed a 1.20-fold increase in the reoperation for LDD in patients with lung disease. The association between lung disease and LDD has not been researched to date. Under adverse microenvironments such as hypoxia, intervertebral disc stem/progenitor cells undergo excessive cell death, which is the major reason for IDD[18]. Chronic obstructive pulmonary disease is associated with the imbalance of oxidants/antioxidants due to exogenous reactive oxygen species[3]. Oxidative stress, such as excessive reactive oxygen species, contributes to the progression of IDD[22]. Chronic inflammation and oxygen stress associated with lung disease may increase the rate of reoperation by accelerating the progression of LDD.

Peptic ulcer

The study results showed a 1.19-fold increase in reoperation for LDD in patients with peptic ulcer. The association between peptic ulcer and LDD has not been researched to date. El Shahawy et al.[7] reported that vitamin D deficiency may be considered a risk factor associated with eradication failure of *Helicobacter pylori* infection. Huang et al.[13] suggested that vitamin D retarded IDD. Possibly, the results indicate a relationship between peptic ulcer and IDD. However, there is no research on this, and further research will be needed.

Diabetes and diabetes complications

In the present study, reoperation rate for LDD in patients with diabetes and diabetes complications increased 1.15 and 1.17 times, respectively. Fabiane et al.[8] reported that increased BMI associated with type 2 diabetes influences LDD. Kim et al.[14] reported the reoperation rate was higher in diabetic patients after lumbar decompression surgery. The strong laboratory evidence implicate diabetes as a distinct contributing factor for IDD[1]. The results indicate diabetes is associated with aggravation and reoperation for LDD as shown in this study.

Spinal degeneration and reoperation

Risk factors for LDD reoperation may be associated with factors for spinal degeneration. In previous studies, a major cause of LDD reoperation was a preexisting and natural history of spine degenerative disease[6,19,24]. Therefore, the reoperation for LDD in the long term observation period is likely associated with risk factors for IDD. The associated factors for IDD have been reported as specific key genes, older age, obesity, BMI, smoking, diabetes, atherosclerosis, dyslipidemia, oxidative stress, inflammation, endplate defect, bone mineral density, occupation, and sporting activities[9,17,22]. Therefore, the long-term study of risk factors for LDD reoperation should be complemented with investigation of factors associated with spinal degeneration.

Strengths and Limitations

The claims data of the HIRA national database are useful for the generalization of the population due to representativeness of the total patient population in South Korea. Despite this strength, the present study had several limitations. First, the accuracy of diagnosis has been an issue due to the nature of claims data which are collected with the purpose of reimbursing healthcare services and not for clinical purposes[16]. The fee-for-service system may contribute to the high incidence of comorbidities because the presence of any comorbidity must be listed when submitting claims to HIRA for insurance-covered medical fees[14]. Second, data were insufficient to clarify the causes of reoperation for LDD such as complications of primary operation, recurrence of index level, and deteriorated degeneration at other levels. However, despite these limitations, this study provides additional information on reoperation for LDD that was not shown in previous studies.

CONCLUSION

The results from the present study indicate the reoperation rate for LDD is associated with patient comorbidities. The comorbidities identified in this study could be helpful in future LDD studies.

CONFLICTS OF INTEREST

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

INFORMED CONSENT

This type of study does not require informed consent.

AUTHOR CONTRIBUTIONS

Conceptualization : HKP
Data curation : PHL
Formal analysis : SYP
Funding acquisition : HKP
Methodology : SYP, HKP
Project administration : HKP
Visualization : SYP, HKP
Writing - original draft : HKP
Writing - review & editing : HRP, SQP, SJC, JCC

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