Influence of osteoporosis following spine surgery on reoperation, readmission, and economic costs : an 8-year nationwide population-based study in Korea

Chang Kyu Lee

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Keung Nyun Kim

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Chang Kyu Lee

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This certifies that the Doctoral Dissertation of
Chang Kyu Lee is approved.

Thesis Supervisor: Keung Nyun Kim

Thesis Committee Member#1: Yoon Ha

Thesis Committee Member#2:Seung-Hwan Yoon

Thesis Committee Member#3: Sang Chul Lee

Thesis Committee Member#4: Sang Kyum Kim

The Graduate School
Yonsei University

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ABSTRACT

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With the rising incidences of degenerative spine diseases and osteoporosis among the aging population, concerns about spine surgery for older patients with osteoporosis have multiplied. Osteoporosis is associated with increased rate of fracture, nonunion, and instrumentation failure resulting from decreased bone mineral density (BMD). It is exceedingly important to prevent these complications that can lead to increased morbidity and mortality in patients. This study aimed to evaluate the relationship between prevalence of osteoporosis and risk factors, medical costs, reoperation, and readmission in patients who have undergone spine surgery, thus attempting to investigate the effects of osteoporosis using a large national sample. Data for this study were drawn from the Korean National Health Insurance Service (KNHIS) database, which contained data on 1 million nationals who were

randomly recruited and nationally represented the entire Korean population. Patients who underwent spine surgery with thoracic or lumbar spine diseases and who were over 50 years between 2005 and 2008 were selected from the KNHIS database for the analysis. The weighting method was used to analyze the data on the entire Korean population that underwent spine surgery during the sample period. From this, 147,676 patients were selected and divided into two groups (Osteoporosis and non-Osteoporosis) and their progress was followed for 5-8 years. Based on the linear regression and multiple Cox regression analyses, in the postoperative 3 months, 12 months, and the whole follow-up period, respectively, patients with osteoporosis showed significant increase in the rate of readmission with or without spine-related issues. (all readmission; OR, 1.16, 1.20, and 1.46, respectively; $p<0.001$) (spine disease related readmission; OR, 1.07, 1.08, and 1.26, respectively; $p<0.001$) Osteoporosis was found to be significantly associated with longer hospital stays and increased medical costs regardless of the cause of spine disease. In spine related readmission, there was a 62-day difference in hospitalization time and a 2,327,262 KRW difference in medical costs between the osteoporosis(OsP) group and the non-osteoporosis group. Total medical costs of the OsP group were more than that of the non-OsP group by 800 billion KRW (about $800 million), and 310 billion KRW (about $310 million) in spine disease related cases. Osteoporosis increased the risk of reoperation in spine surgery, particularly fusion surgery. Moderate to severe osteoporosis was significantly associated with higher reoperation rate,

especially in first 3 years. Among osteoporosis patients, taking anti-osteoporotic medication decreased reoperation rate by 5%.

Osteoporosis was significantly associated with readmission, hospitalization, and medical costs during the 5-8 years follow-up. It also increased the risk of reoperation in patients who underwent spine surgery, particularly fusion surgery. Severity of osteoporosis and use of anti-osteoporotic medication was associated with lowering the reoperation risk for the first 2-3 years. Therefore, proper management of osteoporosis is essential if considering spine surgery, particularly fusion surgery. Moreover, reducing the socioeconomic burden of such patients must be considered to provide greater relief.

Keywords: osteoporosis; spinal surgery; readmission; reoperation; medical cost; socioeconomic burden

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I. INTRODUCTION

Osteoporosis is a skeletal disorder characterized by reduced bone mass and disruption of bone microarchitecture, resulting in increased bone fragility and higher fracture risk.[1] Bone strength depends on the density and quality of bone, which reduces with age or with hormonal changes; it is closely associated with fragility fractures, which commonly occur in the spine, wrist, or hip.[2] The conceptual definition of osteoporosis links the high risk of postmenopausal fractures to low bone mineral density (BMD) and qualitative changes in microarchitecture.[3] The prevalence of osteoporosis varies depending on whether it is defined by fracture incidence or by low BMD (a T score of –2.5 or less).[4] Osteoporosis and associated fractures are primary causes of mortality and morbidity in geriatric populations.[5] Osteoporosis is particularly prevalent in older women, as over 15% of women over 50 and 50% over 85 years are

estimated to have decreased bone density. It has been estimated that more than 200 million people suffer from osteoporosis over the world. Among them, 27.5 million are in Europe and at least 10 million are in the United States.[2,6,7] Osteoporosis and related fragility fractures have a serious impact on people's health and quality of life because they can result in chronic pain, morbidity, and mortality.[8,9] Hip fractures can result in poor quality of life, a dependent living situation, and increased risk of death.[10] Spine fractures are also related with an increased risk of death; they are strong predictors of future fractures and may result in chronic pain, kyphosis, and loss of self-esteem.[4]

Korea is one among the most rapidly aging countries in the world, with the proportion of older people expected to increase to 24.4% (11.7 million) by 2030 and approach 38.8% (15.6 million) in 2050.[11] In the Survey of the Living Condition and Welfare Needs of Korean Older Persons 2014, the prevalence of osteoporosis was found to be 14%, and this disease was ranked sixth among chronic diseases. According to the Health Insurance Review and Assessment Service, the number of patients with osteoporosis increased by 44.3% and osteoporosis medical costs increased by 35% in 2011 compared with the rates in 2007.[12] When the population was classified by age group, osteoporosis incidence rate was found to be 33.1% for patients in their 50s, 41.2% for those in their 60s, and 75.2% for those in their 70s.[13] The number of patients with osteoporosis in Korea is expected to increase continuously, thereby increasing the social and economic burden of osteoporosis in the future.[14] Osteoporotic fractures are known to be the major cause of physical disability and death in the elderly. In Sweden, the cost of hospitalization for osteoporotic fractures in men aged > 50 years was reportedly higher than that for prostate cancer.[15] Additionally, in EU, the overall annual cost of osteoporotic fractures was estimated to be € 37 billion,[6] and in Germany, osteoporotic fractures accounted

for 2.1% (€ 3.3 billion) of the total health care expenditure in 2005.[16]

The yearly medical expenses in spine care in the United States were estimated to be more than $85 billion in 2006 and rising.[17] Surgical complications are an increasing portion of the reducible costs associated with spine surgery.[18] A 30-day readmission cost of $17 billion in 2008 has been identified by the Centers for Medicare and Medicaid Service (CMS) as a target for cost reduction.[19] The United States has therefore conducted research to reduce medical costs using a large sample dataset. Osteoporosis and degenerative spine disease are both serious health problems associated with aging in Korea. With the rising incidences of degenerative spine diseases and osteoporosis in the aging population, concerns about spine surgery for older patients with osteoporosis have multiplied. Osteoporosis is associated with spine-related problems, such as increasing rate of vertebral fracture, nonunion, and instrumentation failure, due to decreased bone mineral density (BMD). Furthermore, elderly patients with osteoporosis show a predisposition to develop progressive spinal deformities and potential neurological compromise, a matter of major concern before performing spine surgery.[20] It is exceedingly important to prevent complications that can result in increased morbidity and mortality in patients. Thus, several studies have suggested how osteoporosis would produce negative outcomes after spine surgery. However, no studies were ever conducted using big data analytics on the effects of osteoporosis on patients who have undergone spine surgery. Therefore, this study aimed to evaluate the relationship between prevalence of osteoporosis and risk factors, medical costs, reoperation, and readmission in patients who have undergone spine surgery and investigate the effects of osteoporosis based on a large national sample.

II. MATERIALS AND METHODS

1. Database

Data were drawn from the Korean National Health Insurance Service (KNHIS) database from 2002 to 2013 on 1 million nationals who were randomly recruited and nationally represented the entire Korean population. In Korea, almost everyone is obligated to enroll in the KNHIS. Nearly 97% of the Korean population is covered by the mandatory health insurance system, and the remaining 3% are covered under Medicaid, a separate program for the poor. After the sample was stratified into 1,476 levels by sex, age, and income, a cohort of 1 million was extracted by the stratified sampling method. Therefore, the KNHIS DB provides the representative nature of the Korean population, with non-sampling error, and accuracy. Using the Korean statistical information service, the entire Korean population was adjusted based on the annual ratio of age and sex by the weighting method. From the KNHIS dataset of 2.8 trillion Korean nationals, information about 2.6 billion is available from the sampling database (DB). The entire database contains smaller databases with information on qualification, DB, medical check-up, and medical care institutions. The Qualification DB provides personally identifiable information; treatment DB includes all information about treatment (statement details [20T], medical details [30T], diagnosis details [40T], and prescription details [60T]). It also includes information about diagnostic codes, procedures, prescription drugs, personal patient information, hospital information, and medical costs. The KNHIS uses the Korean Standard Classification of Diseases (KCD), which was modified from the International Classification of Diseases (ICD). Using all the DBs, particularly those of qualification and treatment, information about the

category of patients we require for this study can be extracted by merging each DB variable.

2. Patient selection

From the KNHIS database, patients over the age of 50 between 2005 and 2008 who underwent surgery with thoracic or lumbar spine diseases were selected for analysis. Patients who underwent a previous spine surgery and were in the wash-out period were excluded from the study. Next, the entire Korean population that underwent spine surgery during that period was estimated by the weighting method. Bill numbers of patients who underwent spinal surgery were extracted from the medical details DB. This was linked with the statement details DB to obtain serial numbers, which substituted the patients' identification numbers. The serial numbers obtained were interconnected with the qualification DB, and a dataset with age (more than 50 years old) and duration (from 2005 to 2008) information was created. The production DB was interworked with the statement details DB, securing all the bill numbers of the subjects from 2002 to 2013. Reoperation information was obtained from the medical details DB, comorbidities from the diagnosis details DB, drug prescription from the prescription details DB, and all medical costs and hospital stays from the statement details DB, organizing the final DB. Finally, 147,676 patients (26,315 for 2005; 33,827 for 2006; 40,654 for 2007; and 46,879 for 2008) were selected, divided into two groups (Osteoporosis and non-Osteoporosis), and followed up for 5-8 years. In the osteoporosis group (OsP), patients were divided by surgical methods (decompression only surgery as Group 1 vs. fusion surgery as Group 2), osteoporosis severity (mild vs. moderate to severe), and use of anti-osteoporosis medication.

3. Variables

Variables included spine surgery of thoracic or lumbar regions (N1492, N1493, N1494, N1498, N 2498, N2499, N0444, N0445, N0446, N0447, N0452, N0453, N0466, N0468, N0469, N1460, N1466, N1469, N2470, N0471, N0472, N0473, and N0474, which include surgeries such as laminectomy, diskectomy, endoscopic diskectomy, corpectomy, interbody fusion with or without screw fixation, vertebroplasty, and kyphoplasty), osteoporosis (determined by the KCD code M80-82 or drug code for osteoporosis), reoperation (determined by the operation code for spine surgery and N2471, N2472, S4722, S5761, SB021, SB022, SB023, SB024, SB025, SB026, SC021, SC022, SC023, SC024, SC025, SC026, and SC027, encompassing surgeries such as removal of fixation implant, cerebrospinal fluid leakage repair, abscess drainage, and wound debridement), household income (<30, 30-60, 60-90, and >90% of the median as low, middle, high, and top classes, respectively), and residential area classified into three regions (Seoul, considered a special metropolitan area in Korea; large city, a metropolitan area with a population of over 1 million; and small city or rural area). Decompression-only surgeries were laminectomy, diskectomy, and endoscopic diskectomy. Fusion surgeries were anterior or posterior interbody fusion, corpectomy, and screw fixation. Osteoporosis was defined as “diagnosed osteoporosis” (when the diagnosis was “osteoporosis” in the diagnosis details DB) or when the subject took anti-osteoporotic medication (there were reports of anti-osteoporotic medication on 20T, 30T, or 60T) at the time of or before the operation. Anti-osteoporotic medications were calcium, vitamin D, bisphosphonates (BP), calcitonin, vitamin K2, and selective estrogen receptor modulators (SERM). Other confounding factors were hypertension (HTN) (determined by the KCD codes I10-15 and drug code for hypertension), diabetes

mellitus (DM) (determined by the KCD codes E10-14 and drug code for DM), cardiovascular disease (CVD) (determined by the KCD codes I20-25), chronic kidney disease (CKD) (determined by the KCD code N18), and cerebrovascular disease (CbVD) (determined by the KCD codes I60-69). Medical cost, as total healthcare expenditure, was calculated as the sum of costs, including outpatient clinics, pain clinics, pain medication, hospital admission, etc., for the 5-8-year follow-up period. Readmission was defined as "admission" at general or university hospital after spinal surgery, but not at personal clinic or sanatorium. Readmission for spine-disease related issue implied that the diagnosis code related to spine disorder exists only in the first or second order in 40T, and readmission for other causes implies that the diagnosis code related to spine disorder exists regardless of the order. Hospitalization time was calculated as the sum of hospital admission days. Reoperation and readmission rates were obtained at 3 months, 12 months, and all periods. Osteoporosis severity was considered "mild" or "moderate to severe" based on the kind of anti-osteoporotic medication. "Mild" condition of osteoporosis was when patients take calcium or vitamin D, and "moderate to severe" was when they take SERM or BP.

4. Statistical analysis

Pearson's chi-square tests were performed to examine the differences between (a) the Osteoporosis (OsP) and non-Osteoporosis groups, (b) decompression-only and fusion operation by surgical methods, and (c) mild and moderate to severe based on osteoporosis severity and anti-osteoporosis medication. Comorbidities and effects of osteoporosis were used to obtain the odd ratios (ORs) and 95% confidence intervals (CIs) by performing univariate and

multivariate Cox regression analyses. The overall survival rates were calculated using Kaplan-Meier curves. All reported *p*-values were two-sided, and *p*-values of ≤ 0.05 were considered significant. Statistical analyses were performed on SAS system using Windows version 9.4 (SAS Inc., Cary, NC, USA).

III. RESULTS

1. Patient characteristics

After follow-up of 5-8 years, readmission rate related to spine disease was estimated at 36.2% (53,516 patients). Reoperation rate was 22.2% (32,716 patients), including 52.9% with osteoporosis (17,297 patients). The proportion of comorbidities was estimated as 16.1% in DM, 49% in HTN, 17.8% in CVD, 3.1% in CKD, and 28.3% in CbVD. Readmission rate was 14.3% (21,046 patients) at 3 months, and 18.1% (26,665 patients) at 12 months, respectively. Reoperation rate was calculated as 1.1% (1,612 patients) at 3 months, and 3.1% (4,617 patients) at 12 months (see Table 1).

Table 1. Baseline characteristics of patients

Variables	Osteoporosis	Non-osteoporosis	*p*- value
Number	82,012	65,664	
Mean ages (yrs)	63.5 ± 5.5	58.5 ± 5.5	
Sex			<0.0001
Male	18,114(22.1%)	40,897(62.3%)	
Female	63,898(77.9%)	24,766(37.7%)	
Surgery			<0.0001
Decompression-only	65,411(79.8%)	53,577(81.6%)	
Fusion	16,601(20.2%)	12,087(18.4%)	
Reoperation			<0.0001
No	64,715(78.9%)	50,245(76.5%)	
Yes	17,297(21.1%)	15,419(23.5%)	
Readmission			<0.0001
No	22,568(27.5%)	23,401(35.6%)	
Yes	59,444(72.5%)	42,263(64.4%)	
Readmission (spine)			<0.0001
No	50,330(61.4%)	43,830(66.8%)	
Yes	31,682(38.6%)	21,833(33.2%)	
DM			<0.0001
No	67,692(82.5%)	56,213(85.6%)	
Yes	14,321(17.5%)	9,450(14.4%)	
HTN			<0.0001
No	37,974(46.3%)	37,338(56.9%)	
Yes	44,038(53.7%)	28,326(43.1%)	

CVD			<0.0001
No	65,208(79.5%)	56,139(85.5%)	
Yes	16,805(20.5%)	9,524(14.5%)	
CKD			<0.0001
No	78,825(96.1%)	64,234(97.8%)	
Yes	3,187(3.9%)	1,430(2.2%)	
CbVD			<0.0001
No	55,630(67.8%)	50,217(76.5%)	
Yes	26,383(32.2%)	15,446(23.5%)	

Decompression; laminectomy, diskectomy, and endoscopic diskectomy

Fusion; anterior or posterior interbody fusion, corpectomy, and screw fixation

Readmission (spine); readmission related to spine disease

DM: diabetes mellitus

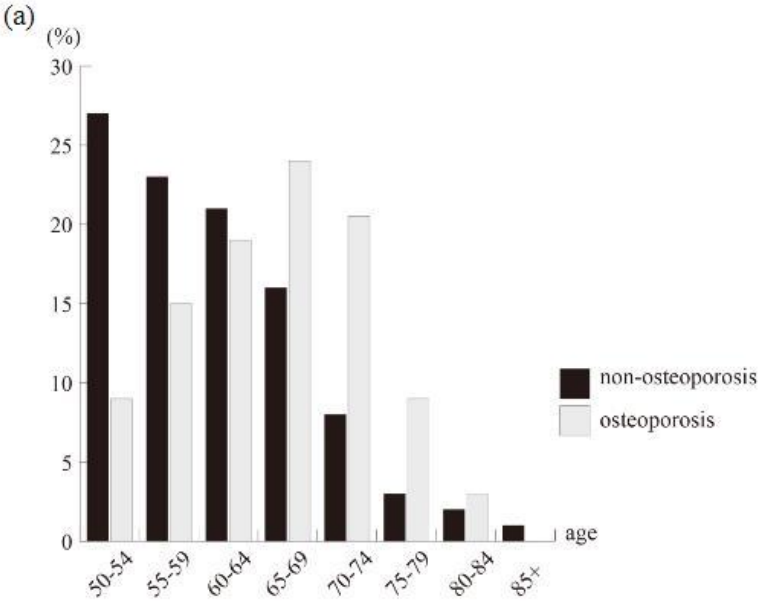
HTN: hypertension

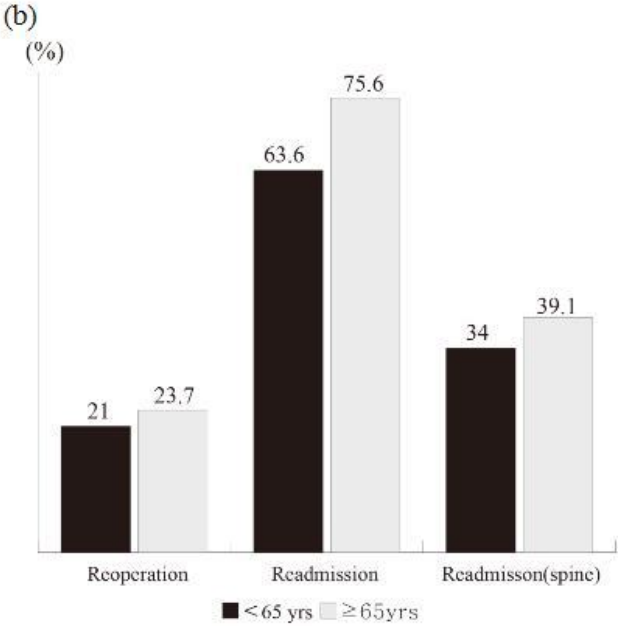
CVD: cardiovascular disease

CKD: chronic kidney disease

CbVD: cerebrovascular disease

The OsP group increased with age peaking at 65-69, and the Non-OsP group decreased with age peaking at 50-54. Patients older than 65 years old had higher rate of reoperation and readmission than those less than 65. Reoperation rate in rural area was higher than that in the urban area. However, regarding income level, a high-income earner had more reoperation and readmission related to spine disease than a low- or middle-income earner (Figure 1).





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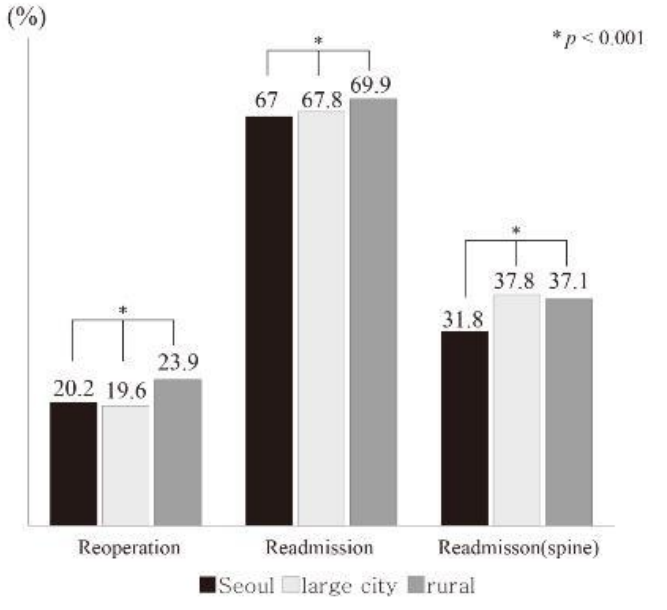

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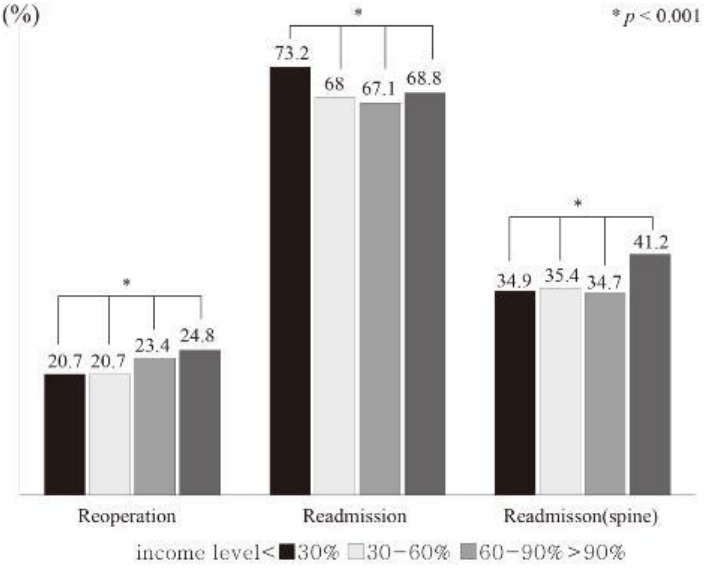


Figure 1. Patient demographic characteristics (percentages with age, residential area, and income level)

(a) proportion of osteoporosis patients by age (%)

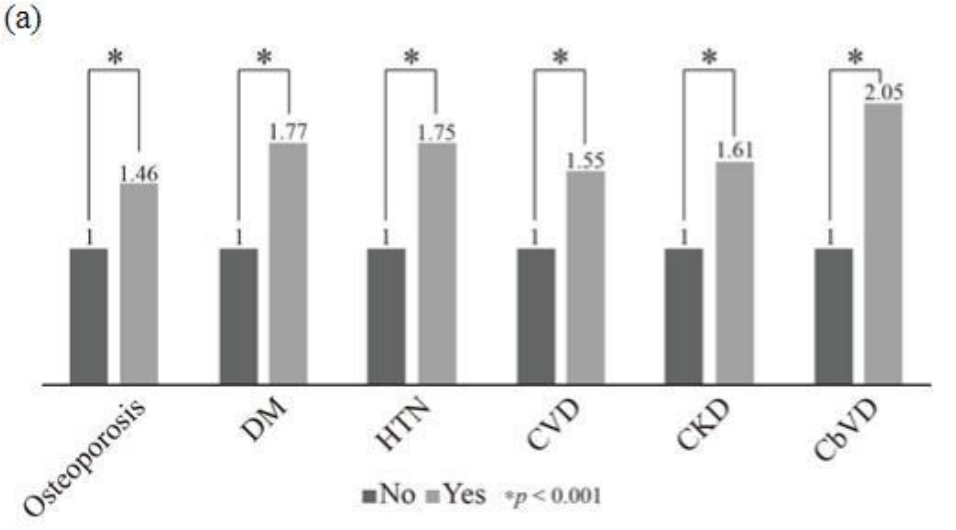
(b) reoperation and readmission rate by age (%)

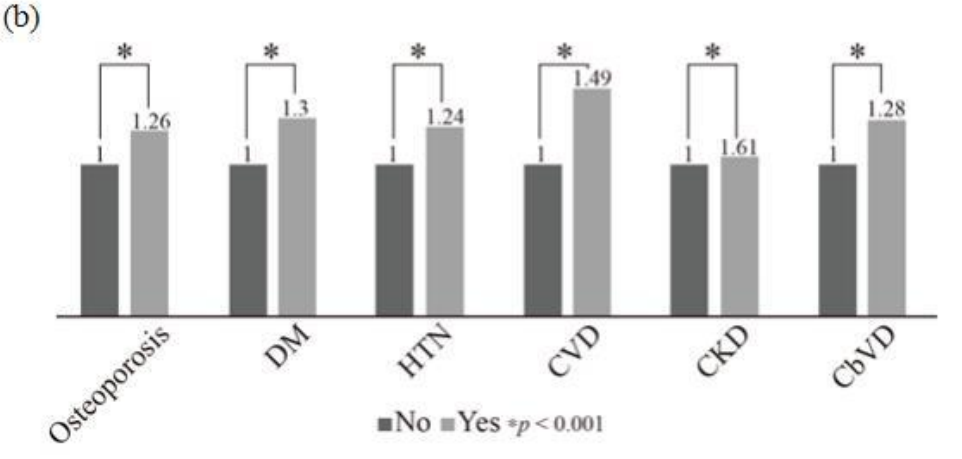
(c) reoperation and readmission rate by residential area (%)

(d) reoperation and readmission rate by income level (%)

2. Relationship between osteoporosis and readmission or reoperation by time period

Osteoporosis significantly increased the rate of readmission regardless of whether it was spine-disease related, based on the linear regression analyses, during postoperative 3 months, 12 months, and the whole follow-up period, respectively: all readmission (3, 12 months, and whole period) (OR, 1.16, 1.20, and 1.46, respectively; $p<0.001$) and spine disease related readmission (3, 12 months, and whole period) (OR, 1.07, 1.08, and 1.26, respectively; $p<0.001$). In other words, during the follow-up period, osteoporosis significantly increased readmission rate by 46% for different causes and by 26% for spine-disease related causes (see Figure 2).





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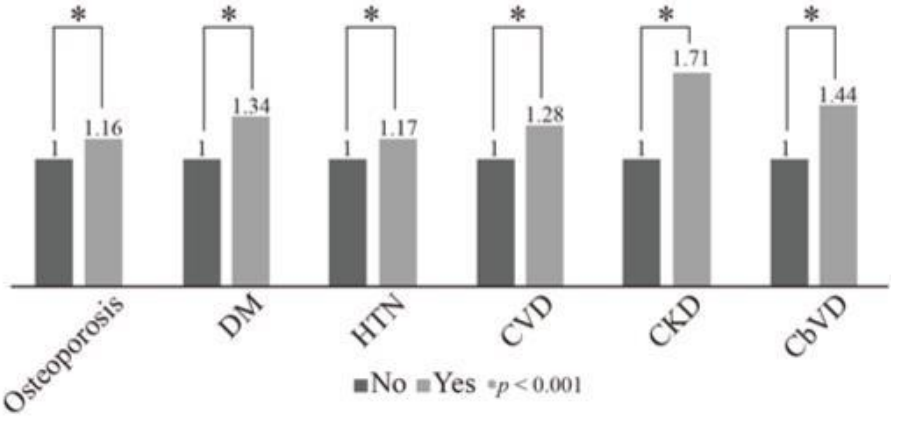

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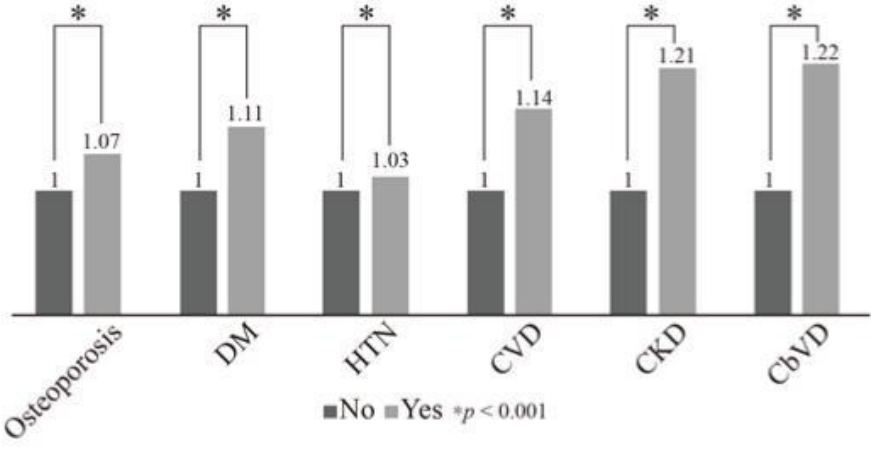

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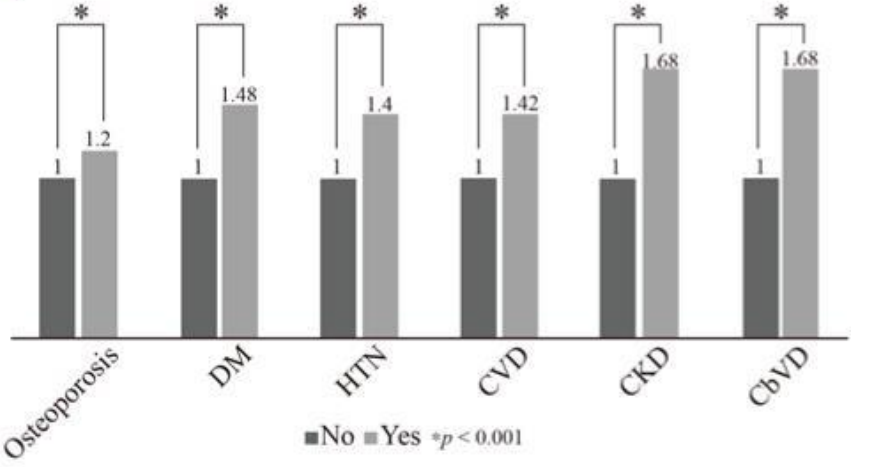

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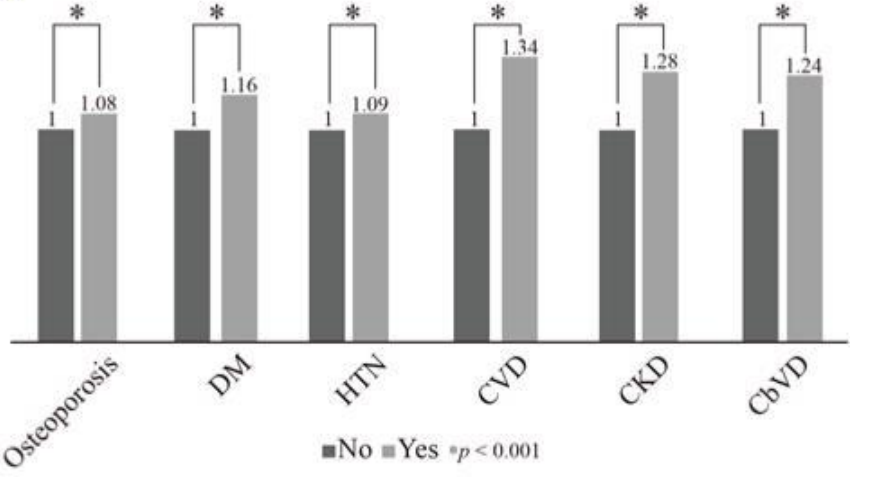


Figure 2. Hazard ratios by linear regression analysis of variables based on risk of readmission

(a) readmission (all causes) over the entire period and odds ratio

(b) readmission (spine-related) over the entire period and odds ratio

(c) readmission (all causes) in 3 months and odds ratio

(d) readmission (spine-related) in 3 months and odds ratio

(e) readmission (all causes) over 12 months and odds ratio

(f) readmission (spine-related) over 12 months and odds ratio

After adjusting age and sex, or all comorbidities, osteoporosis increased readmission by 9-10% (OR, 1.1; 95% CI, 1.07-1.13; $p<0.001$, OR, 1.09; 95% CI, 1.06-1.12; $p<0.001$, respectively) as seen by the multiple regression (Table 2).

Table 2. Multivariate Cox regression analysis of osteoporosis according to adjusting variables in readmission

Variables	**Multiple Cox regression (age/sex)**			**Multiple Cox regression (all)**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis			<0.001			<0.001
No	1	1.07-1.13		1	1.06-1.12	
Yes	1.1			1.09		
Age			<0.001			<0.001
	1	1.07-1.08		1	1.04-1.05	
	1.07			1.05		
Sex			<0.001			<0.001
Female	1	0.83-0.87		1	0.83-0.87	
Male	0.85			0.85		
DM						<0.001
No				1	1.16-1.23	
Yes				1.19		
HTN						<0.001
No				1	1.03-1.08	
Yes				1.05		
CVD						<0.001
No				1	1.3-1.38	
Yes				1.34		
CKD						0.012
No				1	0.87-0.98	
Yes				0.92		

CbVD			<0.001
No	1	1.11-1.16	
Yes	1.13		

OR: odd ratio

DM: diabetes mellitus

HTN: hypertension

CVD: cardiovascular disease

CKD: chronic kidney disease

CbVD: cerebrovascular disease

Table 3 shows that risk of reoperation showed a significant negative correlation with osteoporosis at 3, 12 months, and the entire period. Multivariate Cox regression analysis of osteoporosis showed similar results by adjusting variables, such as, age, sex, or comorbidities, for reoperation showing no association between osteoporosis and reoperation (see Table 4). However, Table 5 shows that the reoperation rate has a significantly high association with male patients, with a hazard ratio of 2.96 at 3 months (p<0.001) and 2.32 at 12 months (p<0.001) after adjusting the variables.

Table 3. Linear regression analysis of variables based on risk of reoperation by time period

Variables	**All**			**3 months**			**12 months**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis			<0.001			<0.001			<0.001
No	1	0.85-0.89		1	0.42-0.49		1	0.52-0.57	
Yes	0.87			0.45			0.54		
DM			<0.001			<0.001			<0.001
No	1	1.17-1.25		1	1.13-1.35		1	1.39-1.55	
Yes	1.21			1.23			1.47		
HTN			<0.001			0.002			<0.001
No	1	1.15-1.21		1	1.04-1.2		1	1.08-1.18	
Yes	1.18			1.12			1.13		
CVD			<0.001			<0.001			<0.001
No	1	1.15-1.23		1	1.15-1.37		1	1.42-1.58	
Yes	1.19			1.26			1.5		
CKD			0.23			<0.001			0.68
No	1	0.89-1.03		1	0.37-0.65		1	0.85-1.1	
Yes	0.96			0.49			0.97		
CbVD			<0.001			<0.001			0.67
No	1	1.18-1.24		1	0.77-0.91		1	0.96-1.06	
Yes	1.21			0.84			1.01		

OR: odd ratio

DM: diabetes mellitus

HTN: hypertension

CVD: cardiovascular disease

CKD: chronic kidney disease

CbVD: cerebrovascular disease

Table 4. Multivariate Cox regression analysis of osteoporosis based on adjusting variables for reoperation by time period

Variables	**All**			**3 months**			**12 months**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis			<0.001			<0.001			<0.001
No	1	0.85-0.89		1	0.42-0.49		1	0.52-0.57	
Yes	0.87			0.45			0.54		
Variables	**All (Multiple regression by age/sex)**			**3months (Multiple regression by age/sex)**			**12 months (Multiple regression by age/sex)**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis			0.43			<0.001			<0.001
No	1	0.98-1.04		1	0.5-0.59		1	0.66-0.74	
Yes	1.01			0.54			0.7		
Variables	**All (Multiple regression by all)**			**3 months (Multiple regression by all)**			**12 months (Multiple regression by all)**		
	*OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis						<0.001			<0.001
No	1	0.98-1.04	0.71	1	0.5-0.6		1	0.65-0.73	
Yes	1.01			0.55			0.69		

OR: odd ratio

Table 5. Multivariate Cox regression analysis of osteoporosis based on adjusting variables for reoperation

Variables	**Multiple Cox regression (adjusting age/sex)**			**Multiple Cox regression (adjusting all factors)**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis			0.43			0.71
No	1	0.98-1.04		1	0.98-1.04	
Yes	1.01			1.01		
Age			<0.001			0.04
	1.03	1.02-1.04		1.01	1.0-1.02	
Sex			<0.001			<0.001
Female	1	1.52-1.61		1	1.53-1.62	
Male	1.56			1.57		
DM						<0.001
No				1	1.09-1.17	
Yes				1.13		
HTN						<0.001
No				1	1.08-1.14	
Yes				1.11		
CVD						<0.001
No				1	1.07-1.15	
Yes				1.11		
CKD						<0.001
No				1	0.82-0.94	
Yes				0.88		

CbVD			<0.001
No	1	1.12-1.19	
Yes	1.15		

OR: odd ratio

DM: diabetes mellitus

HTN: hypertension

CVD: cardiovascular disease

CKD: chronic kidney disease

CbVD: cerebrovascular disease

In all patients who underwent spine surgery, osteoporosis group (OsP) and non-osteoporosis group (non-OsP) were compared in terms of hospitalization time and medical expenses divided into all causes and spine disease related groups. There was a 175-day difference in hospitalization time between OsP and non-OsP, and medical expenses showed a difference of 6,003,268 KRW between the two groups (see Table 6). In spine related admission, there was a 62-day difference in hospitalization time and 2,327,262 KRW was the difference in medical costs between the two groups (see Table 7). Furthermore, the total medical cost related to the OsP group was 2.78 trillion KRW ($ 2.7 billion) and 800 billion KRW (in spine disease related). Total costs of OsP were more than those of Non-OsP by 800 billion KRW (about $800 million), and 310 billion KRW in spine disease related.

Table 6. Comparing hospitalization and medical expenses of the Osteoporosis group and the Non-osteoporosis group in patients who underwent spine surgery

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*-value**
OsP	81,155	557.4 (23~3414)	<0.001	25,610,667 (1,540,240~ 339,490,000)	<0.001
Non-OsP	65,099	382.2 (25~2700)		19,607,399 (1,230,020~ 364,520,000)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

Table 7. Comparing hospitalization and medical expenses of the Osteoporosis group and the Non-osteoporosis group in patients who underwent spine surgery (related to spine disease)

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*-value**
OsP	81,155	176.5 (3~2293)	<0.001	9,870,067 (37,960~ 109,600,000)	<0.001
Non-OsP	65,001	114.5 (2~1270)		7,542,805 (32,900~ 98,612,360)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

3. Relationship between osteoporosis and readmission or reoperation, by surgical method

We also investigated the association between osteoporosis and patients who have undergone spine surgery based on the type of surgery conducted. Group 1 comprised those who underwent decompression-only surgery, such as diskectomy, laminectomy, and endoscopic diskectomy. Group 2 comprised those who underwent fusion surgery, such as corpectomy, interbody fusion, fixation, and arthrodesis for spinal deformity. Table 8 and Table 9 show that osteoporosis increased the risk of readmission, regardless of the admission cause. In decompression-only surgery, osteoporosis increased readmission risk by 44% and 23% during all periods, respectively. In the fusion group, osteoporosis increased readmission rate by 54% and 42% in the follow-up period.

Table 8. Linear regression analysis of osteoporosis based on risk of readmission (Decompression-only surgery group)

Variables	**Readmission (all)**			**Readmission (related to spine disease)**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis (all)			<0.001			<0.001
No	1	1.40-1.47		1	1.2-1.26	
Yes	1.44			1.23		
Osteoporosis (3mo)			<0.001			<0.001
No	1	1.09-1.16		1	1.04-1.11	
Yes	1.12			1.08		
Osteoporosis (12mo)			<0.001			<0.001
No	1	1.15-1.22		1	1.06-1.12	
Yes	1.18			1.09		

OR: odd ratio

Table 9. Linear regression analysis of osteoporosis based on risk of readmission (Fusion surgery group)

Variables	**Readmission (all)**			**Readmission (related to spine disease)**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis (all)			<0.001			<0.001
No	1	1.46-1.62		1	1.35-1.49	
Yes	1.54			1.42		
Osteoporosis (3mo)			<0.001			0.66
No	1	1.21-1.37		1	0.95-1.08	
Yes	1.29			1.01		
Osteoporosis (12mo)			<0.001			0.32
No	1	1.18-1.31		1	0.97-1.09	
Yes	1.24			1.03		

OR: odd ratio

Interestingly, patients with osteoporosis showed a 1.22 times higher risk of reoperation in Group 2, which is related to fusion surgery, and 1.34 times higher in the first 3 months (Table 10). Osteoporosis had a definite influence on fusion surgery, resulting in hardware failure, pseudo-arthrosis, and wound problems. In Group 1, osteoporosis was associated with a high risk of readmission and a low

reoperation rate. Osteoporosis was not found to be related to mortality based on the surgical methods adopted, as per the Kaplan-Meier method (see Figure 3). Furthermore, type of surgery done on osteoporosis group was also not related to survival or mortality, as per the Kaplan-Meier curve (Figure 4).

Table 10. Linear regression analysis of osteoporosis based on surgical method, for reoperation

Variables	**Decompression-only surgery gorup**			**Fusion surgery group**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Osteoporosis (all)			<0.001			<0.001
No	1	0.8-0.85		1	1.15-1.3	
Yes	0.82			1.22		
Osteoporosis (3mo)			<0.001			0.004
No	1	0.34-0.4		1	1.1-1.63	
Yes	0.37			1.34		
Osteoporosis (12mo)			<0.001			0.24
No	1	0.46-0.5		1	0.95-1.2	
Yes	0.48			1.07		

OR: odd ratio

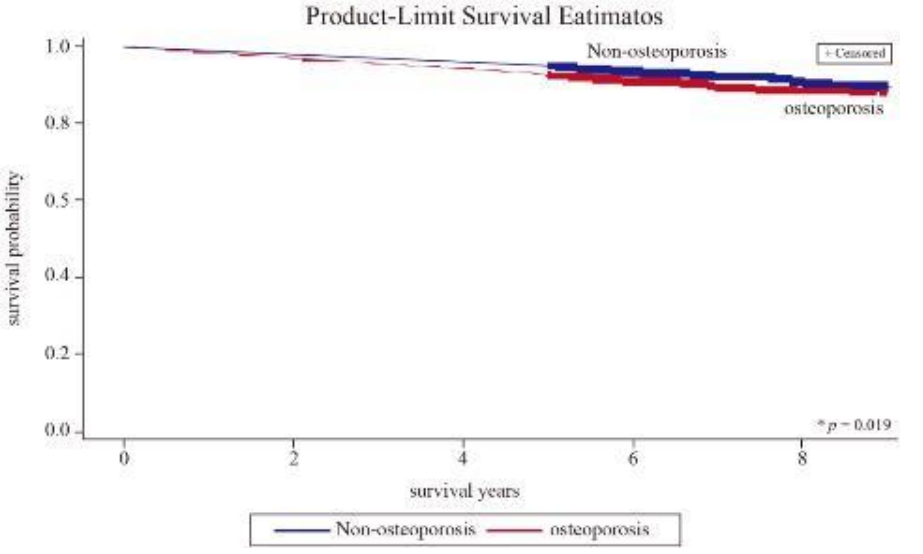
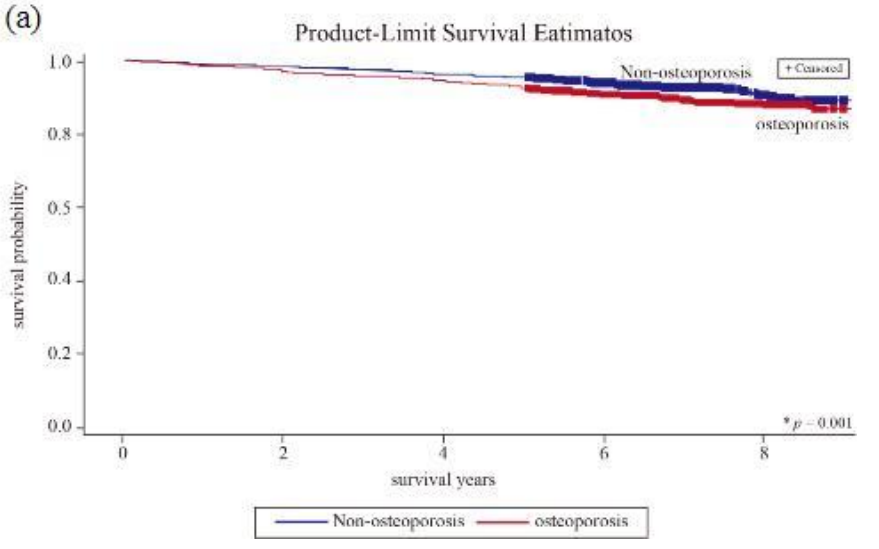


Figure 3. Comparison of mortality based on osteoporosis, by the Kaplan-Meier curve



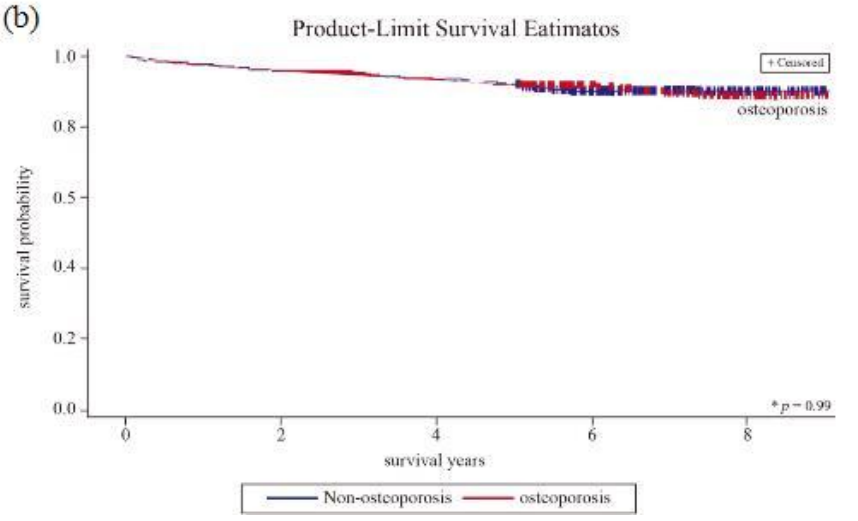


Figure 4. Comparison of mortality based on osteoporosis and the surgical method, by the Kaplan-Meier curve

(a) Group 1 (Decompression-only surgery group)

(b) Group 2 (Fusion surgery group)

In the same manner, based on the type of surgery, OsP and non-OsP were compared by hospitalization and medical expenses. Osteoporosis was significantly associated with longer hospital stays and more medical costs regardless of the disease that led to hospitalization (hospitalization was 94.1 days and 27.3 days, and medical expenses were 3,801,757 KRW and 1,239,474 KRW, respectively, for OsP and non-OsP in Group 1, $p<0.001$; hospitalization was 166.9 days and 70 days, and medical expense was 6,620,845 KRW and 3,015,132 KRW for OsP and non-OsP, respectively, in Group 2, $p<0.001$).

Total medical cost of OsP in Group 1 was overall 1.25 trillion KRW (about $ 1.2 billion) among which 450 billion KRW was for those with spine-related issues. The total medical cost differences between OsP and non-OsP in Group 1

were 426 billion KRW and 150 billion KRW, respectively (see Tables 11 and 12). In Group 2, total cost of OsP was 490 billion KRW, of which, 224 billion KRW was for those with spine-related diseases. The total cost gap between the OsP and the non-OsP was 210 billion KRW and 98 billion KRW, respectively, in Group 2 (see Tables 13 and 14).

Table 11. Comparing hospitalization and medical expenses of the osteoporosis and the non-osteoporosis patients who underwent decompression-only surgery

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*-value**
OsP	64,718	349.5 (9~3022)	<0.001	19,296,974 (1,324,150~ 231,320,000)	<0.001
Non-OsP	53,109	255.4 (11~2363)		15,495,217 (1,173,260~ 326,490,000)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

Table 12. Comparing hospitalization and medical expenses of the osteoporosis and non-osteoporosis patients who underwent decompression-only surgery (related to spine disease)

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*- value**
OsP	64,528	101 (4~1437)	<0.001	7,044,402 (214,170~ 101,790,000)	<0.001
Non-OsP	52,920	73.7 (2~1051)		5,804,928 (79,410~ 97,739,560)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

Table 13. Comparing hospitalization and medical expenses of the osteoporosis and non-osteoporosis patients who underwent fusion surgery

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*-value**
OsP	16,437	577.9 (53~2973)	<0.001	30,019,261 (4,870,060~ 279,840,000)	<0.001
Non-OsP	11,990	411 (49~1775)		23,398,416 (5,580,990~ 160,490,000)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

Table 14. Comparing hospitalization and medical expenses of the osteoporosis and non-osteoporosis patients who underwent fusion surgery (related to spine disease)

	Number	**Hospitalization (mean days) (min~max)**	***p*-value**	**Medical expense (average KRW) (min~max)**	***p*-value**
OsP	16,437	195 (3~1270)	<0.001	13,619,958 (77,120~ 109,600,000)	<0.001
Non-OsP	11,892	125 (8~1232)		10,604,826 (490,480~ 60,038,130)	

OsP: osteoporosis group

Non-OsP: non-osteoporosis group

Table 15 shows that reoperation average was 2.13, and the types of reoperation were wound revision, decompression surgery, fusion surgery, and so on, in order of frequency.

Table 15. Frequency and types of reoperation

op	Mean	SD	Total
Reoperation	2.13	± 1.93	68,918
Decompression	0.73	± 1.08	23,709 (34.4%)
Fusion	0.43	± 0.92	13,922 (20.2%)
Screw removal	0.05	± 0.27	1,651 (2.4%)
CSF repair	0.01	± 0.13	360 (0.5%)
Wound revision	0.9	± 1.26	29,143 (42.3%)

SD: standard deviation

CSF: cerebrospinal fluid

4. Relationship between osteoporosis and readmission or reoperation based on severity of osteoporosis and use of anti-osteoporotic medication

We compared severity of osteoporosis based on use of anti-osteoporotic medication prescribed. The number of mild osteoporosis patients were estimated at 6,200, while those with moderate to severe osteoporosis were estimated at 21,828. Among them, patients who underwent reoperation were overall 1,411 (5%) among those with "mild" and 4,313 (15.4%) among those with "moderate to severe" osteoporosis. Patients who had to be readmitted with spine diseases were overall 2,487 (8.9%) among those with mild osteoporosis and 8,417 (30%) among those with moderate to severe condition. Figure 5 shows the cumulative results of the reoperation rate based on osteoporosis severity. In "moderate to severe" osteoporosis, reoperation rate was higher than that for the "mild" condition for the first three years (21.3% vs. 3.4% in 1 year, 41.8% vs. 19.5% in 2 years, and 55% vs. 43.1% in 3 years, respectively). This result is similar to the finding that patients who underwent fusion surgery and who had osteoporosis were associated with a higher reoperation rate. Readmission rate among the moderate to severe group was higher than that for the mild condition for the first two years (19.3% vs. 16% in 1 year, and 23.6% vs. 19.7% in 2 years, respectively).

Many osteoporosis patients who did not take anti-osteoporotic medication were also estimated. Patients who were diagnosed with osteoporosis, but did not take medication were 53,845 (66.3%). Patients who took anti-osteoporotic medication and underwent reoperation were 5,677 (7%), while those who did not take the medication were 11,620 (14.3%). Comparing the two, those who took anti-osteoporotic medication showed a lower reoperation rate by 5% odds

ratio, which was statistically significant (OR, 0.95; 95% CI, 0.92-0.99; p=0.007) Figure 6 shows osteoporosis patients who took anti-osteoporotic medication and had lower reoperation rate than those who took no medication for the first two years. (17% vs. 19.4% in the first year, and 36.6% vs. 38.4% in 2 years, respectively)

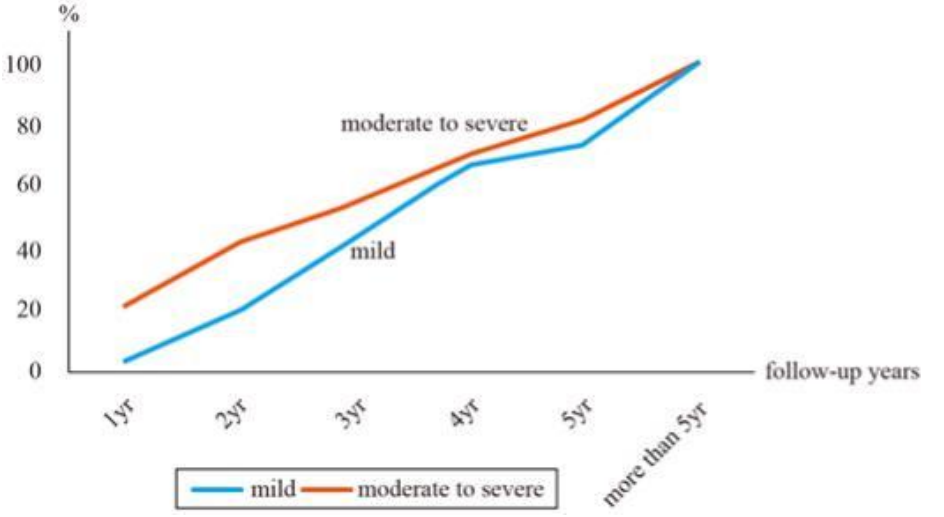


Figure 5. Cumulative effects of reoperation rate based on osteoporosis severity

mild (blue line): patients with mild osteoporosis who take Calcium or Vitamin D

moderate to severe (red line): patients with moderate to severe osteoporosis who take selective estrogen receptor modulator (SERM) or bisphosphonates (BP)

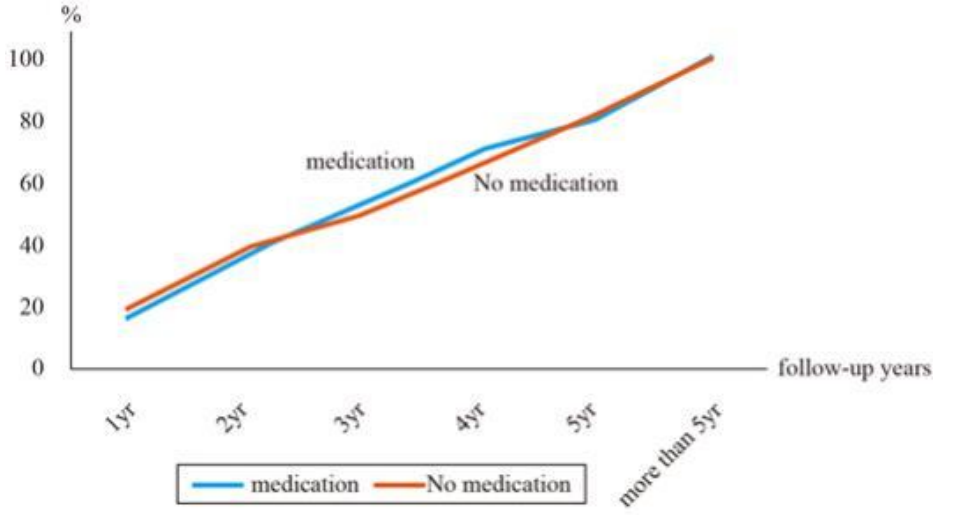


Figure 6. Cumulative effects of reoperation rate based on use of anti-osteoporosis medication

blue line (Yes) - patients diagnosed with osteoporosis who took anti-osteoporotic medication

red line (No) - patients diagnosed with osteoporosis, but did not take anti-osteoporotic medication

IV. DISCUSSION

Big data analyses were performed using information from the Korean national database on osteoporosis and spine surgery. The results are valuable since it helps in understanding the characteristics of Korean nationals. This nationwide study is the first major study in Korea to demonstrate the relationship between osteoporosis and spinal surgery in terms of readmission, reoperation, and the economic costs involved. There is a rising trend in the number of elderly

patients requiring spinal surgery and in the prevalence of osteoporosis among the elderly. In the current data, from 2002 to 2013, the number of spine operations increased by 3 times, and by more than 4 times among those over 50 years. In Korea, the prevalence of osteoporosis in the lumbar spine among women was 33% in the 50-59 age group, 62% in the 60-69 group, and 89% in the 70-79 age group, respectively.[21] Prevalence of osteoporosis in those over 50 years and who underwent spinal surgery was 14.5% among males and 51.3% among female, respectively.[22] Several reports have claimed that decompression and fusion surgeries in elderly patients with spinal stenosis and instability produced favorable outcomes because lumbar arthrodesis with spinal instrumentation led to satisfactory results in elderly patients.[23,24] Therefore, many researchers had been interested in the relationship between osteoporosis and spinal surgery, specially fusion surgery, in the past decades. Low bone quality can reduce the pull-out strength of pedicle screw, resulting in hardware failure, and negative bone remodeling can cause delayed bone fusion and pseudoarthrosis.[25,26] Many studies have demonstrated fusion failure, which can have a negative impact on clinical outcomes, and fusion rates generally ranged from 65% to 100%.[27-30] With these concerns in mind, surgeons are careful about spinal surgery on patients with osteoporosis, which can be closely connected to fusion failure, resulting in negative clinical outcomes.

In the current study, 82,012 (55.5%) patients, over 50 years, with osteoporosis underwent spinal surgery. Among the OsP, the number of female patients (77.9%) was higher than the number of male patients, but among non-OsP, male patients were predominant (62.3%). The patterns of epidemiology of osteoporosis presented in this study are consistent with findings from other countries, including the increased prevalence with age and a higher prevalence among females than among males.[6,31,32] However, the estimates of osteoporosis

patients in this study might be lower than those of other countries as diagnosis and drug codes were used in this study to identify osteoporosis patients while others used bone mineral density (BMD) readings. Moreover, anti-osteoporotic drugs like teriparatide (anabolic parathyroid hormone) or denosumab (anti-resorptive drug) were not included, because these were uninsured items at that time in Korea, and data on them was not available on the KNHIS DB, which does not deal with uninsured items. Although we may have underestimated the number of osteoporosis patients, readmission rates related to osteoporosis have shown an increase by 26%, particularly 7% in 3 months, and 9-10% after adjusting confounders for the follow-up duration. Bernatz et al.[33] report that the 30-day readmission rate following spinal surgery was between 4.2% and 7.4%. Nearly 40% of readmission was related to wound problems, mainly surgical site infection. The American Society of Anesthesiology (ASA) score, operation duration, and medicaid insurance were the risk factors statistically correlated with the increased odds of the 30-day readmission. Wadhwa et al.[34] reported that 90-day readmission was associated with higher ASA class and a history of depression, particularly in medicaid patients younger than 65 years, who were significantly more likely to be readmitted within 90 days after their index surgery. Cusimano et al.[35] reported that readmission rates varied from 2.54% to 14.7%, and risk factors of the 30-day readmission increased with age, poor physical status, and comorbid illnesses. In this study, readmission rate in 3 months was 14.3%, similar to the trend of previous reports although we could not get delicate personal information. In the KNHIS DB, which excludes a medicaid patient's information, significant correlation was seen between patients who were more than 65 years, from rural residential areas, or with higher income level to readmission. Regarding income level, readmission for all causes was higher in the low-income group, but among spine disease related patients, most were in the high-income bracket. Patients who had comorbidities,

like other medical problems, were readmitted, but among spine disease related patients, high-income earners could afford readmission. Medicaid patients also might get readmitted easily as they get aid from the government. Previous studies have examined a retrospective Medicaid cohort to evaluate the 30-day readmission rate. Wang et al.[36] demonstrated a readmission rate of 7.3% after lumbar surgery in Medicare/Medicaid patients. They were mainly for complications related to surgery and musculoskeletal conditions, and included patients from the black race, and those of older age, those with greater comorbidities, and had Medicaid eligibility. Readmission rates were estimated for the anterior approach, for fusion surgery versus decompression alone, and the number of fusion levels.

In the current study, reoperation rate was 22.2% for the entire follow-up duration, 1.1% in 3 months, and 3.1% in 12 months. Osteoporosis was apparently not associated with reoperation rate in this study. This could be because, among the Korean population, female osteoporosis patients (78%) were much more than male (22%), but male patients had 2-3 times higher reoperations than female patients. Therefore, this composition of patients would possible be an influential factor. Reoperation after spinal surgery was commonly for wound infection such as surgical site infection, wound dehiscence, hematoma, cerebrospinal fluid leak, and screw malposition, which are irrelevant to osteoporosis.[37,38] The influence of osteoporosis on the reoperation rate seems to be relevant in instrumental failure, early nonunion, pseudoarthrodesis, and progressive kyphotic deformity or progressive degeneration at the adjacent spine level. In our study, a high frequency of reoperation, in order, was wound revision (42.3%), decompression-only operation (34.4%), and fusion operation (20.2%). Wound revision covers wound infection, dehiscence, and hematoma, and decompression-only operation covers

wound infection, hematoma, and previous incomplete surgery. Previous reports had similar results as the findings from this study. Kim et al.[38] reported that after fusion surgery, the reoperation rates were 4.4% for postoperative 1 to 90 days, 2.3% for postoperative 91 days to 1 year, and 7.2% for more than 1 year. In this study, although osteoporosis was not related to reoperation rate, the reoperation rate increased by 22% in the fusion operation group, especially by 34% in 3 months, implying that fusion operation needing instrumentation is associated with low bone density-related complication like instrumentation failure, early non-union, pedicle fracture, or compression fracture.

We also checked osteoporosis severity and anti-osteoporotic medication. Patients with moderate to severe osteoporosis had higher reoperation rates than mild osteoporosis patients for the first 3 years. This is in conformance with the results of the fusion operation group. On an average, after spinal surgery bone fusion is complete in 2 years. Before bone fusion and during bone remodeling, severe osteoporosis can prevent fusion processing and decrease fixation strength in the bone of osteoporotic patients with low BMD leading to an increased incidence of instrument failure.

Determining osteoporosis severity based on anti-osteoporotic drugs would be inaccurate and improper because calcium and vitamin D supplements are needed first to correct a mild condition and then bisphosphonate, denosumab, or teriparatide are needed to avoid fracture risk, as per the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) guideline.[39] Osteoporosis severity in this study could not be measured by standard criteria like bone mineral density or assumed based on diagnostic code or the anti-osteoporotic drug code. Nevertheless, we can speculate on the osteoporosis severity by estimating from the dataset osteoporosis patients who took calcium or vitamin D (6,262 (22.1%)) and those

who taking the regular osteoporosis medication. In the current study, patients were categorized based on their use of anti-osteoporotic medication before the spinal surgery. Anti-osteoporotic medication lowered the reoperation rate for the first two years for those on medication, but with only a 2-3% difference was seen. Osteoporosis patients, who had a diagnostic code, but no medication, were estimated at 54,390 (66.3%). These results would suggest that (a) osteoporosis treatment and prevention is less optimal resulting in unsatisfying clinical outcome, increasing osteoporotic fracture risk, and imposing a large healthcare burden, and (b) anti-resorptive osteoporosis medication is not related to spinal fusion. Previous studies reported that less than one-third of women and only 10% of men received anti-osteoporosis drugs among the osteoporosis population in Taiwan.[32] Some reported that antiresorptive medication would decrease bone turnover rate and thus might interfere with osteoclast-osteoblast bone remodeling complex needed for successful spinal fusion.[40] Kang et al. reported that long-term use of bisphosphonates might inhibit the spinal fusion process after fusion operation, resulting in delayed union after 6 months.[41]

V. CONCLUSION

We used the KNHIS database for all Koreans as data for analyses in this study. Osteoporosis was found to be significantly associated with readmission, hospitalization, and medical costs during the 5-8-year follow-up. Readmission rates related to spine was 36.2%, which was 14.3% in 3 months, and 18.1% in 12 months. Readmission rates related to osteoporosis showed an increase of 26%, compared with 9-10% after adjusting for confounders. Reoperation rate was 22.2% in the 5-8-year follow-up, 1.1% in 3 months, and 3.1% in 12 months.

Although osteoporosis was not related to the reoperation rate, it increased by 22% in the fusion surgery group, touching 34% at 3 months. Osteoporosis severity was highly associated with reoperation rate, especially in the first 2 years. Moreover, in osteoporosis patients, anti-osteoporotic medication was an important factor to reduce the reoperation rate. Osteoporosis itself needs to be controlled to prevent its impact on the economic burden, such as readmission, reoperation, and total medical cost, even though it is not related to survival rate. Proper management of osteoporosis is essential if considering spine surgery, particularly fusion operation, and this would help reduce patients' socioeconomic burden and produce more satisfying outcomes among those who undergo spine surgery.

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ABSTRACT (IN KOREAN)

골다공증이 척추 수술의 재입원과 재수술, 경제적 비용에 미치는 영향 및 8년 추적 관찰한 결과 : 전국민 대상 연구

<지도교수 김긍년>

연세대학교 대학원 의학과

이창규

고령화 사회가 되면서 퇴행성 척추 질환과 골다공증의 빈도는 증가하고 있고, 이에 따라 골다공증을 가진 고령환자들의 척추 수술에 대한 관심과 걱정도 같이 증가한다. 골다공증은 골감소증으로 인해 골절의 위험성 뿐만 아니라 척추 수술로 인한 불유합과 고정 실패 등을 초래할 수 있다. 따라서 환자의 이병률과 사망률을 증가시킬수 있는 이러한 합병증을 줄이는 것은 굉장히 중요하다. 이 연구에서는 척추 수술 받은 환자들에서 골다공증의 빈도와 위험요소, 의료비용, 재수술, 재입원 등 어떠한 영향을 미치는지에 대해 빅데이터로 조사하였다. 국

민건강보험공단 데이터베이스를 이용하였고, 이는 국민 전체수의 100만명 코호트 자료이다. 2005년도부터 2008년도까지 50세 이상 흉,요추 척추 수술을 받은 환자를 대상으로 하였고, 이를 통계청자료를 이용하여 가중치를 부여해 전체 인구를 추정하는 방식으로 자료를 얻었다. 전체 147,676명이 추정되었고, 이를 골다공증이 있는 군과 골다공증이 없는 군으로 나누어 최소 5년에서 8년까지 추적 관찰하였다. 그 결과, 골다공증은 전체 재입원과 척추 관련 재입원 모두에서 재입원율을 의미있게 높였고, 기간에 따라서도 3개월, 12개월, 전 기간으로 봤을때, 위험도가 의미있게 높은 것으로 나타났다. 또한 골다공증은 전체 입원 일수와 의료비용에도 영향을 주었는데, 골다공증이 있는 군에서 없는 군에 비해 입원일수는 평균 62일 정도 길었고, 의료비용은 개인당 2,327,262원 정도 더 들었다. 총 의료비용은 골다공증군에서 없는 군보다 8000억원 (전체 관련), 3100억원 (척추 관련)의 비용이 더 드는 것으로 파악했다. 골다공증은 재수술에서도 영향을 미쳤는데, 특히 척추 유합술에서 두드러졌다. 골다공증의 심한 정도에 따라서도 골다공증이 중간 단계이상으로 심한 군에서 약한 군보다 첫 3년이내에 재수술률이 더 높았다. 골다공증 환자에서 골다공증 진단은 받았으나 약은 복용하고 있지 않는 환자들이 꽤 많았고, 수술전 골다공증약을 복용하고 있던 군과 복용하고 있지 않던 골다공증환자들을 비교하였을때, 골다공증 약을 복용하고 있던 군에서 5%정도 재수술율이 낮았다.이처럼 골다공증은 5-8년간 추적 관찰한 결과 재입원률과 입원 일수, 의료비용에서는 의미있게 차이를 보였으며, 재수술율은 척추 유합술에서 높았고, 골다공증이 심한 환자에서 3년이내, 골다공증 약을 복용하고 있지 않는 환자에서 조금 더 유의하게 높은 것

으로 확인했다. 따라서 50세 이상 환자에서 척추 수술을 고려한다면, 골다공증을 적절하게 치료하고 예방하는 것이 환자의 만족도와 사회 경제적 비용을 줄이는데 중요한 역할을 할 수 있을 것으로 생각하며, 특히 척추 유합술시에 더 많은 고민이 필요할 것으로 보인다. 이 연구는 한국민 전체를 대상으로, 현재 늘어나는 척추 수술과 골다공증에 대한 국내외 첫 연구이며, 보건 의료 정책 결정에 참고할 수 있는 연구라고 생각한다.

핵심되는 말 : 골다공증, 척추 수술, 재입원, 재수술, 의료 비용, 사회 경제적 부담