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RESEARCH ARTICLE

Chronic Obstructive Pulmonary Disease as a Significant Marker of Prevalent Vertebral Fracture in Patients with Spinal Degenerative Disease: Preoperative Risk Factors Involved in Lifestyle-Related Diseases

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ABSTRACT

Objectives: **It is important to recognize prevalent vertebral fractures before spinal surgery due to the possible complications related to bone fragility. Recently, it has been noted that lifestyle-related diseases are associated with vertebral fractures. In this study, we analyzed prevalent vertebral fractures among patients with spinal degenerative disease and investigated their association with lifestyle-related diseases.**

Methods: **We included patients aged ≥60 years who underwent surgery for spinal degenerative disease between March 2019 and February 2021 at our hospital. The primary outcome measure was radiographically prevalent vertebral fractures from T10 to L5. Univariate analyses were performed for variables obtained from preoperative data related to lifestyle-related diseases between the vertebral fracture and non-fracture groups. Multiple logistic regression was performed with adjustments for variables including patient age, sex, and surgical site, and variables that were found to have a p-value of <0.2 in univariate analyses.**

Results: **A total of 220 patients were enrolled, of which 121 had prevalent vertebral fractures. Multiple logistic analysis was conducted with patient age, sex, and surgical site, and those variables identified p < 0.2 in univariate analyses: eGFR <60 mL/min/1.73 m^2 serum uric acid >7.0 mg/dL, FEV1/FVC <70%, and bone mineral density (BMD) T-score <–1.0. Patients with vertebral fractures were significantly older and had lower BMD, and lower FEV1/FVC.**

Conclusions: **Patients with FEV1/FVC <70% characterizing COPD had a significantly higher risk of vertebral fractures, independent of sex, age, and BMD. The risk of postoperative complications related to bone fragility should be considered in patients with COPD.**

Keywords: Bone fragility, chronic obstructive pulmonary disease, lifestyle-related diseases, vertebral fractures.

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1. Introduction

Vertebral fractures are the most common osteoporotic fractures [1]. While more than two-thirds of patients with vertebral fractures are asymptomatic and radiologically diagnosed [2], previous studies have shown that the presence of a vertebral fracture is a strong predictor of new vertebral and nonvertebral fractures even after adjusting for bone mineral density (BMD) [3]–[6]. Therefore, the presence of vertebral fractures is an important sign of bone fragility. In the surgical management of spinal degenerative disease, complications associated with bone fragility have been recognized, such as screw loosening and postoperative vertebral fractures [7]–[9]. Regarding bone fragility, it is crucial to preoperatively identify the presence of vertebral fractures and plan a treatment strategy to achieve good outcomes.

Recently, lifestyle-related diseases have been reported to be associated with osteoporosis and vertebral fractures [10]. These diseases are a group of conditions whose onset and progress are related to an individual's lifestyle and behavioral factors, such as their dietary habits, physical activity levels, quality and amount of rest, smoking habits, alcohol consumption, etc., [11]. They are considered chronic diseases and include diabetes mellitus, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), heart diseases, and cardiovascular diseases. As the global population ages and gains wealth, the number of patients with lifestyle-related diseases will increase, and more patients are expected to undergo spinal surgery. However, the association between vertebral fractures and lifestyle-related diseases has not been reported in patients with spinal degenerative disease.

In this study, we analyzed prevalent vertebral fractures among patients with spinal degenerative disease who were managed surgically and investigated the association between vertebral fractures and lifestyle-related diseases in such patients.

2. Materials and Methods

This study was approved by the ethics committee of our institute. This retrospective observational study included patients who were aged ≥60 years and underwent surgical management for spinal degenerative disease between March 2019 and February 2021 at our hospital. Spinal degenerative disease was inclusive of both cervical and thoracolumbar degenerative disease. If patients underwent several spinal surgeries during the study period, the preoperative data of the first operation were used. The exclusion criteria for the study were patients who had undergone thoracolumbar instrumentation surgery before the study period and incomplete preoperative data.

The following demographics were collected from the preoperative data: sex, age, body mass index (BMI), estimated glomerular filtration rate (eGFR), hemoglobin A1c (HbA1c) level, serum triglyceride (TG) level, serum uric acid (UA) level, forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC), BMD, and surgical site (thoracolumbar and/or cervical spine). Additionally, data on steroid use were collected. The BMD data, obtained from the proximal femur, were measured by dual x-ray absorptiometry using the Lunar Prodigy equipment (GE Healthcare, Tokyo, Japan). The calculated BMD value was automatically converted to a T-score, which indicated the standard deviation of the patients' BMD compared with that of healthy Japanese adults of the same sex (reference ages were 20–40 years).

Prior to analysis, continuous variables pertaining to lifestyle-related diseases were divided into two groups according to each abnormal criterion. BMI was divided into either <18.5 or ≥18.5 kg/m^2, eGFR into either <60 or ≥60 mL/min/1.73 m^2, HbA1c into either <6.5 or ≥6.5%, TG into either <150 or ≥150 mg/dL, UA into either ≤7.0 or >7.0 mg/dL, FEV1/FVC into either <70% or ≥70%, and BMD T-score into either <−1.0 or ≥−1.0. In terms of BMI and eGFR, patients with lower values were considered to be lean [12] and have CKD [13], respectively. Regarding HbA1c, TG, and UA levels, patients with higher values were considered to have diabetes [14], dyslipidemia [15], and hyperuricemia (characterizing gout) [16], respectively. Those with a lower FEV1/FVC were considered to have an obstructive ventilatory defect, thereby characterizing COPD [17].

The primary outcome measure for this study was preoperative radiographic vertebral fractures from T10 to L5. These were visually diagnosed and graded according to Genant's semi-quantitative (SQ) method [18] using preoperative thoracolumbar sagittal radiographs. Vertebral fractures were categorized as SQ grades 1–3.

Data analysis was performed using SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). The following factors were analyzed for the prevalent vertebral fracture and non-fracture groups: sex, age, surgical site, BMI, eGFR, HbA1c, TG, UA, FEV1/FVC, and BMD. Univariate analyses were performed using a t-test for continuous data and Fisher's exact test for categorical data. We used a multivariable logistic regression model with adjustments for abnormal variables found to be significant (p-value < 0.05) or trending towards significance (p-value <0.2) in the univariate analyses. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were generated for the risk of prevalent vertebral fractures. A p-value of <0.05 in regression testing was considered statistically significant. Subsequently, the risk of vertebral fractures (SQ grades 2–3) and multiple vertebral fractures (n ≥ 2) was analyzed using multiple logistic analyses with adjustments for the same variables.

3. Results

A total of 220 patients were enrolled in this study, of which 130 were women and 90 were men; the mean age of the participants was 74.0 years. Regarding the surgical site, 60 (27.3%), 157 (71.4%), and 3 (1.4%) patients underwent cervical, thoracolumbar, and both cervical and thoracolumbar surgery, respectively. Preoperatively, 121 (55.0%) patients had prevalent vertebral fractures, of which 55 (25.0%) had vertebral fractures with an SQ grade of 2–3. A single vertebral fracture was observed in 52 (23.6%) patients, while 44 (20.0%) patients had two vertebral fractures, and 25 (11.4%) patients had three or more fractures.

Table I shows the means ± standard deviation, the number of patients, and p-values derived from each statistical test. The result showed that patients with older age, lower eGFR, lower FEV1/FVC, and lower BMD were significantly associated with prevalent fractures. Regarding categorical data, Fisher's exact testing showed that eGFR <60 mL/min/1.73 m^2, FEV1/FVC <70%, and a BMD T-score of <−1.0 were significantly associated with prevalent fractures.

Based on univariate analyses, eGFR <60 mL/min/1.73 m^2, UA >7.0 mg/dL, FEV1/FVC <70%, and BMD T-score <−1.0 were included in the multivariable logistic regression model, along with age, female sex, and thoracolumbar surgical site. The results are shown in Table II.

Significant risk factors of vertebral fractures included the following: age (OR = 1.076, 95% CI = 1.021–1.135, p = 0.007), BMD T-score <−1.0 (OR = 3.921, 95% CI

TABLE I: Patient Characteristics

Characteristics	Fracture (N = 121)	No fracture (N = 99)	p-value
Age (years)	75.6 ± 6.97	72.1 ± 7.09	<0.001
Sex-female no. (%)	47 (38.8)	43 (43.4)	0.495
Surgical site-Thoracolumbar no. (%)	88 (72.7)	72 (72.7)	1.000
BMI (kg/m^2)	24.4 ± 3.63	24.4 ± 3.19	0.963
≤18.5 no. (%)	4 (3.3)	3 (3.0)	1.000
eGFR (mL/min/1.73m^2)	57.1 ± 17.6	62.8 ± 20.1	0.025
<60 no. (%)	71 (58.7)	43 (43.4)	0.030
HbA1c (%)	6.07 ± 0.73	6.19 ± 0.83	0.259
≥6.5 no. (%)	24 (19.8)	27 (27.3)	0.203
TG (mg/dL)	160 ± 92.4	181 ± 153	0.223
>150 no. (%)	51 (42.1)	44 (44.4)	0.785
UA (mg/dL)	5.37 ± 1.60	5.12 ± 1.25	0.198
>7.0 no. (%)	17 (14.0)	7 (7.1)	0.128
FEV1/FVC (%)	73.4 ± 8.76	77.2 ± 8.26	0.001
<70 no. (%)	34 (28.1)	10 (10.1)	0.001
BMD (g/cm^2)	0.842 ± 0.189	0.902 ± 0.168	0.015
T score	−0.842 ± 1.60	−0.309 ± 1.33	0.009
T score <−1.0 no. (%)	59 (48.8)	28 (28.3)	0.002
Steroid use no. (%)	5 (4.1)	4 (4.0)	1.000

Note: BMI, body mass index; TG, uremic serum triglyceride level; UA, serum uremic acid level; FEV1/FVC, forced Expiratory Volume in one second/forced Vital Capacity; BMD, bone mineral density.

TABLE II: Results of the Multiple Logistic Analysis for the Risk of Vertebral Fractures

Characteristics	Odds ratio	95% Confidence interval	p-value
Age	1.076	1.021–1.135	0.007
Sex-female	0.534	0.257–1.108	0.092
Surgical site-Thoracolumbar	0.922	0.473–1.794	0.810
eGFR <60 mL/min/1.73 m^2	0.789	0.381–1.634	0.524
UA >7.0 mg/dL	2.598	0.927–7.284	0.070
FEV1/FVC <70%	4.384	1.891–10.161	0.001
BMD T score <−1.0	3.921	1.871–8.215	<0.001

Note: eGFR, estimated glomerular filtration rate; UA, serum uremic acid level; FEV1/FVC, forced expiratory volume in one second/forced vital capacity; BMD, bone mineral density.

TABLE III: Results of the Multiple Regression Analysis for the Risk of Vertebral Fractures with SQ Grades 2–3

Characteristics	Odds ratio	95% Confidence interval	p-value
Age	1.041	0.980–1.105	0.189
Sex-female	1.498	0.679–3.303	0.317
Surgical site-Thoracolumbar	1.345	0.609–2.971	0.464
eGFR <60 mL/min/1.73 m^2	1.466	0.618–3.474	0.385
UA >7.0 mg/dL	1.569	0.519–4.745	0.425
FEV1/FVC <70%	1.066	0.438–2.595	0.888
BMD T score <−1.0	4.078	1.892–8.789	<0.001

Note: eGFR, estimated glomerular filtration rate; UA, serum uremic acid level; FEV1/FVC, forced expiratory volume in one second/forced vital capacity; BMD, bone mineral density.

TABLE IV: Results of the Multiple Regression Analysis for the Risk of Multiple Vertebral Fractures (N ≥ 2)

Characteristics	Odds ratio	95% Confidence interval	p-value
Age	1.017	0.965–1.071	0.529
Sex-female	0.615	0.294–1.287	0.197
Surgical site-Thoracolumbar	1.046	0.530–2.067	0.896
eGFR <60 mL/min/1.73 m^2	1.311	0.613–2.805	0.485
UA >7.0 mg/dL	1.269	0.487–3.307	0.625
FEV1/FVC <70%	2.023	0.976–4.194	0.058
BMD T score <−1.0	2.824	1.374–5.805	0.005

Note: eGFR, estimated glomerular filtration rate; UA, serum uremic acid level; FEV1/FVC, forced expiratory volume in one second/forced vital capacity; BMD, bone mineral density.

= 1.871–8.215, p < 0.001), and FEV1/ FVC <70% (OR = 4.384, 95% CI = 1.884–10.161, p = 0.001). In addition, the results of the multiple regression analysis for the risk of vertebral fractures with SQ grade 2–3 and the risk of multiple vertebral fractures (n ≥ 2) are shown in Tables III and IV. These results showed that a BMD T-score <−1.0 was the only significant risk factor for an SQ grade 2–3 vertebral fracture (OR = 4.074, p < 0.001) and multiple vertebral fractures (OR = 2.824, p = 0.005).

4. Discussion

This study investigated the association between prevalent vertebral fractures in patients with spinal degenerative disease and their preoperative data before spinal surgery, with a specific focus on lifestyle-related diseases. Our results showed that 55% of the patients had prevalent vertebral fractures before surgery. In the multivariate analyses, older age and a BMD T-score of <−1.0 were significant risk factors for prevalent vertebral fractures. In addition, patients with FEV1/FVC <70% were at a significantly higher risk for these fractures. Although the data were not considered significant, such patients were more likely to be at risk of multiple vertebral fractures.

Our study showed that an FEV1/FVC of <70% characterizing COPD was a significant risk factor for prevalent vertebral fractures independent of sex, age, and BMD among patients with preoperative lumbar degeneration. The prevalence of vertebral fractures in COPD patients varies from 24%–79% [19]. Although BMD is lower in patients with COPD than in patients without COPD [20], in several previous studies investigating the association between BMD and vertebral fracture prevalence, BMD was not considered to be a valid predictor of fracture in patients with COPD. In one study, 36.5% of patients with COPD had vertebral fractures, while only 23.6% had low BMD indicating osteoporosis [21]. Another Japanese study revealed that while prevalent vertebral fractures were present in 79.4% of patients, low BMD was present in only 38.8% [22]. In patients with COPD, structural deterioration, which is not estimated by BMD, has been reported to affect bone strength. Postmenopausal women with COPD showed deteriorated cancellous and cortical bone microstructure, which was explained by hypoxia, TNF-α, and smoking [23]. Owing to low bone quality, patients with COPD may be at high risk of prevalent vertebral fractures. Therefore, during surgical intervention for patients with COPD, complications related to bone fragility should be considered.

Prevalent vertebral fractures are known to be risk factors for new fractures, including vertebral fractures. A previous observational study showed that prevalent vertebral fractures increased the risk of subsequent vertebral fractures four times for men and three times for women after adjusting for age and baseline BMD [3]. Generally, BMD comprises only 70% of bone strength, with the other determinants contributing to the remaining 30%, referred to as bone quality [24]. Deterioration of trabecular microarchitecture and cortical thickness has been shown to be associated with vertebral fractures [25]. Thus, patients with vertebral fractures tend to have low bone quality. Complications related to bone fragility, such as pedicle screw loosening and postoperative vertebral fractures, have been reported in surgery for spinal degenerative disease, especially with instrumentation [7]–[9]. Prevention of such complications is considered crucial for improving postoperative outcomes. Therefore, recognizing osteoporotic fractures in patients with spinal degenerative disease is necessary to assess the risk of complications related to bone fragility after surgery and prevent their occurrence.

We analyzed diabetes (HbA1c >6.5%) and CKD (eGFR <60 mL/min/1.73 m^2) as lifestyle-related diseases other than COPD. However, in this study, the multivariate analysis found these associations to be statistically insignificant, although diabetes has been reported as a risk factor for fractures independent of BMD [26]. One reason for this is that our study sample was relatively small, and another is that our patients' general condition may be better for undergoing surgery than that of the general population with diabetes. As no patients with severe diabetes experienced serious complications such as cardiovascular or cerebrovascular diseases, it is possible that the risk of vertebral fractures was lower in these patients. In a systemic review, CKD was also stated to be a risk factor for fractures [27]. However, it showed that in patients with CKD the risk of vertebral fractures was lower than hip or other fractures. Our study also showed that there was no significant association between CKD and vertebral fractures with adjustments for other factors such as age and BMD. As stated above, we found that the risk of vertebral fractures in patients with diabetes or CKD was not as high as that in preoperative patients with spinal degenerative diseases.

The prevalence of morphological vertebral fractures was reported to be 18%–45% among Japanese postmenopausal women aged over 70 years [28]–[30]. In our study cohort, more than 50% of the patients with spinal degenerative disease had vertebral fractures and, therefore, had a higher prevalence of vertebral fractures than the general Japanese community. No difference was observed in the prevalence of vertebral fractures between those who underwent thoracolumbar and cervical surgeries. However, it is possible that there may have been false-positive diagnoses of vertebral fractures in our study owing to the limitations of the SQ method. SQ grade 1 fractures are radiologically distinct and, in some cases, the distinction between borderline deformity and definite mild fracture can be difficult and considered arbitrary [31]. However, approximately 25% of the patients enrolled in our study had SQ grade 2–3 vertebral fractures, which may not be misdiagnosed when semiquantitative methods are used. In this study, regardless of the lesion site that required surgery (thoracolumbar and/or cervical spine), the prevalence of vertebral fractures in patients with spinal degenerative disease was higher than that reported in previous studies. The association between the site of the lesion and the incidence of vertebral fractures was, therefore, considered insignificant. Furthermore, while thoracolumbar degeneration may increase thoracic kyphosis [32], it may not have a similar effect on the incidence of vertebral fractures. One hypothesis is that patients with spinal degenerative disease are more susceptible to falls, explaining the increase in vertebral fractures.

This study had several limitations. First, the data did not reflect the precise diagnosis or severity of lifestyle-related disease since data were extracted from a single point in time (preoperatively). Also, to diagnose COPD, we did not rule out other conditions presenting with obstructive ventilatory defects such as asthma. Ideally, a more precise diagnosis is required to examine the degree to which the control of lifestyle-related diseases is associated with the incidence of vertebral fractures. Second, we did not evaluate other factors affecting vertebral fractures, such as the patients' spinal alignment, social history, daily activity, or smoking and drinking status. Finally, our study was retrospective in nature and only included patients from one institution. Further studies with larger multicenter cohorts are recommended.

5. Conclusions

The prevalence of vertebral fractures among patients with spinal degenerative disease who required surgical intervention was >50%. Patients with FEV1/FVC <70% had a significantly higher risk of vertebral fractures, independent of their sex, age, and BMD. In patients with COPD, clinicians should check the presence of prevalent

vertebral fractures more carefully and be conscious of the risk of postoperative complications related to bone fragility to prevent their occurrence.

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Conflicts of Interest

Authors declare that they do not have any conflict of interest.

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