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Clinical Study

Risk factors for newly developed osteoporotic vertebral compression fractures following treatment for osteoporotic vertebral compression fractures

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Abstract

BACKGROUND CONTEXT: It has been reported that newly developed osteoporotic vertebral compression fractures (OVCFs) occur at a relatively high frequency after treatment. While there are many reports on possible risk factors, these have not yet been clearly established.

PURPOSE: The purpose of this study was to investigate the risk factors for newly developed OVCFs after treatment by vertebroplasty (VP), kyphoplasty (KP), or conservative treatment.

STUDY DESIGN/SETTING: A retrospective comparative study.

PATIENT SAMPLE: One hundred thirty-two patients who had radiographic follow-up data for one year or longer among 356 patients who were diagnosed with OVCF and underwent VP, KP or conservative treatment between March 2007 and February 2016.

OUTCOME MEASURES: All records were examined for age, sex, body mass index (BMI), rheumatoid arthritis and other medical comorbidities, osteoporosis medication, bone mineral density (BMD), history of vertebral and nonvertebral fractures, treatment methods used, level of fractures, and presence of multiple fracture sites.

METHODS: Patients were divided into those who manifested new OVCF (Group A) and those who did not (Group B). For the risk factor analysis, student's *t*-tests and chi-square tests were used in univariate analysis. Multivariate logistic regression analysis was carried out on variables with a $p<.1$ in the univariate analysis.

RESULTS: Newly developed OVCFs occurred in 46 of the 132 patients (34.8%). Newly developed OVCF increased significantly with factors such as average age (p=.047), low BMD T-score of the lumbar spine (p=.04) and of the femoral neck (p=.046), advanced age (>70 years) (p=.011), treatment by cement augmentation (p=.047) and low compliance with osteoporosis medication (p=.029). In multivariate regression analysis, BMD T-score of the lumbar spine (p=.009) and treatment by cement augmentation (p=.044) showed significant correlations with the occurrence of new OVCFs with a predictability of 71.4%.

CONCLUSION: Osteoporotic vertebral compression fracture patients with low BMD T-score of the lumbar spine and those who have been treated by cement augmentation have an increased risk of new OVCFs after treatment and, therefore, require especially careful observation and attention.

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Introduction

Osteoporotic vertebral compression fractures (OVCFs) commonly occur in elderly patients with reduced bone mineral density (BMD). Fractures can occur from minor trauma or without any definite trauma history. Approximately 700,000 OVCFs occur yearly in the United States, 1,416,000 around the world, and about 40% of women experience OVCFs in their lifetime [1,2]. Furthermore, its prevalence is increasing due to an aging society that will lead to an increase in healthcare costs. Thus, it is an important disease from the socioeconomic perspective [3–6].

Osteoporotic vertebral compression fractures may cause continuous pain, reduced quality of life resulting from limited ambulation, progression of kyphosis, and increase in mortality [7–9]. Hence, proper diagnosis and treatment are needed.

Minimally invasive treatments such as percutaneous vertebroplasty (VP) and kyphoplasty (KP) are widely performed for OVCFs. Such procedures insert large cannulated needles through the pedicle percutaneously into the vertebral body, and inject polymethylmethacrylate to stabilize the vertebral body and prevent further collapse and to achieve rapid pain relief and recovery of function [10–12]. It has been suggested by some that VP and KP lead to higher OVCF rates of the adjacent segment vertebrae potentially because stiffness of the cemented vertebral body is increased [11,13–15]. In contrast, Yi et al. reported that there was no significant difference in the incidence of new OVCF between a VP/KP group and a conservative treatment group at 49.4 months of follow-up [16]. Shim et al. reported clinical results after KP among rheumatoid arthritis (RA) patients and found fractures of adjacent segments in 11.5% of the cohort [17]. In the end, it has been difficult to prove whether the effect of VP/KP is most significant or it is a natural course caused by osteoporosis. While there are many reports on the risk factors for new OVCFs, these have not yet been clearly established. This information would be useful in understanding the nature of new fractures.

The purpose of this study was to investigate the risk factors for newly developed OVCFs after treatment by VP, KP or conservative treatment.

Materials and methods

Patients selection

The present study had no funding sources or any potential conflicts of interest associated biases. This study was approved by our institutional review board. It was a single-center, retrospective study. From March 2007 to February 2016, there were 356 patients diagnosed with acute OVCFs after excluding high-energy trauma, pathologic fracture including tumor and infection. Of these patients, 88 had conservative treatment and 268 had VP or KP (considered together). Among them, 224 patients were not followed up for more than one year due to old age, poor general conditions such as dementia, Parkinson's disease, inability to walk independently, among other reasons. Thus, 132 patients with at least one year of radiological data were included. Patients were divided into two groups. Group A included 46 patients who had newly developed OVCFs during follow-up, and Group B included 86 patients without newly developed OVCFs. Differences between the two groups were analyzed by age, gender, body mass index (BMI), fracture region, treatment method used for the fracture, previous history of OVCF, nonvertebral osteoporotic fracture history, BMD, history of osteoporosis medication, and medical comorbidities including RA, cardiovascular, pulmonary, endocrine, Parkinson's disease, hepatic disease, and renal disease.

Treatment

VP was done in cases of acute OVCF documented as a recent fracture on a magnetic resonance imaging (MRI) or bone scan, collapse of the vertebral body less than 30%, and pain that was persistent despite conservative treatment for more than two weeks. Kyphoplasty was done in cases of acute OVCF documented as a recent fracture on an MRI or bone scan, collapse of the vertebral body from 30% to 60%, and pain that was persistent despite conservative treatment for more than three weeks. Patients with congestive heart failure, pneumonia, thrombophlebitis, uncontrolled diabetes, chronic renal failure receiving dialysis, age older than 80 years underwent early VP/KP after diagnosis without conservative treatment. This criterion is mainly based on the national medical insurance guideline of our country.

Conservative treatment was performed with bed rest, medication, physical therapy, at least average eight weeks of TLSO application, and close observation in an outpatient department until three months after diagnosis of OVCF.

Assessment

Radiologic diagnosis of acute OVCF is based on radiographs, MRI or bone scan. Increased signal intensity in T2-weighted fat suppression images, reduced signal intensity in T1-weighted images and fracture lines in vertebral bodies on MRI or increased uptake in vertebral bodies in bone scans was to diagnose acute OVCF.

Newly developed OVCF was diagnosed as a new compression fracture in a different vertebral body compared to

the last follow-up image on plain radiography, MRI, or bone scan. Adjacent-segment fracture was defined as newly developed OVCF within one level above or below from the index fracture. Distant segment fracture was defined as two or more levels away from the index fracture.

Fracture regions were divided into the thoracic region when they occurred in the tenth thoracic vertebra or higher, the thoracolumbar junction when they occurred between the eleventh thoracic vertebra and second lumbar vertebra, and the lumbar region when they occurred in the third lumbar vertebra or lower.

The treatment method for fractures was divided into groups in which only conservative treatment was performed and those in which VP/KP were performed.

BMD was measured at the time of diagnosis of acute OVCF by dual energy x-ray absorptiometry (Hologic Inc., Waltham, MA, USA). T-scores were obtained of the lumbar vertebrae and the bilateral femoral neck. In the lumbar region, the average T-score of the two lowest scoring vertebral bodies between the first lumbar vertebra and the fourth lumbar vertebra was obtained.

The medication possession rate (MPR) was calculated to evaluate compliance with osteoporosis treatment. At least 80% was judged to be good compliance and less than 80% was judged to be poor compliance. The MPR represents the number of prescription days of osteoporosis medication as a percentage of a year [5].

Statistical analysis

For statistical analysis, the SPSS ver. 20 (IBM Corp. NY, USA) program was used. Student's *t*-tests and chi-square tests were used in the univariate analysis. Multivariate logistic regression analysis was carried out with variables that had a $p<.1$ in the univariate analysis and differences were considered to be significant at $p<.05$.

Results

Of the 132 patients, 46 (34.8%) developed new OVCFs at an average of 20.1 (1–70) months after treatment during a mean follow-up period of 28.9 (12–98) months. Of these 46 patients, 21 (45.7%) were adjacent segment fracture and the other 25 (54.3%) were distant segment fracture. Twenty (43.5%) underwent VP/KP after 19.61±15.06 days from diagnosis and the other 26 (56.5%) underwent conservative treatment. Of the 46 patients, 8 (17.4%) developed an additional OVCF an average of 11.3 (1–26) months after the second OVCF.

The average ages of group A and group B were 74.30±8.78 and 70.90±9.57 (p=.047) and the percentages of females were 93.48% and 90.70% (p=.747), respectively. The average BMI was 23.06±4.04 and 23.32±3.52 (p=.706) and medical comorbidity rates were 73.9% and 67.4% (p=.441). The mean follow-up periods were 29.72±17.43 and 28.45±15.91 months and there was no significant difference (p=.675) between groups (Table 1).

Table 1
Demographic data

	Group A (n=46)	Group B (n=86)	p-value
Age	74.30±8.78	70.90±9.57	.047
Sex	M=3, F=43	M=8, F=78	.747
Height (cm)	153.96±4.99	155.93±8.40	.147
Weight (kg)	54.82±10.69	56.82±10.54	.303
BMI (kg/m^2)	23.06±4.04	23.32±3.52	.706
Medical comorbidity	34 (73.9%)	58(67.4%)	.441
Follow-up period (months)	29.72±17.43	28.45±15.91	.675

BMI, body mass index.

Table 2
BMD and MPR

	Group A (n=46)	Group B (n=86)	p-value
BMD of femoral neck (T-score)	−2.91±1.03	−2.53±0.96	.046
BMD of L-spine (T-score)	−3.19±1.10	−2.67±0.94	.004
MPR of osteoporosis medication	61.27±29.17	72.38±26.48	.029

BMD, bone mineral density; MPR, medication possession rate.

The BMD T-scores of the femoral neck were −2.91±1.03 and −2.53±0.96 (p=.046) in group A and group B, respectively, and the BMD T-scores of the lumbar spine were −3.19±1.10 and −2.67±0.94 (p=.004). The MPR was measured at 61.27±29.17 and 72.38±26.48 (p=.029) (Table 2).

In the univariate analysis, the proportions of elderly patients over 70 years were 78.3% and 55.8% in group A and group B, respectively (p=.011, odds ratio 2.85). The percentages of patients undergoing VP/KP were 82.6% and 66.3% (p=.047, odds ratio 2.42). The proportions of patients with MPR<80% were 65.1% and 44.2% (p=.021, odds ratio 2.37). However, there were no significant differences in terms of previous history of OVCF (p=.078), previous nonvertebral osteoporotic fracture (p=.773), multiple-level fracture (p=.151), RA (p=.358), fracture region (p=.523) and type of osteoporosis medication (p=.156) (Table 3).

In multivariate logistic regression analysis, T-score of the lumbar spine (p=.009) and VP/KP (p=.044) were significant risk factors for newly developed OVCF, with a predictability of 71.4% (Table 4).

Discussion

In this study, the overall incidence of new OVCF was 34.8% during a mean follow-up period of 28.9 months. In other studies on patients who underwent cement augmentation such as VP/KP, the incidence of new fractures was reported to be 15%-22% at one year postoperatively and 17.2%-52% at four years postoperatively [11,16,18].

Table 3
Univariate analysis of risk factors for newly developed vertebral compression fractures

	Group A (n=46)	Group B (n=86)	Odds ratio	p-value
Old age (>70)	36 (78.3%)	48 (55.8%)	2.85	.011
VP/KP	38 (82.6%)	57 (66.3%)	2.42	.047
Previous history of OVCF	21 (45.7%)	26 (30.2%)	1.94	.078
History of nonvertebral osteoporotic Fx.	5 (10.9%)	8 (9.3%)	1.19	.773
Multiple level Fx.	11 (23.9%)	12 (14.0%)	1.94	.151
RA	8 (17.4%)	10 (11.6%)	1.60	.358
Fx. region				
Thoracic region	3 (6.5%)	2 (2.3%)		.523
T-L junction	40 (87.0%)	78 (90.7%)		
Lumbar region	3 (6.5%)	6 (7.0%)		
MPR<80%	30 (65.1%)	38 (44.2%)	2.37	.021
Osteoporosis medication				
Bisphosponate	43 (93.5%)	84 (97.7%)		.156
SERM	2 (4.3)	0 (0.0%)		
PTH	1 (2.2)	2 (2.3%)		

KP, kyphoplasty; VP, vertebroplasty; OVCF, osteoporotic vertebral compression fracture; Fx. Fracture; RA, rheumatoid arthritis; T-L, thoracolumbar; MPR, medication possession rate; SERM, selective estrogen receptor modulators; PTH, parathyroid hormone.

Table 4
Multivariate analysis of risk factors for newly developed vertebral compression fractures

	Odds ratio (CI)	p-value
BMD of L-spine (absolute value of T-score)	1.751 (1.151–2.660)	.009
VP/KP	2.817 (1.026–7.736)	.044
Old age (>70)	1.594 (0.606–4.191)	.345
MPR<80%	2.006 (0.872–4.613)	.101

L-spine, lumbar spine; CI, confidence interval; BMD, bone mineral density; KP, kyphoplasty; VP, vertebroplasty; MPR, medication possession rate.

Significant risk factors for newly developed OVCF were age over 70, cement augmentation, low T-scores of the lumbar spine and femoral neck, and low compliance with osteoporosis medication (MPR<80%) in univariate analysis. T-score of the lumbar spine and cement augmentation were significant risk factors in a multivariate logistic regression analysis.

In case of age, it was found that the mean age and percentage of elderly patients over 70 was significantly higher in group A. The BMD T-score of the lumbar spine and femoral neck were significantly lower in group A. Especially in multivariate analysis, low BMD T-score of the lumbar spine had an odds ratio of 1.75. It was therefore considered that the lower it was, the higher the chance that a newly developed OVCF would occur.

Previous studies have reported that the risk of newly developed OVCF rises after VP/KP [11,13–15]. In this study, the rate of patients undergoing VP/KP was found to be significantly higher in group A with an odds ratio of 2.82 according to the multivariate analysis, and therefore, like preceding studies, it was found to be a major risk factor for newly developed OVCF. However, for the average time until new fractures occurred, it was 20.79 months and 21.63 months, respectively for VP/KP and conservative treatment, showing no significant difference (p=.943). Therefore, when choosing the treatment method, clinicians need to take into consideration that VP/KP can achieve rapid pain relief and return to activity of daily living that is important because most of the OVCF patients are quite old.

It was found that MPR was significantly lower in group A, but poor compliance was not significant in a multivariate analysis. However, when considering the effect of improving BMD by osteoporosis medication, additional large-scale studies of the relation between low compliance with osteoporosis medication and newly developed OVCFs are needed.

In a systematic review by Ma et al., strong evidence of newly developed OVCF risk factors was found for low BMD, intradiscal cement leakage, and vertebral height restoration; moderate evidence was found for low BMI, number of pre-existing vertebral fractures, thoracolumbar junction, old age, and number of treated vertebrae [15]. In our study, factors such as previous history of OVCF, multiple level fracture, and fracture region did not show significant differences between the two groups.

Medical comorbidities and RA had no significant differences. However, in the case of RA, it has been reported that BMD decreased due to long-term steroid use. Hiwatashi and Westesson reported that steroid medication is a significant risk factor for newly developed OVCF [19]. Therefore, it is necessary to conduct a large cohort study on RA and steroid medication in the future.

The strengths of this study were as follows. First, the patients included were diagnosed and treated by a single orthopaedic spine surgeon at a single center; therefore, diagnostic and treatment criteria were uniform. Second, this study included both patients who underwent VP/KP

and those who received conservative treatment, whereas most previous studies included only patients who underwent VP/KP.

The limitations of this study are as follows. First, it was a retrospective study and thus selection bias may have been present because only patients with more than one year follow-up radiologic data were included. Second, newly developed OVCF was diagnosed by a variety of different methods. Third, the effect of different osteoporosis medications was not adequately assessed because bisphosphonate was used in most cases.

Conclusions

In this study, the incidence of newly developed OVCF after treatment of OVCF was as high as 34.8% during a mean follow-up period of 28.9 months.

The risk factors for newly developed OVCF were cement augmentation and low BMD T-score of the lumbar spine. And the highest risk factor was cement augmentation in this study with odds ratio of 2.8.

In the treatment of OVCF, patients with these risk factors are at a higher risk of newly developed OVCF; hence, more careful attention, appropriate osteoporosis medication, and efforts to improve compliance with osteoporosis medication are needed.

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