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ORIGINAL ARTICLE

Risk factors for subsequent vertebral fractures following a previous hip fracture

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Abstract

Introduction The purpose of our study was to evaluate the incidence and to identify risk factors of subsequent vertebral fractures after hip fractures, and to determine whether the subsequent vertebral fracture increases the mortality rate of elderly hip fracture patients.

Materials and methods From January 2009 to July 2016, 1,554 patients were diagnosed as having a hip fracture and were treated surgically at our institution. Among them, 1121 patients age > 50 years at the time of injury and were followed up for 1 year or longer after the hip fracture surgery. In these patients, radiographs of the hip and spine were taken at each follow-up. We reviewed medical records and radiographs of these patients. Among the 1121 patients, 107 patients (9.5%) had subsequent vertebral fractures after the hip fracture during entire follow-up periods.

Results In multivariable analysis, previous history of vertebral fracture [odds ratio (OR), 2.62; $p < 0.001$], medication possession rate (MPR) of osteoporosis treatment < 80% (OR, 1.92; $p = 0.014$), and a lower lumbar bone mineral density (BMD) (OR, 2.58; $p = 0.001$) appeared as risk factors for subsequent vertebral fractures.

Conclusion However, the subsequent vertebral fractures did not affect the mortality after the hip fractures. Age ≥ 70 years [hazard ration (HR) 2.70; $p = .039$], body mass index < 18.5 kg/m^2 (HR, 2.57; $p = 0.048$), and Charlson comorbidity index ≥ 2 (HR, 2.04; $p = 0.036$) were risk factors of the death. Timely management is warranted to prevent subsequent vertebral fractures in hip fracture patients with risk factors.

Keywords Mortality · Hip fracture · Osteoporosis · Subsequent fracture · Vertebral fracture

Introduction

Osteoporotic fractures are major socioeconomic burdens worldwide [1]. These fractures seriously limit the patient's activity, degrade the quality of life, and increase the mortality rate [1–10]. In 2000, the number of osteoporotic fractures was more than 9 million over the world [1]. Moreover, the incidence of osteoporotic fractures is projected to increase in accordance with the increment of aging population [11, 12]. Hip fractures and vertebral fractures are the most common osteoporotic fractures [1, 4, 6, 13].

Osteoporotic fracture patients are at risk of subsequent fracture. Two studies, one using Medicare administrative claims data in the United States and one from Swedish national registers, showed that subsequent fractures were likely to occur within 1 year or 2 years after an osteoporotic fracture [14, 15]. In the study from the United States, the risk of subsequent fracture after the initial fracture was 10% in the first year and 18% in the second year. Old age (> 75 years) was a risk factor for the subsequent fracture [14]. In the Swedish study, the subsequent fracture occurred in 7.1% during 1 year and in 12.0% during 2 years after the initial fracture [14, 15]. An Irish study using a local cohort in the greater Reykjavik Area demonstrated that the incidence of a second osteoporotic fracture was high within 1 year after the first fracture and decreased thereafter. At 1 year after the first fracture, the risk of a second fracture

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was 2.7-fold higher than the population risk, while this risk ratio was 1.4-fold at 10 years after the first fracture [16]. These studies evaluated the overall risk of subsequent fracture after prior fracture.

Several studies reported high rates of the subsequent vertebral fractures after a prior fracture [14, 17–21]. A four large 3-year osteoporosis treatment trials were conducted at 373 study centers in North America, Europe, Australia, and New Zealand. Data from these trials showed that the risk of subsequent fractures is two times higher after non-vertebral fractures and four times higher after vertebral fractures [22].

Identification of patients at risk of the subsequent osteoporotic fractures and active measurements are mandatory for the prevention. Hip fractures and vertebral fractures are the most common two osteoporotic fractures, and hip fractures are associated with the highest mortality among the osteoporotic fractures [6]. To date, only one study from Danish registry investigated the incidence of subsequent vertebral fractures after hip fractures [19]. In that study, 10-year cumulative incidence of subsequent vertebral fractures after hip fractures was 3.1% in men and 4.7% in women [19]. Nevertheless, the specific risk factors for new vertebral fracture(s) after a hip fracture are not known.

Therefore, we aimed to analyze the risk factors for the development of subsequent vertebral fractures after a hip fracture, and to determine whether the presence of subsequent vertebral fractures increases the mortality of hip fracture patients.

Materials and methods

Patients' selection

We reviewed the electronic medical record (EMR) database of our hospital, and identified 1,554 patients, who were diagnosed as having a hip fracture and were operated at our institution from January 2009 to July 2016. During this period, we routinely took spine radiographs as well as hip radiographs in hip fracture patients at the initial study and follow-up evaluations.

Among the 1,554 patients, we excluded 433 patients; 36 patients aged < 50 years at the time of hip fracture diagnosis, five patients with pathologic fractures, 16 patients with high-energy trauma, 266 patients with poor quality or insufficient radiographs, and 110 patients who were not followed longer than 1 year.

The remaining 1,121 patients who were followed up for 1 year–9.5 years (mean, 3.0 years) after the initial hip fracture were subjects of this study.

We reviewed patients' age, gender, height, weight, body mass index (BMI), bone mineral density (BMD), type of the primary hip fracture; femoral neck fracture or intertrochanteric fracture, history of a previous vertebral fracture, type of osteoporosis medication after the initial hip fracture, compliance of osteoporosis medication, and medical comorbidities.

Bone mineral density was measured using dual-energy X-ray absorptiometry (Hologic Inc., Waltham, MA, USA). When T score was lower than -2.5, the patients was counted as osteoporotic. Osteoporosis medications were categorized into bisphosphonate versus selective estrogen receptor modulators (SERM) or others. Patient's compliance to the osteoporosis medication was calculated using the medication possession rate (MPR); prescription dates of osteoporosis medication/follow-up period [23]. The MPR was categorized into good (> 80%) and poor (< 80%). Medical comorbidities were scored using Charlson comorbidity index (CCI), which includes cardiovascular disease, cerebrovascular disease, heart failure, dementia, pulmonary disease, gastrointestinal disease, diabetes, renal disease, hematologic disease, liver disease, Acquired immunodeficiency syndrome, and cancer [24]. The CCI scores were divided into three groups: 0, 1, and ≥ 2. In addition, chronic renal disease and dementia were further analyzed. Ambulatory ability after hip surgery was assessed according to Koval's grade system, and the ambulatory status was defined as the best status after surgery during follow-up period [25].

Routine follow-up visits were scheduled for 6 weeks, 3, 6, 9, and 12 months, and every 6 months or 1 year thereafter. Patients who did not visit were contacted by telephone and were asked to return to clinic. All enrolled patients were insured by Health Insurance Review and Assessment (HIRA) service of South Korea. Thus, any patient's death was identified by retrieving e-medical record of the patient. Two independent observers, who did not participate in the index hip fracture surgery, reviewed medical records, and evaluated the radiographs. A diagnosis of new vertebral fracture(s) was made on follow-up medical records and spine radiographs.

Statistical analysis

We compared patients' demographics and other parameters between patients who had newly developed vertebral fractures (VF group) with those who did not have such fractures (non-VF group). Student's *t* test was used for the continuous parameters and the Chi square test for categorical parameters. Statistical significance was determined at two-tailed *p* value < 0.05. Multiple logistic regression analysis was done to identify risk factors for subsequent vertebral fractures in both unadjusted model and in adjusted model. In the latter model, variables including age, sex, BMI, fracture diagnosis, history of a previous vertebral fracture, osteoporosis medication, MPR, BMD, CCI, dementia, chronic renal failure, and Koval's grade were adjusted. Odds ratios (ORs) with

corresponding 95% confidence intervals (95% CI) were calculated. The survival was assessed using Kaplan–Meier analysis in VF group and non-VF group. Log-rank tests were done to evaluate the difference between the two groups. Multivariate Cox proportional hazard regression models were used to calculate the hazard ratio for death according to the presence of a newly developed vertebral fracture.

We used Stata/MP 15.0 (Stata Statistical Software: Release 15; StataCorp LLC, College Station, TX, USA) for the statistical analyses.

Results

Patients' characteristics

After the hip fracture surgery, 107 patients (107/1121, 9.5%) developed a new vertebral fracture during entire follow-up period in each patient, while 1,014 patients did not develop such fracture (Fig. 1). The overall cumulative incidence of subsequent vertebral fracture during follow-up periods was 9.5%. The incidence of subsequent vertebral fracture was 2.85% at 1 year, 3.18% at 2 years, 2.94% at 3 years, 3.91% at 4 years, and 5.75% at more than 5 years. There were significant differences in age, BMI and BMD between the two groups (Table 1). A total of 135 patients died after the surgery during the follow-up.

Risk factors of subsequent vertebral fractures

In unadjusted model, intertrochanteric fracture of the femur (OR, 1.72; 95% CI, 1.11–2.67; $p=0.015$), history of a previous vertebral fracture (OR, 3.19; 95% CI, 2.03–4.99; $p<0.001$), and lower lumbar spine BMD (OR, 3.72; 95% CI, 2.25–6.14; $p<0.001$) were risk factors for subsequent vertebral fractures. In adjusted model, history of a previous vertebral fracture (OR, 2.62; 95% CI, 1.58–4.36; $p<0.001$), MPR < 80% (OR, 1.92; 95% CI, 1.12–3.31; $p=0.014$), and lower lumbar spine BMD (OR, 2.58; 95% CI, 1.44–4.64; $p=0.001$) were the risk factors (Table 2).

Risk of death following hip fracture according to the presence of subsequent vertebral fractures

The mortality rate after a hip fracture was 22.12% (248/1121) during overall follow-up periods after postoperative 1 year. There was no significant difference in the mortality rates between the VF group and non-VF group (Fig. 2). Age ≥ 70 years (HR, 2.70; 95% CI, 1.05– 6.97; $p=0.039$), BMI < 18.5 kg/m^2 compared to ≥ 25.0 kg/m^2 (HR, 2.57; 95% CI, 1.01–6.57; $p=0.048$), and CCI ≥ 2 (HR, 2.04; 95% CI, 1.05–3.98; $p=0.036$) were risk factors of death after hip fractures. However, the development of a new vertebral fracture did not increase the risk of death (Table 3).

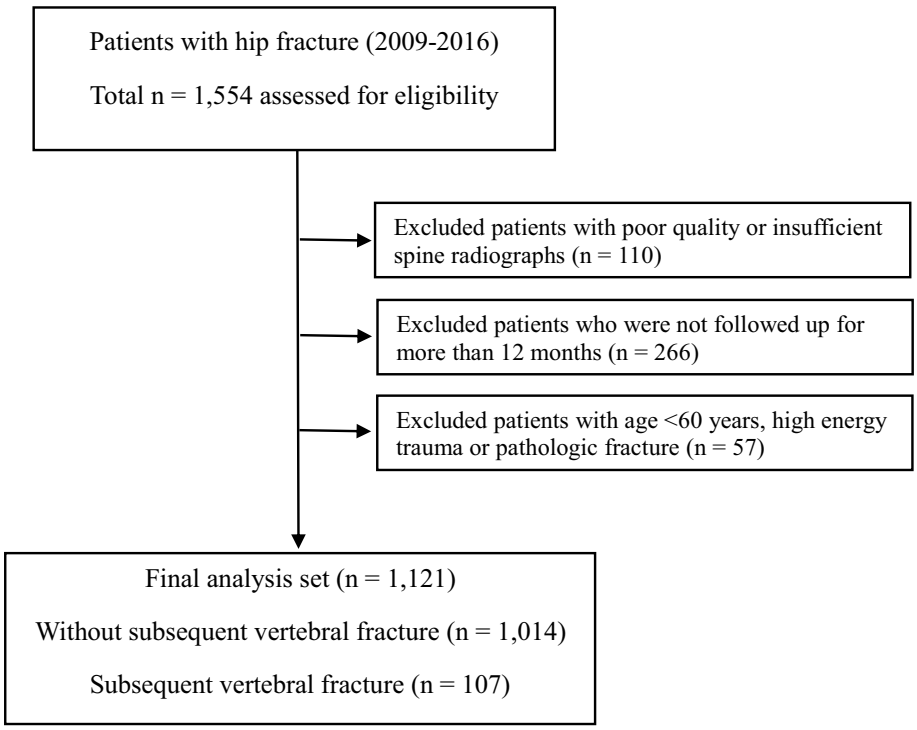

Fig. 1 Selection flow diagram

Table 1 Characteristics of the study population according to the presence of a subsequent vertebral fracture

Variables	Without new vertebral fracture ($n=1014$)	New vertebral fracture ($n=107$)	p value
Age, year	74.5 (60.2–94.5)	77.8 (61.2–91.9)	< 0.001
Age, *n* (%)			
50–59	91 (9.0%)	0 (0%)	0.007
60–69	173 (17.1%)	12 (11.2%)	
70–79	437 (43.1%)	53 (49.5%)	
≥ 80–89	313 (30.8%)	42 (39.2%)	
Gender, *n* (%)			
Male	264 (26.0%)	22 (20.6%)	0.217
Female	750 (74.0%)	85 (79.4%)	
Height, cm	158.4 (135.7–187)	156.3 (139–178)	0.004
Weight, kg	57.2 (34.9–102)	53.6 (29.8–86)	0.029
BMI, kg/m^2	22.7 (14.3–38.9)	21.9 (14.7–36.0)	0.037
Fracture diagnosis*			
Neck fracture	601 (59.3%)	49 (45.8%)	0.014
Intertrochanter fracture	413 (40.7%)	58 (54.2%)	
Previous vertebral fracture history[†]	283 (27.8%)	59 (55.1%)	< 0.001
Osteoporosis medication			
Bisphosphonate	838 (82.6%)	93 (86.9%)	0.459
SERM	19 (1.8%)	1 (0.9%)	
MPR[‡]			
< 80%	513 (50.6%)	61 (57.0%)	0.862
≥ 80%	501 (49.4%)	46 (43.0%)	
BMD			
Lumbar (T-score)	− 2.4 (− 6.3–3.1)	− 3.3 (− 5.7–[− 0.2])	< 0.001
T-score of lumbar ≤ − 2.5	489 (48.2%)	83 (77.6%)	< 0.001
Hip (T-score)	− 2.4 (− 6.8–0.5)	− 2.8 (− 4.6–[− 0.1])	< 0.001
T-score of hip ≤ − 2.5	487 (47.9%)	71 (66.4%)	< 0.001
CCI[§]	1.4 (0–10)	1.6 (0–9)	0.18
0	410 (40.4%)	35 (32.7%)	0.299
1	192 (18.9%)	23 (21.5%)	
≥ 2	412 (40.7%)	49 (45.8%)	
Dementia	115 (93.5%)	8 (6.5%)	0.221
Chronic renal disease	68 (93.2%)	5 (6.8%)	0.508
Koval's grade	3.05 (1–7)	3.20 (1–7)	0.579

Numeric parameters are presented as mean values, with ranges in parentheses

Categorical parameters are presented as counts, with percentages in parentheses

BMI body mass index; *SERM* selective estrogen receptor modulator; *MPR* medication possession rate; *BMD* bone mineral density; *CCI* Charlson's comorbidity index

*Diagnosis of a hip fracture according to its location on the femur

[†]History of a vertebral fracture prior to the hip fracture

[‡]The MPR represents the number of osteoporosis medication prescription days as a percentage of a year

[§]Charlson's comorbidity index score

[‖]The ambulatory status was defined as the best status after surgery during follow-up period

Discussion

Our study demonstrated that a history of a previous vertebral fracture, an MPR < 80%, and a lower lumbar spine BMD are risk factors for subsequent vertebral fracture(s). The subsequent vertebral fractures did not affect the mortality after hip fractures. To the best of our knowledge, our study is the first study to analyze the risk factors for subsequent vertebral fractures after hip fractures and the

Table 2 Univariate and multivariate analysis of risk factors for a subsequent vertebral fracture after a hip fracture

	Unadjusted			Adjusted*		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Fracture diagnosis						
Neck fracture	1			1		
Intertrochanter fracture	1.72	1.11–2.67	0.015	1.42	0.98–2.71	0.061
Previous vertebral fracture history[†]	3.19	2.03–4.99	< 0.001	2.62	1.58–4.36	< 0.001
Osteoporosis medication						
Bisphosphonate	1.35	0.70–2.59	0.369	1.06	0.48–2.36	0.885
SERM and others	0.67	0.07–6.03	0.718	0.52	0.05–5.97	0.599
MPR[‡]						
< 80%	1.29	0.83–2.01	0.249	1.92	1.12–3.31	0.014
≥ 80%	1					
BMD						
T-score of lumbar ≤ − 2.5	3.72	2.25–6.14	< 0.001	2.58	1.44–4.64	0.001
T-score of hip ≤ − 2.5	2.14	1.36–3.38	0.001	1.26	0.74–2.29	0.456
CCI[§]						
0	1			1		
1	1.41	0.77–2.58	0.268	1.17	0.58–2.37	0.651
≥ 2	1.39	0.85–2.28	0.192	1.30	0.74–2.29	0.362
Dementia	0.65	0.32–1.31	0.224	1.42	0.50–4.05	0.508
Chronic renal disease	0.75	0.32–1.77	0.510	1.11	0.33–3.72	0.862
Koval's grade[‖]	1.03	0.94–1.13	0.579	0.92	0.83–1.03	0.162

OR,Odds ratio; 95% *C*, 95% confidence interval, *SERM* selective estrogen receptor modulator; *MPR* medication possession rate; *BMD* bone mineral density; *CCI* Charlson's comorbidity index

*The adjusted model was adjusted for all variables, including age, sex, body mass index, fracture diagnosis, previous vertebral fracture history, osteoporosis medication, MPR, BMD, and CCI

[†]History of a vertebral fracture prior to the hip fracture

[‡]The MPR represents the number of osteoporosis medication prescription days as a percentage of a year

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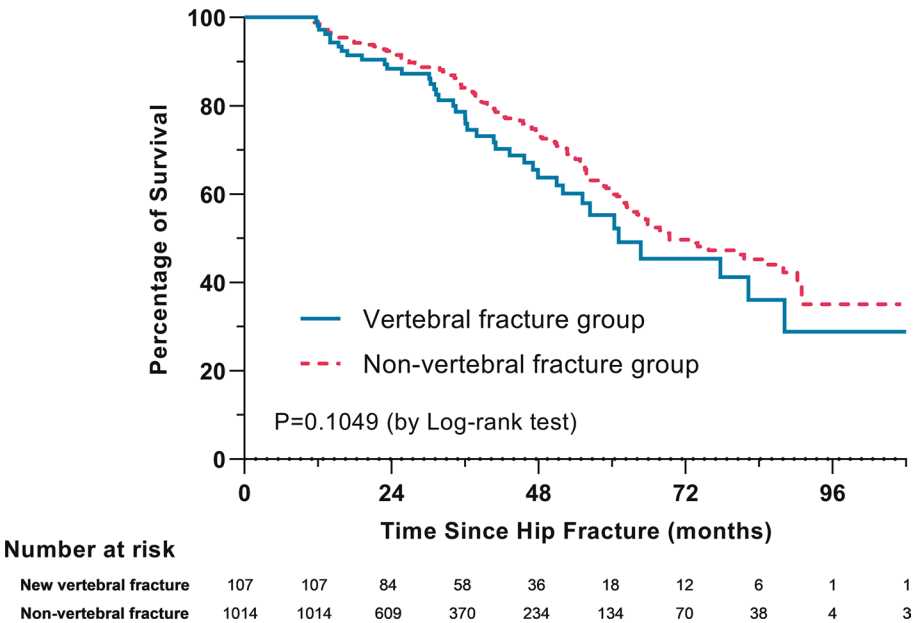

Fig. 2 Survival curve for mortality after hip fractures according to subsequent vertebral fractures

Table 3 Cox proportional hazard model for death after hip fracture in both groups

	Hazard ratio	95% CI	*p* value
Age			
< 70 yr	1		
≥ 70 yr	2.70	1.05–6.97	0.039
Sex			
Male	1.37	0.69–2.70	0.366
Female	1		
BMI*			
Underweight	2.57	1.01–6.57	0.048
Normal	1.83	0.84–4.00	0.129
Obese	1		
Presence of subsequent vertebral fractures	0.70	0.37–1.33	0.281
Fracture diagnosis[†]			
Neck fracture	1		
Intertrochanter fracture	1.38	0.78–2.45	0.262
Previous vertebral fracture history[†]	1.40	0.78–2.50	0.256
Osteoporosis medication	1.21	0.48–3.03	0.688
MPR[‡]			
< 80%	1.39	0.76–2.55	0.285
≥ 80%	1		
BMD			
T-score of lumbar ≤ − 2.5	0.77	0.41–1.45	0.417
T-score of hip ≤ − 2.5	1.66	0.84–3.27	0.142
CCI[§]			
0	1		
1	1.68	0.74–3.80	0.211
≥ 2	2.04	1.05–3.98	0.036

95% *CI* 95% confidence interval; *BMI* body mass index; *MPR* medication possession rate; *BMD*, bone mineral density; *CCI* Charlson's comorbidity index

*According to the BMI, patients were categorized as underweight (< 18.5 kg/m^2), normal (18.5–24.9 kg/m^2), and obese (≥ 25.0 kg/m^2)

[†]History of a vertebral fracture prior to the hip fracture

[‡]The MPR represents the number of osteoporosis medication prescription days as a percentage of a year

[§]Charlson's comorbidity index score

effect of the subsequent vertebral fractures on the mortality after hip fractures.

The incidence of vertebral fractures and that of hip fractures have been increasing worldwide, in accordance with the global trend of aging [4, 6, 26–28]. Patients suffering an osteoporotic fracture have a high risk of subsequent fractures [14, 18, 19]. To date, only one study has investigated the incidence of subsequent vertebral fractures after hip fractures [19]. In a nationwide register-based study from Denmark, 10-year cumulative incidence of subsequent vertebral fractures after hip fractures was 3.1% in men and 4.7% in women [19]. In our study, the incidence of subsequent vertebral fractures was 9.5%, which is much higher than that of the Danish study. Differences in ethnic, the time of patient enrollment and study design might explain the difference in the incidence of subsequent vertebral fracture between the previous Danish study and our study.

In our study, risk factors for subsequent vertebral fractures after hip fractures were previous history of vertebral fractures, a low lumbar BMD, and a low MPR. Our results complied with the results of previous studies [18, 22, 29]. There are many factors that affect the occurrence of subsequent fractures. It is of greatest importance to avoid osteoporotic fractures, but it is also important to prevent subsequent fractures. One of the most important factors for reducing the risk of subsequent fractures is the treatment of osteoporosis [17, 18, 30, 31]. In our study, risk factors for subsequent vertebral fractures after hip fractures included previous vertebral fractures, a low lumbar BMD, and non-continuous osteoporosis treatment. Our results were similar to those of previous studies. In a previous

study, patients with subsequent vertebral fractures had a history of a major osteoporotic or a prior vertebral fracture and most of them were not treated with any anti-osteoporosis medication [18]. In the comparisons between the anti-osteoporosis medications, parathyroid hormone was the most effective treatment for decreasing subsequent vertebral fracture, with high quality of evidence [32]. The anti-osteoporosis treatment with bisphosphonate, denosumab, and SERMs were also effective for preventing subsequent vertebral fracture [32]. Among bisphosphonate and SERMs, zoledronate showed the lowest relative risk (RR, 0.34; 95% CI, 0.17–0.69) compared other bisphosphonates (alendronate: RR, 0.54; 95% CI, 0.43–0.68; risedronate: RR, 0.61; 95% CI, 0.51–0.73; etidronate: RR, 0.50; 95% CI, 0.29–0.87; ibandronate: RR, 0.52; 95% CI, 0.38–0.71) and SERMs (raloxifene: RR, 0.58; 95% CI, 0.44–0.76; bazedoxifene: RR, 0.66; 95% CI, 0.53–0.82) [32]. Thus, continuous osteoporosis treatment with bisphosphonates and SERMs is important for the prevention of subsequent vertebral fractures after hip fractures.

Hip fractures are associated with high mortality rate after the fracture. In a study from South Korea, the mortality rate within the first year after a hip fracture was 21% in men and 15% in women [6]. The 1-year mortality rate after a hip fracture was higher than the mortality after a vertebral fracture (13.6% in men and 5.5% in women) [4]. In our study, the mortality after a hip fracture was 22.12% (248/1121) during overall follow-up periods, which was similar or slightly lower than the mortality rates of previous studies [33–36].

This study has several limitations. First, it was a retrospective study including single institution. Second, the preventive effect of various anti-osteoporosis medications could not be assessed. Over 80% of our patients were treated with bisphosphonate, while only 2% of them were treated with SERM or other medications. Because of the low rate of SERM treatment and no difference between the two groups, we focused on the MPR for anti-osteoporosis treatment. Third, the mortality rate may have been underestimated. Although we performed telephone interviews for all patients, we could not confirm death in some patients due to lost contact details (censored).

In conclusion, it is of crucial importance to prevent subsequent fracture in hip fracture patients. In our study, previous vertebral fractures, a low BMD, and low MPR were risk factors for developing subsequent vertebral fractures after a hip fracture. The use of anti-osteoporosis medication is a modifiable risk factor. We recommend active and continuous osteoporosis medications to prevention subsequent vertebral fractures after hip fractures.

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Compliance with ethical standards

Conflict of interest The authors have no disclosures to declare.

Ethics statement Our study protocol was approved by the institutional review board of our hospital (B-1907/552-101). The requirement for informed consent was waived by the review board due to the retrospective nature of the study.

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