Risk factors for subsequent vertebral fractures following acute osteoporotic vertebral fractures: a prospective single-center study of consecutive patients

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INTRODUCTION:

Preventing subsequent vertebral fractures following an initial osteoporotic vertebral fracture (OVF) is essential for osteoporosis management. These fractures often occur within five years, especially in the first year, and are associated with decreased quality of life, impaired function, and poor clinical outcomes. However, prospective studies investigating risk factors for subsequent fractures in OVF patients remain limited. This study aimed to identify factors associated with subsequent vertebral fractures within five years following an initial OVF in consecutive patients treated conservatively.

METHODS:

This is prospective, single-center study. Consecutive patients of 896 diagnosed with acute OVFs and treated conservatively between January 2017 and December 2023 were included. Patients were eligible for the study if they underwent conservative management with either soft or hard braces. Patients were divided into two groups based on the occurrence of a subsequent fracture within five years following the initial OVF: the subsequent fracture group and the non-subsequent fracture group. Exclusion criteria were: (1) prior thoracic or lumbar surgery, (2) pathological fractures due to tumors or multiple myeloma, and (3) patients in the non-subsequent fracture group failed to follow up at least five years after the initial OVF. Demographic data and anthropometric characteristics data (age, sex, weight, height, and body mass index (BMI)), smoking and alcohol use history, presence of diabetes mellitus, and use of osteoporosis medications prior to the initial OVF were collected. Bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry (DEXA) and evaluated as the young adult mean (YAM) for the spine and femur. Laboratory data included total protein (TP), albumin (Alb), calcium (Ca), Alb-corrected Ca, phosphorus (P), alkaline phosphatase (ALP), procollagen type 1 N-terminal propeptide (P1NP), and tartrate-resistant acid phosphatase 5b (TRACP-5b). We compared demographic data, BMD, and laboratory data between the subsequent and non-subsequent fracture groups using an unpaired t-tests or chi-squared tests. Variables with $p < 0.05$ in univariate analysis were included in multivariate logistic regression analysis. In addition, factors previously reported as risk factors for subsequent fractures after an initial OVF (including age and sex) were set as dependent variables in multivariate logistic regression analysis.

RESULTS:

Among the 896 patients included in the study, 79 (8.8%) had a subsequent fracture during the 5-year follow-up. Finally, 72 patients in the subsequent fracture group and 94 patients in the non-subsequent fracture group were included in the comparative analysis (Figure 1). On univariate analysis, the subsequent fracture group showed significantly higher height (152.4 vs. 149.8 cm, $p = 0.020$) and Alb-corrected Ca (9.5 vs. 9.4 mg/dL, $p = 0.013$) than the non-subsequent fracture group. Furthermore, a significantly higher number of patients in the subsequent fracture group didn't underwent osteoporosis medication after the initial OVF compared to the non-subsequent fracture group ($p = 0.003$). No significant differences were observed between the groups in other demographics, BMD, or laboratory data (Table 1). On multivariate logistic regression analysis, age, sex, height, osteoporosis medication after the initial fracture, and Alb-corrected Ca were set as dependent variables. As a result, osteoporosis medication after the initial fracture (aOR = 0.294, $p = 0.022$) and elevated Alb-corrected Ca levels (aOR = 3.375, $p = 0.013$) were significantly associated with subsequent fractures occurring within 5 years after the initial OVF (Table 2).

DISCUSSION AND CONCLUSION:

This prospective study identified two independent risk factors of subsequent fractures occurring within five years: lack of osteoporosis medication after the initial OVF and elevated Alb-corrected Ca. Importantly, our analysis revealed that prior use of osteoporosis medications and a history of fragility fractures were not associated with the risk of subsequent fractures. These findings suggest that the appropriate initiation of osteoporosis treatment after acute OVF plays a critical role in preventing subsequent fractures, regardless of fragility fracture history, and patients had risk of subsequent fractures with the same management prior to initial OVF. Although the association between elevated Alb-corrected calcium levels and subsequent fractures was statistically significant, this finding should be interpreted carefully. It may indicate increased bone turnover, including enhanced resorption or impaired remodeling. Further studies are needed to better understand this association.

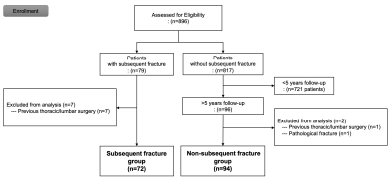

Table 1. Univariate comparisons of variables between groups defined by subsequent fracture.

	Subsequent fracture group N=72	Non-Subsequent fracture group N=94	p-value
Age (years)	75.4 ± 8.4	76.8 ± 8.3	0.221‡
Sex (female / male; n)	58 / 14	83 / 11	0.167†
Height (cm)	152.4 ± 7.1	149.8 ± 7.5	**0.020**‡
Weight (kg)	52.8 ± 9.8	53.0 ± 7.1	0.840‡
BMI (kg/m^2)	22.8 ± 4.2	23.4 ± 3.1	0.278‡
Smoking history (n)	7	3	0.080†
Alcohol consumption history (n)	12	23	0.222†
Diabetes mellitus (n)	6	7	0.833†
History of fragility fractures (n)			0.670†
Spine	24	29	
Others	16	17	
Non	32	48	
Taking osteoporosis medication before the initial fracture (Yes / No; n)	18 / 54	25 / 69	0.816†
Taking osteoporosis medication after the initial fracture (Yes / No; n)	55 / 17	87 / 7	**0.003**†
BMD			
YAM value: Lumbar (%)	71.7 ± 18.0	74.2 ± 15.8	0.357‡
YAM value: Femur (%)	68.5 ± 13.5	68.0 ± 13.9	0.832‡
Laboratory data			
TP (g/dL)	7.0 ± 0.6	7.0 ± 0.4	0.688‡
Alb (g/dL)	4.2 ± 0.4	4.2 ± 0.2	0.236‡
Ca (mg/dL)	9.4 ± 0.4	9.4 ± 0.4	0.210‡
Alb-corrected Ca (mg/dL)	9.5 ± 0.3	9.4 ± 0.4	**0.013**‡
P (mg/dL)	3.6 ± 0.5	3.43 ± 0.5	0.219‡
ALP (U/L)	278.5 ± 159.3	323.03 ± 155.7	0.074‡
P1NP (ng/mL)	67.3 ± 37.9	63.72 ± 30.7	0.709‡
TRACP-5b (mU/dL)	415.4 ± 183.4	398.20 ± 182.8	0.551‡

‡: Unpaired t test, †: chi-square test; Bolded P-values indicate statistical significance.

BMI, body mass index; BMD, Bone mineral density; YAM, young adult mean ; TP, total protein; Alb, albumin; Ca, calcium; P, phosphorus; ALP, alkaline phosphatase; P1NP, procollagen type 1 N-terminal propeptide; TRACP-5b, tartrate-resistant acid phosphatase 5b.

Table 2. Multivariate logistic regression analysis for subsequent fracture

Objective variable: subsequent fracture occurring ≤ 5 years after the initial OVF				
Explanatory variables	Reference	aOR	p-value	95% CI
Age	–	0.968	0.187	0.922 – 1.016
Sex	female	0.962	0.950	0.287 – 3.228
Height	–	1.045	0.148	0.985 – 1.109
Taking osteoporosis medication after the initial fracture	No	0.249	0.007*	0.090 – 0.686
Alb-corrected Ca	–	3.096	0.018*	1.212 – 7.909

*: p<0.05

OVF, osteoporotic vertebral fracture; aOR, adjusted odds ratio; Alb, albumin; Ca, calcium; CI, confidence interval