ORIGINAL ARTICLE

EVALUATION OF MORTALITY AND MORBIDITY ASSOCIATED WITH OSTEOPOROTIC HIP FRACTURE

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Abstract

Introduction: Hip fractures in older adults are associated with significant morbidity, mortality, loss of independence, and financial burdens. In this study, we assessed how factors influenced these effects in elderly patients presenting with hip fractures.

Materials and Method: A prospective observational study was conducted over six months on all patients with fall and hip fractures above 50 years of age who presented to the orthopedics and traumatology clinic of our university hospital. Ambulation status, time until operation, vitamin D level, vertebral fractures, Charlson comorbidity index, and Fracture Risk Assessment Tool score were recorded. The patients' re-evaluated in the sixth month after the fracture. The relationship between death and risk factors was examined by regression analysis.

Results:105 patients were included in the study. The mortality rate was 23.8%. The immobility rate also increased from before the operation to after 1.9% to 31.4%. Univariate regression analysis showed that mortality is related to age, Charlson comorbidity index, smoking history, and Fracture Risk Assessment Tool hip score. At the same time, multivariate regression analysis revealed an association between body mass index, smoking history, and mortality.

Conclusion : Osteoporosis is a widespread disease that may remain hidden until complications, such as fractures, present themselves. Functional loss and mortality risk are high in patients with fractures. Age, Charlson comorbidity index, body mass index, smoking, Fracture Risk Assessment Tool hip score, and pre-fracture ambulation status affect mortality. A decrease in mortality can be achieved by monitoring risky individuals in fracture liaison services.

Keywords: Risk factors; Mortality; Osteoporosis; Hip fractures.

INTRODUCTION

One of the most critical complications of osteoporosis is hip fracture. Low trauma is the leading cause of osteoporotic hip fracture for more than half of the patients, with the rate increasing with age. It has been reported that between 8.4% and 36% of patients die within the first year after the development of the fracture (1). In addition, the ambulation of patients deteriorates after fracture and some even become in need of care. After 1 year, 40% of the patients could not walk independently. Despite increased economic costs and morbidity due to osteoporotic fracture, only 20% of patients receive antiresorptive therapy (2). Therefore, fracture liaison services (FLS) have been used worldwide to treat individuals with osteoporotic fractures, determine fracture risks in patients, and promote the pharmacological and non-pharmacological treatment of osteoporosis. FLS are structures created to include individuals with osteoporotic fractures in a secondary fracture protection program after surgery. They are generally created in tertiary care hospitals and enable many healthcare professionals to follow up and treat patients in a coordinated manner. Thus, the number of patients treated and compliance with treatment increases, and the risk of re-fractures and mortality decreases. Clinical, medical, and laboratory evaluation is indicated in all adults with osteoporotic fractures.

The primary acute treatment for osteoporotic hip fracture is surgery, recommended in the early period of the incident. Although early surgery after the fracture seems to lower mortality, there are still conflicts about delayed surgery time. Apart from mortality, functional outcomes are better in patients who undergo early surgery (3). In addition, gender, age, pre-fracture ambulation status, and comorbidities also affect mortality. The Charlson comorbidity index (CCI) is a validated index that calculates the comorbidities and predicts the risk of death. The index consists of 19 items corresponding to different medical comorbid conditions. A CCI score above 0 was associated with an increased risk of severe disease and death when controlled for age and sex.

Active vitamin D plays an essential role in calcium absorption and bone health. It is also crucial in balance, fall prevention, and muscle strength. If the vitamin D level is 20 ng/ml and below, it indicates deficiency, and if it is between 20 and 30 ng/ml, it indicates insufficiency. It has been shown that there is a significant relationship between low vitamin D levels and hip fractures. Vitamin D levels were found to be low in 96% of individuals who had hip fractures, and it was found to be below 9 ng/ml in 38% (4).

The most common fracture in osteoporosis is vertebral fracture. Even if the bone mineral density (BMD) measurement is standard, having a vertebral fracture is a high-risk indicator for other fractures. Since vertebral fractures may be clinically silent, they may not be detected unless spinal imaging is performed. Former or follow-up shortening may be an indication of vertebral fracture. It is recommended that patients be screened by performing vertebral fracture assessment (VFA) with lateral spinal view direct X-ray or DXA (5).

Fracture Risk Assessment Tool (FRAX) determines fracture risk in patients and includes many risk factors independent of BMD. It determines the 10-year risk of hip and major osteoporotic fractures (i.e., clinical vertebra, hip, forearm, and humerus) and guides the treatment decision. FRAX may be associated with mortality because it contains many risk factors and may indicate osteoporosis and vascular calcification (6). Smoking causes osteoporosis by directly affecting the bone metabolism of cadmium and indirectly by affecting the endogenous estrogen metabolism. Active smokers are at higher risk than those who quit. Smoking cessation for more than 10 years reduces the risk of hip fracture. In addition, a significant correlation was found between smoking and mortality in individuals with osteoporotic hip

fractures (2, 7).

Our study aimed to examine hip fractures and their outcomes in elderly patients in a tertiary care hospital in Turkey. Although risk factors for fracture are well defined, outcomes of patients with hip fractures are still a subject that merits further research.

PATIENTS AND METHOD

A prospective observational study was conducted between June 2019 and December 2019 on all patients who presented to the orthopedics and traumatology clinic with osteoporotic hip fractures above the age of 50. The subjects were followed up for up to 6 months. Patient data were obtained from the patient file and by contacting the patient by phone. All patients over 50 who had a hip fracture because of low trauma and agreed to participate were included in the study.

The study was approved by the Faculty of Medicine Ethics Committee (18-11.1T/10) and was conducted following the Declaration of Helsinki. All participants in the study provided written informed consent to this work and agreed to the scientific use of their data.

Demographic data and clinical assessment

The patients were evaluated at hospitalization and 6 months after hip fracture. Age, gender, height, weight, education level, patient's pre-fracture ambulation status, length of hospital stay, FRAX hip, and FRAX total values, time until the operation, type of operation, vitamin D level, vertebral fractures, smoking, and CCI score were noted at the time of hospitalization for osteoporotic hip fracture. Six months after the hip fracture, the patients were reassessed for mortality, ambulation status, and newly developed osteoporotic fracture. We assessed mobility limitations, which is the most common morbidity after hip fractures. Patients were questioned regarding their need for assistive devices. Ambulation statuses were classified as immobile, needs ambulatory support indoors, needs ambulatory support outdoors, and independently mobile.

For vitamin D levels, the 25-OH vitamin D measurement was evaluated; those patients with below 20 ng/ml were considered vitamin D deficient, and those with between 20 and 30 ng/ml were considered vitamin D insufficient. The radiologist evaluated the lateral spinal view according to the presence of fracture in terms of vertebral fracture, and patients with fractures were classified according to semiquantitative staging. FRAX score calculation was evaluated according to risk factors without bone mineral density. The CCI is a simple, easy-to-perform, and valid method to estimate the risk of death related to comorbid diseases. Classical CCI includes 19 medical conditions weighted 1–6 with total scores ranging from 0 to 33.

Statistical Analysis

IBM SPSS Statistics performed statistical analyses for the Windows 25.0 (IBM Corp., Armonk, NY) package program. The level of significance was determined as α=0.05 in all analyses. Numerical data were summarized as mean, standard deviation, median, and minimum and maximum values, and categorical data were summarized by frequency and percentage.

The primary outcome variable was mortality at the 6-month follow-up. Age, gender, body mass index (BMI), length of hospital stays, time until the operation, type of operation, FRAX hip and FRAX total values, smoking, vitamin D level, fracture presence in lateral vertebral view and CCI were first evaluated using univariate logistic regression analysis. Variables with significance below 0.25 in univariate logistic regression analyses were determined to be candidate variables for the multivariate model. Logistic regression results were given with odds ratios and 95% confidence intervals for these ratios.

The change in pre-fracture and post-fracture 6-month ambulation status were examined using the Wilcoxon signed-rank test. The effect of preoperative ambulation status on mortality was determined with the help of Fisher's exact test.

RESULTS

The study included 105 patients: 79 females and 26 males. The mean age was 77.85. Twenty-five (23.8%) patients were found deceased within 6 months; 4% of deaths occurred during hospitalization, 24% in the first month after discharge, and 72% between 2 and 6 months.

The demographic findings of the patients are summarized in Table 1, and the clinical features of the patients are summarized in Table 2.

Forty-nine percent of patients were already using assistive devices before the fracture, but the requirement for use increased to 92%. Moreover, the immobility rate increased from 1.9% to 31.4%. Thirty-six percent of the patients were mobile independently before the fracture, and only 15% were independently ambulatory in the sixth month after the fracture. The ambulation status of the patients and the use of assistive devices are shown in Table 3. When the change in ambulation status between pre-fracture and post-fracture at 6 months was examined, worsening was observed in 58.1% of the patients ($p<0.001$).

In the univariate regression analysis, age, FRAX hip score, smoking, and CCI showed a statistically significant relationship with mortality ($p < 0.05$; Table 4). Variables with $p < 0.25$ in the univariate logistic regression analysis were analyzed with a multivariate model. In multivariate regression analysis, the relationship between elevated BMI, smoking, and mortality was statistically significant ($p < 0.05$; Table 5). Vertebral fracture distribution could not be analyzed because it was irregular.

The relationship between patients' pre-fracture ambulation status and mortality was examined;

Table 1. Demographic findings

Age (yr), mean ± *SD*	77.85 ± 9.94
Gender, *n* (%)	**Female:** 79 (75.3%) **Male:** 26 (24.7%)
Educational status, *n* (%)	**Illiterate:** 22 (21.2%) **Literate:** 3 (2.9%) **Primary education:** 63 (60.6%) **High school:** 7 (6.7%) **University:** 9 (8.7%)
BMI (kg/m^2), *n* (%)	**Underweight (<18.5):** 3 (2.9%) **Normal (18.5–24.9):** 35 (33.3%) **Overweight (25–29.9):** 39 (37.1%) **Obese (>30):** 28 (26.7%)
Smoking, *n* (%)	**Never smoked:** 70 (66.7%) **Quit:** 28 (26.7%) **Active smoker:** 7 (6.7%)
Alcohol consumption, *n* (%)	**Never drank:** 100 (95.2%) **Quit:** 4 (3.8%) **Active alcohol drinker:** 1 (1%)
Osteoporotic fractures before hip fracture, *n* (%)	**No:** 73 (69.5%) **Yes:** 32 (30.5%) **Clinical vertebral fracture:** 5 (13%) **Hips:** 11 (29%) **Forearm:** 8 (21%) **Proximal humerus:** 8 (21%) **Others:** 6 (16%)
Pre-fracture osteoporosis treatment, *n* (%)	**Bisphosphonate:** 9 (8.5%) **Denosumab:** 2 (1.9%) **Teriparatide:** 0
Use of vitamin D, *n* (%)	**None:** 100 (95.3%) **Yes:** 5 (4.7%)
Use of calcium supplements, *n* (%)	**None:** 96 (91.5%) **Yes:** 9 (8.5%)

Note. BMI, body mass index; n, number; SD, standard deviation.

Table 2. Clinical features

Survival at 6 months, *n* **(%)**	**Alive:** 80 (76.2%) **Dead:** 25 (23.8%) - **Men:** 7 (30% of men) - **Women:** 18 (22.8% of women)
Time of death, *n* **(%)**	**During hospitalization:** 1 (4%) **1 month:** 6 (24%) **2–6 months:** 18 (72%)
Type of operation, *n* **(%)**	**Total hip replacement:** 3(2.8%) **Endoprosthesis:** 38(36.2%) **Proximal femoral nail:** 58(55.2%) **Others:** 6(5.8%)
Time until operation (days), median (min–max)	4 (1–25)
Length of hospital stay (days), mean ± *SD*	7.73 ± 3.21
New fracture development after fracture, *n* **(%)**	**None:** 98 (93.4%) **Yes:** 7 (6.6%)
Control vertebral radiographs, *n* **(%)**	**None:** 56 (53.3%) **Yes:** 49 (46.7%)
Osteoporotic fracture on vertebral radiographs, *n* **(%)**	**None:** 5 (10.2%) **Yes:** 44 (89.8%)
Fracture stage (semiquantitative classification), *n* **(%)**	**Stage 1:** 32 (72.7%) **Stage 2:** 4 (9.1%) **Stage 3:** 8 (18.2%)
Vitamin D level (ng/ml), *n* **(%)**	**<10 ng/ml:** 33 (35.9%) **10–19 ng/ml:**23 (25%) **20–29 ng/ml:** 14 (15.2%) **≥30 ng/ml:** 22 (23.9%)
Vitamin D level (ng/ml), Median (Min–Max)	16 (3–77)
CCI, median (min–max)	5 (1–12)

Note. CCI, Charlson comorbidity index; n, number; SD, standard deviation.

Table 3. Ambulation status and assistive device use

	Pre-fracture	**6-month control**
Use of assistive devices	**None:** 50.5% **Yes:** 49.5%	**None:** 8% **Yes:** 92%
Ambulatory status	**Immobile:** 1.9% **Needs ambulatory support indoors:** 39% **Needs ambulatory support outdoors:** 22.9% **Independent ambulation**: 36.2%	**Immobile:** 31.4% **Needs ambulatory support indoors:** 42.9% **Needs ambulatory support outdoors:** 10.5% **Independent ambulation** 15.2%

Table 4. Univariate regression analysis of mortality

Variable	OR	95% confidence interval		p
		Lower	Upper	
Age	1.091	1.020	1.166	0.011
Gender (male)	1.167	0.425	3.200	0.765
BMİ	1.079	0.994	1.172	0.070
Time of operation	1.001	0.964	1.039	0.971
Length of hospital stay	1.081	0.946	1.235	0.251
FRAX major osteoporotic fracture	1.041	0.999	1.085	0.055
FRAX hip fracture	1.062	1.003	1.125	0.038
Smoking history	2,856	1,132	7,206	0,026
Vitamin D level	1,011	0,982	1,041	0,457
Vitamin D <10 ng/ml	1,024	0,284	3,688	0,971
Vitamin D 11–19 ng/ml	0,889	0,217	3,643	0,870
Vitamin D 20–29 ng/ml	0,533	0,088	3,235	0,494
CCI	1.507	1.120	2.028	0.007

Note. BMI, body mass index; CCI, Charlson comorbidity index; FRAX, Fracture Risk Assessment Tool; OR, odds ratio.

Table 5. Multivariate regression analysis of mortality

Variable	OR	95% confidence interval		p
		Lower	Upper	
Age	1.074	0.979	1.179	0.130
BMI	1.125	1.007	1.256	0.037
FRAX major osteoporotic fracture	0.997	0.853	1.165	0.969
FRAX hip fracture	1.080	0.882	1.323	0.456
Smoking	7,686	1,760	33,562	0,007
CCI	1.386	0.975	1.971	0.069

Note. BMI, body mass index; CCI, Charlson comorbidity index; FRAX, Fracture Risk Assessment Tool; OR, odds ratio.

50% of pre-fracture immobile patients died. This rate was found to be 34% in patients who needed ambulatory support indoors before the fracture, 25% in patients who needed ambulatory support outdoors, and 10.5% in those who ambulated independently. The better pre-fracture ambulation status is related to a lower post-fracture mortality risk with a low correlation (0.256).

DISCUSSION

In this prospective, single-center cohort study, patients operated on for osteoporotic hip fracture were followed up for 6 months, and mortality, changes in ambulation status, and factors affecting mortality were investigated. Even in the first months after osteoporotic hip fractures, mortality rates

were high. In this study, 25 patients died in the first 6 months. Deceased patients constituted 23.8% of all participants. In a study conducted in Spain, the 6-month mortality was 23%, whereas a study from Italy showed a relatively low rate of 14.1% (8, 9). The cause of the low outcomes may be related to including patients who underwent surgery and those who followed conservatively. The mean hospital stay of the patients is 7.7 days. Mortality increases in hospitalizations lasting less than 10 days (10). In patients who are discharged in a short time after the operation, rehabilitation, osteoporosis treatment, and management of postoperative complications may be lacking, which may have led to an increase in mortality. In addition, since the study was conducted in a tertiary hospital, patients referred from secondary hospitals due to the high risk of surgery constitute some of our patients. Surgery on individuals with multiple risk factors may have been another reason for the increase in mortality.

Age is a possible risk factor for mortality in osteoporotic hip fractures. Elderly patients may suffer higher mortality rates. According to the results of this study, each 1-year increase in age raises the risk of death by 9.1%. However, age was not significant when included in the multivariate regression analysis. Although older age was a possible risk factor for death after a hip fracture, we could not find any strong evidence for older age as a risk factor for death after a hip fracture. The higher number of comorbidities in elderly patients affects mortality. It has been reported that heart failure, family history of hip fracture, and pre-fracture ambulation status interact with age and may affect mortality rates (8, 9). Male gender is a risk factor for mortality (8). Twenty-four percent of our patients were men, and 30% of the male and 22% of the female patients died in the first 6 months. Although mortality was higher in male patients, it was not statistically significant. In addition to the male gender, many factors, such as the patient's clinical condition, age, comorbidities, fracture type, type of surgery, length of hospitalization, and complications, can affect mortality (11).

Another affecting factor for osteoporotic hip fracture related to mortality is BMI. In the current literature, hip fracture seems less familiar in obese individuals than in standard and low weights. Some studies have shown that the risk of osteoporotic fractures increases with an increase in BMI. This association is partially explained by worse physical function in obese men (12). Modig et al. found that a BMI below 22 kg/m^2 is associated with higher mortality, called the obesity paradox (13). The study consisted of 8% obese and 26.9% overweight patients. Although complications are higher in obese or overweight patients, mortality rates are lower (14). In this study, in contrast to the literature, mortality was higher in patients with higher BMI. Each unit increase in BMI increases the risk of death by 12.5%. Compared with Modig et al., obese and overweight patients constituted a higher rate (26.7% were obese, and 37% were overweight). Metabolic syndrome and related complications seem more common in people with high-level BMI. Due to the high patient burden, the patients stayed in the hospital for a shorter period, so the complications that developed in the patients may not have been well managed. As a result, an increase in mortality may have been observed in people with high BMI.

The median time until the operation of our patients is 4 (1–25) days. No significant interaction was found when looking at its relationship with mortality. Surgery is recommended in the early period after osteoporotic hip fracture. Mortality is lower in patients who undergo surgery within the first 24 to 48 hours. Some studies found no increase in mortality due to a delayed operation (3, 15). Current guidelines recommend early surgery for patients with hip fractures (16). If the patient has an additional condition that requires treatment before surgery, there may be an increase in mortality by performing surgery without treating the problem

(17). Delaying the operation due to the treatment of comorbid medical conditions of our patients may have prevented an increase in mortality. The mean hospital stay of our patients was 7.73 ± 3.21 days. No significant interaction was found when looking at its relationship with mortality. Patient discharge in fewer than 10 days is associate with mortality (10). Since most of our patients were discharged in fewer than 10 days, the relationship between the length of hospital stay and mortality may not have been observed.

FRAX indicates fracture risk. Because the mortality rate increases in individuals with fractures, we aimed to evaluate the relationship between mortality and FRAX score. This study calculated that the probability of death increased as the FRAX hip fracture probability increased, and each unit increase in the FRAX hip score increased the risk of death by 6.2%. No significant relationship was found when the FRAX hip score was included in the multivariate regression analysis. Although the FRAX hip score was a possible risk factor for death after a hip fracture, we did not find any strong evidence for the FRAX hip score as a risk factor for death after a hip fracture. In a study conducted on patients with end-stage renal disease, FRAX major osteoporotic fracture risk was associated with mortality. FRAX may also be associated with mortality because it contains many risk factors and may indicate osteoporosis and vascular calcification (6).

Control vertebral radiographs of 46.7% of our patients could be taken. Vertebral collapse fracture was found in 89.8% of the patients who had radiographs; 73% of the fractures are Stage 1, 9% are Stage 2, and 18% are Stage 3 fractures. A retrospective study conducted in Japan found a compression fracture in the vertebrae in 78% of individuals with a history of hip fracture, like our study. Mortality was higher in patients with vertebral compression fractures (18). In a study conducted in Ireland, vertebral fractures were detected in 40% of osteoporotic hip fracture patients who underwent vertebral imaging. There was no significant relationship between mortality and the presence of vertebral fractures (19). In our study, however, a relationship between vertebral fracture and mortality could not be examined due to data distribution. Vertebral imaging could not be performed in all patients due to patient density and additional health problems. Since all our patients could not be evaluated, a significant relationship between mortality and vertebral fracture may not have been evaluated.

The mean vitamin D level of the patients was found to be 16 ng/ml. While 24% of the patients have normal vitamin D levels, 15.2% have vitamin D insufficiency, and 60.9% have a vitamin D deficiency. Considering the effect on mortality, no significant interaction was observed in the regression analysis. A study conducted in South Korea reported that 76.5% of individuals who had osteoporotic hip fractures had low vitamin D levels and that there was a relationship between low vitamin D and mortality. However, there was no independent risk factor (20). Vitamin D levels were low in 96% of individuals with osteoporotic hip fractures in the USA and 47% in Norway (21). This difference may have been observed in the patient population for many reasons, such as the study's season of the year, geographical location, diet, and use of food supplements.

In this study, 33.4% of the patients had a smoking history. Cigarette consumption causes a decrease in BMD. Although the mechanism is unclear, it causes a decrease in BMD, since calcium absorption from the intestines decreases by affecting serum estradiol, vitamin D, and PTH levels with cigarette consumption (22). Solbakken et al. found that 24.6% of patients with hip fractures had a smoking history, and there was a significant relationship between smoking and mortality (23). In the study of Bliuc et al., in which the factors affecting mortality due to osteoporotic hip fracture were examined, smoking was associated with mortality (2). Our study found

a significant relationship between smoking history and mortality. If the patient with a hip fracture smoked, the probability of death was 2.9 times higher. When other variables are kept constant, if a patient has a smoking history, the mortality risk increases 7.770 times compared to individuals without a smoking history.

CCI was used to calculate the morbidity risk in patients. This index estimates mortality according to comorbid conditions in patients. Each unit increase in CCI increases the risk of death by 50.7%. In a retrospective cohort study, the authors stated that CCI is the primary determinant of early and long-term mortality. In patients with a score below 5 who underwent early surgery, mortality was significantly lower. We found no relationship between CCI score and mortality after hip fracture, although we observed a significant association with mortality in the univariate analysis (24).

A significant correlation was found between the pre-fracture ambulation status of the patients and mortality, which was similar to previous studies (8, 9). Our subjects' limited ambulatory status before fracture may have resulted in higher mortality. While the ambulation status of 41.9% of the patients remained the same, the ambulation status of 58.1% worsened. Thirty-eight patients ambulated independently before the fracture, decreasing to 16 after the fracture. In a study conducted in Italy, 50.5% of the patients had a worsening ambulation status, and 4.3% showed improvement. Because the ambulation status of the patients was worse before the fracture in our study, it is expected that the ambulation status would be worse at the 6-month follow-up (8, 25).

The strengths of our study are that it is a prospective cohort study, the same person evaluated the patients at the time of and in the sixth month after the fracture, and hospitalization of patients in a center.

The limitations of our study are the absence of a control group, failure to assess patients' mental states, no rehabilitation data, vertebral fracture evaluation not performed in all patients, and 6 months of follow-up.

Osteoporosis is a widespread disease with ambiguous findings that may remain hidden until complications such as fractures are presented. Functional loss and mortality risk are high in patients with fractures. In addition, the cost to the healthcare system is relatively high. Age, CCI, FRAX hip fracture, smoking, BMI, and pre-fracture ambulation status affect mortality. Therefore, patients should be identified and treated before fractures develop. As FLS become more widespread, we expect lower mortality and morbidity in this vulnerable patient population.

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