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Research Article

Effect of osteosarcopenia on the development of a second compression fracture and mortality in elderly patients after vertebroplasty

Gokhan Kursat Kara[1], Cagatay Ozturk[2]

[1]*Department of Orthopaedics and Traumatology, Liv Hospital Ulus Istanbul, Istanbul, Turkey*
[2]*Department of Orthopaedics and Traumatology, Istinye University, Istanbul, Turkey*

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ORCID iDs of the authors:
G.K.K. 0000-0002-2058-6534;
C.O. 0000-0003-3133-206X.

ABSTRACT

Objective: This study aimed to investigate the effect of osteosarcopenia on second fracture development and mortality in patients aged above 60 years undergoing vertebroplasty because of osteoporotic vertebral compression fracture (OVCF).

Methods: A retrospective evaluation was conducted on 104 patients treated by vertebroplasty because of OVF between 2016 and 2021. The L3 vertebra Hounsfield unit values and the psoas muscle index (PMI) values measured at the L3 vertebra level were obtained from the patients' medical data and computed tomography images. Using these measurements, the patients were divided into 3 groups: only osteoporosis (OO group), only sarcopenia (OS group), and osteosarcopenia (OSP group). Differences between the groups were evaluated regarding second OVCF development and mortality.

Results: The study included 104 patients, comprising 30 males and 74 females aged 60-92 years. The OS group included 10 patients, the OO group included 54 patients, and the OSP group consisted of 40 patients. A single vertebral fracture occurred in 72 patients, and 2 vertebral fractures occurred in 32 patients. The chi-square test, Mann–Whitney *U*-test, Kruskal–Wallis test, and Kaplan–Meier survival analysis results showed no statistically significant difference between the 3 groups for the risk of second vertebral fracture. Sarcopenia, either alone or in combination with osteoporosis, was seen to have a negative effect on the survival of patients who underwent vertebroplasty following a vertebral fracture.

Conclusion: This study has shown that osteosarcopenia did not increase the risk of developing a second vertebral fracture, but it increased mortality 2.8-fold for those who underwent vertebroplasty after vertebral fracture.

Level of Evidence: Level III, Prognostic study.

Introduction

Osteoporosis is a systemic disease of the skeletal system characterized by the deterioration of bone quality and low bone mass, which lead to increased bone fragility. Due to the increase in life expectancy and the consequent increase in the elderly population, osteoporotic fractures have become a public health concern.[1]

One of the most common complications of osteoporosis is osteoporotic vertebral compression fracture (OVCF), which results from low-energy traumas in the elderly population and causes severe pain, progressive kyphosis, compromised quality of life, and increased mortality.[2] Classic treatment for OVCF includes bed rest and the use of analgesics and corsets. Fracture healing and pain control are required for patients to return to their daily life activities, which may promote new health problems in elderly patients with comorbidities.

Therefore, percutaneous vertebroplasty and kyphoplasty have become the most widely performed minimally invasive approaches in spinal surgeries for the treatment of OVCF in recent years.

Sarcopenia, a term first introduced in 1989 by Rosenberg, refers to age-related loss of muscle mass and is thus considered as a type of geriatric syndrome.[3] Since then, sarcopenia and its association with various diseases (i.e., malignancy, cirrhosis, etc.) have been the subject of several studies. Most studies have shown that sarcopenia has a negative effect on postoperative complications, morbidity, and mortality.

Osteosarcopenia is a condition in which osteoporosis and sarcopenia occur at the same time in a patient. This study aimed to investigate the effect of osteosarcopenia on the development of a second compression vertebral fracture and mortality in patients with OVCF who had undergone vertebroplasty.

Material and Methods

This retrospective study included patients who underwent vertebroplasty because of a thoracic or lumbar vertebral fracture performed by a senior orthopedic surgeon between August 2016 and December 2021. This study was approved by the Ethics Committee of Istinye University Faculty of Medicine (3/2022.K-79), and informed consent was obtained from all patients.

Corresponding author:
Gokhan Kursat Kara
drkursatkara@yahoo.com

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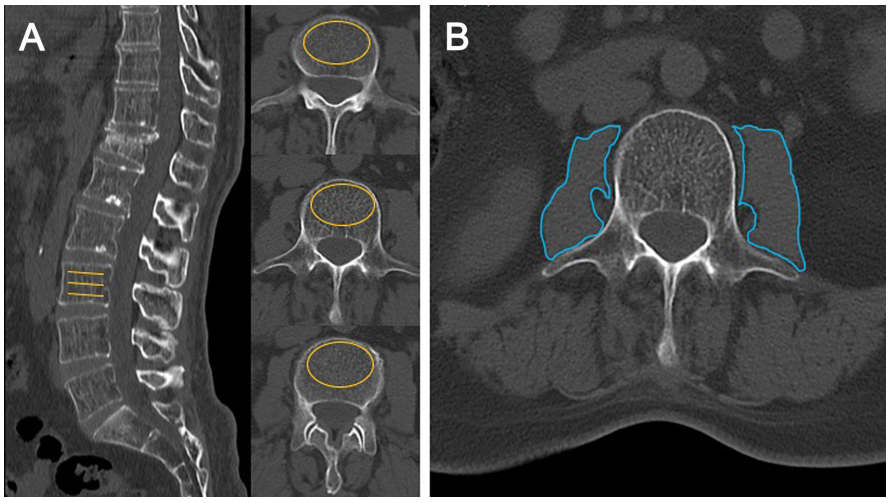

Figure 1. Hounsfield unit and psoas muscle index measurements on computed tomographic images.

The study criteria were defined as age ≥ 60 years, vertebral compression fracture resulting from low-energy trauma, fracture as the first acute or subacute symptomatic vertebral compression fracture, and availability of computed tomography (CT) images including L3 vertebra axial slices taken before or after 3 months of vertebral augmentation (spinal or abdominal CT).

The exclusion criteria included: (1) patients with incomplete radiological examination; (2) fractures caused by severe trauma or pathological fractures due to tumor, infection, or bone metabolic disease; and (3) previous spinal fusion surgery.

Surgical Procedure and Follow-Up

All patients underwent surgery performed by a single senior surgeon (C.O.) under general anesthesia or sedation+local anesthesia. With the patient in the prone position, bilateral transpedicular polymethylmethacrylate was injected under anteroposterior and lateral continuous fluoroscopic guidance. A biopsy specimen was obtained for the pathological evaluation. All patients were discharged on the same day or 1 day after the operation. Treatment for osteoporosis was initiated by an endocrinologist after the procedure in all patients. Outpatient clinic evaluations were performed at 2, 4, and 12 weeks, 6 months, and once a year thereafter, until death. During the study, all patients were contacted via telephone to obtain information about their current status.

Radiological Measurements

All the images were obtained from the hospital picture archiving and communication system.

HIGHLIGHTS

- Osteosarcopenia is a condition in which osteoporosis and sarcopenia occur at the same time in a patient. This study aimed to investigate the effect of osteosarcopenia on the development of a second compression vertebral fracture and mortality in patients with osteoporotic vertebral compression fracture (OVCF) who undergone vertebroplasty.
- The results showed no statistically significant difference between the osteoporosis, sarcopenia and osteosarcopenia groups for the risk of second vertebral fracture. However, sarcopenia,either alone or in combination with osteoporosis, was seen to have a negative effect on the survival of patients.
- The results indicate that identifying high-risk patients early and implementing special preoperative and postoperative management strategies to decrease the risk of mortality in elderly patients after vertebroplasty is necessary.

Radiological Evaluation of Osteoporosis

The L3 vertebrae average Hounsfield Unit (HU) value was calculated as follows: the vertebral body was divided into 3 equal parts in the sagittal plane, and the largest elliptical region of interest (ROI) containing only bone trabeculae was drawn in the axial plane to obtain the average CT value, avoiding the cortical bone and posterior venous plexus[4] (Figure 1A).

When L3 was fractured (12 patients), HU value measurements were obtained from L2 and L4 using the same technique, and the average was obtained.

L3 HU average: HU1+HU2+HU3 / 3.

Based on a previous study of a Turkish population, osteoporosis was defined as an HU value <102, and osteopenia was defined as an HU value >102 and <165.[5]

Radiological Evaluation of Sarcopenia

The right and left psoas muscle borders were manually drawn on axial CT images with a ROI at the level of the L3 vertebra without fatty infiltration. The left psoas area (LPA) and right psoas area (RPA) were measured in mm^2 (Figure 1B).

The psoas muscle index (PMI) was calculated in mm^2/m^2 using the following equation:

$PMI = (RPA + LPA)/height^2$.

A PMI < 540 mm^2/mm^2 for male patients and < 360 mm^2/m^2 for female patients were determined as the cutoff points to define sarcopenia, based on a previous study of a Turkish population.[6]

Statistical Analysis

The data obtained in this study were analyzed statistically using Statistical Package for Social Sciences Statistics software, version 25.0 (IBM SPSS Corp.; Armonk, NY, USA). Conformity of the variables to a normal distribution was examined using histograms, graphs, and the Kolmogorov–Smirnov test. Descriptive statistics are presented as mean ± SD, median, and minimum–maximum values. Categorical variables were compared using the Pearson Chi-square test. The Mann–Whitney *U*-test was used when comparing 2 groups

of non-normally distributed (nonparametric) variables, and the Kruskal–Wallis test was applied to evaluations between more than 2 groups. Survival analysis was performed using the Kaplan–Meier test, and factors affecting mortality were examined using Cox regression analysis. A value of $P < .05$ was accepted as statistically significant.

Results

After exclusion of 36 patients (25 met the exclusion criteria and 11 were lost to follow-up), 104 patients (30 males and 74 females between 60 and 92 years old) were evaluated. Patients were classified into 3 groups: 10 patients with only sarcopenia (OS), 54 patients with only osteoporosis (OO), and 40 patients with osteosarcopenia (OSP). A single vertebral fracture occurred in 72 patients, whereas 2 vertebral fractures occurred in 32 patients. In patients with a second vertebral fracture, the mean time between the 2 fractures was 15.62 ± 16.18 months. Hounsfield unit values of L3 were below the limit for osteopenia (165 HU) in all patients, and below the limit for osteoporosis (102 HU) in 94 patients. The mean L3 HU value of all patients was 69.69 ± 22.57. During the follow-up period after vertebroplasty, 34 patients died. The mean survival time of the exitus patients was 23.56 ± 17.53 months. The mean follow-up period, PMI, and body mass index (BMI) of all patients were 30.57 ± 19.84 months, 415.43 ± 141.74, and 27.05 ± 3.89, respectively (Table 1). Sarcopenia and osteoporosis were diagnosed in 50 and 94 patients, respectively.

Statistical analysis using the chi-square test showed that all osteoporotic patients (OO group+OSP group) had a significantly higher number of fractures compared to OS patients, who had no second fracture. No significant relationship was observed between fracture number and the OO, OS, and OSP groups ($P = .065$) (Table 2).

Kruskal–Wallis analysis showed no significant difference between the 3 groups with respect to age and sex. A significant difference was determined between the OS, OO, and OSP groups in terms of time between 2 fractures, survival time after the first fracture, PMI, and BMI. Time between 2 fractures was longer in the OO group than in the OSP group. Survival time after the first fracture was longer in the OO group than in the OS and OSP groups. The PMI was higher in the OO group than in the OS and OSP groups. The BMI was lower in the OS group than in the OO and OSP groups (Table 3).

Table 1. Patient Demographics

	n	%
Age	74.79 ± 8.68	75 (60-92)
Gender		
Male	30	(28.85)
Female	74	(71.15)
Group		
Only sarcopenia	10	(9.62)
Only osteoporosis	54	(51.92)
Osteosarcopenia	40	(38.46)
Fracture number		
1	72	(69.23)
2	32	(30.77)
Time to second fracture (months)	15.62 ± 16.18	8 (1-48)
L3 Hounsfield unit average	69.69 ± 22.57	66 (30-122)
Mortality		
Absent	70	(67.31)
Present	34	(32.69)
Survival time after first fracture (months)	23.56 ± 17.53	24 (2-61)
Follow-up (months)	30.57 ± 19.84	24.5 (2-72)
Psoas muscle index	415.43 ± 141.74	437.58 (187.89-723.27)
Body mass index	27.05 ± 3.89	26.94 (18.07-37.11)

The relationships between fracture number and age, sex, time to second fracture, mortality, survival time after the firstfracture, PMI, and BMI were examined with the Mann–Whitney *U*-test (Table 4). Patients who had a second fracture were older than those who did not.

The relationships between survival and the OS, OO, and OSP groups and fracture number were examined with Kaplan–Meier survival analysis (Table 5). A significant reverse correlation was observed between survival and OS and OSP groups. The survival rates of

Table 2. Chi-Square Test

	OS Group (n=10)		OO Group (n=54)		OSP Group (n=40)		
	n	%	n	%	n	%	
Second vertebral fracture	0	(0.00)	20	(37.04)	12	(30.00)	$P = .065$

OO, only osteoporosis; OOS, osteosarcopenia; OS, only sarcopenia.

Table 3. Kruskall–Wallis Test Analysis

	Only Sarcopenia	Only Osteoporosis	Osteosarcopenia	*P*
Age				
Average ± SD	74 ± 4.11	74.07 ± 9.42	75.95 ± 8.5	.563
Median (minimum–maximum)	75 (67-78)	75 (60-92)	77 (63-88)	
Gender				
Male, n (%)	2 (20.00)	14 (25.93)	14 (35.00)	.511
Female, n (%)	8 (80.00)	40 (74.07)	26 (65.00)	
Time to second fracture (months)				
Average ± SD		22 ± 16.83	5 ± 7.16	.001
Median (minimum–maximum)		21.5 (2-48)	1.5 (1-20)	
Survival time after first fracture (months)				
Average ± SD	11.5 ± 2.89	37.43 ± 17.57	14.44 ± 9.98	.002
Median (minimum–maximum)	11.5 (9-14)	30 (16-61)	12 (2-27)	
Psoas muscle index				
Average ± SD	250.26 ± 101.36	518.32 ± 89.34	317.82 ± 91.75	<.001
Median (minimum–maximum)	208.59 (187.89-440.82)	508.22 (365.09-723.27)	289.9 (193.35-498.15)	
Body mass index				
Average ± SD	23.19 ± 3.85	27.48 ± 3.56	27.43 ± 3.88	.016
Median (minimum–maximum)	21.64 (18.07-27.76)	27.31 (20.96-35.38)	26.33 (22.03-37.11)	

Bold text indicates statistically significant values.

Table 4. Mann–Whitney *U*-Test Analysis

		Fracture Number				
		1		2		
		n/Average ± SD	%/ Median (minimum–maximum)	*n*/Average ± SD	%/ Median (minimum–maximum)	*P*
Age		73.06 ± 8.69	73 (60-92)	78.69 ± 7.4	79.5 (60-90)	.001
Gender	Male	24	(33.33)	6	(18.75)	.130
	Female	48	(66.67)	26	(81.25)	
Time to second fracture (months)			15.63 ± 16.18	8 (1-48)	***	
Survival time after first fracture (months)		18.9 ± 13.65	19 (2-48)	30.21 ± 20.65	25.5 (6-61)	.083
Psoas muscle index		415.1 ± 152.24	437.36 (187.89-723.27)	416.17 ± 116.92	438.06 (193.35-603.79)	.905
Body mass index		26.83 ± 4.02	26.6 (18.07-37.11)	27.53 ± 3.59	27.21 (22.27-35.38)	.472

Bold text indicates statistically significant values.

Table 5. Kaplan–Meier Survival Analysis

				95% Confidence Interval		
		Estimate	Std. Error	Lower Bound	Upper Bound	*P*
Overall		50.048	2.870	44.422	55.673	
Group	Sarcopenia	32.800	5.522	21.976	43.624	.010
	Osteoporosis	57.507	3.025	51.577	63.437	
	Osteosarcopenia	37.121	4.930	27.459	46.784	
Fracture number	1	49.575	3.635	42.451	56.700	.762
	2	49.377	4.519	40.520	58.234	

Bold text indicates statistically significant values.

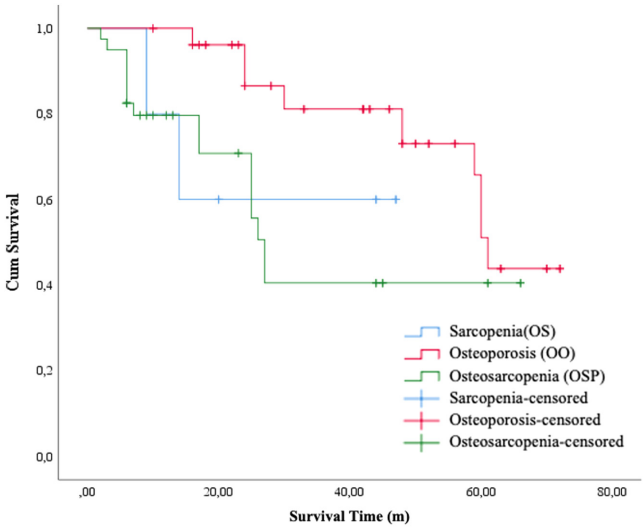

Figure 2 . Kaplan–Meier survival graphic.

Table 6. Cox Regression Analysis

					95% CI for Exp(*B*)	
	B	SE	Significance	Exp(*B*)	Lower	Upper
Only osteoporosis group			0.016			
Only sarcopenia group	0.976	0.577	0.091	2.654	0.857	8.224
Osteosarcopenia group	1.031	0.371	0.005	2.803	1.354	5.802

patients with sarcopenia and osteosarcopenia were significantly low ($P = .01$) (Figure 2). No relationship was determined between the number of fractures and survival.

The effects of sarcopenia and osteosarcopenia on mortality were examined using Cox regression analysis. The presence of sarcopenia was found to increase mortality by 2.654-fold, and the presence of osteosarcopenia increased mortality by 2.803-fold (Table 6).

Discussion

Osteoporosis, Dual-Energy X-Ray Absorptiometry vs. Hounsfield Unit Value

Osteoporosis is a significant health problem with high prevalence that contributes to morbidity and the incidence of fracture. Reportedly, 200 million people worldwide have osteoporosis, and this prevalence is expected to increase by 310% and 240% in men and women, respectively, by 2050.[7]

Bone mineral density (BMD) measurement using dual-energy x-ray absorptiometry (DEXA) is the gold standard for osteoporosis diagnosis. The World Health Organization (WHO) has classified patients according to BMD measured with DEXA as osteoporotic (*T*-score ≤ -2.5), osteopenic (*T*-score between -2.5 and -1.0), and normal (*T*-score ≥ -1.0).[8] However, this method has some limitations (spinal deformity, spinal instrumentation, vertebroplasty, kyphoplasty, etc.) and potential incorrect results (osteoarthritis, aortic calcification, severe osteophytes, or incorrect patient positioning).[5] The CT-derived bone HU values may be used to identify patients with osteoporosis and decreased BMD.

Pickhardt et al[9] reported that 52.1% of patients with vertebral compression fractures had false-negative results when DEXA was used to diagnose osteoporosis. The authors clearly defined how bone HU values can be measured and used as an alternative for osteoporosis diagnosis. The cancellous bone is the most accurate site to assess BMD, and the ROI of HU is placed in the cancellous area of the vertebral body, thus rendering the HU value less sensitive to lumbar degenerative changes, aortic calcification, osteophytes, incorrect patient positioning, and spinal deformity. In addition, vertebral HU has excellent validity in detecting osteoporosis, along with good interexamination and inter-observer reliability.[10]

In studies with different patient cohorts conducted to determine the threshold for osteoporosis, the following cutoff values have been reported: 110 HU for L1 by Pickhardt et al[9] and Zou et al,[11] 80 HU for L1 by Buckens et al,[12] and 95 HU for L1-3 by Kim et al.[13] These differences between studies may be due to measurements acquired from different areas and/or racial differences. Therefore, in the current study, 102 HU was used as the threshold for osteoporosis measured on L3 axial CT slices, as described by Cansu et al[5] in abdominal CT measurements in 111 Turkish patients.

Sarcopenia and Psoas Muscle Index

The word "sarcopenia" derives from the Greek words "sarx" and "penia," which mean "flesh" and "loss," respectively.[14] The European Working Group on Sarcopenia in Older People (EWGSOP) defines sarcopenia as "a syndrome characterized by a progressive and

generalized loss of skeletal muscle mass and strength, with a risk of adverse outcomes, such as physical disability, poor quality of life, and high mortality."[15]

In 2016, Bokshan et al[16] demonstrated a correlation between sarcopenia and postoperative morbidity and mortality after thoracolumbar decompression or decompression with fusion surgery. It was reported that patients with sarcopenia had longer hospital stay and higher complication rate compared with patients without sarcopenia. In 2020, Bayram et al[17] demonstrated that age, American Society of Anesthesiologists (ASA) classification, and sarcopenia were independent risk factors for mortality after spinal surgery.

Various measurement methods and threshold values have been described for sarcopenia diagnosis. According to the EWGSOP2 algorithm, magnetic resonance imaging and CT are accepted as the gold standards for noninvasive evaluation of muscle quantity and mass.[18]

The EWGSOP2 has recommended values of <7.0 kg/m^2 and <5.5 kg/m^2 (appendicular skeletal muscle/height^2) for men and women, respectively. However, these values were determined based on studies conducted in the USA and Australia. The EWGSOP and other consensus series have also stated that variability in threshold values is likely between different populations because of potential ethnic and cultural variations, nutritional habits, and physical activity levels.[19]

In studies of the Turkish population by Bahat et al[6,19] conducted to determine the threshold for sarcopenia diagnosis, the skeletal muscle mass index for men and women was determined as 9.2 kg/m^2 and 7.4 kg/m^2, respectively; hand grip threshold values were 32 kg and 22 kg, respectively; calf circumference was 33 cm for both men and women; and PMI was 540 mm^2/m^2 and 360 mm^2/m^2 for men and women, respectively. In the current study, we used the PMI threshold recommended by Bahat et al[6,19] for the diagnosis of sarcopenia.

Osteosarcopenia

The combination of sarcopenia with several acute and chronic diseases has been investigated, and most studies have shown that prognosis is negatively affected by sarcopenia.[20,21] Although osteoporosis and sarcopenia seem to be independent of each other, their incidence increases with age. Furthermore, bones and muscles feedback to each other through endocrine and paracrine mechanisms; therefore, bone loss can contribute to muscle loss, and vice versa.

In 2009, Binkley and Buehring[22] examined a subgroup of weak, elderly patients with both osteoporosis and sarcopenia and concluded that these patients were at high risk of fall, fracture, disability, and fragility. This new syndrome was initially named sarco-osteopenia and changed over time to osteosarcopenia. Since then, the relationship between advanced age and osteosarcopenia has been well documented.

Osteosarcopenia is a condition in which osteoporosis and sarcopenia occur simultaneously in the same patient. Additionally, the combined effects of osteoporosis and sarcopenia increase the risk of fall in the elderly, resulting in bone fractures. Yu et al[23] reported that the fracture risk increased by 3.5-fold in male patients with osteosarcopenia, which was significantly higher than that in male patients with only sarcopenia or osteoporosis.

Trajanoska et al[24] examined 5911 individuals and determined that sarcopenia did not increase the risk of fractures in individuals with osteoporosis. Consistent with that, a prospective study in elderly females by Harris et al[25] revealed that sarcopenia was not an additional risk factor for fractures in female patients with osteoporosis. In the current study, sarcopenia or osteosarcopenia did not increase the risk of new vertebral fracture in patients who underwent vertebroplasty following OVCF. However, we think that sarcopenia increases the frequency of falls, because the time between 2 fractures was significantly shorter in patients with OSP compared to patients with OO.

Kim et al[26] reported a significant difference between the postoperative 5-year mortality rate of patients with osteosarcopenia and healthy control individuals. In particular, the mortality rate was 30% higher in the osteosarcopenia group than in the control group in hip fracture cases. Yoo et al[27] reported similar results in a study with 324 patients who had undergone hip surgery. The postoperative 1-year mortality rate was twice as high in the osteosarcopenia group than in the control group. Similarly, in our study, the survival time after first OVCF was significantly lower in patients with sarcopenia (OS+OSP groups) compared to OO patients; in addition, we found that osteosarcopenia increased mortality by 2.803-fold, compared to osteoporosis, which may account for the longer follow-up period observed in OO patients.

In our study, we observed that the number of fractures was positively correlated only with age, while it was not significantly correlated with mortality. In addition, OS patients had the lowest BMI.

Study Limitations

The primary limitations of this study include the small sample size and retrospective design. Inherent biases of retrospective studies cannot be avoided and include possible selection or misclassification bias. Second, conditions that may increase the risk of a new fracture after OVCF, such as fracture level, restoration of vertebral corpus height, kyphotic angulation, cement leakage, vertebral cleft, pelvic incidence, and other spinopelvic parameters, were not evaluated in this study. Third, comorbidities that may affect morbidity and mortality [ASA classification, additional fractures (such as distal radius, proximal humerus, and hip fractures), chronic and systemic diseases (such as steroid use, chronic liver disease, chronic obstructive lung disease, diabetes, and cancer without spine metastasis)], mean age of patients that died, and causes of death were not included in this study. Since the treatment of osteoporosis was performed in another clinic (endocrinology), it could not be standardized.

Unlike previous studies, mortality and the occurrence of a second compression fracture after vertebroplasty were examined in groups of patients with osteoporosis, sarcopenia, and osteosarcopenia. The results demonstrated that osteosarcopenia did not increase the risk of a second vertebral fracture. We concluded that osteosarcopenia had a 2.8-fold negative effect on the survival of patients who had undergone vertebroplasty after vertebral fracture. Therefore, identifying high-risk patients early and implementing special preoperative and postoperative management strategies to decrease the risk of mortality in elderly patients after vertebroplasty is necessary.

Ethics Committee Approval: This study was approved by Ethics Committee of Istinye University Faculty of Medicine (Approval No: 3/2022.K-79, Date: October 18, 2022).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.O., G.K.K.; Design – C.O., G.K.K.; Supervision – C.O., G.K.K.; Resources – C.O., G.K.K.; Materials – G.K.K.; Data Collection – G.K.K.;

Analysis – G.K.K.; Literature Search – G.K.K.; Writing – G.K.K.; Critical Review – C.O., G.K.K.

Declaration of Interests: The authors have no conflict of interest to declare.

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