

# Subcutaneous fat area at the upper thigh level is a useful prognostic marker in the elderly with femur fracture

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## Abstract

**Background** The aim of this study was to evaluate prognostic value of body tissue composition at the upper thigh level for 1 year mortality in elderly patients with proximal femur fracture.

**Methods** This retrospective cohort study included consecutive elderly (aged  $\geq 65$ ) patients diagnosed with proximal femur fracture based on the findings of pelvic bone computed tomography (CT) performed at the emergency department of a tertiary care hospital and treated with surgery between 2010 and 2017. The cross-sectional area of subcutaneous fat and skeletal muscle at the upper thigh level was measured using CT. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for 1 year mortality were estimated using a Cox proportional hazards model. Survival based on the SFA quartiles was assessed using nonparametric Kaplan–Meier survival analysis and compared used log-rank tests.

**Results** Among 876 elderly patients included in this study, the median age was 79.0 years, and 646 (73.7%) patients were female. A total of 93 (10.6%) died within 1 year after admission to the emergency department. Survivors had a significantly higher median subcutaneous fat area (SFA) than non-survivors (170.2 vs. 133.0 cm<sup>2</sup>,  $P < 0.001$ ), but no significant difference was observed between the skeletal muscle area (median, 156.7 vs. 160.3 cm<sup>2</sup>,  $P = 0.504$ ) and muscle density (median, 19.0 vs. 19.1 HU,  $P = 0.861$ ) of both groups. After adjustment of other clinical characteristics and body compositions, the multivariate Cox proportional hazard analysis showed that SFA (adjusted HR, 0.987; 95% CI, 0.982–0.992;  $P < 0.001$ ) was independently associated with 1 year mortality. With 384 deaths during 51 322 person-months of follow-up, the median estimated survival duration of all the patients was 92.8 months (95% CI, 80.8–104.7 months). The patients with SFA in the third (165.6–195.0 cm<sup>2</sup>) and fourth ( $>195.0$  cm<sup>2</sup>) quartiles showed significantly longer survival duration than those with SFA in the first ( $<131.4$  cm<sup>2</sup>; median survival time, 51.3 months) and second (131.4–165.5 cm<sup>2</sup>; median survival time, 88.7 months) quartiles ( $P < 0.001$  by log-rank test).

**Conclusions** The SFAs measured at the upper thigh level and 1 year mortality are positively associated in elderly patients with proximal femur fracture. SFA may be an independent prognostic biomarker for 1 year mortality of femur fracture.

**Keywords** Elderly; Femur fracture; Upper thigh; Body composition; Mortality

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## Introduction

Femur fracture represents a global health concern as a major cause of physical disability and mortality among elderly individuals. The incidence of femur fracture among individuals aged >60 has increased 2.4-fold since 1980, and the increased medical costs are a burden for both individuals and society.<sup>1–3</sup> Unlike the younger subset of patients who sustain multiple injuries from high-energy mechanisms, elderly patients are often injured as a result of low-energy falls from a standing height or less (a low energy trauma). These falls and injuries are consequences of deterioration in the properties of bones, muscles and joints, which is associated with advancing age.<sup>2,4</sup>

Decline in muscle mass and decrease in bone density contribute to impaired balance and increased risk of fracture in a synergistic manner.<sup>5</sup> These changes, which are associated with aging, have been suggested as not only risk predictors for femur fracture but also as prognostic factors for clinical outcomes, including perioperative bleeding, length of hospital stay, and survival, among patients with hip fracture.<sup>6–8</sup> Moreover, recent studies have revealed that changes in body composition, including skeletal muscle mass, subcutaneous and visceral fat mass and muscle fat infiltration, have a collaborative impact on elderly patients.<sup>9</sup>

Although the relationship between reduced muscle mass, that is, sarcopenia, and increased risk of femur fracture or poor outcomes in patients with femur fracture have been studied,<sup>6–8,10</sup> the prognostic value of body composition measured at the upper thigh in elderly patients with femur fracture has not been properly investigated. Measurement of body composition at the upper thigh level using pelvic bone computed tomography (CT), which is performed during routine clinical examination, is practical and reliable without the additional risk of exposure to radiation.<sup>11</sup>

The aim of this study was to evaluate the association between body tissue composition measured at the upper thigh level and 1 year mortality in elderly patients who presented to the emergency department (ED) with proximal femur fracture.

## Methods

### *Study design and population*

This retrospective cohort study was conducted at the ED of a tertiary care university-affiliated hospital in Seoul, Korea, which has an annual census of about 110 000 visits. Our institutional review board approved this study (study number: 2018-0806) before its commencement and waived the requirement for informed consent due to the retrospective nature of the study.

Consecutive elderly patients (aged  $\geq 65$ ) who underwent pelvic bone CT and were diagnosed with pelvic bone fracture

at the ED between January 2010 and December 2017 were eligible to participate in this study. From this population, we selected and included patients with proximal femur fracture, that is, femoral neck and intertrochanteric fractures, documented using pelvic bone CT. Patients were excluded if they were diagnosed with pathologic fractures, refused surgical treatment, had poor mobility functions before trauma, had no available CT images for body morphometry analysis, or medical records with insufficient data. All the study participants were followed up for more than 1 year after hospital admission or until the time of death, and they were categorized into 1 year survivor and non-survivor groups. Survival time was calculated as the date from ED admission to the date of death or 31 August 2020. Throughout the study period, operative management, including surgical timing and surgical options, was determined by an orthopaedic surgeon.

### *Collection of clinical data*

Demographic and clinical data, such as age, sex, comorbidity, mobility function before trauma, trauma mechanism, fracture site, the type of surgery, laboratory data at ED admission and clinical outcomes including length of hospital stay, mobility function at discharge and in-hospital mortality were extracted from electronic medical records. We retrieved the data on body weight, height and body mass index (BMI) entered into the electronic health records at hospital admission. BMI was automatically calculated as weight in kilograms divided by height in metres squared ( $\text{kg}/\text{m}^2$ ) in our medical record system. BMI was used to categorize the patients as underweight ( $<18.5 \text{ kg}/\text{m}^2$ ), of normal weight ( $18.5\text{--}25.0 \text{ kg}/\text{m}^2$ ) or overweight ( $>23.0 \text{ kg}/\text{m}^2$ ) according to the World Health Organization (WHO) criteria for Asian populations.<sup>12</sup> We also retrieved data on the bone mineral density of the lumbar spine and femoral neck of the study participants who underwent dual-energy X-ray absorptiometry within 90 days before ED admission or during hospitalization. Patients were diagnosed with osteoporosis (T score of  $\leq -2.5$ ) and osteopenia ( $-2.5 < \text{T score} < -1.0$ ) based on data from a working group of the WHO.<sup>13</sup>

The primary endpoint was 1 year all-cause mortality after ED presentation. The date of a patient's death was obtained by reviewing the electronic medical records or using the database of National Health Insurance Service System in South Korea.

### *Acquisition of computed tomography images and body morphometry analysis*

Pelvic bone CT was performed using a 128-channel multi-detector CT scanner (Somatom Definition AS Plus; Siemens Healthineers, Erlangen, Germany) with the following protocols: tube voltage, 120–130 kVp; effective tube current,

120–150 mAs; matrix,  $512 \times 512$ ; and slice thickness, 3 mm. The pelvic bone CT was performed by scanning from the mid-abdomen to the upper thigh without injection of a contrast agent.

The overall procedure of the body morphometry analysis is summarized in Figure 1. An experienced radiologist (K. W. K) analysed the CT images using the AsanJ-Morphometry™ software, which was developed for the measurement of body composition based on ImageJ (NIH, Bethesda, MD, USA).<sup>14</sup> We selected the CT slice at the upper thigh level, which was defined as the inferior tip of the ischial tuberosity, that is, the lowest CT slice where the ischial bone was visible on a pelvic bone CT image. The boundary between the subcutaneous fat and skeletal muscle was demarcated. Within the boundary, the cross-sectional area of the skeletal muscle area (SMA) was segmented using predetermined thresholds ( $-29$  to  $+150$  Hounsfield units). Outside the boundary, the subcutaneous fat area (SFA) was segmented using thresholds ranging from  $-190$  to  $-30$  HU. The muscle density within the muscle boundary was assessed as the mean radiodensity in HU.

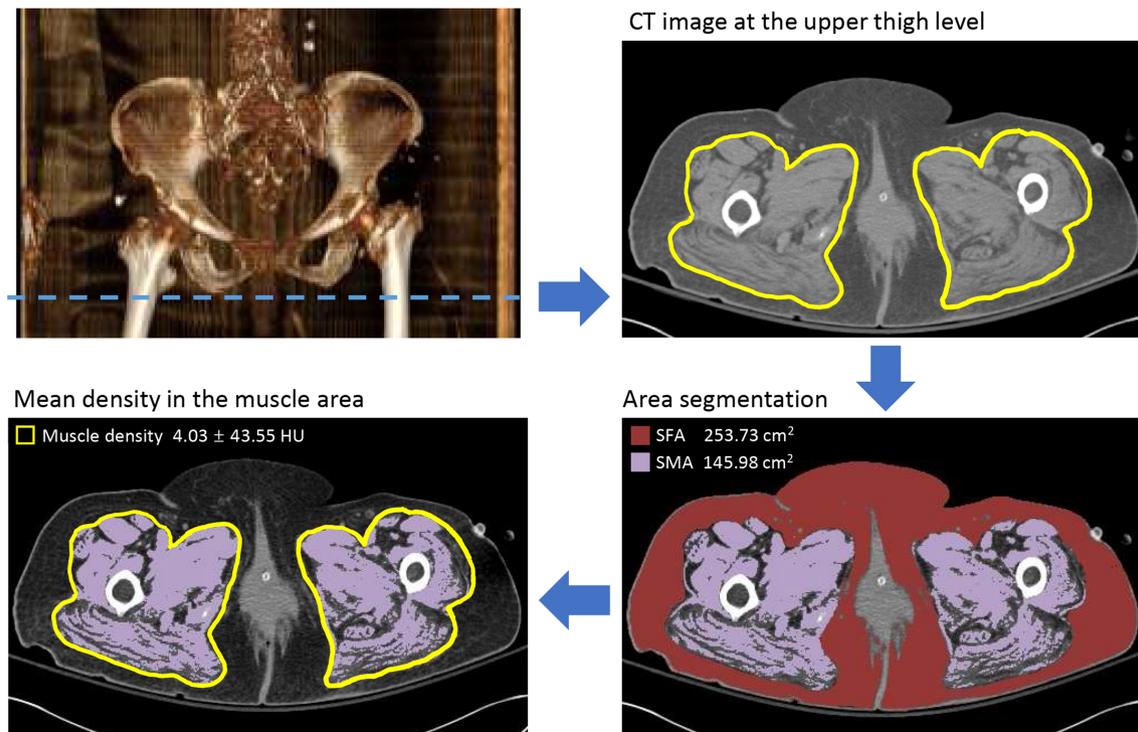
### Statistical analysis

Continuous variables were presented as medians with interquartile ranges (IQRs) due to the non-normal distribution

based on the Kolmogorov–Smirnov test. Categorical variables were presented as numbers and percentages.

Clinical characteristics were compared between the 1 year survivor group and non-survivor group. The Student *t* test was used to compare the means of continuous variables, whereas the Mann–Whitney *U* test was used to compare the medians. The  $\chi^2$ -test or Fisher's exact test was used to compare categorical variables.

Univariate Cox proportional hazard analysis was performed to evaluate the prognostic ability of each variable. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for 1 year mortality were estimated using multivariate Cox proportional hazards regression analyses with the forward conditional method. The final model was adjusted for age, sex and other variables that were shown to significantly affect 1 year mortality in the univariate Cox proportional hazards regression analyses. The proportional hazards assumption was assessed by examining graphs of the estimated log minus log plots; no violation of the assumption was found. Regarding the body composition factors, survival based on the SFA quartiles was assessed using nonparametric Kaplan–Meier survival analysis and compared used log-rank tests using the survival package version 3.2-7.<sup>15</sup> A two-sided *P* value  $<0.05$  was considered statistically significant. All statistical analyses were performed using both SPSS for Windows version 21.0 (Armonk, NY, USA: IBM Corp.) and R version 4.1.0.



**Figure 1** Body morphometry analysis. The axial computed tomography image at the upper thigh level is selected. The boundary between the subcutaneous fat and skeletal muscle is drawn. Then, the skeletal muscle area (SMA) and subcutaneous fat area (SFA) are segmented using predefined thresholds ( $-29$  to  $150$  HU for SMA,  $-190$  to  $-30$  HU for SFA). The mean density of the muscle area is calculated within the boundary of the skeletal muscle.

## Results

### Patients

From January 2010 to December 2017, 1102 elderly patients with a proximal femur fracture were admitted to the ED of our hospital. Among these cases, 876 patients were finally included in our study after the exclusion of 226 patients who had no available CT images for body morphometry analysis ( $n = 102$ ), had poor mobility function before trauma ( $n = 35$ ), had medical records with insufficient data ( $n = 23$ ), refused surgical treatment ( $n = 62$ ) or were diagnosed with pathologic fracture (Figure 2). A total of 93 patients (10.6%) in this cohort died within 1 year after ED admission.

### Characteristics between survivors and non-survivors

Table 1 presents the demographic and clinical characteristics of the study patients. The median age of the cohort was 79.0 (73.0–83.0) years, and 646 (73.7%) patients were female. Significant differences were found between the 1 year survivor and non-survivor groups regarding the sex distribution of the patients (female, 76.4% vs. 51.6%;  $P < 0.001$ ), chronic kidney disease (CKD) (5.5% vs. 15.1%;  $P < 0.001$ ), independent ambulatory function before trauma (78.3% vs. 66.7%;  $P = 0.012$ ), and laboratory results including haemoglobin count (median, 11.5 vs. 10.3 g/dL;  $P < 0.001$ ), creatinine level (median, 0.73 vs. 0.89 mg/dL;  $P < 0.001$ ), and albumin level (median, 3.5 vs. 3.2 g/dL;  $P < 0.001$ ). However, other comorbidities, trauma mechanisms, fracture locations and surgical treatments did not differ statistically between the two groups. Patients in the non-survivor group showed longer length of hospital stay (median, 10.0 vs. 12.0 days;

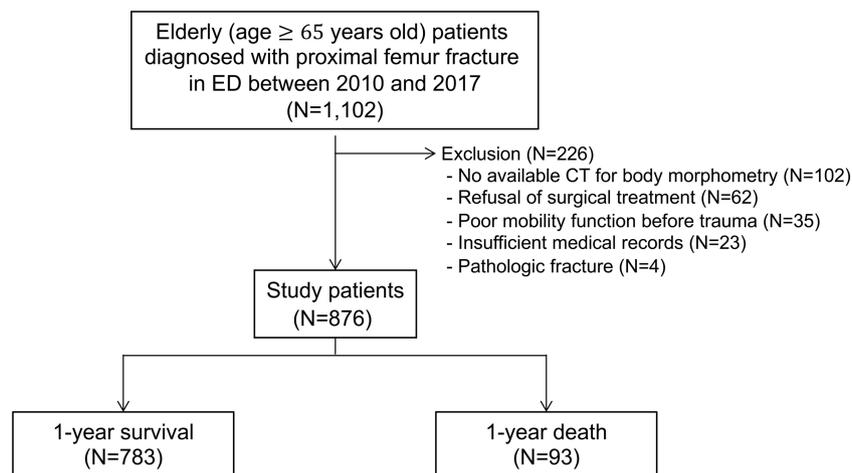
$P = 0.047$ ) and poorer mobility function at hospital discharge than patients in the 1 year survivor group. Four patients in non-survivor group (4.3%) died during hospitalization.

The comparison of body compositions between the 1 year survivor and non-survivor groups are presented in Table 2. BMI was significantly higher in the 1 year survivor group than in the non-survivor group (median, 32.5 vs. 21.9 cm<sup>2</sup>/m<sup>2</sup>,  $P = 0.006$ ); however, no significant difference was observed between the SMA (median, 156.7 vs. 160.3 cm<sup>2</sup>,  $P = 0.504$ ) and muscle density (median, 19.0 vs. 19.1 HU,  $P = 0.861$ ) of both groups. In contrast, survivors had significantly higher SFA than non-survivors (median, 170.2 vs. 133.0 cm<sup>2</sup>,  $P < 0.001$ ). The body morphometry analyses for representative cases of a survivor and a non-survivor are illustrated in Figure 3.

### Prognostic model for the 1 year mortality

Table 3 shows the univariate and multivariate Cox proportional hazards analyses of the associations between clinical characteristics and body compositions and 1 year mortality. The results of the multivariate Cox proportional hazard analysis showed that CKD (adjusted HR, 2.326; 95% CI, 1.303–4.152;  $P = 0.004$ ) and impaired mobility function before trauma (ambulation with walker; adjusted HR, 1.655; 95% CI, 1.072–2.555;  $P = 0.023$ ) were significantly associated with worse prognosis. In contrast, albumin level (adjusted HR, 0.338; 95% CI, 0.226–0.505;  $P < 0.001$ ) and SFA (adjusted HR, 0.987; 95% CI, 0.982–0.992;  $P < 0.001$ ) were significantly associated with better prognosis in elderly patients with proximal femur fracture.

There were 384 deaths during 51,322 person-months of follow-up. The median duration of follow-up was 53.2 months (IQR, 35.6–84.4 months). The median survival time of all the patients was 92.8 months (95% CI, 80.8–104.7 months),



**Figure 2** Patient flow diagram. CT, computed tomography; ED, emergency department.

**Table 1** Demographic and clinical characteristics of the study patients stratified according to 1 year mortality

Variables	Total (n = 876)	Survivor (n = 783)	Non-survivor (n = 93)	P value
Age, years	79.0 (73.0–83.0)	79.0 (73.0–83.0)	79.0 (72.0–84.0)	0.445
65–74 years	263 (30.0%)	236 (30.1%)	27 (29.0%)	0.523
75–84 years	444 (50.7%)	400 (51.1%)	44 (47.3%)	
≥85 years	169 (19.3%)	147 (18.8%)	22 (23.7%)	
Female	646 (73.7%)	598 (76.4%)	48 (51.6%)	<0.001
Comorbid disease				
Hypertension	577 (65.9%)	517 (66.0%)	60 (64.5%)	0.771
Diabetes mellitus	312 (35.6%)	273 (34.9%)	39 (41.9%)	0.178
Chronic kidney disease	57 (6.5%)	43 (5.5%)	14 (15.1%)	<0.001
Dementia	75 (8.6%)	62 (7.9%)	13 (14.0%)	0.181
Current medication				
Anticoagulants	53 (6.1%)	49 (6.3%)	4 (4.3%)	0.454
Antiplatelets	233 (26.6%)	216 (27.6%)	17 (18.3%)	0.055
Bone density*	n = 649	n = 582	n = 67	0.068
Normal	5 (0.8%)	3 (0.5%)	2 (3.0%)	
Osteopenia	157 (24.2%)	146 (25.1%)	11 (16.4%)	
Osteoporosis	487 (75.0%)	433 (74.4%)	54 (80.6%)	
Mobility function before trauma				0.012
Ambulation	675 (77.1%)	613 (78.3%)	62 (66.7%)	
Ambulation with walker	201 (22.9%)	170 (21.7%)	31 (33.3%)	
Trauma mechanism				0.311
Ground-level fall	789 (90.1%)	708 (90.4%)	81 (87.1%)	
Others	87 (9.9%)	75 (9.6%)	12 (12.9%)	
Fracture location				0.825
Femoral neck	405 (46.2%)	361 (46.1%)	44 (47.3%)	
Intertrochanteric region	422 (53.8%)	422 (53.9%)	49 (52.7%)	
Surgical treatment				0.615
Internal fixation	474 (54.1%)	428 (54.7%)	46 (49.5%)	
Hemiarthroplasty	250 (28.5%)	220 (28.1%)	30 (32.3%)	
Total hip arthroplasty	152 (17.4%)	135 (17.2%)	17 (18.3%)	
Other concomitant injuries	51 (5.8%)	47 (6.0%)	4 (4.3%)	0.508
Laboratory test				
Haemoglobin, g/dL	11.4 (10.0–12.6)	11.5 (10.2–12.7)	10.3 (8.9–12.1)	<0.001
Creatinine, mg/dL	0.75 (0.60–1.03)	0.73 (0.60–1.00)	0.89 (0.66–1.35)	<0.001
Albumin, g/dL	3.5 (3.2–3.7)	3.5 (3.2–3.7)	3.2 (2.8–3.5)	<0.001
Length of hospital stay, days	10.0 (8.0–17.0)	10.0 (7.0–17.0)	12.0 (8.5–18.0)	0.047
Mobility function at discharge				<0.001
Ambulation with or without walker	388 (44.3%)	362 (46.2%)	26 (28.0%)	
Wheelchair	406 (46.3%)	363 (46.4%)	43 (46.2%)	
Bed-ridden state	78 (8.9%)	58 (7.4%)	20 (21.5%)	
In-hospital death	4 (0.5%)	0 (0%)	4 (4.3%)	

Continuous variables are expressed as median (interquartile range) and categorical variables are expressed as absolute number (percentage).

\*A total of 227 patients did not undergo bone density measurement test.

whereas that for patients with SFA in the first and second quartiles was 51.3 months and 88.7 months, respectively. The patients with SFA in the third and fourth quartiles showed significantly longer survival duration than those with SFA in the first and second quartiles ( $P < 0.001$  by log-rank test; Figure 4).

## Discussion

In this retrospective cohort study, we found that increased SFA measured at the upper thigh level was independently associated with reduced 1 year mortality in elderly patients with proximal femur fracture, who had good mobility function before trauma and underwent surgical treatment.

Moreover, the estimated survival duration for the patients in this study was significantly different according to their SFA quartiles at the time of ED presentation. To the best of our knowledge, this is the first study to demonstrate that the impact of SFA measured at upper thigh using pelvic CT is far more important than that of SMA or muscle density on the clinical outcomes of elderly patients with proximal femur fracture. The measurement of SFA at the upper thigh level using pelvic CT is a relatively practical and simple procedure for physicians compared with that of SMA or muscle density. This implies that the subcutaneous fat thickness or circumference of the upper thigh would be another easily applicable method that can be used to predict outcomes in the ED.

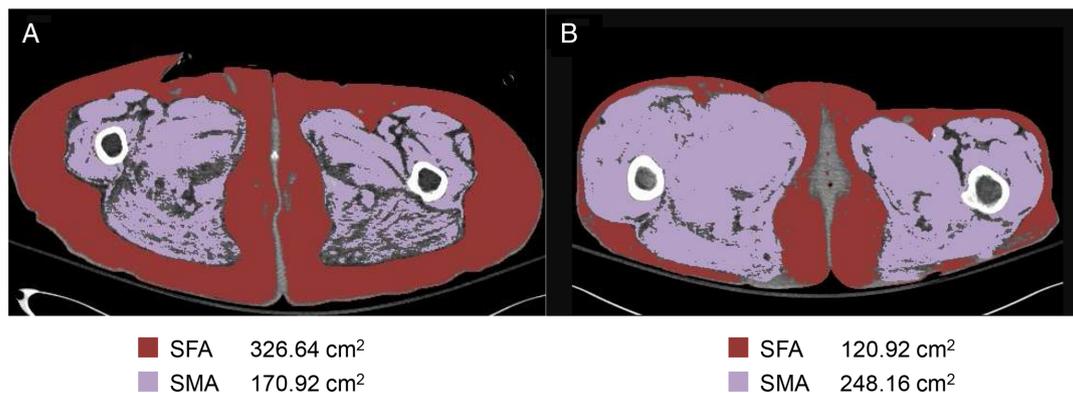
In the present study, a total of 93 of 876 (10.6%) elderly patients with proximal femur fracture died within 1 year.

**Table 2** The body composition of the elderly patients with proximal femur fracture according to 1 year mortality

Body composition	Total (n = 876)	Survivor (n = 783)	Non-survivor (n = 93)	P value
Height, cm	156.0 (151.0–162.0)	156.0 (150.0–162.0)	159.0 (152.3–167.7)	0.002
Weight, kg	55.0 (48.9–63.0)	55.0 (49.0–63.0)	54.5 (46.4–65.0)	0.616
BMI, kg/m <sup>2</sup>	22.5 (20.0–24.8)	22.5 (20.3–25.0)	21.9 (19.0–23.5)	0.006
BMI categorization				0.023
Underweight	113 (12.9%)	93 (11.9%)	20 (21.5%)	
Normal	381 (43.5%)	340 (43.4%)	41 (44.1%)	
Overweight	170 (19.4%)	152 (19.4%)	18 (19.4%)	
Obese	212 (24.2%)	198 (25.3%)	14 (15.1%)	
SMA, cm <sup>2</sup>	157.0 (135.1–187.8)	156.7 (135.4–187.8)	160.3 (130.0–187.7)	0.504
SFA, cm <sup>2</sup>	165.6 (131.4–195.1)	170.2 (135.0–197.1)	133.0 (115.5–165.1)	<0.001
Muscle density, HU	18.8 (12.4–26.1)	19.0 (10.65)	19.1 (10.28)	0.861

Continuous variables are expressed as median (interquartile range) and categorical variables are expressed as absolute number (percentage).

Abbreviations: BMI, body mass index; HU, Hounsfield units; SFA, subcutaneous fat area; SMA, skeletal muscle area.



**Figure 3** Representative pelvic bone computed tomography images used for measurement of skeletal muscle and subcutaneous fat area and muscle density. (A) An 84-year-old female survivor whose axial image shows a high subcutaneous fat area of 326.6 cm<sup>2</sup> with a low skeletal muscle area of 170.9 cm<sup>2</sup>. (B) An 82-year-old female non-survivor whose axial image shows a low subcutaneous fat area of 120.9 cm<sup>2</sup> with a high skeletal muscle area of 248.2 cm<sup>2</sup>.

The estimated median survival duration for the patients in this study was 92.8 months (95% CI, 80.8–104.7 months). The mortality rate for the first 12 months after femur fracture varied according to population, and ranged from 10% to 47% according to the comorbidities and performance functions of the patients prior to femur fracture.<sup>2,16,17</sup> Our study included relatively healthy patients with preserved independent performance, whose 1 year mortality rates were consistent with those reported in previous studies. For survivors, up to 70% are expected to recover their functional performance before trauma within the first 6 months after discharge, whereas approximately 10% to 20% of patients require residential and nursing home care, which tends to extend for more than 10 years after discharge.<sup>2,17,18</sup> Considering the maintenance of the functional performance of the patients at 6 months after discharge and during their relatively long remaining life, early and systemic interventions for improving functional performance after hip fracture surgery would be warranted.<sup>2,19</sup>

With the acceleration of population aging and increase in life expectancy, the prevalence of CKD also increased. CKD

is a known risk factor for fragility fractures such as hip and vertebral fractures and is associated with increasing mortality.<sup>20–22</sup> Also, CKD contributes the development of mineral bone disorder, osteoporosis, fragility and impaired muscle strength.<sup>20,23</sup> According to previous studies, CKD was associated with an almost two-fold increase in hip-fracture-related mortality in elderly, similar to our results (adjusted HR, 2.326; 95% CI, 1.303–4.152;  $P = 0.004$ ).<sup>21,22</sup>

Among elderly, body composition has been suggested as a surrogate marker for baseline health status and future healthy life. However, studies on the impact of sarcopenia or muscle mass reduction on functional prognosis or mortality showed conflicting results.<sup>9,24–27</sup> Two prospective cohort studies demonstrated weak or no association between low muscle mass measured in the inferior limbs and long-term mortality risk in elderly individuals.<sup>25,28</sup> In line with those previous studies, the patients in the 1 year survivor and non-survivor groups of the present study who had good mobility function before trauma showed no differences in SMA and muscle density at the upper thigh level.

**Table 3** Cox proportional analysis for 1 year mortality in elderly patients with proximal femur fracture

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	Adjusted HR	95% CI	P value
Age, years	1.017	0.988–1.047	0.244			
Male	2.835	1.887–4.258	<0.001			
Comorbid disease						
Hypertension	1.066	0.697–1.630	0.788			
Diabetes mellitus	1.316	0.872–1.987	0.191			
Chronic kidney disease	2.862	1.621–5.053	<0.001	2.326	1.303–4.152	0.004
Dementia	1.785	0.993–3.208	0.053			
Current medication						
Anticoagulants	0.686	0.252–1.869	0.462			
Antiplatelets	0.602	0.356–1.019	0.059			
Mobility function before trauma						
Ambulation	Reference			Reference		
Ambulation with walker	1.731	1.125–2.664	0.013	1.655	1.072–2.555	0.023
Fracture location						
Intertrochanteric region	Reference					
Femoral neck	1.041	0.693–1.564	0.846			
Surgical treatment						
Internal fixation	Reference		0.616			
Hemiarthroplasty	1.269	0.779–2.067	0.339			
Total hip arthroplasty	1.172	0.650–2.112	0.598			
Other concomitant injuries	0.710	0.261–1.934	0.503			
Laboratory test						
Haemoglobin (g/dL)	0.781	0.704–0.866	<0.001			
Creatinine (mg/dL)	1.174	1.066–1.293	0.001			
Albumin (g/dL)	0.252	0.172–0.370	<0.001	0.338	0.226–0.505	<0.001
Body mass index, kg/m <sup>2</sup>	0.922	0.870–0.978	0.007			
SMA, cm <sup>2</sup>	0.997	0.992–1.003	0.320			
SFA, cm <sup>2</sup>	0.967	0.957–0.977	<0.001	0.987	0.982–0.992	<0.001
SMA attenuation, HU	1.000	0.981–1.019	>0.999			

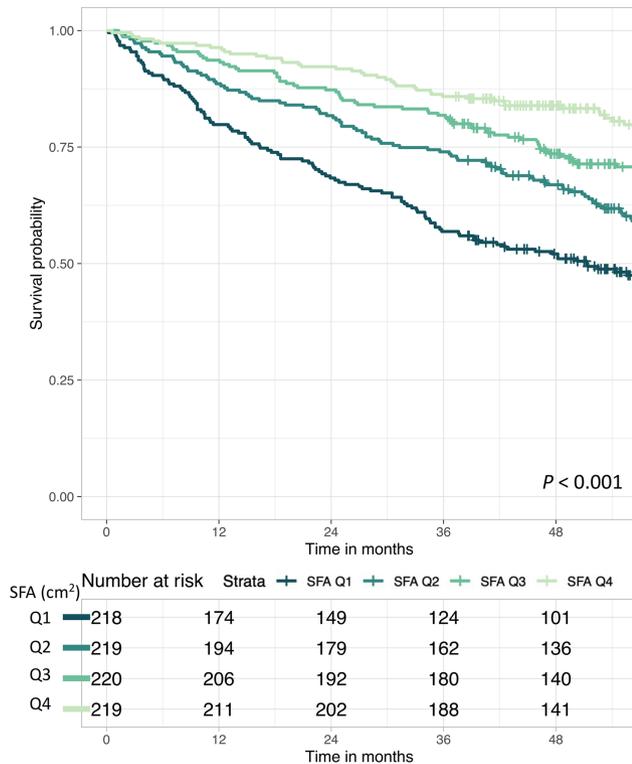
Abbreviations: CI, confidence interval; HR, hazard ratio; HU, Hounsfield units; SFA, subcutaneous fat area; SMA, skeletal muscle area.

Regarding body composition, the results of this study showed that SFA was an independent predictor for 1 year mortality (adjusted HR, 0.987; 95% CI, 0.982–0.992;  $P < 0.001$ ) in elderly patients with proximal femur fracture. A positive association was also observed between SFA and survival duration. A similar association has been reported for patients with cancers and end-stage liver disease.<sup>29–32</sup> Body fat redistribution and reduction of subcutaneous fat mass with increasing age have been observed.<sup>9</sup> Subcutaneous fat tissue would be potentially favourable on mortality and healthy life expectancy due to its metabolic and endocrine function in energy storage and production of leptin, which regulates insulin sensitivity, glucose and lipid metabolism and immune response.<sup>29,33</sup> However, several assessments are needed to understand the association between SFA at the upper thigh and 1 year mortality among elderly individuals with proximal femur fracture. As subcutaneous fat mass, which contributes to the stability of the metabolic and endocrine systems in the body, decreases with aging, it is reasonable to hypothesize that SFA mirrors the physiologic age rather than the chronological age. Low SFA could be described as an indicator of frailty in the elderly, which is defined as diminished reserve and resistance to stressors.<sup>24,34</sup> In addition, a recent meta-analysis of prospective cohort studies suggested that obesity can significantly decrease the risk of hip fracture.<sup>35</sup> Furthermore, obese patients may

benefit from cushioning of their hip by abundant fat, which may decrease impact forces when they fall.<sup>36</sup>

Body composition has been considered to reflect a patient's health status and reserve. However, presence of various measurement locations, assessment methods and diagnostic criteria have been the main obstacles to the effective utilization of body composition as a marker in clinical practice.<sup>37</sup> In the present study, body composition was measured at the upper thigh level, which was defined as the inferior tip of the ischial tuberosity and can be easily identified on abdominal and pelvic bone CT images to perform body morphometry analysis in reliable manner. Although the mid-thigh level is traditionally employed as a measurement location, selecting the mid-thigh level on axial CT images is difficult due to the lack of exact anatomic landmarks. Moreover, several studies have used different definitions for the mid-thigh level, and this may hamper consistent muscle measurements.<sup>38,39</sup> Therefore, the upper thigh level may be a good alternative measurement location to provide body composition values consistently without additional scanning and time.

This study had several limitations. First, although this was a relatively large cohort study of 876 elderly patients with proximal femur fracture who underwent surgical treatment, the intrinsic limitations of the retrospective design of the study were inevitable. In addition, mobility function before trauma



**Figure 4** Kaplan–Meier survival curve estimates of elderly patients with proximal femur fracture according to their subcutaneous fat area (SFA) (cm<sup>2</sup>) measured at the upper thigh level. SFA were defined as Q1: <math>< 131.4\text{ cm}^2</math>; Q2:

and at hospital discharge was assessed based on electronic medical records; however, inter-rater reliability was not warranted. Furthermore, there was no detailed information on functional performance measured using an objective assessment tool such as gait speed or hand-grip strength, which could affect long-term mortality. Second, this study was performed between 2010 and 2017, and the treatment strategies for femur fracture among the elderly have improved over the long study period. This could affect the outcomes as well as the clinical decision-making of the attending physicians during presentation. These potential confounding factors were not standardized in this study. Finally, this study was conducted at the ED of single tertiary center in South

Korea, and all the study participants were Northeast Asians. This weakens the generalizability of the study findings. Notably, changes in body composition according to race have been reported.<sup>40</sup>

In conclusion, our findings suggest the importance of SFA measured at the upper thigh using pelvic CT scans as an independent prognostic marker for elderly patients with proximal femur fracture who underwent surgical treatment. Our findings also imply that SFA would be a simple and reliable screening tool that reflects a patient's health status and reserve. Although further studies are required to elucidate the beneficial role of subcutaneous fat tissue in elderly patients with proximal femur fracture, personalized treatment strategies including nutritional support and rehabilitation interventions based on body composition may improve recovery of function and survival in elderly patients after femur fracture.

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## Conflicts of interest

The authors declare that they have no competing interests.

## Ethical guidelines statement

This study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. It was approved by the institutional review board (approval number: 2018-0806) before its commencement. The requirement for informed consent due to the retrospective nature of the study.

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