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Computed tomographic measurements of the psoas muscle as a predictor of mortality in hip fracture patients: Muscle attenuation helps predict mortality in hip fracture patients

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ABSTRACT

Introduction: In recent years, sarcopenia has been identified as an important risk factor of patient prognosis. The aim of this study was to determine the association between prognosis of hip fracture and sarcopenia and to evaluate the prognostic performance of psoas muscle volume and attenuation measurements in hip computed tomography (CT).

Material and methods: This was a retrospective cohort study of patients with hip fracture in our institution from 2014 to 2017. Baseline character data and hip CT scans were obtained. Two readers independently measured muscle size (cross-sectional area) and attenuation of the psoas muscle at the L4 vertebra on CT scans. Logistic regression analysis was used to identify the association between mortality and muscle index (the sum of the left and right muscle sizes divided by patient height) and muscle attenuation after adjusting for demographic variables. In addition, receiver operating characteristic (ROC) curves were obtained.

Results: In the 462 patients included in the study, in-hospital mortality was 4%. Multivariate logistic regression analysis revealed that muscle attenuation was a risk factor for mortality. Among baseline characteristics, age, sex, diastolic blood pressure, and albumin were significant variables for mortality. The area under the ROC curve (AUC) of muscle attenuation for prediction of death was 0.839 (0.803–0.872) with 84.2% sensitivity and 69.5% specificity. Furthermore, when we combined all independent factors according to the results, the AUC was 0.929 (0.902–0.951) with 84.2% sensitivity and 93.6% specificity for prediction of mortality among hip fracture patients.

Conclusion: Among many variables, the most significant was muscle attenuation. CT is the most typical modality to determine treatment of hip fracture patients. Measuring muscle size and attenuation is simple using PACS software. Muscle attenuation has significant value for predicting the prognosis of hip patients.

Introduction

Hip fracture is a musculoskeletal trauma that occurs in a large proportion of elderly patients. Which tend to have comorbidity compared to young patients might occur patients' morbidity, mortality and medical burden for both caregivers and health systems. The number of hip fractures in the United States has doubled in 20 years, with 340,000 hip fractures in 2000, and the medical cost has reached 9 billion dollars [1,2]. The 1-year mortality rate among elderly patients is generally 20%–30% [3–5].

Prognosis prediction is essential and affects treatment decision, such as surgical or conservative treatment, total hip arthroplasty or hemiarthroplasty, and post-operative conservative or intensive care, which influences patient health care, safety, and quality of life as well as cost [6]. Physicians often predict prognosis based on their clinical experience, which is highly subjective with low reproducibility [7,8].

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Several reports have shown independent risk factors for mortality of increased age, male sex, and increased number of comorbidities during treatment including conservative treatment, surgery, and post-operative procedures [9]. However, there is no consensus for prediction of prognosis in hip fracture patients with imaging modalities. CT is considered an essential diagnostic modality for hip fracture patients and is used to evaluate occult fractures and aid surgical planning [10].

In recent years, sarcopenia has been demonstrated as one of the important risk factors of prognosis in both non-orthopedic and orthopedic patients [11]. In particular, recently studies have shown that sarcopenia is important in hip fracture patients [12,13]. Sarcopenia is defined as significant loss of muscle mass and function and affects physical disability and falls and contributes to prolonged hospitalization and increasing health care costs [14]. Age-related loss of skeletal muscle and muscle strength are consequences of dysfunction of several physiological systems, including endocrine, neurological, cardiovascular, and immunological systems [15,16]. Sarcopenia can be measured using various imaging modalities including dual x-ray absorptiometry, ultrasound, MRI, and CT [14].

Although there are few reports that suggested prognosis in hip fracture patients can be predicted with measurement of muscle size (muscle volume) and attenuation (muscle fatty infiltration) [17], no report has used CT alone to measure the psoas muscle in hip fracture patients. In this study, we evaluated the prognostic performance of psoas muscle volume and attenuation in hip CT, which does not require additional radiologic evaluation.

Material and methods

Study design

This was a single-center, retrospective study that used the electronic medical records (EMRs) of patients who presented in the ED with hip fracture. The study was approved by the institutional review board, and the requirement for written informed consent was waived.

Study setting and population

This study included patients who visited a tertiary university teaching hospital with 65,000 annual emergency visits from January 2014 through December 2017. The inclusion criteria were 1) age 18 years or older who visited the ED with hip fracture and 2) hip CT performed simultaneously in the ED. The exclusion criteria were 1) metallic hip prostheses due to previous fracture or surgery, which can produce metal artifact on hip CT; 2) multiple trauma including brain hemorrhage, abdomen, and chest injuries that could result in mortality rather than hip fracture; 3) muscle-related disease such as sarcoma; and 4) incomplete EMR data (Fig. 1).

Data collection and outcome measurement

One board-certified emergency physician without knowledge of the aim of this study and final diagnosis collected data from EMRs of eligible patients that were stored in a picture archiving and communication system (PACS) (Maroview 5.4, Infinitt, Seoul, Republic of Korea).

The following data were collected: patient demographics, including sex, age, and body mass index (BMI; weight in kilograms divided by the square of height in meters); initial vital signs in the ED, including systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, body temperature, and mental status; and clinical details including laboratory findings, general ward or intensive care unit (ICU) admission, hospital length, and mortality. Comorbidity was used as a classification of the American Society of Anesthesiologists (ASA) and the Charlson Comorbidity Index (CCI), which are useful in predicting morbidity and mortality from a variety of diseases [18,19].

Image acquisition, psoas muscle size, and Hounsfield unit measurement

Hip CT examinations were performed in the hospital using a 64-slice multidetector CT scanner (Somatom Perspective ONE Dynamic Volume CT, Siemens Healthineers Corporation, Erlangen, Germany).

For evaluation of cross-sectional area and attenuation of muscle, images were obtained with PACS software. All images were retrospectively and independently evaluated by two board-certified emergency physicians (10 years of experience and 9 years of experience) who were not involved in patient selection and who were blinded to the final diagnosis and outcome. The physicians performed measurements in random order with respect to patient numeric code and radiographic image.

Measurements were conducted on axial images by outlining a freehand ROI around the circumference of the psoas muscles at the L4 pedicle level using a method similar to that reported for pancreatic adenocarcinoma [20] (Fig. 2). The muscle was measured bilaterally, which helps account for any muscle asymmetry associated with scoliosis, and the measurement was used to calculate the average of the left and the right psoas muscle sizes and attenuation (measured in Hounsfield units [21]). Muscle size was presented as muscle index, which is total psoas muscle area (square millimeters) divided by patient height (square meters); muscle attenuation was presented in Hounsfield units [21]

Reference standard

Hip fracture was confirmed by either radiological or intra-operative findings. Radiologic report confirmed by a senior musculoskeletal radiologic faculty with 15 years of experience was considered a reference standard for patients who did not undergo surgery. Intra-operative findings by the orthopedic department were considered a reference standard for patients with underwent surgery.

Statistical analysis

Continuous variables are presented as mean with SD (standard deviation) and range, while categorical variables are presented as count (percentage). Baseline clinical and demographic characteristics were summarized using the independent *t*-test for continuous variables and Pearson's chi-square test for numerical variables.

To establish the independent factors for prognosis of hip fracture patients (mortality), we performed multivariate logistic regression analysis of the variables that were statistically significant in the univariate analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from the multivariate analyses. The area under the receiver operating characteristic (AUROC) curve analysis was performed to identify prognostic accuracy. AUROC between 0.8–0.9 is considered good, between 0.7–0.8 is considered adequate, and between 0.6–0.7 is considered poor [22].

The intraclass correlation coefficients (ICCs) with 95% CIs were calculated to determine reliability between reviewers' measurements. ICCs of 0–0.20 indicated poor agreement, 0.21–0.40 indicated fair agreement, 0.41–0.60 indicated moderate agreement, 0.61–0.80 indicted good agreement, and 0.81–1.00 indicated excellent agreement [23]. The significance level was set as $p < 0.05$. All statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA).

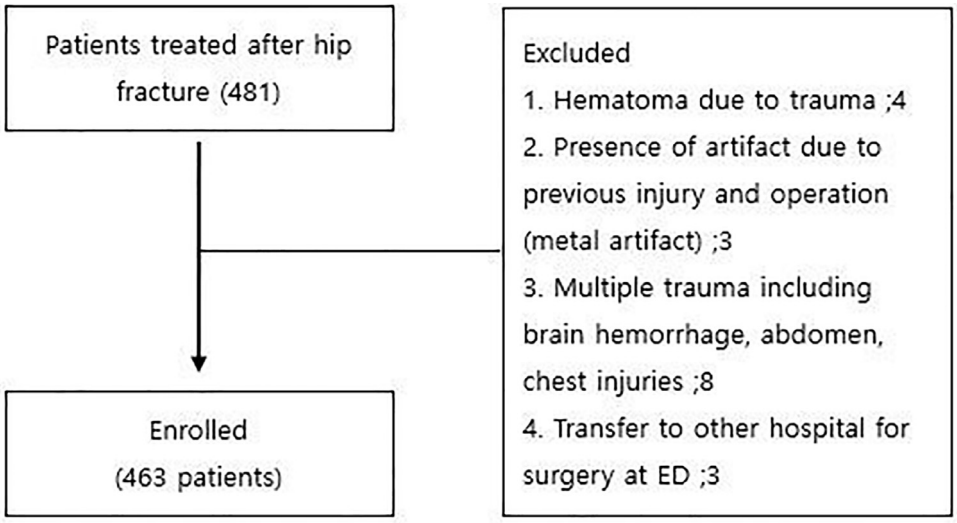

Fig. 1. Flowchart of patients enrolled in the study.

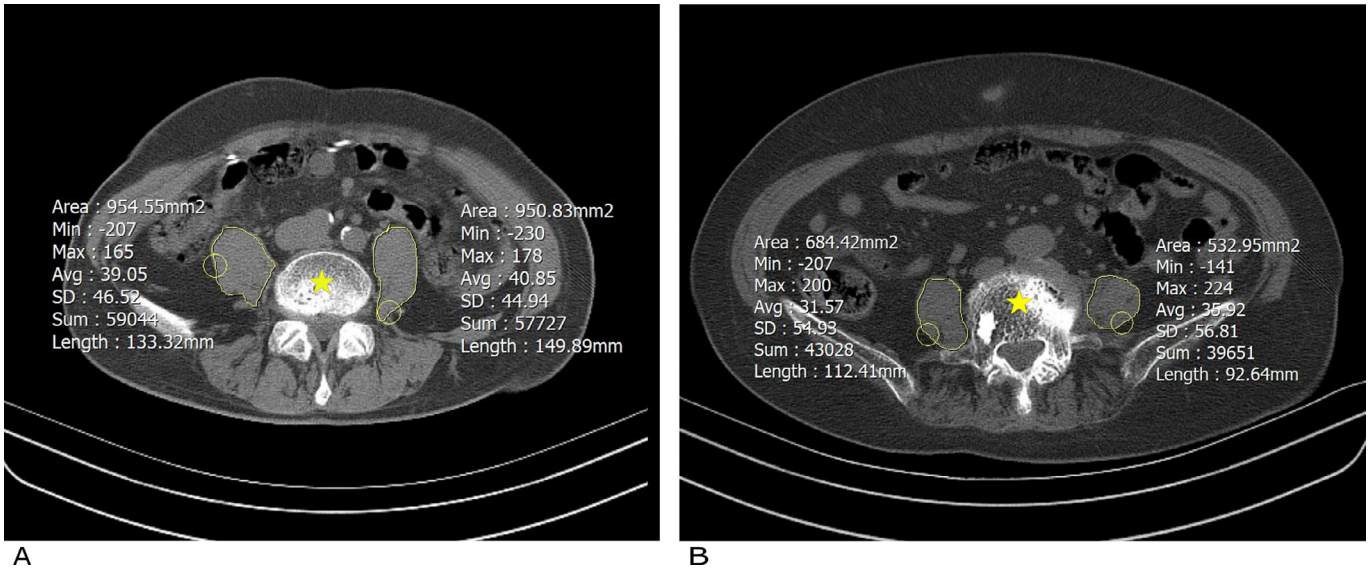

Fig. 2. Two different patients. Axial CT images outlining the psoas muscles bilaterally were obtained at L4 level (yellow stars).
A, 55-year-old man, image shows a cross-sectional area (yellow outline) measuring left side and right side which were 950.83mm^2 and 954.55mm^2 and mean muscle attenuation measuring left side and right side which were 40.85 HU (SD, 44.94 HU) and 39.05 (SD, 46.52), respectively.
B, 87-year-old woman, image shows a cross-sectional area (yellow outline) measuring left side and right side which were 532.95mm2 and 684.42mm2 and mean muscle attenuation measuring left side and right side which were 36.92 HU (SD, 56.81 HU) and 31.57 HU (SD, 54.93), respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

Results

Baseline characteristics

From January 2014 through December 2017, a total of 462 patients was enrolled in the study (Fig. 1). The baseline characteristics of patients are presented in Table 1. The mean age of enrolled patients was 74.3 years (SD: 16.2), and 30.7% of patients were male. The mean CCI was 4.4 (SD: 1.7), and ASA physical status classification was 2.2 (SD: 0.6). A total of 431 patients underwent surgery (93.3%); 19 (4.1%) died during the clinical process.

Measurement of psoas muscle area and attenuation

The psoas muscle size and attenuation were measured in the 462 patients by two reviewers. For reviewer 1, the mean muscle areas on the left, right, and average (mm^2) were 552.3, 555.4, and 553.9, respectively; the mean attenuation (HU) values were 35.5, 36.0, and 35.8, respectively. For reviewer 2, the mean muscle areas on the left, right, and average (mm^2) were 547.8, 532.5, and 540.1, respectively; the mean attenuation (HU) values were 35.8, 35.7, and 35.8, respectively. The muscle index (mm^2/m^2) based on each reviewer's measurements were 418.3 and 408.2, respectively. Agreement for muscle size and attenuation between reviewers 1 and 2 was excellent. The ICCs between the two reviewers for muscle size on the left and right were excellent at 0.968 [95% CI: 0.961–0.973] and 0.915 [95% CI: 0.898–0.929], respectively. The ICCs for attenuation on left and right sides were also excellent at 0.938 [95% CI: 0.925–0.948] and 0.908 [95% CI: 0.890–0.924], respectively.

Table 1
Demographic, laboratory and clinical variables of patients (Total $n = 462$).

Variable	Value
Age (years)	74.3 ± 16.2
Sex	
Male	142 (30.7)
Female	320 (69.3)
Body mass index[a] (kg/m^2)	23.2 ± 9.8
Charlson comorbidity index (CCI)	4.4 ± 1.7
American Society of Anesthesiologists score (ASA)	2.2 ± 0.6
Systolic Blood Pressure (mmHg)	136.3 ± 25.1
Diastolic Blood Pressure (mmHg)	76.4 ± 12.1
Pulse rate (beats/min)	82.3 ± 12.6
Respiratory rate (breath/min)	20.0 ± 1.5
Body temperature (°C)	36.6 ± 0.5
Mental status	
Alert	457
Verbal response	4
Painful response	1
Unresponsive	0
Laboratory test	
Hemoglobin (g/dL)	11.8 ± 2.0
Hematocrit (%)	35.0 ± 5.5
White blood cell (10^9/L)	10.7 ± 3.9
Platelet(10^9/L)	209.9 ± 80.3
C-reactive protein (mg/dL)	2.4 ± 3.7
Aspartate aminotransferase (IU/L)	36.2 ± 35.7
Alanine aminotransferase (IU/L)	19.7 ± 21.4
Blood urea nitrogen (mg/dL)	20.3 ± 10.7
Creatinine (mg/dL)	1.0 ± 0.8
Glucose (mg/dL)	147.3 ± 57.3
Albumin (g/dL)	3.8 ± 0.4
Sodium (mmol/L)	136.2 ± 3.9
Potassium (mmol/L)	4.0 ± 0.5
Troponin-T (ng/mL)	0.10±0.95
Operative treatment	
Yes	431 (93.3)
No	31 (6.7)
Hospital day (days)	27.8 ± 19.7
ICU admission	16 (3.5)
In-hospital mortality	19 (4.1)
Psoas muscle index (mm^2/m^2) [†]	
Reviewer 1	418.3 ± 232.7
Reviewer 2	408.2 ± 209.0
Muscle attenuation (HU)	
Reviewer 1	35.8 ± 8.1
Reviewer 2	35.7 ± 7.5

[a] The values are given as mean ± standard deviation.[b]The values are given as number (%).
[†] Psoas muscle index is calculated in sum of muscle sizes divided by patient's height.

Clinical factors associated with prognosis of hip fracture patients

The associations between death and clinical and laboratory variables are presented in Table 2. In a total of 462 patients, univariate logistic regression analysis was performed for in-hospital mortality. On univariate analysis, CCI, DBP, albumin, muscle attenuation, age, sex, BUN, creatinine, and troponin-T were significant risk factors for death. Multivariate logistic regression analysis was performed for these variables . In multivariable analysis, significant predictors of in-hospital mortality were age, sex, diastolic blood pressure, albumin, and muscle attenuation (Table 2).

Predictive performance of psoas muscle measurement in hip fracture patients

According to multivariate logistic analyses, muscle size was not an independent factor. The ROC curves of the significant factors for prediction of death are shown in Fig. 3. The AUC of muscle attenuation for prediction of death was 0.839 [95% CI: 0.803–0.872], and the cut-off value was 32 with 84.2% sensitivity and 69.5% specificity. To increase sensitivity and specificity, we combined other independent factors with muscle attenuation, as is presented in Table 3. When we combined muscle attenuation and albumin level, the AUC was 0.904 [95% CI: 0.874–0.930] with 84.2% sensitivity and 82.1% specificity. Furthermore, when we combined all independent factors, the AUC was 0.929 [95% CI: 0.902–0.951] with 84.2% sensitivity and 93.6% specificity for prediction of mortality among hip fracture patients.

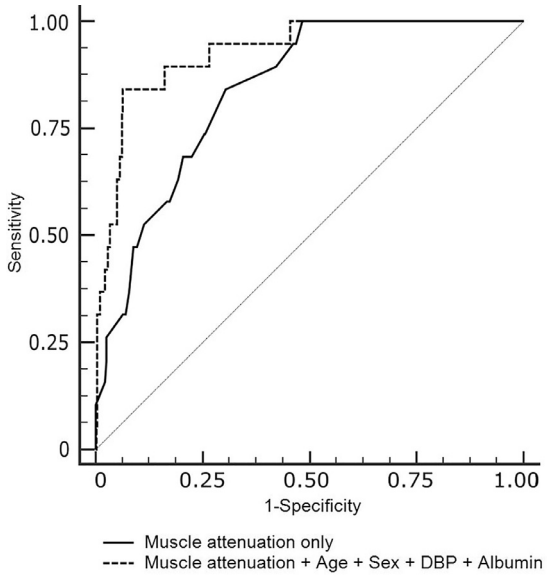

Fig. 3. The AUROCs for the prediction of mortality
The area under the receiver operating characteristic (AUROC) curves for the prediction of mortality. AUROC curve for muscle attenuation and the combination of muscle attenuation, age, sex, diastolic blood pressure and albumin to predict mortality of patients with hip fracture.

Discussion

As population aging accelerates, studies are focusing on diseases in the elderly, death from trauma, and risk factors related to aging. There are many issues with aging, but this study focused on loss of muscle mass and muscle strength due to muscle atrophy and fatty infiltration that may be clinically occult or ignored [24]. Our results revealed that muscle attenuation was an independent predictor of hip fracture patient mortality. To the best of our knowledge, this is the first study to evaluate the association between muscle attenuation and prognosis of hip fracture using hip CT alone. A positive association was observed between muscle attenuation and poor prognosis of hip fracture as evidenced by in-hospital mortality. This is consistent with other reports that demonstrated that sarcopenia measured in the ED was independently associated with in-hospital mortality and morbidity [17,25,26]. In addition, we presented the cut-off value of poor prognosis of hip fracture.

Increases in adiposity of skeletal muscle and other tissues have been reported as age-related processes that can result in mitochondrial dysfunction and impaired oxidative metabolism [15,27,28]. Aging has been linked to the increasing tendency of precursor cells such as bone marrow mesenchymal cells or muscle satellite cells to express an adipocytic phenotype instead of osteoblastic or myocytic phenotype with age [29]. Moreover, in skeletal muscle, age-related decreases in the ability of muscle fibers to process triglyceride result in increased storage of lipid in the form of droplets that form along the cell membrane [30]. Sarcopenia is evaluated as an independent factor in assessing the prognosis of patients with medical problems such as endovascular aortic aneurysm and pulmonary embolism [25,26]. The replacement of

Table 2
Univariate analysis of mortality predictors.

Variable	Univariate analysis[a] Non-mortality group $n = 443$	Mortality group $n = 19$	*P*-value	Multivariate analysis[+] OR	B	*P*-value
Age (years)	74.0 ± 16.3	82.5 ± 10.1	**0.023**	1.09 (1.01, 1.17)	0.082	**0.030**
Sex; Male	132	10	**0.041**	4.42 (1.33, 14.69)	1.487	**0.015**
Body mass index[a] (kg/m^2)	23.3 ± 10.0	22.0 ± 3.9	0.332			
Charlson comorbidity index (CCI)	4.4 ± 1.7	5.5 ± 1.0	**0.005**	1.27 (0.62, 2.60)	0.238	0.517
American Society of Anesthesiologists score(ASA)	2.2 ± 0.6	2.4 ± 0.6	0.272			
Systolic Blood Pressure (mmHg)	136.6 ± 25.0	130.2 ± 26.3	0.274			
Diastolic Blood Pressure (mmHg)	76.7 ± 12.1	68.7 ± 11.7	**0.006**	0.93 (0.88, 0.98)	−0.069	**0.011**
Pulse rate (beats/min)	82.3 ± 12.4	82.4 ± 15.4	0.977			
Respiratory rate (breath/min)	20.0 ± 1.5	20.2 ± 1.7	0.516			
Body temperature (°C)	36.6 ± 0.5	36.4 ± 0.3	0.070			
Laboratory test						
Hemoglobin (g/dL)	11.8 ± 2.0	11.2 ± 2.0	0.202			
Hematocrit (%)	35.0 ± 5.5	33.7 ± 6.4	0.298			
White blood cell (10^9/L)	10.6 ± 3.9	11.9 ± 5.4	0.162			
Platelet(10^9/L)	209.7 ± 81.1	214.1 ± 60.5	0.813			
C-reactive protein (mg/dL)	2.4 ± 3.7	2.8 ± 3.5	0.620			
Aspartate aminotransferase (IU/L)	36.2 ± 36.0	35.6 ± 29.4	0.938			
Alanine aminotransferase (IU/L)	19.7 ± 21.6	18.0 ± 17.1	0.723			
Blood urea nitrogen (mg/dL)	20.0 ± 10.3	25.8 ± 17.7	**0.041**	1.02 (0.98, 1.06)	0.018	0.351
Creatinine (mg/dL)	1.0 ± 0.8	1.5 ± 1.4	**0.026**	1.11 (0.58, 2.12)	0.104	0.752
Glucose (mg/dL)	147.2 ± 57.0	149.1 ± 65.4	0.890			
Albumin (g/dL)	3.9 ± 0.4	3.4 ± 0.5	**<0.001**	0.22 (0.07, 0.72)	−1.508	**0.012**
Sodium (mmol/L)	136.2 ± 3.8	134.6 ± 5.0	0.073			
Potassium (mmol/L)	4.0 ± 0.5	4.2 ± 0.7	0.177			
Troponin-T (ng/mL)	0.05±0.5	1.0 ± 3.8	**0.025**	1.61 (0.82, 3.17)	0.475	0.169
Hospital day (days)	27.1 ± 17.3	43.2 ± 47.8	**0.003**	1.02 (1.00, 1.05)	0.023	**0.031**
ICU admission	15 (3.4)	1 (5.3)	0.192			
Psoas muscle index (mm^2/m^2)	418.6 ± 230.8	411.1 ± 279.1	0.890			
Muscle attenuation (HU)	36.2 ± 8.0	26.9 ± 5.0	**<0.001**	0.82 (0.74, 0.90)	−0.202	**<0.001**

OR odds ratio, B regression coefficient.
Boldface type indicates statistical significance ($p < 0.05$).
[a] Data are mean (standard deviation) or number (%).
[+] Data in parentheses are 95% confidence intervals, conducted on variables with a p value of < 0.05 on univariate analysis.

Table 3
AUROC, sensitivities, specificities of sepsis criteria.

	Sensitivity,% (95% CI)	Specificity,% (95% CI)	AUROC (95% CI)
Muscle attenuation only	84.2 (60.4 - 96.6)	69.5 (65.0 - 73.8)	0.839 (0.803 – 0.872)
Muscle attenuation + Age	94.7 (74.0 - 99.9)	71.3 (66.9 - 75.5)	0.871 (0.837 - 0.900)
Muscle attenuation + Sex	94.7 (74.0 - 99.9)	62.75 (58.1 - 67.3)	0.863 (0.828 - 0.893)
Muscle attenuation + DBP	94.7 (74.0 - 99.9)	62.75 (58.1 - 67.3)	0.863 (0.828 - 0.893)
Muscle attenuation + Albumin	84.2 (60.4 - 96.6)	82.1 (78.1 - 85.5)	0.904 (0.874 - 0.930)
Muscle attenuation + Age + Sex + DBP + Albumin	84.2 (60.4 - 96.6)	93.6 (90.9 - 95.7)	0.929 (0.902 – 0.951)

AUROC Area under the ROC curve.
DBP diastolic blood pressure.

skeletal muscle by non-contractile components such as lipids appears to contribute to age-related losses in skeletal muscle function, along with loss of muscle mass. This results in loss of muscle strength and reduced performance, as well as loss of mobility, and increases the risk of trauma such as falls. In addition, impaired muscle strength and reduced physical function may cause loss of bone strength.

Although sarcopenia is especially important in elderly patients, the gold standard measurement method of dual energy X-ray absorptiometry (DXA) has drawbacks. Bioelectrical impedance analysis is not specific to muscle, but also indicates alteration in body water, so overhydration or dehydration can lead to substantial errors [31]. Despite these errors, DXA is widely used, but it is not practical for patients with acute hip fracture. In contrast, CT is mostly performed to determine treatment of hip fracture patients. Therefore, in this study, we examined if size and attenuation of the fracture were significant using CT.

There are numerous studies on age, sex, comorbidity, fracture location, and fracture treatment as postoperative prognostic factors of patients with hip fractures [32]. The baseline characteristics of patients, especially age and sex, were significant factors in this study, consistent with previous reports. In addition, we obtained CT findings of muscle size and attenuation. CT has been validated for the measurement of muscle size and attenuation and may be performed for patients presenting with hip fractures. Few studies have examined the association of CT measurements of muscle size and attenuation, especially in hip CT alone, with mortality for hip fracture patients.

In this study, poor prognosis was determined as in-hospital mortality. Various variables such as age, sex, vital signs, and laboratory tests were investigated, and the most significant variable in the multivariate logistic analysis was muscle attenuation. An increase in skeletal muscle lipid content can be quantified accurately by CT scan; an increase in lipid concentration of 1 g/100 ml causes an approximately 1 HU decrease in CT attenuation [33]. Muscle attenuation analyzed using the ROC curve showed good predictability for mortality (AUROC between 0.8 and 0.9). In addition, when we combined muscle attenuation with other significant factors such as age, sex, DBP, and albumin, the highest sensitivity and specificity were noted for albumin. When we combined

all significant factors, the AUC, sensitivity, and specificity showed large improvement. Therefore, we propose that muscle attenuation is useful for prediction of prognosis of patients with hip fracture in combination with baseline characteristics and lab findings such as age, sex, blood pressure, and albumin.

This study has several limitations. First, this was a single-centered retrospective study. Thus, selection bias may be present. Caution should be used in generalizing our results, and further studies are required with multi-centered, prospective designs. Second, the relatively small sample size of in-hospital mortality compared with survivors may not be sufficient for identifying definite associated factors. Third, there is a potential selection bias for patient inclusion in the study group. Because only hip fracture patients who underwent CT were included in the first step. Use of manual muscle outlining was another limitation and can lead to incorrect inclusion of perimuscular fat in the measurement area. However, to minimize this bias, two board-certified emergency physicians measured the psoas muscle, and the reliability was verified.

Conclusion

This study's results were consistent with those of other studies regarding baseline characteristics such as age and sex or laboratory tests. Among multiple variables, the most significant was muscle attenuation. Muscle size and attenuation are not routinely analyzed in patients with hip fractures, but CT examinations include these measurements on every scan. In addition, measuring muscle size and attenuation is very simple using PACS software. The poor prognosis in elderly patients and in males is similar to results in previous studies. The present study is important because it verified the ability to predict prognosis with muscle attenuation as measured using hip CT, which can be easily performed.

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None.

Previous presentation

None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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