Rectus Femoris Muscle Mass Measured by Ultrasound is an Indicator of Whole-Body Muscle Mass at Intensive Care Unit Admission: A Retrospective Study

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Research

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Abstract

Background: Muscle mass is an important biomarker of survival from a critical illness, but it is not a widely accepted method to assess whole-body muscle mass when patients are admitted to the intensive care unit (ICU). We hypothesize that ultrasound-based muscle mass assessments can reflect whole-body muscle mass.

Methods: We conducted a retrospective analysis of prospectively obtained ultrasound data at ICU admission. We included patients who underwent computed tomography (CT) imaging at the third lumbar vertebral level, within 2 days before and after ICU admission. Primary outcomes included the correlation between the muscle mass (thickness and cross-sectional area) of the rectus femoris measured using ultrasound and whole-body muscle mass measurements obtained from CT. We aimed to determine whether ultrasound assessments can identify sarcopenia, defined as a skeletal muscle index of 29.0 cm^2/m^2 for males and 36.0 cm^2/m^2 for females. Secondary outcomes included the ultrasound measurements of the biceps brachii muscle mass and diaphragm thickness.

Results: Among 133 patients, 89 patients underwent CT imaging, which included the third lumbar vertebra. The patients' mean age was 72 ± 13 years, and 60 patients were male. The correlation between rectus femoris muscle ultrasound and CT was $\rho = 0.57$ ($p < 0.01$, n = 89) and $\rho = 0.48$ ($p < 0.01$, n = 89) on thickness and cross-sectional area, respectively. The thickness of the rectus femoris and cross-sectional area had the discriminative power to assess sarcopenia when the areas under the curve were 0.84 and 0.76, respectively. Ultrasound measurements of the biceps brachii muscle mass and diaphragm thickness were correlated with CT imaging [$\rho = 0.57$–0.60 ($p < 0.01$, n = 52) and $\rho = 0.35$ ($p < 0.01$, n = 79)].

Conclusions: Ultrasound measurements of muscle mass are a promising method to assess whole-body muscle mass and sarcopenia at ICU admission.

Trial registration: UMIN000044032. Retrospectively registered on 25 April 2021

Background

Muscle mass is an important biomarker of survival from a critical illness, because lower muscle mass at intensive care unit (ICU) admission is associated with higher mortality and ICU-acquired weakness [1, 2]. Recently, the notion that a state of low muscle mass is representative of sarcopenia has been gaining increased attention [3]. The identification of sarcopenia is important in planning nutrition and rehabilitation management strategies. Both are needed to maintain muscle mass during ICU hospitalization. However, to date, there is no widely accepted method to assess low muscle mass and sarcopenia at the time of ICU admission.

Several methods have been used to assess muscle mass [4]. Generally, dual-energy X-ray absorptiometry and bioelectrical impedance analyses have been used to assess whole-body muscle mass and sarcopenia [5]. However, these indirect muscle mass assessments are inaccurate in critically ill patients because these are influenced by dynamic fluid changes [6–8]. During a critical illness, computed tomography (CT) is considered the gold standard to assess whole-body muscle mass because it can visually separate muscle mass from other tissues [9]. Although CT is a reliable method to measure muscle mass, prospective CT evaluation is infeasible because of patient transportation risks and radiation exposure [10]. Alternatively, ultrasound is an emerging tool used to measure muscle mass noninvasively at the bedside [11]. Although ultrasound is used to assess limb muscles, it is unclear whether the partial muscle mass assessments reflect whole-body muscle mass in critically ill patients. To validate ultrasound assessments of whole-body muscle mass, it is important to show the measurement correlation between ultrasound and CT.

The rectus femoris muscle is assessed commonly using ultrasound, in which muscle thickness or cross-sectional area measurements are conducted. The measurement of the cross-sectional area is preferable because it correlates with the patient’s physical functions [12, 13]. However, it is unclear if these mass measurements reflect whole-body or partial-body muscle mass in critically ill patients. Given that a previous study reported that the cross-sectional area of the rectus femoris is preferable for muscle mass assessments, we hypothesized that this area (not the thickness) is associated with whole-body muscle mass. We retrospectively evaluated the muscle mass area at the level of the third lumbar vertebra using CT, and compared the outcomes with those obtained from prospectively obtained ultrasound data at ICU admission. This study aimed to investigate whether ultrasound measurements can replace CT regarding whole-body muscle mass measurements at ICU admission.

Methods

Study design

This two-center retrospective study was conducted in the mixed medical/surgical ICUs of Tokushima University Hospital and Tokushima Prefectural Central Hospital. The study was based on Declaration of Helsinki, and approved by the clinical research ethics committees at Tokushima University Hospital (approval number 2593) and Tokushima Prefectural Central Hospital (approval number 1739). Prospectively obtained data from May 2016 to June 2020 were retrospectively analyzed. This trial was retrospectively registered as a clinical trial (UMIN-Clinical Trials Registry: 000044032). At the time of data acquisition, written informed consent was obtained from patients or their relatives. One part of this study was published previously [7, 14].

Study population

We included patients who met the following criteria: (1) adults (≥ 18 years) admitted to the ICU; (2) those expected to stay in the ICU for more than 5 days; (3) those who underwent ultrasound assessments of the rectus femoris muscle at the day of ICU admission; and (4) those who underwent CT assessments of the third lumbar vertebra within 2 days before and after ICU admission. The following patients were excluded from the studies conducted previously: those with (1) primary neuromuscular disease and (2) obstacles at the ultrasound measurement site.

Ultrasound

We used a linear transducer and conducted B-mode imaging. The measurements were taken at the dominant limb, with elbows and knees extended in the spine position. The transducer was placed perpendicular to the long axis of the limbs. The thickness and cross-sectional area of the rectus femoris were measured. Measurements were taken midway between the anterior superior iliac spine and the proximal end of the patella. The thickness, including the underlying vastus intermedius muscle, was measured from the superficial fascia of the rectus femoris to the uppermost part of the femur. The cross-sectional area was measured by outlining the area shown in the transverse plane. The biceps brachii muscle was measured at a distance equal to two-thirds of the distance from the acromion to the antecubital crease. The thickness, including the underlying brachialis muscle, was defined as the depth between the superficial fascia of the biceps brachii muscle and the uppermost part of the humerus. The diaphragm was measured at the end expiration on the right chest wall at the zones of apposition 0.5–2 cm below the costophrenic sinus between the antero-axillary and the midaxillary lines. Ultrasound measurements were taken by a physician (N.N.) three times, and the median value was used for evaluation. The reliability of measurements was confirmed by another ICU physician. The intraclass and interclass correlation coefficients were 0.96–0.99 and 0.99 for limbs and 0.92 and 0.96 for the diaphragm, respectively, as reported previously [14].

Computed tomography

CT was used to evaluate whole-body muscle mass. The CT image at the level of the third lumbar vertebra is reported to correlate with whole-body muscle mass. A board-certified radiologist (A.Y.) retrospectively measured the total muscle mass in the CT image at the middle point of the third lumbar vertebra (L3) where transverse processes were visualized. At this slice level, the total muscle area included the psoas, quadratus lumborum, transversus abdominis, external and internal obliques, and rectus abdominis muscles. CT images acquired within 2 days before and after ICU admission were included in the analyses, and examinations conducted close to the day of ICU admission were used for comparisons in patients with multiple CT examinations. The radiologist was blinded to all clinical characteristics. Images were analyzed using ImageJ software (National Institutes of Health, Bethesda, MD, USA) [15]. The reliability of measurements was confirmed in 10 patients by two examiners (Y.A. and N.N.). The intraclass correlation coefficient was $\rho = 0.98$ ($p < 0.01$) and the interclass value was $\rho = 0.94$ ($p < 0.01$). The Bland–Altman plot yielded a bias of − 1.24 ± 1.58 and − 4.83 to 2.34 at the 95% limits of agreement regarding intraobserver reproducibility, and a bias of − 0.94 ± 2.67 and − 6.98 to 5.10 at the 95% limits of agreement regarding interobserver reproducibility.

We used the skeletal muscle index to discriminate sarcopenia at ICU admission. The sex-specific cutoff point was set to 29.0 cm^2/m^2 for males and 36.0 cm^2/m^2 for females, as one of the commonly used cutoff points for sarcopenia in the Asian population [16]. This cutoff point was previously reported to be important in the Japanese population [17].

Outcomes

The primary outcome was the relationship between ultrasound assessments of the rectus femoris muscle mass and CT assessments. We also assessed whether ultrasound assessments of the rectus femoris muscle can predict sarcopenia in the same manner as that assessed by CT. Secondary outcomes of this study included the relationship between ultrasound assessments at the biceps brachii muscle and diaphragm and CT assessments.

Statistics

Continuous variables were presented as the mean (standard deviation) or median values [interquartile range (IQR)], whereas categorical data were presented as counts and proportions. Variables were compared using either the t-test or the Mann–Whitney U-test. The Spearman correlation coefficient was used to investigate relationships in primary and secondary outcomes. The area under the receiver operating characteristic curve (AUC) was generated to determine the cutoff values of ultrasound assessments for sarcopenia. For reproducibility, the Spearman correlation coefficient and Bland–Altman plot were determined using JMP statistical software, version 13.1.0 (SAS Institute Inc., Cary, NC, USA).

Results

In total, 133 patients had ultrasound measurements of the rectus femoris muscle mass. Among them, 89 patients underwent CT imaging at the level of the third lumbar vertebra within 2 days of ICU admission (Fig. 1). Of the patients included, CT examinations were conducted on the median day of 0 (IQR, 0–0 days). Fifty-nine patients had CT examinations immediately after ICU admission. CT examinations were conducted in 10 and 4 patients on days 1 and 2 after ICU admission, respectively, and in 13 and 3 patients on days 1 and 2 days before ICU admission, respectively.

The patients’ characteristics are summarized in Table 1. The patients’ mean age was 72 ± 13 years, and 60 patients were male. The median Acute Physiology and Chronic Health Evaluation II score was 27 (IQR, 24–30) and the median length of ICU stay was 7 (IQR, 5–14) days. Seventy-eight (88%) patients were mechanically ventilated, and 15 (16%) were admitted postoperatively. Sarcopenia, assessed by CT, was present in 24 (27%) patients. The median rectus femoris thickness and cross-sectional area were 23.7 (IQR, 17.7–31.0) mm and 4.9 (IQR, 3.9–6.5) cm^2, respectively. There were body mass index ($p < 0.01$), rectus femoris thickness ($p < 0.01$), rectus femoris cross-sectional area ($p < 0.01$), and muscle mass differences on CT between sarcopenia and non-sarcopenia ($p < 0.01$).

Table 1
Patients' characteristics

	All patients	Sarcopenia	Non-Sarcopenia	
Variables	(n = 89)	(n = 24)	(n = 65)	p-value
Age, mean ± SD, y	72 ± 13	76 ± 11	70 ± 13.6	0.07
Male/Female	60/29	16/8	44/21	0.93
Body mass index, mean ± SD, kg/m^2	22.2 ± 4.4	18.6 ± 3.0	23.5 ± 4.0	< 0.01
APACHE II score	27 (24–30)	28 (25–32)	27 (23–30)	0.31
SOFA	8 (6–11)	8 (6–11)	10 (6–12)	0.66
Sepsis (Sepsis-3 criteria), n (%)	40 (49)	24 (56)	16 (41)	0.27
Postoperative admissions, n (%)	14 (16)	1 (4)	13 (20)	0.07
Mechanical ventilation, n (%)	78 (88)	19 (79.2)	59 (90.8)	0.16
Length of ICU stay, d	7 (5–14)	6 (4–11)	7 (5–17)	0.13
Length of hospital stay, d	29 (18–51)	22 (15–44)	30 (21–51)	0.39
Mortality in the ICU, n (%)	16 (18.0)	4 (17)	12 (19)	0.85
Mortality in the hospital, n (%)	25 (28.1)	10 (41.7)	15 (23.1)	0.08
Thickness (mm)	23.7 (17.7–31.0)	17.4 (14.0–19.9)	28.3 (21.1–32.3)	< 0.01
Cross-sectional area (cm^2)	4.9 (3.9–6.5)	3.9 (2.9–4.6)	5.4 (4.1–7.1)	< 0.01
Muscle mass in computed tomography (cm^2)	102.8 (77.1–133.2)	69.2 (54.1–80.5)	118.9 (97.0–143.5)	< 0.01
APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; SD: standard deviation; ICU: intensive care unit; IQR: interquartile range				
Data were presented as median (IQR) unless otherwise indicated.				

Ultrasound measurements of the rectus femoris muscle at ICU admission were correlated with the muscle mass at the third lumbar vertebra, as measured by CT (Fig. 2). The correlations of the thickness of the rectus femoris and its cross-sectional area were $\rho = 0.57$ ($p < 0.01$, n = 89) and $\rho = 0.48$ ($p < 0.01$, n = 89), respectively. The thickness of the rectus femoris had the discriminative power to assess sarcopenia at the AUC of 0.84 (95% Confidence Interval [CI], 0.74–0.94), in which the cutoff value of 20.2 mm had a sensitivity of 83.3% and a specificity of 78.5% (Fig. 3). Conversely, the rectus femoris cross-sectional area had the discriminative power to assess sarcopenia at the AUC of 0.76 (95% CI, 0.65–0.88), in which the cutoff value of 4.66 cm^2 had a sensitivity of 79.2% and a specificity of 66.2%.

Among the secondary outcomes, the biceps and diaphragm muscles were assessed in 52 and 79 of the 89 patients included, respectively (Fig. 4). Ultrasound measurements of the biceps and diaphragm muscles at ICU admission were correlated with the muscle mass at the third lumbar vertebra, as measured by CT. The biceps brachii thickness and cross-sectional area yielded the following correlations: $\rho = 0.57$ ($p < 0.01$, $n = 52$) and $\rho = 0.60$ ($p < 0.01$, $n = 52$), respectively. The diaphragm muscle thickness yielded a correlation of $\rho = 0.35$ ($p < 0.01$, $n = 79$).

Discussion

In this study, we investigated whether ultrasound-based rectus femoris muscle thickness and cross-sectional area measurements are indicators of whole-body muscle mass in 89 critically ill patients. Contrary to our hypothesis, both the thickness and cross-sectional area were good indicators of whole-body muscle mass at ICU admission. The biceps brachii and diaphragm muscles were also weak to moderate indicators of whole-body muscle mass. Given that CT is not routinely available to critically ill patients, ultrasound measurements of the rectus femoris thickness and cross-sectional area can be an alternative for noninvasive assessments of muscle mass and sarcopenia at ICU admission.

This study adds several important intellectual contents. First, we found that both the rectus femoris thickness and cross-sectional area are good indicators of whole-body muscle mass. A previous study investigated the quadriceps muscle thickness in 35 critically ill patients, and showed that the thickness was correlated with muscle mass measured using CT [18]. However, the differences between the thickness and cross-sectional area had not been clarified in previous studies. Although thickness measurement is not correlated with functional impairments [12, 13], the thickness measurement reflects whole-body muscle mass. Second, this study sets the standard values of the rectus femoris thickness and cross-sectional area at ICU admission. Few studies have investigated subject groups using ultrasound at ICU admission. The rectus femoris thickness of 20.2 mm and the cross-sectional area of 4.66 cm^2 can be set as the cutoff values for sarcopenia at ICU admission. Hida et al. investigated the cutoff value of the rectus femoris muscle for sarcopenia in healthy volunteers, but the values in critically ill patients have not been reported [19].

Interestingly, the biceps brachii muscle mass was correlated with the whole-body muscle mass. This finding is important because muscle mass assessments of the biceps brachii muscle may replace the rectus femoris muscle for whole-body muscle mass assessments. The extension of the lower limb for rectus femoris muscle measurements requires the critically ill patients to be placed in a supine position because the bed angle affects lower limb extension [20]. During a critical illness, especially at ICU admission, the flat position may be risky in some patients. On the other hand, the extended biceps brachii muscle can be held regardless of the bed angle. Furthermore, the upper limb can be measured more easily because the biceps brachii muscle is exposed to the outside, whereas the rectus femoris muscle measurements need preparation pertaining to the removal of the patient’s cloth. A previous study reported that the sum of upper and lower limb muscle masses is useful to evaluate whole-body muscle mass [21]. However, it was unclear whether the biceps muscle alone can be correlated with whole-body muscle mass. The upper limb circumference has been used to calculate the upper limb muscle mass, but it is not accurate to evaluate the muscle mass in critically ill patients [22]. This is reasonable because the circumference indirectly evaluates the upper limb muscle mass, whereas ultrasound evaluates it directly. Therefore, the ultrasound biceps brachii muscle measurements are promising for whole-body muscle mass assessments.

In addition to the biceps brachii muscle, the diaphragm was also correlated with whole-body muscle mass. We found that the diaphragm thickness is different among critically ill patients. Sklar et al. reported that a diaphragm thickness less than 2.3 mm is associated with prolonged mechanical ventilation and mortality [23]. Our finding suggests that patients with frailty likely have low diaphragm thickness. Thus, preventing further diaphragm atrophy is an urgent matter in these patients. Diaphragm atrophy may be prevented by avoiding excessive ventilatory support and inflammation [24, 25]. Furthermore, diaphragm muscle training can preserve diaphragm muscle thickness [26]. The prevention and treatments of diaphragm atrophy are being investigated globally, but few treatments exist [27]. Physical rehabilitation, such as mobilization, may contribute to treating diaphragm muscle atrophy as well as whole-body muscle mass because of the associated relationship [28].

Based on this study’s outcomes, we propose using ultrasound to assess whole-body muscle mass at the time of ICU admission. The recognition of sarcopenia at ICU admission is important for nutritional and rehabilitation intervention. Sarcopenia at ICU admission carries a risk of mortality and prolonged physical impairments. As early enteral nutrition and early mobilization are recommended in critically ill patients, personalized nutrition and rehabilitation management schemes could prevent further muscle loss. Given that we provided the cutoff value of ultrasound assessments, it may be possible to assess sarcopenia using ultrasound. Additional studies are needed to confirm that ultrasound muscle mass assessments can be used to improve patient management in the ICU.

Limitations

First, this is a retrospective analysis of an observational study. Therefore, prospective studies should be conducted to validate these findings. Second, the reliable cutoff value of sarcopenia is unclear for the entire ICU population. Therefore, we used a cutoff value for the Japanese population to avoid ethnicity differences. Third, CT and ultrasound examinations were conducted within 2 days before and after admission and not on the same day. However, the CT examination was conducted at the median day of 0 (IQR, 0–0 days). Thus, temporal differences were not considered to be influential.

Conclusions

We retrospectively evaluated the relationship between ultrasound and CT muscle mass assessments and found that ultrasound measurements of the rectus femoris muscle thickness and cross-sectional area can serve as indicators of whole-body muscle mass. Furthermore, the biceps brachii and diaphragm muscles are weak to moderate indicators of whole-body muscle mass. At ICU admission, ultrasound assessments of muscle mass can be a promising method to identify low whole-body muscle mass and sarcopenia.

Abbreviations

AUC: area under the receiver operating characteristic curve; CT: computed tomography; ICU: intensive care unit; IQR: interquartile range; CI: confidence interval

Declarations

Ethics approval and consent to participate

Ethics approval and consent to participate: Ethics approval was obtained from the clinical research ethics committee at Tokushima University Hospital (approval number 2593) and Tokushima Prefectural Central Hospital (approval number 1739). Informed consent to participate in the study was also obtained from patients or from an authorized surrogate.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

AY took part in the acquisition of dada and drafting of the manuscript. NN took part in study design, acquisition of dada, analysis, and drafting of the manuscript. The first two authors contributed equally to this study as first authors. YO took part in the revision of the manuscript. Profs SI, JK, MH, and JO supervised all aspects of this study. All authors read and approved the final manuscript.

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Figures

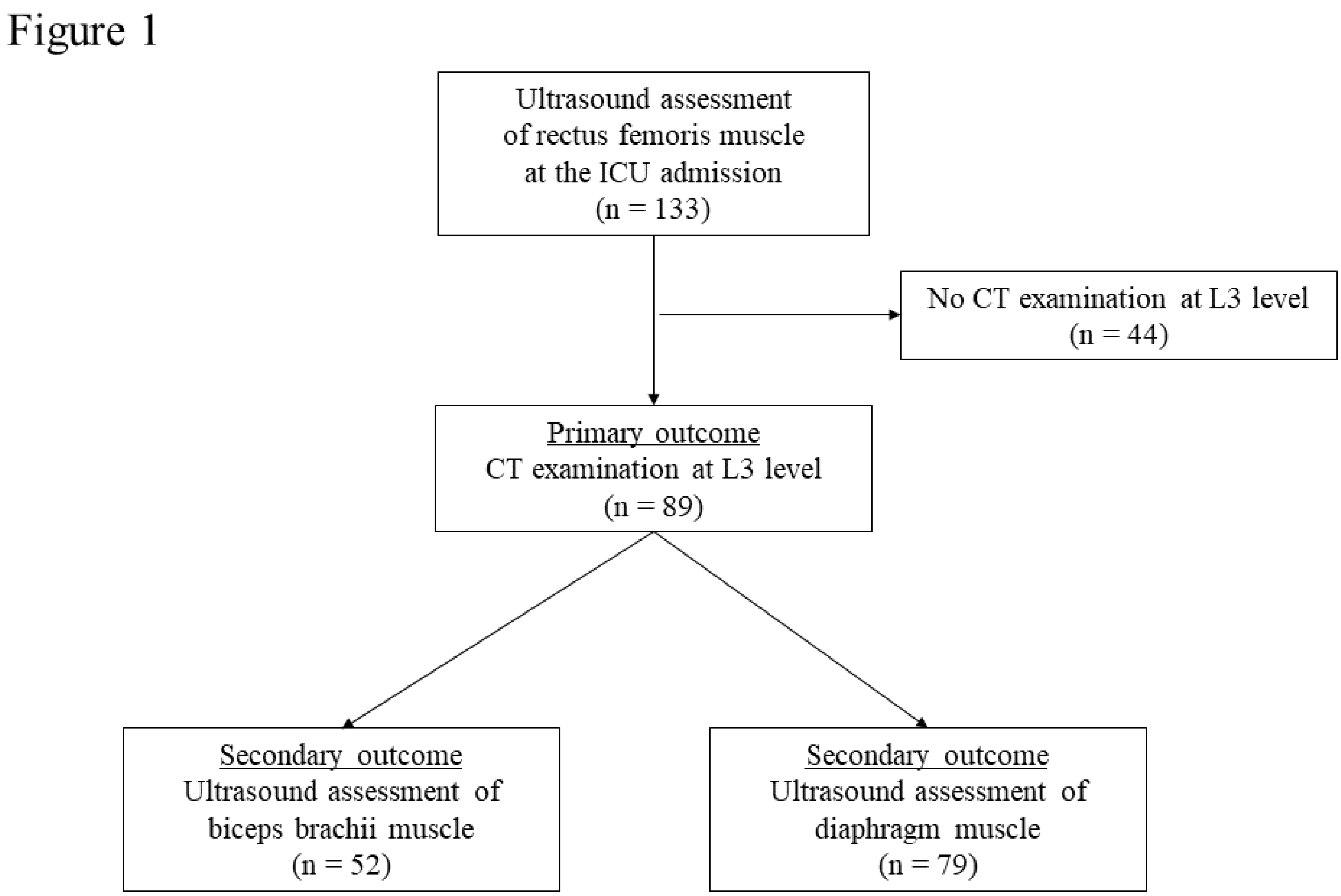

Figure 1

Flowchart of patients included in this study. Among the 133 patients screened, 89 underwent computed tomography (CT) examinations at the level of the third lumbar vertebra. Secondary outcomes included ultrasound assessments of the biceps brachii muscle (n = 52) and diaphragm muscle (n = 79) (CT, computed tomography; L3, third lumbar vertebra).

Figure 2

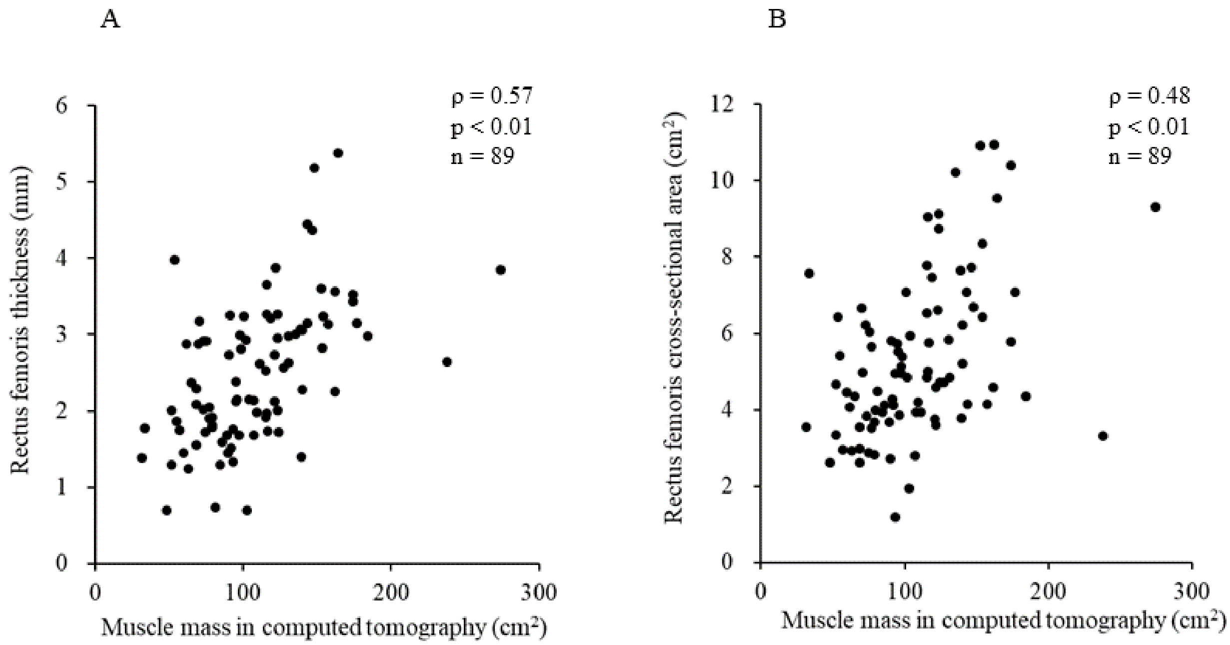

Figure 2

Relationships between ultrasound measurements of the rectus femoris muscle and CT measurements of whole-body muscle mass. (A) Rectus femoris thickness and (B) cross-sectional area. The Spearman correlation coefficient was used to investigate the relationships.

Figure 3

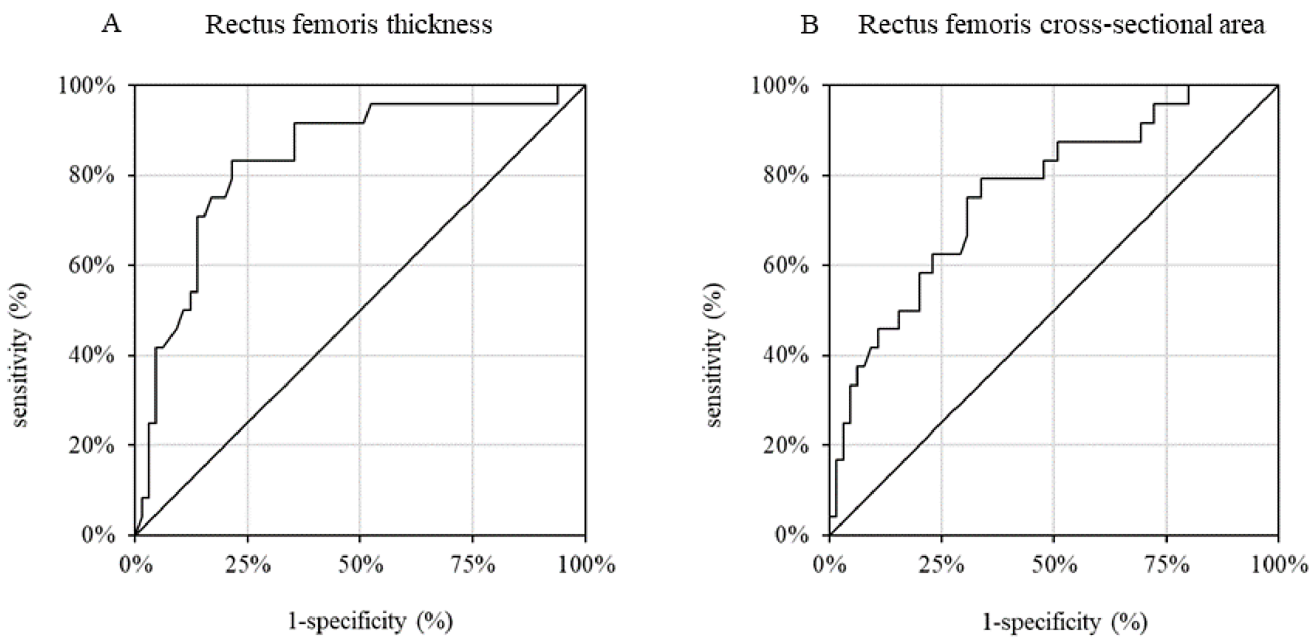

Figure 3

Areas under the receiver operating characteristic curves (AUCs) were estimated to determine the cutoff values of ultrasound assessments for sarcopenia. The Youden index was used to identify the optimal cutoff value. (A) Rectus femoris thickness and (B) cross-sectional area. (A) AUC = 0.84 (95% CI, 0.74–0.94) at the cutoff value of 20.2 mm (sensitivity: 83.3%, specificity: 78.5%) and (B) AUC = 0.76 (95% CI, 0.65–0.88) at the cutoff value of 4.66 cm2 (sensitivity: 79.2%, specificity: 66.2%).

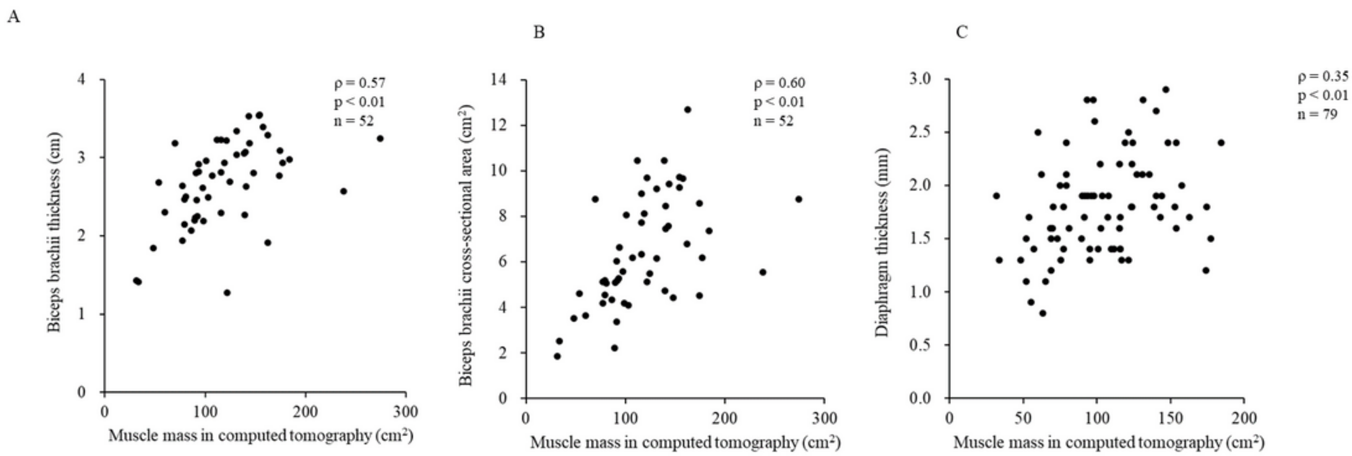

Figure 4

Relationships between ultrasound measurements of the biceps brachii and diaphragm muscles and CT measurements of whole-body muscle mass. The Spearman correlation coefficient was used to investigate the relationships.