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Ultrasound-based upper limb muscle thickness is useful for screening low muscularity during intensive care unit admission: a retrospective study

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Abstract

Background & Aims: Malnutrition is associated with poor outcomes. Muscle mass is an important malnutrition indicator included in Global Leadership Initiative on Malnutrition (GLIM) criteria. Although bioelectrical impedance analysis and dual-energy X-ray absorptiometry are common muscle mass assessment methods, they are unreliable during intensive care unit (ICU) admission due to the influence of dynamic fluid changes. We hypothesized that ultrasound-based upper limb muscle assessment would be useful for assessing muscularity at ICU admission.

Methods: We retrospectively analyzed prospectively obtained ultrasound data from patients admitted to an ICU. We excluded patients without computed tomography (CT) imaging of the third lumbar vertebra within 2 days of ICU admission. Primary outcomes were the diagnostic utility of ultrasound-based upper limb muscle thickness for assessing low muscularity by CT. Low muscularity was defined as a skeletal muscle index of 36.0 cm^2/m^2 for males and 29.0 cm^2/m^2 for females at the cross-sectional area of the third lumbar vertebrae. Secondary outcomes of this study included the relationships between upper limb muscle thickness and biceps brachii muscle cross-sectional area, quadriceps femoris thickness, rectus femoris cross-sectional area.

Results: Among 64 patients assessed by ultrasound, 52 had CT examination records and were included in the analysis. The mean age was 70 ± 13 years, and the mean body mass index was 23.3 ± 4.2 kg/m^2. Upper limb muscle thickness had the discriminative power to assess low muscularity at an area under the curve of 0.77 (95% CI [confidence interval], 0.63–0.91); the cutoff value (26.8 cm) had 84.6% sensitivity and 66.7% specificity. The upper limb muscle index had the discriminative power to assess low muscularity at an area under the curve of 0.80 (95% CI, 0.68–0.93); the cutoff value (9.9 mm/m^2) had 76.9% sensitivity and 71.8% specificity. Upper limb muscle thickness was correlated with upper limb muscle cross-sectional area, quadriceps femoris muscle thickness, rectus femoris muscle cross-sectional area ($r = 0.39$–0.76, $p < 0.01$, $n = 52$).

Conclusions: Ultrasound-based upper limb muscle thickness assessments can screen for low muscularity upon ICU admission.

Keywords: muscle, malnutrition, sarcopenia, ultrasound, upper limb, computed tomography

BACKGROUND

Malnutrition has negative clinical consequences in critically ill patients [1] and is associated with longer intensive care unit (ICU) stays and increased mortality [2, 3]. Therefore, identifying malnutrition is important for critically ill patients [4]. A worldwide consortium of experts from various clinical nutrition societies have proposed Global Leadership Initiative on Malnutrition (GLIM) criteria [5], which require muscle mass assessments because muscle mass is an important reflection of nutritional status [5].

Muscle mass is generally assessed using biological impedance analysis or dual-energy X-ray absorptiometry [6, 7]. However, these indirect methods are unreliable during the acute phase of an illness due to dynamic fluid balance [8]. Arm anthropometry is also an indirect muscle mass assessment affected by fluid changes [9]. Computed tomography (CT) is a reliable method for assessing muscle mass; however, it is not feasible for prospective screening assessments because of its associated radiation exposure, transportation risk, and high cost. Alternatively, ultrasound-based muscle mass assessments are increasingly used to assess muscularity [10] and direct visualizations by ultrasound are not critically affected by dynamic fluid changes [11].

Ultrasound-based muscle mass assessments generally evaluate the quadriceps femoris muscles. However, such assessments require strict conditions, including flatbed positioning [12]. These conditions may be burdensome for patients with cardiopulmonary diseases and trauma and these factors are obstacles to the clinical application of ultrasound-based lower limb muscle mass assessments [13]. Although upper limb muscle mass assessments are easier to obtain from critically ill patients, their usefulness is unknown. We hypothesized that an ultrasound-based upper limb muscle mass assessment could predict low muscularity during the acute illness phase. If confirmed, ultrasound-assessed upper limb muscle thickness assessments could be a useful screening test for low muscularity in patients admitted to ICUs.

METHODS

Study design

This was a retrospective study of prospective data obtained from May 2016 to June 2020 in the mixed medical-surgical ICUs of Tokushima University and Tokushima Prefectural Central Hospitals. This study was approved by the clinical research ethics committees of Tokushima University Hospital (#2593) and Tokushima Prefectural Central Hospital (#1739). At the time of inclusion, written informed consent was obtained from patients or their relatives. This study was registered at UMIN-Clinical Trials Registry (UMIN 000051202).

Study population

Inclusion criteria were as follows: (1) adults (≥18 years) admitted to ICU and (2) with an expected ICU stay of >5 days. (3) All patients underwent upper limb muscle ultrasound assessments on the day of ICU admission. We excluded patients with (1) primary neuromuscular disease and (2) obstacles at the ultrasound measurement site.

Ultrasound

Ultrasound measurement was conducted by a physician (N.N.), as previously reported[14, 15]. A linear transducer was used with B-mode imaging. Measurements were conducted on the dominant limb or, if the dominant limb was unknown, on the right limb. The patient's elbow was extended in supine position, and the transducer was placed perpendicularly using generous gel for accurate measurement. Upper limb muscle thickness was measured at a point two-thirds from the acromion to the antecubital crease (Figure 1A). This thickness measure included biceps brachii and brachialis muscles from the superficial fascia of the biceps brachii muscle to the uppermost part of the humerus (Figure 1B). The median value of three-time ultrasound measurements was taken as the "official" measure. Ultrasound assessment reliability was confirmed with the intra-observer and inter-observer reproducibility $r = 0.99$, $p < 0.01$, and $r = 0.99$, $p < 0.01$, respectively. The upper limb muscle index was calculated by dividing muscle thickness by square height meter (mm/m^2) [16].

The cross-sectional area of the biceps brachii was measured at the same site as the upper limb thickness measurement. Lower limb muscles were measured midway between the anterior superior iliac spine and the proximal end of the patella. Quadriceps femoris thickness included the rectus femoris and vastus intermedius muscles from the rectus femoris's superficial fascia to the femur's uppermost part. The rectus femoris's cross-sectional area was measured by outlining the area in the transverse plane. The intra-observer and inter-observer reproducibility were $r = 0.96–0.99$, $p < 0.01$, and $r = 0.99$, $p < 0.01$, respectively, for biceps brachii muscle cross-sectional area, quadriceps femoris thickness, and rectus femoris cross-sectional area.

Computed tomography

A board-certified radiologist (A.Y.) measured the muscle mass area at the middle level of the third lumbar vertebra (Figure 1 C). The evaluator was blinded to all clinical characteristics. CT images obtained within 2 days of ICU admission were included in the analyses. Images were analyzed using ImageJ software (National Institutes of Health, Bethesda, MD, USA) [17]. Ultrasound assessment reliability was confirmed with the intra-observer and inter-observer reproducibility $r = 0.98$ ($p < 0.01$) and $r = 0.94$ ($p < 0.01$), respectively. The cutoff value of low muscularity was defined as 29.0 cm^2/m^2 for females and 36.0 cm^2/m^2 for males, which were reported in the Japanese population [18].

Outcomes

The primary outcome was the diagnostic utility of upper limb muscle thickness and index for assessing low muscularity, as determined by CT. Secondary outcomes of this study included the relationships between upper limb muscle thickness and biceps brachii muscle cross-sectional area, quadriceps femoris thickness, and rectus femoris cross-sectional area.

Statistical analyses

Continuous data are shown as means (standard deviations) or medians [interquartile ranges (IQRs)]. Categorical data are shown as counts and proportions. Between-group comparisons of continuous data were made using the unpaired t-test or the Mann–Whitney U test. The area under the receiver operating characteristic curve (AUC) was calculated to assess the diagnostic utility of ultrasound-based upper limb muscle thickness for low muscularity. The Youden index was used to identify the optimal cutoff value. The Pearson correlation coefficient was used to investigate relationships between upper limb muscle thickness and other muscles. Due to the study's retrospective nature, an a priori sample size was not calculated. Analysis was conducted using JMP statistical software, version 13.1.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

In total, 64 patients had ultrasound measurements of upper limb muscle thickness. Among them, 52 patients had CT imaging at the third lumbar vertebra level within 2 days of ICU admission. The patients' characteristics are summarized in Table 1. The mean age was 70 ± 13 years, and 43 patients (67%) were male. The body mass index was 23.3 ± 4.2 (kg/m^2). The median Acute Physiology and Chronic Health Evaluation II score was 27 (interquartile range [IQR], 22–30). Thirty-four (53%) patients were sepsis, and 16 (25%) were postoperative admissions.

Among the 64 patients, the median of upper limb muscle thickness was 27.3 (22.6–31.4) mm, and the upper limb muscle index was 10.6 (9.2–11.7) mm/m^2. Upper limb muscle thickness was higher in males aged <70 compared with females aged ≥70 ($p < 0.01$). Contrary to that, the upper limb muscle index showed no difference by sex ($p = 0.39$) or age ($p = 0.51$). Among the 52 patients who also had CT-based muscularity assessments, the upper limb muscle thickness, and index were higher in patients with normal muscularity compared to those with low muscularity across all patients, males, females, those aged <70, and those aged ≥70 with and without a statistical difference (Table 2).

Upper limb muscle thickness and index were moderately correlated with CT-assessed muscularity with $r = 0.51$, $p < 0.01$ ($n = 52$) for thickness and $r = 0.36$, $p < 0.01$ ($n = 52$) for the index. Upper limb muscle thickness had the discriminative power to assess low muscularity at an AUC of 0.77 (95% CI, 0.63–0.91). Here the cutoff value of 26.8 cm had a sensitivity of 84.6% and a specificity of 66.7% (Figure 2). On the other hand, the upper limb muscle index had the discriminative power to assess low muscularity with an AUC of 0.80 (95% CI, 0.68–0.93). Here the cutoff value of 9.9 cm^2 had a sensitivity of 76.9% and a specificity of 71.8%.

Regarding the secondary outcomes, upper limb muscle thickness was strongly correlated with upper limb muscle cross-sectional area ($r = 0.76$, $p < 0.01$, $n = 52$, Figure 3). In addition, upper limb muscle thickness was moderately correlated with quadriceps femoris muscle thickness ($r = 0.43$, $p < 0.01$, $n = 52$) and rectus femoris muscle cross-sectional area ($r = 0.39$, $p < 0.01$, $n = 52$)

DISCUSSION

This retrospective study found that ultrasound-based upper limb muscle thickness and index were low muscularity indicators. Upper limb muscle index was less affected by age and sex and had a higher predictive value of low muscularity than upper limb muscle thickness. Upper limb muscle assessment was moderately correlated with widely used lower limb muscle assessments. Because the upper limb is relatively accessible, ultrasound-based upper limb muscle thickness assessments could be readily deployed in clinical practice settings for muscularity assessments. Furthermore, ultrasound-based upper limb assessments may contribute to applying GLIM criteria for malnutrition assessment during the acute phase.

Malnutrition can be assessed using various methods [19], and GLIM criteria are recommended during the acute phase [20]. Although arm or calf circumferences assess muscularity [21], edema can easily affect these measures [22, 23]. A previous study found that arm circumference was only 31%–38% accurate for assessing low muscularity [9]. Therefore, ultrasound is a promising alternative tool for muscularity assessment. Although most studies evaluate lower limb muscles [15, 24], we showed upper limb muscle assessments can predict whole-body muscle mass. In our previous study, quadriceps muscle layer thickness and rectus femoris cross-sectional area had the discriminative power to assess low muscularity at the AUC of 0.84 (95% CI, 0.74-0.94) and 0.76 (95% CI, 0.74-0.94), respectively [15]. The predictive utility is almost the same with upper limb muscle thickness measurement and the index at the AUC of 0.77 (95% CI, 0.63–0.91) and 0.80 (95% CI, 0.68–0.93), respectively. Considering the relatively easy access to upper limbs in bed-ridden patients, upper limb thickness measurement may change the clinical assessments of muscularity in critically ill patients.

We focused on muscle thickness rather than cross-sectional area. Although the cross-sectional area indicates physical function [25, 26], thickness measures are convenient and easily obtained using a portable ultrasound device [27]. Cross-sectional area measurements indicate changes in muscle mass; however, thickness measures are likely sufficient to screen muscularity upon ICU admission. Indeed, ultrasound-based upper limb muscle thickness was correlated with CT, ultrasound-based lower limb muscle assessments and upper limb cross-sectional area. Interestingly, the upper limb muscle index was not significantly different in patients of different ages, or when we compared males and females. Therefore, the cutoff value of 9.9 cm^2 can be widely applied in clinical practice.

Healthcare providers can use convenient, ultrasound-based upper limb muscle thickness assessments. A prior study found that healthcare providers (including dietitians) could improve the accuracy of their muscle mass measures through ultrasound training [28]. In addition, ultrasound can assess nutritional status upon ICU admission. A previous questionnaire survey found that 86% of dieticians have conducted muscle mass assessments; however, most only used bioelectrical impedance analysis (61%) and anthropometric upper limb circumference (45%). In addition, ultrasound-based muscle mass assessments were conducted by only 6% of dieticians [13]. Our results may incentivize dieticians to use ultrasound to assess malnutrition in patients admitted to ICUs.

This study has several limitations. First, the sample size was limited and could have produced insufficient statistical significance, especially concerning age. Furthermore, the sample size prevented us from proposing sex-specific cutoff values. Second, this study was conducted only in two facilities in Japan; the generalizability requires further prospective observational studies in different countries. Third, we did not evaluate GLIM criteria in this study; these require further validation.

Conclusion

Ultrasound-based upper limb muscle thickness and index assessments accurately indicate low muscularity. The upper limb muscle index was less affected by age and sex and had a higher predictive value for low muscularity than upper limb muscle thickness. Therefore, upper limb muscle thickness measurement can be an alternative method for assessing muscularity upon ICU admission.

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Data statement

Data are available upon reasonable requests to the corresponding author.

Author contributions

N.N. participated in study design, data acquisition, analysis, and manuscript drafting. Y.O. and K.N. participated in manuscript revision. A.Y. participated in data acquisition. S.I., J.S., K.T., J.O., and J.K. supervised this study. All authors read and approved the final manuscript.

Disclosure of potential conflicts of interest

The authors declare that they have no competing interests

Figure captions

Figure 1. Ultrasound-based upper limb thickness measurement A. upper limb muscle measurement; B. ultrasound image of upper limb muscle thickness; C. muscle mass measurement using computed tomography

A. Measures were performed at two-thirds of the distance from the acromion to the antecubital crease. B. Thickness is measured from the superficial fascia of the biceps brachii muscle to the uppermost part of the humerus. C. Muscle mass is measured by tracing the cross-sectional area at the middle level of the third lumber vertebra.

Figure 2. Areas under the receiver operating characteristic curves (AUCs) are used to assess low muscularity from ultrasound-based upper limb muscle thickness

measurements

A. upper limb muscle thickness; B. upper limb muscle index

A. The cutoff value was 26.8 mm, with a sensitivity of 84.6% and a specificity of 66.7%.

B. The cutoff value was 9.9 cm^2, with a sensitivity of 76.9% and a specificity of 71.8%.

AUC: areas under the receiver operating characteristic curves

Figure 3. Relationship of upper limb muscle thickness with upper limb cross-sectional area, quadriceps femoris muscle thickness, and rectus femoris cross-sectional area

A. upper limb muscle thickness; B. quadriceps femoris muscle thickness; C. rectus femoris cross-sectional area

Upper limb muscle thickness was moderately to strongly correlate with upper limb cross-sectional area, quadriceps femoris muscle thickness, and rectus femoris cross-sectional area.

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Table 1. Baseline information

Variables	All patients (n = 64)
Patient characteristics	
Age, mean ± SD, y	70 ± 13
Male/Female	43/21
Height ± SD, cm	160.2 ± 9.6
Weight ± SD, kg	60.3 ± 14.4
Body mass index, mean ± SD, kg/m^2	23.3 ± 4.2
APACHE II score	27 (22–30)
SOFA	8 (5–10)
Sepsis (Sepsis-3 criteria), n (%)	34 (53)
Postoperative admissions, n (%)	16 (25)
Mechanical ventilation, n (%)	78 (88)
Length of ICU stay, d	10 (6–16)
Length of hospital stay, d	38 (18–57)
Mortality in the hospital, n (%)	21 (32.8)
Upper limb muscle thickness (mm)	
All patients, n = 64	27.3 (22.6–31.4)
Male, n = 43*	29.6 (25.0–32.3)
Female, n = 21	23.1 (19.3–26.5)
Age < 70, n =30†	30.6 (24.3–33.2)
Age ≥ 70, n = 34	25.2 (21.8–28.5)
Upper limb muscle index (mm/m^2)	
All patients, n = 64	10.6 (9.2–11.7)
Male, n = 43‡	10.5 (9.4–11.7)
Female, n = 21	10.6 (8.6–11.7)
Age < 70, n =30§	10.6 (9.4–11.7)
Age ≥ 70, n = 34	10.5 (9.1–11.6)

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.

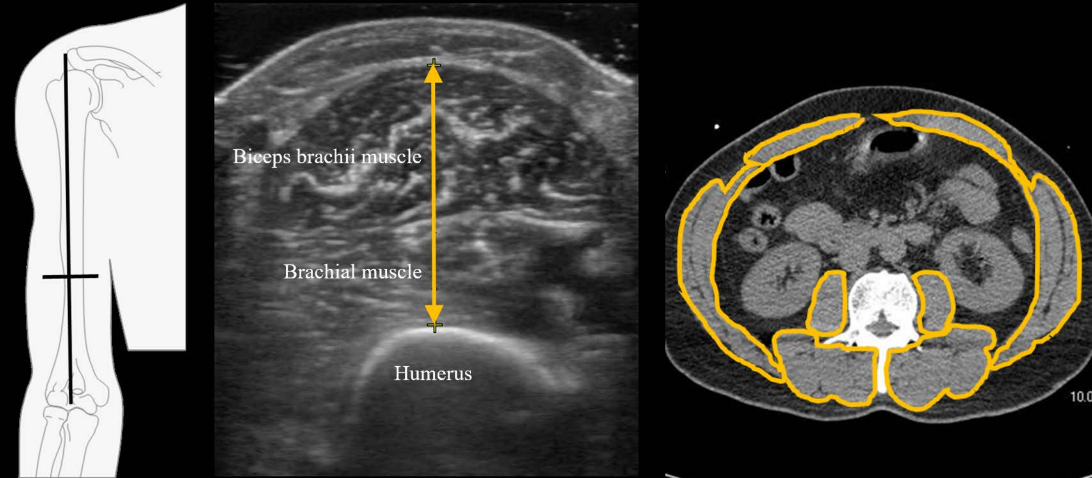
* vs. female, $p < 0.01$, † vs. Age ≥ 70, $p < 0.01$, ‡ vs. female, $p = 0.39$, § vs. Age ≥ 70, $p = 0.51$

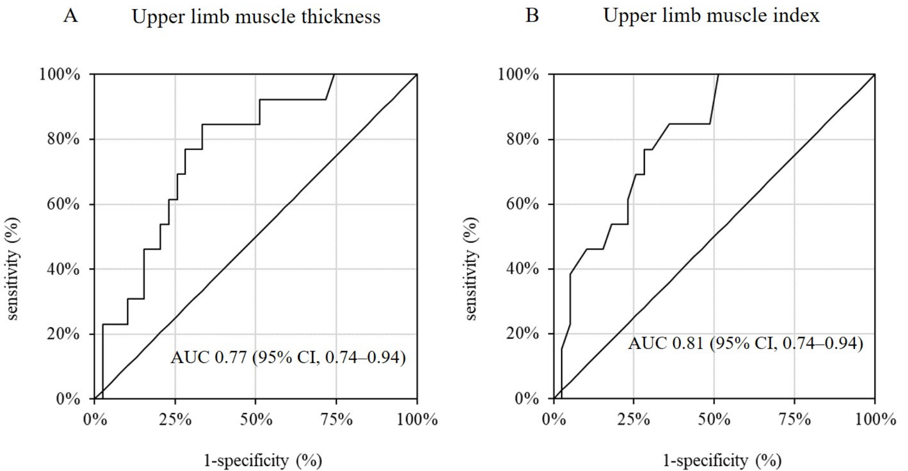
Table 2. Upper limb muscle thickness and index value in different sex and age

Variables	Low muscularity	Normal muscularity	p-value
Upper limb muscle thickness (mm)			
All patients, n = 13, 39	23.0 (20.0–26.5)	28.2 (24.9–32.2)	< 0.01
Male, n = 10, 29	24.9 (22.5–27.4)	30.4 (26.0–32.4)	0.02
Female, n = 3, 10	14.3 (14.1–18.4)	27.1 (22.2–28.1)	0.01
Age < 70, n = 5, 18	22.5 (20.4–28.3)	30.8 (28.0–33.2)	0.01
Age ≥ 70, n = 8, 21	24.0 (16.1–26.6)	26.9 (22.0–29.6)	0.17
Upper limb muscle index (mm/m^2)			
All patients, n = 13, 39	9.2 (7.8–10.1)	10.7 (9.6–11.7)	< 0.01
Male, n = 13, 39	9.6 (8.7–10.3)	10.9 (9.5–11.7)	0.02
Female, n = 3, 10	6.7 (5.9–7.7)	10.7 (9.9–11.9)	0.01
Age < 70, n = 5, 18	8.7 (7.8–10.1)	11.1 (10.3–11.7)	< 0.01
Age ≥ 70, n = 8, 21	9.4 (7.2–10.4)	10.4 (9.2–11.8)	0.10

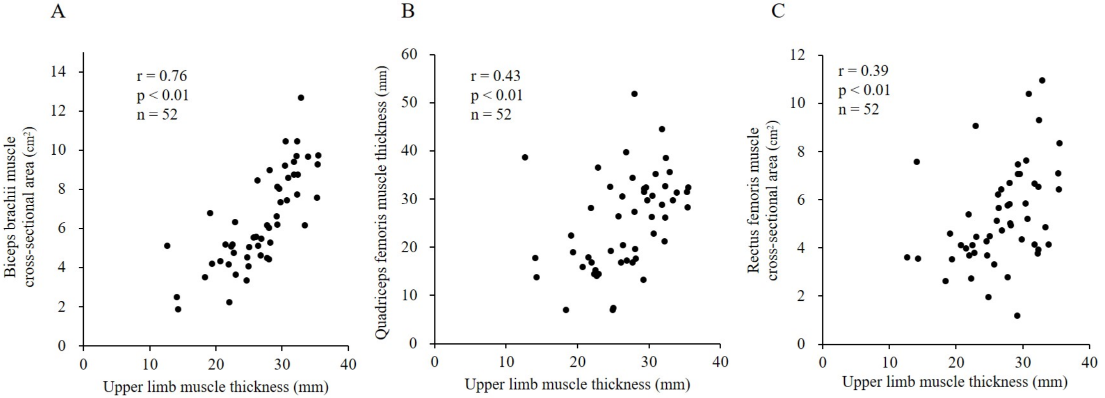
Data were presented as median (IQR) unless otherwise indicated.

IQR: interquartile range


Biceps brachii muscle
Brachial muscle
Humerus
10.0



A
Upper limb muscle thickness
100%
80%
60%
40%
20%
0%
sensitivity (%)
0%
25%
50%
75%
100%
1-specificity (%)
AUC 0.77 (95% CI, 0.74–0.94)
B
Upper limb muscle index
100%
80%
60%
40%
20%
0%
sensitivity (%)
0%
25%
50%
75%
100%
1-specificity (%)
AUC 0.81 (95% CI, 0.74–0.94)



A
r = 0.76
p < 0.01
n = 52
Biceps brachii muscle cross-sectional area (cm²)
Upper limb muscle thickness (mm)
B
r = 0.43
p < 0.01
n = 52
Quadriceps femoris muscle thickness (mm)
Upper limb muscle thickness (mm)
C
r = 0.39
p < 0.01
n = 52
Rectus femoris muscle cross-sectional area (cm²)
Upper limb muscle thickness (mm)