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ORIGINAL REPORT

CAN WE DIAGNOSE SARCOPENIA USING ANTERIOR FEMORAL MUSCLE THICKNESS IN PATIENTS WITH CARDIOVASCULAR DISEASE?

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Objective: **Making the diagnosis of sarcopenia is not always easy and this is especially true for those with cardiovascular disease. The purpose of this study is to investigate whether it is possible to diagnose sarcopenia by using ultrasound-guided measurements of anterior femoral muscle thickness.**

Methods: **We investigated the utility of ultrasound-guided measurements of anterior femoral muscle thickness in 1075 hospitalized patients with cardiovascular disease (675 men). As a comparison, sarcopenia was assessed by skeletal muscle mass index using bioelectrical impedance analysis and the Asia Working Group for Sarcopenia criteria.**

Results: **When the receiver operating characteristic curve using muscle thickness was examined, we found this could be used to make the diagnosis of sarcopenia (men: cutoff value 2.425 cm, area under the curve 0.796; women: cutoff value 1.995 cm, area under the curve 0.746). The prevalence of sarcopenia according to the criteria with skeletal muscle mass index was 34.2% in men and 51.8% in women, while its prevalence according to the cutoff value of muscle thickness was 29.2% in men and 36.7% in women.**

Conclusion: **Ultrasound-guided measurement of the anterior femoral muscle thickness is a simple and useful method to help make the diagnosis of sarcopenia in patients with cardiovascular disease.**

Key words: cardiovascular diseases; sarcopenia; ultrasonography.

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LAY ABSTRACT

A decrease in muscle mass and physical function are symptoms of sarcopenia, but making this diagnosis is not always easy. This is especially true for those with cardiovascular disease. Therefore, to diagnose sarcopenia, we investigated the utility of ultrasound-guided measurements of anterior femoral muscle thickness in 1075 hospitalized patients with cardiovascular disease. When the receiver operating characteristic curve using muscle thickness was examined, we found that this could be used to make the diagnosis of sarcopenia. This study also showed that this muscle thickness criteria may be more specific than the Asia Working Group for Sarcopenia criteria. Measurement of the anterior femoral muscle thickness using ultrasound is a simple and useful method to help make the diagnosis of sarcopenia in patients with cardiovascular disease. In clinical practice, it may be useful to first rule out sarcopenia by using ultrasound of the anterior femoral muscle thickness.

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The proportion of elderly people in advanced economies has increased dramatically over the past 70 years. In Japan, the estimated number of people aged 65 years and older increased to 28.4% by 2019, the highest among the world's 201 countries and regions (1). The problems associated with a growing older population include increasing immobility and a higher dependence

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on the healthcare system. Sarcopenia, or age-related skeletal muscle atrophy, is one of the leading causes of disability in the elderly. Approximately 30% of skeletal muscle mass is lost between the ages of 50 and 80 (2). In addition, denervation of motor units occurs primarily after age 70, and other mechanisms such as endocrine, immunologic, metabolic, and nutritional are implicated in the development of sarcopenia (3). Furthermore, muscle wasting is frequently observed among hospitalized patients and those with cardiovascular disease (CVD) (4, 5). Thus, sarcopenia is one of the most important factors that reduces quality of life. It is also associated with medical complications and higher mortality rates (6, 7).

Low muscle mass, low muscle strength, and poor physical functioning are used as diagnostic criteria for sarcopenia (8, 9), and bioelectrical impedance analysis (BIA) method is widely used to measure low muscle mass. The BIA method is non-invasive and easy to use, but it cannot be used in people with pacemakers because it uses weak electricity (10). However, ultrasonography has no contraindications for all people and thus, measuring muscle thickness (MTH) using ultrasound is a reasonable option for most people. While marked atrophy of the quadriceps muscles tends to occur in the elderly (11, 12), the relationship between anterior femoral MTH and sarcopenia remains unclear, especially in those with CVD (10). On the other hand, the anterior thigh MTH measured by ultrasound has been significantly correlated with the thigh muscle cross-sectional area (CSA) obtained by magnetic resonance imaging (MRI) (13), and with the thigh lean mass obtained by dual energy X-ray absorptiometry (DEXA) (14). In this study, we aimed to investigate the usefulness of ultrasound-guided measurements of anterior femoral MTH in making the diagnosis of sarcopenia in those with CVD.

METHODS

Table I shows the baseline characteristics of the patients. Patients with CVD (1075 patients, average age 71.0 years, 675 men) were included in this study. Out of these, 256 individuals had chronic heart failure and 240 had ischemic heart disease. Patients who had undergone coronary artery bypass grafting (CABG), aortic valve replacement (AVR), transcatheter aortic valve implantation, mitral valve replacement (MVR), mitral valve plasty (MVP), tricuspid valve replacement (TVR), tricuspid annuloplasty (TAP) and CABG combined with valve replacement or repair (AVR, MVR, MVP, TVR, TAP) were all included in this study. The study protocol was approved by our institution's human research committee, and it conformed to the ethical guidelines of the Declaration of Helsinki. The proposal was also approved by the Regional Ethics Committee of Dokkyo Medical University Hospital.

Table I. Patients' physical characteristics

Patients (n=1,075)	Males (n=675)	Females (n=400)
Specific diseases, *n* (%)		
Surgical disease		
Coronary artery bypass graft	162 (24.0)	49 (12.3)
Valve surgery	213 (31.6)	124 (31.0)
Aortic surgery	82 (12.1)	25 (6.3)
Arteriosclerosis obliterans	15 (2.2)	4 (1.0)
TAVI	54 (8.0)	79 (19.8)
Others	33 (4.9)	20 (5.0)
Internal disease		
Congestive heart failure	149 (22.1)	107 (26.8)
Ischemic heart disease	177 (26.2)	63 (15.8)
Others	307 (45.5)	226 (56.5)

TAVI: transcatheter aortic valve implantation.

Ultrasound was conducted using a LOGIQe ultrasound (GE Healthcare Japan, Tokyo, Japan). Measurements were taken with a real-time linear electronic scanner with a 10.0 MHz scanning head and ultrasound probe (L4-12t-RS Probe, GE Healthcare Japan) (15, 16). Measurements were taken mid-thigh, and the subcutaneous adipose tissue-muscle interface and the muscle-bone interface were identified from the ultrasound images. The perpendicular distance from the adipose tissue-muscle interface to the muscle-bone interface was considered to represent the anterior femoral MTH. The measurement was performed twice in the supine position, and the average value was adopted. BIA measurements (skeletal muscle mass index [SMI] etc.) were performed with a multi-frequency BIA (InBody S10 Biospace, Biospace Co. Ltd., Korea/Model JMW 140) in patients in the spine position, as previously described (15, 16). Maximum voluntary isometric contraction (MVIC) of the handgrip was determined using a factory-calibrated hand dynamometer (TKK 5401, TAKEI Scientific Instruments Co., Ltd., Tokyo, Japan). MVIC of the knee extensors was determined using a digital handheld dynamometer (μTas MT-1, ANIMA Co., Ltd., Tokyo, Japan). Gait speed was determined as the time needed to walk 4 m at a typical pace. Short physical performance battery (SPPB) was measured according to the National Institute on Aging protocol. A SPPB, a brief performance battery, was based on a timed short-distance walk, repeated chair stands, and a set of balance tests (17, 18). Sarcopenia was assessed using the Asia Working Group for Sarcopenia (AWGS) criteria (grip strength $<$ 26 kg or gait speed $\leq$ 0.8 m/s, and SMI $<$ 7.0 kg/m^2 for men; grip strength $<$ 18 kg or gait speed $\leq$ 0.8 m/s, and SMI $<$ 5.7 kg/m^2 for women) (9).

The data are presented as the mean $\pm$ standard deviation, or median and interquartile range on their distributions. Data normality was evaluated using the Kolmogorov–Smirnov test. Anterior femoral MTH was compared between groups using the Mann–Whitney U test. Associations between clinical data were evaluated with Pearson correlation coefficients for normally distributed parameters and with Spearman correlation coefficients for non-normally distributed parameters. To construct the receiver operating characteristic (ROC) curves, different cutoff values of anterior femoral MTH were used to predict sarcopenia. True-positives (sensitivity) were plotted on the vertical axis and false-positives (1 – specificity) were plotted on the horizontal axis. At this time, the Youden index (sensitivity + specificity – 1) was calculated from the obtained sensitivity and specificity, and the point at the maximal value was taken as the optimal cutoff value. All statistical analyses were performed using SPSS version 28 for Windows (IBM Corp., New York, USA). A p-value of $<$0.05 was regarded as significant.

RESULTS

Anterior femoral MTH positively correlated with grip strength (r=0.515, p<0.001), knee extension strength

(r=0.546, p<0.001), gait speed (r=0.288, p<0.001), and SPPB (r=0.272, p<0.001) in men. It also positively correlated with grip strength (r=0.322, p<0.001), knee extension strength (r=0.393, p<0.001), gait speed (r=0.257, p<0.001), and SPPB (r=0.276, p<0.001) in women. Compared to no sarcopenia, the mean anterior femoral MTH was significantly lower in those with sarcopenia in both men and women (men: 1.92 [1.64–2.42] vs 2.66 [2.32–3.24] cm, p<0.001; women: 1.80 [1.56–2.13] vs 2.40 [1.90–2.72] cm, p<0.001). The area under the curve (AUC) for anterior femoral MTH was 0.796 and 0.746 in men and women, respectively. Sensitivity and specificity of anterior femoral MTH in the diagnosis of sarcopenia were 68.5 and 77.6% for men, and 70.5 and 66.0% for women, respectively. The optimal cutoff value of anterior femoral MTH was 2.425 cm in men and 1.995 cm in women, as shown in Fig. 1. When using these MTH cutoff values, the prevalence of sarcopenia was 29.2% in men and 36.7% in women. When using AWGS criteria with SMI, the prevalence of sarcopenia was 34.2% in men and 51.8% in women.

DISCUSSION

This study showed that in both male and female hospitalized patients with CVD, anterior femoral MTH in the supine position had a significant positive correlation with grip strength, knee extension, gait speed, and SPPB. Also, in the ROC curve for detecting sarcopenia, anterior femoral MTH was a determining factor for sarcopenia, with cutoff values of 2.425 cm for men and 1.995 cm for women. Furthermore, the prevalence of sarcopenia according to the AWGS criteria with SMI was 34.2% in men and 51.8% in women, while the prevalence of sarcopenia according to the cutoff value of MTH was 29.2% in men and 36.7% in women.

Ultrasound is extremely safe and suitable in all patient groups. It is also portable, can be performed quickly, and can be interpreted at the bedside by a trained sonographer. One of the limitations of ultrasound is that the quality and interpretation of images is user dependent (10). On the other hand, BIA is dependent on hydration status, not universally portable, and cannot be used if a patient has metal work or electronic device implants (10). Thus, out of all the tools available such as BIA and ultrasound, ultrasound may be one of the more promising options for making the diagnosis of sarcopenia. This is especially true when considering frail older adult populations.

Ultrasound has recently received attention as a technique to measure muscle quality (10, 19, 20). The presence of intramuscular extracellular connective tissue and fat has qualitative effects (19, 20) and can overestimate the true muscle cell volume. However, measuring MTH using ultrasound has been reported to correlate positively with muscle strength (21), muscle CSA by MRI (13, 22), lean thigh mass by DEXA (14) and skeletal muscle mass by MRI (23). A previous study showed that the sum of 9 sites (lateral forearm, anterior upper arm, posterior upper arm, abdomen, subscapula, anterior thigh, posterior thigh, anterior lower leg and posterior lower leg) MTH by ultrasound × height was closely correlated with MRI-measured total body skeletal muscle mass (n=48, r=0.98, p<0.001) (23). We also previously examined the association between anterior femoral MTH and quadriceps muscle CSA using MRI in elderly subjects (approximately 70 years old, 5 men and 14 women) and found a significant correlation (r=0.821, p<0.01; unpublished data) between the two.

This study was the first to evaluate the usefulness of anterior femoral MTH using ROC analysis to detect sarcopenia in patients with CVD. In this study, the cutoff value of MTH was 2.425 cm for men and 1.995 cm for women. Using MTH, the prevalence of sarcopenia was found to be lower than when the AWGS criteria with SMI was applied. Thus, the MTH criteria may be more specific than the AWGS criteria. In clinical practice, it may be useful to first rule out sarcopenia by using ultrasound of the anterior femoral MTH before performing BIA.

This study has several limitations. Firstly, there is heterogeneity regarding the selected patient group in this study. Also, sub-analyses were not performed in terms of factors such as age range, gender difference, disease severity, immobilization period due to disease. Therefore,

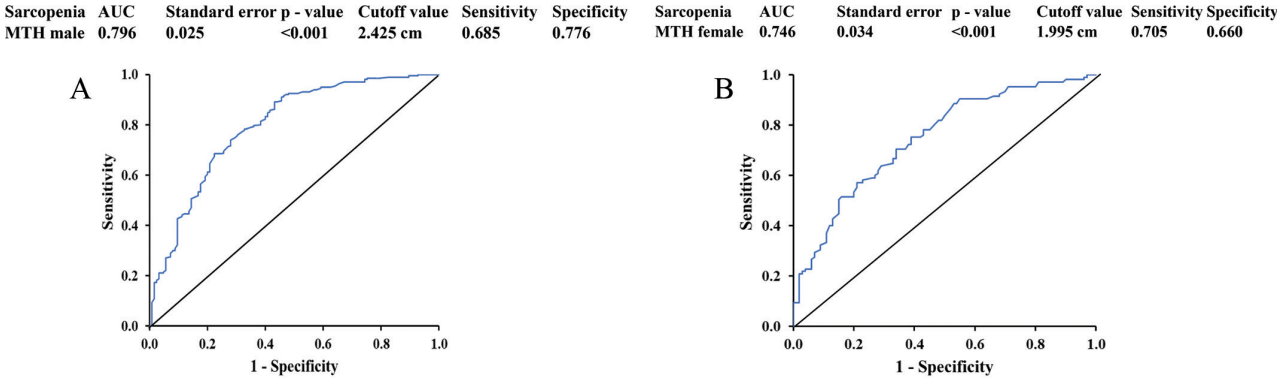

Fig. 1. Receiver operating characteristics curves to identify the optimal cutoff of MTH for detecting sarcopenia in male (A) and female (B) patients. To generate receiver operating characteristics curves shown, MTH cutoffs were used to predict sarcopenia, with true positives (sensitivity) plotted on the vertical axis and false positives (1 – specificity) plotted on the horizontal axis. MTH: muscle thickness.

our findings may not necessarily be applicable to the general population of patients with CVD, and further studies including sub-analyses are needed. Secondly, in this study, the sensitivity and specificity were slightly low, suggesting that sarcopenia cannot be assessed simply by measuring anterior femoral MTH. Furthermore, previous studies have shown a good correlation between MTH by ultrasound and CSA and skeletal muscle mass measured by MRI (13, 22, 23). Therefore, anterior femoral MTH may help to make a simple and useful method to evaluate muscle mass and help make the diagnosis of sarcopenia.

In conclusion, measurement of anterior femoral MTH using ultrasonography is a simple and useful method to evaluate muscle mass and help make the diagnosis of sarcopenia in patients with CVD.

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The authors have no conflict of interest to declare.

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