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Maximal calf circumference reflects calf muscle mass measured using magnetic resonance imaging

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ABSTRACT

Background: Calf circumference (CC) has been used as a surrogate for calf muscle mass, which facilitates venous blood return to the heart through active skeletal muscle. However, the correlation between CC and calf muscle mass has not been extensively examined. This study aimed to examine the relationship between CC and calf muscle mass considering differences in sex and physique in elderly individuals.
Methods: A total of 124 community-dwelling elderly individuals ≥60 years of age (61 men, mean [± SD] age 74.3 ± 5.7 years) were enrolled. Maximal CC was measured using a tape measure with the subject supine. The cross-sectional area of skeletal muscle tissues was measured using magnetic resonance imaging from the point of greatest calf circumference to 5 cm proximal and distal. Calf muscle mass was calculated by multiplying the area of each slice by slice thickness (5 mm).
Results: CC was strongly correlated with calf muscle mass in male and female subjects (male: r = 0.908, $P < 0.001$; female: r = 0.892, $P < 0.001$). Multiple regression analysis revealed that CC and body mass index (BMI) were independent associate factors of calf muscle mass. The following estimation formulae were derived: (male) calf muscle mass (cm^3) = 47.82 × CC (cm) − 12.50 × BMI (kg/m^2) −732.80; (female) calf muscle mass (cm^3) = 32.23 × CC (cm) −4.85 × BMI (kg/m^2) −429.94.
Conclusions: A strong correlation was found between CC and calf muscle mass according to magnetic resonance imaging. Sex differences and BMI should be considered for accurate estimation of calf muscle mass using CC.

1. Introduction

Skeletal muscle mass has been measured using several methods including magnetic resonance imaging (MRI) (Abe, Kearns, & Fukunaga, 2003; Janssen, Heymsfield, Wang, & Ross, 2000), bioelectrical impedance (Miyatani, Kanehisa, Masuo, Ito, & Fukunaga, 2001), dual-energy X-ray absorptiometry (DXA) (Rolland, Lauwers-Cances, & Cournot, 2003), and computed tomography (Mitsiopoulos, Baumgartner, & Heymsfield, 1998). However, these measurements are not commonly available in clinical settings. Instead, limb circumference is often used for screening muscle mass (Evans, Chumlea, Guo, Vellas, & Guigoz, 1995) because of its simplicity in measurement. Calf circumference (CC) is strongly correlated with appendicular muscle mass and useful as a tool for screening sarcopenia (Kawakami, Murakami, & Sanada, 2015; Maeda, Koga, Nasu, Takaki, & Akagi, 2017). CC also serves as a screening tool for nutritional status and physical frailty in elderly individuals (Bonnefoy, Jauffret, Kostka, & Jusot, 2002; Landi, Onder, & Russo, 2014) based on the premise that CC reflects calf muscle mass.

Additionally, CC has been used as a clinical measure of the calf muscle pump (Stewart, Medow, Montgomery, & McLeod, 2004). The skeletal muscle pump is an important mechanism that facilitates venous blood return to the heart through active skeletal muscle (Nådland, Walløe, & Toska, 2009). Our previous study described an index of CC divided by height, known as "calf mass index", and confirmed its validity as a screening tool for orthostatic hypotension in elderly individuals (Kobayashi & Yamada, 2012). More recently, we demonstrated the association between leg ejection fraction measured in lower skeletal muscle and exercise capacity in patients with heart failure (Kondo et al., 2018). These results suggest the importance of measuring

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calf muscle mass in terms of hemodynamic assessments in the clinical setting.

However, there is scope for calf muscle mass estimation using CC because previous studies have not focused on calf muscle mass, but on total-body muscle mass. Additionally, limb circumference is susceptible to sex differences and soft tissue including skin and adipose. Fat infiltration in skeletal muscle increases with aging (Marcus, Addison, Kidde, Dibble, & Lastayo, 2010), which possibly attenuates the correlation between CC and calf muscle mass. To improve the predictive value of CC for calf muscle mass, additional variables, such as sex and physique, may be useful.

This study, therefore, aimed to examine the relationship between CC and calf muscle mass in a healthy elderly population evaluated using MRI. Considering the influence of sex and adipose tissue, we explored a possible estimation formula to predict calf muscle mass using CC and additional variables related to physique.

2. Methods

2.1. Study area and population

Participants were recruited from the Research of Health Promotion at Nagoya University, School of Health Science in Nagoya city, Japan. The inclusion criterion was a community-dwelling elderly individual ≥ 60 years of age. Participants with contraindications to MRI, including pacemaker, artificial ear, tattoo and those who refused to undergo MRI, were excluded. All participants provided informed consent before participation in this study. The Ethics Review Committee of Nagoya University Graduate School of Medicine approved the study (approval no. 10-524, 12-504).

2.2. Study design and protocol

A cross-sectional, correlational research project was designed. Calf muscle mass and CC were measured on the same day. Only one calf was measured, which was the supporting leg on which subjects were able to stabilize on one foot. All measurements were performed in the morning to mitigate the influence of edema. In addition, demographic information (age, sex) and anthropometric measurements (height, weight, BMI) were assessed. BMI was defined as weight (kg) divided by height squared (m^2). The study was performed at the Health and the Disease Prevention Study of Community-dwelling Older Adults at Nagoya University School of Health Sciences.

2.3. CC

CC was measured using a non-elastic, flexible plastic tape at the point of greatest circumference while subjects were supine with the knee extended; subcutaneous tissues were not compressed.

2.4. MRI acquisition and data analysis

MRI studies were performed using a 3.0 Tesla scanner (MAGNETOM Verio; Siemans, Germany). T1-weighted and T1-weighted imaging with fat suppression was performed. A T1-weighted, spin echo, axial plane sequence was performed with a repetition time of 600 ms and an echo time of 11 ms. A T1-weighted with fat suppression, spin echo, axial plane sequence was performed with a repetition time of 628 ms and an echo time of 13 ms. Both images, contiguous transverse images with 0.5 cm slice thickness, were obtained from the point of greatest CC to a point each 5 cm proximal and distal (21 slices per subject). Each subject was in the supine position with their arms and legs extended and relaxed during MRI measurements. ImageJ 1.43 (Wayne Rasband, National Institutes of Health, Bethesda, MD, USA) was used to analyze the T1-weighted with fat suppression images, and skeletal muscle tissue cross-sectional area was measured. The T1-weighted image was reference for line drawing. The volume of skeletal muscle was calculated by multiplying the area of each slice by the slice thickness (5 mm).

2.5. Statistical analysis

All continuous data are presented as mean ± standard deviation. Characteristics between men and women were compared using the unpaired t-test. The correlations between calf muscle mass and CC or BMI were assessed using Pearson's correlation coefficient. Multiple linear regression analysis was subsequently performed with calf muscle mass as a dependent variable. CC, BMI, age, height, and body weight were entered as independent variables, and a stepwise variable selection procedure was adopted. Multiple linear regression analysis was performed according to gender if an interaction between CC and gender was significant. All analyses were performed using SPSS version 16 (SPSS Inc., Tokyo, Japan); $P < 0.05$ was considered to be statistically significant.

3. Results

From March 2011 to January 2013, 124 community-dwelling elderly individuals (61 male, 63 female) were enrolled. Subject characteristics are summarized in Table 1. Height, weight, CC, and calf muscle mass were significantly higher in males than in females. No subjects exhibited severe edema.

The correlation between calf muscle mass and CC is shown in Fig. 1. In the univariate analysis, CC was strongly correlated with calf muscle mass; this strong relationship was also observed when analyzed separately in males and females (male: $r = 0.908$, $P < 0.001$; female: $r = 0.892$; $P < 0.001$). However, the slope of the regression line indicated a difference according to sex. Indeed, there is a significant interaction between CC and gender ($P < 0.001$) shown in Table 2. Pearson's correlation coefficient also showed the positive association between calf muscle mass and BMI ($r = 0.439$; $P < 0.001$).

Table 1
Subject characteristics.

	Total (N = 124)	Male (n = 61)	Female (n = 63)	*P*
Age (years old)	74.3 ± 5.7	75.0 ± 5.4	73.5 ± 5.9	0.112
Height (cm)	157.1 ± 8.9	163.8 ± 5.7	150.6 ± 6.1	< 0.001
Weight (cm)	55.9 ± 9.0	60.4 ± 7.8	51.5 ± 7.9	< 0.001
Body mass index (kg/m^2)	22.6 ± 2.8	22.5 ± 2.4	22.7 ± 3.1	0.612
< 18.5 kg/m^2	4 (3.2)	0 (0)	4 (6.4)	0.047
18.5-24.9 kg/m^2	98 (79.0)	53 (86.9)	45 (71.4)	
25.0-29.0 kg/m^2	21 (17.0)	7 (11.5)	14 (22.2)	
30.0 kg/m^2 ≤	1 (0.8)	1 (1.6)	0 (0)	
Calf circumference (cm)	34.0 ± 2.6	34.6 ± 2.6	33.3 ± 2.5	0.004
Calf muscle mass (cm^3)	588.0 ± 109.7	643.4 ± 111.7	534.4 ± 76.6	< 0.001

The data are presented as the mean ± standard deviation or number (percentage).

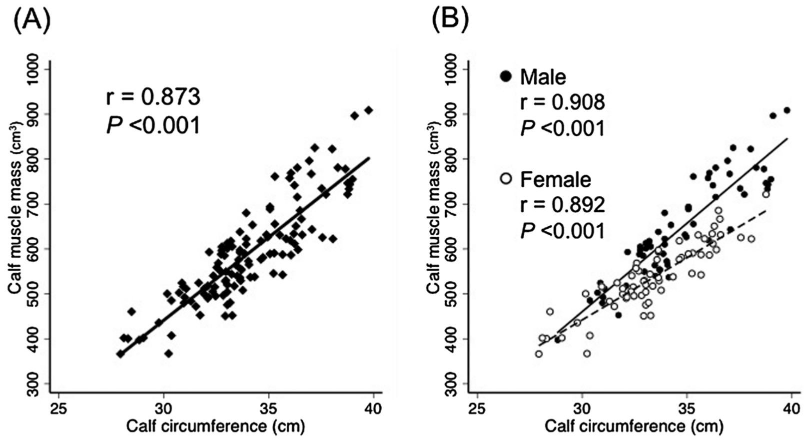

Fig. 1. Correlation between calf circumference and calf muscle mass in total subjects (A) and stratified according to sex (B). Male and female are shown as black circles + solid regression line and white circles + dashed regression line, respectively (B).

The results of multivariate linear regression analysis revealed that CC and BMI were independent associate factors of calf muscle mass regardless of gender (Table 3). An estimated regression equation is reported in Table 3.

4. Discussion

The results of the present study clarified that CC is strongly correlated with calf muscle mass in elderly individuals. To our knowledge, this is the first study to identify the relationship between CC and calf muscle mass evaluated using MRI. Moreover, our data indicated that sex differences influenced this relationship.

The relationship between CC and calf muscle mass indicated a strong correlation (r = 0.908 for male; r = 0.892 for female). The correlation between CC and calf muscle mass in this study was stronger than the correlation between CC and appendicular muscle mass evaluated by DXA in a previous study (r = 0.81 for male, r = 0.73 for female) (Kawakami et al., 2015). A possible explanation for this finding was that we measured muscle mass using MRI, which provides higher-accuracy measurements of skeletal muscle than the DXA and bioelectrical impedance used in previous studies. In particular, the analysis of bioelectrical impedance was not designed to measure the skeletal muscle mass, and it estimates skeletal muscle mass using an equation proposed by Janssen, Heymsfield, Baumgartner, and Ross (2000). MRI has been considered to be a highly precise imaging system that can clearly separate fat from other soft tissues of the body, making this method the gold standard for estimating muscle mass in many studies (Cruz-Jentoft, Baeyens, & Bauer, 2010). Another possible reason was that we focused on only calf muscle mass. Our findings suggest that CC is a surrogate indicator for calf muscle mass in a community-dwelling elderly population. In this study, the relationship between CC and calf muscle mass had a sex difference. Previous studies have reported that muscle mass is larger in males than in females (Abe et al., 2003; Janssen, Heymsfield, Wang et al., 2000), and the proportion of body fat is higher in females than in males (Li, Ford, Zhao, Balluz, & Giles, 2009). Therefore, sex differences should be considered when evaluating CC as an alternative indicator of calf muscle mass.

Another finding was that stepwise multiple regression analysis revealed CC and BMI as independent associated factors of calf muscle

Table 3
Results of stepwise multiple linear regression according to gender.

	Regression coefficient	[95% confidence interval]	Standardized beta	P
(Male)				
CC, cm	47.82	[41.60, 54.04]	1.10	< 0.001
BMI, kg/m^2	−12.50	[−19.17, −5.82]	−0.27	< 0.001
Intercept	−732.80	[−882.05, −583.55]		
R^2 = 0.86				
(Female)				
CC, cm	32.23	[27.00, 37.46]	1.04	< 0.001
BMI, kg/m^2	−4.85	[−9.05, −0.64]	−0.19	< 0.001
Intercept	−429.94	[−551.07, −308.80]		
R^2 = 0.81				

Male: calf muscle mass (cm^3) = 47.82 × CC (cm) −12.50 × BMI (kg/m^2) −732.80.
Female: calf muscle mass (cm^3) = 32.23 × CC (cm) −4.85 × BMI (kg/m^2) −429.94.
The R^2 indicates that 86% in male and 81% in female of the variance in calf muscle mass can be predicted from the variables CC and BMI.
A dependent variable is calf muscle mass. CC, BMI, age, height, and body weight are entered as independent variables using stepwise variable selection procedure.
CC, calf circumference; BMI, body mass index.

Table 2
Results of linear regression analysis in total participants.

		Regression coefficient	[95% confidence interval]	P	Standardized beta
Model 1	CC, cm	33.71	30.60, 36.83	< 0.001	0.80
	Gender	−64.68	−80.79, −48.57	< 0.001	−0.30
	Intercept	−459.88	−574.64, −345.13	< 0.001	
Model 2	CC, cm	39.40	35.29, 43.51	< 0.001	0.93
	Gender	332.15	131.35, 532.94	0.001	1.52
	CC × Gender	−11.68	−17.58, −5.79	< 0.001	−1.79
	Intercept	−721.61	−864.48, −578.74	< 0.001	

CC, calf circumference; Gender (male = 0, female = 1).
CC × Gender means an interaction of CC and gender.

mass. A previous study reported that BMI is a strong predictor of skeletal muscle mass in both women and men (Iannuzzi-Sucich, Prestwood, & Kenny, 2002) and, moreover, is a simple index for assessing total muscularity in the older Japanese population (Kanehisa & Fukunaga, 2013). In contrast, our data suggested that BMI was negatively correlated with calf muscle mass in multiple linear regression analysis, although BMI was positively associated with calf muscle mass in simple correlation. This result may be caused by the interaction of CC and BMI, and implies that larger BMI in the regression model indicated more adipose tissue. This study clarified that 86% (male) and 81% (female) of the variance in calf muscle mass are due to CC and BMI, suggesting that calf muscle mass can be precisely predicted from CC and BMI.

Because of a limited number of extremely obese subjects in this study, estimation of calf muscle mass among this population may need to be examined in future studies. In case of sarcopenic obesity, a coexistence of sarcopenia and obesity (Cruz-Jentoft, Bahat, & Bauer, 2018), the prediction of calf muscle mass may need to be examined by adding functional measurements such as walking speed or grip strength. Another issue is that calf muscle mass may function to increase cardiac output by generating cardiac preload. A previous report demonstrated that leg ejection fraction measured using strain gauge plethysmography in calf muscle was correlated to exercise capacity in patients with heart failure (Kondo et al., 2018), suggesting the importance of measuring calf muscle mass in terms of cardiac hemodynamics during exercise. Estimated calf muscle mass has a possibility to be an alternative index of leg ejection fraction, which may lead to further studies to examine a role of calf muscle mass in the calf muscle pump. In addition, the estimated calf muscle mass is likely to be a more precise indicator of functional decline than CC. A cut-point of CC < 31 cm has been considered lower muscle mass and functional performance (Landi et al., 2014; Rolland et al., 2003). The usefulness of estimated calf muscle mass for assessing functional decline will be another theme of future studies.

This study, however, had several limitations. First, our participants voluntarily participated in the study, potentially causing selection bias. Second, as discussed before, the applicability of the estimated formula proposed in this study to obese individuals is unclear due to the limited number of participants with obesity. Moreover, there are other confounding factors that may affect the relationship between CC and calf muscle mass, including edema and sarcopenic obesity.

In conclusion, CC was strongly correlated with calf muscle mass evaluated using MRI in a population of community-dwelling elderly individuals. Our results suggest that CC may serve as an alternative indicator of calf muscle mass considering sex and BMI.

Disclosure statement

The authors declare no conflict of interest.

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