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Utility of ultrasound as a promising diagnostic tool for stroke-related sarcopenia

A retrospective pilot study

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Abstract

Stroke patients undergo extensive changes in muscle mass which lead to stroke-related sarcopenia. Stroke-related sarcopenia has a significant impact on the functional outcome of stroke survivors. So, it is important to measure muscle mass in stroke patients. This study aimed to examine the correlation between ultrasonographic quadriceps muscle thickness (QMT) and dual-energy X-ray absorptiometry (DXA) derived appendicular lean mass (ALM) in patients with acute hemiplegic stroke. Twenty five participants were included (13 men and 12 women) in this study, who were diagnosed with stroke within 1 month. For both paretic and non-paretic legs, QMT was measured by an ultrasound and ALM was obtained by performing DXA scan. We analyzed the difference and the correlation between ultrasonographic QMT and DXA-derived lean body mass of both paretic and non-paretic legs. Stroke patients were divided into 2 groups according to the paretic knee extensor power. Ultrasonographic QMT, DXA scan findings, and functional parameters were compared. There was a significant correlation between QMT and ALM index, and between QMT and site-specific lean mass (SSLM) of both the legs for both the sexes ($P < .05$). In multivariate linear regression model, we made adjustments for the confounding factors of age, sex, body mass index (BMI) and paretic knee extensor power. We observed a positive relationship between QMT and ALM index ($P < .05$), and between QMT and SSLM of both the legs ($P < .05$). The % QMT showed higher difference than % SSLM between paretic and non-paretic legs (10.25% vs 4.58%). The QMT measurements of ultrasound show a great relationship with DXA scan findings. Ultrasound better reflects the change of muscle mass between paretic and non-paretic legs than DXA scan at an acute phase of stroke. Ultrasound could be a useful tool to evaluate stroke-related sarcopenia.

Abbreviations: ALM = appendicular lean mass, BMI = body mass index, DXA = dual-energy X-ray absorptiometry, QMT = quadriceps muscle thickness, SSLM = site-specific lean mass

Keywords: dual-energy x-ray absorptiometry, quadriceps muscle, stroke, ultrasonography

1. Introduction

Sarcopenia is characterized by low muscle mass, low muscle strength and impaired physical function.[1] It is strongly related with age and predominantly affects the elderly. Stroke is one of the leading causes of disability and death worldwide.[2] Stroke patients undergo extensive changes in muscle mass due to following reasons: disuse, denervation/reinnervation, muscle fiber type shift, spasticity and local inflammation. These complex changes lead to the development of sarcopenia in stroke patients.[3] Stroke-related sarcopenia, particularly muscle wasting of lower limbs has a significant impact on the functional outcome of stroke survivors. Jang et al[4] reported that the presence of sarcopenia 2 weeks after stroke is significantly related to poor functional outcome 6 months after stroke. So, it is helpful to measure muscle mass at an early stage in stroke patients to predict the functional outcome. Currently, dual-energy X-ray absorptiometry (DXA) is considered as a gold standard for assessing the body composition. Recent literature highlights that musculoskeletal ultrasonography would be useful for assessment of muscle mass. The reliability and repeatability of ultrasonographic muscle thickness is high,[5,6] and it revealed good interobserver and intraobserver reliability.[7]

After stroke, robust muscle changes occur in the quadriceps femoris muscle compared with other muscles.[8] Several literature reviews reported that quadriceps muscle thickness (QMT) measurement is a useful indicator for assessing muscle wasting and physical function in stroke patients.[9–11] In addition, several studies have proved that the degree of quadriceps muscle power, as knee extensor, plays an important role in functional recovery in stroke patients.[12,13] Several research studies reported that ultrasonographic muscle thickness is positively correlated with the DXA-derived appendicular lean

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

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mass (ALM).[14,15] Although there are some researches suggesting an association between ultrasonographic QMT and DXA-derived lean body mass, no study has investigated the correlation for both paretic and non-paretic legs among acute hemiplegic stroke patients.

The aim of this study was to determine whether it is beneficial to use ultrasound for the evaluation of sarcopenia of stroke patients. The purposes of the present study were as follows: (1) to compare the ultrasonographic QMT in both paretic and non-paretic legs, (2) to analyze the relationship between ultrasonographic QMT and DXA-derived lean body mass, and (3) to identify the difference of QMT, ALM, and functional parameters between the 2 groups classified according to the paretic knee extensor power.

2. Methods

2.1. Study design and patients

This pilot study was single-centered, retrospective, and cross-sectional. In this study, we evaluated patients with ischemic or hemorrhagic strokes who were admitted to the Department of Rehabilitation Medicine between December 2020 and May 2021. The inclusion criteria were as follows: (1) first incidence of stroke; (2) unilateral brain lesion confirmed by radiological evidence; (3) patients with poststroke hemiplegia; (4) acute stroke events having a duration of within 1 month; (5) the absence of spasticity confirmed by neurological examination. The exclusion criteria were as follows: (1) a history of brain lesions; (2) bilateral brain lesions; (3) patients with neuromuscular diseases that would cause muscle weakness or muscle atrophy. The eligible patients were divided into 2 groups: Group A (less than grade 3 of paretic knee extensor power) and Group B (greater than or equal to grade 3 of paretic knee extensor power), based on the medical research council scale for muscle strength (0, zero; 1, trace; 2, poor; 3, fair; 4, good; 5, normal). The study protocol was approved by the Institutional Review of Board (No.2021–08-023).

2.2. Measurement

In total, 25 patients were included in this study. The following parameters of patients were analyzed: the age, gender, height (cm), weight (kg), body mass index (BMI) (kg/m²), the type of stroke (ischemic or hemorrhagic), the hemiplegic side, the duration from the onset of the stroke to the measurements of parameters (days), the risk factors of stroke (Hypertension, Diabetes, Atrial fibrillation, Hypercholesterolemia), ultrasonographic QMT (cm), ALM index (height-adjusted ALM) (kg/m²), the proportion of low muscle mass (The number of patients with low ALM index were divided by the total number of patients), and site-specific lean mass (SSLM) (kg). The following parameters were used to evaluate the patients' balance function and functional independence of daily activities: the Berg-Balance scale (BBS),[16] the Korean version of the Modified Barthel Index (K-MBI) and the modified Rankin Scale (mRS).[17] All data were based on the initial evaluation within a week after the transfer. Ultrasonographic measurement and DXA scan were performed on the same day.

2.3. Muscle mass

2.3.1. Ultrasonographic muscle thickness. A single sonographer performed ultrasonographic measurement with an E-CUBE 9 Diamond US system (Alpinion, Seoul, Korea) with a high density linear array transducer (3–12 MHz). The physiatrist, who has had a 10-year experience in musculoskeletal US at the time of the investigation, reviewed all imaging findings. All system-setting parameters were maintained constant throughout the study with the exception of depth (initially set 40 mm), which was modified during the measurement (range, 30–60 mm) to allow visualization of the entire muscle thickness.

Ultrasonographic measurements were performed at paretic and non-paretic quadriceps femoris muscle, which included the rectus femoris and vastus intermedius muscles in the supine position with hips and knees extended. The patients were asked to relax without causing a strain on the body. The examiner applied a sufficient amount of transmission gel on the scanning head, which provided an acoustic contact without compressing the skin. The transducer was placed midway between the anterior superior iliac spine and the proximal end of the patella which is known to be a landmark for measuring QMT.[18,19] Then, the transducer was placed perpendicular to the long axis of the limbs. After identifying the subcutaneous tissue–muscle interface and the muscle–bone interface, the perpendicular distance from the subcutaneous tissue–muscle interface to the muscle–bone interface was recorded using electronic calipers (Fig. 1). Each measurement was performed in triplicate; the angle of the transducer was slightly changed to facilitate clear visualization. The mean value of each measurement was used for data analysis.

2.3.2. Dxa-derived lean body mass. Appendicular lean body mass was analyzed by DXA scan (GE Healthcare, Lunar Prodigy Advance, enCORE 2008, Version 12.20.023, Madison, WI). Patients were laid down in supine position on the scanning table; their forearms were extended parallel to the table, and their legs were also extended. To ensure accurate measurement, the patients were instructed not to move when the examiner performs the scanning procedure. A certified radiologic technologist performed the scanning procedure on patients.

Low muscle mass was diagnosed according to the guidelines of the Asian Working Group for Sarcopenia (AWGS); the cutoff point for low muscle mass is defined by ALM index as < 7.0 kg/m² for

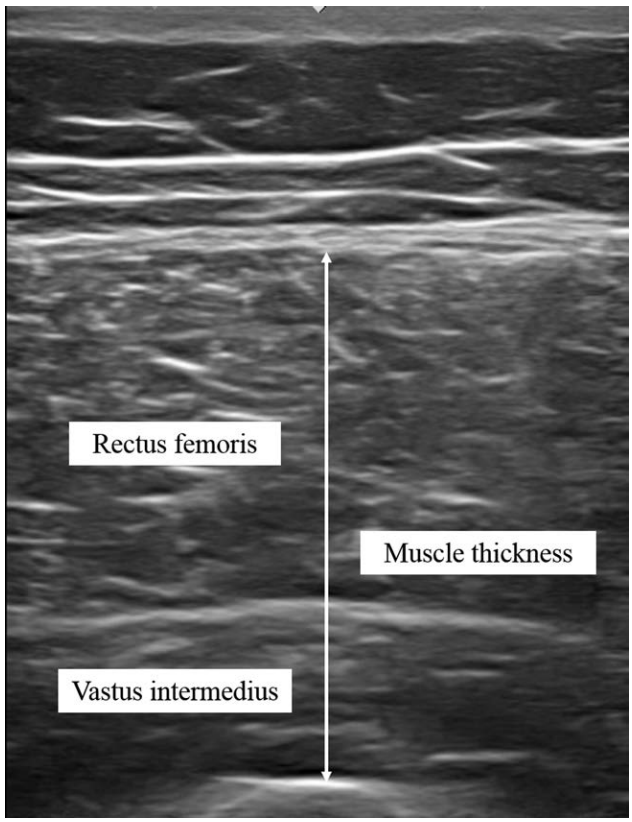

Figure 1. A representative ultrasound image of quadriceps femoris muscle.

males and < 5.4 kg/m^2 for females.[20] Furthermore, the ALM was calculated by adding the lean mass of upper and lower extremities. The SSLM refers to the lean mass of the lower extremity from the buttock to the toe; it is matched with paretic/non-paretic leg.

2.4. Statistical analyses

Mann–Whitney U test was performed, and the mean ± standard deviation for continuous variables was expressed. Fisher test was performed as expressing number and the percentage of categorical variables. Spearman correlation analysis was performed to determine the correlation between QMT and ALM index, and the correlation between QMT and SSLM. Multivariate linear regression analysis was performed to determine whether there was a significant relationship between the following parameters: (i) QMT and ALM index, and (ii) QMT and SSLM. Thereafter, β coefficients were calculated by adjusting confounding factors. Mann–Whitney U test was also applied to investigate the differences of % QMT and % SSLM between paretic and non-paretic legs in the patient groups. All statistical analyses were performed by using SPSS version 26.0 software (IBM SPSS, Armonk, NY). The significance level was 0.05 or less.

3. Results

3.1. Patient characteristics

Table 1 summarized the characteristics of patients. There were 25 patients (13 men, 12 women) in 2 groups (Group A, n = 12; Group B, n = 13). There were no statistically significant differences between the groups in terms of ALM index, QMT and SSLM. Group B showed higher average QMT on both paretic and non-paretic legs than Group A. However, Group B revealed smaller average SSLM on both paretic and non-paretic legs than Group A. There were statistically significant differences of sex (P = .009), BBS (P = .01), mRS (P = .02) and MBI (P = .022) between the 2 groups. Also, within each group, the QMT and SSLM showed a significant difference between paretic and non-paretic legs (P < .001).

3.2. A correlation between QMT and ALM

Figure 2 and Table 2 shows the association between the following parameters of both legs: i) QMT and ALM index, and ii) QMT and SSLM. There were positive correlations between the QMT and ALM index on the paretic/non-paretic sides of both sexes (Spearman correlation coefficient [r], paretic side, R = 0.796, P = .001, men, R = 0.814, P = .001, women; non-paretic side, R = 0.835, P < .001, men, R = 0.813, P < .001, women) (Fig. 2). There were also significant correlations between QMT and SSLM on the paretic/non-paretic sides of both sexes (paretic side, R = 0.752, P = .003, men, R = 0.871, P < .001, women; non-paretic side, R = 0.707, P = .007, men, R = 0.860, P < .001, women).

In this study, the relationship between QMT and ALM index, and the relationship between QMT and SSLM were analyzed on paretic/non-paretic legs by performing multivariate linear regression. This statistical method of analyses was performed after adjusting for confounding factors of age, sex, BMI, and paretic knee extensor power. We used confounding factors with

Table 1

Demographics and baseline characteristics of 25 patients.

Characteristics	Total	Group A	Group B	*P* value
No. of subjects	25	12	13	
Age	69.6 ± 11.9	69.8 ± 13.6	69.5 ± 10.5	.892
BMI (kg/m^2)	24.0 ± 2.9	23.9 ± 3.0	24.0 ± 3.0	.935
Sex				
Male	13 (52)	10 (83.3)	3 (23.1)	.009*
Female	12 (48)	2 (16.7)	10 (76.9)	
Stroke type				
Hemorrhagic	12 (48.0)	7 (58.3)	5 (38.5)	.553
Ischemic	13 (52.0)	5 (41.7)	8 (61.5)	
Duration from stroke onset to USG (d)	24.7 ± 8.8	26.8 ± 11.3	22.8 ± 5.3	.413
Duration from stroke onset to DXA (d)	24.4 ± 9.2	27.3 ± 10.9	21.6 ± 6.6	.173
Stroke risk factors				
Hypertension	24 (96.0)	12 (100)	12 (92.3)	
Diabetes	2 (8.0)	2 (16.7)	0 (0.0)	
Atrial fibrillation	4 (16.0)	2 (16.7)	2 (15.4)	
Hypercholesterolemia	6 (24.0)	2 (16.7)	4 (30.8)	
Paretic side				
Right	16 (64.0)	7 (58.3)	9 (69.2)	.688
Left	9 (36.0)	5 (41.7)	4 (30.8)	
BBS	21.6 ± 19.8	8.3 ± 14.3	33.9 ± 16.0	.01*
mRS	4.0 ± 0.9	4.5 ± 0.5	3.5 ± 1.0	.02*
MBI	34.4 ± 24.5	21.9 ± 19.4	45.9 ± 23.4	.022*
Paretic knee extensor power	2.3 ± 1.3	1.2 ± 0.8	3.4 ± 0.5	<.001*
Proportion of low muscle mass	13 (52.0)	7 (58.3)	6 (46.2)	.835
ALM index (kg/m^2)	6.2 ± 1.1	6.6 ± 1.2	5.8 ± 0.9	.097
QMT (cm)				
Paretic	2.4 ± 0.7	2.4 ± 0.8	2.5 ± 0.6	.531
Non-paretic	2.7 ± 0.7	2.7 ± 0.7	2.7 ± 0.7	.978
SSLM (kg)				
Paretic	5.7 ± 1.4	6.0 ± 1.4	5.5 ± 1.4	.301
Non-paretic	6.0 ± 1.4	6.5 ± 1.6	5.6 ± 1.2	.157

Data are presented as means ± standard deviation or number (%).

ALM = appendicular lean mass, BMI = body mass index, BBS = Berg-Balance Scale, MBI = Modified Barthel Index, mRS = modified Rankin Scale, QMT = quadriceps muscle thickness, SSLM = site specific lean mass.

*P < .05 by Mann–Whitney U test or Fisher test.

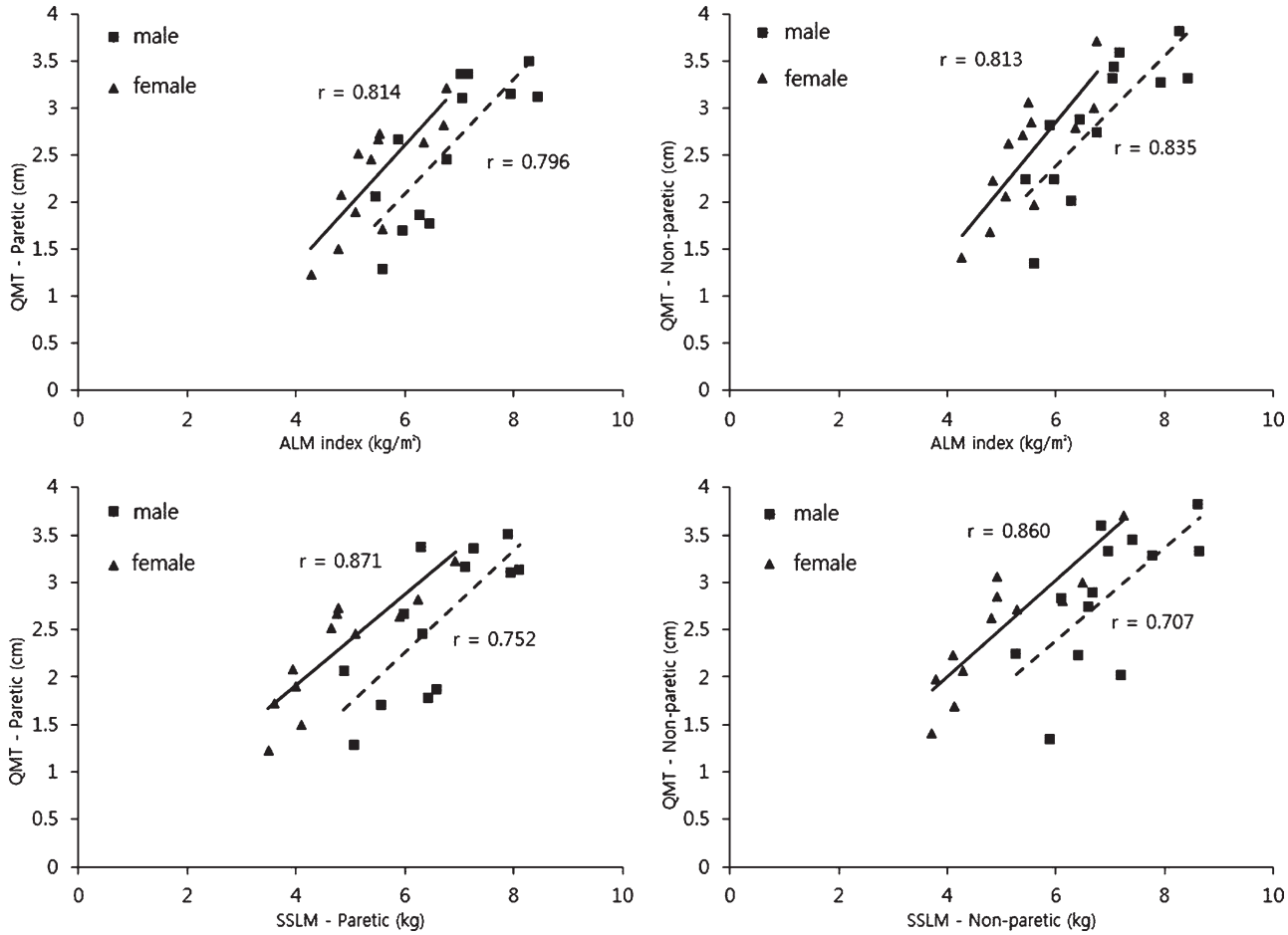

Figure 2. A correlation between QMT and ALM index, and between QMT and SSLM on paretic and non-paretic legs.

Table 2

A correlation between (A) QMT and ALM index, (B) QMT and SSLM by using multivariate linear regression model

	(A) QMT and ALM index								
	Total			Group A			Group B		
	Model 1 †)	Model 2 ‡)	Model 3§)	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Paretic leg	0.474* (0.295–0.653)	0.597* (0.388–0.806)	0.574* (0.396–0.752)	0.538* (0.290–0.786)	0.617* (0.276–0.958)	0.387* (0.113–0.660)	0.630* (0.426–0.834)	0.571* (0.310–0.833)	0.556* (0.261–0.851)
Non-paretic leg	0.504* (0.344–0.665)	0.589* (0.409–0.769)	0.578* (0.401–0.755)	0.538* (0.305–0.771)	0.583* (0.264–0.902)	0.466* (0.069–0.862)	0.638* (0.411–0.865)	0.598* (0.324–0.872)	0.566* (0.270–0.862)
	(B) QMT and SSLM								
	Total			Group A			Group B		
	Model 1†)	Model 2‡)	Model 3§)	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Paretic leg	0.360* (0.213–0.506)	0.494* (0.309–0.679)	0.053* (–0.056–0.163)	0.368‖ (0.097–0.639)	0.554‖ (0.103–1.004)	0.366* (0.151–0.581)	0.403* (0.249–0.557)	0.416* (0.212–0.621)	0.408* (0.173–0.642)
Non-paretic leg	0.350* (0.212–0.489)	0.461* (0.284–0.638)	0.449* (0.267–0.631)	0.341‖ (0.103–0.579)	0.525‖ (0.117–0.932)	0.397‖ (0.028–0.767)	0.468* (0.300–0.636)	0.464* (0.283–0.644)	0.452* (0.239–0.665)

The data are presented as β value and 95% confidence intervals; β (95% CI).

ALM = appendicular lean mass, BMI = body mass index, SSLM = site specific lean mass, QMT = quadriceps muscle thickness.

*$P < .01$.

†Unadjusted model.

‡Adjusted by age, sex and BMI.

§Adjusted by age, sex, BMI and paretic knee extensor power.

‖$P < .05$.

proven association with sarcopenia in the previous studies. Model 1 (without adjusting any confounding factor), model 2 (adjusted for age, sex, and BMI), and model 3 (adjusted for age, sex, BMI, and paretic knee extensor power) were applied (Table 2). With QMT as the dependent variable, R^2 value and beta values for standardized coefficients were calculated. The r-square values increased from model 1 to model 3. In total, Group A and Group B showed a statistically significant correlation between QMT and ALM index, and also between QMT and SSLM in both the paretic and non-paretic legs.

3.3. Paretic and non-paretic side difference

The % QMT, SSLM differences between paretic and non-paretic legs are shown in Table 3. The % QMT showed higher difference than % SSLM between paretic and non-paretic legs (10.3% vs 4.8%). Group A showed higher differences of % QMT and % SSLM between paretic and non-paretic legs than Group B (P = .014, P = .001, respectively).

4. Discussion

The purpose of this study was to examine the relationship between ultrasonographic QMT and DXA-derived lean body mass on both paretic and non-paretic legs in acute hemiplegic stroke patients. In this study, we analyzed the correlation between QMT and ALM index, and between QMT and SSLM of paretic/non-paretic legs. Moreover, the QMT and ALM index showed a positive correlation and the QMT and SSLM also showed a significant relationship even after adjusting several confounding factors. The % QMT showed higher difference than % SSLM between paretic and non-paretic legs. The % QMT and % SSLM difference between the paretic and non-paretic legs were higher in Group A than in Group B.

Several studies have reported that ultrasonographic muscle measurements have a positive relationship with other muscle measurements tools, such as CT, MRI, and DXA scan.[14,15,21] To the best of our knowledge, this is the first study to investigate the relationship between ultrasonographic QMT and DXA-derived lean body mass of both paretic and non-paretic legs in acute hemiplegic stroke patients.

Previous studies have noted that quadriceps is the main muscle responsible for ambulatory capacity, functional mobility, and would be a predictor of walking performance in stroke patients.[12,13] The earlier studies reported that a minimum of grade 3 of knee extensor strength is required for community ambulation.[22,23] Accordingly, we divided the patients into 2 groups based on the grade 3 of the paretic knee extensor power, and compared several parameters between the 2 groups. However, the simple comparison of several parameters of muscle mass between 2 groups had some limitations because it was not possible to correct for all of differences in male-female ratio, age and individual muscle mass. In particular, the proportion of men in Group A was significantly higher than that of Group B (P = .009). Therefore, in this study, we additionally observed the changes of QMT and SSLM between the paretic and non-paretic legs of the same patient.

Since the 2 groups were classified on the basis of paretic knee extensor power, we expected that QMT and SSLM would be higher in Group B than in Group A. However, there were no significant differences in QMT and SSLM of the 2 groups. This was attributed to the discrepancies in the ratio of men and women in the 2 groups. The proportion of men was 83.3% in Group A, whereas it was only 23.1% in Group B. Therefore, the SSLM value in Group A was higher than in group B contrary to our expectations. But, the QMT of Group A was lower than that of Group B despite differences in the gender ratio. In our study, the % QMT difference was greater than the % SSLM difference (10.3% vs 4.8%) between paretic and non-paretic legs. According to previous studies, the DXA scan underestimates the loss of lean mass compared to the loss of muscle mass measured by CT and MRI.[24–26] Based on our results, in the acute phase of stroke, the change of QMT was greater than the change of SSLM as consistent with the underestimation of muscle loss by DXA scan. Subsequently, we could predict that QMT reflects the changes of muscle mass more sensitively than SSLM in patients with an acute phase of stroke.

In addition, the % QMT difference and the % SSLM difference between paretic and non-paretic legs was greater in Group A than in Group B (QMT, 13.6 vs 7.2 %; SSLM, 7.6 vs 2.2 %). A previous study reported that leg extensor power asymmetry after stroke was strongly related to reduced walking performance and poor gait quality.[27] Similarly, another study reported that knee extensor strength is closely related to gait endurance of stroke survivors.[13] Between Group A and Group B, there were statistically significant differences of BBS, mRS, and MBI. This indicates that paretic knee extensor power has an influence on the standing balance and physical functions of stroke survivors.

Stroke-related sarcopenia has a different mechanism from age-related sarcopenia. However, there are no definite diagnostic criteria for stroke-related sarcopenia. The stroke patients have clinical difficulties in executing several tests of muscle strength and physical performance among the criteria for sarcopenia due to paralysis, cognitive impairment, abnormal muscle tone, impaired sensation, poor balance and proprioception deficits. Therefore, the importance of measuring muscle mass among the criteria for sarcopenia becomes more prominent in stroke patients. The ultrasound-based muscle thickness measurement is clinically useful in the aspects of low cost, noninvasiveness, portability and harmlessness. Although DXA scan is a current gold standard for assessing body components, it does not provide the information of distinct muscle structure, whereas it can be easily obtained by ultrasonography. Moreover, DXA scan, compared to ultrasound, can only be performed with appropriate facilities to which many hospitals do not have access. Several studies have reported that the lack of accuracy of DXA scan in assessing changes of lean mass with strength training compared to MRI-derived muscle mass.[26,28] The ultrasonographic muscle thickness is known to be a useful indicator of muscle growth with strengthening training.[29] Furthermore, Franchi et al[30] demonstrated that the muscle thickness changes after strengthening training are related to the parallel changes of muscle cross-sectional area. This finding reinforces the usefulness of ultrasound as a reliable method for the measurement of muscle mass, both in terms of longitudinal aspects as well as in cross-sectional analysis.

Table 3

The % QMT, % SSLM difference in the patient groups.

	Total	Group A	Group B	*P*-value
% QMT difference between paretic and non-paretic leg (%, mean (SD))	10.3 (7.5)	13.6 (9.1)	7.2 (3.8)	.014
% SSLM difference between paretic and non-paretic leg (%, mean (SD))	4.8 (4.5)	7.6 (3.4)	2.2 (4.0)	.001

QMT = quadriceps muscle thickness, SD = standard deviation, SSLM = site-specific lean mass.

The proximal muscles of lower extremity are preferentially affected than distal muscles in the aspect of muscle loss. In a recent study, it was found that thigh muscles were affected earlier and showed a higher rate of decline than the total muscle mass.[31] Additionally, it reported that the thickness of the thigh had a stronger relationship with physical performance than total muscle mass. In the present study, only 13 (52%) out of 25 patients met the diagnostic criteria for low muscle mass; however, only 3 patients were able to walk independently or under supervision. This implies that the ALM index does not adequately reflect the current level of physical performance in agreement with the finding of the previous study. Recently, thickness measurements of quadriceps muscle have shown remarkable findings for evaluating sarcopenia, and numerous studies are in progress to suggest the cut-off values for sarcopenia. Although this study did not evaluate the long-term prognosis of stroke patients as a cross-sectional study, we proved how ultrasound could be a promising tool for the evaluation of sarcopenia in acute stroke patients.

This study has some limitations. First, although we have proved several significant findings in this study, the generalization is difficult due to small sample size. Second, there was a large difference in the gender ratio between the 2 groups, limiting the intuitive comparison of muscle mass indicators when comparing the groups. Therefore, we additionally examined the difference of QMT and SSLM between the paretic and non-paretic legs of the same patient. Third, it is unknown whether the patients already had age-related sarcopenia before stroke. Fourth, the quadriceps muscle was used as a representative muscle, and other muscles were not measured in this study. Finally, this study was a cross-sectional study without additional follow-up evaluation of QMT or lean body mass to monitor the patients' progress or changes.

In conclusion, the ultrasonographic QMT is strongly associated with DXA-derived lean body mass of both paretic and non-paretic legs in patients with acute hemiplegic stroke. Ultrasound reflects better the change of muscle mass between paretic and non-paretic legs than DXA scan at an acute phase of stroke. Therefore, ultrasonographic evaluation of quadriceps muscle could be a pragmatic diagnostic tool, enabling an early detection of stroke-related sarcopenia in the future.

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Author contributions

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Writing—review & editing: Kim YT, Kim DE, Kim SA, Hwang IS.

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