Assessment of changes in muscle mass, strength, and quality and activities of daily living in elderly stroke patients
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Introduction
Numerous studies have shown that poststroke muscle weakness can be partially alleviated through stroke rehabilitation [1–3]. Muscle strength has been the most used parameter for evaluating muscle; however, the importance of muscle mass and quality is increasingly being recognized [4–6]. No studies have investigated whether recovery of muscle strength during poststroke rehabilitation is accompanied by restoration of muscle mass and muscle quality.

Lower limb muscle strength is known to be related to the walking ability and activities of daily living (ADL) status of stroke patients [7, 8]. Skeletal muscle mass is related to muscle strength; in addition, studies have demonstrated a strong correlation between the diameter and tension of extracted human muscle fibers [9]. Several studies have indicated the relationship between lower limb skeletal muscle mass and strength in stroke patients [10–14]. On the other hand, this finding has been questioned in more recent studies have found only a moderate correlation between muscle mass and muscle strength; it has become clear that muscle weakness cannot be explained only by the reduced muscle mass [15–17]. Reduced muscle mass is attributable to the presence of extracellular fat and extracellular fluid in the skeletal muscle tissue. Ryan et al. [15] measured intramuscular fat mass in stroke patients using computed tomography (CT); they found that the intramuscular fat mass on the paralyzed side increased by approximately 25% compared with that on the nonparalyzed side. Presence of intramuscular fat should be considered during the assessment of skeletal muscle mass in stroke patients. Moreover, a high level of intermuscular fat is liable to reduce muscle strength [18]. Therefore, both muscle quality as well as muscle mass should be considered during the assessment of muscle strength. Muscle quality is commonly assessed by CT, MRI, and ultrasound [19]; however, phase angle (PhA), measured by body composition monitors, has recently been shown to reflect muscle quality. The European Working Group on Sarcopenia in Older People 2019 consensus statement suggested that PhA can be regarded as an index of overall muscle quality [20].

Muscle strength, mass, and quality are measures of muscle condition. Investigating the changes in these indices...
after stroke and their relationship with recovery of ADLs would help improve the efficiency of stroke rehabilitation. Understanding the muscle-related factors that affect ADL recovery in stroke patients may accrue benefits in terms of ADL improvement and reduced healthcare costs. Therefore, the aim of this study was to examine the relation of muscle strength, mass, and quality with ADL recovery in stroke patients.

Materials and methods
This prospective study was conducted at two stroke rehabilitation units in Japan between January 2017 and June 2018. Written informed consent was obtained from all subjects before their enrollment. The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of each hospital. The study initially included 210 consecutive patients with stroke. Patients with a pacemaker, high ADL score [motor functional independence measure (FIM) items > 81], severe cognitive impairment, severe dysphasia, and early discharge were excluded from the study. Eventually, 179 patients (90 female and 89 male patients; mean age 79.7 years) were included.

Bioelectrical impedance analysis
Bioelectrical impedance analysis (BIA) was performed using the InBody S-10 analyzer (InBody Japan, Tokyo, Japan), which applies a 200-μA current at frequencies of 5, 50, and 250 kHz after 10 min of rest at ambient temperature. All patients underwent BIA immediately after their admission to the rehabilitation unit. For 3 h before the measurements, the patients did not consume any liquids or solids. The same operator performed the analysis in all patients. For BIA, one electrode each was placed on all four limbs of each patient in the supine position. Before attaching the electrodes, the areas chosen for attached placements were prepared by shaving (if needed) and cleaned. The body weight of the patients was measured during hospitalization using a folding stretcher, and the weight of the empty stretcher was subtracted from the total weight. In the BIA, total body water composition, total body fat, skeletal muscle mass, and PhA were measured. PhA for the whole body at 50 kHz was calculated from the impedance values. In order to standardize the values, we determined the body muscle percentage by dividing the total body skeletal muscle mass by weight.

Muscle strength assessment
Manual dynamometer is a quick, convenient, and low-cost tool for the clinical assessment of global muscle strength in older people. Studies have demonstrated the validity and reliability of manual dynamometer for measurement of grip strength [21]. A manual dynamometer was used to assess grip strength (Grip A TKK5001, Takei Scientific Instruments Co. Ltd., Niigata, Japan), in line with the recommendations of the American Society of Hand Therapy [22] and the American College of Sports Medicine [23]. The test was conducted with the nonaffected side. The participant was seated on a chair (with a back and no arm rests) with the lower limbs resting on the ground. The shoulder of the limb to be tested remained adducted and neutral for rotation, the elbow flexed at 90°, the forearm neutral for pronosupination, and the wrist extended between 0° and 30° with 0°–15° of ulnar deviation. During the test, the participants were verbally encouraged to use their maximum strength. The test was repeated three times and the mean value was recorded.

Functional measurements
The ADL status of patients was assessed using the FIM motor scores. The FIM contains 13 items related to motor tasks, each of which is rated on a 7-point ordinal scale; higher scores are indicative of greater independence [24]. The scale has been used mainly during neuropsychological rehabilitation (including patients with stroke and brain injury) and geriatric rehabilitation [25]. The FIM was scored by members of the multidisciplinary rehabilitation team on the day of admission to the stroke rehabilitation unit and four weeks later. The amount of change in the motor FIM score over 4 weeks was used as the index of functional recovery. We performed BIA, muscle strength and ADL assessments on all subjects at admission to the stroke rehabilitation unit and at 4 weeks postadmission.

Statistical analysis
Continuous variables are expressed as mean ± SD. Independent t-test was used to assess differences between male and female patients. P values less than 0.05 were considered indicative of statistical significance.

Owing to the sex-related differences in muscle mass, muscle strength, and muscle quality, the analysis was performed disaggregated by sex [26]. The relationships between high muscle strength recovery (>4 kg), high PhA recovery (>0.4°), high body muscle recovery (>0%), and functional recovery (motor FIM items > 15) were estimated using odds ratios and 95% confidence intervals obtained from multivariate logistic regression models. All statistical analyses were performed using IBM SPSS Statistics ver. 25 (IBM Corp., Armonk, New York, USA).

Results
Descriptive characteristics
The descriptive and functional characteristics of the study population are presented in Table 1. All participants were Japanese (Asian). The mean time elapsed from stroke onset to admission in the stroke rehabilitation unit was 27.6 days. All participants received stroke rehabilitation program for about 160 min/day in the stroke rehabilitation unit. Male participants were significantly taller (P < 0.05) and heavier (P < 0.05) than female participants; however, there were no significant differences between male and...
Female participants with respect to age or BMI (Table 2). Male participants had greater muscle strength, higher muscle quality, and greater muscle mass than female participants. Both male and female patients showed significant improvement in motor FIM scores at 4 weeks (P < 0.05 for both). There was significant improvement in muscle strength and muscle quality at 4 weeks in both male and female patients (P < 0.05 for all). However, muscle mass showed a tendency to decrease during 4 weeks in both male and female patients (Tables 3 and 4).

**Statistical analysis**

We investigated ADL recovery and assessed its correlation with muscle mass, strength, and muscle quality. We observed a significant correlation of ADL recovery with muscle strength and muscle quality (r = 0.66 and 0.55 for men and r = 0.45 and 0.31 for women, respectively). The correlation was stronger in males. There was a mild negative correlation between muscle mass and ADL recovery (r = −0.14 and r = −0.22) (Figs. 1a–c and 2a–c). We also investigated which covariates were associated with functional recovery. In the univariate analysis, no malnutrition, a high body muscle percentage, and a high PhA were associated with functional recovery (Table 5).

**Discussion**

In the present study, we compared ADL recovery and changes in muscle mass, strength, and muscle quality in patients undergoing stroke rehabilitation. After stroke, both muscle strength and muscle mass decrease in the affected and nonaffected sides [27]. Muscle strength has been shown to affect the walking ability and ADL status of stroke patients [7,8]. Studies have also reported a strong relationship between lower limb muscle strength and walking ability of stroke patients [10–14]. However, although muscle strength has been suggested to correlate with muscle mass, this correlation has recently been reported to be weaker in the elderly [15–17].

Assessment of limb circumference is the simplest approach for measuring skeletal muscle mass. Local muscle mass measurements are performed by CT, MRI, and ultrasound. Dual-energy X-ray absorption and BIA are used to measure muscles throughout the body.

In the BIA method, a weak current is passed through the body, and its electrical impedance is used to indirectly determine the amount of water, body fat, and muscle mass. Although BIA is minimally invasive and simple, the results are liable to be affected by body water status (such as dehydration and edema) and changes in conductivity due to body temperature [28].

We observed differences in body muscle mass, muscle strength, and PhA between male and female patients. These findings are consistent with those of previous studies [29, 30]. Therefore, the analysis was performed separately for male and female participants. In our study, both male and female participants showed faster functional recovery when the body muscle percentage and PhA were high. Body fat percentage and body water composition percentage were not found to affect functional recovery.

PhA is the most frequently applied BIA parameter in clinical settings. It reflects both the quantity and quality of soft tissue and is currently regarded as a composite measure of tissue resistance and reactance [31]. Increased PhA reflects the structural integrity of the cell membrane and improved cellular function while structural damage of the cell leads to decrease in PhA. In a pure cell membrane mass, PhA is 90°, whereas that in pure electrolyte water is 0°. In healthy subjects, PhA typically ranges from 8° to 15° [32]. A previous study also showed a significant decrease in PhA with age after showing a peak between the age of 20 and 40 years in healthy subjects [31]. The decrease in PhA with increasing age may reflect cell function and general health conditions in addition to body composition [32]. PhA in our study participants was lower than that in a previous study. This is likely attributable to the reduced cell function and general health status of stroke patients as compared with healthy elderly individuals.

Muscle quality has received significant attention in recent years as an indicator for muscle assessment.

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**Table 1** Characteristics of the study population

| Characteristic                      | Mean | SD |
|------------------------------------|------|----|
| Number of patients                 | 179  | ND |
| Age (years)                        | 79.7 | 11.5 |
| Sex (female/male)                  | 90/89| ND |
| Mini-Mental State Examination      | 20.2 | 8.0 |
| Days after stroke                  | 276  | 8.7 |
| Duration of rehabilitation program (min/day) | 159.8| 21.6 |
| Motor FIM score on admission       | 39.0 | 19.9 |
| Motor FIM score at 4 weeks         | 53.6 | 28.8 |

FIM, functional independence measure; ND, no data.

**Table 2** Characteristics of the study population disaggregated by sex

| Characteristic          | Men (n = 89) | Women (n = 90) | P     |
|------------------------|-------------|---------------|-------|
| Age (years)            | 78.6        | 80.7          | 0.21  |
| Height (cm)            | 158.1       | 153.2         | <0.05 |
| Weight (kg)            | 52.4        | 45.7          | 0.13  |
| BMI (kg/m²)            | 20.0        | 19.4          | 0.57  |

*P < 0.05.

**Table 3** Changes in muscle strength, quality, and mass in male patients

| Parameter               | Muscle strength (kgw) | Muscle quality (degree) | Muscle mass (%) | Motor FIM items |
|-------------------------|-----------------------|-------------------------|-----------------|----------------|
| On admission            | 18.6                  | 4.2                     | 40.0            | 39.5           |
| After 4 weeks           | 22.9                  | 4.5                     | 39.6            | 55.7           |

P < 0.001, < 0.001, < 0.001, < 0.001.

FIM, functional independence measure.
Skeletal muscle mass in stroke patients should be considered along with this intramuscular fat. Muscle quality decreases with increase in intermuscular fat.

Studies have shown a direct relation between PhA and muscle strength [33, 34]; for instance, PhA was higher in athletes [35], and declined with aging. PhA decreases in the setting of disease, inflammation, malnutrition, and prolonged physical inactivity [30]; in addition, it is associated with impaired quality of life [36] and poor prognosis in various chronic diseases [37–39]. In the elderly, it is also an independent predictor of clinical adverse outcomes such as frailty [40], falls [41], incident disability [42], and mortality [43, 44]. Furthermore, in our previous

| Parameter        | Muscle strength (kgw) | Muscle quality (degree) | Muscle mass (%) | Motor FIM items |
|------------------|-----------------------|-------------------------|-----------------|-----------------|
| On admission     | 12.4                  | 3.3                     | 35.8            | 38.6            |
| After 4 weeks    | 16.8                  | 3.5                     | 35.4            | 52.8            |
| *P*              | *<0.001*              | *<0.001*                | 0.24            | *<0.001*        |

FIM, functional independence measure.

Fig. 1

(a) The relationship of changes in muscle strength and ADL improvement (male). (b) The relationship of changes in muscle quality and ADL improvement (male). (c) The relationship of changes in muscle mass and ADL improvement (male). The vertical axis shows the change in ADL in 4 weeks, and the horizontal axis shows the change in grip strength, muscle quality, and muscle mass, respectively. The broken line shows the regression line. A significant correlation of ADL recovery with muscle strength and muscle quality (*r* = 0.66 and 0.55). However, there was a mild negative correlation between muscle mass and ADL recovery (*r* = −0.14). ADL, activities of daily living.
Irisawa and Mizushima's study found PhA to predict ADL recovery in elderly stroke patients [45]. Interestingly, from a practical standpoint, the EWGSOP 2019 consensus on sarcopenia suggested that PhA may be regarded as an index of overall muscle quality [20].

Decrease of muscle strength is commonly observed in the elderly. This is due to a primary disturbance of the neuromuscular junction with a progressive decrease in the trophic function of nerve cells, resulting in the random loss of muscle fibers and consequently the decrease of the size of the motor unit [46]. However, rehabilitation for the elderly can increase muscle strength and muscle activation (neural factors) [46]. Our results show that muscle strength and muscle quality can be restored by poststroke rehabilitation. Although several studies have suggested that muscle strength can be restored during poststroke rehabilitation, this is the first study to show that muscle quality plays a role in muscle strength recovery. In contrast, we found a decrease in muscle mass at 4 weeks, although the difference was not statistically significant. This may seem like a surprising result; however,
Muscle strength showed a correlation with ADL recovery. This is consistent with several previous studies [7, 8, 49, 50]. Improvement in muscle quality also showed a correlation with recovery of ADL status; this finding is entirely plausible as improvement in muscle quality correlated with improvement in muscle strength. Male patients showed a stronger correlation of improvement in muscle strength and muscle quality with improvement in ADL status than female patients. In a previous study, men were found more likely to benefit from muscle hypertrophy from exercise than women [51]; this may explain why muscle strength and muscle quality improved with rehabilitation in men and correlated more strongly with ADL. Furthermore, the results of multivariate analysis revealed that the recovery of muscle strength and muscle quality both affected the recovery of ADL. Muscle mass showed a very weak negative correlation with ADL and multivariate analysis did not find a relationship between muscle mass and ADL recovery. As mentioned above, muscle mass may decrease with rehabilitation in the elderly; therefore, it may be inappropriate to use muscle mass as an indicator of the effectiveness of rehabilitation in elderly stroke patients.

Some limitations of our study should be considered while interpreting our results. PhA values vary widely by race and age, and the mean values obtained in this study were smaller than those in previous studies; small PhA values may have increased the risk of sarcopenia, which may have led to muscle weakness.

We also did not take into account the nutritional status or any changes in diet or route of administration. Although the stroke rehabilitation unit provides the nutritional requirements for each patient, the actual intake varies according to dietary patterns and individual appetite due to swallowing status, which may also affect the changes in muscle strength, muscle quality, and muscle mass.

**Conclusion**

Muscle strength and muscle quality, as determined by BIA, correlate with ADL recovery during stroke rehabilitation. Muscle mass is not an indicator of ADL recovery in the elderly. Muscle strength and quality should be emphasized in the rehabilitation of the elderly.

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**Conflicts of interest**

There are no conflicts of interest.

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