Ultrasound Assessment of Changes in Muscle Architecture of the Brachialis Muscle After Stroke—A Prospective Study

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Abstract  Objective: To investigate changes in ultrasound-derived muscle architecture parameters of the brachialis and correlations in patients with subacute stroke.

Design: Prospective longitudinal observational study.

Setting: Tertiary inpatient rehabilitation centre.

Participants: Fifty adult patients (N=50) who were recruited within the first month poststroke. The patients had a mean age of 57.2±12.3 years and 68.0% were male. The majority of patients had significant upper limb weakness with a low mean Motricity Index of 18.5±24.7 and median elbow flexor strength of grade 0.

Intervention: Not applicable.

Main Outcome Measures: Ultrasound of the intact and hemiparetic brachialis was performed at 3-time intervals: within 1 month of stroke onset and at 1 and 6 months after first assessment. Clinical variables captured included upper limb motor power and elbow flexor spasticity.

Results: Compared to the intact brachialis, there was reduced muscle thickness (1.93 cm vs 2.07 cm, 1.86 cm vs 2.08 cm, 1.85 cm vs 2.05 cm; P=.022) and increased echo intensity (63.3 arbitrary units [AU] vs 56.8 AU, 69.4 AU vs 56.6 AU, 77.4 AU vs 58.2 AU; P<.001) in the hemiparetic brachialis at all assessment intervals (baseline, 1 month, 6 months). Reduction in muscle...
Motor weakness of the upper limb is a major complication of stroke, with less than half of stroke survivors regaining useful upper limb function after 6 months poststroke. Upper limb rehabilitation is therefore a significant area of research interest in stroke rehabilitation, because motor impairment restricts stroke survivors in their activities of daily living such as feeding, dressing, and grooming. Exercise-based rehabilitative modalities are especially crucial during the first 4 months after stroke, when the majority of upper limb motor recovery occurs. Complications arising from the loss of motor function include learned non-use, spasticity, and contractures, and these can potentially result in changes in muscle architecture. Muscle changes documented in previous studies include reduction in muscle volume and thickness as well as number of motor units, shortening of muscle fibers and increased fibrosis. However, almost all of these studies are limited to evaluation of the hemiparetic lower limb in chronic stroke survivors. It is difficult to determine whether these findings are also applicable to the hemiparetic upper limb given the scarcity of such studies. One small study of 17 patients with stroke utilizing dual-energy x-ray absorptiometry found no significant change in muscle mass of the hemiparetic upper arm between 3 weeks and 6 months after stroke. Understanding changes in muscle architecture of the hemiparetic upper limb and when these changes occur after stroke onset may allow one to provide appropriate rehabilitation interventions in a timely manner. For example, early atrophy and changes in muscle fiber structure are linked with reduced muscle force generation. Early detection of these changes can identify patients at risk of emergent strength and functional deficits, who may then require select high-intensity and repetitive task-specific therapy to attenuate further muscle atrophy.

The elbow flexors are muscles that are commonly affected after stroke. Elbow flexors are also prone to the development of spasticity, with 1 study citing it as the commonest form of poststroke spasticity with a prevalence of 79%. The biceps brachii, brachialis, and brachioradialis are the primary elbow flexors. Of these, the brachialis muscle contributes to the largest force to elbow flexion torque (47%).

With the above in mind, we conducted a longitudinal study in a cohort of patients with stroke using ultrasound to evaluate changes in brachialis muscle architecture and to establish clinical variables associated with changes in brachialis muscle architecture.

Methods

Study design

This was a prospective observational study that recruited patients with stroke admitted consecutively to a rehabilitation center from October 2018 to December 2020. Patients were included based on the following criteria: age between 21 and 80 years old, a first-ever clinical unilateral stroke (ischemic or hemorrhagic) confirmed on computed tomography or magnetic resonance brain imaging, duration of <1 month poststroke, premorbid modified Rankin scale of 0, and presence of elbow flexion weakness in the hemiparetic upper limb of Medical Research Council (MRC) grade 4 or less. The exclusion criterion was limitation of full elbow extension; for example, due to contracture or joint deformity of the hemiparetic upper limb.

Ultrasound measurement of muscle parameters

Ultrasound evaluation was performed on the brachialis of both the hemiparetic and normal upper limbs. Ultrasound images were obtained using B-mode ultrasound with a 15-4 MHz linear array probe. Ultrasound measurements were obtained with patients in a supine position with fully extended elbow joints. The brachialis was measured at 1 cm proximal to the elbow crease on the anterior part of the upper arm.

The following ultrasound parameters were measured:

a. Muscle thickness. This was assessed using the longest distance between the superficial aponeurosis and uppermost part of the bone echo of the humerus. Muscle thickness is a reflection of muscle mass.

b. Anterior pennation angle and fascicle length. The anterior pennation angle and fascicle length were measured between the humeral surface and the most clearly visualized fascicle for the brachialis on longitudinal views. In cases where the fascicle extended outside the acquired image, the fascicle length was derived by dividing the muscle thickness by the hypotenuse of the anterior pennation angle. The fascicle length and pennation angle affect force production in a muscle. A lower fascicle length reflects lower contraction strength and a larger pennation angle reflects a lower muscle tension applied to the bone tendon unit.
c. Muscle echo intensity. This was measured using ImageJ software for analysis. Muscle echo intensity was assessed at the grayscale level and expressed as a number between 0 and 255 arbitrary units (AU), with 0 representing black and 255 representing white. A large region of interest, as large as possible, was established in the muscle, excluding bone or surrounding fascia. The mean echo intensity inside the region of interest was then calculated. Echo intensity is a measure of muscle quality, and an increased echo intensity reflects increased intramuscular fibrosis and adipose tissue.

A single examiner (JMK) with more than 10 years of experience in musculoskeletal ultrasound performed all muscle ultrasound imaging.

Clinical evaluation

The following outcome measures were also captured: (1) Elbow flexor spasticity of the hemiparetic upper limb using the Modified Ashworth Scale (MAS). The 6-point MAS ranges from 0 (no increase in muscle tone) to 4 (rigid in flexion or extension). A value of 1.5 for MAS was assigned to ratings of 1+ to maintain equal intervals for statistical analysis; (2) Motor strength of the hemiparetic upper limb using the MRC scale and Motricity Index. The Motricity Index measures shoulder abduction, elbow flexion, and pinch grip in the upper limb and is scored from 0 to 100 for each limb, with 100 indicating normal motor power.

Other clinical parameters captured included patient demographics (age and sex), premorbid functional status as measured on the modified Rankin Scale and type of stroke (infarct vs hemorrhagic), presence of sensory loss and unilateral spatial neglect as measured on the Sensation and Unilateral Spatial Neglect subscales of the National Institute of Health Stroke Scale, and duration from stroke onset to study enrollment.

Ultrasound evaluation, MAS, Motricity Index, and sensation and unilateral spatial neglect measurements were performed at 3 time intervals: on study enrollment (baseline), 1 month after baseline, and 6 months after baseline. Baseline and 1-month assessments were done in the inpatient setting and the 6-month assessment was done in the outpatient setting. All clinical parameters were performed by the first 2 authors.

Statistical analysis

Descriptive statistics were utilized to illustrate clinical characteristics of the study population. The Student t test was used for analysis of continuous variables for independent samples and the Pearson test for correlation between continuous variables. For assessment of repeated measures over time, analysis of variance was used for continuous variables and the nonparametric Friedman test was used for ordinal variables. Factors analyzed for association with ultrasound parameters were age, elbow flexor spasticity, and elbow flexor strength. Elbow flexor spasticity was dichotomized as absent (MAS score of 0) and present (MAS score of 1 or greater), and elbow flexor strength was dichotomized as severe weakness (MRC score of 0-2) and mild weakness (MRC score of 3-4). The level of significance was set at P<0.05 for a 2-tailed test. Statistical analyses were generated using SPSS v25.0.

Ethics approval was obtained from the institution’s ethics board and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients or their legally acceptable representative where relevant.

Results

A total of 50 patients with a mean age of 57.2±12.3 years were enrolled in the study. No patients were excluded because of limitation of full elbow extension. None of the patients had pharmacologic or interventional treatments for spasticity. Baseline patient characteristics are shown in table 1. Most of the patients were male (68.0%), of Chinese ethnicity (78.0%), and had stroke of an ischemic origin (54.0%). The average duration after stroke to study enrollment was 16.9±6.74 days. Sensory impairment was present in 39 patients (78.0%) and visuospatial neglect in 21 patients (42.0%). The majority of patients had significant upper limb

| Table 1 Baseline characteristics of study population (n=50) |
|-----------------------------------------------------------|
| Characteristics                                          | N (%)/Median (25th Percentile-75th Percentile)/Mean±SD |
| Age (y) (mean)                                           | 57.2±12.3                                                |
| Sex: Male/female                                         | 34 (68.0%)/18 (32.0%)                                   |
| Ethnicity: Chinese/Malay/Indian                          | 39 (78.0%)/8 (16.0%)/8 (16.0%)                           |
| Premorbid modified Rankin Scale: 0; 1                    | 49 (98.0%)/1 (2.0%)                                      |
| Nature of stroke: Ischemic/hemorrhagic                   | 27 (54.0%)/23 (46.0%)                                   |
| Duration from stroke onset to study enrollment (days) (mean) | 16.9±6.74                                               |
| Side of hemiparesis: Left/right                           | 32 (64.0%)/18 (36.0%)                                   |
| Sensation on hemiparetic side: Normal/reduced            | 11 (22.0%)/39 (78.0%)                                   |
| Hemispatial neglect                                      | 21 (42.0%)                                               |
| Elbow flexor spasticity: (MAS elbow flexor score>0)      | 17 (34.0%)                                               |
| MAS elbow flexors (median)                               | 1.5 (1, 1.5)                                             |
| MRC grade elbow flexion (median)                         | 0 (0, 2)                                                 |
| Motricity Index (mean)                                   | 18.5±24.7                                                |
weakness as evidenced by a low mean Motricity Index of 18.5±24.7 and median elbow flexor strength of grade 0. Although elbow flexor spasticity (defined by MAS score of greater 0) was present in 17 patients (34.0%), this was mild in severity as reflected by the median elbow flexor MAS score of 1.5. No patient had an MAS score of more than 2.

The number of patients evaluated at 1 and 6 months after study enrollment was 42 (84.0%) and 38 (76.0%), respectively. Reasons for failure to complete the study included transfers back to the acute facility because of medical complications (5) and loss to follow-up (7).

Changes in motor strength and spasticity of the stroke-affected upper limb

There was a significant increase in elbow flexion strength in the affected upper limb from a median MRC grade of 0 (interquartile range [IQR]=0-2) at baseline to 3 (IQR=0-4) at 1 month and 3 (IQR=1-4) at 6 months (P=.027). There was also a significant increase in the severity of elbow flexor spasticity over time, with the median MAS increasing from 1.0 (IQR=1.0-1.5) at baseline to 1.5 (IQR=1.0-1.5) at 1 month and 1.5 (IQR=2-4) at 6 months.

The percentage of patients with elbow flexor spasticity increased from 34.0% at baseline to 54.7% at 1 month and 68.4% at 6 months. The Motricity Index increased from 18.5±24.7 at baseline to 41.0±29.2 at 1 month and 48.8±24.0 at 6 months.

Changes in ultrasound parameters of the brachialis muscle

Changes in ultrasound parameters of the hemiparetic brachialis muscle were statistically significant with respect to baseline. Comparison of baseline ultrasound parameters of both the stroke-affected and unaffected upper limbs are shown in table 2. Comparison of baseline ultrasound parameters between the hemiparetic and nonhemiparetic brachialis revealed statistically significant differences in muscle thickness (P=.034) and echo intensity (P=.002) but not fascicle length or pennation angle. Compared to the nonhemiparetic brachialis, the hemiparetic brachialis had lower muscle thickness (1.93 cm vs 2.07 cm) and increased echo intensity (63.3 vs 56.8).

In the hemiparetic brachialis, there was a significant reduction in muscle thickness from baseline to 1 month (P=.022) but not from 1 month to 6 months. Significant increase in echo intensity was noted from baseline to 1 month and from 1 month to 6 months (P<.001). No significant changes were noted in fascicle length and pennation angle. In the nonhemiparetic brachialis, no significant changes in ultrasound parameters were noted over time.

Factors correlated with ultrasound parameters of the hemiparetic brachialis muscle

Analysis of factors revealed that elbow flexor strength was not statistically correlated with any of the ultrasound parameters of the hemiparetic brachialis at all assessment intervals. Only age and elbow flexor spasticity were significantly correlated to certain ultrasound parameters.

Age was inversely correlated to muscle thickness at all assessment intervals, with the correlation coefficient ranging from −0.30 (P=.03) at baseline to −0.50 (P<.001) at 6 months. Age was not significantly correlated with echo intensity, pennation angle, or fascicle length. There was also no significant correlation between age and Motricity Index at all assessment intervals (P>.05).

Significant associations between elbow flexor spasticity and fascicle length, muscle thickness, and echo intensity at 1 month and elbow flexor spasticity with fascicle length at 6 months were noted (table 3). Presence of elbow flexor spasticity was associated with longer fascicle lengths, greater muscle thickness, and lower echo intensity at 1 month with longer fascicle lengths at 6 months (table 3).

Discussion

This study reports longitudinal changes in ultrasound parameters of the brachialis muscle of both the intact and hemiparetic upper limbs from the subacute to chronic stage of stroke in a cohort of 50 patients with stroke. We recruited patients as early as 6 days and followed patients up to 7 months after stroke onset.

Compared to the unaffected brachialis, there was a reduction in muscle thickness of the hemiparetic brachialis muscle as early as slightly more than 2 weeks after stroke onset, with further loss noted at 1 month before stabilizing at 6 months. The echo intensity of the hemiparetic brachialis muscle was increased at baseline and continued to increase at 1 month and 6 months. Increased echo intensity

| Table 2 | Changes in ultrasound parameters over 6 months |
|---------|---------------------------------------------|
| Measurement                      | Baseline: (n=50) | 1 Month: (n=42) | 6 Months: (n=38) | P Value |
| Hemiplegic brachialis            |                 |                 |                 |        |
| Fascicle length (cm)             | 12.4±3.45       | 11.20±3.40      | 12.10±3.21      | .162   |
| Pennation angle (degree)         | 9.49±2.05       | 10.0±2.23       | 9.77±1.96       | .371   |
| Muscle thickness (cm)            | 1.93±0.31       | 1.86±0.332      | 1.85±0.39       | .022   |
| Echo intensity (AU)              | 63.3±11.0       | 69.4±12.8       | 77.4±14.9       | <.001  |
| Nonhemiplegic brachialis        |                 |                 |                 |        |
| Fascicle length (cm)             | 11.9±2.17       | 12.2±2.18       | 12.4±3.37       | .736   |
| Pennation angle (degree)         | 10.5±2.19       | 10.3±1.95       | 10.1±1.81       | .509   |
| Muscle thickness (cm)            | 2.07±0.33       | 2.08±0.33       | 2.05±0.37       | .460   |
| Echo intensity (AU)              | 56.8±10.7       | 56.6±13.1       | 58.2±10.9       | .478   |

Significant P values in bold.
of hemiparetic upper limb muscles has been reported previously in 2 previous cross-sectional studies of patients with chronic stroke. Berenpas et al reported an increase in echo intensity in hemiparetic biceps brachii and forearm flexors in patients with stroke of >6 months' duration when compared with reference values obtained from healthy patients. Similarly, Lee et al reported increased muscle echo intensity of the hemiparetic upper limb compared to the nonparetic side in patients with a mean poststroke duration of 11.6 years. Our finding of reduction in muscle thickness and increased muscle echo intensity over time reflects ongoing loss of muscle mass and increased intramuscular fibrosis and adipose tissue of the hemiparetic brachialis muscle, and this is likely due to denervation and disuse. As for the parameters of fascicle length and pennation angle, we did not note any significant changes over time in either the intact or hemiparetic brachialis muscle.

The majority of patients had severe upper limb weakness with a mean Motricity Index of 18.5±24.7 at baseline and, as such, are dependent on the unaffected upper limb to perform most, if not all, activities of daily living. With increased use of the unaffected upper limb, we had entertained the possibility of increased muscle thickness of the unaffected brachialis over time, but this was not demonstrated in this study.

Of the factors analyzed for correlation to ultrasound parameters in the hemiparetic brachialis, only age and elbow flexor spasticity were found to be significant. Age was inversely correlated to muscle thickness at all assessment intervals, meaning that older patients were more likely to lose muscle mass than younger patients over time. The lack of correlation between age and Motricity Index at all assessment intervals suggests that this muscle loss is not a result of poorer motor recovery in older patients. This accentuated loss of muscle mass in older patients is consistent with current evidence of aging-associated muscle loss.

This study demonstrated that elbow spasticity at 1 month was correlated to greater muscle thickness, lower echo intensity, and longer fascicle lengths. In other words, compared to patients without elbow flexor spasticity, we found that patients with elbow flexor spasticity were more likely to have less muscle mass loss and intramuscular fibrosis and adipose tissue of the hemiparetic brachialis at 1 month. Longer fascicle lengths also suggested greater force production when the brachialis muscle is contracted. In trying to understand why these findings were not present at baseline, we note that elbow flexor spasticity at baseline was very mild as evidenced by the median MAS score of 1. On the other hand, elbow flexor spasticity at 1 and 6 months was significantly more severe, as reflected in median MAS scores of 1.5. Muscles that are spastic are in a state of tonic contraction, and we postulate that the greater degree of spasticity at 1 month resulted in greater tonic muscle contraction, with better preservation of muscle mass and architecture. The duration of this protective effect of muscle spasticity appeared to diminish over time, because at 6 months, only fascicle length, but not muscle thickness and echo intensity, was significantly correlated to elbow flexor spasticity.

Ultrasound assessment of pennation angle and fascicle length of the spastic brachialis has been studied previously. In a study by Li et al involving 7 patients with chronic stroke (2-11 years poststroke) with median elbow flexor spasticity of MAS 2, ultrasound assessment of the affected and unaffected brachialis was done at different elbow flexion angles. Those authors reported that pennation angles and fascicle lengths were joint angle dependent in both affected and unaffected brachialis. Overall, pennation angles were greater and fascicle lengths shorter in the spastic brachialis. In another study, Theliam and Yourey performed ultrasound assessment of the brachialis with the elbow flexed at 90 degrees in 11 patients with chronic stroke (4-15 years poststroke) with brachialis spasticity. They reported greater pennation angles and longer fascicle lengths in the spastic brachialis when compared to the unaffected brachialis.

When comparing results of our study to the abovementioned studies, we recognize that it is important to acknowledge that significant differences in study methodology, sample size, and patient selection exist between studies, and these could have contributed to differences in study findings. These include duration poststroke when patients were recruited (subacute vs chronic, where muscle disuse is expected to be more prominent in patients with chronic stroke), elbow position at which ultrasound of the brachialis was performed (extended vs flexed), and severity of elbow flexor spasticity.

**Study limitations**

There are a few limitations worth highlighting. Firstly, because we did not examine other upper limb muscle groups, we are uncertain whether similar findings exist. Secondly, because patients were only followed up to 7 months after stroke onset, changes in brachialis muscle architecture beyond this period are uncertain. Thirdly, we were not able to determine the cause of muscle loss in older patients, meaning that older patients were more likely to have less muscle mass loss and intramuscular fibrosis and adipose tissue of the hemiparetic brachialis at 1 month. Longer fascicle lengths also suggested greater force production when the brachialis muscle is contracted. In trying to understand why these findings were not present at baseline, we note that elbow flexor spasticity at baseline was very mild as evidenced by the median MAS score of 1. On the other hand, elbow flexor spasticity at 1 and 6 months was significantly more severe, as reflected in median MAS scores of 1.5. Muscles that are spastic are in a state of tonic contraction, and we postulate that the greater degree of spasticity at 1 month resulted in greater tonic muscle contraction, with better preservation of muscle mass and architecture. The duration of this protective effect of muscle spasticity appeared to diminish over time, because at 6 months, only fascicle length, but not muscle thickness and echo intensity, was significantly correlated to elbow flexor spasticity.

**Table 3** Analysis of elbow flexor spasticity and ultrasound parameters

|                  | Elbow Flexor Spasticity | P Value |
|------------------|-------------------------|---------|
|                  | Yes                     | No      | |
| Baseline         |                         |         | |
| Fascicle length (cm) | 13.82±4.61             | 11.72±2.13 | .09 |
| Pennation angle (degree) | 9.1±2.4               | 10.2±2.9 | .13 |
| Muscle thickness (cm) | 2.02±0.41              | 1.92±0.32 | .40 |
| Echo intensity (AU) | 67.0±13.0              | 62.6±13.0 | .27 |
| 1 month          |                         |         | |
| Fascicle length (cm) | 12.92±3.02              | 9.83±2.93 | .002 |
| Pennation angle (degree) | 9.5±2.1               | 9.9±2.4 | .58 |
| Muscle thickness (cm) | 1.93±0.32              | 1.74±0.33 | .017 |
| Echo intensity (AU) | 65.1±11.1              | 75.1±15.0 | .023 |
| 6 months         |                         |         | |
| Fascicle length (cm) | 13.33±4.33              | 11.02±2.12 | .047 |
| Pennation angle (degree) | 9.3±2.1               | 10.3±1.9 | .18 |
| Muscle thickness (cm) | 1.93±0.32              | 1.83±0.32 | .30 |
| Echo intensity (AU) | 76.0±13.7              | 77.6±16.7 | .80 |

*Significant P values in bold.*
to ascertain the influence of rehabilitation intensity on study findings at 6 months because the relevant data on these were not captured. Fourth, the examiners performing ultrasound and clinical assessments were not blinded to their previous findings. Another limitation associated with this study is that the increase in familywise error rate across the reported statistical analyses was not controlled for. Hence, we consider this study relatively preliminary and encourage replication. Finally, due to the relatively small numbers recruited in this study and substantial dropout rate, caution is required when extrapolating the results found. On the other hand, to the best of our knowledge, this study is the first to look at longitudinal changes in an upper limb muscle after stroke, with all ultrasound assessments performed by an experienced rehabilitation physician.

Conclusions

Our study details quantitative and qualitative changes that occur in the hemiparetic brachialis in the first 7 months after stroke onset, with the main findings of decreased muscle thickness and increased echo intensity over time. We also show that obtaining measurements of muscle architecture is an easily accessible and feasible task. A growing body of evidence suggests that nutritional supplementation, pharmacologic administration of anti-inflammatory agents, and increased rehabilitation exercise may mitigate loss of muscle mass and function after stroke. Future studies should look at changes in muscle architecture of other upper limb muscles, along with the role of various interventions in modifying muscle architecture changes and disability outcomes.

Suppliers

a. Terason t3200, Terason.
b. ImageJ, National Institutes of Health.
c. SPSS v25.0, IBM Corporation.

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