Site-specific thigh muscle loss as an independent phenomenon for age-related muscle loss in middle-aged and older men and women

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Abstract The purpose of this study was to examine the relationships between dual-energy X-ray absorptiometry (DXA)-determined appendicular lean mass (aLM) and ultrasound-measured thigh muscle thickness (MTH) ratio and between aLM or thigh MTH ratio and zigzag walking performance. Eighty-one middle-aged and older adults (41 men and 40 women) aged 50 to 74 years volunteered for the study. Approximately two thirds of the subjects (34 men and 17 women) carried out regular sports activity (at least >2 times a week) including running and cycling exercise. MTH was measured using B-mode ultrasound at two sites on the anterior (A50) and posterior (P50) aspects of the mid-thigh. A50:P50 MTH ratio was calculated to evaluate site-specific thigh muscle loss. aLM and percent body fat were also determined using a DXA. Men had lower body fat and higher aLM than women. Anterior and posterior thigh MTH as well as A50:P50 MTH ratio was higher in men than in women. Zigzag walking time was faster in men than in women. Anterior and posterior thigh MTH was positively ($p < 0.001$) correlated to aLM and aLM index in men and women. However, A50:P50 MTH ratio was not significantly correlated with aLM

and aLM index in both sexes. There was no significant correlation between aLM index and zigzag walking time in men and women. A50:P50 MTH ratio was inversely ($p < 0.05$) correlated to zigzag walking time in both men and women. Our results suggest that thigh MTH ratio is independent of age-related muscle mass loss detected by aLM.

Keywords Aging · Thigh muscle thickness · Appendicular lean mass · DXA · B-mode ultrasound

Introduction

Since Rosenberg coined the term *sarcopenia*, many researchers have been interested in the age-related loss of skeletal muscle mass (SM) and muscular function as well as how it is influenced by physical disability and metabolic disorders (Rosenberg 1997; Janssen 2010). Now, it is known that the prevalence of age-related severe muscle loss dramatically increases after the age of 60 (Baumgartner et al. 1998; Abe et al. 2014) and that severe muscle loss leads to increased risk of physical disability (Baumgartner et al. 1998), cognitive decline (Burns et al. 2010), metabolic disorders (Park et al. 2009; Abe et al. 2012a), and mortality (Bunout et al. 2011). Dual-energy X-ray absorptiometry (DXA) has been the most widely preferred technique for the assessment of SM in older adults. The DXA-determined appendicular lean tissue mass (aLM) as a major criterion of diagnosis for age-related SM loss has been previously reported in many studies (Baumgartner et al. 1998;

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Cruz-Jentoft et al. 2010). However, this technique is costly and exposes participants to radiation, and access to the equipment is limited. In addition, DXA is limited to regional estimation of SM and cannot determine the anterior and posterior SM in the limb. Because the ability to complete normal daily physical activities is highly dependent on different muscle groups located in the anterior and posterior aspects of the limbs, the ability of DXA to detect muscle loss leading to physical disability may be limited.

Recently, our laboratory (Ogawa et al. 2012a; Abe et al. 2011) and others (Maden-Wilkinson et al. 2013) have reported that age-related loss of SM is observed as a site-specific loss of SM, especially for the quadriceps muscle (Abe et al. 2013b; 2014). A follow-up observation of approximately 9 years also observed a significant reduction in anterior mid-thigh muscle cross-sectional area (CSA), while posterior muscle CSA did not change (Frontera et al. 2008). In our previous study, the prevalence of site-specific thigh muscle loss, as well as ultrasound-estimated whole body SM loss, was determined from a relatively large sample of Japanese men and women. With this cohort, we observed a higher percentage of age-related site-specific thigh muscle loss compared to whole body SM loss in each age category sampled (Abe et al. 2014). However, the association between site-specific thigh muscle loss and whole body SM loss was not directly investigated (Abe et al. 2014). Furthermore, our previous study used muscle thickness (MTH) for estimating whole body SM, whereas DXA-estimated aLM may be more appropriate as it is currently considered the gold standard and most widely used in evaluating sarcopenia status. If MTH decreases in both the anterior and posterior compartments of the thigh, the MTH ratio may not change significantly, but whole body SM estimated via DXA may be decreased. Conversely, if there are decreases in only anterior thigh MTH, and either no change or slightly increases in muscles of the posterior compartment, the anterior/posterior thigh MTH ratio would be decreased while DXA-estimated aLM may not be a sensitive enough measure to detect such a small but important change. Therefore, it is not clear whether site-specific thigh muscle loss is an independent phenomenon for age-related loss of skeletal muscle mass.

Age-related site-specific muscle loss of the quadriceps is inversely associated with zigzag walking performance in middle-aged and older women (Abe et al. 2012b) and is positively correlated to one-leg standing

balance in active healthy women before adjusting for physical activity level (Abe et al. 2013a). Thus, the site-specific thigh muscle loss may lead to increased functional impairment during specific task performance. Both SM loss detected by whole body SM methods (e.g., aLM via DXA) as well as site-specific muscle loss of the thigh is strongly correlated with age (Baumgartner et al. 1998; Mitchell et al. 2012; Abe et al. 2013b; 2014). However, it is unknown whether or not site-specific thigh sarcopenia is independent of age-related muscle loss of the whole body.

The purpose of the present study was to examine the relationships between DXA-determined aLM and ultrasound-measured thigh muscle thickness (MTH) ratio and between aLM or thigh MTH ratio and zigzag walking performance. A secondary purpose was to determine if age-related site-specific thigh muscle loss and aLM loss were observed equally between age groups.

Methods

Participants

Eighty-one middle-aged and older adults (41 men and 40 women) aged 50 to 74 years volunteered for the study. The subjects were recruited from the university campus and surrounding area. Prior to obtaining informed consent, a written description of the purpose of the study and its safety was distributed to potential subjects. All subjects were free of overt chronic disease (e.g., neuromuscular, diabetes, angina, myocardial infarction, cancer, stroke, etc.) as assessed by self-report. Approximately two thirds of the subjects (34 men and 17 women) reported participation in regular sports activity (at least twice a week) including running and cycling exercise. This study was conducted according to the Declaration of Helsinki and was approved by the university's Institutional Review Board.

Ultrasound-measured thigh muscle thickness ratio

Muscle thickness (MTH) was measured using B-mode ultrasound (Aloka SSD-500, Tokyo, Japan) at two sites on the anterior and posterior aspects of the thigh as previously described (Abe et al. 1994). Because MTH for the evaluation of site-specific muscle loss was previously measured in a standing position (Abe et al. 2013b; 2014), the measurements were taken while the

subjects stood with their knees extended and relaxed. A 5-MHz scanning head was placed on the measurement site without depressing the dermal surface. The subcutaneous adipose tissue-muscle interface and the muscle-bone interface were identified from the ultrasonic image, and the distance between two interfaces was recorded as MTH. Test-retest reliability of MTH measurements using intraclass correlation coefficient ($ICC_{3,1}$), standard error of measurement (SEM), and mean difference was previously determined from 15 middle-aged subjects for anterior (0.98, 0.07, and 0.01 cm) and posterior (0.95, 0.10, and 0.04 cm) thigh (Abe et al. 2013b). To evaluate site-specific muscle loss of the thigh, the ratio of anterior to posterior thigh MTH (A50:P50 MTH) was calculated.

DXA-determined appendicular lean tissue mass

Subjects underwent dual energy X-ray absorptiometry scans (DXA) (Discovery A, Hologic Inc., Bedford, MA, USA) to determine percent body fat (%fat) and appendicular lean tissue mass (aLM). aLM index was calculated as aLM divided by height in meters squared (kg/m^2). Quality assurance testing and calibration was performed the morning of data collection days to ensure that the DXA was operating properly. Subjects were asked to refrain from eating for at least 4 h prior to scans. Test-retest reliability using $ICC_{3,1}$, SEM, and minimal difference to be considered real were previously determined from 17 subjects scanned twice for aLM (0.99, 0.21, and 0.58 kg) and %fat (0.99, 0.49, and 0.95 %).

Zigzag walking performance

Zigzag walking time was measured using a 10-m walkway. Four cones were placed 2-m apart on the floor between the start and finish points (Abe et al. 2012b). The cones were set to alternate from side to side with a distance of 0.5 m from a line drawn through the start and finish points. The test started with the subject standing on the start point. The subject then walked around the outside of each cone and walked through the finish point. Subjects were instructed to complete the walking course as quickly as possible. The elapsed time from the start to finish points was recorded. Times were calculated using a digital stopwatch (ADMD-

001; Seiko, Tokyo, Japan). The best time of two trials was used for zigzag walking time. Test-retest reliability of zigzag walking tests using $ICC_{3,1}$, SEM, and minimal difference was determined from 21 older adults (11 men and 10 women) for the zigzag walking test (0.96, 0.21, and 0.59 s).

Statistical analysis

Results are expressed as means and standard deviations (SD). Differences in the dependent variables between men and women were tested for significance using unpaired Student's *t* tests. The differences between age groups (ages 50–57, ages 58–65, and age >65) for selected dependent variables were tested for significance by one-way analysis of variance. If a significant *F* test was observed, pairwise comparisons were run using Tukey's multiple comparison procedure. If variances were unequal, Dunnett's C procedure was performed. Pearson's product correlation coefficients were performed to determine the relationship between DXA-determined aLM and ultrasound-measured MTH ratio as well as between zigzag walking performance and aLM index or MTH ratio. Statistical significance was set at $p \leq 0.05$.

Results

Age and BMI were similar between sexes, although men were taller and heavier than women. Men had lower percent body fat and higher aLM than women. Anterior (A50) and posterior (P50) thigh MTH as well as A50:P50 MTH ratio was higher in men than in women. Zigzag walking time was faster in men than in women (Table 1). After classifying men and women by age (Table 2), BMI was not significantly different between age groups for either sex. aLM and aLM index were also similar among the age groups in both men and women. However, the A50:P50 thigh MTH ratio was significantly lower in the oldest group (age >65) than in the younger group (ages 50–57 or ages 58–65).

Anterior and posterior thigh MTH was positively ($p < 0.001$) correlated to aLM and aLM index in both men and women. In contrast, A50:P50 MTH ratio was not significantly correlated with aLM and aLM index in both sexes (Table 3). There was no significant

Table 1 DXA-determined appendicular lean mass (aLM) and ultrasound-measured thigh muscle thickness (MTH) in middle-aged and older men and women

	Men	Women	<i>p</i> value
<i>N</i>	41	40	
Age (yr)	61 (6)	59 (7)	0.134
Height (m)	1.77 (0.07)	1.63 (0.05)	<0.001
Body mass (kg)	82.7 (13.6)	69.9 (18.2)	<0.001
Body mass index (kg/m ²)	26.1 (3.5)	26.3 (6.3)	0.846
Body fat (%)	19.3 (5.0)	31.8 (8.1)	<0.001
Legs lean mass (kg)	20.9 (2.9)	14.4 (2.6)	<0.001
Arms lean mass (kg)	7.5 (1.5)	4.3 (0.8)	<0.001
aLM (kg)	28.3 (4.3)	18.6 (3.4)	<0.001
aLM index (kg/m ²)	8.9 (1.0)	7.0 (1.1)	<0.001
Thigh MTH (cm)			
Anterior 50 % (A50)	5.38 (0.54)	4.41 (0.62)	<0.001
Posterior 50 % (P50)	6.50 (0.53)	5.93 (0.70)	<0.001
A50:P50 MTH ratio	0.83 (0.10)	0.75 (0.11)	<0.001
Zigzag walk time (s)	5.4 (0.8)	6.1 (1.0)	<0.001

correlation between aLM index and zigzag walking time in men and women. However, the A50:P50 MTH ratio was inversely ($p<0.05$) correlated to zigzag walking time in both sexes (Table 4).

Discussion

The main findings of the present study were that (1) although DXA-measured aLM was similar among age groups, A50:P50 thigh MTH ratio was lower in oldest group than in younger group, (2) thigh MTH was correlated to aLM and aLM index in middle-aged and older men and women, while (3) thigh MTH ratio did not correlate to aLM or aLM index in both sexes, and (4) zigzag walking performance was associated with thigh MTH ratio, but not aLM index in both men and women.

Previous studies have reported that anterior thigh MTH is strongly correlated with anatomical mid-thigh muscle CSA ($r=0.91$, $n=52$) (Abe et al. 1997) and muscle volume ($r=0.92$, $n=23$) (Miyatani et al. 2002) in the quadriceps. Although correlation coefficients are relatively weak, anterior and posterior thigh MTH is also correlated with whole body fat-free mass (FFM) in men ($r=0.67$ and $r=0.54$, respectively; $n=62$) and women ($r=0.55$ and $r=0.53$, respectively; $n=55$) (Abe et al. 1994). A recent study (Takai et al. 2013)

Table 2 Comparison among age groups (ages 50–57, ages 58–65, and age >65) in appendicular lean mass index and thigh muscle thickness ratio

	Ages 50–57	Ages 58–65	Age >65
Men			
<i>N</i>	15	14	12
Age (yr)	54 (2)	61 (2) ^a	68 (3) ^{a, b}
Height (m)	1.80 (0.05)	1.76 (0.07)	1.78 (0.08)
Body mass (kg)	85.1 (8.6)	83.8 (17.4)	78.5 (13.9)
Body mass index (kg/m ²)	26.3 (2.7)	27.1 (4.4)	24.7 (2.9)
aLM (kg)	29.4 (3.4)	28.1 (5.1)	27.4 (4.3)
aLM index (kg/m ²)	9.0 (0.9)	9.1 (1.3)	8.6 (0.9)
Thigh MTH (cm)			
Anterior 50 % (A50)	5.36 (0.44)	5.56 (0.57)	5.18 (0.60)
Posterior 50 % (P50)	6.59 (0.55)	6.35 (0.53)	6.58 (0.49)
A50:P50 MTH ratio	0.82 (0.10)	0.88 (0.12)	0.78 (0.07) ^b
Women			
<i>N</i>	20	13	7
Age (yr)	53 (2)	61 (2) ^a	69 (5) ^{a, b}
Height (m)	1.64 (0.05)	1.62 (0.06)	1.62 (0.06)
Body mass (kg)	68.9 (18.0)	68.7 (21.9)	75.4 (10.7)
Body mass index (kg/m ²)	25.5 (5.5)	26.1 (7.7)	29.0 (5.9)
aLM (kg)	19.0 (3.5)	18.0 (3.9)	18.7 (1.7)
aLM index (kg/m ²)	7.1 (1.1)	6.8 (1.2)	7.2 (1.0)
Thigh MTH (cm)			
Anterior 50 % (A50)	4.68 (0.51)	4.16 (0.63) ^a	4.09 (0.61) ^a
Posterior 50 % (P50)	5.93 (0.72)	5.86 (0.76)	6.07 (0.59)
A50:P50 MTH ratio	0.79 (0.09)	0.72 (0.11)	0.68 (0.12) ^a

aLM appendicular lean mass, MTH muscle thickness

Significance was set at $p<0.05$

^aSignificant group difference for ages 50–57

^bSignificant group difference for ages 58–65

investigated the relationships between ultrasound-measured MTH and DXA-based FFM in older adults

Table 3 Correlation coefficients between appendicular lean mass (aLM) and thigh muscle thickness (MTH) ratio in middle-aged and older men and women

	Men (<i>n</i> =41)		Women (<i>n</i> =40)	
	aLM	aLM index	aLM	aLM index
Anterior 50 % MTH	0.591**	0.518**	0.550**	0.631**
Posterior 50 % MTH	0.543**	0.530**	0.693**	0.679**
A50:P50 MTH ratio	0.113	0.055	−0.047	0.029

** $p<0.001$

Table 4 Correlation coefficients between zigzag walking time and appendicular lean mass (aLM) index or thigh muscle thickness (A50:P50 MTH) ratio in middle-aged and older men and women

	Zigzag walking time	
	Men (<i>n</i> =41)	Women (<i>n</i> =40)
aLM index	−0.163	0.143
A50:P50 MTH ratio	−0.367*	−0.305*

*p<0.05

and found that there were strong correlations between limb MTH and DXA-based FFM. In support of these data, our findings in the present study showed significant correlations between anterior and posterior thigh MTH and absolute and relative aLM in middle-aged and older men and women.

In the present study, thigh MTH ratio as an index of site-specific thigh muscle loss did not correlate to DXA-determined aLM or aLM index in middle-aged and older adults. Furthermore, the thigh MTH ratio was lower in oldest men and women than that of corresponding younger group. These results suggest that the age-related change in thigh MTH ratio is an independent phenomenon for age-related muscle mass loss detected by aLM. The reasons for the discrepancy between age-related declines in aLM index and thigh MTH ratio are unknown. Considering the age-related changes in MTH for each segment, main etiologic factors may differ between age-related whole body and site-specific thigh muscle loss (Abe et al. 2013b). The major reason for decreasing anterior to posterior thigh MTH would be due to lower anterior thigh MTH because posterior thigh MTH was not significantly decreased among age groups under the age of 60 in men and under the age of 70 in women (Abe et al. 2013b, 2014). In this study, a similar phenomenon was observed in middle-aged and older men and women. A study reported that the ratio of anterior to posterior thigh MTH was inversely correlated to duration of vigorous physical activity in middle-aged and older women (Ogawa et al. 2012b). In addition, we recently examined whether chronic vigorous exercise (master athletes) prevents the site-specific thigh muscle loss experienced in sedentary adults and found that the thigh MTH ratio was similar between master athletes (both cyclists or swimmers) and young active men (unpublished observation). Interestingly, this is supported by research that has observed site-specific losses in motor units with advancing age (Aagaard et al. 2010).

A recent study demonstrated that lifelong running can provide a localized maintenance of motor units in exercising muscle, but not systemically (Power et al. 2012). Thus, changes in the intensity and/or duration of weight-bearing physical activity may be a main factor for decreasing anterior thigh MTH with age. On the other hand, age-related muscle loss detected by aLM may be associated with a combination of age-related declines in physical activity and systemic etiologic factors (i.e., circulating anabolic hormones and cytokines, chronic low grade inflammation, insulin resistance, and nutrition) for age-related muscle loss (Ryall et al. 2008; Beyer et al. 2012; Mitchell et al. 2012).

Our findings showed that zigzag walking performance was inversely associated with thigh MTH ratio, but not aLM index in middle-aged and older men and women. Consistent with our results in the present study, a study of Japanese middle-aged and older women reported that the ratio of anterior to posterior thigh MTH is inversely correlated with zigzag walking performance (Abe et al. 2012b). Furthermore, knee extension strength index (torque divided by body mass) is also inversely associated with zigzag walking performance in both older men and women (unpublished observation). The ability to make quick, lateral movements is a crucial factor during zigzag walking. A recent study (Inaba et al. 2013) reported the biomechanical factors contributing to quickness in lateral movements and found that extension torques of the hip, knee, and ankle joints contribute substantially to the changes in side-step distances, while hip abduction torque accelerates the center of mass laterally in the earlier phase of the movement. Thus, it is possible that the site-specific loss of anterior thigh muscle as well as reduced knee extensor (quadriceps) muscle strength may play a significant role in zigzag walking performance in older adults.

In conclusion, our results demonstrate that the ratio of anterior to posterior thigh MTH did not correlate to aLM and aLM index in middle-aged and older men and women. Thus, thigh MTH ratio may be independent of age-related whole body muscle mass loss detected by aLM. In contrast, anterior to posterior thigh MTH ratio was inversely correlated with zigzag walking performance in men and women. These results suggest that measurement of thigh MTH ratio using ultrasound and zigzag walking performance may be possible criteria for assessing site-specific thigh sarcopenia in middle-aged and older men and women.

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