Review

Age-related muscle loss of the anterior and posterior thigh assessed by means of MRI/CT and ultrasound

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Site-specific thigh muscle loss may be independent of age-related whole body muscle mass loss detected by using dual-energy X-ray absorpotiometry (DXA). Site-specific thigh muscle loss can be assessed by two major methods, i.e., magnetic resonance imaging (MRI) or computed tomography (CT) and ultrasound.

Objectives: The purpose of this review is to discuss whether the magnitude of age-related declines in anterior and posterior thigh muscle size differs among previous studies with different methods for assessing muscle size. Age-related changes in absolute and relative knee extension (KE) and flexion (KF) strength and possible reasons for the age-related site-specific thigh muscle loss are discussed.

Design and Method: Non-systematic review.

Results: The results of MRI/CT and ultrasound studies both suggest that age-related thigh muscle loss differs between the anterior compartment (i.e., quadriceps) and posterior compartment (i.e., hamstring) with much larger losses occurring in the anterior thigh compared with the posterior thigh. Previous studies investigating the age-related changes in absolute KE and KF strength are not as consistent. However, age-related change in muscle quality (strength per unit of muscle size) may not differ between KE and KF in an individual, although the values may differ among individuals. A major reason for the site-specific thigh muscle loss with advancing age may be the intensity and duration of daily physical activity which may secondarily influence other factors such as motoneuron loss and muscle protein metabolism.

Conclusions: A ratio of anterior to posterior MT determined by ultrasound may correspond well to a multidimensional variable (CSA or MV) of the quadriceps to other thigh muscles (including both hamstring and adductor muscles) ratio, but not to the quadriceps to hamstring ratio. If there are similar changes in muscle quality with advancing age between knee extensor and flexor muscles, the anterior to posterior MT ratio may be involved in a ratio of muscle force of knee extensor and flexor muscles.

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Key words: sarcopenia ■ MRI ■ B-mode ultrasound ■ muscle thickness ■ muscle cross-sectional area

INTRODUCTION

Age is associated with a progressive loss of skeletal muscle mass, muscular strength and physical function.[1-3] The term sarcopenia was originally defined as a decline in only skeletal muscle mass with advancing age[4]; however, it has now generally become a term to define both a loss of muscle mass and physical function[5]. Many countries including Japan are rapidly aging and approximately 10% of Japanese aged 65 years or older were classified as having sarcopenia.[6] Further, sarcopenia is problematic given that it is closely associated with an increased risk of physical disability[7], cognitive decline[8], metabolic disorders[9], and mortality[10].

Interestingly, one longitudinal study demonstrated that there is a significant reduction in mid-thigh anterior (quadriceps) muscle cross-sectional area (CSA), while the posterior (hamstring) muscle CSA did not change.[11] Similarly, isokinetic knee extension strength decreased significantly at follow-up, while no significant change was observed in isokinetic knee flexion strength.[11] In line with the results of that study, a limited number of studies have reported that an age-related site-specific thigh muscle loss is observed not only in Japanese men and women[12,13] but also in German and American men and women[14,15]. This site-specific anterior thigh muscle loss is associated with decreasing zigzag walking performance, but not straight walking performance in middle-aged and older men and women.[16,17] However, it is unknown whether the magnitude of age-related declines in anterior and posterior thigh muscle size differs among the previous studies with different methods for assessing muscle size. Ultrasound determined muscle thickness is a single dimensional variable that can include intermuscular adipose tissue while magnetic resonance imaging (MRI) or computed tomography (CT) measured muscle CSA/muscle volume (MV) is a multidimensional variable that can exclude intermuscular adipose tissue.[18,19] Thus, knowledge of the difference in magnitude of age-related declines in thigh muscle size assessed by single and multidimensional

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variables may be useful for clinical application in the area of gerontology and rehabilitation.

In this review, we summarize previously published articles demonstrating the age-related loss of the anterior and posterior thigh muscle compared between two major methods for assessing muscle size (MRI/CT and ultrasound). Absolute and relative knee extension and flexion strength are also summarized. Finally, we discuss possible mechanisms for the age-related site-specific muscle loss of the thigh.

AGE-RELATED CHANGES IN MUSCLE CSA/MV IN THE ANTERIOR AND POSTERIOR THIGH

To our knowledge, only five studies[20-24] are published for demonstrating the age-related changes in anterior and posterior thigh muscle CSA and/or MV measured using MRI and CT scans (Table 1). For example, Overend and colleagues[20] investigated the differences in muscle CSA and strength of knee extensor and flexor between young and older men. The study used a CT scan and separated muscle and non-muscle tissue (fat plus loose connective tissue) of the quadriceps and hamstring compartments. They found that the quadriceps muscle CSA was significantly smaller in older men than in young men, however, the hamstring muscle CSA did not significantly differ between two groups. Macaluso and colleagues[22] examined the differences between young and older women in contractile MV and strength of the knee extensors and flexors. The authors found that MV was significantly lower in the older than in the young women both in the knee extensors and flexors. Recently, Ogawa and colleagues[23] investigated the component characteristics of thigh MV (quadriceps, hamstring and adductors) and compared the average muscle CSA (MV divided by muscle length) of each thigh muscle in young and older men. Compared with the young men, mid-thigh quadriceps muscle CSA was 24% lower in the older men. However, mid-thigh hamstring muscle CSA was similar, with the difference between the two groups being only 7%. Average muscle CSA in the quadriceps was also 16% lower in the older than in the young men, while hamstring and adductors average muscle CSA was almost the same in both groups.

Maden-Wilkinson and colleagues[24] examined the age and sex differences in MV of the quadriceps and other thigh muscles (knee flexor, hip abductors and adductors). They reported that the quadriceps as well as other thigh MV was significantly lower in the older than in the young men and women. When expressed as percentage of the young values, the differences were 68% for older men and 72% for older women in the quadriceps and 78% for older men and 86% for older women in the other thigh muscles. Calculated percent difference between young and old groups in each study vary a great deal in the hamstring compared to the quadriceps; however, all the studies reported a high percent difference between the two groups for the quadriceps.

Table 1. Age-related changes in the quadriceps and hamstring muscle cross-sectional area (CSA) and muscle volume (MV) measured using magnetic resonance imaging or computed tomography and in anterior and posterior thigh muscle thickness (MT) measured using ultrasound

Authors	Year	# of subject Young/Old	Sex	Mean age (yr) Young/Old	Method	Variable & unit	Quadriceps (anterior thigh)			Hamstring (posterior thigh)		
							Young	Old	%Diff	Young	Old	%Diff
MRI and CT study												
Overend et al.	1992a	13/12	M	24.5/70.7	CT	CSA, cm^2	84.7	65.7*	22	38.5	33.1	14
Overend et al.	1992b	13/11	M	24.5/71.0	CT	CSA, cm^2	84.7	63.9*	25	38.5	31.6*	18
Macaluso et al.[†]	2002	10/10	W	22.8/69.5	MRI	MV, cm^3	1230	860*	30	445	360*	19
Ogawa et al.	2012	15/13	M	24.3/68.6	MRI	CSA, cm^2	72	55*	24	26	24	7
						MV, cm^3	1716	1382*	20	704	641	9
Maden-Wilkinson et al.[‡]	2013	20/25	M	22.4/72.3	MRI	MV, cm^3	2237	1523*	32	2309	1805*	22
		18/28	W	22.1/72.0			1374	991*	28	1537	1321*	14
Ultrasound study												
Miyatani et al.	2003	61/62	M	24.2/72.6	Ultra	MT, cm	5.46	4.06*	26	6.52	6.14*	6
Abe et al.	2014a	103/63	M	24/73	Ultra	MT, cm	5.31	3.83*	28	5.90	5.47*	7
		124/76	W	23/76			4.68	3.28*	30	5.19	5.02	3
Abe et al.	2014b	119/79	M	36/74	Ultra	MT, cm	4.95	3.37*	32	5.94	5.44*	8
		88/87	W	36/73			4.25	3.17*	25	5.60	5.23*	7

M, men; W, women; CT, computed tomography; MRI, magnetic resonance imaging; Ultra, B-mode ultrasound

* Significant group difference between young and old

[†] The study measured muscle volume of the knee extensor and flexor

[‡] The study measured muscle volume of the quadriceps and other thigh muscles

Percent difference (%Diff) was calculated as follows: (Young − Old) ÷ Young × 100

AGE-RELATED CHANGES IN MUSCLE THICKNESS IN THE ANTERIOR AND POSTERIOR THIGH

Age-related changes in muscle thickness (MT) of the anterior and posterior aspect of the thigh have been observed in three ultrasound studies[13,25,26] (Table 1). For example, Miyatani and colleagues[25] investigated the age-related changes in MT at nine sites of the body in men aged 20 to 79 years. Decreases in anterior thigh MT could be observed for the 50-59 year old group and for the posterior thigh in the 70-79 year old group when compared to the younger age groups (age 20-29 and age 30-39 years). When the 70-79 year old group was expressed as a percentage of the young values (20-29 years), the differences were lower at the anterior thigh (74.4%) than at the posterior thigh (94.2%). Abe and colleagues[26] also investigated the age-related changes in MT at nine sites in both men and women and found a significant decline in anterior thigh MT for age 40-49 and posterior thigh MT for age 60-69 when compared to the younger age group (age 20-29) in men. In women, posterior thigh MT did not show a significant decline with age, while anterior thigh MT gradually decreased with age.

RELATIONSHIP BETWEEN AGE-RELATED MUSCLE LOSS IN THE ANTERIOR AND POSTERIOR THIGH

To compare MRI/CT studies with ultrasound studies, we calculated the percent difference between young and old groups (% Diff) in each study. Figure 1 illustrates the relationship between the age-related decline (% Diff) in anterior and posterior thigh muscle size. For all studies, the plots are located directly below the line of identity. These results suggest that the age-related muscle loss of the thigh differs between the anterior compartment (i.e., quadriceps) and posterior compartment (i.e., hamstring) with much larger losses occurring in the anterior thigh compared with the posterior thigh. In addition, there seems to be a difference between the plots of ultrasound studies and the plots of MRI/CT studies. Although speculative, this difference may be caused by age-related changes in muscle shape of the thigh (how the shape of a transverse section diverges from an ellipses) and/or intermuscular adipose tissue.

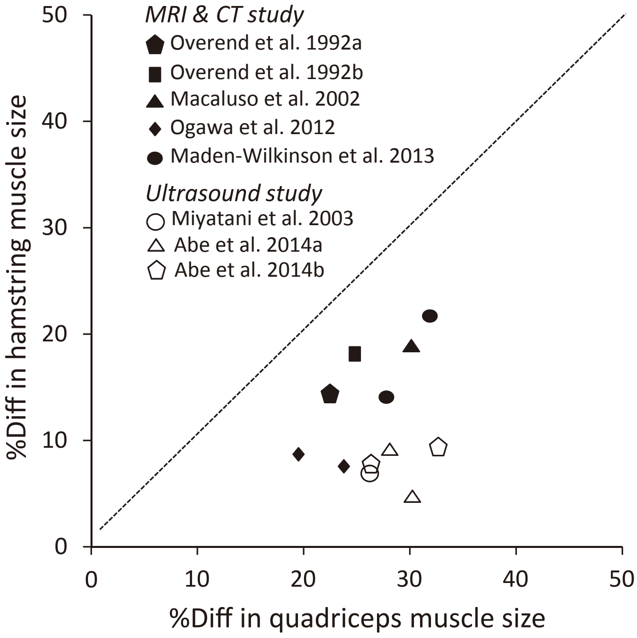

Figure 1. Relationship between age-related decline (percent difference between young and old groups in each study) in anterior and posterior thigh muscle size.

INDEXES FOR EVALUATING AGE-RELATED SITE-SPECIFIC MUSCLE LOSS OF THE THIGH

In previous studies, site-specific thigh muscle loss is often evaluated using the ratio of anterior to posterior thigh MT.[13,15,26] However, the difference between assessing single and multidimensional variables is not well known. To compare MRI/CT studies with ultrasound studies, we calculated the ratio of quadriceps to hamstring muscle CSA or MV for MRI/CT studies and the ratio of anterior to posterior MT for ultrasound studies (Table 2). The quadriceps/hamstring CSA or MV ratio ranged from 2.20 to 2.77 (average 2.47) for young and from 1.98 to 2.39 (average 2.17) for old adults. Interestingly, one study measured MV of the quadriceps and other thigh muscles include hamstring.[24] The ratio of quadriceps to other thigh muscles was, respectively, 0.97 and 0.84 in young and old men and 0.89 and 0.75 in young and old

Table 2. Quadriceps/hamstring muscle ratio in young and old groups as well as young/old ratio of quadriceps and hamstring muscle

Authors	Year	Method	Variable & Unit	Quadriceps/ Hamstring ratio (Anterior/ Posterior ratio)	
				Young	Old
MRI and CT study					
Overend et al.	1992a	CT	CSA, cm^2	2.20	1.98
Overend et al.	1992b	CT	CSA, cm^2	2.20	2.02
Macaluso et al.[†]	2002	MRI	MV, cm^3	2.76	2.39
Ogawa et al.	2012	MRI	CSA, cm^2	2.77	2.29
			MV, cm^3	2.44	2.16
Maden-Wilkinson et al.[‡]	2013	MRI	MV, cm^3	0.97	0.84
				0.89	0.75
Ultrasound study					
Miyatani et al.	2003	Ultra	MT, cm	0.84	0.66
Abe et al.	2014a	Ultra	MT, cm	0.90	0.70
				0.90	0.65
Abe et al.	2014b	Ultra	MT, cm	0.83	0.62
				0.76	0.61

CT, computed tomography; MRI, magnetic resonance imaging; Ultra, B-mode ultrasound; CSA, cross-sectional area; MV, muscle volume; MT, muscle thickness

[†] The study measured muscle volume of the knee extensor and flexor

[‡] The study measured muscle volume of the quadriceps and other thigh muscles

women. These values are similar to the values of ultrasound studies[13,25,26] where anterior to posterior thigh MT ratio ranged from 0.76 to 0.90 in young men and women and from 0.61 to 0.70 in old men and women. The ratios derived from ultrasound (anterior/posterior ratio) and MRI/CT (quadriceps/hamstring ratio) are different. The reason for this is due to the ultrasound posterior measurement including both hamstrings and adductor muscles. Thus, a ratio of anterior to posterior MT determined by ultrasound may correspond well to a multidimensional variable of the quadriceps to other thigh muscles (including both hamstring and adductor muscles) ratio, but not the quadriceps to hamstring CSA or MV ratio.

AGE-RELATED CHANGES IN ABSOLUTE AND RELATIVE KNEE EXTENSION AND FLEXION STRENGTH

Three of the five MRI/CT studies[20,22,23] measured age-related changes in absolute (Table 3) and relative (strength per unit of muscle CSA or MV) (Table 4) knee extension and flexion strength in men and women. For example, Overend and colleagues[20] reported that there were no differences in the relative strength of knee extensor and flexor between young and older men for the isometric testing, although absolute isometric strength was lower in the older group. However, the young men had higher relative strength obtained during isokinetic (at 120°/s) contraction in both extension and flexion. Ogawa and colleagues[23] also reported that isometric relative strength of knee extensor was similar between young and older men, although knee flexor isometric relative strength was lower in the older than in the young men. On the other hand, Macaluso and colleagues[22] found that compared to young women, isometric relative strength was lower in older women both in the knee extensors and flexors. Surprisingly, there is not full agreement on the results from the previous studies. However, it is expected that the differences in relative strength between young and old groups are similar between knee extensors and flexors in each study. These results suggest that muscle quality (strength per unit of muscle CSA or MV) may not differ between knee extensors and flexors in an individual, even if these values differ among individuals, especially for older adults.

POSSIBLE REASONS FOR AGE-RELATED SITE-SPECIFIC MUSCLE LOSS OF THE THIGH

The reasons for the site-specific thigh muscle loss with advancing age are not well known. It is well known that the reduction of muscle mass with aging is mainly attributed to a decline in the size of the fast-twitch (type II) muscle fibers.[27] Insulin-resistant men have greater muscle mass loss with age when compared to insulin-sensitive men[28], and there may be differential responses in different muscle groups. Fast-twitch fibers have been shown to have higher levels of insulin resistance.[29] However, autopsy studies have revealed that the hamstrings have a higher percentage of fast-twitch fibers compared with the quadriceps in both young[30] and older[31] adults. Thus, this discrepancy may not directly explain the age-related site-specific thigh muscle loss, although secondary effects of insulin resistance may be a contributing factor.

One possible factor may be the intensity and duration of physical activity completed over a lifetime. Exercise and sport/fitness activities make up a greater proportion of total moderate and vigorous physical activity time in young adults, whereas domestic activities make up a greater proportion of total moderate and vigorous physical activity time in older adults.[32] A limited number of studies reported that muscle activation patterns during ambulation differed among lower extremity muscles.[33] The muscle activation levels while walking on a downward slope and jogging are greater in the posterior thigh muscle compared with those in the anterior thigh.[33] A study examining muscle activity in the quadriceps during 24 hours of daily activity using electromyography (EMG) found that the quadriceps was active for only a short amount of time (1-3 hr) and at relatively low intensities (3-11% of maximal voluntary isometric contraction), although only one muscle was measured.[34] Compared to the hamstring, lower EMG activity is observed in the quadriceps during slow walking (50 m/min), although EMG activity is similar between the two muscles during free (85 m/min) and fast (100 m/min) walking.[35] The difference in this muscle activation may correspond to changes (stimulations) in muscle protein metabolism in the quadriceps and hamstring muscle. A study reported that the ratio of anterior to posterior thigh MT was positively correlated with duration of vigorous physical activity in middle-aged and older women.[36]

Table 3. Age-related changes in knee extension and flexion strength

Authors	Year	Mode	Sex	Knee extension (Nm)			Knee flexion (Nm)		
				Young	Old	%Diff	Young	Old	%Diff
Overend et al.	1992a	Isometric	Men	262	199*	24	144	109*	24
		Isok 120		204	138*	32	103	70*	32
Macaluso et al.	2002	Isometric	Women	138	79*	43	65	35*	47
Ogawa et al.	2012	Isometric	Men	246	167*	32	90	73*	19

Isok 120, isokinetic contraction at 120°/sec
* Significant group difference between young and old
Percent difference (%Diff) was calculated as follows: (Young − Old) ÷ Young × 100

Table 4. Age-related changes in relative strength (strength per unit of muscle cross-sectional area) of knee extensor and flexor

Authors	Year	Mode	Unit	Knee extension			Knee flexion		
				Young	Old	%Diff	Young	Old	%Diff
Overend et al.	1992a	Isometric	N/cm^2	9.6	9.8	-2	11.7	10.6	9
		Isok 120		7.5	6.7*	10	8.4	6.8*	19
Macaluso et al.	2002	Isometric	N/cm^2	11.1	9.3*	16	14.2	9.9*	30
Ogawa et al.	2012	Isometric	Nm/cm^2	5.4	4.6	15	4.2	3.4*	19

Isok 120, isokinetic contraction at 120°/sec
* Significant group difference between young and old
Percent difference (%Diff) was calculated as follows: (Young − Old) ÷ Young × 100

In addition, recent studies[37,38] examined whether chronic vigorous exercise (master athletes) prevents site-specific thigh muscle loss experienced in sedentary adults and found that anterior/posterior MT ratio was similar between master athletes and young moderate active men. This evidence is supported by research that has observed site-specific losses in motor units with increasing age.[39] Furthermore, a study demonstrated that the lifelong running can provide a localized maintenance of motor units in exercising muscle but not systemically.[40]

Another player in site-specific muscle loss may be changes in anabolic hormones and cytokine milieu[39] outside of the normal physiologic range. It is well known that there are marked changes in endocrine status associated with aging[41] and these changes particularly at the local level, may create a muscular microenvironment less capable of mounting an anabolic response. Hormone receptors are upregulated in exercising muscle, but not in nonexercising muscle. Because possible site-specific reductions in muscle activation in the thigh, it may be that there is also a decrease in hormonal binding in the anterior thigh muscle.

CONCLUSIONS

Site-specific thigh muscle loss can be assessed by two major methods, i.e., MRI or CT and ultrasound. A ratio of anterior to posterior MT determined by ultrasound may correspond well to a multidimensional variable (CSA or MV) of the quadriceps to other thigh muscles (including both hamstring and adductor muscles) ratio, but not to the quadriceps to hamstring ratio. If there are similar changes in muscle quality with advancing age between knee extensor and flexor muscles, the anterior to posterior MT ratio may be involved in a ratio of muscle force of knee extensor and flexor muscles.

CONFLICT OF INTEREST STATEMENT

None of the authors had financial or personal conflict of interest with regard to this study.

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