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Published version

MADEN-WILKINSON, Tom, MCPHEE, J S, RITTWEGER, J, JONES, D A and DEGENS, H (2014). Thigh muscle volume in relation to age, sex and femur volume. Age, 36 (1), 383-393.

AGE (2014) 36:383–393
DOI 10.1007/s11357-013-9571-6

Thigh muscle volume in relation to age, sex and femur volume

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Received: 3 December 2012 / Accepted: 16 July 2013 / Published online: 11 August 2013

Abstract Secular changes and intra-individual differences in body shape and size can confound cross-sectional studies of muscle ageing. Normalising muscle mass to height squared is often suggested as a solution for this. We hypothesised that normalisation of muscle volume to femur volume may be a better way of determining the extent of muscle lost with ageing (sarcopenia). Thigh and femur muscle volumes were measured from serial magnetic resonance imaging sections in 20 recreationally active young men (mean age 22.4 years), 25 older men (72.3 years), 18 young women (22.1 years) and 28 older women (72.0 years). There were no age-related differences in femur volume. The relationship between thigh muscle volume and femur volume (R^2=0.76; exponent of 1.12; P<0.01) was stronger than that with height (R^2=0.49; exponent of 3.86; P<0.01) in young participants. For young subjects, the mean muscle/bone ratios were 16.0 and 14.6 for men and women, respectively. For older men and women, the mean ratios were 11.6 and 11.5, respectively. The Z score for the thigh muscle/bone volume ratio relative to young subjects was −2.2±0.7 for older men and −1.4±0.8 for older women. The extent of sarcopenia judged by the muscle/bone ratio was approximately twice that determined when normalising to height squared. These data suggest that the muscle/bone ratio captures the intra-individual loss of muscle mass during ageing, and that the age-related loss of muscle mass may be underestimated when normalised to height squared. The quadriceps seems relatively more affected by ageing than other thigh muscles.

Keywords Muscle-to-bone ratio · Sarcopenia · Ageing

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Introduction

Frailty, decreased mobility and the consequent loss of independence are common features of old age, and there are compelling reasons to understand the underlying causes of these problems. One aspect that has received considerable attention is the age-related loss of muscle bulk and strength, often referred to as "sarcopenia" (Rosenberg 1989) that has been linked to reduced mobility, disability, decreased quality of life and mortality (Hairi et al. 2010; Janssen et al. 2002; Lauretani et al. 2003). It is important, therefore, to be able to accurately document the extent of muscle wasting with age and to identify possible differences in the extent of atrophy between muscle groups that may have different metabolic profiles or be used in particular ways.

It is notable, however, that while the time course and extent of muscle changes over many decades are widely discussed, the evidence is almost entirely based on cross-sectional data for the obvious reasons that it is almost impossible to fund and undertake a longitudinal study lasting 50–70 years. When interpreting cross-sectional data as evidence for longitudinal change, the assumption is often made that old people measured today were of the same stature and physical development in their youth, some 50 to 70 years ago, as the young people of today. However there are well-known secular changes in height, mass and rates of maturation possibly associated with changing diet, levels of physical activity and general health care. In addition, Europeans in their seventh and eighth decade today probably had a much-restricted diet during and immediately after the Second World War (Heijmans et al. 2008; Lumey et al. 2007) as well as higher levels of habitual physical activity than people born in the latter part of the last century (Prentice and Jebb 1995). For these reasons, we cannot be certain that a direct comparison of the muscle mass in today's older population with that of younger adults gives an adequate reflection of the age-related muscle loss. In judging the extent of sarcopenia, either from a single measurement of an individual or in a cross-sectional study, it would be valuable to have a reference measure of body shape or size that could be used to normalise the data.

Mass and height, the two most obvious indicators of body size, have equally obvious disadvantages. Mass has the disadvantage that body fat is a significant component which can vary independently of muscle mass and since the majority of people tend towards higher BMI as they age, using body mass as a standard would overestimate muscle loss with age. Height, or height squared, has been proposed as a way of normalising lean body mass (Baumgartner et al. 1998), but there are two objections to this. First, height squared has the wrong dimensions for normalising a volume, which might be better reflected by height cubed. In addition, height can decrease by as much as 1 cm per year in older age, mainly as a result of increased spinal curvature and vertebral compaction (Moayyeri and Luben 2008; Sorkin et al. 1999), and normalising muscle mass to height will thus underestimate changes in muscle mass.

An alternative rationale starts with the observation that bones and muscles are adapted to each other at young age (Rittweger et al. 2000; Schiessl et al. 1998). Whilst bone mass seems to be lost during ageing from the upper extremities and from the spine, such bone losses seem to be moderate in the lower extremities (Riggs et al. 2004; Wilks et al. 2009). In the shafts, those small changes are conveyed through thinning of the cortex, with the total bone cross section undergoing no or only small changes (Garn et al. 1967; Wilks et al. 2009). Another option would be to use femur length since this does not change after growth plate fusion and the cessation of longitudinal growth, and femur length cubed might be used to provide the correct dimensions for normalising thigh muscle volume and provide a better estimate of changes in muscle mass. However, multiplying femur length by its cross-sectional area to give a nominal femur volume may be more appropriate, as muscle forces on the bone are important factors determining bone cross-sectional area during the critical growth period (Rittweger 2008; Schoenau et al. 2002). Jones et al. (1983) used total bone cross-sectional area as a standard against which to judge muscle development in boys with muscular dystrophy, and growth of bone relative to muscle has been used as a way of gauging bone development in children with underlying skeletal problems (Schoenau et al. 2002).

The aim of the work described here was to develop a more valid indicator of sarcopenia than the commonly used muscle mass per height squared. We hypothesised that femur muscle volume would be a better measure with which to normalise muscle volume than height squared when comparing young and older subjects. To substantiate this argument, it was first necessary to show that muscle volume correlates well with bone volume in young subjects. Having established this, we have assessed muscle and bone size in the thigh of young and older participants by magnetic resonance imaging (MRI).

Methods

Participants and ethical approval

The study was approved by the local ethical committee of Manchester Metropolitan University and conformed to the Declaration of Helsinki. Written informed consent was obtained from each volunteer prior to participating. Young participants (20 men, 18 women) were recruited from amongst the university student population

and older participants (25 men, 28 women) from the local community; participant characteristics are presented in Table 1. These volunteers were recruited in the UK as part of a larger study of ageing (the MYOAGE study, EU-FP7 nr: 223576) (McPhee et al. 2013). All the subjects were healthy and participated in recreational physical activities but none were training to compete in athletic competitions. Older participants were all socially active, and their General Practitioner confirmed there was no medical reason not to take part in the study.

Magnetic resonance imaging

The volume of the quadriceps femoris muscle group was measured with a 0.25 T MRI scanner (G-Scan, Esaote, Genova, Italy) in the dominant leg. The participant was positioned supine in the scanner. A turbo 3D-T1-weighted protocol was used (matrix 256×256, TR 40 ms, TE 16 ms) and multiple 6-mm thick serial transverse sections were obtained along the entire length of the thigh with no inter-slice gap. Computing imaging software (OsiriX medical imaging software, OsiriX, Atlanta, USA) was used to determine the total cross-sectional area of each of the four muscles of the quadriceps group as well as total bone cross-sectional areas. This analysis was completed using manual tracing in MRI slices at distances of 24 mm along the entire length of the quadriceps muscles, from the most distal point of the vastus medialis to the most proximal origin of the rectus femoris. Obvious visible deposits of fat infiltration were subtracted from the cross-sectional areas (Fig. 1).

Muscle volumes were obtained by summation of the cross-sectional areas in each slice (16–19, depending on femur length) multiplied by the distance between slices. Femur length was obtained from total-body DXA scans (Lunar Prodigy Advance, GE Healthcare) by using the computer software (Lunar EnCore version 10.50.086) tools to draw a straight line from the proximal point of the greater trochanter to the distal region of the lateral condyle. A nominal value for femur volume was obtained by multiplying femur cross-sectional area at 60 % (from proximal femur end) by femur length, but the precise location is not critical since the femur cross-sectional area is relatively constant in this region.

Muscle data were normalised using Z scores with individual data expressed as the number of standard deviations from the mean of the young men or women, calculated as:

$$z = \frac{\chi - \mu}{\sigma}$$

where χ is the value for the individual subject, and μ and σ the mean and standard deviation, respectively, of the corresponding young population.

Statistics

Data were analysed using SPSS v19 (IBM, New York, USA; 2011). Univariate two-way ANOVA was used with age and sex as "between factors" to examine differences between groups. Significant interactions indicate that the effects of age differed between men and women. Pearson's product moment correlation was used to determine the relationships between variables. Data are expressed as mean ± standard deviation unless stated otherwise. Differences were considered significant with p values ≤ 0.05.

Results

Participant characteristics

Data for age, height, body mass and femur dimensions are given in Table 1. Both older men and women were ~7–8 cm shorter than their younger counterparts ($p<0.005$). Femur length was ~1.5 cm shorter in both older men and women than the younger people ($p=0.012$). Femur cross-sectional areas at 60 % femur length were marginally, but not significantly ($p=0.11$), larger in the older subjects, and there were no significant differences in the nominal femur volumes between young and old.

Muscle volumes

Figure 1 shows typical scans at 60 % femur length for a young (Fig. 1a) and older (Fig. 1b) man indicating the measured areas of muscle and bone. Values for total thigh muscle volume and for the two major components, the quadriceps and "other muscles,"

Table 1 Participant characteristics

	Young men (n=20)	Older men (n=25)	Young women (n=18)	Older women (n=28)	Significant difference
Age (years)	22.4±4.5	72.3±4.9	22.1±4.5	72.0±4.5	Y < O
Height (m)	1.81±0.05	1.73±0.08	1.67±0.06	1.60±0.06	Y > O; M > W
Body mass (kg)	72.8±9.8	77.9±13.2	61.7±9.5	64.1±11.2	M > W
Femur Length (cm)	45.4±1.6	43.8±3.0	41.5±1.7	40.6±2.0	Y > O; M > FW
Femur CSA 60 % (cm^2)	6.3±0.8	6.6±0.8	4.9±0.5	5.0±0.6	M > W
Nominal femur volume (cm^3)	285±38	289±49	200±20	205±32	M > W

There were no significant age × gender interactions. *Femur CSA 60 %*: Femur cross-sectional area at 60 % femur length from proximal. Significant differences $p<0.05$

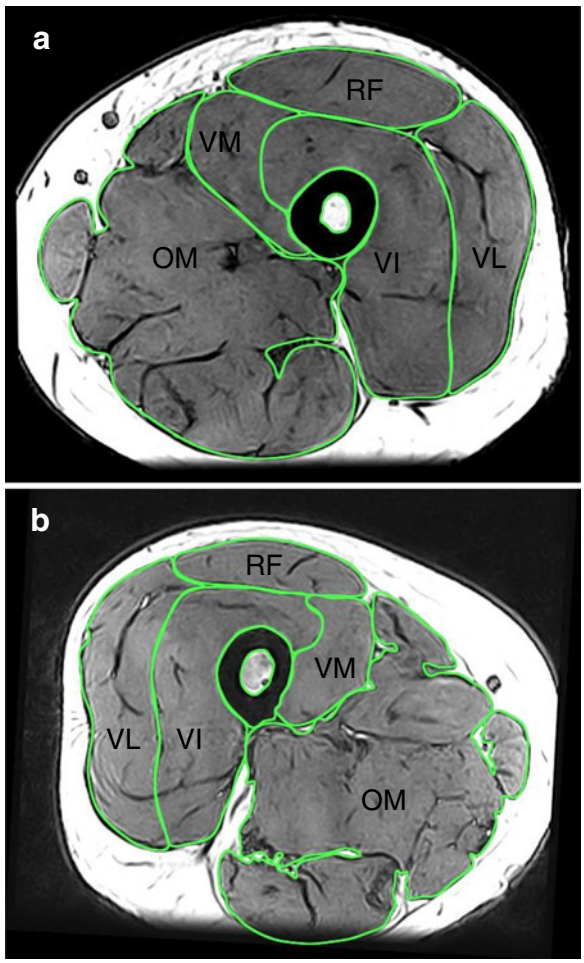

Fig. 1 Magnetic resonance image of the thigh of **a** a young man (22 years) and **b** an older man (76 years) at 60 % of femur length. Highlighted are the cross-sectional areas of the femur, *RF* rectus femoris, *VL* vastus lateralis, *VI* vastus intermedius, *VM* vastus medialis and *OM* other muscles

the latter including the hamstrings, adductor and abductor muscles, are given in Table 2. Total thigh muscle volumes of the older subjects were, respectively, 80 and 73 % of the values for young women and men ($p<0.001$). Of the two components of the thigh muscle volume, the quadriceps group was more affected than the other muscles for both men and women ($p<0.001$).

When expressed as Z scores (Fig. 2 and Table 2), it can be seen that the mean score of the total thigh volume for the older subjects was about 1.5 SD below the mean value for the young. For the quadriceps, the Z score approached 2 and for the other muscles, it was closer to 1. The difference in Z score between quadriceps and other muscles was highly significant ($p<0.0001$).

It is notable that the distribution of Z scores for the old subjects, evident by eye in Fig. 2 and numerically in Table 2, was as tight, if not slightly tighter (i.e. a standard deviation<1), than the distribution of the young subjects.

In Fig. 2, it can be seen that only one older man (indicated by the arrow) had Z scores that were above the mean Z scores for the young subjects, both for the total thigh muscle volume and the component parts. This subject, at the age of 76, was the tallest and heaviest of all the subjects and had the largest femur cross-sectional area. The obvious question is whether he had exceptionally large and strong muscles in his youth and had become merely average, compared to the young, as a result of ageing, or whether he was always this strong but had, as a consequence of lifestyle choices, good fortune or genetics, managed to avoid the effects of ageing. We will come back to this question below.

Table 2 Muscle volumes of the thigh in young and older men and women

	Young men (n=20)	Older men (n=25)	Young women (n=18)	Older women (n=28)	Significant difference
Thigh muscle volume (cm^3)	4,549±740	3,338±512 (73 % Young)	2,905±407	2,314±360 (80 % Young)	Y > O; M > W*
Mean Z score	0±1	−1.64 ±0.88	0±1	−1.45±0.88	Y > O
Quadriceps volume (cm^3)	2,240±366	1,533±306 (68 % Young)	1,368±204	993±181 (73 % Young)	Y > O; M > W*
Mean Z score	0±1	−1.93±0.84	0±1	−1.84±0.89	Y > O
Other muscle volume (cm^3)	2,309±431	1,805±276 (78 % Young)	1,536±238	1,321±212 (86 % Young)	Y > O; M > W*
Mean Z score	0±1	−1.17±0.64	0±1	−0.91±0.89	Y > O

Data for the old subjects are also expressed as a percentage of the young in brackets. In addition, the data for the older subjects are expressed as Z scores (for calculation, see "Methods")

*p<0.05 (significant age × gender interactions)

Normalising muscle volume

The relationships between height and thigh muscle volume for the combined young male and female subjects are shown in Fig. 3a. The best fit to the data (R^2=0.49; p<0.01) had an exponent of 3.86. Plotting muscle volume against femur length (Fig. 3b) gave a best fit with an exponent of 2.89 (R^2=0.38; p<0.01). However, the fit to the data was very much improved (R^2=0.76; p<0.01) when plotting muscle volume against the nominal femur volume (Fig. 3c) with an exponent of 1.12.

It is evident in Fig. 3a, c that muscle volume correlated better with femur volume than height in the young subjects. In Fig. 3d, comparison of the older

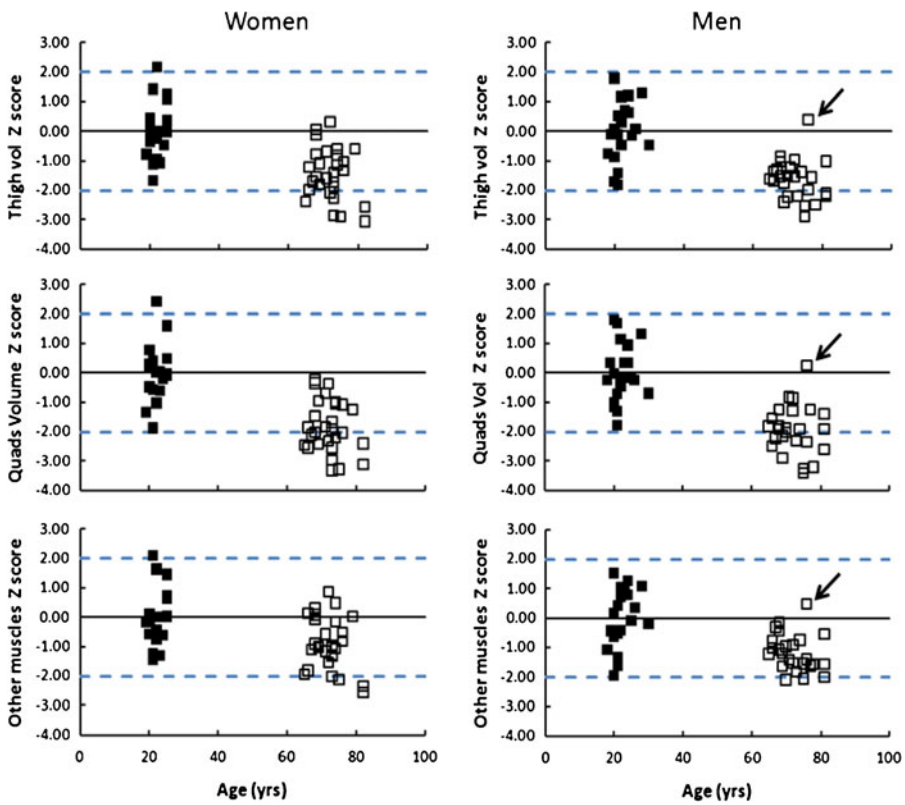

Fig. 2 Muscle volume Z scores as a function of age. Z scores (for calculation, see "Methods") for the total thigh muscle volume, quadriceps and hamstring muscles. The mean values for the young subjects (0, *solid line*) and ±2 SD (*dashed lines*) are shown

and the young data normalised in this way shows that despite a similar range of femur volumes, all the muscle volumes of the older people fell below the regression line for the young subjects.

The one data point from an older subject on the extreme right of Fig. 3d (indicated by arrow) is the older man referred to above, and indicated in Fig. 2, whose *Z* score for muscle volume was just above the mean for the young men. It is evident that while he had a large muscle volume compared with all older subjects, and many of the young, his muscle to bone volume ratio was below that in the young men. This is evident in Fig. 4 where muscle volumes are shown normalised for femur volume and expressed as *Z* scores.

Height squared is commonly used to normalise for body size when defining sarcopenia. Therefore, values for thigh muscle volume are given in Table 3 together with thigh muscle volume data relative to nominal femur volume. It can be seen that the latter approach indicates a greater degree of muscle loss associated with ageing than estimates based on muscle volume corrected for height squared; the mean *Z* score for the thigh volume of older men adjusted to femur volume was −2.2, while it was −1.17 when adjusted for height squared. The *Z* score for total thigh volume divided by femur volume for the one large older man (arrow in Figs. 2, 3d and 4) was −2.85, suggesting he had even experienced somewhat greater muscle loss compared to the average older man (Table 3).

A similar difference between normalising muscle volumes by height squared and femur volume was evident for the women and when considering the quadriceps and hamstring muscles separately.

Finally, the *Z* scores for the muscle volumes and muscle/bone ratio were larger in the quadriceps muscle group than the other muscles (Fig. 2; Tables 2 and 3), indicating that the quadriceps was relatively more affected by ageing than other thigh muscles.

Discussion

The loss of muscle mass that occurs with advanced age is a matter of considerable interest and concern, but studies in this area have tended to be limited by two factors. One is the fact that almost all studies of muscle changes over several decades have, out of necessity, been cross-sectional in design. There is no argument that 70–80-year-old people have a smaller muscle mass than people currently in their third decade. However, it is possible that this is a consequence of the older generation having had a smaller muscle mass in their youth, either as a consequence of secular changes or a lower protein and calorie-rich diet in the years during and immediately after WWII (Lumey et al. 2007). We have addressed this possibility by normalising muscle volumes to the volume of the femur and conclude that this is a better way of determining sarcopenia in an individual than the more commonly used method of dividing muscle mass by height squared. Judging by this muscle/bone ratio, thigh muscle mass was reduced by about 2 SD by the age of around 70 years with slightly greater differences seen in the extensor muscles than the other muscles of the thigh. There were no significant effects of age upon total bone cross-sectional area in the cohort studied here, so that any existing and possibly marginal periosteal expansion with age is unlikely to affect the muscle/bone ratio.

Leaving aside methodological problems and measurement errors, there are four reasons why the muscle mass may vary between people of different ages. First, subjects differ in body size, and the larger the person, the more muscle they are likely to have. Secondly, they may differ in somatotype where for a given body size, mesomorphs will have a greater proportion of muscle than ectomorphs. Thirdly, there may have been secular changes with the phenotype of the population changing in the years over which the ageing process has its effects. For instance, the body height in the western world increased in the last generation by around 1 cm (Lissner et al. 2013). Finally, the ageing process may have affected some individuals more than others (Degens and Korhonen 2012). It is this latter ageing process that most research, including the present study, is concerned with. Longitudinal studies are the only certain way of revealing the true effects of ageing, but practical issues make this impossible over a 50-year span. Given that most studies are cross-sectional and have relatively small sample sizes, it is necessary to have some way of allowing for differences in body size and composition and, if possible, accounting for secular changes. Normalising muscle mass to height squared is the most common procedure (Baumgartner et al. 1998; Dufour et al. 2013; Estrada et al. 2007; Gillette-Guyonnet et al. 2003; Iannuzzi-Sucich et al. 2002; Kenny et al. 2003; Morley et al. 2001), but despite the fact that this is also the basis for calculating

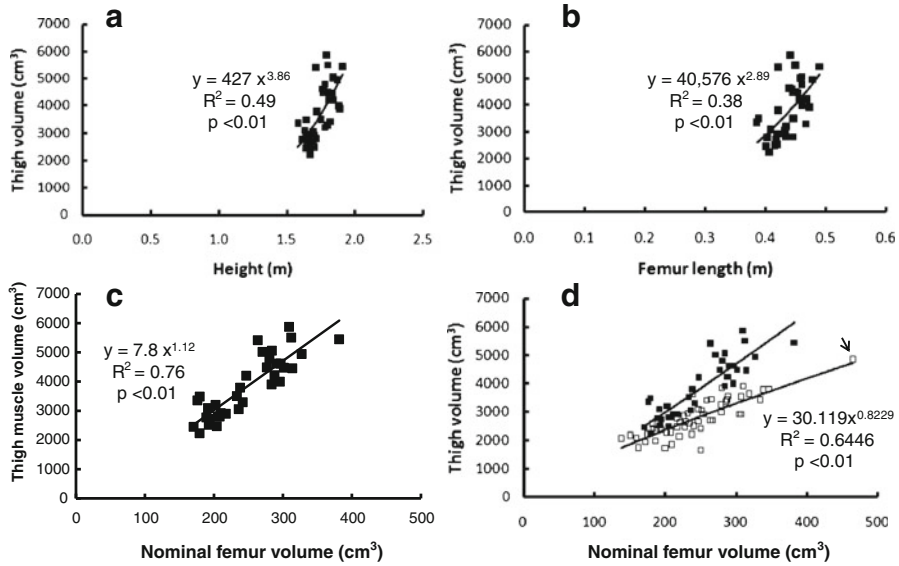

Fig. 3 Relationship between thigh muscle volume as a function of **a** height and **b** femur length and **c** nominal femur volume (cross-sectional area multiplied by length) in young people and **d** nominal femur volume for all young subjects (*solid symbols*; as in **c**) and that of all older subjects (*open symbols*) both $p<0.01$

body mass index, it has no theoretical justification since volume would be expected to vary as the third power of a linear measurement. In fact, the data in Fig. 3a show an exponent of 3.85. There is an additional objection to using height to normalise muscle mass when comparing young and old since stature is

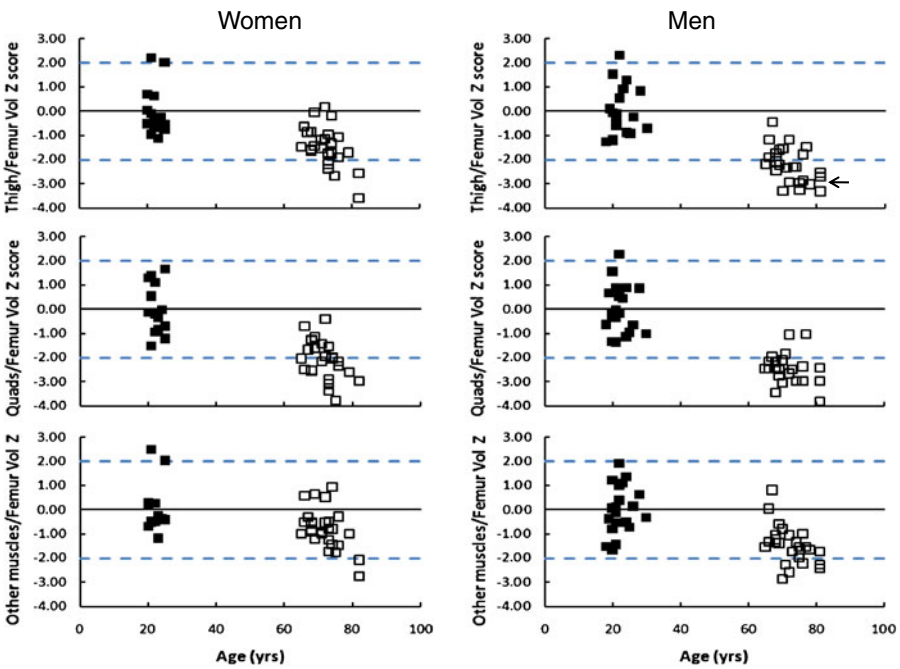

Fig. 4 *Z* scores (for calculation, see "Methods") for muscle volume divided by femur volume as a function of age. *Left panels* are the women, the *right panels*, men. The mean values for the young subjects (0, *solid line*) and ±2 SD (*dashed lines*) are shown

Table 3 Muscle volumes of the thigh normalised for femur volume or height squared in young and old men and women

	Young men (n=20)	Older men (n=25)	Young women (n=18)	Older women (n=28)	Significant difference
Thigh muscle volume/femur volume	16.0±2.0	11.6±1.5	14.6±2.2	11.5±1.8	Y > O, M > W
Mean Z score	0±1	−2.2±0.7	0±1	−1.4±0.8	Y > O, M > W*
Quadriceps volume/femur volume	7.9±1.0	5.3±0.8	6.8±0.9	4.9±0.8	Y > O, M > W
Mean Z score	0±1	−2.7±0.8	0±1	−2.2±0.9	Y > O
Other muscle volume/femur volume	8.1±1.2	6.3±1.0	7.7±1.5	6.6±1.2	Y > O
Mean Z score	0±1	−1.5±0.8	0±1	−0.8±0.8	Y > O
Thigh muscle volume/Ht^2 ($cm^3.m^{-2}$)	1,390±241	1,108±124	1,040±151	900±112	Y > O, M > W*
Mean Z score	0±1	−1.17±0.5	0±1	−0.92±0.7	Y > O

Data are the different muscle groups together with the data expressed as Z scores (for calculation, see "Methods")

*p<0.05 (significant age × gender interactions)

well known to change with advancing years, mainly as a result of shrinkage and increased curvature of the spine, with up to 8 cm lost over the lifespan (Moayyeri and Luben 2008; Sorkin et al. 1999), which is similar to the differences between the young and older cohorts reported here.

Thigh muscle volume in the young subjects was related to femur length with an exponent of 2.89, close to the third power that might be expected (Fig. 3b). However, thigh muscle volume correlated even better with nominal femur volume with an exponent of 1.12 and R^2=0.76. It seems likely that taking femur cross-sectional area into account when calculating femur volume allows for variation in somatotype so that for a given femur length, we might expect mesomorphic subjects to have both greater muscle mass and greater femur cross-sectional area. In addition to somatotype, adjusting muscle to femur volume may also allow for differences in muscle and bone development as a result of training or differences in habitual activity in the adolescent and early adult years.

Here, we calculated a nominal femur volume as the cross-sectional area at 60 % femur length multiplied by femur length. The cross-sectional area of the femur at 60 % femur length is representative of the shaft of the femur and excludes the mass of bone at the two ends of the femur. One possible drawback to using femur volume to normalise muscle volume is that it assumes the outer dimensions of the mid-shaft region remain constant throughout life. The bone is constantly being remodelled, and it is thought that the rate of periosteal apposition increases during ageing, with this increase being greater in men (Ahlborg et al. 2003; Rittweger 2008; Ruff and Hayes 1988). In line with previous studies (Feik et al. 1996; McNeil et al. 2009; Riggs et al. 2004), we found no significant change in total bone shaft CSA, and studies where an age-related increase was reported, it was only 5 % in a small population (Allen et al. 2011). Bone size is therefore a suitable internal standard against which to normalise muscle size.

There were considerable differences in the extent of sarcopenia depending on whether muscle volume is normalised to height squared or to femur volume. When normalising to height squared, only 1 out of 25 older men fell 2 SD below the mean of the young men (giving a prevalence of just 4 %), while when normalising for femur volume, 24 of the 25 were more than 2 SD below the corresponding young average (giving a 96 % prevalence of sarcopenia). For the female subjects, 3 out of 28 older women were more than 2 SD below the young when thigh volume was adjusted for height squared (prevalence of 11 %) but this rose to 16 out of 28 when normalised to femur volume (prevalence of 57 %). It appears, therefore, that adjusting muscle volume for height squared may seriously underestimate the effect of age on muscle mass. It should also be noted that although every effort was made to exclude non-muscle components from the measured cross-sectional areas, it is impossible to account for small fat deposits and connective tissue that can infiltrate the muscles of older people. Consequently, the extent of the loss of contractile material must be greater than the extent of sarcopenia we report. This is most likely to be at least part of the explanation of the commonly reported reduction in specific tension with ageing (Rutherford and Jones 1992; Hairi et al. 2010).

The few longitudinal studies of muscle ageing show a loss of muscle size of about 1 % per year. Delmonico et al. (2009) report a 5 % decrease in thigh muscle cross-sectional area of the knee extensors in men over a 5-year period in participants aged between 71 and 79 years, and Frontera et al. (2000) found a 16 % decrease in quadriceps and 14 % decrease in knee flexors over a 12-year period in men aged around 65 year at the start of the study. The data in Table 3 suggest a loss of around 0.5 % per year of the original muscle volume over a 50-year period. Given that the observed rate of muscle wasting in longitudinal studies is higher, this suggests that sarcopenia may begin around the age of 45 years as is also suggested by cross-sectional data over the 18–88-year age range (Janssen et al. 2000), or simply be a reflection of the fact that a reduction in muscle mass in a year as a percentage of the muscle mass in young people is less than when the same loss is expressed as a percentage of the mass at the start of that year (Degens 2012).

Most large studies of sarcopenia have assessed muscle mass by dual energy X-ray absorptiometry, which cannot distinguish between different component muscle groups in, for instance, the thigh and thus cannot detect any differential effects of ageing on various muscle groups. Using MRI, we were able to determine the size of different components of the thigh muscles; the knee extensors (quadriceps) and all the other muscles of the thigh, which includes the flexors, abductors and adductors, revealing that the quadriceps muscles were more affected by age than the other muscles. While the total thigh muscle volume was 20 % lower in the older subjects, the quadriceps were 27–28 % smaller and the other muscles about half this, at 14–15 % smaller. The reason for this differential susceptibility is not obvious but might reflect different patterns of activity of the various muscle groups or possibly differences in fibre type composition since studies have shown that type II fibres atrophy more during ageing than type I fibres (Andersen 2003). However, a study by Garrett et al. (1984) observed that the knee flexors have a greater proportion of type II fibres than quadriceps or adductor muscles suggesting this is not the explanation.

The definition of sarcopenia as muscle size falling below some lower limit, often defined as −2SD of young values, gives the impression that the extent of muscle loss with age is a phenomenon that affects some individuals to a greater extent than others; i.e. that some older people "suffer" from sarcopenia, while others are little or not affected at all by this condition. If this were the case, the effect would be a greater dispersion of the muscle data for old subjects in comparison with the young subjects. However, it is evident in Figs. 2 and 4 that the variances of the muscle data for young and old subjects were similar in both male and female; the standard deviation of *Z* scores for the older subjects was less than 1. The most likely explanation is that, when young, the older subjects had a similar mean and range of muscle volumes as the present-day young, and the effect of ageing has lead to a similar loss of muscle volume in all subjects. The results suggest therefore that all the older subjects had age-related thigh muscle loss to a similar extent of around 20 % for women and 27 % for men. Those older subjects who were at the lower end of the distribution and had the lowest *Z* scores probably had small muscle mass when young while those at the top of the range and who might have been thought to not have suffered the effects of ageing (such as subjects identified by the arrows in Figs. 2 and 3) had, in fact, considerably larger muscles when young which with age had shrunk to what would be average for a young person. Overall, the effect is that the decrease with age is approximately 2 SD, taking the top of the range down to the mean and the mean to the bottom of the range of the corresponding young people. This observation may reflect the fact that our older sample were relatively homogeneous, remaining active and in good health. In a larger sample of the population, inactivity, disease or strength training may increase the dispersion.

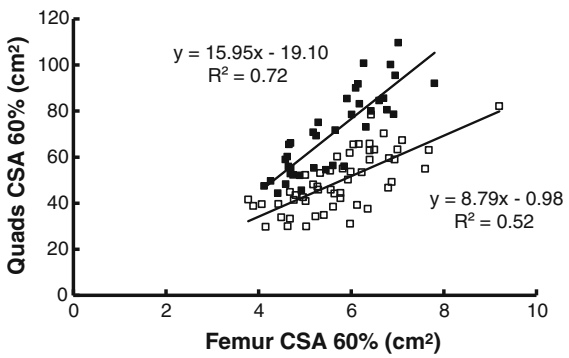

Fig. 5 Relationship between quadriceps muscle cross-sectional area (*Quads CSA*) and femur cross-sectional area (*Femur CSA*) measured at 60 % femur length. Young subjects: *solid symbols*; older subjects: *open symbols*

Measuring muscle volume with multiple MRI scans is demanding in terms of time and equipment and simply comparing muscle to bone cross-sectional areas from a single scan at 60 % femur length showed a similar relationship between bone and muscle cross-sectional areas (Fig. 5) to that obtained comparing bone and muscle volumes (Fig. 3d). *Z* scores for the quadriceps/femur cross-sectional areas (−2.27 for the older female −3.2 for the older men) are similar, although slightly larger than those for muscle/bone volumes (Table 3). We have previously shown that it is possible to estimate quadriceps muscle volume of young male subjects from a single MRI scan if the length of the femur is known (Morse et al. 2007), and it appears therefore that the same is true for women and older subjects. It also implies that sarcopenia affects all the components of the quadriceps to a similar extent, a conclusion we have reported elsewhere (Maden-Wilkinson et al. 2013).

In summary, the data presented here lead to the following conclusions. First, normalising upper leg muscle volumes to height squared has little validity and leads to a substantial underestimation of the differences in muscle volume between young and old. Secondly, the differences in muscle volume between young and old are a consequence of the ageing process and have not arisen because the older subjects were of a smaller stature when they themselves were young; this removes one of the concerns about interpreting cross-sectional data in terms of longitudinal changes. Thirdly, muscle changes with age appear to have affected all subjects to a similar degree as there was no evidence of individuals who were protected from the ageing process. Fourth, the extent of muscle changes was greater in the quadriceps than in the other muscles of the thigh.

Acknowledgments JMcP was supported by Myoage EU FP7 223576.

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