Appendicular Lean Tissue Mass and the Prevalence of Sarcopenia Among Healthy Women

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Studies indicate that deficient skeletal muscle mass or sarcopenia is a major cause of disability and morbidity among the elderly. In part, due to the lack of generally applicable normal values, there is still insufficient epidemiologic data available on the frequency and severity of sarcopenia in health and under various disease-related conditions. The objectives of the present study were to (1) characterize the age- and menopause-related variations in appendicular lean tissue mass (LTM_A), (2) provide young-normal means and estimate the age-specific prevalence of sarcopenia among healthy women. A total of 754 healthy women were included in the study of cross-sectional design. LTM_A was estimated by dual-energy x-ray absorptiometry (DEXA). Physical characteristics and menopausal status were also registered. LTM_A as well as height showed significant negative correlation with age with Pearson's r values of −0.43 and −0.06, respectively ($P < .05$). Trend of finding lower mean values with advancing age remained even when LTM_A was adjusted for height^2 (ht^2). Menopause did not seem to have any influence on LTM_A. Young-normal means were obtained from 216 premenopausal women aged 18 to 39 years. Prevalence rates of sarcopenia in healthy women were determined with reference to a cut-off line corresponding to LTM_A or LTM_A/ht^2 less than young-normal mean 2 SD and were found to be 40.2% and 12.3%, respectively, among the healthy elderly (>70 years of age). Results of the present study provide further evidence that sarcopenia exists even among otherwise healthy women with increasing age-specific prevalence. Further studies are needed (1) to estimate the prevalence of sarcopenia under various health and disease-related conditions with reference to the hereby given cut-off values and (2) to find therapeutic strategies with beneficial effects in conserving skeletal muscle mass.

ADVANCING AGE IN women is accompanied with changes in body composition characterized by an increase in fat tissue mass and a decline in both bone and skeletal muscle mass.[1-8] Insufficient skeletal muscle mass has been linked to disability, morbidity, and mortality in the geriatric population.[3]

Until recently, the vast majority of clinical investigations addressing the age and menopause-related changes in muscle mass used total lean tissue mass (LTM_T) as study parameter. Dual-energy x-ray absorptiometry (DEXA), which has proved itself as a useful and convenient technique for body composition measurements,[9-12] has set a new stage on the musculoskeletal research field. With appropriate definitions of arm and leg regions,[11-13] DEXA is able to provide an estimate of fat-free lean tissue mass of the trunk and the limbs separately. The sum of arm and leg lean tissue masses, termed as appendicular lean tissue mass (LTM_A) has been reported to correlate well with computer tomography (CT)-determined skeletal muscle mass and total body K^+.[13-16] Based on these characteristics, LTM_A has received increasing physiologic and clinical interest in the past years. However, there is a lack of generally applicable young-normal values making it difficult to quantify the severity of skeletal muscle loss and estimate the prevalence of sarcopenia in healthy and diseased populations.

Recent data suggest that, in addition to aging, the menopause transition also contributes to the changes in body composition.[17,18] Although there are some observations suggesting an accelerated muscle loss coinciding with the menopause transition, most of the previous epidemiological and interventional studies are not in line with this concept. However, as pointed out above, these studies focused on LTM_T measurements, and thus, it is still under debate whether changes in estrogen status has any major impact on LTM_A.

Therefore, the main purpose of the present study was to characterize the age and menopause-related variations in LTM_T and LTM_A in a larger representative subpopulation of healthy Danish women aged 18 to 85 years using the DEXA technique. In addition, we intended to provide young-normal means for LTM_A and estimate the age-specific prevalence of sarcopenia among healthy women.

SUBJECTS AND METHODS

The study population consisted of 754 healthy women aged 18 to 85 years, who participated in various studies investigating changes in bone mass, lipid metabolism, and total body composition performed at 2 study sites of the Center of Clinical and Basic Research. Subjects were enrolled in the present cross-sectional study, if meeting the following selection criteria: (1) absence of serious chronic medical illnesses, (2) absence of ongoing medication known to affect body composition, and (3) no history of reduced ambulation or prolonged immobilization. When comparing mean body mass index (BMI), height, and weight values calculated on an age decade basis with those obtained from other Danish reference populations,[19] no significant differences were found. Thus, subjects of the present study can be considered as a representative subpopulation of healthy Danish women.

All investigations were performed in accordance with the Declaration of Helsinki II and approved by the Ethical Committee of Copenhagen and of North Jutland counties.

Physical Parameters and Menopausal Status

On participants wearing light indoor clothes and no shoes, body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Women were considered as postmenopausal if not experiencing any signs of menstrual bleeding within the past 6 months. None of the participants has undergone ovariectomy or hysterectomy.

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Submitted February 19, 2001; accepted June 6, 2001.

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0026-0495/02/5101-0002$35.00/0
doi:10.1053/meta.2002.28960

Table 1. LTM_T and LTM_A Measured by DPX and QDR4500A Scanners in Age- and Height-Matched Groups of Women

	DPX	QDR4500A
No.	379	358
Age	48.2 ± 0.8	48.2 ± 0.8
Height	1.65 ± 0.01	1.64 ± 0.01
LTM_T	41.0 ± 0.30	41.6 ± 0.30
LTM_A	18.00 ± 0.14	17.65 ± 0.13

NOTE. No significant differences were found between the groups.

DEXA

Total and regional lean tissue masses of healthy women were determined from a whole body scan obtained by DEXA using a QDR4500A scanner (Hologic, Waltham, MA; software version V8.10a:3) and a DPX scanner (Lunar Radiation, Madison, WI; software versions 3.1 and 3.2). These scanners have both been validated against CT for the measurements of LTM_T and LTM_A.[12,14] In our comparison, the mean LTM_T and LTM_A of age- and height-matched groups of healthy women measured with the DPX or QDR4500A scanner showed negligible differences (Table 1).

Estimation of LTM_A has been described previously in detail.[11-13] Briefly, with the use of specific landmarks, the legs and arms can be separated on the anterior view of the skeletal x-ray planogram. The arm encompasses all soft tissues extending from the center of the arm socket to the phalange tips, and contact with the ribs, pelvis, or greater trochanter can be avoided. The leg consists of all soft tissues extended from an angled line drawn through the femoral neck and to the phalangeal tips. These landmarks defining the legs and arms were the same for the DPX and QDR4500 scanners. The fat and bone mineral-free portion of the extremities were assumed to represent LTM_A. LTM_A shows a strong association with appendicular muscle mass, yet the contribution of a small and relatively constant amount of skin, underlying connective tissue, and fat-free part of the adipose tissue cannot be ignored.[11]

Because muscle mass strongly correlates with body size, we adjusted both LTM_T and LTM_A for ht^2 analogously with the calculation of BMI. However, because changes in lean tissue mass and body height is due to different pathomechanisms, normalizing for height may, to some extent, obscure the real muscle loss that occurs with aging. For this reason, the prevalence rate of sarcopenia was estimated in the mirror of corresponding cut-off values of both LTM_A and LTM_A/ht^2. Muscle mass parameters had approximately normal distribution as indicated by quantile-quantile plots.

Because mean LTM_A/ht^2 of women belonging to the second and third age decade showed no differences, young-normal means were determined from 216 women aged 18 to 39 years. Prevalence rates of sarcopenia were determined according to the definition first proposed by Baumgartner et al[20]; LTM_A/ht^2 < young-normal mean 2 SD. Low skeletal muscle mass was also estimated according to an approach somewhat similar to that assessing osteopenia (1 to 2 SD below young-normal means).

Statistical Analysis

Data on physical and muscle mass characteristics shown in Table 2 were expressed as mean ± SD. All other results are shown as mean ± SEM. Data analysis was performed using the GraphPad Analysis Software 2.01 (GraphPad, San Diego, CA). Student's unpaired *t* test was used to compare baseline characteristics, LTM_T, and LTM_A indices of pre- and postmenopausal women. One-way analysis of variance (ANOVA) followed by Bonferroni's test was used to compare the aforementioned parameters of the various age groups. Pearson's correlation coefficients were used to establish the univariate relationship between muscle parameters, age, height, and weight. The relationship between muscle mass and height, weight, age, and years after menopause were also investigated by multiple-regression analysis performed by using the SPSS 8.0 data analysis software (SPSS, Chicago, IL). LTM_T and LTM_A were used as dependent variables and height, weight, age, menopausal status, and years since menopause were used as independent variables in the multiple-regression models. Differences were considered significant if *P* values were less than .05.

RESULTS

Physical and Lean Mass Characteristics of the Study Population

The physical and LTM characteristics of the 754 participants stratified according to age-decade are shown in Table 2. Mean values of body weight and BMI calculated in the different age groups increased with advancing age up to the sixth decade followed by a decline thereafter. In contrast, mean values of body height of the different age groups decreased progressively with increasing age.

LTM_T and LTM_A showed a strong correlation characterized

Table 2. Variations in Physical and Lean Mass Characteristics as Measured by DEXA in Healthy Women of Different Age Decades

	18-29 Years (n = 97)	30-39 Years (n = 119)	40-49 Years (n = 121)	50-59 Years (n = 265)	60-69 Years (n = 85)	>70 Years (n = 67)
Age (yr)	25.7 ± 2.5	34.4 ± 3.1	45.1 ± 2.9	54.0 ± 2.6	64.5 ± 2.9	75.2 ± 3.4
Weight (kg)	62.9 ± 7.7	64.2 ± 9.8	66.3 ± 10.1	65.5 ± 9.8	67.6 ± 10.1*	62.3 ± 10.7*‖
Height (m)	168.4 ± 5.9	1.67 ± 0.06	1.66 ± 0.05*	1.63 ± 0.06*†‡	1.60 ± 0.05*†‡§	1.59 ± 0.06*†‡§
BMI (kg/m^2)	22.2 ± 2.5	22.9 ± 3.3	24.0 ± 2.8*	24.5 ± 3.5*†	26.3 ± 4.1*†‡§	24.6 ± 4.2*†
LTM_T (kg)	43.4 ± 4.3	43.0 ± 5.2	42.4 ± 4.4	40.3 ± 4.0*†‡	39.4 ± 4.37*†‡	38.5 ± 4.4*†‡
LTM_T/ht (kg/m)	25.7 ± 2.2	25.6 ± 2.4	25.5 ± 2.3	24.7 ± 2.2	24.5 ± 2.6	24.2 ± 2.4
LTM_T/ht^2 (kg/m^2)	15.3 ± 1.3	15.3 ± 1.5	15.3 ± 1.3	15.1 ± 1.4	15.2 ± 1.6	15.2 ± 1.5
LTM_A (kg)	19.4 ± 2.3	19.0 ± 2.6	18.3 ± 2.5*	17.2 ± 2.0*†‡	16.5 ± 2.13*†‡	15.7 ± 2.4*†‡§
LTM_A/ht (kg/m)	11.5 ± 1.2	11.4 ± 1.5	11.0 ± 1.3*	10.5 ± 1.1*†‡	10.3 ± 1.2*†‡	9.8 ± 1.3*†‡§
LTM_A/ht^2 (kg/m^2)	6.8 ± 0.7	6.8 ± 0.8	6.6 ± 0.7*	6.4 ± 0.6*†‡	6.3 ± 0.7*†‡	6.2 ± 0.8*†‡§

*$P < .05$ *v* 18-29 years.
†$P < .05$ *v* 30-39 years.
‡$P < .05$ *v* 40-49 years.
§$P < .05$ *v* 50-59 years.
‖$P < .05$ *v* 60-69 years.

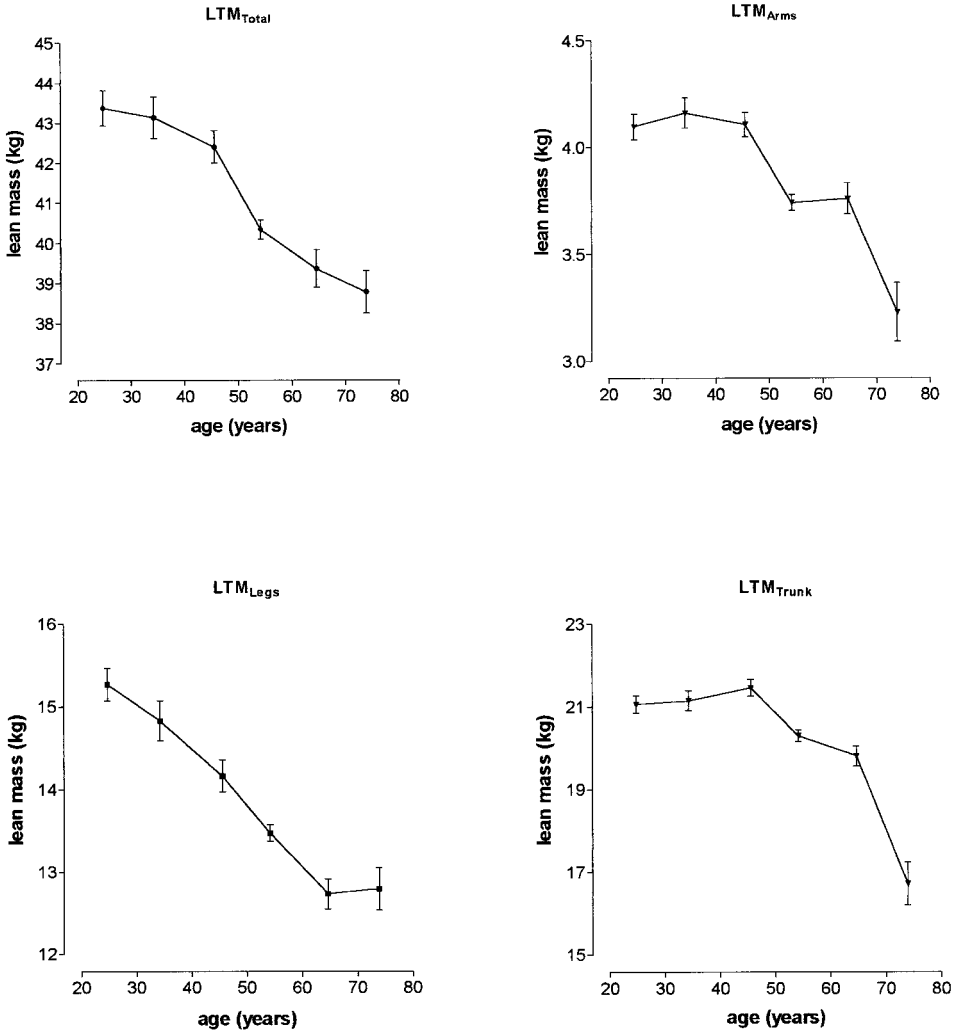

Fig 1. Age-dependent variations in total (LTM_T) and regional lean tissue masses (LTM_{legs}, LTM_{arms}, and LTM_{trunk}). Results shown are means ± SEM. Number of subjects in the respective age group is indicated in Table 2. *$P < .05$.

with Pearson's r value of .79 (n = 754, $P < .0001$). Both LTM_T and LTM_A showed strong negative correlation with age with respective Pearson's r values of .58 and .65, respectively (n = 754, $P < .0001$). The data were best fit with straight lines with characteristics as follows: $LTM_T = 46.3$ kg − 0.11 [age (years)] (n=754, $P < .0001$), whereas $LTM_A = 28.4$ kg − 0.10 [age (years)] (n=754, $P < .0001$). LTM parameters showed strong correlation with height and weight as well, but not with menopausal status or years since menopause.

To assess the contribution of major physical characteristics to the variations in LTM_T and LTM_A, we have established multiple regression models describing the relationship between these parameters as dependent variable and age, weight, height, menopausal status, years since menopause as independent variables. All of the independent variables except for menopausal status and years since menopause contributed significantly ($P < .0001$) to the variations in the 2 muscle parameters. Predictive equations for the 2 muscle parameters were as follows: $LTM_T = -11.9 - 0.06$ [age (years)] + 0.20 [weight (kg)] + 26.3 [height (m)] with a SEE of 3.4 kg (SEE% = 8%); $LTM_A = -13.3 - 0.05$ [age (years)] + 0.11 [weight (kg)] + 16.1 [height (m)] with a SEE of 1.7 kg (SEE% = 9%). Correlation coefficients of the models were: $R_{LTMT} = 0.70$ and $R_{LTMA} = 0.76$. Thus, variations in age, weight, and height explained 49% of the variance in LTM_T and 58% of the variance in LTM_A.

Variations in LTM_T and LTM_{leg} with age showed similar patterns (Fig 1). Although there was a slight, nonsignificant decrease in absolute LTM_A between women belonging to the third and fourth age-decade, means of ht and ht^2-adjusted LTM_A showed no differences. However, in those older than 39 years, there seemed to be a linear tendency for decreasing values with age. In contrast, variations in the LTM_{arm} and LTM_{trunk} were of somewhat different patterns (Fig 1); no differences in means were seen between 18 and 50 years of age, but there were significantly lower values seen in the 50s and the 70s.

Postmenopausal women had significantly less LTM_T and LTM_A compared with premenopausal women. Thus, the mean LTM_T of pre and postmenopausal women were 42.8 ± 0.3 kg (n = 336) and 39.9 ± 0.2 kg (n = 418), respectively ($P < .0001$), whereas means of LTM_A were 18.9 ± 0.2 kg (n = 336)

Table 3. Prevalence of Sarcopenia Among Healthy Women

		T-SCORE = −1-2 SD		T-SCORE less than −2 SD	
Age	No.	LTM_A (%)	LTM_A/Ht^2 (%)	LTM_A (%)	LTM_A/Ht^2 (%)
40-49 yr	121	26.4	29.7	7.4	3.3
50-59 yr	265	35.8	32.1	14.3	3.8
60-69 yr	85	43.5	24.0	20.0	9.4
> 70 yr (healthy)	67	40.3	32.9	40.2	12.3

and 16.9 ± 0.1 kg (n = 418), respectively ($P < .0001$). However, the average age of postmenopausal women (60.4 ± 9.9 years, n = 418) was obviously higher compared with that of premenopausal women (36.0 ± 8.8 years, n = 336; $P < .0001$). When minimizing age differences between premenopausal (48.2 ± 1.5 years, n = 31) and postmenopausal (49.6 ± 0.8 years, n = 42) women and comparing their mean LTM_T and LTM_A, differences remained nonsignificant. Thus, LTM_T of pre and postmenopausal women were 42.4 ± 0.8 kg (n = 31) and 40.9 ± 0.6 kg (n = 42), respectively ($P = .15$), whereas LTM_A were 18.2 ± 0.5 kg (n = 31) and 17.9 ± 0.3 kg (n = 42), respectively ($P = .63$). There were no significant differences in the BMI values of these premenopausal (24.4 ± 2.7 kg/m^2; n = 31) and postmenopausal (23.4 ± 3.1 kg/m^2; n = 42) women ($P = .15$).

As shown in Table 2, there were no significant differences between ht and ht^2-adjusted LTM_A of women aged 18 to 29 years and 29 to 39 years. Therefore, young-normal means of LTM_A-derived muscle parameters were obtained from the pooled group of women aged 18 to 39 years (n = 216).

If sarcopenia is defined as previously proposed by Baumgartner et al,[20] LTM_A/ht^2 < young-normal mean –2 SD, age-specific prevalence rates can be given as shown in the right column of Table 3. Cut-off values for LTM_A and LTM_A/ht^2 were 14.0 kg and 5.4 kg/m^2, respectively. Age-specific prevalence rates increased with age, regardless of which parameter was used (Table 3), and reached 40.3% and 12.3%, respectively, among the healthy elderly (>70 years of age).

In the present study, we have also calculated the prevalence rates of sarcopenia according to the approach similar to that used to define osteopenia (1 to 2 SD below young-normal means). Cut-off values for LTM_A and LTM_A/ht^2 according to this definition were 16.6 kg and 6.1 kg/m^2, respectively. Prevalence rates of sarcopenia are indicated in Table 3. Interestingly, age-specific prevalence rates were found increasing when estimated as a function of LTM_A, however, it was quite uniform in the various age-groups when estimated with reference to cut-off values of LTM_A/h^2. Corresponding age-specific prevalence rates among the elderly (>70 years of age) were found 40.3 % and 32.9%, respectively.

DISCUSSION

Advancing adult age is associated with prominent changes in body composition, an important component of which is a decline in skeletal muscle mass.[2-8,17,21-24] Due to the lack of sufficient epidemiologic data, incomplete knowledge of the pathophysiologic consequences and poor understanding of the underlying mechanisms, the extent of this potential public health burden posed by sarcopenia continues to be largely unknown.

Values of LTM_T and LTM_A found in the present study were comparable to those reported by previous studies.[23,25,26] Furthermore, results of the present study are consistent with previous reports insofar as LTM_T and LTM_A among healthy volunteer women show a strong negative correlation with age.[23,25,26] It is to be pointed out that approximately three quarters of the loss of LTM_T from young to old age can be attributed to losses in LTM_A. In our data, each year of age was associated with 0.10 kg reduction in LTM_A. This value is in line with that recently reported by a longitudinal study reporting 1 kg of muscle decline per decade[4] and with findings of the Rochester, MN Study showing a yearly skeletal muscle loss of 0.09 kg.[25] A somewhat lower value was found by the Rosetta study, 0.06 kg/year.[23] With the use of multiple regression analysis to predict LTM_A, height and weight explained 53% of the LTM_A variance. Contribution of age was an additional 5%. These results are similar to those reported in the Rosetta study, in which weight and height explained 67%, while age contributed an additional 6% to the variation in total skeletal muscle mass.[23] Further studies are needed to define physical variables that could further improve the predictive equation of skeletal muscle mass.

Although the issue of aging and concomitant changes in skeletal muscle mass have been extensively studied over the past decade, the metabolic alterations underlying muscle loss are yet to be clarified. Poehlman et al[27] observed an accelerated loss of LTM_T coinciding with the menopause transition. On the basis of this finding, it was speculated that estrogen might play an important role in the preservation of muscle mass. Results of the present study, in accordance with the vast majority of previous investigations (reviewed in Poehlman and Tcherof[17]), however, could not provide support for this hypothesis.

The failure of not seeing any effect on LTM_T, however, could be attributed to a methodological drawback of DEXA, namely that it is unable to differentiate between muscle mass, extracellular water, and other fat-free lean tissue masses.[28] A major advantage of using LTM_A is that it minimizes errors of the aforementioned origin and thus provides a more homogenous estimate of muscle mass in healthy women without extracellular edemas. The differences between LTM_A and LTM_T were also indicated by the correlation analysis showing an association characterized by a Pearson's *r* value of .79 (n = 754). Nevertheless, when comparing LTM_A of pre and postmenopausal women of the same age, we, in accordance with others,[29] still found no significant differences. Further, interventional studies assessing the effect of estrogen on LTM_A are required to provide the ultimate answers.

Results of the present study indirectly suggest that ht and ht^2-adjusted LTM_A do not undergo changes during the third and fourth decades. Therefore, mean values obtained from women aged 18 to 39 years (30.4 ± 5.3 years, n = 216) seem to represent peak muscle mass and thereby a relevant reference for the calculation of *t* scores. The fact that the present study and the Rosetta study, calculating young-normal means of LTM_A/ht^2 from practically the same (age-class) population found the same cut-off values of 5.4 kg/m^2,[20] appears to support the above statement. The Rochester study, which included

in the reference population all premenopausal women younger than 50 years of age, found a significantly lower cut-off value of 4.5 kg/m^2.[25] The differences could be explained, at least in part, by a notable decline in LTM_A in those in the forties, as also suggested by our results (see Table 2). Collectively, these findings seem to argue for the selection of healthy women aged 18 to 39 years as a valid reference population to set young-normal means.

Regarding the reference parameter to be used for estimation of the prevalence and severity of sarcopenia, similar uncertainties exist. Baumgartner et al[20] arbitrarily suggested the use of LTM_A/ht^2, because this parameter in their study had eliminated the strong correlation between ht and LTM_A ($r = .09$, $P = .107$). In contrast, in the present study, as well as in the Rochester, MN Study,[25] significant residual correlation remained between ht and LTM_A/ht^2, leaving some questions behind as to whether this parameter is the most optimal for the estimation of sarcopenia. Moreover, it is to be pointed out that changes in muscle mass and body height are due to different pathomechanisms and are not correlated. Normalization for ht may, therefore, obscure the real muscle loss that occurs with aging. Clearly, further studies are needed to refine the estimation of the changes in LTM with aging. Due to considerable differences in the composition of study and/or reference populations used, it is somewhat difficult to make valid comparisons between findings of these 3 cross-sectional studies. However, it appears that prevalence rates of sarcopenia found in the present study are comparable to those found by Melton et al[25]; age-specific prevalence rates among the elderly (>70 years): 12.3% *v* 8%, respectively. These values are practically the same, especially if taking into account that the latter study used lower cut-off values compared with ours, as also pointed out above. In comparison, the New Mexico Elder Health Study[20] found markedly higher prevalence rates compared with the present study even though the cut-off values were the same. These discrepancies could be, at least in part, due to the smaller number of elderly participating in our study. However, it should also be pointed out that Baumgartner et al[20] measured skeletal muscle mass by DEXA only in a smaller subsample ($n = 199$) of their study population ($n = 883$), while LTM_A of the remaining participants was estimated by a predictive equation, which might introduce some degree of errors. Finally, it must be emphasized that our study focused only on healthy and physically active individuals, while participants of the New Mexico Elder Health Study were of a much more heterogeneous background. Therefore, factors other than age might also influence the LTM_A of their participants, which may also account for the pronounced differences in the prevalence rates found by the 2 studies.

In summary, results of the present study suggest that both LTM_T and LTM_A show strong negative correlation with age, whereas the menopause transition does not seem to be a major contributor. The prevalence of sarcopenia among women increases with age reaching 12.3% in the healthy elderly aged older than 70 years. Further studies are required to obtain further insights in the mechanisms underlying the age-related decline in LTM_A and to establish a clinically relevant criteria to define those being in the relative risk of facing disability, morbidity, and mortality due to sarcopenia at an elderly age.

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