Total-body skeletal muscle mass: estimation by a new dual-energy X-ray absorptiometry method[1–3]

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ABSTRACT

Background: Skeletal muscle (SM) is an important body-composition component that remains difficult and impractical to quantify by most investigators outside of specialized research centers. A large proportion of total-body SM is found in the extremities, and a large proportion of extremity lean soft tissue is SM. A strong link should thus exist between appendicular lean soft tissue (ALST) mass and total-body SM mass.

Objective: The objective was to develop prediction models linking ALST estimated by dual-energy X-ray absorptiometry (DXA) with total-body SM quantified by multislice magnetic resonance imaging in healthy adults.

Design: ALST and total-body SM were evaluated with a cross-sectional design in adults [body mass index (in kg/m^2) < 35] with an SM-prediction model developed and validated in model-development and model-validation groups, respectively. The model-development and model-validation groups included 321 and 93 ethnically diverse adults, respectively.

Results: ALST alone was highly correlated with total-body SM (model 1: $R^{2=}$ 0.96, SEE = 1.63 kg, $P < 0.001$), although multiple regression analyses showed 2 additional predictor variables: age (model 2: 2-variable combined $R^{2=}$ 0.96, SEE = 1.58 kg, $P < 0.001$) and sex (model 3: 3-variable combined $R^{2=}$ 0.96, SEE = 1.58 kg, $P < 0.001$). All 3 models performed well in the validation group. An SM-prediction model based on the SM-ALST ratio was also developed, although this model had limitations when it was applied across all subjects.

Conclusion: Total-body SM can be accurately predicted from DXA-estimated ALST, thus affording a practical means of quantifying the large and clinically important SM compartment. *Am J Clin Nutr* 2002;76:378–83.

KEY WORDS Body composition, nutritional assessment, skeletal muscle mass, magnetic resonance imaging, dual-energy X-ray absorptiometry

INTRODUCTION

Skeletal muscle (SM), the largest component of adipose tissue–free body mass in humans, is central to the study of nutritional, physiologic, and metabolic processes (1–3). Total-body and regional SM mass can now be accurately quantified with imaging methods, including computed axial tomography (CT) and magnetic resonance imaging (MRI) (4, 5). However, CT and MRI are costly methods and instrument access is limited.

An alternative approach for measuring total-body SM is dual-energy X-ray absorptiometry (DXA), because DXA instruments are widely available and are relatively inexpensive; in addition, radiation exposure is minimal with this technique (2, 6, 7). DXA systems provide a measure of appendicular lean soft tissue (ALST), a fat- and bone mineral–free component that includes muscle and other components such as skin, tendons, and connective tissues (8–11). SM constitutes the largest fraction of ALST, and previous investigators proposed several models for predicting SM with DXA (7, 8, 12, 13). The 2 main proposed models (8, 12) are now recognized as being either inaccurate or of limited applicability because of model imprecision or because of the complexity of the required measurements and calculations. These 2 models were reported before the availability of reference methods for measuring total-body and regional SM mass on large and diverse subject populations such as those now provided by MRI (1).

A large proportion of total-body SM is found in the extremities, and a large proportion of ALST is SM (**Figure 1**). Therefore, DXA potentially affords a practical and available means for quantifying total-body SM mass. The aim of the present study was to develop and subsequently validate a total-body DXA SM-prediction model with the use of MRI as the reference method.

SUBJECTS AND METHODS

Protocol and design

The adult subjects underwent 2 evaluations within 1 d of each other: ALST was estimated by DXA (12), and total-body SM mass was estimated by MRI (14). Subjects were recruited into 2 groups, the first group served as a model-development sample (group 1) and the second group as a model-validation sample (group 2). The subjects in group 1 were recruited first, followed by the recruitment of the subjects in group 2. Total-body SM-prediction models were developed by using simple and multiple linear regression

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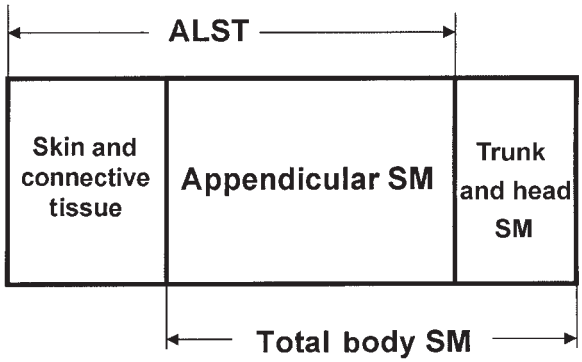

FIGURE 1. Relations between appendicular lean soft tissue (ALST) and total-body skeletal muscle (SM) mass. ALST is the sum of lean soft tissue from both arms and legs.

methods in which total-body SM mass estimated by MRI was set as the dependent variable and ALST estimated by DXA was set as the independent variable, along with other potential covariates such as age, sex, and race.

Subjects

Subjects were healthy men and women aged ≥ 18 y with a body mass index (BMI; in kg/m^2) < 35 who had participated in previous multiethnic investigations of body composition (15). The subjects were recruited over 5 y through advertisements in newspapers, on radio stations, and in flyers posted in the local community. To be eligible for inclusion, the subjects had to be ambulatory and have no orthopedic problems that could affect any of the variables under investigation. Persons who regularly participated in vigorous physical activity training programs were excluded. Each subject completed a medical examination that included screening blood tests. Only healthy subjects with no diagnosed medical conditions were enrolled in the study. The study was approved by the Institutional Review Board of St Luke's–Roosevelt Hospital Center, and all subjects gave written consent before participating.

Body-composition analysis

Body mass and height were measured to the nearest 0.1 kg and 0.5 cm with a digital scale (Weight Tronix, New York) and wall-mounted stadiometer (Holtain, Crosswell, United Kingdom), respectively.

Dual-energy X-ray absorptiometry

Whole-body and regional body composition were estimated by using DXA (software version 3.6; Lunar DPX, Madison, WI). The system software provided the mass of lean soft tissue, fat, and bone mineral for both the whole body and specific regions. ALST mass was considered equivalent to the sum of lean soft tissue in both the right and left arms and legs. Appendages were isolated from the trunk and head by using DXA regional computer-generated default lines, with manual adjustment, on the anterior view planogram. With the use of specific anatomic landmarks, the legs and arms were defined by this method as the soft tissue extending from a line drawn through and perpendicular to the axis of the femoral neck and angled with the pelvic brim to the phalange tips and the soft tissue extending from the center of the arm socket to the phalange tips, respectively. Repeated daily measurements over 5 d in 4 subjects showed a CV (100% × SD/mean) of 1.7% for leg lean soft tissue, 2.0% for arm lean soft tissue, and 2.6% for ALST (16). DXA was also used to provide descriptive measures of total-body fat across the 2 subject groups.

Magnetic resonance imaging

Total-body SM mass was measured by using whole-body multislice MRI as reported by Ross (14). Subjects were placed on the 1.5-T scanner (6X Horizon; General Electric, Milwaukee) platform with their arms extended above their heads. The protocol involved the acquisition of ≈40 axial images across the whole body with 10-mm thickness and 40-mm intervals (14, 17). Images were analyzed by using SliceOmatic image analysis software (TomoVision Inc, Montreal), and SM volume by MRI was converted to mass by using an assumed density of 1.04 kg/L for SM (18). The CV for repeated measurements of the same scan by the same observer of MRI-measured total-body SM volumes in our laboratory is 0.7% (17).

Statistical analysis

Differences in between-group characteristics were tested for statistical significance by using Student's *t* tests. Pearson's correlation coefficients were used to explore the associations between DXA-measured ALST and MRI-measured total-body SM in the model-development group. The simplest empirical SM-prediction model is SM = k × ALST, where k is the established ratio of SM to ALST. We therefore explored mean k values in men and women along with their respective SDs and CVs.

SM-prediction equations were first developed in the model-development group with the use of multiple linear regression analysis. Potential independent variables included ALST, age, sex, and race (African American, Asian, white, and Hispanic). Prediction equations were developed by stepwise multiple regression analysis with MRI-measured total-body SM set as the dependent variable. The adjusted R^2 values were used to quantify model-fitting

TABLE 1
Subject characteristics[1]

	Model-development group		Model-validation group	
	Men (n = 145)	Women (n = 176)	Men (n = 26)	Women (n = 67)
Age (y)	41 ± 17 (18–84)	49 ± 19[2] (18–88)	43 ± 18 (21–81)	39 ± 15 (19–92)
Body mass (kg)	80.4 ± 13.2 (47.4–114.0)	65.2 ± 13.1[2] (40.6–100.2)	79.3 ± 11.4 (61.2–104.8)	67.6 ± 14.6[2] (40.8–101.6)
Height (cm)	177.0 ± 7.0 (153.5–191.5)	161.9 ± 7.5[2] (143.1–182.6)	176.3 ± 6.9 (164.2–187.8)	164.0 ± 7.4[2] (149.7–185.3)
BMI (kg/m^2)	25.6 ± 3.6 (17.1–34.6)	24.8 ± 4.3 (15.9–34.8)	25.5 ± 3.6 (19.2–32.2)	25.0 ± 4.7 (16.5–34.9)
Fat (%)	20.7 ± 7.5 (4.3–35.7)	32.7 ± 9.1[2] (7.8–51.7)	19.8 ± 11.9 (5.4–48.8)	31.8 ± 10.5[2] (8.6–52.4)
ALST mass (kg)	28.7 ± 4.5 (18.4–39.7)	18.0 ± 2.8[2] (11.4–28.0)	28.4 ± 4.4 (20.7–41.5)	19.0 ± 3.3[2] (11.7–31.2)
Total-body SM mass (kg)	33.2 ± 5.7 (19.2–45.9)	20.3 ± 3.4[2] (12.9–31.3)	33.1 ± 6.0 (23.9–50.0)	21.7 ± 3.9[2] (12.0–32.0)

[1] $\bar{x}$ ± SD; range in parentheses. ALST, appendicular lean soft tissue; SM, skeletal muscle.
[2] Significantly different from men within group, $P < 0.001$.

TABLE 2
Developed models for predicting total-body skeletal muscle mass[1]

Model	Independent variable			Intercept	Adjusted R^2	SEE
	ALST mass (kg)	Age (y)	Sex[2]			
						kg
1	1.19 ± 0.01[3,4]			−1.01 ± 0.33[5]	0.96	1.63
2	1.17 ± 0.01[4]	−0.02 ± 0.01[4]		0.35 ± 0.45	0.96	1.58
3	1.13 ± 0.02[4]	−0.02 ± 0.01[4]	0.61 ± 0.31[6]	0.97 ± 0.55	0.96	1.58

[1] ALST, appendicular lean soft tissue.
[2] 0 = female; 1 = male.
[3] Estimate of regression coefficient ± SEE.
[4] $P < 0.001$.
[5] $P = 0.003$.
[6] $P = 0.052$.

performance. In the next phase, the value for total-body SM mass was calculated for each subject in the validation group by using the developed prediction equations. Correlations were then explored between the predicted SM values and the corresponding actual values measured by MRI. The observed differences between predicted and actual total-body SM mass were tested for significance by using Student's *t* tests, and the level of agreement was assessed according to the method of Bland and Altman (19). Data were analyzed by using SPSS version 8.0 (1997; SPSS Inc, Chicago), and statistical significance was set at $P < 0.05$. Group data are expressed as means ± SDs.

RESULTS

Subject characteristics

The baseline characteristics of the model-development group (n = 145 men and 176 women) and of the model-validation group (n = 26 men and 67 women) are presented in **Table 1**. There was no significant difference in BMI between the men (25.6 ± 3.6) and women (24.8 ± 4.3) in the model-development group, although men were heavier, taller, and younger than the women (all $P < 0.001$).

Men had a lower percentage body fat (20.7 ± 7.5% compared with 32.7 ± 9.1%) and a greater total-body SM mass than did the women (33.3 ± 5.7 kg compared with 20.3 ± 3.4 kg; both $P < 0.001$). Men and women in the model-validation group were similar to those in the model-development group, except that women in the model-validation group were younger ($P < 0.001$), were taller ($P = 0.046$), and had greater amounts of ALST ($P = 0.025$) and total-body SM mass ($P = 0.007$) than did the women in the model-development group.

The total sample of 414 subjects was ethnically diverse across both groups: 139 African Americans, 48 Asians, 177 whites, and 50 Hispanics. The racial distribution (%) in the model-development group was as follows (men and women, respectively): 39 and 38 whites, 30 and 39 African Americans, 15 and 12 Hispanics, and 15 and 11 Asians. The racial distribution in the validation group was as follows (men and women, respectively): 58 and 57 whites, 16 and 33 African Americans, 12 and 6 Hispanics, and 16 and 4 Asians.

Prediction models

Model-development

Women had a greater MRI-measured total-body adipose tissue mass than did the men (22.3 ± 9.4 kg compared with 17.6 ± 7.2 kg, $P < 0.001$). Total-body adipose tissue mass was positively correlated with age in men ($r = 0.33$) and in women ($r = 0.34$) (both $P < 0.001$). The slope of the regression line between total-body adipose tissue and age was 0.14 ± 0.03 kg/y in the men and 0.17 ± 0.04 kg/y in the women ($P < 0.001$).

ALST (in kg) was the strongest predictor ($P < 0.001$) of total-body SM mass, explaining 95.7% of the between-subject variance in MRI-measured SM mass (in kg) in model 1 (**Table 2** and **Figure 2**):

$$\text{Total-body SM} = (1.19 \times \text{ALST}) - 1.01 \quad (1)$$

The ratio of total-body SM to ALST was 1.15 ± 0.06 in the men and 1.13 ± 0.08 in the women ($P < 0.001$); the corresponding CVs were 5.2% and 7.1%, respectively.

The inclusion of age ($P < 0.001$) along with ALST in the multiple regression models explained an additional 0.2% of the variance in measured total-body SM mass in model 2 (Table 2):

$$\text{Total-body SM} = (1.17 \times \text{ALST}) - (0.02 \times \text{age}) + 0.35 \quad (2)$$

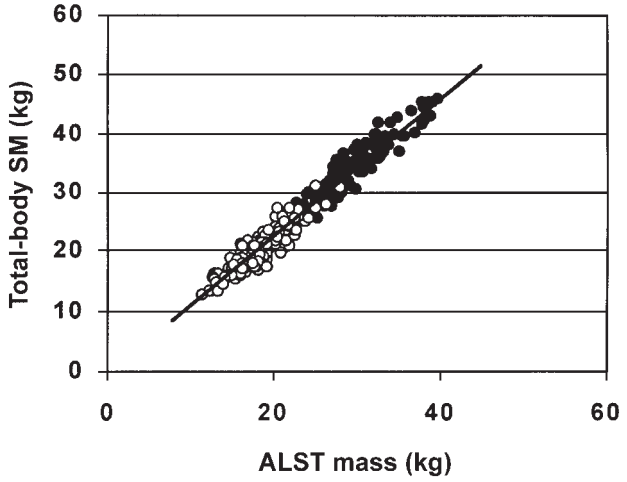

FIGURE 2. Correlation between total-body skeletal muscle (SM) mass estimated by magnetic resonance imaging and appendicular lean soft tissue (ALST) mass estimated by dual-energy X-ray absorptiometry in men (●) and women (○) in the model-development group. Total-body SM mass = (1.19 × ALST) − 1.01. $R^2 = 0.96$, $P < 0.001$, SEE = 1.63 kg. n = 321.

TABLE 3
Skeletal muscle (SM) mass and correlation coefficients in the model-validation group[1]

Model	Independent variable	Measured total-body SM mass	Predicted total-body SM mass	*r*
		kg	*kg*	
1	ALST	24.9 ± 6.9[2]	24.7 ± 6.6	0.96
2	ALST and age	24.9 ± 6.9	24.8 ± 6.6	0.96
3	ALST, age, and sex	24.9 ± 6.9	24.8 ± 6.5	0.97

[1] ALST, appendicular lean soft tissue. The *r* values are for predicted versus measured total-body SM mass.
[2] $\bar{x}$ ± SD.

The ratio of SM to ALST decreased significantly with age in both men (SM/ALST = −0.001 × age + 1.20; $r = 0.27$, $P = 0.001$) and women (SM/ALST = −0.001 × age + 1.18; $r = 0.22$, $P = 0.003$).

Sex (0 = female; 1 = male) was a borderline contributor to predicted total-body SM mass ($P = 0.052$), and the addition of race failed to contribute significantly ($P = 0.42$) to the developed model (model 3, Table 2):

$$\text{Total-body SM} = (1.13 \times \text{ALST}) - (0.02 \times \text{age}) + (0.61 \times \text{sex}) + 0.97 \quad (3)$$

There were no statistically significant interaction terms in model 3.

Model validation

The mean values and correlations between MRI-measured and model-predicted SM mass are presented in **Table 3**. Predicted total-body SM mass values derived from all 3 models did not differ significantly from measured SM mass. Predicted total-body SM mass was highly correlated (all $r \geq 0.96$, $P < 0.001$) with measured SM mass for all 3 models. The addition of age and sex to ALST in the prediction models led to a small increase in the correlation between measured and predicted total-body SM mass (ie, from $r = 0.96$ to 0.97). A Bland-Altman analysis showed no significant between-method bias (eg, model 3, **Figure 3**).

DISCUSSION

The primary aim of this study was to develop and validate a total-body SM mass prediction model based on the widely available DXA method, with MRI used as the reference standard. Practical prediction models were developed and successfully validated in a sex-diverse and ethnically diverse adult population.

SM-prediction models

SM-ALST ratio

Our first level approach was to explore the use of DXA-estimated ALST as the sole SM predictor (ie, SM = $k \times$ ALST). We based this strategy on 2 observations: that ALST is mainly muscle (≈76%) (15, 20) and that a large proportion (≈74%) of total-body SM is in the extremities (Figure 1) (18). These observations indicate that ALST and total-body SM are 2 overlapping components and suggest that there may be a high correlation between the two. The results of the present study support this hypothesis (model 1: $R^2 = 0.96$, SEE = 1.63 kg).

Rough estimates based on earlier reports (15, 18, 20) suggest a *k* value (ie, SM/ALST) of ≈1.0 (ie, 0.76/0.74 = 1.03). Our observed mean values for men (ie, $k = 1.15$) and women (ie, $k = 1.13$) were reasonably close to this estimated value, given the exigencies of defining the appendicular portion of body mass. However, we found in simple and multiple regression analyses that both sex and age moderate the relation between SM and ALST. After adjustment for ALST, women had a smaller SM mass than did men, and the elderly had a smaller SM mass than did young subjects. A smaller *k* value in women may be, in part, secondary to a larger adipose tissue contribution to ALST compared with men. Similarly, the smaller *k* value in the elderly may be secondary to a larger adipose tissue contribution to ALST compared with that observed in young subjects. ALST is composed of muscle,

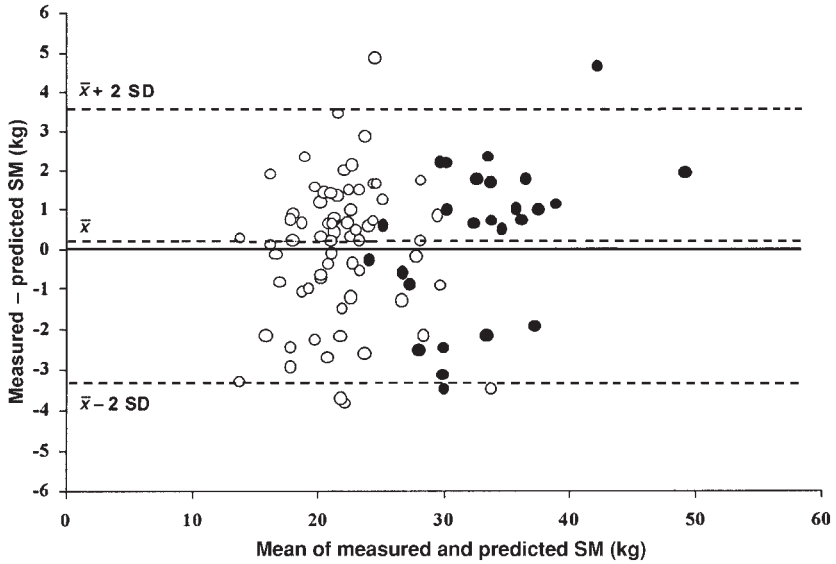

FIGURE 3. Correlation between the difference in measured and predicted total-body skeletal muscle (SM) mass and the mean of measured and predicted SM mass in men (●) and women (○) in the model-validation group. The dashed lines indicate 95% CIs. $n = 93$.

skin, connective tissue, and the lean portion of adipose tissue. In the aging process, SM decreases but other components such as connective tissue and the lean portion of adipose tissue increase. As a result, the SM-ALST ratio probably decreases during the aging process, as observed in our study.

An example of this age and sex effect on the SM-ALST ratio is as follows. Assuming that both SM and ALST are equal to 25 kg in men and young subjects, the corresponding ratio of SM to ALST would be 25/25 = 1.0. If we then assume the same SM mass for women and elderly subjects, there would be an appropriate increase in appendicular adipose tissue of ≈5 kg. About 20% of adipose tissue mass is lean soft tissue (ie, water and protein) and the remaining ≈80% is fat. Therefore, 5 kg adipose tissue includes 1 kg lean soft tissue. When body composition is determined with DXA, this 1 kg lean soft tissue is included in the ALST compartment. The corresponding ratio of SM to ALST is then 25/(25 + 1) = 0.96 for the women and elderly subjects. Women and elderly subjects thus have a smaller SM-ALST ratio than do men and young subjects with an equivalent appendicular SM mass.

Therefore, a simple proportionality SM-prediction model based on an assumed constant *k* value would not be very accurate (CVs for men and women: 5.2% and 7.1%, respectively), and the predicted SM values would also have an age and sex bias. However, this does not negate the possibility of using ALST per se as a surrogate body-composition marker of total-body SM mass, particularly because the R^2 of SM versus ALST was 0.96 with an SEE of 1.63 kg.

Composite regression model

Accordingly, the final developed multiple regression model controlled for age and sex after adjustment for ALST (Table 2; model 3: R^2 = 0.96, SEE = 1.58 kg). Race was not a significant predictor of SM after the 3 other predictor variables were controlled for. Because age and sex are easily acquired predictors, it is reasonable to apply this last model for clinical and research purposes. The low SEE for this model can be compared with the corresponding SM-prediction model SEEs for anthropometry (ie, 2.8 kg), bioimpedance analysis (ie, 2.7 kg), urinary 3-methyl histidine (ie, 2.3 kg), and urinary creatinine (ie, 1.9 kg) (5).

Study limitations

In the present study we applied the regional default option of DXA with manual adjustment to evaluate regional ALST mass. This approach was applied for practical reasons because most trained DXA technicians can obtain the data required for SM mass estimation. However, the possibility exists that even more specific regional appendicular anatomic landmarks can be developed. Moreover, our DXA system was purchased from Lunar Corporation, and we have no information on the comparability of regional estimates across instruments from different manufacturers.

A second proviso regarding the developed models is that the equations are population specific. The models would be inappropriate for use in body builders or in any group that differs substantially from the subjects evaluated in this report. Additionally, the models are not appropriate for use in younger age groups, and there remains a need to develop similar prediction formulas for use in children and adolescents.

A third limitation involves the assumed constant density of SM tissue of 1.04 kg/L (18). Variability in actual SM density may introduce a small error into the MRI-estimated SM.

Last, our models were developed in a cross-sectional cohort and similarly validated in a study group evaluated at only one time point. A need exists for establishing the validity of the models in longitudinally monitored populations, particularly those in whom interventions are part of the study protocol.

Conclusions

In summary, 3 new models for predicting total-body SM mass with the use of DXA were developed and then validated in a large sample of ethnically diverse, healthy, adult men and women. This observation suggests that the new DXA models can provide reliable and accurate estimates of total-body SM mass in adult populations. Further studies are needed to validate the models in other study populations and DXA systems and to evaluate the applicability of these developed formulas in longitudinal studies for the detection of change in SM mass in response to interventions.

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