Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study

BRET H. GOODPASTER,1 CATHERINE L. CARLSON,1 MARJOLEIN VISSER,2,4 DAVID E. KELLEY,1 ANN SCHERZINGER,3 TAMARA B. HARRIS,2 ELIZABETH STAMM,3 AND ANNE B. NEWMAN1

1Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania 15261; 2National Institute on Aging, Bethesda, Maryland 20892; 3Department of Radiology, University of Colorado Health Sciences Center, Denver, Colorado 80261; and 4Institute for Research in Extramural Medicine, Vrije University, Amsterdam, The Netherlands

Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. J Appl Physiol 90: 2157–2165, 2001.—Although loss of muscle mass is considered a cause of diminished muscle strength with aging, little is known regarding whether composition of aging muscle affects strength. The skeletal muscle attenuation coefficient, as determined by computed tomography, is a noninvasive measure of muscle density, and lower values reflect increased muscle lipid content. This investigation examined the hypothesis that lower values for muscle attenuation are associated with lower voluntary isokinetic knee extensor strength at 60°/s in 2,627 men and women aged 70–79 yr participating in baseline studies of the Health ABC Study, a longitudinal study of health, aging, and body composition. Strength was higher in men than in women (132.3 ± 34.5 vs. 81.4 ± 22.0 N·m, P < 0.01). Men had greater muscle attenuation values (37.3 ± 6.5 vs. 34.7 ± 7.0 Hounsfield units) and muscle cross-sectional area (CSA) at the midthigh than women (132.7 ± 22.4 vs. 93.3 ± 17.5 cm², P < 0.01 for both). The strength per muscle CSA (specific force) was also higher in men (1.00 ± 0.21 vs. 0.88 ± 0.21 N·m·cm⁻²). The attenuation coefficient was significantly lower for hamstrings than for quadriceps (28.7 ± 8.7 vs. 41.1 ± 6.9 Hounsfield units, P < 0.01). Midthigh muscle attenuation values were lowest (P < 0.01) in the eldest men and women and were negatively associated with total body fat (r = −0.53, P < 0.01). Higher muscle attenuation values were also associated with greater specific force production (r = 0.26, P < 0.01). Multivariate regression analysis revealed that the attenuation coefficient of muscle was independently associated with muscle strength after adjustment for muscle CSA and midthigh adipose tissue in men and women. These results demonstrate that the attenuation values of muscle on computed tomography in older persons can account for differences in muscle strength not attributed to muscle quantity.

Address for reprint requests and other correspondence: B. H. Goodpaster, E 1140 Biomedical Science Tower, University of Pittsburgh, Pittsburgh, PA 15261 (E-mail: bgood+pitt.edu).

http://www.jap.org

Sarcopenia, the reduction in muscle mass that normally occurs with aging, has been interpreted as the primary reason for the age-related loss of strength (4, 7, 19, 23). However, whether loss of muscle strength in aging can be solely attributed to decreased muscle mass is uncertain (12, 22, 28, 30). Age-related changes in muscle “quality,” in addition to changes in skeletal muscle quantity, may contribute to loss of muscle function in old age. Aging human skeletal muscle has a reduced proportion of glycolytic type II muscle fibers (15) and a diminished muscle fiber contractile ability (16). One query that deserves further consideration is whether there is increased fat content within skeletal muscle in aging and whether this may influence muscle strength and function.

In aging, there is an increased adipose tissue accumulation around muscle concomitant with a reduced muscle cross-sectional area (CSA) (3, 12). These studies have typically quantified muscle and adipose tissue but have not taken advantage of the capability of computed tomography (CT) or magnetic resonance imaging (MRI) to characterize the composition of muscle itself (10). CT differentiates tissues on the basis of their attenuation characteristics, which in turn are primarily a function of tissue density (5). The tissue attenuation characteristics of skeletal muscle therefore provide information about skeletal muscle composition and produce accurate images of the distribution of adipose tissue interspersed around muscle (9, 11, 13). For example, an altered skeletal muscle composition in obese individuals is manifest by a reduced attenuation coefficient on CT, suggestive of an augmented fat infiltration within muscle (11, 13). This regional body composition parameter has been associated with a reduced oxidative enzyme capacity (25) and insulin resistance (11) in muscle. Muscle wasting diseases such as Duchenne muscular dystrophy are also characterized by reductions in muscle mass and attenuation of muscle on CT coincident with impaired muscle function (17). Attenuation characteristics of skeletal muscle have been reported in middle-aged adults (9, 11, 13). Although adipose tissue accumulation in and

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

2157
around muscle has been associated with aging, the attenuation characteristics of aging muscle have not been well described. In addition, data regarding the association between the attenuation characteristics of muscle on CT and muscle strength in the elderly are not available. The purpose of the present study was to test the hypothesis that skeletal muscle composition, assessed by the attenuation characteristics or density of muscle on CT, is associated with muscle strength in elderly individuals. To test this hypothesis, mean CT attenuation values of skeletal muscle were determined in the Health, Aging, and Body Composition (ABC) Study, along with measures of isokinetic strength.

**METHODS**

Participants in the study were recruited for baseline studies of the Health ABC Study, a longitudinal study of 3,075 non-disabled men and women aged 70–79 yr residing in Pittsburgh, PA, and Memphis, TN. The population was 48.5% male and 51.5% white and had a mean age of 73.6 yr. Participants were selected from a random sample of Medicare-eligible adults >65 yr of age from a list provided by the Medicare Agency. Persons were ineligible if they reported difficulty getting around without assisted devices, reported difficulty in performing basic activities of daily living, or reported one-quarter mile or climbing 10 steps without resting, reported life-threatening cancers, were not planning to remain in the area for >=3 yr, or were participating in any research study involving medications or modification of eating or exercise habits. Exclusions from the strength testing were participants with a diagnosis of cerebral aneurysms or bleeding, stroke, hypertension (blood pressure = 200/110 mmHg), severe bilateral knee pain, or prior bilateral knee replacement. Thus 2,627 men and women from the entire Health ABC Study cohort were included in the study. The study was approved by the Universities of Pittsburgh and Tennessee, and written, informed consent was obtained from each volunteer.

Age of participants was determined to the nearest year. Standing height and weight were obtained from each volunteer, and a body mass index (BMI) was calculated as weight (kg)/height (m²). Total body fat was determined using dual-energy X-ray absorptiometry (model QDR 4500, Hologic, Waltham, MA).

**CT of the mid thigh.** Axial CT scans at the mid thigh level were obtained on each participant during their first examination of the Health ABC Study protocol. CT images were acquired in Pittsburgh (9800 Advantage, General Electric, Milwaukee, WI) or Memphis (Somatom Plus 4, Siemens, Erlangen, Germany, or PQ 2000S, Marconi Medical Systems, Cleveland, OH). Patients were imaged in the supine position with the arms above the head and toes directed toward the top of the gantry, with legs extended flat on the table. An anterior-posterior scout scan of the entire femur was used to localize the mid thigh position. The femoral length was measured in cranial-caudal dimension, and the scan position was determined as the midpoint of the distance between the medial edge of the greater trochanter and the intercondylar fossa. This measurement was done on the same leg that was used for isokinetic strength testing, usually the right. A single, 10-mm-thick axial image was obtained at the femoral midpoint, with care taken that the entire circumference of both thighs was included in the field of view. The scanning parameters for this image were 120 kVp and 200–250 mA. Images were then network transferred (TCP/IP protocols) to a SUN workstation (SPARCstation II, Sun Microsystems, Mountain View, CA) for review. A quality review was performed on each subject's images to ensure that all images were present, that the proper scan techniques were used, and that the image was of appropriate quality for analysis.

Skeletal muscle and adipose tissue areas of the thigh were calculated from the axial CT images using proprietary IDL software (RSI Systems, Boulder, CO). Muscle and adipose tissue areas were calculated by multiplying the area of a given pixel as extracted from the image header. The mean attenuation coefficient values of muscle within the regions outlined on the images were determined by averaging the CT number (pixel intensity) in Hounsfield units. The methodological variability of this measure is quite small (8). Skeletal muscle and adipose tissue areas were distinguished by a bimodal image histogram resulting from the distribution of CT numbers in adipose tissue and muscle (24). These peaks are readily separable (10), and the areas of adipose tissue and muscle in the entire image were determined by the areas under their respective peaks of the histogram.

Intermuscular adipose tissue was distinguished from the subcutaneous adipose tissue by manual drawing of a line along the deep fascial plane surrounding the thigh muscles. Once the adipose tissue was segmented from the images, the individual muscles were identified. Muscle borders that were not already defined by adipose tissue were outlined manually, with care taken that no pixels for bone were included in the muscle area. Quadriceps muscles were separated from hamstring muscles with manual tracing (Fig. 1).

**Isokinetic strength testing.** Isokinetic strength of the knee extensors was determined at 60°/s with a dynamometer (model 125 AP, Kin-Com, Chattanooga, TN). Before strength testing, participants warmed-up by performing a long-distance corridor walk as another part of the Health ABC Study.

Fig. 1. Typical computed tomography (CT) image depicting muscle area (gray), subcutaneous adipose tissue (large arrow), and intermuscular thigh adipose tissue (small arrows). Quadriceps (Q) and hamstring (H) muscle groups were distinguished by manual tracing.
protocol. The right leg was tested unless it was injured or weaker by self-report or restricted in motion. After instruction on the procedure, the participant was positioned so that the lateral femoral epicondyle of the knee joint was aligned with the rotational axis of the dynamometer. The participant’s limb was weighed for gravity correction, and start-stop angles were set at 90° and 30°. Two practice trials were performed at 50% effort to familiarize the participant with the procedure and to provide a warm-up period. At least three maximal efforts were performed by each participant. Beginning with the first maximal effort, the torque production over the entire range of motion was plotted, and the plot of each subsequent effort was overlaid on the previous efforts until three similar curves were obtained. Participants were not asked to perform more than six trials. Maximal torque production was recorded as the mean peak torque production from three similar trials. A methodological consideration was whether maximal voluntary effort during isokinetic strength testing represents the true contractile ability of muscle. Electrical stimulation superimposed on maximal voluntary contraction has been demonstrated to produce no additional torque in elderly men and women (14, 28), suggesting that the maximal voluntary effort is a valid measure of strength.

Statistical analysis. ANOVA was used to compare mean muscle and adipose tissue areas, the mean muscle attenuation values, and strength with respect to gender, race, and age. The association between thigh composition and isokinetic knee extensor strength and specific torque (strength/CSA) was determined using simple linear regression analysis. Gender-specific forced multiple linear regression models were fit to determine the independent associations of thigh muscle area and muscle attenuation with maximal isokinetic strength, controlling for age, race, height, and thigh adipose tissue. Gender-specific forced multiple linear regression models were also fit to determine the independent association of thigh muscle attenuation values with specific torque, controlling for age, height, and thigh adipose tissue. Gender-specific models were used in the analysis, because there was little overlap between strength and lean mass in men and women. Because there were no significant race interactions, blacks and whites were collapsed for presentation. All analyses were performed using SAS 6.12 for Windows (SAS Institute, Cary, NC).

RESULTS

Subject characteristics. Subject characteristics are presented in Table 1. The study population was 60% white and 40% black, divided approximately equally among men and women between 70 and 80 yr of age. Because of exclusion criteria for strength testing, 2,627 subjects out of the entire Health ABC Study cohort were included in the study. However, the demographics of the present study participants were similar to those of the entire Health ABC Study cohort. The age of the cohort was well matched according to gender and race. As expected, men were taller and heavier than women, but women had more total body fat than men. Black women had a greater BMI and a higher proportion of body fat than white women, but white men had more body fat than black men.

Muscle attenuation values and CSA by CT. Skeletal muscle attenuation values in this cohort are presented in Table 2. The mean attenuation value for muscle and muscle CSA represent the entire midthigh of the respective leg, i.e., right or left, that was used for isokinetic strength testing. The mean skeletal muscle attenuation values were lower in these elderly women than in men (P < 0.01). Black women had lower mean attenuation values in both muscle groups than white women, but white men had slightly lower mean attenuation values in hamstrings than black men (P < 0.01). CSA of the midthigh was greater in men than in women (Table 2), and this was true for quadriceps and hamstrings (P < 0.01). The mean CT attenuation values and the CSA were lower for hamstrings than for quadriceps across all groups (P < 0.01).

Values for the attenuation of muscle were decreased across increasing quartiles of BMI (Fig. 2) and were negatively associated with BMI in men (r = −0.44, P < 0.01) and women (r = −0.43, P < 0.01). Similarly, the attenuation value for muscle had negative associations with total body fat (r = −0.53, P < 0.01) and total percent fat (r = −0.49, P < 0.01) in this cohort. However, thigh muscle CSA was higher in men and women in the higher-BMI quartiles, and BMI was positively associated with muscle CSA in men (r = 0.61, P < 0.01) and women (r = 0.60, P < 0.01). Thus increased body fatness was associated with larger thigh muscle but with muscle of different composition than in leaner subjects. Figure 2 also illustrates that the attenuation value for muscle decreased as a function of increasing age, so that the oldest men and women had the lowest muscle density. In addition, muscle CSA was also lower with increasing age in these elderly men and women (data not shown). Thus, although advancing age and increased obesity are associated with reduced muscle density in older, healthy adults, the respective effects on muscle size are opposite.
Midthigh adipose tissue content. Adipose tissue area within the midthigh was divided into subcutaneous and intermuscular depots, inasmuch as this later compartment better describes the infiltration of adipose tissue around muscle (Fig. 1). Absolute amounts of intermuscular adipose tissue were much smaller than subcutaneous adipose tissue areas in this cohort (Table 2), representing only 11.7% of the total thigh adipose tissue area. Women and men had similar amounts of intermuscular thigh adipose tissue, but women had substantially more subcutaneous thigh adipose tissue than men, so that the proportion of thigh intermuscular adipose tissue relative to the total thigh adipose tissue was lower in women than in men (8.6 vs. 17.4%, P < 0.01). Black men and women had higher absolute areas of intermuscular and subcutaneous thigh adipose tissue than white men and women, but there were no racial differences in the relative amount of intermuscular adipose tissue depots (12.2 and 11.2% for black and white participants, respectively).

The amount of intermuscular thigh adipose tissue was higher in obesity (BMI) in these elderly men (r = 0.56) and women (r = 0.61, both P < 0.01). Similar associations were observed between the amount of subcutaneous thigh adipose tissue and BMI in men and women (r = 0.69 and 0.73, both P < 0.01, respectively). Moreover, lower mean muscle attenuation values were related to more intermuscular (r = −0.55) and subcutaneous (r = −0.42) thigh adipose tissue (both P < 0.01). Neither of these adipose tissue depots was associated with age within these elderly participants.

Association between attenuation of muscle and strength. Isokinetic strength was greater (P < 0.01) in men than in women (Table 3); black women had higher absolute strength than white women, but there were no racial differences in strength in men. There was a 19% decrease in absolute strength in men and women across this age range. There was a strong association between strength and the CSA of muscle in men (r = 0.55, P < 0.01) and women (r = 0.48, P < 0.01); thus muscle CSA accounted for 25% of the variance in muscle strength independently of gender. To account for the effect of muscle size, strength per unit of CSA

Table 2. Midthigh composition characteristics

<table>
<thead>
<tr>
<th></th>
<th>White Men</th>
<th>Black Men</th>
<th>All Men</th>
<th>White</th>
<th>Black Women</th>
<th>All Women</th>
<th>Entire Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM area, cm²</td>
<td>128.5 ± 19.5</td>
<td>140.2 ± 25.2</td>
<td>132.7 ± 22.4</td>
<td>86.0 ± 14.1</td>
<td>102.5 ± 17.0</td>
<td>93.3 ± 17.5</td>
<td>112.6 ± 28.1</td>
</tr>
<tr>
<td>Quadriceps</td>
<td>60.6 ± 9.4</td>
<td>65.2 ± 12.2</td>
<td>62.2 ± 10.7</td>
<td>40.0 ± 7.0</td>
<td>46.4 ± 8.4</td>
<td>42.9 ± 8.3</td>
<td>52.3 ± 13.6</td>
</tr>
<tr>
<td>Hamstrings</td>
<td>30.0 ± 5.7</td>
<td>33.8 ± 6.8</td>
<td>31.4 ± 6.3</td>
<td>21.3 ± 4.1</td>
<td>25.7 ± 4.5</td>
<td>23.3 ± 4.8</td>
<td>27.2 ± 6.9</td>
</tr>
<tr>
<td>SM attenuation, HU</td>
<td>37.5 ± 6.4</td>
<td>37.0 ± 6.6</td>
<td>37.3 ± 6.5</td>
<td>34.7 ± 7.0</td>
<td>32.7 ± 6.9</td>
<td>33.8 ± 7.0</td>
<td>35.5 ± 7.0</td>
</tr>
<tr>
<td>Quadriceps</td>
<td>43.6 ± 5.8</td>
<td>42.9 ± 6.6</td>
<td>43.4 ± 6.1</td>
<td>39.8 ± 6.9</td>
<td>37.7 ± 6.8</td>
<td>38.9 ± 6.9</td>
<td>41.1 ± 6.9</td>
</tr>
<tr>
<td>Hamstrings</td>
<td>30.0 ± 8.4</td>
<td>31.3 ± 8.5</td>
<td>30.5 ± 8.4</td>
<td>27.4 ± 8.7</td>
<td>26.7 ± 8.7</td>
<td>27.1 ± 8.7</td>
<td>28.7 ± 8.7</td>
</tr>
<tr>
<td>AT area, cm²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermuscular</td>
<td>9.3 ± 5.9</td>
<td>11.2 ± 8.9</td>
<td>10.0 ± 7.2</td>
<td>8.7 ± 4.4</td>
<td>12.5 ± 6.9</td>
<td>10.4 ± 6.0</td>
<td>10.2 ± 6.6</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>46.3 ± 19.7</td>
<td>49.3 ± 21.2</td>
<td>47.4 ± 20.3</td>
<td>96.3 ± 38.6</td>
<td>120.4 ± 52.9</td>
<td>107.0 ± 47.1</td>
<td>77.9 ± 47.1</td>
</tr>
</tbody>
</table>

Values are means ± SD. SM, skeletal muscle; HU, Hounsfield units; AT, adipose tissue. Attenuation refers to the mean attenuation coefficient of muscle. P values for specific comparisons are as follows: gender differences: SM area, 0.0001; SM attenuation, 0.0001; quadriceps area, 0.0001; hamstring area, 0.0001; quadriceps attenuation, 0.0001; hamstring attenuation, 0.0001; intermuscular AT, 0.0760; subcutaneous AT, 0.0001; men race differences: SM area, 0.0001; SM attenuation, 0.1661; quadriceps area, 0.0001; hamstring area, 0.0001; quadriceps attenuation, 0.0668; hamstring attenuation, 0.0076; intermuscular AT, 0.0001; subcutaneous AT, 0.0114; women race differences: SM area, 0.0001; SM attenuation, 0.1661; quadriceps area, 0.0001; hamstring area, 0.0001; quadriceps attenuation, 0.0001; hamstring attenuation, 0.1260; intermuscular AT, 0.0001; subcutaneous AT, 0.0001.

Fig. 2. Mean midthigh muscle attenuation values determined by CT in men and women were lower across increasing body mass index (BMI) quartiles (A) and increasing age (B). HU, Hounsfield units. Differences in mean attenuation coefficients with respect to BMI and age were analyzed using one-way ANOVA. Error bars, SE.
was calculated, and this value was termed specific force.

Men were able to generate higher ($P < 0.01$) specific force than women (Table 3). Specific force in black men and women was reduced compared with that in white men and women. Higher values for the attenuation of muscle were associated with greater torque as well as higher specific force production (Fig. 3). These associ-

**Table 3. Isokinetic strength**

<table>
<thead>
<tr>
<th></th>
<th>White Men</th>
<th>Black Men</th>
<th>All Men</th>
<th>White Women</th>
<th>Black Women</th>
<th>All Women</th>
<th>Entire Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal torque, N•m</td>
<td>130.6 ± 33.1</td>
<td>134.4 ± 37.6</td>
<td>132.3 ± 34.5</td>
<td>78.3 ± 20.0</td>
<td>85.1 ± 24.0</td>
<td>81.4 ± 22.0</td>
<td>106.0 ± 38.5</td>
</tr>
<tr>
<td>Specific torque, torque/cm²</td>
<td>1.02 ± 0.20</td>
<td>0.97 ± 0.22</td>
<td>1.00 ± 0.21</td>
<td>0.91 ± 0.20</td>
<td>0.84 ± 0.21</td>
<td>0.88 ± 0.21</td>
<td>0.94 ± 0.22</td>
</tr>
</tbody>
</table>

Values are means ± SD. See Table 2 footnote for abbreviations. Specific torque, torque per unit cross-sectional muscle area. $P$ values for specific comparisons are as follows: gender differences: torque, $0.0001$; specific torque, $0.0001$; men race differences: torque, $0.0586$; specific torque, $0.0001$; women race differences: torque, $0.0001$; specific torque, $0.0001$.

Fig. 3. Associations between midthigh attenuation values and torque (A) and specific torque (B) in all subjects ($n = 2,627$). Correlation coefficients determined using simple linear regression were 0.20 for attenuation value vs. torque and 0.26 for attenuation value vs. specific torque ($P < 0.01$ for both).
Multivariate models accounting for variance in isokinetic strength in men and women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SE</th>
<th>P</th>
<th>Partial $R^2$</th>
<th>Mean ± SE</th>
<th>P</th>
<th>Partial $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thigh muscle area, cm$^2$</td>
<td>0.857 ± 0.039</td>
<td>0.0001</td>
<td>0.304</td>
<td>0.641 ± 0.035</td>
<td>0.0001</td>
<td>0.248</td>
</tr>
<tr>
<td>Thigh MA, HU</td>
<td>0.455 ± 0.153</td>
<td>0.0029</td>
<td>0.016</td>
<td>0.558 ± 0.090</td>
<td>0.0001</td>
<td>0.030</td>
</tr>
<tr>
<td>Age, yr</td>
<td>−1.034 ± 0.279</td>
<td>0.0002</td>
<td>0.007</td>
<td>−0.608 ± 0.184</td>
<td>0.0010</td>
<td>0.009</td>
</tr>
<tr>
<td>Race</td>
<td>−5.166 ± 1.688</td>
<td>0.0003</td>
<td>0.007</td>
<td>−2.919 ± 1.158</td>
<td>0.0119</td>
<td>0.004</td>
</tr>
<tr>
<td>Height, cm</td>
<td>72.547 ± 12.142</td>
<td>0.0001</td>
<td>0.017</td>
<td>57.307 ± 8.392</td>
<td>0.0001</td>
<td>0.023</td>
</tr>
<tr>
<td>AT, cm$^2$</td>
<td>−0.242 ± 0.140</td>
<td>0.0848</td>
<td>0.002</td>
<td>−0.060 ± 0.112</td>
<td>0.5941</td>
<td>0.000001</td>
</tr>
<tr>
<td>Intermuscular AT</td>
<td>−0.056 ± 0.044</td>
<td>0.2118</td>
<td>0.001</td>
<td>0.029 ± 0.012</td>
<td>0.1711</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Table 4. Multivariate models accounting for variance in isokinetic strength in men and women

Strength values are expressed as units of torque (N·m). Partial variance ($partial R^2$) is the explained variance for each specific parameter in the model. Total variance ($R^2$) by the models was 0.355 for men, 0.315 for women, and 0.628 combined. MA, muscle attenuation for total mid-thigh.
Muscle CSA was lower with age but higher in association with obesity in this cohort. Because of the close association between the loss of muscle mass and diminished muscle function in aging, the precise determination of skeletal muscle mass has been an important consideration in studies of aging and muscle strength. Several indirect methods have been used to quantify muscle CSA in older persons, including anthropometry (2, 23) and manual outlining of muscle area on CT images (27). CT (3) and MRI (7, 12) image analysis software has recently been used to obtain specific measures of muscle CSA in the elderly on the basis of the ability to precisely distinguish muscle from adipose tissue. Our results concur with these CT (3) and MRI (7, 12) studies demonstrating lower muscle CSA in older individuals. The composition of muscle defined by its mean attenuation value was altered independently of these measurable changes in muscle quantity. This result is in accord with prior exercise (26) or weight loss (10) intervention studies reporting changes in muscle density independently of changes in muscle CSA.

Muscle CSA was positively associated with knee extensor strength in these elderly men and women, accounting for ~25% of the variance in strength in men and women. Thus our results confirm those of prior studies (4, 7, 19, 23) in demonstrating that lower muscle strength with age can be largely attributed to a reduction of skeletal muscle. However, the difference in muscle strength between men and women could not be explained solely by differences in muscle size, inasmuch as the explained variance in strength increased to ~50% for the entire cohort when gender was included as a covariate. On the basis of differences in attenuation characteristics between skeletal muscle and adipose tissue, we systematically separated muscle from subcutaneous adipose tissue and, in addition, determined the amount of adipose tissue interspersed between muscle, termed intermuscular adipose tissue. In this process, we were able to quantify muscle CSA exclusive of these different adipose tissue depots but not necessarily the amount of lipid within muscle itself. Subcutaneous and intermuscular thigh adipose tissue were increased with obesity in this older cohort, a result congruent with prior studies in middle-aged adults (10). However, the amount of adipose tissue in the thigh was not associated with the strength or specific force production by muscle. Thus lower muscle CSA, but not the accumulation of these fat depots outside muscle, impacts negatively on strength in these older individuals.

Another important finding in the present study was that higher values for the attenuation of muscle density were associated with greater absolute muscle strength after accounting for the quantity of muscle. Greater muscle attenuation values were also related to better muscle quality as defined by greater specific force production by muscle, i.e., force production per unit muscle size (18, 20). Nearly half the explained variance in specific torque was due to the attenuation values of muscle. Metter and colleagues (18, 20), using CSA or fat-free mass to measure the quantity of muscle, found that specific force production declines with age. Other investigations have also found an altered muscle quality in older persons, as evidenced by a reduced proportion of type II fibers (15) and a reduced force production by individual muscle fibers (16). The age-related increase in the relative proportion of type I muscle fibers, which are known to have a greater lipid content (1), may partly explain the age-associated decrease in muscle density. Our results demonstrate that lower muscle attenuation values are associated with lower muscle quality in the elderly. Quantification of skeletal muscle attenuation characteristics may help define the nonfat component of skeletal muscle, thereby accounting for additional variance in muscle strength.

In support of our findings of an association between altered muscle density and strength, strength training in elderly women has been shown to increase the attenuation of muscle and strength (26). In studies performed in muscular dystrophy (17) and neurological patients (21), whose muscle wasting closely resembles that of age-related sarcopenia, it was noted that an increased fatty infiltration was associated with reduced force generation in skeletal muscle. However, these studies were based on a small number of patients, and only one of these studies quantified the muscle density (17). It is possible that factors other than lipid contained within muscle, such as connective tissue, contribute to alterations in the attenuation characteristics of muscle. However, attenuation of muscle is correlated with direct measures of muscle fiber lipid content determined by muscle biopsy (8).
Lower skeletal muscle attenuation values on CT have also been associated with diminished muscle function as defined by reduced oxidative enzyme capacity (25), lower maximal aerobic capacity (11), and insulin resistance (11). It is possible that lower physical activity levels correspond to lower muscle attenuation values in this elderly cohort and that fatty infiltration of muscle as captured by muscle density (8, 17) is a marker for these other physiological parameters. Whether an altered muscle composition is a cause or a consequence of diminished function and the influence of physical activity levels on muscle density and muscle quality is a topic for further investigation.

A large number of elderly adults were included in the present investigation, but only relatively healthy older adults were recruited to the study at baseline; the most frail men and women, whom we can assume were weaker, were excluded on the basis of the criteria set forth. Omitting these very frail individuals from the study likely limited our power to examine the relationships between muscle composition and strength in the elderly. Another limitation of this present cross-sectional study was that a relatively narrow age range of individuals was recruited to the study, severely challenging the ability of regression analysis to detect meaningful associations between muscle attenuation characteristics and strength by age. Thus the associations between parameters of muscle composition and strength by age were likely underestimated because of the relatively homogenous age range studied. Nevertheless, one of the major strengths of this study was that important associations between muscle composition and strength were observed, since the heterogeneity within the cohort was not due to age but, rather, to differences in BMI and muscle composition. It is likely that only a large-scale study with a broad range of body composition such as this could detect these associations in such a narrow age range of nondisabled elderly adults. Thus this study serves as a valuable reference for examination of age-associated changes in muscle composition and function.

In summary, these results demonstrate that that lower attenuation values for muscle on CT, but not the adipose tissue around muscle, were associated with lower muscle strength in these older adults and that this was independent of the muscle CSA or quantity of muscle. The other novel and important finding was that the attenuation of skeletal muscle was lower in older men and women and was lower with obesity. We have provided detailed quantification of the attenuation characteristics of muscle, which represent an important and novel parameter of muscle composition. These findings will be important in interpreting results from interventional investigations directed at preventing sarcopenia associated with aging. Future longitudinal studies examining changes in muscle composition will provide further insight into factors contributing to the loss of muscle strength and function in older adults independent of the age-related loss of skeletal muscle.

We thank the volunteers for their participation in the study. We also appreciate the technical expertise of the clinical and radiology staffs.

This project was supported by National Institute on Aging Grants N01-AG-6-2106, N01-AG-6-2102, and N01-AG-6-2103. B. H. Goodpaster was supported by National Institute on Aging Career Development Award K01-AG-00851.

REFERENCES


