Muscle-specific atrophy of the quadriceps femoris with aging

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Trappe, T.A., D.M. Lindquist, and J.A. Carrithers. Muscle-specific atrophy of the quadriceps femoris with aging. J Appl Physiol 90: 2070–2074, 2001.—We examined the size of the four muscles of the quadriceps femoris in young and old men and women to assess whether the vastus lateralis is an appropriate surrogate for the quadriceps femoris in human studies of aging skeletal muscle. Ten young (24 ± 2 yr) and ten old (79 ± 7 yr) sedentary individuals underwent magnetic resonance imaging of the quadriceps femoris after 60 min of supine rest. Volume (cm³) and average cross-sectional area (CSA, cm²) of the rectus femoris (RF), vastus lateralis (VL), vastus intermedius (VI), vastus medialis (VM), and the total quadriceps femoris were decreased (P < 0.05) in older compared with younger women and men. However, percentage of the total quadriceps femoris taken up by each muscle was similar (P > 0.05) between young and old (RF: 10 ± 0.3 vs. 11 ± 0.4; VL: 33 ± 1 vs. 33 ± 1; VI: 31 ± 1 vs. 31 ± 0.4; VM: 26 ± 1 vs. 25 ± 1%). These results suggest that each of the four muscles of the quadriceps femoris atrophy similarly in aging men and women. Our data support the use of vastus lateralis tissue to represent the quadriceps femoris muscle in aging research.

magnetic resonance imaging; rectus femoris; vastus lateralis; vastus intermedius; vastus medialis

THE QUADRICEPS FEMORIS MUSCLE is composed of the rectus femoris, vastus lateralis, vastus intermedius, and vastus medialis. However, the vastus lateralis muscle has been used for nearly 40 yr to represent the quadriceps femoris in human muscle physiology and biochemistry studies (4–6). Many aerobic and resistance exercise investigations have studied muscle samples from the vastus lateralis while simultaneously examining function of the entire quadriceps femoris (1, 22, 23, 25). This vastus lateralis–quadriceps femoris supposition is also being used extensively in aging muscle research (8–11, 13, 26). However, it has never been determined whether all four muscles of the quadriceps femoris change similarly with aging.

Recently, noninvasive measures such as computed tomography (CT) and magnetic resonance imaging (MRI) have allowed for the accurate determination of muscle size (7, 15, 20). In particular, MRI resolution allows for the discrimination of the muscles of a specific muscle group (e.g., the four muscles of the quadriceps femoris). The purpose of this study was to address the appropriateness of the vastus lateralis as a surrogate for the quadriceps femoris in aging studies. Specifically, we hypothesized that the vastus lateralis would atrophy to the same degree as the other three muscles of the quadriceps femoris in aging women and men.

METHODS

Subjects. Ten young (5 male, 5 female) and ten old (5 male, 5 female) individuals were included in this investigation (Table 1) after a physical examination that included blood and urine analyses and an interview documenting the subject’s life history of physical activity. Subjects were excluded if they had any acute or chronic illness, cardiac abnormalities, uncontrolled hypertension, insulin- or non-insulin-dependent diabetes, abnormal blood or urine chemistries, arthritis, or history of neuromuscular problems or if they smoked cigarettes. Women taking oral contraceptives or hormone replacement therapy were included. It was our intent to carefully screen the subjects so as to include lifelong-sedentary, healthy older and younger individuals; therefore, we excluded individuals who had ever completed any formal exercise programs or physical activity outside of their activities of daily living. Body composition was determined using whole body air displacement plethysmography (Life Measurement Instruments, Concord, CA) (14). All procedures, risks, and benefits associated with the experimental testing were explained to the subjects before they signed a consent form adhering to the guidelines of the Institutional Review Board of the University of Arkansas for Medical Sciences.

MRI. After 1 h of supine rest to control for the influence of posturally related fluid shifts on muscle size (3), MRIs were obtained for each subject. Subjects were supine, and their heels were fixed on a nonmetallic support to control joint and scan angle and to minimize compression of the legs against the patient’s back. MRI investigations were explained to the subjects before they signed a consent form adhering to the guidelines of the Institutional Review Board of the University of Arkansas for Medical Sciences. Subjects underwent MRI scanning in the axial and coronal orientations. A pretest axial scout scan (repetition time/echo time [TR/TE] = 500/14, field of view 48, 256 x 160 matrix) was acquired for each subject. An axial T1-weighted spin echo scan was obtained (TR/TE = 500/14, field of view 48, 256 x 160 matrix) for the left and right quadriceps femoris muscles. 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.

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Muscle volume (cm³) was calculated by multiplying the RF, VL, VI, and VM and summed for the total quadriceps analyzed slices for an individual muscle and determined for the ant leg of each subject was analyzed for CSA and volume. The average CSA (cm²) was taken as the average of all the slices containing RF (7), because this region has been shown to represent the maximal CSA of the thigh (17, 20). The dominant leg of each subject was analyzed for CSA and volume. The average CSA (cm²) was taken as the average of all the analyzed slices for an individual muscle and determined for the RF, VL, VI, and VM and summed for the total quadriceps femoris. Muscle volume (cm³) was calculated by multiplying the CSA of each individual muscle by the slice thickness (1 cm) for all analyzed images of the RF, VL, VI, and VM and summed for the total quadriceps femoris.

All measurements were made by the same investigator. In our laboratory, coefficients of variation for measurements made on separate days on the same individuals were 3.6, 1.4, 2.9, 2.6, and 1.4% for RF, VL, VI, VM, and total quadriceps femoris, respectively. The coefficients of variation measuring the same image were 0.3, 1.1, 0.2, 1.3, and 0.2% for RF, VL, VI, VM, and total quadriceps femoris. 

Statistics. A one-way analysis of variance was completed on the group (men and women combined) data for subject characteristics, individual muscle volume, and CSA of the quadriceps femoris, and the percentage of the individual muscle volume and CSA of the quadriceps femoris. Significance was accepted at $P < 0.05$.

RESULTS

Both the volume and average CSA decreased from young to old in the individual muscles and the whole quadriceps femoris (Tables 2 and 3). However, the percentage (volume or average CSA) of the quadriceps that each muscle comprised was unchanged with aging (Fig. 3). Figure 2 shows a representative MRI and CSA data from an old and young subject.

**DISCUSSION**

Two important findings in the present study support the use of the VL as a surrogate of the quadriceps femoris in studies of aging skeletal muscle. First, significant differences existed between the old and young in absolute size of each of the four quadriceps femoris muscles (i.e., aging muscle atrophy). Second, the proportion of the total volume or area of the quadriceps femoris that each of the four muscles comprised was not different between old and young individuals. Taken together, these two findings suggest that the four muscles that make up the quadriceps femoris likely atrophy to the same extent in aging men and women.

These findings are important when one considers the large number of cross-sectional and longitudinal investigations of aging human skeletal muscle that have used or are using the vastus lateralis muscle tissue to represent the quadriceps femoris. For example, studies have examined the CSA of muscle fibers from the vastus lateralis of young to old individuals and then compared these differences with knee extensor (quadriceps femoris) strength in the same individuals (12, 24). Other studies have examined the fractional synthetic rate of muscle proteins from vastus lateralis biopsy tissue of 20- to 92-yr-old women and men and related the differences to quadriceps femoris muscle strength (2). From our data, it appears that these and other similar comparisons are likely appropriate.

To our knowledge, no one has previously addressed the issue presented in the present paper with a direct

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Age, yr</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>Body Fat, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Young</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YM</td>
<td>24 ± 2 (22–27)</td>
<td>173 ± 9 (160–188)</td>
<td>67.8 ± 12.3 (49.7–89.4)</td>
<td>23 ± 8 (12–37)</td>
</tr>
<tr>
<td>OM</td>
<td>79 ± 7 (72–83)</td>
<td>167 ± 10 (150–152)</td>
<td>71.5 ± 7.8 (58.3–83.9)</td>
<td>35 ± 11 (18–51)*</td>
</tr>
<tr>
<td><strong>Old</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YM</td>
<td>24 ± 2 (22–27)</td>
<td>180 ± 6 (175–188)</td>
<td>77.4 ± 8.2 (67.0–89.4)</td>
<td>20 ± 7 (12–31)</td>
</tr>
<tr>
<td>OM</td>
<td>81 ± 8 (73–93)</td>
<td>175 ± 5 (170–182)</td>
<td>74.6 ± 5.7 (69.0–83.9)</td>
<td>25 ± 5 (18–30)</td>
</tr>
<tr>
<td>*<em>Values are means ± SD. n = 10 in young (Y) and old (O) groups; 5 men (M) and 5 women (F). Nos. in parentheses are range. <em>Different (P &lt; 0.05) from young group.</em></em></td>
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<tr>
<th>Table 2. Volumes of the quadriceps femoris muscles</th>
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<tbody>
<tr>
<td><strong>Rectus Femoris</strong></td>
</tr>
<tr>
<td><strong>Young</strong></td>
</tr>
<tr>
<td><strong>Old</strong></td>
</tr>
<tr>
<td><strong>YM</strong></td>
</tr>
<tr>
<td><strong>OM</strong></td>
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<tr>
<td><strong>YP</strong></td>
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<tr>
<td><strong>OF</strong></td>
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</tbody>
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*Values are means ± SE in cm³. *Different (P < 0.05) from young group.
or indirect sampling of all of the quadriceps femoris muscles. However, we do recognize the underlying methodological impediment as the basis for the lack of relevant data. Recently, using similar MRI methodology to that used in the present study, it has been shown, in a nonaging model of human muscle atrophy, that the individual muscles of the quadriceps femoris atrophy to varying degrees (27). Thus, in conjunction with our ongoing studies of aging skeletal muscle, we thought it was necessary to address this issue in an aging population.

Our data compare favorably with literature values of total quadriceps femoris muscle size in young and old (7, 10, 11, 15–17) and individual muscles of the quadriceps femoris from young subjects by means of MRI (7, 15, 17). Furthermore, the 27% difference in CSA (−31% in volume) of the total quadriceps femoris from young to old in the present study is comparable to calculated differences in reported values from studies that have examined only young (7, 15–17) or old individuals (10, 11).

The young and old study groups contained equal numbers of men and women. However, we did not power the study to examine gender responses as well as aging responses. We have included the subset of male and female data in Tables 1–3 to represent the gender responses. These data show that the gender response is similar to the group (men and women combined) response. That is, the absolute size of the muscles was smaller in both older women and men,

<table>
<thead>
<tr>
<th></th>
<th>Rectus Femoris</th>
<th>Vastus Lateralis</th>
<th>Vastus Intermedius</th>
<th>Vastus Medialis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>6.0 ± 0.3</td>
<td>20.9 ± 0.9</td>
<td>19.6 ± 1.4</td>
<td>16.9 ± 1.3</td>
<td>63.4 ± 3.7</td>
</tr>
<tr>
<td>Old</td>
<td>5.0 ± 0.3*</td>
<td>15.1 ± 1.0*</td>
<td>14.5 ± 1.0*</td>
<td>11.8 ± 1.1*</td>
<td>46.4 ± 3.4*</td>
</tr>
<tr>
<td>YM</td>
<td>6.8 ± 0.2</td>
<td>22.8 ± 1.3</td>
<td>23.3 ± 1.0</td>
<td>20.6 ± 0.5</td>
<td>73.5 ± 2.5</td>
</tr>
<tr>
<td>OM</td>
<td>5.8 ± 0.4</td>
<td>17.2 ± 1.4</td>
<td>16.8 ± 1.3</td>
<td>14.2 ± 1.5</td>
<td>53.9 ± 4.1</td>
</tr>
<tr>
<td>YF</td>
<td>5.3 ± 0.2</td>
<td>19.0 ± 0.7</td>
<td>16.0 ± 1.0</td>
<td>13.2 ± 1.0</td>
<td>53.4 ± 1.8</td>
</tr>
<tr>
<td>OF</td>
<td>4.2 ± 0.3</td>
<td>13.0 ± 0.8</td>
<td>12.1 ± 0.7</td>
<td>9.5 ± 0.7</td>
<td>38.8 ± 2.3</td>
</tr>
</tbody>
</table>

Values are means ± SE in cm². *Different (P < 0.05) from young group.

thought it was necessary to address this issue in an aging population.

Our data compare favorably with literature values of total quadriceps femoris muscle size in young and old (7, 10, 11, 15–17) and individual muscles of the quadriceps femoris from young subjects by means of MRI (7, 15, 17). Furthermore, the 27% difference in CSA (−31% in volume) of the total quadriceps femoris from young to old in the present study is comparable to calculated differences in reported values from studies that have examined only young (7, 15–17) or old individuals (10, 11).

The young and old study groups contained equal numbers of men and women. However, we did not power the study to examine gender responses as well as aging responses. We have included the subset of male and female data in Tables 1–3 to represent the gender responses. These data show that the gender response is similar to the group (men and women combined) response. That is, the absolute size of the muscles was smaller in both older women and men,
comparing with their younger gender counterparts. Furthermore, the percentage of the total quadriceps femoris taken up by each muscle was similar in both women and men with aging.

In presenting these data, we realize that specific biochemical, molecular, or physiological analyses were not completed on tissue obtained from each muscle of the quadriceps femoris from our subjects. One further consideration when interpreting our data is the possibility of age-related increases in nonmuscle (i.e., fat and connective) tissue. It has been shown that the amount of nonmuscle tissue increases in both arm (21) and leg (19) muscles with aging. However, there are no data to suggest that with aging there is a disproportionate increase in the nonmuscle composition of the individual quadriceps femoris muscles. This does, however, emphasize the need for more studies of muscle specific atrophy.

Other methodologies are needed to address the issue of muscle specific atrophy, especially for those muscles that are unavailable to the muscle biopsy technique due to location or size. Promising approaches for the study of multiple components of the quadriceps femoris and other muscle groups are magnetic resonance spectroscopy coupled with MRI as well as positron emission tomography (18, 28). Both of these methods allow for study of multiple components of the quadriceps femoris that are unavailable to the muscle biopsy technique and are magnetic resonance specific atrophy, especially for those muscles that are unavailable to the muscle biopsy technique due to location or size. Promising approaches for the study of multiple components of the quadriceps femoris and other muscle groups are magnetic resonance spectroscopy coupled with MRI as well as positron emission tomography (18, 28). Both of these methods allow for study of multiple components of the quadriceps femoris that are unavailable to the muscle biopsy technique and are magnetic resonance imaging.

In conclusion, the present data support the continued use of the vastus lateralis as a surrogate for the quadriceps femoris in studies of aging human skeletal muscle. Future studies of muscle samples, or other innovative measurements, taken from more than one muscle of the quadriceps femoris in cross-sectional and longitudinal studies of aging would further help address this issue.

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