significant increase in fat-free mass (FFM) (11). This of the midthigh, whereas DEXA could not detect an increase in muscle mass was detected by using a single-slice CT subject to a strength-training program, an increase of DEXA (11). Specifically, in elderly women documented (9), concerns have been raised regarding relationship between adipose tissue and skeletal muscle measures is well evidenced in wasting illnesses (5, 18), and obesity (7). Determinations of skeletal muscle mass and body fat distribution largely depend on imaging techniques (computed tomography (CT) or magnetic resonance imaging (MRI)) (6, 13, 18) or dual energy X-ray absorptiometry (DEXA) (7). Although the accuracy of CT and MRI with respect to adipose tissue and skeletal muscle measures is well documented (9), concerns have been raised regarding the validity of DEXA (11). Specifically, in elderly women subjected to a strength-training program, an increase in muscle mass was detected by using a single-slice CT of the midthigh, whereas DEXA could not detect a significant increase in fat-free mass (FFM) (11). This might indicate that DEXA provides inaccurate or imprecise measures of appendicular tissue composition.

Jensen et al. (3) and others (15) have noted that DEXA compares favorably with imaging assessments of truncal body fat. If DEXA does not perform equally well over the extremities, this could explain the reported inability of DEXA to detect the increase in muscle size (11). Wang et al. (18) reported a good (r = 0.95, P = 0.0001) correlation between DEXA measures of appendicular FFM and a multislice-CT assessment of skeletal muscle mass but noted that DEXA consistently overestimated muscle mass relative to the CT technique. They suggested that differences in the ratio of appendicular to total body skeletal muscle obtained by using the DEXA might account for the discrepancies, but, because the 22-slice CT method did not provide sufficiently accurate measures of appendicular skeletal muscle, this possibility could not be directly tested.

Another possible explanation for the observed discrepancy is the differences in tissue "types" assessed by the two different approaches. CT and MRI can provide volume (and, therefore, mass) measures of skin, skeletal muscle, and adipose tissue (with its attendant nonfat components), whereas DEXA provides information regarding the mass of fat (primarily triglyceride) and nonfat tissues being scanned (8). Although extremity FFM determined by DEXA is primarily skeletal muscle (2), there may be systematic differences between DEXA-measured FFM and CT-measured skeletal muscle (18). These differences could vary among individuals depending on the amount of non-skeletal muscle fat-free tissue in the extremity.

Multislice CT is considered a "gold standard" for measurement of tissue mass in light of the extensive validation studies confirming its accuracy (9) for body composition studies. A single-slice-CT-measured thigh appears to be quite useful in the context of muscle strength determinations (12), but the relationship between this measure and tissue mass measurements such as DEXA does not appear to have been specifically addressed. This study was originally designed to determine whether the relationship between DEXA-measured thigh FFM and thigh skeletal muscle (single-slice CT) was sufficiently good to allow one to be used in place of the other. On the basis of our initial findings, we proceeded with additional studies to examine the potential reasons for the lack of ideal agreement between these two measures.

Accurate measurements of skeletal muscle and fat mass in humans are important for studies of aging (10), wasting illnesses (5, 18), and obesity (7). Determinations of skeletal muscle mass and body fat distribution largely depend on imaging techniques (computed tomography (CT) or magnetic resonance imaging (MRI)) (6, 13, 18) or dual energy X-ray absorptiometry (DEXA) (7). Although the accuracy of CT and MRI with respect to adipose tissue and skeletal muscle measures is well documented (9), concerns have been raised regarding the validity of DEXA (11). Specifically, in elderly women subjected to a strength-training program, an increase in muscle mass was detected by using a single-slice CT of the midthigh, whereas DEXA could not detect a significant increase in fat-free mass (FFM) (11). This
MATERIALS AND METHODS

Subjects

Informed, written consent was obtained from all volunteers that participated in the two separate studies described in this report. The first study was conducted to test the relationship between skeletal muscle area measured by single-slice midthigh CT scan and thigh FFM measured by DEXA. Forty-three volunteers (25 women and 18 men, age 39 ± 13 yr) participated in this study. A second study was deemed necessary on the basis of the result of the first experiment. For the second experiment, measures of thigh muscle and adipose tissue volume were made by using multislice CT of the legs. These results were compared with thigh fat and FFM measured by DEXA. Fifteen men and fifteen women, age 33 ± 8 yr, participated in the second study.

Measurements

CT measurements of thigh tissue composition. CT was performed with an Imatron C150 (Imatron, San Francisco, CA) CT scanner. Scanning was performed at 130-kVp exposure; exposure and scanning times were 0.1 and 0.4 s. Slice thickness was 6 mm. For the first study, the location of the single-slice CT of the midthigh was one-half of the distance from the cephalad aspect of the patella to the greater trochanter. For the second study, CT images were obtained beginning 5 cm below the perineum in men (to avoid testicular X-ray exposure) and beginning at the perineum in women, continuing at 2-cm intervals to the level of the knee. CT images from each volunteer were examined to assess the Hounsfield units (HU) most representative of adipose tissue and muscle (3). After identification of the appropriate HU for nonbone, nonadipose tissue (primarily skeletal muscle and skin), the entire area with these HU was measured for each slice, after which the skin was erased from the image to assess the amount of skeletal muscle in each CT image. To more easily “erase” skin (which has the same HU as skeletal muscle), a software program was written (by J. E. Reed) that automatically removes the outer two voxel layers (1.83–2.62 mm) of the air-tissue interface for each image.

DEXA measurements of thigh tissue composition. A DPX-IQ (Lunar Radiation, Madison, WI) (4) was used to obtain regional tissue composition analysis (software version 4.1) for both the first and second study. For the second study, care was taken to ensure that identical lengths of thigh were included for the CT scans and the DEXA. This was accomplished by using the cephalad margin of the patella as a landmark (it can be readily identified on both the CT and DEXA images) and including as many CT slices in the direction of the perineum as were available. The distance covered by these slices for each individual was then used to ensure that the identical distance was included in the DEXA region of interest, also by using the cephalad aspect of the patella as a landmark.

Chemical analysis (1) of human adipose tissue obtained from a surgical panniculectomy specimen was performed to assess the relative proportions of fat and nonfat in our laboratory.

Calculations and Statistics

Because the CT images collected for the second study were taken at 2-cm intervals, total thigh tissue composition was calculated by summing the areas of the slices and multiplying the value by 2. We also estimated a more gradual transition between slices by interpolating a value one-half way between each slice as the “1-cm” value for bone, adipose, and nonadipose (skeletal muscle and skin) area. These areas were also summed to predict the volumes. The interpolation method yielded values ~1.5% less than the noninterpolated method for both muscle and adipose volumes. The interpolated volumes were used for comparison with DEXA values. To convert the volume of thigh muscle and skin measured by CT, we assumed their density to be 1.04 (14) and 1.1 g/cm³ (14), respectively. This permitted comparison with the thigh FFM (g) measured by DEXA.

All values are expressed as means ± SD. To compare the thigh tissue volumes assessed by CT vs. thigh tissue mass assessed by DEXA, a paired t-test was used. DEXA-measured total thigh fat was compared with CT-measured thigh adipose tissue by using a paired t-test. Univariate linear regression analysis was used to assess the predicted value of DEXA- to CT-measured thigh adipose tissue and muscle mass. To determine whether the measure of DEXA-measured fat mass contributed to the ability of DEXA-measured FFM to predict CT-measured skeletal muscle mass, multivariate linear regression analysis was used.

RESULTS

Subjects

The volunteers in study 1 were 172 ± 9 cm tall and weighed 75.9 ± 12.1 kg. The body mass index (BMI) of these volunteers was 25.5 ± 6.6 kg/m². The volunteers in study 2 were 170 ± 9 cm tall, weighed 78.0 ± 16.1 kg, and had BMI of 27.0 ± 5.4 kg/m².

Fat Content of Human Adipose Tissue

As determined by chemical analysis, the human adipose tissue block was 87% lipid.

CT vs. DEXA: Study 1

The CT areas for adipose tissue and muscle were 196 ± 87 and 266 ± 70 cm², respectively. Thigh fat and FFM as measured by DEXA for the same subjects was 5.38 ± 1.43 and 9.46 ± 2.30 kg, respectively. There was a positive (r = 0.86, P < 0.0001) correlation between CT-measured muscle area and thigh FFM as measured by DEXA (Fig. 1). Thus DEXA measures of leg FFM accounted for <75% of the interindividual variance in CT-measured skeletal muscle area. To determine whether this less-than-ideal agreement was related to problems with the DEXA measurements or the possibility that a single CT image provides an insufficient sample of thigh tissue composition, the second study was performed.

CT vs. DEXA: Study 2

The length of thigh tissue included in the comparison analysis was 25 ± 3 cm. The thigh adipose tissue volume by CT was 3,764 ± 2,184 cm³, and thigh fat mass by DEXA was 3,394 ± 1,957 g. Adipose tissue volume by CT was, therefore, ~10% greater (P < 0.0001) than DEXA-measured fat mass. There was a strong relationship (Fig. 2) between CT-measured leg adipose tissue volume and DEXA-measured leg fat (r² = 0.96, P < 0.0001). The intercept was not significantly different from 0; however, the slope (1.08) was significantly >1.0.
CT-measured leg muscle and skin mass were 5,852 ± 1,251 and 400 ± 93 g, respectively. Leg FFM as measured by DEXA (6,557 ± 1,385 g) was greater than leg muscle mass (P < 0.00001) or leg muscle plus skin (6,251 ± 1,242 g; P < 0.001) as measured by CT. The relationship between CT-determined leg muscle mass and DEXA-measured leg FFM was excellent (r² = 0.96, P < 0.0001). The intercept of the formula describing this relationship was not significantly different from 0; however, the slope was significantly, 1 (Fig. 3) at 0.88. DEXA overestimated thigh muscle mass by 705 ± 306 g (a 12 ± 5% overestimate) and thigh muscle plus skin mass by 306 ± 350 g (a 5 ± 6% overestimate).

DEXA-measured leg FFM could be greater than CT-measured muscle mass for several reasons. Skin would be included in leg FFM assessed by DEXA, but it is excluded by CT techniques. This does not explain the discrepancy completely, however, because CT-measured skin plus muscle mass was significantly less than DEXA-measured leg FFM. Adipose tissue is only ~85% lipid (16), and, therefore, the nonfat components of adipose tissue might be included in DEXA-measured leg FFM, leading to an overestimate of skeletal muscle mass. To test this possibility, we performed multiple linear regression analysis by using CT-measured skeletal muscle as the dependent variable and DEXA-measured FFM and fat mass as independent variables; DEXA-measured fat contributed (P = 0.06) to the ability of DEXA-measured FFM to predict CT-measured skeletal muscle mass. There was not a statistically significant relationship between the DEXA-measured FFM overestimate of skeletal muscle (DEXA-measured thigh FFM – CT-measured thigh skeletal muscle mass) and DEXA-measured thigh fat mass. We note, however, that only four of the volunteers had more that 6.0 kg of thigh fat, which might make it difficult to detect such a statistical association given the relatively minor contribution of nonfat components to adipose tissue mass.

Effects of Position on CT-Measured Thigh Tissue Areas

Some investigators use a single mid thigh CT image to assess leg skeletal muscle and adipose tissue areas, relying on exact repositioning to make comparison measurements. To assess the effects of slight differences in positioning on CT measures of mid thigh tissue areas, we compared two consecutive CT slices from the mid thigh region from each individual in the second study. The differences in CT areas between the first and second images for skeletal muscle and adipose tissue...
Discussion

The cross-sectional muscle area, as measured by a midthigh CT, is an excellent correlate of muscle strength (12), and DEXA are also used to measure appendicular tissue composition, which are important data for studies of energy and adipose tissue metabolism. Systematic differences between DEXA and CT measures of skeletal muscle mass have been reported (9); however, the nature of these differences has not been completely identified. The present studies were initially conducted to determine whether DEXA-measured leg tissue composition is an acceptable substitute for CT imaging of the midthigh. Because the DEXA results and the single-slice CT values were in less-than-ideal agreement, we performed additional studies to test the hypothesis that the majority of the discrepancy was related to adequate sampling of leg tissue composition by CT. We found that multislice CT and DEXA measures of thigh soft tissue composition were extremely well correlated; however, thigh FFM by DEXA consistently overestimates CT-measured thigh skeletal muscle, and DEXA thigh fat was consistently less than CT-measured thigh adipose tissue. The significant non-fat component (~15%) of adipose tissue (16) might contribute to the systematic discrepancies between the two methods. It could also account for the apparent contribution of DEXA-measured thigh fat (in addition to DEXA FFM) to explain the interindividual variation in skeletal muscle mass in our multiple linear regression analysis.

DEXA measures of appendicular FFM include skin, which in this study contributed 9 ± 2% (range 6–13%) of values in the HU range of muscle and skin, as well as the fat-free components of adipose tissue. The range of values for thigh adipose tissue volume in study 2 was 0.819–7.342 liters, which could potentially contribute from 0.123 to 1.101 liters of “fat free tissue” to thigh mass. DEXA-measured appendicular FFM would likely be less representative of skeletal muscle mass in the later case than in the former. Despite the excellent agreement between CT (or MRI) and DEXA measures of limb tissue composition, DEXA estimates of skeletal muscle mass will not likely be as sensitive to small changes as would CT measures, because variations in adipose tissue (or skin) mass over time could confound the values. We do not interpret this to indicate that DEXA measures are inaccurate, merely that they are fundamentally different and must be interpreted with caution. Similarly, if thigh soft tissue composition is being measured for the primary purpose of relating muscle strength to tissue composition, and comparisons are to be made between individuals with substantially different amount of adipose tissue, it may not be appropriate to rely solely on DEXA estimates of skeletal muscle mass.

The significant variability in thigh skeletal muscle and adipose tissue areas between two consecutive CT slices 2 cm apart merits comment. If paired measures are planned, extreme care must be taken with regard to positioning of the volunteers, or the ability to detect changes over time will be severely limited. Similarly, our results indicate that a single-slice CT of the midthigh is not a good predictor of the tissue composition of the entire thigh. Within the limits described above, the combined use of DEXA and a single-slice CT of the thigh may provide comprehensive tissue composition information that can be used in relating both muscle strength and metabolic measures to leg tissue composition, even when paired studies are planned in heterogeneous groups.

Wang et al. (17) recently reported that DEXA estimates of regional skeletal muscle in men were slightly, but significantly, greater than CT-measured skeletal muscle mass, despite the application of a sophisticated model that attempted to account for skin, adipose tissue FFM, and connective tissue. Their new model provided much more accurate estimates of regional skeletal muscle mass relative to the previous DEXA-based model (17), but the authors note the r² and SE of estimate were not improved with the newer model. They considered possible implication from the use of only three to four CT images per region, model errors, and the use of multiple measurements from the DEXA to derive compartments as potential explanations for the failure to observe a better correlation between the two approaches. They also noted the need to include obese individuals and women in future studies examining these two body composition techniques. Our results would tend to confirm their suppositions: using multiple CT slices to compare with simple DEXA-measured FFM and fat mass values resulted in better and greater r² and lesser SE of the estimate. The data from the obese individuals and women included in our study did not worsen the relationship between DEXA and CT, suggesting that the findings of Wang et al. (17) are applicable to these groups also.

In summary, DEXA measures of thigh fat mass correlate extremely well with adipose tissue mass measured by using a multislice-CT technique. Similarly, DEXA thigh FFM correlates well with CT-determined skeletal muscle mass. Nevertheless, there are systematic differences between the two techniques that seem to relate to nonskeletal muscle tissues that are measured as FFM by DEXA. If appendicular tissue composition were to be measured for the purpose of relating it to muscular strength, a single-slice CT would appear to be most satisfactory (12), whereas, if tissue mass is needed as a denominator for metabolic measurements, DEXA is preferred over a single-slice CT. DEXA-determined fat mass compares well with multislice-CT measures, in both the abdomen (3, 15) and thigh. Appreciation of the strengths and weakness of each method can facilitate selecting the appropriate body composition techniques for a given study.

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REFERENCES