Sarcopenia: Assessment of Muscle Mass

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ABSTRACT Despite general information that skeletal muscle mass is the largest organ in the body and despite increased awareness of the importance of skeletal muscle in biological function, methods and techniques for its routine assessment in humans are generally lacking. One important reason for the paucity of assessment tools is the relative lack of direct data on anatomical skeletal muscle mass in humans. J. Nutr. 127: 994S–997S, 1997.

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As discussed by Martin et al. (1990), assessment of skeletal muscle mass, as determined by dissection in conjunction with measurements of body mass in the same cadavers, was limited to only 25 men. Thus, development and validation of most current methods of assessment of skeletal muscle mass were hampered by inadequate reference data and confounded by the reliance on indirect methods that employed some biochemical or physical characteristic of skeletal muscle.

A variety of methods and approaches are available for estimation of regional and whole-body skeletal muscle mass in humans. These techniques range from simple anthropometric measurements requiring inexpensive equipment to the use of sophisticated and costly radiologic instrumentation.

ESTIMATION OF HUMAN MUSCLE MASS

Anthropometry. Measurements of skinfold thicknesses and body circumferences have been used to estimate muscle mass. This approach requires selection of muscle groups with the assumption that site-specific physical measurements reflect the mass of that muscle and that the mass of the estimated muscle group is proportional to the whole-body skeletal muscle mass.

Anthropometric measurements of the upper arm as an estimation of muscle mass are frequently reported (Jelliffe and Jelliffe 1969), with measurements of the lower leg also used, albeit much less frequently (Heymsfield et al. 1979). These estimates have served as a functional index of protein-energy malnutrition (Jelliffe and Jelliffe 1969). Simple measurements of upper arm circumference, corrected for triceps skinfold thickness, are used to calculate muscle cross-sectional area.

The validity of anthropometric estimation of upper arm muscle circumference has been examined. Heymsfield et al. (1979) indicated that each assumption of the anthropometric approach was limited to some degree, and they demonstrated that anthropometric mid-arm muscle area among non-obese adults was overestimated by 15–25% as compared with computed tomographic (CT) determinations. Furthermore, subsequent evaluation of derived sex-specific models, corrected for errors in basic assumptions of the anthropometric method, yielded within-subject errors of 7–8% in the calculated mid-arm muscle area relative to CT values. In subjects with body weights exceeding 150% of ideal body weight, the anthropometric estimates were in error by more than 50%, even after the application of the revised prediction models.

The use of regional body circumferences and skinfold thicknesses to estimate whole-body muscle mass has also been proposed. Mattega (1921) developed a model based on measurements of circumferences of the forearm, upper arm, thigh and calf, corrected for skinfold thicknesses to calculate an average muscle limb radius. This value was squared, multiplied by standing height, then multiplied by 6.5. This initial model was neither validated nor examined by other investigators.

In contrast to previous studies, the Brussels Cadaver Study (Clarys et al. 1984) used skinfold thickness measurements, body circumferences, and skeletal muscle mass determinations to generate and validate prediction models in male cadavers. The model was generated by using regression analysis in one group of cadavers, then cross-validated in a second group of cadavers. Martin et al. (1990) found no difference between the predicted and measured whole-body skeletal muscle mass. When the data from the two cadaver samples were combined, a final model was produced:

\[
MM = \text{STAT (0.0553CTG}^2 + 0.0987FG^2 + 0.0331CCG^2) - 2445
\]

SEE (standard error of estimate) = 1.53 kg, \(R^2 = 0.97\)

in which MM is total skeletal muscle mass (g), STAT is stature (cm), CTG is thigh circumference corrected for skinfold thickness (cm), FG is forearm circumference uncorrected for skinfold thickness (cm), and CCG is calf circumference corrected for skinfold thickness (cm).

The derived model was evaluated in relation to values predicted by using other published prediction equations. The multicomponent anthropometric model of Martin et al. (1990) yielded errors (observed minus predicted values) ranging from...
0 to 2 kg, in contrast to errors of −5 to −7 kg with the anthropometric model of Matiega (1921). The largest errors (−5 to −10 kg) were found with the model that used upper arm anthropometric measurements to predict total body skeletal muscle mass (Heysmfield et al. 1982).

The use of anthropometric measurements, combined limb circumferences and skinfold thicknesses to predict regional and total body skeletal muscle mass, yields qualitative measurements. It is not known at present if anthropometric estimations are either sufficiently accurate or sensitive enough to monitor small changes in muscle mass associated with an individual’s weight loss or gain. There is concern that the use of four independent variables based on a small sample size (n = 6) may yield a highly specific model that is not adequately robust for general use in the population.

Endogenous muscle metabolites. It has been hypothesized that endogenous components or metabolites of skeletal muscle metabolism can be used as an index of muscle mass. This hypothesis assumes that 1) the chemical marker is found only in skeletal muscle, 2) the pool size of the marker is constant, 3) the rate of turnover is relatively constant, and 4) the marker compound is unchanged after it has been released from the skeletal muscle. Two specific metabolites, creatinine and 3-methylhistidine (3-MH), have been used as indices of skeletal muscle mass.

Endogenous creatinine is formed by the nonenzymatic hydrolysis of creatine, which is formed in the kidney and liver (Borsook and Dubnoff 1947). Creatine is formed primarily in skeletal muscle, principally in the form of creatine phosphate (Borsook and Dubnoff 1947).

Estimation of total skeletal muscle mass presumes a constant relationship between these variables. Experimental evidence from humans (Cheek 1968, Talbot 1938) indicates that 1 g of creatinine is derived from 18 to 20 kg of muscle mass, which may be termed creatinine equivalence. The variability in the constancy of creatinine excretion per unit muscle mass may reflect differences in muscle sampling and methodologic variation between the studies.

Alternatively, the ratio of endogenous creatinine excretion to skeletal muscle mass may vary among individuals (Forbes and Bruining 1976). Factors such as physical activity, maturity, metabolic state, sex and non-skeletal muscle sources of creatinine may all contribute to variability in the creatinine to muscle mass ratio. The magnitude of these attenuating influences remains to be determined.

Endogenous excretion of 3-MH in the urine has been suggested as an indirect measure of muscle protein breakdown (Young and Munro 1978). This amino acid is located primarily in skeletal muscle from the post-translation modification of specific histidine residues in myoﬁbrilla. During muscle catabolism, the released 3-MH is neither re-utilized for protein synthesis nor metabolized oxidatively but, instead, is quantitatively excreted in the urine (Young and Munro 1978). These characteristics contributed to the hypothesis that 3-MH might be a useful indicator of skeletal muscle mass.

In two separate studies of men consuming controlled diets (Lukaski and Mendez 1980, Lukaski et al. 1981), endogenous 3-MH was significantly correlated with urinary creatinine excretion, densitometrically determined fat-free mass, and muscle protein mass as estimated by determinations of total body potassium and nitrogen.

The use of endogenous 3-MH as a marker of skeletal muscle mass has received some criticism because of the potential contribution from non-skeletal muscle protein sources. In rats, for example, smooth muscle protein turnover from the gastrointestinal tract and skin contribute significantly to urinary 3-MH output (Millward and Bates 1983, Wassner and Li 1982). In humans, however, the relative rates of muscle to non-muscle protein synthesis and turnover are greater than for rats (37% vs. 12%). A compilation of data from humans indicates that the majority (75%) of endogenous 3-MH in urine emanates from skeletal muscle turnover (Lukaski 1996).

Although creatinine and 3-MH are generated principally from skeletal muscle, their relationship to muscle mass requires a further analysis of factors that affect their pool sizes and turnover rates, including the non-skeletal muscle sources of these markers. However, studies that examine these factors pose some practical limitations, including consumption of a meat- and creatine-free diet and timed urine collections. Renal handling of creatinine and 3-MH poses another concern: changes in rate of creatinine secretion affect daily excretion, and 3-MH is filtered only at the kidney. These factors limit the general use of endogenous muscle metabolites for assessment of skeletal muscle mass.

**RADIOGRAPHIC OR IMAGING METHODS**

In contrast to other methods that indirectly assess muscle mass, imaging techniques offer unique opportunities for direct visualization and measurement of compositional variables, including adipose tissue, bone and muscle. These methods rely on the differing responses among tissues, based on their chemical composition, as the tissue interacts with applied electromagnetic energy. Thus, these techniques facilitate the regional, and in some cases whole-body, assessment of body composition.

**Computed tomography.** Computed tomography exposes a subject to a collimated beam of X-rays that are attenuated as they pass through the body. These attenuations are related to differences in the physical density of the tissues examined. This physical effect is depicted quantitatively as the CT number and is expressed in Hounsfield units, a measure of tissue attenuation relative to air. Because physical density and atomic number are the principal determinants of the chemical components of a tissue, there is a general linear relationship between CT number and tissue density. For example, air, adipose tissue and muscle have average CT numbers of −1000, −70 and +20, respectively.

The CT method offers high image contrast and clear separation of fat from other soft tissues. The differing attenuation of adipose tissue and skeletal muscle permits visual and mathematical separation of image components.

The use of CT has provided unique measurements of change in regional body composition of humans. Fiaratore et al. (1990) found a significant increase in mid-thigh muscle area with marked increases in both quadriceps (9%) and hamstring and adductor areas (8.4%) in response to 8 wk of resistance training, without changes in subcutaneous or intramuscular adipose tissue. These gains were not accompanied by a measurable parallel increase in densitometrically determined fat-free mass.

Caution should be taken with regard to using CT as an assessment of muscle mass in some patient populations. There is a variation of +30 to +80 Hounsfield units in the attenuation of normal muscle. There is also wide variation in the size or volume of muscles on contralateral sides of the body. Because of the variation in muscle size associated with physical training and nutrition status, general reductions in muscle size may be difficult to determine in the early stages of disease without baseline measurements.

**Magnetic resonance imaging.** Nuclear magnetic resonance (MR) is a powerful technique that can provide both images and chemical composition of tissues. As with CT, mag-
Magnetic resonance imaging (MRI) can be used to assess regional and whole-body composition.

Magnetic resonance imaging is based on the interaction between nuclei of hydrogen atoms and the magnetic fields generated and controlled by the MRI instrument. When a subject is placed inside the magnet of an MR imager, the magnetic moments of the protons tend to align themselves with the magnet's field. When a pulsed radiofrequency (RF) field is applied to the body tissues, the hydrogen protons absorb energy. When the RF field is turned off, the protons gradually return to their previous state and release the absorbed energy in the form of another RF signal that is used to develop the MR images. To increase the contrast between adipose tissue and skeletal muscle, MRI data acquisition systems are programmed to take advantage of the specific proton density and relaxation times of the various tissues. The spin-echo data acquisition technique uses the T1 relaxation times of adipose tissue and skeletal muscle to provide high quality MR images. Specifically, the T1 relaxation time for adipose tissue is much faster than its counterpart for skeletal muscle.

The interaction of energy restriction and exercise on appendicular skeletal muscle volume was examined recently with MRI (Ross et al. 1995). Obese women treated with diet only showed a significant decrease in skeletal muscle volume in arms and legs compared with women treated with diet and aerobic exercise. This finding indicates the specificity and sensitivity of MRI to small changes in skeletal muscle mass.

**Dual X-ray absorptiometry.** Dual X-ray absorptiometry (DXA) exposes the patient to a collimated beam of X-rays to determine bone mineral and soft tissue (fat and lean) composition (Laskey 1996, Lukasik 1993). The X-rays are attenuated in proportion to the composition and thickness of the region of the body through which the X-ray beam is passed. The attenuation is also influenced by the energy of the X-rays. Specifically, soft tissues that contain water and organic compounds restrict the flux of X-rays much less than bone.

The DXA method permits assessment of whole-body and regional body composition assessment, with a particular emphasis on appendicular skeletal muscle mass. Heymsfield et al. (1990) compared estimates of limb muscle mass assessed with dual photon absorptiometry, a method similar to DXA, in healthy men and women with measurements of total body potassium and nitrogen, as well as with anthropometric assessments of muscle mass. There were significant correlations with total body potassium \(r = 0.94\), total body nitrogen \(r = 0.78\), and upper arm \(r = 0.82\) and thigh \(r = 0.88\) muscle plus-bone areas. These findings indicate the potential use of DXA in healthy individuals.

The DXA method has also been used to monitor body composition in hemodialysis patients before and after dialysis therapy (Horber et al. 1992). No changes in bone or fat mass were found after dialysis, but lean mass was significantly decreased. The largest proportion of lean mass lost was attributed to the trunk (61%) and legs (30%), with minimal losses in the arms (5.5%) and remainder of the body (3.5%). Thus, DXA partitions fluid accumulation into the lean component of the body.

**Bioelectrical impedance.** Another potentially useful approach for assessment of regional muscle mass is bioelectrical impedance (BI). This method relies on the conduction of an applied electrical current to index conductor volume, which, in the region of the upper arm, is muscle mass. Brown et al. (1988) used a four-electrode system and 1 mA at 50 kHz to measure the resistance of the upper arms of 20 healthy men. A parallel resistance model was used on an equivalent circuit, assuming that the resistivities of muscle, fat and bone were 1.18, 16, and >100 W·cm\(^{-1}\), respectively. Reference muscle and fat area data were derived from CT and anthropometry.

The areas of muscle and fat estimated with BI were significantly correlated with CT determinations \((r = 0.981, 0.943, 0.934)\) with mean differences (errors) of 0.22 and 0.73 cm\(^2\). Anthropometric estimates of muscle and fat areas also were significantly related to CT determinations \((r = 0.943, 0.876)\), respectively. However, the mean differences between the CT and the anthropometric values were significantly different from zero for muscle and fat \((-2.62, 2.61)\) cm\(^2\), respectively. These findings indicate the feasibility of using BI to assess regional muscle area, and BI may offer a practical method for routine measurement of muscle mass.

Some caution for the general use of BI in patients is indicated. Additional work is needed to determine the type and size of electrodes for optimal BI measurements. The advantage of a multifrequency rather than a single frequency BI instrument also needs to be established. The influence of regional edema on BI measurements and hence on estimation of muscle mass also requires further investigation.

**SUMMARY AND CONCLUSIONS**

Clinicians and researchers both seek the availability of practical, accurate and reproducible methods for routine assessment of whole-body and regional skeletal muscle mass. Anthropometric methods offer a low cost approach but are limited in their accuracy of estimation of regional muscle mass, and extrapolation of the data to whole-body muscle mass is limited by validity of the assumptions of the extrapolation. Excretion of endogenous muscle metabolites (creatinine and 3-MH) can be influenced by physical factors (physical activity, sex, age) and the use of measurements of these metabolites is further complicated by the need for controlled diets (meat- and creatine-free) and timed urine collections. Imaging techniques provide the most accurate determinations of regional muscle mass but are hampered both by radiation exposure and/or by the cost and availability of instrumentation. Regional BI, a potentially useful technique, requires additional research to evaluate its strengths and weaknesses.

**LITERATURE CITED**


