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COMMENTARY

Lean body mass should not be used as a surrogate measurement of muscle mass in malnourished men and women: Comment on Compher et al.

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The assessment of body composition and its relation to health outcomes has been an integral component of medical research. Whereas body mass index (BMI) is used as an index of overweight and obesity, the effects of the major individual components of body mass, including fat and skeletal muscle, on outcomes depend on the accuracy of the assessment method being used. Body composition may be measured by using several different methods, each of which relies on assumptions that may not be true in all populations, ages, or clinical conditions. The Global Leadership Initiative on Malnutrition has provided an update of their consensus criteria of malnutrition.[1] Three of the criteria are and have been used as strong indicators of malnutrition. However, the third criterion, low skeletal muscle mass, is problematic. Although skeletal muscle is a highly plastic tissue that is extremely responsive to reduced energy and protein intake and physical activity, inflammation, and disease, the assessment of total-body muscle mass represents several methodological challenges that are not well described or recognized by the Global Leadership Initiative consensus group. In particular, the assessment of lean body mass (LBM) or fat-free mass should not be used as a surrogate for the estimation of skeletal muscle mass.

The measurement of muscle mass and changing muscle mass for a diagnosis of malnutrition is an important goal. This may be an important step in the identification of the potential causes of malnutrition that are of critical importance for nutrition interventions.[2] Muscle represents a large storage depot for protein, and inadequate dietary protein in adults can result in a relatively rapid decrease in muscle mass to maintain protein synthetic rate in tissues vital to survival. However, skeletal muscle represents only about 50% of LBM, and the nonmuscle components can change dramatically in malnourished or ill patients. Hydration status can be highly variable with illness, aging, exercise, and exposure to heat.[3] In addition, extracellular water volume is also variable in many common disease states, including heart failure, kidney disease, and edematous conditions. Chronic exposure to heat can result in heat acclimation and a large expansion of plasma volume (up to 20%).[4] Malnourished patients are often dehydrated, and as a result, LBM will be low because of reduced total body water. Refeeding a poorly nourished patient may have an immediate effect on body water content, which may be misinterpreted as increasing muscle mass. Effects of body water on dual-energy x-ray absorptiometry (DXA)–derived or bioimpedance spectroscopy (BIS)–derived estimates of muscle mass may be large and unpredictable. However inaccurate the proposed estimates of muscle mass may be, the expert commentary provides no information on the accuracy or, indeed, how changes in the proposed surrogate estimates of muscle mass should be interpreted. As a result, clinical decisions that result from inaccurate estimates of muscle mass or changes in these estimates can have inappropriate and unintended consequences.

The D_3-creatine (D_3Cr) dilution method measures total-body creatine pool size, approximately 98% of which is sequestered in skeletal muscle. By this method, an oral tracer dose of D_3Cr is administered, absorbed, and transported against a large concentration gradient into the sarcomere. The enrichment of urine D_3-creatinine thereby reveals the enrichment of intramyocellular D_3Cr and provides a noninvasive measurement of total-body muscle mass. The method has been validated in rodents, adult humans,[5] and premature infants cared for in a neonatal intensive care unit (NICU).[6] In these neonates, substantial increases in muscle mass (measured

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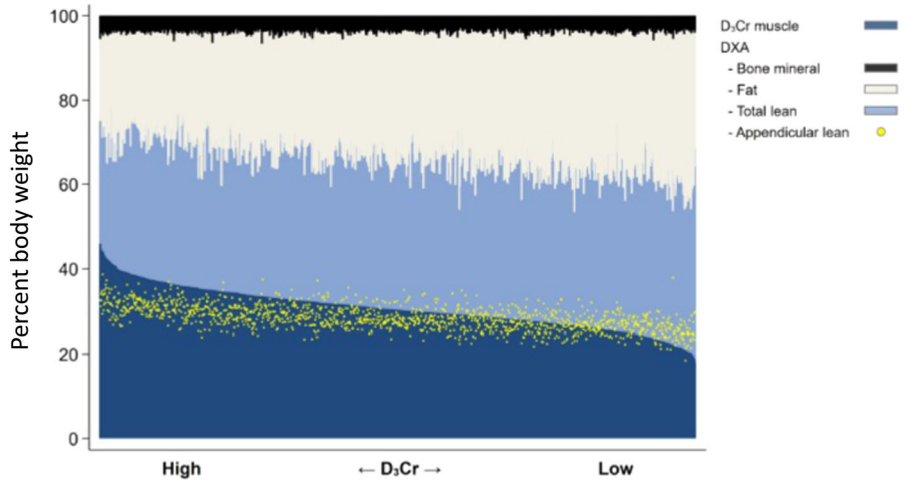

FIGURE 1 In >1300 older men, body composition was measured by using dual-energy x-ray absorptiometry (DXA) and D_3-creatine (D_3Cr) dilution to assess muscle mass.[10] Yellow circles represent appendicular lean mass (ALM), also estimated by using DXA. Muscle mass is ranked from highest to lowest. Light blue represents nonmuscle lean mass. These data demonstrate that, in older men, muscle is only a component of and not strongly associated with lean body mass. There was no relationship between ALM and D_3Cr muscle mass.

every 2 weeks during care in the NICU) were observed. Importantly, the method was able to determine changes of 100–200 g. The method only requires a single "spot" urine sample, and there is no need for a skilled technician to administer a dose or collect a urine sample. The method was introduced into the Osteoporotic Fractures in Men (MrOS) cohort study of older men, and several resulting publications show that muscle mass determined by the D_3Cr dilution method (but not DXA lean mass or appendicular lean mass [ALM]) was strongly related to functional capacity along with risk of disability, hip fracture, and mortality.[7–9] In a recent commentary, Schaap[10] wrote, "In contrast to DXA, deuterated creatine (D_3-creatine) assesses muscle mass directly," and, "By isolating contractile muscle mass from noncontractile components including fat, the D_3-creatine assessment is not only an accurate method to assess muscle mass but is less biased by obesity and aging than DXA ALM." Body composition in >1300 older men, measured by using DXA and D_3Cr dilution, is shown in Figure 1.[11] DXA estimates of LBM, ALM, fat mass, and bone mass are shown along with muscle mass. In this population, LBM provides a substantial and inaccurate overestimate of muscle mass, with muscle representing only about 50% of LBM. There was no relationship between DXA ALM and muscle mass ($r = 0.2$, $P = 0.335$). A similarly poor relationship between DXA LBM and D_3Cr muscle mass was reported in older women.[12] Although these comparisons provide important new data to help interpret surrogate estimates of muscle mass, there is still an inadequate amount of data on D_3Cr muscle mass to base clinical decisions regarding treatment of malnutrition. This will come as data emerge that use this method to measure muscle in patients with cachexia and malnourishment.

The expert commentary provides little or no information on exactly how body composition data should be used by a healthcare provider. As they suggest, none of these measurements are widely available to clinicians, and, at least in the United States, there is no reimbursement from third-party payers. Because the most commonly used indicators of malnutrition in adults are involuntary weight loss or low BMI, strong recommendations should be made for systematic and frequent measurements of body weight. Just because an estimate of LBM is available does not mean that it should be used unless a healthcare professional understands what is being measured and the limitation of the measurement. Most importantly, emerging data show that LBM is not an accurate or appropriate estimate of muscle mass.

CONFLICTS OF INTEREST

Although Dr. Evans is listed as an inventor for the issued patents for the D_3-creatine dilution method, he does not own or derive any income from this intellectual property.

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