The authors reply:

Letter on: "Pitfalls in the measurement of muscle mass: a need for a reference standard" by Clark et al.

Abstract

However, semantics aside, we think that DXA can indeed serve as a reference standard for measuring muscle mass. Obviously, CT and MRI are advanced techniques that can and have been used to obtain important information such as muscle size/volume and more recently amount and distribution of intra- and intermuscular adipose tissue. Also individual muscles can be assessed separately. However, with respect to muscle mass, the comparison of DXA with CT/MRI is rather difficult because DXA and QCT/MRI measure different physical parameters

Keywords   Lean body mass; Lean mass; Muscle mass; Reference standard

We very much appreciate your valuable comments and your interest in the topic raised in our paper.[1] One of your main concerns seem to be the statement at the end of our contribution suggesting that 'DXA is the gold standard for the measurement of muscle mass'. Perhaps the term 'gold' could have been omitted. However, semantics aside, we think that DXA can indeed serve as a reference standard for measuring muscle mass as concluded in the discussion and summarized in the abstract. Obviously, CT and MRI are advanced techniques that can and have been used to obtain important information such as muscle size/volume and more recently amount and distribution of intramuscular and intermuscular adipose tissue.[2,3] Also, individual muscles can be assessed separately. However, with respect to muscle mass, the comparison of DXA with CT/MRI is rather difficult because DXA and QCT/MRI measure different physical parameters.

As you correctly describe, primary outcome of DXA is lean mass in g, of CT is muscle volume in cm^3 or area in cm^2 and CT density in Hounsfield units [HU] and of MRI is also muscle volume in cm^3 or area and proton density fat and water fraction in % when using advanced Dixon sequences.[4] None of the three techniques measures muscle mass in g or muscle density in g/cm^3. CT and MRI do not even directly measure a mass in g. Thus, from a physics point of view, none can serve as a gold standard for any of the other two methods, with the exception of volume/area measurements of CT and MRI.

For the further discussion, it is important to remember that all current definitions of sarcopenia include appendicular lean mass but not muscle area/volume.[5,6] You refer to accuracy validation studies with MR and CT[7–10] but all evaluated area, not mass. Correlations reported between DXA lean mass and CT muscle area in the thigh were moderate in young subjects ($r^2 = 0.74$)[11] and even lower in premenopausal lean and obese women ($r^2 = 0.59$ and $r^2 = 0.58$, respectively),[12] thus a substitution of DXA by CT in the definition of sarcopenia, i.e. of mass by volume, will be problematic.

There are indeed some studies that report muscle mass from CT and MRI scans.[13–15] In these studies, muscle mass has been estimated by multiplying measured muscle volume with a density of 1.06 or 1.04 g/cm^3, values based on publications summarized in the ICRP reference man report from 1972.[16] In this report, the proportion of fat of wet skeletal muscle in adults is given as a range from 2.2% to 9.4%. Thus, accuracy of assuming a muscle density of 1.06 or 1.04 g/cm^3 is questionable if higher degrees of muscle fat infiltration occur, because higher proportions of fat will decrease density. Correlation coefficients of $r^2 \geq 0.96$ have been reported in young and elderly healthy volunteers[11,15] between muscle mass in the thigh estimated with CT and fat free mass (FFM) measured by DXA but results are likely to change in subjects with a higher amount of intramuscular adipose tissue of let's say greater than 10%. Thus, these studies for a specific population serve more as a validation of the simplifying assumptions made to obtain CT/MRI muscle mass than a validation for DXA.

Finally, you point out only moderate correlations between longitudinal changes in lean mass and muscle volume. But with the current definitions of sarcopenia,

wouldn't this be an argument in favour of DXA? One could criticize that definitions of sarcopenia inherently favour DXA and should have been better tailored towards CT or MR measurements in the first place. They even use appendicular lean instead of muscle mass,[17] which has been rightfully criticized. However, the real problem is the rather poor correlation of the common DXA/CT/MRI measurements with function, which has caused the integration of functional measurements in the definitions of sarcopenia. Thus, we do not imply that DXA will be the gold standard for the diagnosis of sarcopenia, which requires a functional component. However, DXA can serve as a reference standard for lean mass, considering the limitations described in our article.[18] Similar to osteoporosis, DXA may become the workhorse in clinical routine of sarcopenia. CT and MRI should be regarded as a complementary more powerful imaging method to DXA that may improve our understanding on intervention and may eventually better explain effects on functional muscle outcome than simple lean mass or area/volume measurements.

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