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Dual energy X-ray absorptiometry: gold standard for muscle mass?

Since the late 90s, dual energy X-ray absorptiometry (DXA) has been validated against so-called gold standards for body composition (BC) by comparison to chemical analysis, dissection, and anatomy-based imaging methods (CT or MRI).[1–3] Today, DXA is being used in a variety of clinical settings with the prospect of diagnosing osteoporosis, obesity, and sarcopenia. With this in mind, we read with great interest the article 'Pitfalls in the measurement of muscle mass: a need for a reference standard'.[4] This paper states that DXA is a gold standard for the measurement of muscle mass on behalf of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis working group on frailty and sarcopenia.

Lean soft tissue mass by DXA has proved to be a reliable method for the estimation of muscle mass in groups using prediction equations.[1] Individual discrepancies related to lean tissue hydration and tissue thickness have been repeatedly reported in literature.[5–7] Because of its imprecise definition, lean or lean body mass (LBM) leads to much confusion in the literature and is often erroneously used as a synonym for fat-free mass (FFM).

In attempts to identify physiological relevant tissues, the concept of LBM has been introduced almost 8 decades ago.[8] LBM was used to represent the body's active protoplasm (i.e. bone salts, essential lipoids, and tissue each with their specific gravity). LBM and FFM are not interchangeable as the former consists of the FFM plus the essential fat which may vary from 2 to 10% for the FFM.[9,10] DXA pretends to measure lean or LBM as opposed to FFM.[2] However, DXA produces results also for fat (essential and non-essential lipids) and bone mineral content (dry salts). Thus, lean mass by DXA compares to FFM minus bone minerals. As a result, lean by DXA is quantitatively smaller than FFM which in turn is smaller than LBM.[5] This confusion in terminology adds to the ongoing difficulties with the interpretation of BC output produced by different methodologies.

The authors state that in a previous study, the agreement between appendicular lean mass assessed by DXA and predicted by bio-electrical impedance analysis (BIA) was found to be low with a potential large prediction error on the individual level. Comparing two indirect BC methods to each other with the purpose of validation is subject to misinterpretation. Both methods are often used to estimate FFM, notwithstanding they may represent different compartments. Compartments different from FFM may be typically estimated depending on which BC technique was used to develop the BIA system's equation.[11] As such, the systematic underestimation of LBM measurements by BIA as reported in the present paper might not be valid.[4] In fact, recent evidence suggests that when using raw BIA data (resistance and reactance) to produce population specific equations, BIA rather overestimates DXA in subjects with low muscularity.[12,13] This observation, of course, does not ignore the fact that prediction errors at individual level remain possible.

Fundamental research has proven that lean mass by DXA is almost equal to the sum of muscle, skin, and viscera by dis section.[2] Lipid-free skeletal muscle by underwater weighing has been estimated at 1.04 g/cm^3 and skin at 1.07 g/cm^3 in an older sample.[3] Since CT or MRI cannot distinguish between intramyocellular lipids, the use of a constant density to convert volume to weight is prone to interindividual variation. This is also the case when lean mass by DXA is used as a synonym for muscle mass, taking into account the variation of water, protein, and glycogen content in a limb and between different tissue compartments. As lean and muscle belong to two different organization levels of BC, their interrelationship remains predictive with a given residual uncertainty.[14]

In summary, the clinical interpretation of DXA outcome measures may lead to elevated expectations regarding the diagnosis of sarcopenia. As long as there is no clarity about the way manufacturers use their mathematical algorithms to produce quantitative results, the status of gold standard for DXA is premature. Upgrading DXA to gold standard for muscle mass measurement opens the doorway to inaccurate validation of other indirect BC techniques by DXA (e.g. ultrasound). Moreover, this may create unreliable diagnoses in clinical settings. In patients, the cumulative impact of biological variability on muscle mass measurement is not yet established.

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