Lean Tissue and Protein in Health and Disease: Key Targets and Assessment Strategies

Written by Dennis Bittner

The Dudrick Research Symposium is named for Dr Stanley J. Dudrick, a researcher whose groundbreaking work brought parenteral nutrition to the bedside, among many other important contributions to the field of nutrition support. Carrie P. Earthman, PhD, RD, University of Minnesota–Twin Cities, Minneapolis and St Paul, Minnesota, USA, chaired the symposium this year and was the first of 3 speakers to explore the opportunities and challenges inherent to the accurate assessment of lean tissue.

Lean tissue, with skeletal muscle as its principal constituent, is critical to the body's healthy response to both acute and chronic illnesses. Lean tissue is also a key indicator of nutritional status, with estimation of lean tissue loss cited as one of the primary criteria in recent consensus definitions of malnutrition published jointly by the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) and the Academy of Nutrition and Dietetics (AND). Despite the utility of lean tissue loss as a marker of malnutrition in chronic and acute disease, estimation of lean mass is not commonly performed in US hospital settings. One of the primary reasons for this is the limited availability of valid methods for measuring lean mass at the bedside.

One advantage of bedside body composition assessment is the ability to identify individuals with loss of lean tissue who might not otherwise be detected through more gross physical examination techniques (eg, patients with sarcopenic obesity). In one recent study, >50% of patients with sarcopenia were misclassified as normally nourished using subjective global assessment, underscoring the need for body composition assessment [Sheean PM et al. *JPEN J Parenter Enteral Nutr*. 2014]. There has been substantial interest in the use of bioelectrical impedance analysis (BIA) techniques because they are affordable, reliable, and noninvasive and are easily used at the bedside; however, their accuracy for whole-body lean tissue estimates in clinical populations, particularly those with fluid overload and obesity, is questionable. Dr Earthman stressed that all body composition methods are indirect and are associated with underlying assumptions that may lead to potential inaccuracies.

In general, BIA techniques can provide estimates of lean mass that compare favorably with more expensive reference methods when considering groups of patients, but they can be too variable at the individual level. Dr Earthman reviewed the theory underlying the 3 main bioimpedance techniques typically used to assess lean tissue and their various limitations, and provided tips for how to best interpret various BIA validation studies. The use of multiple-frequency BIA (MF-BIA) and bioimpedance spectroscopy (BIS) approaches in the clinical setting is more promising (compared with single-frequency [SF]-BIA) because they can theoretically distinguish between the extracellular and intracellular water compartments. BIS is being utilized by some large dialysis centers where new physiologic models are employed to discriminate between excess fluid and normally hydrated lean tissue [Chamney PW et al. *Am J Clin Nutr.* 2007]. However, Dr Earthman said that although BIS has theoretical advantages over both SF- and MF-BIA, the technology of BIS devices needs to be refined before being made widely available.

Challenges to the more commonly seen techniques of SF- and MF-BIA can arise from the need to choose appropriate population-specific prediction algorithms in order to estimate whole-body lean mass values. Manufacturers often will not disclose the methods and algorithms used to analyze the data collected by their devices, creating a "black box" that can be a hindrance to clinical nutrition researchers. Dr Earthman urged her audience to choose carefully when purchasing a bioimpedance device, advising them to ensure that the device provides the raw data, not just whole-body composition values. Having the raw data allows researchers to compute

Official Peer-Reviewed Highlights From

cnw Clinical Nutrition Week2015

February 14–17, 2015
Long Beach, CA, USA

body composition parameters with the appropriate validated equation, as well as utilize the phase angle and/or high-to-low impedance ratio for comparison with reference values that might help to identify individuals with malnutrition. Dr Earthman called for additional studies to help validate diagnostic criteria for malnutrition that would include bedside methods such as bioimpedance in addition to reference measures of body composition such as computerized tomography and/or dual-energy x-ray absorptiometry (DXA) scans. Dr Earthman advised that bedside measures of lean tissue can aid in identifying malnutrition and monitoring nutritional interventions, particularly in patients not showing outward signs of malnutrition.

Robert Wolfe, PhD, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA, reviewed techniques to determine protein requirements for maintenance of lean tissue. The first of these techniques, nitrogen balance, is conceptually simple, and there is an extensive database of results supporting its use. However, the method is subject to some degree of variability, as it can be difficult to measure nitrogen balance accurately, with patients required to remain in a steady state of nitrogen balance for several days to record valid readings [Rand WM et al. *Am J Clin Nutr*. 2003].

Another approach is determination of arterial-venous balance. The advantage of this technique is that it is a direct measurement of muscle metabolism, providing physiologically relevant data. Maintenance of steady-state conditions is not required, and the method reacts quickly to register changes in amino acid availability. However, this technique is not only invasive but also highly dependent on accurate measurement of blood flow. Another approach to determining protein requirements, measuring the muscle protein fractional synthesis rate (FSR) and the fractional breakdown rate (FBR), requires direct sampling of muscle tissue. Therefore, although the procedure is responsive to changes in protein intake levels, the muscle biopsy it entails not only is invasive but also provides data from just a single sample site.

Dr Wolfe described another means for determining protein synthesis and degradation rates, indicator amino acid oxidation (IAAO). This method gauges the partitioning of an essential amino acid (the indicator) between protein synthesis and protein degradation. However, the IAAO method assumes not only that the estimated average requirement for protein reflects protein synthesis but also that protein degradation does not vary with protein intake levels.

The last technique addressed by Dr Wolfe for measuring protein requirements was calculation of whole-body protein turnover. Here, protein synthesis and breakdown rates are calculated using single amino acid tracer kinetics, where tracer infusion of essential amino acids is tracked by minimally invasive sampling of peripheral blood. The rate of amino acid appearance in plasma reflects the rate of protein breakdown, whereas the rate of disappearance of the amino acid gives oxidation plus synthesis. The net balance between appearance and disappearance represents breakdown minus synthesis. Although whole-body protein turnover does require researchers to measure the rate of absorption of exogenous amino acids, and data for specific tissues are not provided, Dr Wolfe said that the advantages of whole-body protein turnover are that the procedure is relatively noninvasive and easily performed. It can also measure both acute and long-term response to different protein intake levels.

The final speaker, Steven Heymsfield, MD, Louisiana State University, Baton Rouge, Louisiana, USA, covered state-of-the-art techniques for lean tissue assessment.

Imaging technologies such as computed tomography and magnetic resonance imaging revolutionized measurement of lean mass beginning in the 1990s. The power of these techniques is their ability to separately measure both subcutaneous and visceral adipose tissue in addition to skeletal muscle and even intermuscular adipose tissue. Dr Heymsfield talked about ultrasound as another potential bedside option, although more work needs to be done to refine protocols to standardize measurements to improve reliability and reproducibility. Dr Heymsfield also discussed more cutting-edge techniques for measuring lean mass, including magnetic resonance proton spectroscopy, diffusion tensor imaging, dual photon absorptiometry, DXA, and magnetic resonance elastography.

Although these more sophisticated and technically advanced methods of lean mass measurement provide some of the most detailed and accurate measurements of lean mass available, their expense and size make them impractical for bedside use. More focus on developing useful technologies in the acute care environment is needed.