

Bioelectrical impedance analysis for diagnosing sarcopenia and cachexia: what are we really estimating?

Maria Cristina Gonzalez^{1,2*} & Steven B. Heymsfield²

¹Postgraduate Program in Health and Behavior, Universidade Católica de Pelotas, Pelotas, RS, Brazil; ²Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA 70803, USA

Abstract

As reference methods are not available for identifying low skeletal muscle mass in clinical practice, the European Group on Sarcopenia in Older People the Asian Working Group for Sarcopenia and the International Consensus for Cancer Cachexia guidelines accept bioelectrical impedance analysis (BIA) as an option for sarcopenia and cachexia assessment. Using different BIA equations, several components that represent ‘muscularity’ can be assessed. Total skeletal muscle mass or appendicular skeletal muscle mass normalized in relation to height (skeletal muscle mass index or appendicular skeletal muscle index, respectively) is the most common term used in the consensus. These terms are similar, but they should not be used as synonymous. Both terms can be used to define sarcopenia, but adequate equations and cut-off values should be used according to the studied population. However, there is a disagreement between the sarcopenia definition assessed by using BIA from the European Group on Sarcopenia in Older People and Cachexia Consensus, and this can lead to an overestimation of sarcopenia and, consequently, cachexia. An effort should be made to standardize the terminology employed by the Societies to define low muscularity and sarcopenia by using BIA. Future validation studies may show the need for specific cut-off values for each population using this method.

Keywords bioelectrical impedance analysis; sarcopenia; cachexia; body composition; muscularity

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*Correspondence to: Maria Cristina Gonzalez, Postgraduate Program in Health and Behavior, Catholic University of Pelotas, R. Gonçalves Chaves, 377 - Room #411, CEP 96015-560 Pelotas, RS, Brazil. Tel: +55 53 9982 1328, Email: cristinagbs@hotmail.com

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Although dual-energy X-ray absorptiometry (DXA), computed tomography and magnetic resonance imaging (MRI) are considered reference methods for identifying low skeletal muscle mass in elderly persons and patients with chronic diseases, access to these instruments may be limited in clinical practice. For this reason, bioelectrical impedance analysis (BIA) can be a useful tool to assess skeletal muscle mass, and three available consensus statements (European Working Group on Sarcopenia in Older People, Asian Working Group for Sarcopenia and

International Consensus for Cancer Cachexia)^{1–3} accept BIA as an option for identifying sarcopenia and cachexia.

However, BIA, differently from the other body composition tools, does not actually measure a specific body component. Body composition assessment from BIA relies on a calibration equation developed using a reference method such as DXA, computed tomography or MRI. Early BIA systems employed fat-free mass (FFM) prediction equations developed using traditional two-compartment reference methods such as underwater weighing or total body water. More recently, other more sophisticated imaging methods have been used to develop BIA prediction formulas, and new equations were developed to identify body components beyond that of FFM and related %fat.

Within the sarcopenia and cachexia areas, BIA is now used to estimate several components that represent 'muscularity'. Although these terms are often used as synonymous to FFM, they may not actually represent this component. Depending on which body composition technique was used to develop the BIA system's equation, compartments different from FFM are typically estimated. This has led to some confusion in the literature, and we now review some of these measures with the aim of clarifying the role in patient assessment.

Total body skeletal muscle mass

Janssen *et al.*⁴ validated BIA against skeletal muscle mass (SM) obtained from MRI, and a BIA prediction equation to estimate SM was generated from this study. Usually, 73–75% of total body SM is located in the limbs and represents appendicular SM. The same authors defined SM index (SMI) as a % of total body mass (SM/body weight, %) X 100, and SMI is expressed in % units. Low SMI was defined as a SMI below one standard deviation of young adult values according to the data from the Third National Health and Nutrition Examination Survey (NHANES III).⁵ The cut-off values suggested from this study were <37% and <31.5% (class I and II sarcopenia for men) and <27.6% and <22.1% (class I and II sarcopenia for women).

Another definition for SMI was created some years later, considering SMI as SM (in kg, obtained from the same BIA equation) adjusted for the squared height (SM/height², kg/m²). Based in physical disability risk also assessed in the NHANES III elderly population, the authors defined the usual cut-off used to define sarcopenia with SMI: moderate sarcopenia when SMI is between 8.51 and 10.75 kg/m² (men) or 5.76 and 6.75 kg/m² (women) and severe sarcopenia when SMI is ≤8.50 kg/m² (men) or ≤5.75 kg/m² (women).⁶ These cut-off values are used in the European Working Group on Sarcopenia in Older People consensus, when absolute SM is estimated from BIA.²

In the Cachexia Consensus statement, Fearon *et al.*³ proposed three criteria for diagnosing cancer cachexia:

- Weight loss >5% over past 6 months (in the absence of simple starvation); or
- Body mass index < 20 kg/m² and any degree of weight loss >2%; or
- Appendicular skeletal muscle index consistent with sarcopenia.

Sarcopenia can be assessed by several techniques, as described in the paper, including BIA. The authors used the term whole body FFM index without bone and defined the cut-off

as <14.6 kg/m² (men) and <11.4 kg/m² (women).³ The term whole body FFM index without bone is not exactly the same thing as SM, estimated from BIA as described in the cited reference.⁵ There was likely confusion here with the term lean tissue without bone (compartment obtained from DXA). Based in the study from Janssen *et al.*, the cut-off values cited by Fearon *et al.*³ are much higher than those used to define low muscularity in the Sarcopenia Consensus. This would lead to a misclassification of subjects according to SMI using BIA, diagnosing almost everyone as sarcopenic, and consequently, cachectic.

Appendicular skeletal muscle mass

Appendicular skeletal muscle mass (ASMM) is another term given to the assessed 'soft lean appendicular tissue' (the fat and bone-mineral free tissue, obtained from DXA) assessed in the four limbs. It should be a little larger than the actual appendicular skeletal muscle mass, because the skin and connective tissue are included in this measurement. This compartment can be estimated when a BIA equation is derived from a validation study where ASM was assessed from DXA.^{7–10} ASMM can also be normalized in relation to height, giving the appendicular SMI (ASMI = ASMM/height², kg/m²). Different equations were developed from different populations (adults, elderly, Caucasian and Asian subjects). Only the Asian Consensus suggests cut-off values of ASMI by using BIA (7.0 kg/m² in men and 5.7 kg/m²).¹ These values were established from 1719 young healthy Japanese volunteers, and ASMI was defined as the sum of the muscle mass of the arms and legs divided by height in meters squared, assessed directly by using segmental BIA.^{11,12}

Appendicular lean mass

Recently, this new term was introduced to describe exactly the same compartment as appendicular SM from DXA: the lean mass without bone and fat assessed by DXA in the four limbs.¹³ The authors obtained two different equations to estimate appendicular lean mass using BIA, depending of the type of DXA systems used in the validation (GE Lunar or Hologic). Although these equations were developed from a sarcopenic population (defined by the previously described Janssen's equation for BIA) obtained from a large European multicentre study (PROVIDE nutritional intervention study), no cut-off values were shown, and the authors suggested that the reference values from Hologic and Lunar should be used to characterize sarcopenia.

Can bioelectrical impedance analysis be used to identify sarcopenia/cachexia?

Bioelectrical impedance analysis can estimate different compartments that are used to define sarcopenia and cachexia, as described earlier. As they were estimated using different BIA equations, they are valid for the same population from the validation study, using the same BIA device, and the subjects should be classified according to the adequate suggested cut-off values. For this reason, it is important to standardize not only the terminology employed to define low muscularity and sarcopenia but also the cut-off values for diagnostic purposes in each population. The terms and cut-off values suggested in the Cancer Cachexia International Consensus to diagnose sarcopenia by using BIA should be reviewed, as an

overestimation of cachexia can result with the actual values. Further research may show the need for specific cut-off values to define sarcopenia in different populations.

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Conflict of interest

Maria Cristina Gonzalez and Steven B. Heymsfield declare that they have no conflict of interest.

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