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Review

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Measuring Muscle Mass to Identify Sarcopenia Via Bioelectrical Impedance Analysis in Hemodialysis: Importance of Timing and Equipment Choice

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ABSTRACT

Measurement of muscle mass is an integral part of sarcopenia diagnosis. Bioelectrical impedance analysis has been commonly used for muscle mass assessment in many clinical and research settings as it is non-invasive, practical, and portable. However, one of the major handicaps of this measurement technique is that the validity and precision of bioelectrical impedance analysis measurements can be affected by hydration status. In hemodialysis patients, the volume status fluctuates easily and continuously, which is most significant between the immediate pre-dialysis and post-dialysis periods. Thus, a significant difference in the results of bioelectrical impedance analysis measurement is obviously expected between that obtained before and after hemodialysis. In fact, many centers perform measurements before hemodialysis, since it is more convenient for both staff and patients. However, the confounding effect of excess water on correct bioelectrical impedance analysis estimations seems substantial. For this reason, it seems more appropriate to perform bioelectrical impedance analysis measurements in chronic hemodialysis patients when they are closer to their dry weight, i.e., after the dialysis rather than before it. Accordingly, we searched the literature to identify the ideal timing of bioelectrical impedance analysis measurements in patients undergoing hemodialysis. The literature data on this subject indicate that performing bioelectrical impedance analysis measurements in the period after 15 minutes and within 2 hours after hemodialysis session will aid in a better estimation of muscle mass in terms of reliability and reproducibility.

Keywords: Bioelectrical impedance analysis, hemodialysis, sarcopenia, spectroscopy

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The incidence and prevalence of end-stage kidney disease (ESKD) have been increasing continuously.[1] The number of people receiving kidney replacement therapy (KRT) exceeded 2.5 million worldwide in 2015 and is projected to double to 5.4 million in 2030.[2] One of the main causes of this continuous rise is the aging population. Aging brings a vulnerability to kidney diseases because glomerular filtration rate decreases gradually with aging and common comorbidities (e.g., hypertension and diabetes) affect kidney functions adversely. Therefore, older adults receiving KRT are more prone not only to major problems like cardiovascular events, stroke, or death,[3,4] but also to specific conditions like frailty,[5] protein-energy wasting,[6] and sarcopenia.[7] All of the last stated conditions overlap and are related to the catabolic state and protein wasting caused by the increased level of pro-inflammatory cytokines, inadequate protein intake, insulin resistance, and other multiple metabolic derangements due to uremia.[8-11] Since the mean age of dialysis patients is increasing worldwide, identifying these conditions means a lot for those patients, as these outcomes are associated with poor prognosis and survival.[12] Thus, identification of sarcopenia deserves special attention. Sarcopenia is defined as a progressive and generalized skeletal muscle disorder, and several studies have demonstrated an association between sarcopenia and/or the individual components of sarcopenia (i.e., low muscle mass, low muscle strength, and slow gait speed) and high mortality in patients undergoing dialysis.[13-17] Also, sarcopenia stands as a major underlying cause and one of the core components of frailty, which is a significant contributor to adverse outcomes in hemodialysis (HD) patients.[18]

Several recent international consensus definitions have been reported to diagnose sarcopenia in clinical and research settings, which all share the common diagnostic components, i.e., identification of low muscle mass and low muscle strength/impaired physical performance. The European Working Group on Sarcopenia in Older People (EWGSOP) consensus definition is the most commonly used and cited definition in the literature. The EWGSOP2, representing its most updated version, recommends detecting low muscle quantity and/or quality to confirm the diagnosis of sarcopenia.[19] Thus, muscle mass measurement is an integral part of assessments for sarcopenia.

Bioelectrical impedance analysis (BIA) has been commonly used as a tool for muscle mass assessment in many clinical and research settings, as it is non-invasive, inexpensive, practical, and portable. It allows measurement of fat-free mass (FFM), fat mass (FM), and other body compartments by giving estimations based on electrical conductivity of tissues.[20] Bioelectrical impedance analysis also has a special significance for HD patients as it can be additionally utilized for nutritional assessment and dry weight estimation, which are important for patients' prognosis and quality of life.[21] However, the validity and precision of the BIA measurements are influenced by various factors that affect the hydration status.[22] In HD patients, the volume status fluctuates easily and continuously, which is most significant between pre-dialysis and post-dialysis periods. Thus, a significant difference in the results of BIA measurements is obviously expected between that obtained before HD and after HD. Because sarcopenia is a major factor that increases the likelihood of adverse outcomes in this patient population,[13-17] and muscle mass measurement is an integral part of sarcopenia assessment, there is a need to clarify the ideal timing of BIA measurements to come up with reliable results in HD patients.

In the HD population, there have been debates about whether hydration status has a significant impact on BIA measurements, as some studies reported changes with hydration status[21] while others came up with little effects.[23] Furthermore, whether the timing of performing BIA matters for reliable estimations is an issue that needs to be enlightened. Water is the major determinant of impedance and as is well known, skeletal muscles contain high amounts of water both extracellularly and intracellularly.[24] Therefore, one can suggest that the accumulation of excess water in the intra- and extracellular compartments due to kidney failure would confound the muscle mass estimations. Panorchan et al[25] evaluated whether fluid status would affect BIA measurements in 676 HD patients and suggested that overhydration overestimates muscle mass and underestimates fat mass (FM). They concluded that BIA measurements of body composition should be made "when patients are closer to their target weight" than when overhydrated. Studies in the literature suggest that hydration status significantly impacts body composition evaluation and emphasize that overhydration overestimates muscle mass values in HD patients.[21,26,27] Moreover, FFM estimations were derived from prediction equations developed in healthy individuals with stable fluid status.[28-32] For this reason, to remove the confounding effect of excess water, it seems more appropriate to perform BIA measurements in chronic HD patients when they are closer to their dry weight, i.e., after the dialysis rather than before it. At this point, one should consider that dialysis itself can change electrolyte concentrations, which may result in resistance changes[33]and may also affect the accuracy of post-dialysis measurements. So, the other question comes forward: what should be the exact time to perform BIA after an HD session? In fact, a limited number of studies present a strong recommendation. Pupim et al[34] suggested that this problem can be minimized with measurements performed not earlier but 30 minutes after HD, since fluid shifts caused by osmotic imbalance related to HD would subside approximately 20-30 minutes after the session. More recently, Di Iorio et al[35] reported that BIA variables "remain constant and reproducible over the 120 minutes after the end of HD," which they call as a dry weight state.They suggested that, without any food/drink consumption, one can obtain stable body composition values over 2 hours post-dialysis. Carrero et al[36] also recommended that measurements should be performed preferably between 15 and 120 minutes post-dialysis, since the patients would be closer to their target weight after HD compared to the overhydrated pre-dialytic period. Hence, it seems that performing BIA measurements in the period after 15 minutes and within the following 2 hours after the HD session will aid in a better estimation of muscle mass in terms of reliability and reproducibility. Many centers perform measurements before HD session because it is more convenient for both staff and patients. Asking patients

MAIN POINTS

- As a diagnostic method for sarcopenia, bioelectrical impedance analysis might be affected by the hydration status. Therefore, there is a need to clarify the ideal timing of bioelectrical impedance analysis measurements in hemodialysis patients.
- In the light of the recent literature, it seems more appropriate to perform bioelectrical impedance analysis measurements in the period starting from 15 minutes and within 2 hours after hemodialysis sessions, in order to provide reliability and reproducibility.
- Although bioimpedance spectroscopy represents the ideal bioimpedance technology for assessing muscle mass in hemodialysis population, the confounding effect of excess fluid on estimations still may not be subsided. Therefore, it seems proper that measurements are better to be performed in the post-hemodialysis period regardless of the preferred bioimpedance technology.

to stay after the session and making them take the necessary steps for measurements seem difficult, especially for older HD patients. However, as outlined above, the confounding effect of excess water on the correct BIA estimations seems substantial, and the assessment of body composition via BIA in the immediate pre-dialysis period is an important limitation point of those assessments (Figure 1).

Bioimpedance techniques are classified with regards to the frequencies of electric current they use, i.e., single frequency (sfBIA) and multi-frequency (mfBIA).[37] The sfBIA measures whole-body bioimpedance with a frequency of 50 kHz and mfBIA with several frequencies ranging from 5 to 1000 kHz. These 2 BIA technologies express body composition as a 2-compartment model (FM and FFM) and have been used more frequently in clinical settings.[37-39] In recent years, a relatively new bioimpedance technology, bioimpedance spectroscopy (BIS), has been introduced that is not affected by the hydration status. The BIS uses all frequencies ranging from 0 to 1000 kHz and expresses the whole body as a 3-compartment model (FM, lean tissue mass, and water). These devices are designed to separate extracellular water excess from normohydrated, fat-free tissues. In this way, they provide more accurate muscle mass estimates even if the fluid distribution is altered. This 3-compartment model of the BIS has been validated against standard reference methods for assessment of fluid status and body composition in dialysis patients.[20,40-44] For all these reasons, BIA has been largely replaced by BIS recently to assess fluid status and body composition in chronic kidney disease and ESKD researches and clinical evaluations. However, although BIS promises to give more accurate estimations of body composition with the promise of not being affected by the hydration status, few studies[45,46] showed that BIS also had a potential to overestimate FFM when it is performed before HD. Tangvoraphonkchai et al[45] aimed to determine whether pre-HD measurements of body composition alone would suffice by being unaffected by volume overload in 48 patients undergoing HD. Accordingly, they compared corresponding pre- and post-HD body composition data driven via BIS and found out that both FM index (FMI) and FFM index (FFMI) were confounded by the hydration status, as FFMI was overestimated and FMI was underestimated with pre-HD measurements.

While BIS may appear to give more accurate results post-HD according to these findings, it still provides an indirect measure of body composition and is therefore prone to error. In a longitudinally designed study, the accuracy of predictive equations

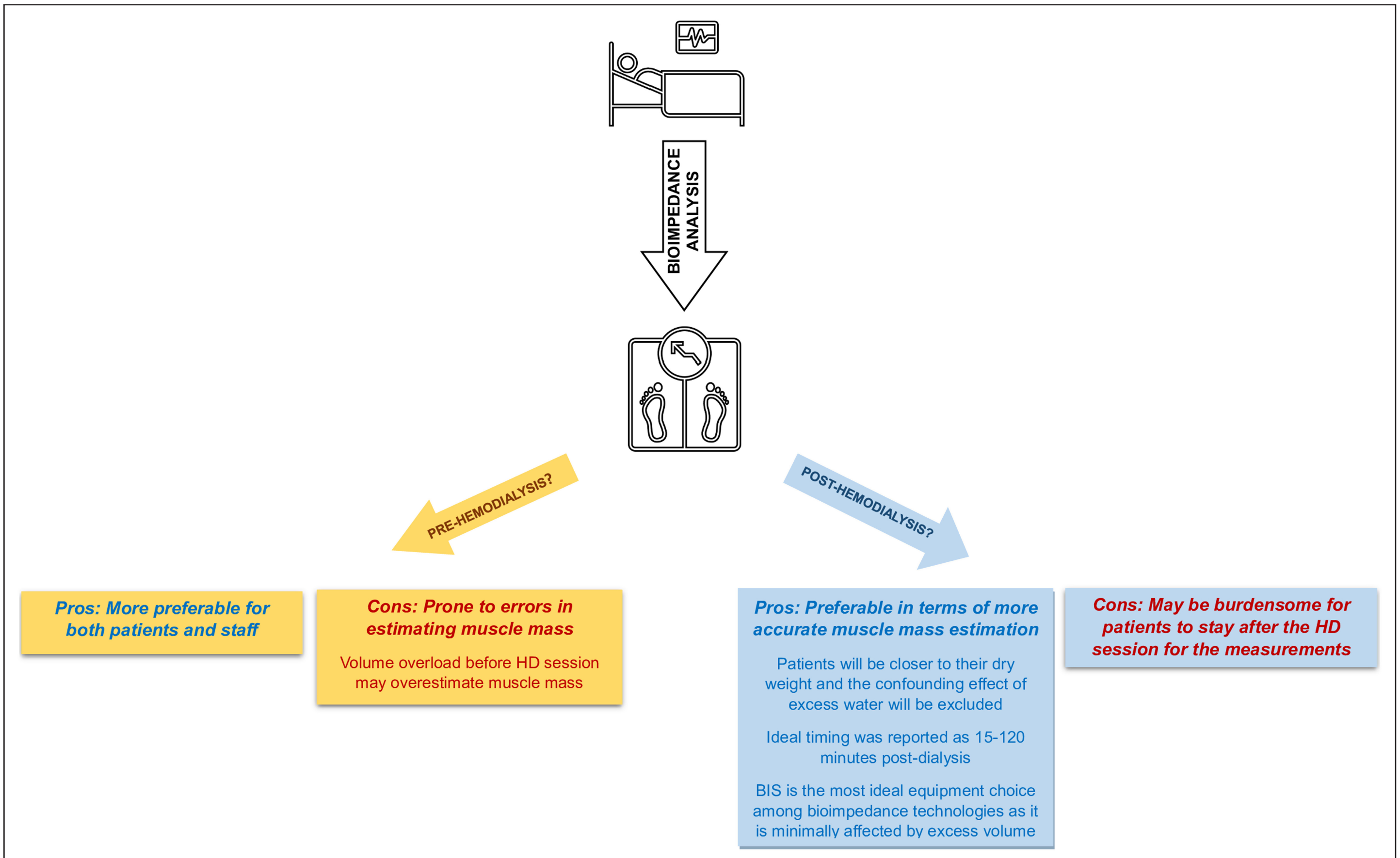

Figure 1. Pros and cons of bioelectrical impedance analysis measurements performed before vs. after hemodialysis sessions for muscle mass assessment in patients undergoing hemodialysis. BIS, Bioimpedance spectroscopy; HD, hemodialysis.

based on BIS for estimating FFM and appendicular FFM was studied in comparison with dual-energy x-ray absorptiometry (DXA) as the reference method. In a more general population of patients with chronic kidney disease (non-dialysis-dependent patients, patients undergoing HD or peritoneal dialysis (PD), or kidney transplant patients), it was reported that total body water is one of the main factors affecting the bias encountered between BIS and DXA measurements. Of note, measurements were performed 30 minutes after the HD session in patients undergoing HD and after drainage of the effluent in PD patients to exclude the confounding effect of excess water.[47] Therefore, although BIS is considered as the ideal bioimpedance technology for assessing muscle mass in HD patients, the confounding effect of hydration status on estimations may not be subsided with its use. It is clear that evidence is limited and conflicting as to whether BIS provides an accurate estimation without being affected by the hydration status, and further studies are needed to demonstrate that it works well in this particular patient population. Nevertheless, it seems proper that measurements are better to be performed in the post-HD period via either bioimpedance technologies in the context of muscle mass assessment.

In conclusion, while assessing muscle mass in patients undergoing HD via bioimpedance technologies, BIS is considered preferable over sfBIA or mfBIA. Furthermore, all these techniques should preferably be performed in the post-dialytic period, specifically within 15-120 days following the end of the dialysis.

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