Editorial Review

Current state of bioimpedance technologies in dialysis

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Keywords: bioimpedance; body composition; body hydration; dialysis; dry weight

Introduction

Determination of body hydration and nutritional status are significant problems in dialysis patients. In practice, clinical evaluation is usually used to estimate the ultrafiltration target, since accurate knowledge of dry weight is lacking. Several methods have been proposed for non-clinical dry weight assessment; these include natriuretic peptides, measurement of inferior vena cava diameter and collapsibility on inspiration by ultrasound and intradialytic relative blood volume change. Unfortunately these methods suffer from several shortcomings, such as poor specificity (natriuretic peptides), operator dependence (inferior vena cava diameter measurements) and poor correlation with extracellular volume (continuous blood volume measurement) [1].

After years of bioimpedance analysis (BIA) research in dialysis patients, this technique is now increasingly used clinically. BIA as a means to determine extracellular volume (ECV) or/and intracellular volume (ICV) has been validated by applying dilution methods as the gold standard. Body composition analysis by BIA has been compared to magnetic resonance imaging (MRI) and appropriate regression models have been developed to estimate fat and muscle content [2,3]. This editorial deals with the principles of BIA techniques, and their clinical application in fluid management, body composition and nutrition.

Principles of bioimpedance techniques

Impedance (Z) denotes the opposition to injected alternating and/or direct electric current; Z has two components (Figure 1A): resistance (R; x-axis) and reactance (Xc; y-axis). Resistance is the opposition to the flow of direct and alternating electric current and reactance is the opposition to the passage of alternating current. Resistance and reactance decrease with higher frequencies of the alternating current. The fluid component is largely reflected in the resistance, whereas reactance might represent the cell membrane that is related to nutrition. Tissue volume (V; cm³) can be calculated as

\[ V = \rho \frac{L^2}{Z}. \]  

The resistivity \( \rho \) (\( \Omega \text{ cm} \)) describes how strongly a certain material opposes the flow of electric current; \( L \) is the conductor length (cm).

In biological tissues lower frequency currents travel preferentially in the extracellular space, whereas high frequency currents traverse both ECV and ICV.

With the injection of multifrequency currents [multifrequency bioimpedance spectroscopy (MFBIS); standard range 5 kHz to 1000 kHz] ECV and ICV can be computed using the Cole–Cole model [4]. Single frequency bioimpedance analysis (SFBIA) with an injection current frequency of 50 kHz is simpler and easier to use than MFBIS [5], but the inability to make an accurate distinction between ECV and ICV is a major limitation. The various BIA techniques are summarized in Table 1.

Clinical application in dialysis

The clinical use of BIA is currently focused on two major fields, firstly the management of extracellular fluid (dry weight) and secondly the assessment of nutritional status.

Assessment of hydration status and dry weight in hemodialysis patients

Over-hydration is frequent in dialysis patients. In the course of clinical probing for dry weight [1] hypotension may frequently occur, resulting in uncomfortable events, such as muscle cramps, dizziness and fatigue. Non-clinical dry weight assessment is very much needed, and BIA has gained widespread interest in that respect.

Different approaches such as wrist-to-ankle ("whole body") or segmental BIA (SBIA) [6–13] have been used to measure ECV, ICV and total body water (TBW) in...
dialysis patients. These studies aimed to measure hydration status and estimate dry weight by employing ratios of ECV to ICV, ECV to TBW or ECV to body weight \[14–18\].

Unfortunately, with current BIS techniques, the standard error of ECV measurement in healthy subjects is \(\geq 1\) L and that of ICV is \(\geq 1.5\) L \[18\], limiting their clinical utility to dry weight determination. However, accuracy may be improved by a new modeling equation, taking differences in body composition into account \[19\].

To overcome these limitations, we applied continuous monitoring of the segmental ECV with SBIA to assess hydration states during subsequent hemodialysis sessions \[20–22\]. Thereby, calf ECV is monitored continuously (Figure 2) by BIS (calf BIS; cBIS). When dry weight is approached, no further decline of calf ECV takes place and resistivity should—ideally—rise to the normal range. Because of gravitational forces, the lower limb is more likely to be over-hydrated than other anatomical sites, and may thus represent the best single location to delineate total body hydration. Notwithstanding, elevated venous pressure (e.g. right-sided heart failure; postphlebitic syndrome) may result in reduced reabsorption of extracellular fluid from the limb. Therefore, the use of lower limb resistivity from a normal population as a confirmatory measurement in dialysis patients is not sufficient due to the individual variation in body composition.

### Table 1. Comparison of bioimpedance techniques used in dialysis

<table>
<thead>
<tr>
<th>Technique</th>
<th>Applications</th>
<th>Advantage</th>
<th>Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole body</td>
<td>Measurement of whole body ECV, ICV and TBW using a regression model, assessment of body composition from a specific model</td>
<td>Simple, relative lower cost for device and operation. Calculation is easy and fast</td>
<td>Accuracy is not enough for clinical use due to the individual variation in body composition</td>
</tr>
<tr>
<td>MFBIS</td>
<td>Measurements of total body ECV, ICV and TBW by Cole–Cole model, estimation of body composition based on the volume measured</td>
<td>Provide stable and relative accurate ECV, ICV, TBW and muscle mass</td>
<td>Accuracy can be affected by the amount of subcutaneous fat</td>
</tr>
<tr>
<td>Vector BIA</td>
<td>Assessment of nutrition and hydration state</td>
<td>Simple and observable from the R–Xc graph</td>
<td>Accuracy limited by the lack of independence of R and Xc</td>
</tr>
<tr>
<td>Segmental</td>
<td>Measure ECV, ICV or muscle in the one of the segments</td>
<td>Relative accuracy using a model by comparing MRI data</td>
<td>Depend on an empirical model that limits the application of subjects</td>
</tr>
<tr>
<td>measurement</td>
<td>Measurement of ECV, ICV and TBW, muscle in each segment or sum of segments</td>
<td>Provide fluid and muscle in the segment separately as well as total body with an acceptable accuracy</td>
<td>Need more electrodes, additional switch and careful placement of electrodes</td>
</tr>
<tr>
<td>Calf BIS</td>
<td>Measure resistance and resistivity in the calf to predict the hydration state</td>
<td>It can be continuously monitored and provide accurate hydration state</td>
<td>Initial measurement of the circumference of the calf</td>
</tr>
</tbody>
</table>

BIA, bioimpedance analysis; SBIA, single frequency BIA; MFBIA, multiple frequency BIA; ECV, extracellular volume; ICV, intracellular volume; TBW, total body water; MRI, magnetic resonance imaging.

**Assessment of body composition and nutritional status**

Nutritional status relates strongly to morbidity and mortality in dialysis patients. BIA-based measurements of muscle mass, subcutaneous and total adipose tissues have been validated by MRI and can now be done on a routine basis. BIA estimates of body cell mass and TBW are highly correlated with the results from DEXA and D2O dilution, respectively \[18\]. Relating the patient’s impedance vector in the R–Xc plane to tolerance ellipses defined in healthy subjects (Figure 1B) has been proposed as a means to assess body composition and nutritional state \[24–27\]. However, since HD patients have abnormal distribution of body fluid content, thus affecting resistance, the error of estimation may be significant. SBIA of the arm or leg has been suggested as an alternative approach \[2,28\]. Kaysen \[2\] developed a model to estimate total body muscle mass based on BIS-derived ICV, which was as precise as methods based on total \(40\)K counting. Knowledge of muscle mass can provide an indirect assessment of creatinine generation, which in turn could be used to correct the current eGFR calculations, so as to apply these to racial and ethnic groups not examined in the initial studies. Although current techniques use improved methods to assess the nutritional state of dialysis patients, the accuracy of fat-free mass estimates is still limited, due to dialysis patients’ over-hydration state.

**BIA in peritoneal dialysis (PD)**

The use of BIA in PD has been reviewed recently \[29\]. PD over-hydration is as common as in HD. The continuous
Fig. 1. (A) Impedance (Z) is a two-dimensional vector consisting of two independent scalar (one-dimensional) phenomena (both expressed in ohms): resistance (R; x-axis) and reactance (Xc; y-axis). Resistance and reactance can vary independently of each other. (B) Phase angle method using an ellipse (dash line) to represent a normal range of the resistance and reactance. Patient’s hydration state can be obtained by comparing the range of ellipse, where R, Xc and H represent resistance reactance and body height, respectively [27].

cBIS technique discussed earlier for hemodialysis may not be practicable to assess dry weight in PD patients, because fluid change is slow in the absence of rapid ultrafiltration techniques. A useful alternative may be the sum of segmental body resistivity measurement with comparison to a normal control group.

Outflow failure, defined by the incomplete recovery of instilled fluid, is observed frequently in PD patients. Kinking of the catheter, malpositioning, omental occlusion and constipation are commonly observed, but it is important to exclude dialysate leakage as the underlying cause. The initial manifestations of dialysate leakage may be subtle. Intra-abdominal fluid volume determined by bioimpedance could aid differential diagnosis of outflow failure (catheter problem versus leakage) and reduce the need for imaging studies. Continuous monitoring of the intra-abdominal fluid volume by BIA in the course of a modified peritoneal equilibration test may help to diagnose ultrafiltration failure, especially when due to rapid absorption. Calibration of BIA by infusion of PD fluid enables accurate assessment of intra-abdominal fluid volume [30].

Problems and future areas of research

What are the practical differences between segmental and wrist-to-ankle methods?

According to basic assumptions, the measured subject should be cylindrical, with isotropic conductivity in its segments and uniform current density across its cross-sectional area. It is obvious that wrist-to-ankle BIA violates this
requirement. Wrist-to-ankle BIA provides a sum of measurements from the arm and leg but neglects much of the trunk. According to some studies, SBIA is superior to wrist-to-ankle BIA for the estimation of fluid volumes. Unfortunately, it is difficult to compare the results of many methods, since no uniform SBIA methodology has been fully established yet [31].

Which method is superior, SBFIA or MFBIS?
This question has been posed since the advent of MFBIS devices [32]. SFBIA is technically simpler but less informative, since resistance and reactance from a single frequency only are collected. In contrast, MFBIS provides information on body components, whereas SFBIA applies regression models to calculate body components. Reproducibility of SFBIA heavily depends on the subject’s physical and chemical characteristics. MFBIS is based on the Cole–Cole [4] model using curve fitting methods to delineate ECV and ICV.

Is the current body composition model correct?
This fundamental question applies to both SFBIA and MFBIS. Current models ignore the effect of subcutaneous adipose tissue, the interface between electrodes and the skin and the skin resistance. These factors must be considered in models of bioimpedance. Recently, an electrical equivalent circuit model was proposed, to take into account the effect of skin and subcutaneous fat on bioimpedance measurement [33].

Conclusion
BIA is a readily available operator-independent method for assessment of the hydration status in dialysis patients. Estimation of dry weight may be facilitated by recently developed techniques, such as the dynamic intra-dialytic SBIS of the calf. With respect to the detailed assessment of body composition and nutritional analysis, in terms of fat and muscle mass, further improvement in BIA techniques is needed.

Conflict of interest statement: Nathan W. Levin holds stocks in Fresenius.

References


Received for publication: 7.11.06
Accepted in revised form: 22.11.07