Bioelectric Impedance Measurement for Fluid Status Assessment

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Abstract

Background: Adequacy of body fluid volume improves short- and long-term outcomes in patients with heart and kidney disorders. Bioelectrical impedance vector analysis (BIVA) has the potential to be used as a routine method at the bedside for assessment and management of body fluids. Methods: Impedance (Z vector) is a combination of resistance, R (function of intra- and extracellular fluid volume) and reactance, Xc (function of the dielectric material of tissue cells), with the best signal to noise ratio at 50 kHz. BIVA allows a direct assessment of body fluid volume through patterns of vector distribution on the R-Xc plane without the knowledge of the body weight. Reference tolerance ellipses (50, 75 and 95%) for the individual vector were previously calculated in the healthy population. Results: We determined the optimal vector distribution in patients undergoing hemodialysis without hypotension or intradialytic symptoms. Most vectors lay within the reference 75% tolerance ellipse of the healthy population indicating full electrical restoration of tissues. We also determined the optimal vector distribution of patients undergoing continuous ambulatory peritoneal dialysis without edema and with a residual urine output. The vector distribution was close to the distribution of both healthy subjects and pre-session distribution of hemodialysis patients. We established the relationship between central venous pressure and BIVA in critically ill patients. Shorter vectors (overhydration) were associated with increasing venous pressure, whereas longer vectors were associated with decreasing venous pressure. The association between BIVA and NT-proBNP has been evaluated in patients with acute cardiac-related dyspnea. In the ‘gray zone’ of NT-proBNP values between ‘ruling out’ and ‘ruling in’ acute heart failure, BIVA detected latent peripheral congestion. Conclusion: Simple patterns of BIVA allow detection, monitoring, and control of hydration status using vector displacement for the feedback on treatment.
volume control improves short- and long-term outcomes. The routine evaluation of hydration status based on body weight and blood pressure changes over time can be misleading, since changes are not uniquely determined by body fluid volume variations. Edema is not usually detectable until the interstitial fluid volume has risen to about 30% above normal (4–5 kg of body weight), while severe dehydration can develop before clinical signs [1].

Hemodialysis (HD) is an excellent model of fluid removal (1–5 l in 4 h) and overload (1–5 l in 2–3 days). HD often results in bringing the patient either to dehydration or to fluid repletion. Dehydration can be symptomatic (decompensated, with hypotensive episodes in the latter part of the session, malaise, washed-out feeling, cramps, and dizziness after dialysis) or asymptomatic (compensated). Fluid overload is mostly symptomatic with pitting edema, worsening of hypertension, and pulmonary congestion during the interdialysis interval. The so-called dry weight is the postdialysis weight at which all or most excess body fluid has been removed [2] (generally as the lowest weight a patient can tolerate without intradialytic symptoms or hypotension).

Treatment with diuretics and ultrafiltration (UF) of decompensated HF patients remove pulmonary and peripheral congestions until a ‘dry weight’ is achieved often resulting in dehydration. Therefore, prescription of treatment for the HF cycle of hydration can take advantage of the observations collected from the HD cycle of hydration.

**Tools for Detecting Hydration**

*Anthropometry*

Anthropometry formulas recommended in the literature [2] for estimation of total body water (e.g. Watson, Hume-Weyers, Chertow, Johanssohn) are of limited value because they are functions of body weight [3–6]. It has been shown that these formulas are completely insensitive to fluid overload with apparent edema [7].

*Dilutometry*

At the top of total body water measurement, utilization of dilutometry (e.g. tritium and deuterium) is implemented in unique centers evaluating plasma activity 3–4 h after isotope ingestion. But estimates are obtained with a relevant within-subject measurement error (up to 10%) even in the absence of delayed gastric emptying. Furthermore, three available isotopes measure different water spaces (by 3–4%). Therefore, dilutometry cannot be considered an optimal method for monitoring hydration in the clinical setting [6].

*Bioelectrical Impedance*

Bioelectrical impedance analysis (BIA) is a property-based method of body composition specifically detecting soft tissue hydration with a 2–3% measurement error,
which is comparable to routine laboratory tests [8]. The usefulness of body impedance measurement derives from its immediate availability as a noninvasive, inexpensive and highly versatile test that transforms electrical properties of tissues into clinical information [8]. Conventional BIA is based on electric models supporting quantitative estimates of body compartments through regression equations which are not valid in individuals with altered hydration. Bioelectrical impedance vector analysis (BIVA) is based on patterns of the resistance-reactance graph (RXc graph) relating body impedance to body hydration without equations [8–10]. A simple algorithm with few operational rules has been derived for interpreting impedance vector position and migration on the RXc graph at the bedside in any clinical condition. Changes in tissue hydration status below 500 ml are detected and ranked.

Body impedance is generated in soft tissues as an opposition to the flow of an injected alternate current and is measured from skin electrodes that are placed on hand and foot (whole body analysis) or on segments and regions of the body (segmental, regional analysis). Impedance (Z vector, ohm) is represented with a point in the R-Xc plane which is a combination of resistance, R, i.e. the opposition to the flow of an injected alternating current, at any current frequency, through intra- and extracellular ionic solutions and reactance, Xc, i.e. the dielectric or capacitative component of cell membranes and organelles, and tissue interfaces. The impedance of a cylindrical conductor is proportional to its impedivity (i.e. impedance per meter) and to its length, and is inversely proportional to its transverse area. Hence, whole-body impedance is determined by limbs up to 90% and by trunk up to 10% [11]. Therefore, changes in bioimpedance measurements reflect changes in the hydration of lean and fat soft tissues of limbs, whereas ascites and effusions do not contribute to the measured impedance. Vector normalization by the subject’s height (Z/H, in Ω/m) controls for the different conductor length [8–10, 12].

**Basic Patterns of BIVA**

Clinical information on hydration is obtained through patterns of vector distribution with respect to the healthy population of the same race, sex, class of BMI, and class of age [7–10, 13–23]. Unfortunately, the reference vector distribution may change with different analyzers due to the lack of one universal method of calibration of impedance devices. Our reference distribution and subsequent clinical validation studies were performed using the phase-sensitive analyzers produced by Akern-RJL Systems (Florence, Italy). Although BIVA can be done on R and Xc components at any current frequency, the optimal performance of the method is obtained with the standard, single frequency, 50 kHz current that allows impedance measurements with the best signal to noise ratio [8, 11, 13] (fig. 1). The RXc graph is a probability chart (50, 75, and 95% tolerance ellipses, i.e. bivariate percentiles) that classifies and ranks individual vectors according to the distance
from the mean value of the reference population (fig. 1 and 2). From clinical validation studies in adults, vectors falling out of the 75% tolerance ellipse indicate an abnormal tissue impedance (i.e. abnormal hydration) [7, 14, 17–20, 22].

Vector position on the RXc graph is interpreted following two directions on the R-Xc plane, as depicted in figure 2: (1) Vector displacements parallel to the major axis of tolerance ellipses indicate progressive changes in tissue hydration (dehydration with long vectors, out of the upper poles of the 75 and 95%, and hyperhydration with apparent edema, with short vectors, out of the lower poles of 75 and 95%); (2) Peripheral vectors lying on the left side of the major axis, or on the right side of the major axis of tolerance ellipses indicate more or less cell mass, respectively (i.e. vectors with a comparable R value and a higher or lower Xc value, respectively).

**BIVA in Hemodialysis**

Figure 2 shows vector trajectories observed in a dialysis session (measurements at the start and every hour) spanning within (solid circles) or out (open circles)
of the 75% tolerance ellipses during 3–4 h of UF in representative HD patients (several with HF). Vector displacement occurs following fluid volume changes below 500 ml (fig. 1 and 2) [19].

The first and more frequent pattern is a vector displacement parallel to the major axis of the tolerance ellipses. According to the basic patterns, long vectors overshooting the upper poles indicate dehydration (dry vectors), and short vectors migrating across the lower poles indicate fluid overload (wet vectors). Vector trajectories spanning on the left side versus trajectories on the right side of ellipses are from patients with more versus less soft tissue mass, respectively. The second pattern of UF is a flat vector migration to the right, due to an increase in R/H without a proportional increase in Xc/H due to loss of cells in soft tissue. This pattern is characteristic of patients with severe malnutrition or cachexia, including cardiac cachexia. It is never observed in vectors lying on the left of the ellipses. R is resistance, Xc reactance, and H height.

The second pattern associated with UF is a flat vector migration to the right side, due to an increase in R/H without a proportional increase in Xc/H caused by severe loss of soft tissue mass. This pattern is characteristic of patients with severe malnutrition or cachexia, in particular with cardiac cachexia following congestive HF. It is never observed in vectors lying on the left of the ellipses.

**Fig. 2.** Solid and open circles indicate vector trajectories that spanned within (normal) or out (abnormal) of the 75% tolerance ellipses, respectively, during 3–4 h of UF in representative HD patients (several with HF). The first and more frequent pattern is a vector displacement parallel to the major axis of the tolerance ellipses. Long vectors overshooting the upper poles indicate dehydration (dry vectors), and short vectors migrating across the lower poles indicate fluid overload (wet vectors). Vector trajectories spanning on the left side versus trajectories on the right side of ellipses are from patients with more versus less soft tissue mass, respectively. The second pattern of UF is a flat vector migration to the right, due to an increase in R/H without a proportional increase in Xc/H due to loss of cells in soft tissue. This pattern is characteristic of patients with severe malnutrition or cachexia, including cardiac cachexia. It is never observed in vectors lying on the left of the ellipses. R is resistance, Xc reactance, and H height.
Better Information from BIVA than BIS

The analysis of the HD cycle highlighted pitfalls in the BIS model [13] (fig. 1). Intra- and extracellular flows of current at any frequency, due to tissue anisotropy, cause equivalence of information based on functions of R and Xc measurements made at 50 kHz versus other frequencies (4–1,024 kHz). With whole-body BIS before and during fluid removal (0, 60, 120, 180 min, 2.5 kg) in HD patients, one can observe that with increasing current frequency, R decreases and Xc moves along the Cole’s semicircle on the R-Xc plane (fig. 1). The Cole’s semicircles progressively enlarge and move to the right on the R-Xc plane following fluid removal (increase in both R and Xc values at any given frequency). Xc values at 5 kHz (expected values close to 0 Ω) reached 70% of the maximum Xc, indicating an intracellular current flow also at low frequencies. The correlation coefficient between R at 50 kHz and R at other frequencies ranged from 0.96 to 0.99. In the clinical setting, the comparison of vector position and migration with target reference intervals represents an additional advantage of BIVA, which is not allowed with BIS (fig. 1).

BIVA in Peritoneal Dialysis

In continuous ambulatory peritoneal dialysis, peritoneal UF is obtained with 2 l of hypertonic glucose solutions or icodextrin infused within the abdomen and exchanged with 2 l of fresh solution every 6 h. More glucose in the solution drives more UF. The process is continuous rather than cyclical as in HD. Adequate UF should keep hydration of CAPD patients close to normal [2].

With BIVA, we established the optimal tissue hydration in CAPD patients. We studied 200 patients, 149 without edema and asymptomatic, and 51 with pitting edema due to fluid overload. There was no difference in impedance measurements before and after 2 l of fluid infusion in the abdomen. In asymptomatic CAPD patients, we found a vector distribution close to the healthy population and to the distribution of asymptomatic HD patients before the dialysis session [7]. Vectors from patients with edema were displaced downward on the RXc graph, out of the 75% ellipse and close to vectors from nephrotic patients not undergoing dialysis. Therefore, the pattern of fluid overload with the vector displacement in the direction of the major axis was also observed in CAPD patients. This pattern can be utilized in dialysis prescription using vector displacement for the feedback on glucose solutions in order to keep or achieve a normal hydration without the knowledge of the body weight.

BIVA in Congestive Heart Failure

The clinical validation of BIVA in HD patients allows direct extension of the same BIVA patterns to the congestive HF. Similar to the HD cycle, HF is
characterized by a cyclical fluid overload (pulmonary and peripheral congestion) and removal (diuretics, extracorporeal fluid removal with UF). Despite current therapy, the high rate of readmission indicates that the present criteria for discharge, typically based mostly on subjective impressions, correlates poorly with clinical stabilization.

Current practice uses the biomarker NT-proBNP for interpretation of overhydration in the diagnosis of HF [24]. Values between the lower threshold point for ‘ruling out’ acute HF and the higher, aged-adjusted cutoff point for ‘ruling in’ acute HF are referred to as gray zone values. In the situation of a ‘gray zone’ diagnosis, clinical judgment of congestion is often necessary to ascertain the correct diagnosis. It is possible that the diagnostic and prognostic values of the NT-proBNP depend on the level of congestion (i.e. ‘wet’ worse than ‘dry’ NT-proBNP). In 315 patients admitted to the emergency department for acute dyspnea, NT-proBNP was used as biomarker of HF, lung ultrasound was used to detect pulmonary congestion, and BIVA was used to detect peripheral congestion. Peripheral congestion was either apparent with edema or latent without edema (unpubl. obs.). Patients were classified into two categories: cardiac-related dyspnea (n = 169) or noncardiac-related dyspnea (n = 146).

The mean impedance vector was significantly shorter in patients with cardiac-related dyspnea, with a parallel decrease in both R and Xc components according to the pattern of fluid overload. BIVA was able to detect a ‘latent peripheral congestion’ in dyspneic patients with NT-proBNP in the ‘gray zone’. Ongoing intervention studies are needed to establish the region of the R-Xc plane where the individual vectors should be brought following an adequate fluid removal which is the region where an optimal ‘dry’ patient will decrease the rate of death and readmission, and also decrease the incidence of acute renal dysfunction.

**BIVA in Critically Ill Patients**

Determination of fluid volumes in patients in the intensive care unit is neither practical nor reliable. Limitations in the use of tracer dilution methods and violations of the assumption of constant hydration of soft tissues severely diminish the validity of the dilution method and conventional BIA in critically ill patients. In the critical care setting, however, central venous pressure (CVP) values are used as a guide for fluid infusion. Low CVP values are observed with true or relative hypovolemia, once a negative intrathoracic pressure has been excluded. Conversely, high CVP values indicate true or relative hypervolemia and fluid overload.

BIVA was examined as an indicator of fluid status compared to CVP in 121 ICU patients [18]. Both components of the impedance vector were significantly, linearly, and inversely correlated with CVP values. A progressive increase in the CVP corresponded in the R-Xc plane with backward and downward
displacement of the impedance vector to the region of fluid overload out of the lower pole of the 75% tolerance ellipse. Low CVP values were associated with most vectors of normal length or long vectors overshooting the upper pole of the 75% reference ellipse (e.g. BIVA pattern indicating tissue dehydration).

The combined evaluation of peripheral tissue hydration with BIVA and of central filling pressure with CVP provides a useful clinical evaluation tool in the planning of fluid therapy for ICU patients, particularly in those patients with low CVP. Indeed, a different response or tolerance to fluid infusion is expected in patients with peripheral dehydration compared to well-hydrated patients with a same low CVP where BIVA can identify those with reduced, preserved, or increased peripheral tissue fluid content.

**BIVA in Localized Edema**

Direct measurements of segmental Z can be evaluated with BIVA. Edema localized in one leg frequently follows a femoral-popliteal bypass. Localized edema can bias the interpretation of whole-body impedance [12]. Limbs and trunk contribute to whole-body Z by 90 and 10%, respectively [11]. The R and Xc components of Z vector were measured at 50 kHz in 20 adult male patients without edema, before and 3 days after a femoral-popliteal bypass that induced pitting edema in the leg. Whole-body Z was measured from hand to foot of the right and left side. The impedance of each leg was measured from the pair of electrodes on foot and the other pair on the trochanter.

After surgery, mean whole-body and leg Z vectors from the side without edema did not change position in the R-Xc plane with respect to the position before surgery. In contrast, mean whole-body and leg Z vectors of the body side with edema significantly shortened according to the BIVA patterns of fluid accumulation along a down-sloping trajectory, due to a combined decrease in both vector components (R and Xc).

Because whole-body Z vector from the side of the body without edema was not sensitive to the edema localized in the leg of the opposite side, it can be utilized in the assessment of body composition also in patients with edema in one leg. Furthermore, a complete resolution of the fluid accumulation in the leg is expected to bring Z-leg to the baseline position before surgery. Similar evidence cannot be obtained with other BIA methods.

**Conclusions**

Tissue hydration changes that are cyclical in HD and HF patients or slow over days in CAPD and ICU patients are detectable as changes in the whole-body impedance, which can be utilized with BIVA patterns in monitoring and
prescribing optimal hydration independent of the body weight. Wet-dry weight prescription based on BIVA indication would bring abnormal vectors back into the 75% reference ellipse, where tissue electrical properties are restored. A simple algorithm with few operational rules is provided for interpreting impedance vector position and migration on the RXc graph at the bedside. Longitudinal and intervention studies are required to establish whether patients with vectors cycling within the normal third quartile ellipse have better outcomes than those cycling out of the target interval.

References


