Relationship between central venous pressure and bioimpedance vector analysis in critically ill patients

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Objective: To assess the relationship between central venous pressure values and bioelectrical impedance vector analysis (BIVA), which may be used as complementary methods in the bedside monitoring of fluid status.

Design: Cross-sectional evaluation of a consecutive sample.

Setting: Intensive care unit of a university hospital.

Patients: One hundred and twenty-one consecutive Caucasian, adult patients of either gender, for whom routine central venous pressure measurements were available.

Interventions: None.

Measurements and Main Results: Central venous pressure values and impedance vector components (i.e., resistance and reactance) were determined simultaneously. Total body water predictions were obtained from regression equations according to either conventional bioimpedance analysis or anthropometry (Watson and Hume formulas). Variability of total body water predictions was unacceptable for clinical purposes. Central venous pressure values significantly and inversely correlated with individual impedance vector components ($r^2 = .28$ and $r^2 = .27$ with resistance and reactance, respectively), and with both vector components together ($R^2 = .31$). Patients were classified in three groups according to their central venous pressure value: low (0 to 3 mm Hg); medium (4 to 12 mm Hg); and high (13 to 20 mm Hg). Three BIVA patterns were considered: vectors within the target (reference) 75% tolerance ellipse (normal tissue hydration); long vectors out of the upper pole of the target (dehydration); and short vectors out of the lower pole of the target (fluid overload). The agreement between BIVA and central venous pressure indications was good in the high central venous pressure group (93% short vectors), moderate in the medium central venous pressure group (35% normal vectors), and poor in low central venous pressure group (10% long vectors).

Conclusions: Central venous pressure values correlated with direct impedance measurements more than with total body water predictions. Whereas central venous pressure values >12 mm Hg were associated with shorter impedance vectors in 93% of patients, indicating fluid overload, central venous pressure values <3 mm Hg were associated with long impedance vectors in only 10% of patients, indicating tissue dehydration. The combined evaluation of intensive care unit patients by BIVA and central venous pressure may be useful in therapy planning, particularly in those with low central venous pressure in whom reduced pressure, or increased tissue fluid content can be detected by BIVA.

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Key Words: bioelectrical impedance; electric conductivity; water balance; total body water; central venous pressure; critical care; monitoring

Weight changes in patients cannot be used to estimate tissue changes, because changes in body mass are predominantly caused by large changes in total body water (TBW), even with an expansion of the extracellular water (1). In intensive care unit (ICU) patients, reliable water measurements with reference methods such as isotope dilution are much more difficult to obtain than in normal subjects or even the majority of sick patients, because of either fluid sequestration or abnormal penetration of tracers into cells (1). In the critical care setting, central venous pressure values, obtained from either central venous pressure catheter or more invasive hemodynamic monitoring (e.g., pulmonary artery flotation catheter) are used as a guide in fluid infusion. Low central venous pressure values are observed with true or relative hypovolemia, once a negative intrathoracic pressure has been excluded. On the other hand, high central venous pressure values indicate true or relative hypervolemia and fluid overload, in the absence of a number of conditions (right ventricular dysfunction, hindrance to right atrial emptying, tricuspid regurgitation, cardiac tamponade or constrictive pericarditis, and positive intrathoracic pressure) (2, 3).

Body composition methods using bioelectrical impedance analysis (BIA) are property-based methods (4). Impedance is a measurable property of electrical conduction of soft tissues, because fat and bone are poor conductors (5–7). Whole-body impedance, a complex number represented in the real-imaginary plane by the Z vector (5–7), is a combination of resistance (R) (i.e., the opposition to flow of an alternating current through intra- and extracellular solutions, representing the real part of Z) and reactance (Xc) (i.e., the capacitance produced by tissue interfaces and cell membranes, representing the imaginary part of Z) across tissues.

In BIA studies, the height is used as a measure of the human conductor length (5, 6). Many conventional BIA predictions of TBW from $H^2/R$ (called the
impedance index), while requiring model assumptions, are nevertheless accurate in healthy adults (4, 5, 6, 8). In patients with abnormal hydration (e.g., critically ill patients), predictions of body compartments from conventional BIA equations can be biased, because of violation of the assumption of fixed (73%) hydration of tissues (4–6, 8, 9).

We overcame any need of assumptions for BIA and avoided biased estimates by using direct measurements from the analyzer of the impedance vector components, namely R and Xc. These values used with the RXc graph method (10, 11) will be referred to as the bioelectrical impedance vector analysis (BIVA). Tissue hydration can be qualitatively evaluated by BIVA in any clinical condition and without knowledge of the body weight (10, 12–14), simply by comparison with reference vector distribution (11).

In BIVA, we used the standard 50-kHz frequency, because measurements of R and Xc at multiple frequencies, despite the promising theory, did not provide any clinically significant improvement over measurements at only 50 kHz for the estimation of extracellular water and TBW (5, 15–19). In fact, in muscle cells, the current passes according to an electrical behavior more complex than in suspended cells, where the extracellular or intracellular current path predominates at low or high frequencies, respectively (5, 7).

In this study, using a heterogeneous ICU population, we sought to determine relationships between venous pressure and tissue electrical conductivity measurements according to the BIVA approach. We designed the protocol on the hypothesis that a combined utilization of two methods measuring different entities related to body fluid content could improve bedside monitoring of the patient's hydration status. For comparison of methods, we also considered TBW predictions based both on anthropometry and conventional BIA regression equations.

**MATERIALS AND METHODS**

**Study Design**

A cross-sectional study of consecutive patients admitted to the ICU of our university hospital was designed to establish whether the central venous pressure correlated with whole-body, tetrapolar impedance measurements.

**Study Populations**

We studied 121 consecutive patients (70 males and 51 females; age range, 18–80 yrs) undergoing treatment in the ICU. The study did not interfere with the patient's treatment. Approval was obtained by the local ethics committee, and subjects had obtained signed written informed consent.

**Inclusion Criteria.** Adult Caucasians of both genders undergoing intensive care treatment with routine monitoring of central venous pressure were eligible for the study. Sixty-eight patients were admitted to the ICU after abdominal surgery (37 with liver transplant, 16 with gastrointestinal surgery, and 15 with aortic aneurysm repair), and 53 patients with cerebrocerebral injuries (23 with cerebrocerebral hemorrhage, ten with cerebrocerebral/meningeal tumor, ten with carotid artery surgery, and ten with cranioencephalic trauma).

**Exclusion Criteria.** Patients with amputated limbs, those with diffuse cutaneous or traumatic muscle lesions, and cardiac patients (cardiac surgery, acute myocardial infarction, and coronary care) were not considered. As a reference normal group for impedance measurements, we considered 726 healthy healthy Italian subjects (354 males and 372 females, aged 15–85 yrs, with body mass indices of 17–31 kg/m²) who also participated in a previous study (11).

**Protocol Variables**

Age, body weight, and H were recorded on the day of admission. Body mass index was calculated as body weight divided by the H squared. Central venous pressure and impedance measurements were conducted by the same operator no more than 15 mins apart. Central venous pressure measurements (in mm Hg) were obtained according to standard methods either through a central venous (65 patients) or a pulmonary artery flotation catheter (56 patients), inserted in the subclavian vein and connected to a calibrated transducer that was zeroed using the level of the right atrium as a reference point (2, 3). Impedance measurements were obtained using a plethysmograph that emitted 800-µA and 50-kHz alternating sinusoidal current (BIA-101, RJL Systems, Clinton, MI) and was connected to surface electrodes (standard, tetrapolar placement on the hand and foot) strictly according to the method reported previously elsewhere (6). The external calibration of the instrument was checked with a calibration circuit of known impedance value (R = 470 Ω, and Xc = 90 Ω, error 1%). The mean coefficient of variation was 1% for intrindividual within-day impedance measurements. According to the RXc graph method (10), we standardized the impedance vector Z by the H of the subjects, thus expressing both R/H and Xc/H in Ω/m.

TBW was estimated by regression equations, on the basis of either anthropometry data, known as the Watson (20) and Hume (21) formulas, or conventional BIA prediction equations recommended in the literature (8), indexed in the following equations as TBW, 

**TBW** = 2.447 – 0.0952 **Age** + 0.1074 **H** + 0.3362 **Weight** (for males), and

**W-TBW =** −2.097 + 0.1069 **H** + 0.2466 **Weight** (for females), Watson formula (20);

**H-TBW** = −14.013 + 0.1948 **H** + 0.2968 **Weight** (for males), and

**H-TBW** = −35.270 + 0.3445 **H** + 0.1838 **Weight** (for females), Hume formula (21);

**BIA-TBW** = 1.726 + 0.556 **H**/R + 0.095 **Weight** (equation a) (22);

**BIA-TBW** = 0.040 + 0.590 **H**/R + 0.065 **Weight** (equation b) (23);

**BIA-TBW** = 4.65 + 0.377 **H**/R + 0.14 **Weight** = 0.08 **Age** + 2.90 **Sex** (0, female; 1, male) (equation c) (24).

Serum Na, osmolality, creatinine, and protein concentrations were determined with routine laboratory methods. The plasma oncotic pressure was calculated from albumin and total protein concentration (25).

**Statistical Analysis**

The programs of the statistical package BMDP (26) were used for standard calculations: the Student's t-test; the Hotelling's T² test for vector analysis (program 3D); the two-way analysis of variance with Bonferroni adjustment for multiple comparisons (program 7D); the chi-square test for frequency analysis (program 4F); and the linear, simple and multiple regression analysis (simple r and multiple R correlation coefficients, programs 6D and 1R, respectively). Agreement between TBW prediction equations was assessed according to Bland and Altman method (27).

Impedance vectors from ICU patients were also plotted on the RXc graph (10) using the bivariate, gender-specific, 50%, 75%, and 95% tolerance limits (28) of the impedance vector in the reference healthy population (11) (i.e., the ellipses within which the vector of the individual subject falls with a probability of 50%, 75%, and 95%, respectively).

**RESULTS**

Characteristics of ICU patients are reported in Table 1. At the time of measurements, the body temperature of patients ranged from 36 to 38°C (96.8–100.4°F). In no patient was there detectable, segmental fluid collection or sequestration (i.e., ascites, pleural or pericardial effusion, and extensive muscle hematomas). Central venous pressure values were 8.1
Table 1. Characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>All (n = 121)</th>
<th>Males (n = 70)</th>
<th>Females (n = 51)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>Mean (sd)</td>
<td>Mean (sd)</td>
<td>Mean (sd)</td>
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<tr>
<td></td>
<td>55 (15)</td>
<td>55 (13)</td>
<td>55 (17)</td>
<td>0.1</td>
<td>NS</td>
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<tr>
<td>Height (cm)</td>
<td>167 (9)</td>
<td>172 (6)</td>
<td>159 (7)</td>
<td>10.8</td>
<td>.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.9 (11.0)</td>
<td>75.3 (9.5)</td>
<td>64.7 (9.9)</td>
<td>5.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 (3.5)</td>
<td>25.5 (3.1)</td>
<td>25.5 (4.0)</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>s-Na (mmol/L)</td>
<td>139.5 (6.2)</td>
<td>139.4 (6.0)</td>
<td>139.6 (6.6)</td>
<td>0.2</td>
<td>NS</td>
</tr>
<tr>
<td>s-Osmolality (mosm/L)</td>
<td>292.2 (17.5)</td>
<td>293.0 (16.9)</td>
<td>291.2 (19.0)</td>
<td>0.5</td>
<td>NS</td>
</tr>
<tr>
<td>s-Creatinine (mg/dL)</td>
<td>1.8 (2.6)</td>
<td>1.4 (1.4)</td>
<td>2.2 (2.4)</td>
<td>2.2</td>
<td>.03</td>
</tr>
<tr>
<td>s-Protein (g/L)</td>
<td>58.2 (9.9)</td>
<td>56.2 (8.7)</td>
<td>61.5 (10.9)</td>
<td>2.3</td>
<td>.02</td>
</tr>
<tr>
<td>P&lt;sub&gt;aco&lt;/sub&gt; (mm Hg)</td>
<td>18.1 (4.8)</td>
<td>17.0 (4.1)</td>
<td>19.8 (5.5)</td>
<td>2.5</td>
<td>.01</td>
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<tr>
<td>Hematocrit (%)</td>
<td>29.9 (5.6)</td>
<td>29.8 (5.4)</td>
<td>29.9 (5.7)</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>131.3 (21.8)</td>
<td>135.8 (24.4)</td>
<td>126.3 (17.2)</td>
<td>2.2</td>
<td>.03</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>73.1 (14.1)</td>
<td>76.9 (15.7)</td>
<td>73.1 (11.8)</td>
<td>1.4</td>
<td>NS</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>8.1 (5.0)</td>
<td>9.5 (5.0)</td>
<td>6.1 (4.2)</td>
<td>3.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>R (Ω)</td>
<td>474.6 (129.2)</td>
<td>408.3 (104.9)</td>
<td>501.6 (140.5)</td>
<td>4.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>R/H (Ω/m)</td>
<td>270.4 (83.1)</td>
<td>237.9 (62.6)</td>
<td>315.1 (87.5)</td>
<td>5.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Xc (Ω)</td>
<td>34.2 (19.1)</td>
<td>30.6 (16.7)</td>
<td>39.0 (21.1)</td>
<td>2.4</td>
<td>.02</td>
</tr>
<tr>
<td>Xc/H (Ω/m)</td>
<td>20.6 (11.6)</td>
<td>17.8 (9.8)</td>
<td>24.4 (12.9)</td>
<td>3.2</td>
<td>.002</td>
</tr>
<tr>
<td>W-TBW (L)</td>
<td>36.7 (6.0)</td>
<td>41.0 (3.7)</td>
<td>30.9 (2.8)</td>
<td>16.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>H-TBW (L)</td>
<td>37.5 (6.1)</td>
<td>41.8 (3.4)</td>
<td>31.5 (3.4)</td>
<td>16.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BIA-TSWa (L)</td>
<td>46.8 (14.3)</td>
<td>52.2 (13.5)</td>
<td>38.9 (11.6)</td>
<td>5.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BIA-TBWb (L)</td>
<td>46.1 (15.0)</td>
<td>50.9 (14.1)</td>
<td>37.1 (12.2)</td>
<td>5.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BIA-TBWc (L)</td>
<td>37.7 (11.1)</td>
<td>43.1 (9.8)</td>
<td>30.4 (8.3)</td>
<td>7.5</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

BMI, body mass index; s, serum; P<sub>aco</sub>, onocotic pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVP, central venous pressure; R/H, resistance/height; Xc/H, reactance/height; TBW, total body water; BIA, bioelectrical impedance analysis; W-TBW, H-TBW, TBW calculated following Watson formula (20) and Hume formula (21); TBWa, TBWb, TBWc, TBW calculated following BIA equation a, b, and c, respectively (22); NS, not significant; t, Student's t-test.

To obtain creatinine in μmol/L, multiply mg/dL by 88.5.

mm Hg on average, and ranged from 0 to 20 mm Hg (males, 0–17 mm Hg; females, 0–20 mm Hg).

Both components of the impedance vector were significantly (p < .01), linearly, and inversely correlated with central venous pressure values, namely r² = .28 for R/H (males, r² = .15; females, r² = .29) and r² = .27 for Xc/H (males, r² = .25; females, r² = .22) (Fig. 1).

Because the two components of the impedance vector were significantly (p < .01) linearly correlated with each other (r² = .59; r² = .41 in males, and r² = .69 in females), and average values of central venous pressure, R/H, and Xc/H differed by gender (Table 1), we assessed the relationship between central venous pressure and vector components by multiple linear regression analysis (with a test for equality of regression parameters by gender). We documented a significant multiple correlation coefficient between central venous pressure, as dependent variable, and the vector components R/H and Xc/H as predictor variables (R² = .31, p < .01). The standardized, partial regression coefficients indicated that both components similarly contributed to the central venous pressure prediction (−0.30 for R/H, and −0.29 for Xc/H; p < .01). Furthermore, multiple regression parameters did not differ significantly (F = 2.3; p, not significant) between males (R² = .26, p < .01) and females (R² = .29, p < .01). However, despite the statistically significant correlation coefficients, the square of the highest R indicated that no more than 31% of central venous pressure variability could be explained by simultaneously considering both vector components.

Central venous pressure values were weakly correlated with TBW estimates provided by either the Watson (r² = .15, p < .01) or Hume (r² = .13, p < .01) formula only on combined data from male subjects (r² = .04 with Watson, and r² = .03 with Hume; p, not significant) and female subjects (r² = .05 and r² = .03, respectively; p, not significant). TBW values predicted by either formula were strongly correlated with each other (r² = .96; r² = .79 in males and r² = .90 in females) and were mostly dependent on gender, which accounted for the spurious correlation of pooled data.

Central venous pressure values correlated significantly with TBW estimates obtained by conventional BIA regression equations, with r² values ranging from .24 to .26 in pooled data (males, r² = .10–.11; females, r² = .30–.31), consistent with direct impedance measurements and correlating more than anthropometry. However, the variability of estimates using conventional equations was high, as indicated by the bias and limits of agreement (LA) between prediction for-
mulas, ranging from 1.3 to 9.1 L in male subjects (95% LA, 1.4 and 7.9 L, respectively) and from 1.7 to 8.5 L in female subjects (95% LA, 1.3 and 7.5 L) (Table 1, BIA-TB Wa vs. TB Wb, and BIA-TB Wa vs. TB Wc, respectively).

To further investigate the association between BIVA and central venous pressure indications at bedside, we classified patients with respect to their central venous pressure values into three groups, namely low, medium, and high. A low central venous pressure was defined as 0–3 mm Hg (average, 1.6 mm Hg [SEM 0.4] in nine male subjects and 1.6 mm Hg [SEM 0.3] in 12 female subjects). This central venous pressure group included ten patients from the abdominal surgery group and 11 patients with cerebrovascular injuries. Five patients were on mechanical ventilation. A medium central venous pressure was defined as 4–12 mm Hg (average, 7.9 mm Hg [SEM 0.4]) in 39 males and 6.0 mm Hg [SEM 0.4] in 32 females). This central venous pressure group included 37 and 34 patients from the abdominal surgery and the cerebrovascular groups, respectively. Twelve patients were on mechanical ventilation. A high central venous pressure was defined as 13–20 mm Hg (average, 15.4 mm Hg [SEM 0.4]) in 22 males and 14.3 mm Hg [SEM 0.5] in seven females). This central venous pressure group included 21 patients from the abdominal surgery group and eight patients with cerebrovascular injuries. Five patients were on mechanical ventilation. However, the frequency distribution of patients after abdominal surgery vs. cerebrovascular injuries into the three central venous pressure groups did not differ significantly (χ² = 4.2; p, not significant). Furthermore, by two-way analysis of variance, considering gender (Fsex) and central venous pressure group (FCVP) as factors, we documented no significant difference among groups in average plasma oncotic pressure (Fsex = 3.1, FCVP = 2.3) and Na concentration (Fsex = 0.2, FCVP = 0.5). There were mild differences among the 12 groups means of other laboratory variables, namely plasma osmolality (Fsex = 0.5, p is not significant; FCVP = 4.4, p = 0.02), creatinine (Fsex = 0.5, p is not significant; FCVP = 4.1, p = 0.02), and hematocrit (Fsex = 0.9, p is not significant; FCVP = 5.0, p = 0.01). However, differences were not statistically significant after adjustment for multiple comparisons.

Average vectors were longer in female than in male subjects in low central venous pressure (Hotelling’s T² = 7.9, p = .04), and medium central venous pressure (T² = 19.7, p = .0002), but were comparable in the high central venous pressure group (T² = 1.0; p, not significant) (Fig. 2).

We then plotted the average central venous pressure values and the corresponding average impedance vectors on the RX graph (i.e., the gender-specific reference 50%, 75%, and 95% tolerance ellipses of the healthy population). As depicted in Figure 2, the average impedance vectors from patients of either gender with low central venous pressure fell within the 50% reference interval, and the vectors from patients with high central venous pressure fell out of the lower pole of the 95% reference tolerance ellipse. Vectors from patients with medium central venous pressure were distributed across the lower pole of the 75% ellipse, out of the pole in male subjects and within the pole in female subjects. Therefore, progressively higher central venous pressure values were associated with shorter and more down-sloping impedance vectors plotted on the RX graph, where the lower pole of the 75% tolerance ellipse was identified as a threshold for fluid overload in renal patients (10, 13, 14). However, the distribution of individual vectors on the RX graph was highly scattered within each central venous pressure group (Fig. 2). Indeed, 62% of vectors from the low central venous pressure group fell within the 75% tolerance ellipse (67% in males and 58% in females), 35% from the medium central venous pressure group (33% in males and 38% in females), and 7% from the high central venous pressure group (5% in males and 14% in females). Furthermore, short vectors, falling out of the lower pole of the target ellipse, indicating fluid overload, were 29%, 61%, and 93% in the low, medium, and high central venous pressure groups, respectively. Finally, long vectors overshooting the upper pole of the 75% tolerance ellipse, indicating tissue dehydration, were observed in 10%, 4%, and 0% of patients from the low, medium, and high central venous pressure groups, respectively.

DISCUSSION

In this study, we evaluated the relationship between two methods used at bedside for the monitoring of patient’s fluid status, namely the central venous filling pressure and the whole-body bio-
only 35% of vectors were within the reference 75% tolerance ellipse. No agreement was found for lower central venous pressure values, which were associated with most vectors of normal length (62%) and with only 10% long vectors overshooting the upper pole of 75% reference ellipse (indicating tissue dehydration).

In the clinical setting, these results support a new operative definition of the optimal hydration status in ICU patients, considering that tissue hydration is governed by capillary and venous pressure together with systemic and local control factors. Indeed, by combining at bedside a measure of effective tissue hydration (i.e., tissue electrical conductivity) with one of venous system pressure, it is consistent to score a patient with both central venous pressure values and impedance vectors within norms of the reference population as a patient with optimal hydration status. A patient with a BIVA pattern of tissue dehydrating and with low central venous pressure values then can be scored clinically worse than one with normal central venous pressure values. Similarly, a patient with a BIVA pattern of tissue hyperhydration and with high central venous pressure values can be scored clinically worse than one with normal central venous pressure values.

The combined evaluation of tissue hydration by BIVA and central venous pressure might be useful in the therapy planning of ICU patients, particularly in those with low central venous pressure. Indeed, a different response/tolerance to fluid infusion is expected in dehydrated vs. well-hydrated patients with the same low central venous pressure value (in the range of 0–3 mm Hg), where BIVA could identify those with reduced, preserved, or increased tissue fluid content. However, only a longitudinal study will establish whether patients from different central venous pressure groups with vectors within the 75% tolerance ellipse have a different response to fluid infusion/removal than those falling out of the 75% tolerance ellipse.

The true hydration of ICU patients could not be determined in the present study without reference body composition methods, whose reliability, however, can be low in these patients (1, 4). Our results cannot be compared with BIA studies in the literature, because the relationship between impedance and central venous pressure has never, to our knowledge, previously been studied. In published studies comparing impedance values with clinical assessment of fluid status in ICU patients, neither the gender nor the Xc component was considered in the statistical analysis (19, 29–32). Interestingly, in 31 ICU patients of either gender, with clinical evaluation of hydration scored as dehydrated, euolemic, and edematous, Roos et al. (29) reported R/H and Xc/H values of 458 and 22 Ω/m, 332 and 19 Ω/m, and 217 and 9 Ω/m, respectively. These values, plotted as RXC graphs, were in agreement with our BIVA pattern (i.e., progressively shorter and down-sloping vectors on the R-Xc plane corresponding to a progressive fluid repletion). Furthermore, in 12 male subjects with central venous pressure < 5 mm Hg, the impedance (expressed as length of Z vector) ranged from 118 to 275 Ω/m (19), partially overlapping the vector distribution of our patients with low central venous pressure values. These studies indicate a great variability of impedance measurements in patients clinically classified as hypovolemic-dehydrated, accounting for the low agreement between low central venous pressure and BIVA indications in our patients.

On the basis of clinical practice, we assumed that patients with low central venous pressure values had true or relative hypovolemia and were likely less hydrated than patients with higher central venous pressure values (2, 3, 19). Surprisingly, BIVA indicated that only 10% of vectors from these patients were overshooting the upper pole of the 75% tolerance ellipse (i.e., the region of dehydration in the R-Xc plane), whereas 29% of vectors were abnormally short, falling out of the lower pole of the 75% tolerance ellipse (i.e., the region of fluid overload in the R-Xc plane). However, we are aware that invasive cardiovascular monitoring via pulmonary artery catheterization may result in a major change in therapy in 45% of patients who did not respond to the initial trial of therapy (33).

With BIVA, a qualitative indication for hydration is obtained through a comparison of the measured tissue property with percentiles from a reference healthy population. The method is noninvasive, rapid, reproducible, and simple, demanding comparable skills necessary for doing an electrocardiogram. Plotting the point corresponding to R/H and Xc/H readings with a pen on the bedside chart with the reference tolerance ellipses (as in Fig. 2) allows one to draw immediate conclusions regarding body composition independent of body weight, which results in an appropriate utilization of impedance in body composition analysis (34). For instance, we recently established that the cyclic removal and repletion of 2.7-kg fluid (0.5–0.0 kg) in 1116 uremic, asymptomatic patients (of comparable age and body mass index as ICU patients) undergoing hemodialysis was associated with a cyclic shortening (fluid removal) and shortening (interdiatry fluid repletion) of the impedance vector from the lower to upper pole of the reference 75% tolerance ellipse (14). In obese subjects, we also observed that a body weight loss of ~9 kg after energy restriction was associated with no vector displacement, in contrast with a definite vector lengthening and steepening after fluid removal of only 3 kg with hemodialysis (13).

We question the literature stating that either individual component of the impedance vector reflects changes in specific fluid compartments (e.g., intracellular, extracellular, or their ratio) (5, 18, 19, 31, 32). In fact, anisotropic structure of tissues is thought to invalidate even multifrequency BIA models predicting extracellular and intracellular fluid compartments, on the basis of current flow through suspended cells (5, 7). Finally, the variability of conventional BIA prediction equations, even in healthy subjects, could be explained, in part, by the geometrical properties of the impedance index (i.e., hyperbolic function predicting more biased TBW and fat-free mass for shorter vectors) (35). The same geometrical properties may also account for the different correlation coefficient in studies relating body weight changes to impedance changes (e.g., the shorter the vector, the lower the correlation coefficient).

The different agreement between BIVA and central venous pressure indications in different fluid states cannot be explained by data collected in the present study. Indeed, factors possibly influencing impedance measurements (1, 5, 6), such as febrile conditions, disorders in electrolyte concentration and fluid distribution or sequestration, and surgical involvement of abdominal vs. cranial regions, were either absent or uniformly distributed in central venous pressure groups. However, because of the sample’s demographics and comorbidities, extrapolation of our results may not be possible to races other than Caucasian, to patients with heart failure or shock, and to patients with nonuniform fluid distribution among body segments. A better under-
standing of the relationship between BIVA and hemodynamic data in these patients might be obtained from current studies considering longitudinal and more invasive protocols, including pulmonary artery catheterization.

In conclusion, central venous pressure values were inversely correlated with impedance measurements, and a progressive increase of the central venous pressure was represented on the Rxc plane with backward and downward displacement of the impedance vector from the target 75% tolerance ellipse to the region of fluid overload. The agreement between methods in determining the fluid status in the individual patient was greater for higher central venous pressure values, associated with short impedance vectors out of the target ellipse (BIVA pattern indicating fluid overload), moderate for medium central venous pressure values, and poor for lower central venous pressure values, which were associated with most vectors of normal length (62%) and with only 10% long vectors overshooting the upper pole of the 75% reference ellipse (BIVA pattern indicating tissue dehydration).

APPENDIX

**RXc graph, charts and calculations:** Free software available at E-mail: apiccoli@ux1.unicp.it.

**Drawing tolerance ellipses:** Using the scale of the Figure 2 for V/H and Xc/H, we drew ellipses with major and minor axes slopes of 69.30 degrees and −20.70 degrees, respectively, in the male panel, and of 69.27 degrees and −20.73 degrees in the female panel. The semiaxes lengths of the male panel ellipses were 89 and 43 Ω/m for the 50% tolerance, 127 and 61 Ω/m for the 75% tolerance, and 187 and 89 Ω/m for the 95% tolerance ellipses. In the female panel ellipses, the semiaxes lengths were 95 and 50 Ω/m for the 50% tolerance, 135 and 71 Ω/m for the 75% tolerance, and 199 and 105 Ω/m for the 95% tolerance ellipses (11).

REFERENCES