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# Rapid Measurement of Total Body Water to Facilitate Clinical Decision Making in Hospitalized Elderly Patients

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***Background.*** Bioelectrical impedance analysis (BIA) is a noninvasive rapid and simple bedside technique that can be used to predict total body water (TBW), extracellular water (ECW), and intracellular water (ICW) and identify altered fluid distribution following critical illness.

***Methods.*** An equivalence study of BIA in 32 hospitalized elderly patients was compared with reference standard dilutional measurements of deuterated water (TBW) and sodium bromide (ECW). The results were compared with anthropometric equations commonly used to predict TBW.

***Results.*** There was variability in TBW content among the participating hospitalized elderly patients. This variability was within (±5 L) and the percent difference between the standard and BIA was as follows: mean (range) –4.1% (–18.5 to 11.2). BIA reliably predicted TBW and ECW in individual participants, whereas standard prediction equations uniformly over- or underestimated TBW in individuals and whole group population.

***Conclusion.*** TBW in hospitalized elderly patients can be estimated noninvasively by bedside BIA. Standardized anthropometric equations have to be used with caution in this population.

***Key Words:*** Total body water—Body composition in aging—Bioelectrical impedance.

BODY composition measurements are important to assess nutritional depletion and lean muscle mass wasting in elderly individuals and acutely ill patients. Information on the total body water (TBW) can be used to estimate body composition and its compartments such as fat-free mass, fat mass, and body solids (1–4). Rapid knowledge of patient TBW can contribute to diagnosis, and management of fluid and electrolyte imbalance. TBW is composed of two compartments: intracellular water (ICW) and extracellular water (ECW). ICW consists of the fluid in the muscle and organ cells and ECW includes plasma, interstitial fluid, and connective tissue fluids.

In healthy humans, for rapid approximate estimates of TBW, simple anthropometric measurements can be used with considerable accuracy (5–9). However, in acutely ill patients, estimated TBW does not reliably reflect fat-free mass due to disturbances of ICW caused by protein malnutrition, changes in TBW, and changes in the ratio of ICW and ECW due to injury and inflammation (10–14). ECW occupies approximately 25% of the total body mass; however, a 40% increase in ECW would result in only a 10% increase in total volume, which may not be detected (15). This is of considerable clinical importance because excessive fluid retention in the extracellular space is known to cause increased morbidity in acutely ill patients (15–17). Moreover, a shift in the ICW/ECW ratio could occur without a large change in total volume.

To accurately measure TBW and the distribution of water between the ICW and ECW compartments, isotopic dilutions are used. Briefly, TBW is measured after oral administration of deuterated water into the blood stream and measuring the exchange of labeled hydrogen atoms with hydrogen atoms associated with carboxyl, hydroxyl, and amino acid groups. ECW is measured after oral administration of sodium bromide and measuring the bromide blood concentrations. Bromide space is determined by the area under the curve as compared with known bromide standards. The ICW is calculated as the difference between TBW and ECW. Although these methods are considered the "gold standard" methods to determine TBW, they are expensive, time consuming, and not readily available at the bedside. Urine osmolality is another important indicator of hydration status (18), but does not permit quantification of TBW.

An alternative technique to predict TBW in acutely ill patients is bioelectrical impedance analysis (BIA). This simple technique introduces a single-frequency (50 kHz) signal through two outer pairs of electrocardiograph-type electrodes placed on the right wrist and right ankle. Two inner pairs of electrodes detect resistance to the introduced signal as a function of body conductance. The circuits are designed to measure two components of the alternating current signal: resistance and reactance. The resistance reflects extracellular space, and the reactance indicates cellular activity. These currents are conducted almost

Table 1. Participants

| Characteristics | Mean (range) | | |
|---|---|---|---|
| | Total, $N = 32$ | Men, $n = 21$ | Women, $n = 11$ |
| Age (y) | 77.1 (67–87) | 79 (67–87) | 75.2 (67–84) |
| Height (cm) | 166.2 (149.9–182.9) | 169.1 (159–182.9) | 159.2 (149.9–166.4)) |
| Weight (kg) | 74.9 (43.2–114) | 73.2 (43.2–114) | 78.1 (56.6–109.3) |
| Body mass index (kg/m$^2$) | 27.2 (17.1–41) | 25.3 (17.1–33.2) | 30.7 (21.4–41) |
| Albumin (g/dL) | 3.37 (2.1–4.4) | 3.1 (2.1–3.7) | 3.78 (3.1–4.4) |

completely through the fluid compartment of the fat-free mass, which is an equivalent of TBW. The opposition to the flow of current, or resistance, is measured and used to predict TBW (3,4). BIA has been shown to be a simple, rapid, noninvasive, and reproducible technique to measure total body impedance in healthy adults (19–21). It has previously been used in assessing TBW in malnourished patients who underwent abdominal surgery (12,16,22). What is not clear is whether BIA is a useful and an accurate tool to predict TBW in acutely ill patients with nonuniform fluid distribution.

In acutely ill patients, the amount of lean muscle mass is often overestimated by anthropometric equations when compared with actual values measured by the segmental compartments of TBW or ECW. Once validated, BIA could be used to determine fluid status, estimate fat and fat-free mass, assess nutritional states, and test hypotheses related to drug doses on the individualized level in acutely ill elderly patients.

The goal of the study was to determine the agreement between TBW for commonly used equations for the prediction of TBW against the reference methods, deuterium oxide and sodium bromide dilution, in acutely ill hospitalized elderly persons.

## Methods

### *Participants*

Thirty-two acutely ill hospitalized patients were randomly recruited between 2002 and 2006 from elderly medical and surgical patients admitted to either a 10-bed veterans affairs (VA) geriatric evaluation and management unit or the 10-bed university hospital senior care service. Fifty-six individuals were consented; 14 were excluded due to current smoking, having amputations, or had implanted cardiac devices, metal pins, plates, or joint prostheses; and 10 withdrew. This study was approved by both the Vanderbilt and VA institutional review committees, and all participants provided informed consent.

### *Study Procedures*

All studies were completed at patient's bedside, after an overnight fast.

*Anthropometric measurements.*—Body height and weight were recorded from the patients' charts.

*Bioelectrical impedance measurement.*—TBW and ECW were measured using bioelectrical impedance real-time RJL Systems analyzer (RJL Systems, Clinton Twp, MI).

Participants were studied in the supine position, with arms and legs abducted at a 30°–45° angle from the trunk to avoid medial body contact by upper and lower extremities. After careful skin cleansing with alcohol, two electrocardiograph-like electrodes (Model LMP3; RJL Systems) were placed on the dorsal surfaces of the right hand and foot proximal to the metacarpal phalangeal and metatarsal phalangeal joints, respectively. Two additional electrodes were applied at the pisiform prominence of the right wrist and between the medial and lateral malleoli of the right ankle. Resistance to a tiny (undetectable by participants) electrical current (50 kHz) was measured, corresponding to TBW. Resistance, reactance, and demographic data (age, height, body weight, sex, and amount of exercise) of the patients were entered into the Cyrus software program for the graphic display of TBW and intra- and extracellular fluid content, as well as other variables related to body cell mass and energy requirements. Major assumptions for the calculation of TBW from bioelectrical impedance measurements are based on the principle that the impedance of a biologic system is related to conductor length, cross section, and frequency (23,24).

*Dilution measurements.*—TBW was measured by $^2H_2O$ dilution (25), and ECW was determined by using sodium bromide (NaBr) dilution (26). After providing a baseline blood sample, the participant drank water containing $^2H_2O$ and NaBr in the amount of 30 and 70 mg/kg body weight, respectively. Three to 4 hours after the oral dose, a second blood sample was obtained. Plasma was separated from the blood samples and frozen at 70°C for later analysis. $^2H_2O$ enrichment was determined in plasma by isotope ratio mass spectroscopy (26). The baseline (0 hour) value was used to correct the background $^2H_2O$ concentration value for the 3- to 4-hour sample. All assays were performed in duplicate, and repeat assays indicated an analytical precision of 2%. The calculation of TBW can be described by the following equation:

$$TBW = [^2H_2Odose/(^2H_2O_{3h} - ^2H_2O_{0h})]/1.04,$$

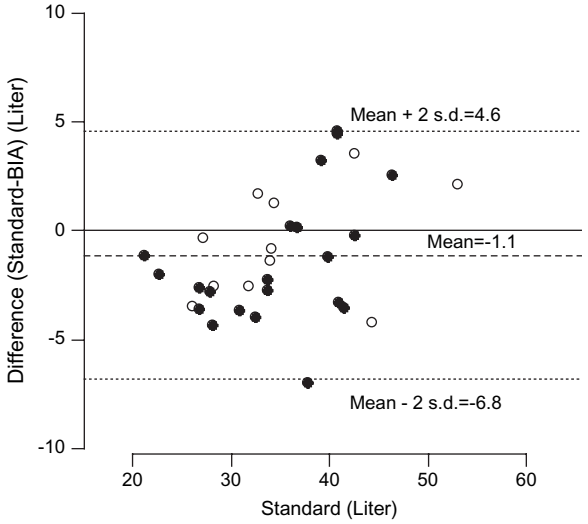


Figure 1. Total body water bioelectrical impedance analysis (BIA) measurement compared with deuterated water standard. Solid circles represent men, open circles women.

where [$^2H_2O$] denotes plasma concentration, and the constant (1.04) was used to adjust for exchange of $^2H_2O$ with nonaqueous hydrogen in the body.

NaBr dilution was assayed by using a high-performance liquid chromatography anion-exchange method, after serum ultrafiltration (26). ECW was calculated as follows:

$$ECW = [Br\ Dose/(Br\ dose_{3h} - Br\ dose_{0h})] \times 0.90 \times 0.95,$$

where [Br] denotes the serum Br concentration, and the constants (0.90, 0.95) were used to adjust for the overexpansion of Br into nonextracellular sites and for the Donnan equilibrium effect. Duplicate samples within an assay were performed with an analytic precision 2%–3%; intra-assay precision was less than 3% (Metabolic Solutions, Merrimack, NH). ICW volume was defined as TBW – ECW.

*Statistical Analysis*

Values are means and *SD*. Data analysis was performed by a random-effects model with generalized least square estimators, and Huber–White sandwich estimator of variance was used to test whether the TBW predicted by each equation or measured by BIA was different from the TBW measured by the deuterated water standard. All tests were two tailed, and a $p$ value of less than .05 was considered significant. Analyses were performed with STATA 9.2 (StataCorp, College Station, TX) and R (www.r-project.org).

## Results

Clinical characteristics of the 32 participants are shown in Table 1. The TBW measured by BIA was not significantly different from that measured by the standard (mean of difference 1.1; 95% confidence interval: –0.5 to 2.7; $p = .163$; Figure 1). Other published prediction equations (Table 2) significantly overestimated TBW and one significantly underestimated TBW compared with the standard. There was no difference in TBW measured by BIA or the standard

Table 2. Comparison of Bioelectrical Impedance Analysis Prediction Equations for TBW in the Elderly Patients

| Study | Prediction Equation |
|---|---|
| Watson* | Male: TBW-W = 2.447 – (0.09156 × age) + (0.1074 × BH) + (0.3362 × BW)<br>Female: TBW-W = –0.2097 + (0.1069 × BH) + (0.2466 × BW) |
| Chertow† | TBW-C = (–0.07493713 × age) – (1.01767992 × male) + (0.12703384 × BH) – (0.0412056 × BW) + (0.57894981 × BW) + (0.57894981 × DM) – (0.00067247 × BW2) – (0.03486146 × age × male) + (0.11262857 × male × BW) + (0.00104135 × age × BW) + (0.0186104 × BH × BW), where male = 1 and DM = 1 |
| Chumlea‡ | Male: TBW-Ch = 23.04 – (0.03 × age) + (0.50 × BW) – (0.62 × BMI)<br>Female: TBW-Ch = –10.50 – (0.01 × age) + (0.20 × BW) + (0.18 × BH) |
| Lee§ | Male: TBW-L = –28.3497 + (0.243057 × BH) + (0.366248 × BW)<br>Female: TBW-L =–26.6224 + (0.262513 × BH) + (0.232948 × BW) |
| TBW-58 | TBW-58 = 0.58 × BW |

*Notes*: BH = body height; BMI = body mass index; BW = body weight; DM = diabetes mellitus; TBW = total body water.

*TBW Watson (TBW-W; kg) predicted from bioelectrical impedance analysis developed by Watson and associates (8).

†TBW Chertow (TBW-C; kg) predicted from bioelectrical impedance analysis developed by Chertow and associates (27).

‡TBW Chumlea (TBW-Ch; kg) predicted from bioelectrical impedance analysis developed by Chumlea and associates (28).

§TBW Lee (TBW-L; kg) predicted from bioelectrical impedance analysis developed by Lee and associates (29).

Formula (TBW-58): 58% of BW.

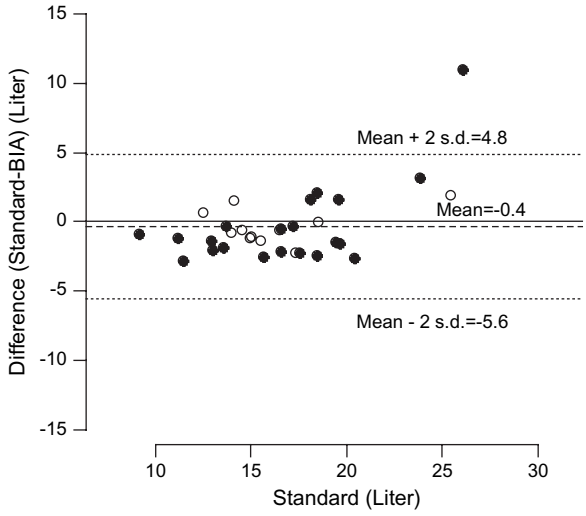


Figure 2. Extracellular water bioelectrical impedance analysis (BIA) measurement compared with sodium bromide standard. Solid circles represent men, open circles women.

Table 3. Individual Characteristics of Study Participants

| Patient No. | Race | Sex | Age (y) | Major Diagnosis at Admission | Weight (kg) | Body Mass Index (kg/m$^2$) | TBW Standard (%) | TBW BIA (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | Black | Female | 69 | CHF | 108.4 | 41 | 53.03 | 50.93 |
| 2 | Black | Female | 84 | DM | 62.7 | 27 | 27.18 | 27.50 |
| 3 | White | Female | 83 | ASCVD | 56.6 | 21.4 | 26.12 | 29.57 |
| 4 | White | Female | 83 | Falls | 67.3 | 30 | 32.67 | 31.01 |
| 5 | White | Female | 76 | CHF | 87.1 | 35.1 | 42.48 | 38.93 |
| 6 | White | Female | 74 | Pneumonia | 109.3 | 38.9 | 44.25 | 48.46 |
| 7 | White | Female | 67 | UTI | 86.6 | 35.5 | 33.95 | 35.32 |
| 8 | White | Female | 75 | CHF | 72.2 | 26.1 | 31.83 | 34.40 |
| 9 | White | Female | 73 | UTI | 71.1 | 28.5 | 34.35 | 33.12 |
| 10 | White | Female | 66 | CHF | 64.4 | 25.8 | 28.29 | 30.84 |
| 11 | White | Female | 77 | UTI | 73.5 | 28.7 | 34.06 | 34.86 |
| 12 | White | Male | 82 | CHF | 71.3 | 25.1 | 32.44 | 36.38 |
| 13 | White | Male | 87 | CHF | 80.1 | 30.1 | 39.14 | 35.89 |
| 14 | White | Male | 78 | Hip fx | 75.3 | 25.4 | 33.66 | 36.37 |
| 15 | White | Male | 67 | Pneumonia | 75.7 | 23.6 | 40.89 | 44.21 |
| 16 | White | Male | 85 | Cellulitis | 58.9 | 18.1 | 26.78 | 29.41 |
| 17 | White | Male | 82 | Prostate cancer | 57.4 | 21.4 | 26.69 | 30.28 |
| 18 | Black | Male | 72 | SDH | 83.7 | 25.0 | 37.75 | 44.75 |
| 19 | White | Male | 80 | CHF | 61.0 | 21.9 | 30.86 | 34.49 |
| 20 | White | Male | 82 | CHF | 55.7 | 20.0 | 28.16 | 32.51 |
| 21 | White | Male | 76 | Renal failure | 87.9 | 31.2 | 40.77 | 36.32 |
| 22 | White | Male | 79 | COPD | 43.2 | 17.1 | 21.18 | 22.34 |
| 23 | White | Male | 83 | CHF | 81.3 | 28.1 | 39.86 | 41.08 |
| 24 | Black | Male | 67 | CHF | 89.4 | 28.9 | 41.43 | 44.97 |
| 25 | White | Male | 82 | CHF | 54.0 | 18.3 | 27.83 | 30.61 |
| 26 | White | Male | 85 | CHF | 114.0 | 35.1 | 46.29 | 43.72 |
| 27 | White | Male | 77 | CHF | 86.0 | 30.5 | 40.77 | 36.21 |
| 28 | Black | Male | 86 | CHF | 48.3 | 16.7 | 22.68 | 24.68 |
| 29 | White | Male | 77 | CHF | 101.8 | 33.2 | 42.59 | 42.81 |
| 30 | White | Male | 75 | Pneumonia | 64.7 | 25.3 | 36.71 | 36.55 |
| 31 | White | Male | 79 | Endocarditis | 75.8 | 28.5 | 36.07 | 35.77 |
| 32 | White | Male | 79 | UTI | 72.2 | 27.5 | 33.68 | 35.92 |

*Note*: ASCVD = atherosclerotic coronary vascular disease; BIA = bioelectrical impedance analysis; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; SDH = subdural hematoma; TBW = total body water; UTI = urinary tract infection.

between the male and female patients ($p$ = .444), nor between patients with congestive heart failure (CHF) and other participants ($p$ = .151). The ECW measured by BIA was not significantly different from that measured by the standard (mean of difference 0.4; 95% confidence interval: −0.5 to 1.3; $p$ = .432; Figure 2).

Although there was some interindividual variability in TBW measured by BIA (Table 3), it was smaller than that measured by all other equations we compared. The percent difference between the standard and BIA (STD – BIA) was as follows: mean (range) −4.1% (−18.5 to 11.2).

## Discussion

BIA is a noninvasive, rapid, and simple bedside technique that can be used to predict TBW, ECW, and ICW to quantitate altered fluid distribution following critical illness.

Ritz (30) found that TBW spaces can be estimated accurately in geriatric patients with BIA and that it could be used to monitor changes in fluid balance in patients across a range of hydration disorders. BIA has been found valid in elderly patients with CHF (31) and pancreatic cancer (32). Standard prediction equations have been shown to overestimate TBW in peritoneal dialysis patients particularly with increased body mass index (33). Knowledge of TBW can also estimate lean and fat mass, as well as urea volume of distribution to monitor appropriate dialytic treatment (34). Others have found that BIA may be helpful to follow TBW changes over time as shown with growth in adolescent girls (35) and to assess body composition and nutritional status in gastrointestinal disease (36).

Rapid TBW estimates by BIA can be used to more safely and appropriately guide clinical decision making in acutely ill elderly patients regarding fluid and electrolyte status. Standard clinical anthropometric formulae also overestimate elderly TBW, free-water and sodium deficits. This also includes usual bedside clinical estimates often used to guide treatment for fluid and electrolyte imbalances. These equations use TBW calculated from either BW (TBW [L] = 0.7 × [kg lean body mass]) or lean body mass predicted from total body mass. Calculated TBW is then used in several equations used for calculating normal TBW (L) = TBW × (serum Na [meq/L]/140), free body water deficit (L) = (TBW – normal TBW), or sodium deficit (meq) = (TBW [L] × [140 – serum Na (meq/L)]).

Clinical formulae assume 50%–70% TBW; however, BIA and reference standard measurements among elderly hospitalized patients show a much lower TBW. This could result in a 10%–30% (7–21 L in our study population) overestimation of TBW when using anthropometric-based formulae. BIA variability was much lower with percent difference between the standard and BIA: mean (range) –4.1% (–18.5 to 11.2). The clinical significance of this variability will depend on clinical judgment and individual patient condition.

TBW has not been found to correlate with red blood cell mass in elderly patients (37) such that intravascular volume cannot be predicted from the packed cell volume. Individual variation has limited BIA guidance of hydration therapy in cancer patients (38). Although theoretically promising, TBW measurement has not been found to reliably predict drug pharmacokinetics due to aberrant physiology in different populations and lack of multicentered large-scale population data needed to provide prediction equations applicable to a wide variety of patient populations (39).

Our study has also limitations. The study sample was relatively small and heterogeneous as it relates to age, ethnic background, and diagnosis at admission. From a clinical perspective, however, the study is informative because it shows that in individual patients with different clinical conditions, use of predictive equations based on anthropometric measurements alone could over- or underestimate TBW. Future studies should include assessment of changes in TBW occurring during the clinical course of acute illness in hospitalized elderly patients.

In conclusion, TBW in hospitalized elderly patients on the individual level can be estimated noninvasively by bedside BIA. Commonly used standardized anthropometric-based equations have to be used with caution in this population.

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