The prediction of total body water from bioelectrical impedance in patients with anorexia nervosa

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Total body water (TBW) was measured by deuterium oxide (D2O) dilution and predicted from bioelectrical impedance (Z) in nineteen anorexic and twenty-seven control women. The equation of Kushner et al. (1992) based on the impedance index (ZI = height2/Z) gave biases of 0.9 (SD 2.5) and 0.8 (SD 2.5) litres in controls and patients respectively (NS, ANOVA). The ZI-based equation of Deurenberg et al. (1993) gave biases of 1.5 (SD 2.4) litres (NS) and 3.0 (SD 2.1) litres (P < 0.001) in controls and patients respectively. Despite the fact that weight was the most powerful predictor of TBW on the study sample (n=46, r2 0.90, P < 0.0001, SE of the estimate 1.6 litres, CV 5.7%), the formulas of Segal et al. (1991) and Kushner et al. (1992) based on the association of weight and ZI gave an inaccurate prediction of TBW in both control and anorexic subjects, with a bias ranging from −3.2 (SD 2.4) to 2.9 (SD 2.1) litres (P ≤ 0.001). Population-specific formulas based on ZI (n=46) gave a more accurate prediction of TBW by bioelectrical impedance analysis on the study subjects, with biases of −0.1 (SD 1.8) and 0.5 (SD 1.7) litres in controls and patients respectively (NS). However, the individual bias was sometimes high. It is concluded that bioelectrical impedance analysis can be used to predict TBW in anorexic women at a population level, but the predictions are less good than those based on body weight alone.

Anorexia nervosa: Body composition: Bioelectrical impedance

Subjects suffering from anorexia nervosa (AN) lose weight as a consequence of extreme energy restriction. While their weight loss consists mainly of fat, their fat-free mass (FFM) also undergoes wasting as the disease proceeds (Dempsey et al. 1984; Forbes 1987; Vaisman et al. 1988a,b; Russell et al. 1994a,b). The composition of FFM of anorexic patients influences the efficacy of refeeding therapy and the prognosis of AN (Russell et al. 1994a,b). For example, Russell et al. (1994a) have shown that the loss in total body N, which is an index of protein mass, is predictive of the number of hospitalizations in subjects with AN. Together, these studies suggest that the assessment of body composition has the potential to improve the clinical management of patients with AN.

Water is the main component of FFM (Heymsfield & Waki, 1991). Total body water (TBW) is characteristically decreased in anorexic subjects (Dempsey et al. 1984). The assessment of TBW requires the use of expensive and time-consuming tracer-dilution techniques (Schoeller, 1996). Bioelectrical impedance analysis (BIA) offers an accurate assessment of TBW in healthy subjects and has the potential to be employed as a ‘bedside’
technique to assess the hydration status of ill subjects (Heitmann, 1994). However, while BIA has been studied for the assessment of FFM in subjects with AN (Hannan et al. 1990, FFM evaluated by TBW, total body N and total body K; Hannan et al. 1993, FFM evaluated by dual-energy X-ray absorptiometry), no data are available on the accuracy of this technique for the prediction of TBW in these patients.

The aim of the present study was, therefore, to assess the accuracy of BIA for predicting TBW in patients with AN.

MATERIALS AND METHODS

Subjects

Nineteen female patients affected by AN were consecutively enrolled into the study at the Institute of Internal Medicine and Metabolic Diseases of the University of Napoli (Italy). The diagnosis of AN was made according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994). Twenty-seven age-matched healthy women were recruited as controls among the members of the medical staff and medical students. The study protocol required that patients and controls had a stable body weight (±1 kg) during the month before the study. Control women were studied during the 6th and 10th days of their menstrual cycle (follicular phase). AN patients were amenorrheic. The study protocol was approved by the Ethical Committee at the University of Napoli.

Anthropometry

Body weight (Wt) and height (Ht) were measured following the Anthropometric Standardization Reference Manual (Lohman et al. 1988). BMI was calculated as Wt (kg)/Ht² (m).

Total body water assessment

TBW was measured by deuterium oxide (D₂O) dilution. A preliminary study aimed at establishing the equilibration time of D₂O was performed on the plasma of three unselected AN patients. The tracer reached equilibrium 3.0 h after its administration, a time similar to that observed in healthy individuals (Lukaski & Johnson, 1985; Battistini et al. 1995a). Subjects had fasted for at least 8 h and voided the bladder before receiving orally a precisely weighed solution made up of D₂O and drinkable water. Plasma samples were collected before the administration of this solution and 3.5 h later, as described in detail elsewhere (Battistini et al. 1995b). Deuterium concentration in plasma samples was measured by infrared spectrophotometry according to the method of Lukaski & Johnson (1985). Deuterium dilution space was corrected for the water fraction of plasma (0.94). TBW was calculated as deuterium dilution space × 0.95, taking into account non-aqueous distribution of D₂O (Heymsfield & Waki, 1991). The CV for duplicate measurements of D₂O was <2.0%. Body hydration (TBW%) was calculated as (TBW × 100)/Wt.

Bioelectrical impedance analysis

The determination of bioelectrical impedance (Z) was made with a tetrapolar impedance plethysmograph (Human IM Scan, Dietsystem, Milano, Italy) at frequencies of 1, 5, 10,
25, 50 and 100 kHz. Current-injecting electrodes were placed on the dorsal surfaces of the hand and foot proximal to metacarpal-phalangeal and metatarsal-phalangeal joints respectively and voltage-sensing electrodes were placed between wrist and ankle, as described in detail by Lukaski et al. (1985). The reproducibility of measurements was between 1 and 3Ω at frequencies <100 kHz and between 2 and 4Ω at 100 kHz. Only values of Z at 50 and 100 kHz were used for the present study. Measurements of BIA were performed following the Rome guidelines (Deurenberg, 1994). TBW was calculated from the impedance index (\(ZI = Ht^2 / Z\)) at 50 kHz (\(Z_{50}\)) by applying the formulas of Kushner et al. (1992) and at 100 kHz (\(Z_{100}\)) by applying the formulas of Deurenberg et al. (1993) and Segal et al. (1991). The formulas of Kushner et al. (1992) and Segal et al. (1991) employ bioelectrical resistance (R) instead of Z. In a study on healthy subjects we found that replacing R with Z at frequencies of 50 and 100 kHz did not modify the accuracy of the prediction of TBW obtained by these equations (Borghi et al. 1996; A. Borghi, G. Bedogni, E. Rocchi, S. Severi, F. Farina and N. Battistini, unpublished results). This was in agreement with the data presented by Lukaski (1990). Therefore, we used Z instead of R to predict TBW from the equations of Kushner et al. (1992) and Segal et al. (1991). One of the two equations of Kushner et al. (1992) and the equation of Segal et al. (1991) include \(Wt\) along with \(ZI\) among the predictor variables.

**Statistics**

Descriptive statistics, ANOVA, analysis of covariance, correlations and regressions were performed on an Apple Macintosh computer using the Statview 4.5 and SuperAnova 1.1 software packages (Abacus Concepts, Berkeley, CA, USA). The significance level was set to a value of \(P < 0.05\). Values are presented as means and standard deviations.

**RESULTS**

The characteristics of anorexic and control women are given in Table 1. Fifteen patients exhibited a `restrictive' and four a `purging' (self-induced vomiting) pattern of AN (Garner, 1993; American Psychiatric Association, 1994). As expected, \(Wt\) and BMI were significantly lower in anorexic than in control women \((P < 0.0001)\). As an absolute value,
TBW was lower in anorexic than in control subjects. However, when standardized per kg Wt, TBW was higher in patients than controls \((P < 0.0001)\). Moreover, values of \(Z\) were higher in anorexic compared with control subjects \((P < 0.0001)\).

To test whether the relationship between Wt, ZI and TBW was similar in anorexic and control women, a linear model was constructed using TBW as the dependent variable and Wt or ZI as the independent (predictor) variable. AN status (0 for controls and 1 for patients) was entered in the model as a covariate and comparison of intercepts and regression coefficients of the regression lines was performed to determine if the relationship was the same in both groups (Norgan, 1995). Since AN status had no effect on the prediction (NS, analysis of covariance), it was removed from the model. According to the final model, Wt explained 90\% of the variance of TBW in the pooled sample \(n = 46; P < 0.0001\) while ZI\(_{50}\) and ZI\(_{100}\) explained 76 and 77\% of its variance respectively \(n = 46; P < 0.0001\) for both). The regression plots of TBW v. Wt and ZI\(_{100}\) and the corresponding equations are given in Figs. 1 and 2 respectively. It should be pointed out that ZI explained less variance of TBW at frequencies < 50 kHz \((r^2 = 0.70, P < 0.0001)\).

Values of TBW predicted by the formulas of Kushner \textit{et al.} (1992), Deurenberg \textit{et al.} (1993) and Segal \textit{et al.} (1991) were highly correlated with those measured by D\(_2\)O dilution \((n = 46)\), with values of \(r\) ranging between 0.874 (Kushner \textit{et al.} (1991); ZI-based equation) and 0.917 (Segal \textit{et al.} (1991); ZI and Wt-based equation). However, the difference between predicted and measured values (bias) of TBW was statistically significant in all cases except the ZI-based equation of Kushner \textit{et al.} (1992) (Table 2). This was the only equation to allow an accurate prediction of TBW in both controls and patients. However, the equation of Deurenberg \textit{et al.} (1993) gave an accurate prediction of TBW in controls. The bias of the latter formula (Deurenberg \textit{et al.} 1993) was similar to that we observed in other studies of healthy subjects (Battistini \textit{et al.} 1995a; Borghi \textit{et al.} 1996).

Not surprisingly, population-specific formulas based on Wt (Fig. 1), ZI\(_{100}\) (Fig. 2) and their association, gave a more accurate prediction of TBW than those developed by other authors (Table 2). However, the association of Wt and ZI\(_{100}\) did not improve the prediction of TBW compared with Wt alone \((n = 46; r^2 = 0.90, \text{SE of the estimate} 1.6 \text{litres}, P < 0.0001)\);
TOTAL BODY WATER IN ANOREXIA NERVOSA

Fig. 2. Regression of total body water (TBW) v. impedance index at 100 kHz (ZI_{100}) on a pooled sample (n 46) of anorexic women (●) and age-matched controls (○). TBW = 0.563 × ZI_{100} + 2.695; r 0.876, P < 0.0001, SE of the estimate 2.4 litres, CV 8.6%.

Fig. 1 and Table 2). Partial correlation analysis confirmed this finding showing that ZI_{100} was no longer correlated with TBW after correction for Wt (NS); the correlation coefficient between ZI_{100} and Wt after correction for TBW was 0.501 (P < 0.05).

The individual bias ranged between −3.9 and 6.0 litres for the ZI-based equation of Kushner et al. (1992), between −4.1 and 2.0 litres for the ZI_{100}-based population-specific formula, between −0.5 and 0.5 litres for Wt, and between −3.2 and 3.2 litres for the population-specific formula including both ZI_{100} and Wt (Fig. 3).

Table 2. Bias associated with the prediction of total body water (TBW) from formulas available in the literature and from population-specific formulas in anorexic subjects and age-matched controls

(Mean values and standard deviations)

<table>
<thead>
<tr>
<th>Formula</th>
<th>All (n 46)</th>
<th>Controls (n 27)</th>
<th>Anorexic (n 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Segal et al. (1991)</td>
<td>2.8***</td>
<td>2.0</td>
<td>2.9***</td>
</tr>
<tr>
<td>Deurenberg et al. (1993)</td>
<td>2.2*</td>
<td>2.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Kushner et al. (1992) (ZI_{50})</td>
<td>0.9</td>
<td>2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Kushner et al. (1992) (ZI_{50} and Wt)</td>
<td>−2.8***</td>
<td>2.3</td>
<td>−3.2****</td>
</tr>
<tr>
<td>Wt†</td>
<td>0.0</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>ZI_{100}‡</td>
<td>0.0</td>
<td>1.8</td>
<td>−0.1</td>
</tr>
<tr>
<td>ZI_{100} and Wt‡</td>
<td>0.0</td>
<td>1.5</td>
<td>0.1</td>
</tr>
</tbody>
</table>

ZI_{1}, impedance index (height^2/Z) at a frequency of x kHz.
Mean bias was statistically significant: *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001 (ANOVA).
† TBW measured by bioelectrical impedance analysis minus TBW measured by D_2O dilution.
‡ The prediction equation was generated from the pooled sample (n 46).
Fig. 3. Individual differences (litres) between the values of total body water measured by deuterium oxide (D$_2$O) dilution and those predicted by (a) Kushner's equation (based on the impedance index (ZI) at 50 kHz (ZI$_{50}$); Kushner et al. 1992), (b) ZI at 100 kHz (ZI$_{100}$), (c) weight (Wt) and (d) the association of ZI$_{100}$ and Wt in anorexic women (■) and age-matched controls (□).
DISCUSSION

Our anorexic patients had higher values of TBW% and Z than controls, thus confirming the results of previous studies (Dempsey et al. 1984; Scalfi et al. 1993). The increase in TBW% of AN patients is to be ascribed to a preferential loss of fat (which is anhydrous) with respect to fat-free tissues (Dempsey et al. 1984). Interestingly, the CV of TBW% in controls was nearly double that in anorexic women (76 v. 39%), confirming the lower inter-individual variability in body composition of the latter, suggested by their values of BMI (Table 1).

Despite significant differences in their values, the relationship between TBW and ZI was similar in AN patients and control women. The same was true for the relationship between TBW and Wt. This latter finding is of interest because it suggests that the physiological relationship between Wt and TBW is not altered in patients with AN. Wt was nonetheless the best predictor of TBW on the pooled sample. It explained 13% more variance of TBW than ZI100 (Figs. 1 and 2). This is not surprising because of the homogeneity of the study sample, which is known to improve the predictive power of Wt with respect to ZI (Kushner, 1992; Kushner et al. 1992). Moreover, our AN patients were weight-stable, suggesting that their body composition had not been acutely perturbed. These factors are likely to be responsible for the high predictive power of Wt in the present study (Kushner, 1992). Our data are nonetheless in agreement with those of Hannan et al. (1990) which showed that Wt was the more powerful predictor of FFM calculated from TBW, total body N and total body K in a sample of AN patients.

Unexpectedly, however, predictive formulas based on Wt in association with ZI (Segal et al. 1991; Kushner et al. 1992) gave a significantly biased prediction of TBW in both control and anorexic women (Table 2). The ZI-based formulas of Kushner et al. (1992) and Deurenberg et al. (1993) gave, however, an accurate prediction of TBW in controls and the former also in AN patients. The formula of Kushner et al. (1992) was developed on subjects with a high inter-individual variability in TBW% (sixty-two adults, thirty-seven prepubertal children, forty-four preschool children and thirty-two premature low-weight neonates). Moreover, Goran et al. (1993) have established the accuracy of this formula on an external group of preschool children. Thus, it is likely that the accuracy achieved by the equation of Kushner et al. (1992) in the present study is due to the high variability in TBW% of the originating population. The age of our subjects was also closer to that of the subjects studied by Deurenberg et al. (1993) (thirty-three males and twenty-seven females of 25.5 (SD 8.5) and 22.8 (SD 1.6) years respectively) than those studied by Segal et al. (1991) (19–64 years, n 36). Moreover, all the subjects studied by Segal et al. (1991) were male and we have recently shown that this formula offers an accurate assessment of TBW in male subjects (Borghi et al. 1996). It appears, therefore, that TBW%, age and sex of the populations on which these formulas were developed were the major determinants of their accuracy in our study population. Not surprisingly, population-specific formulas offered more accurate estimates of TBW from Wt and ZI (Figs. 1, 2 and Table 2) in both control and AN subjects.

Taken together, these data suggest that when formulas based on ZI are applied to external populations (in this case composed of both healthy and ill subjects), they offer more accurate predictions of TBW than those based on an association of ZI and Wt. In other terms, predictive algorithms including Wt appear to be more ‘population-specific’ than those based on ZI alone. This is in agreement with the demonstration that ZI (calculated as Ht^2/R) is the more powerful predictor of TBW across a wide span of ages and TBW% (Kushner et al. 1992). The present study shows, however, that while selected predictive algorithms may be used to obtain a satisfactory prediction of TBW from BIA in...
AN subjects at a population level (Table 2), they are less likely to be of clinical utility owing to their bias at the individual level (Fig. 3). This bias is reduced when ZI-based population-specific formulas are used or TBW is predicted from Wt.

In conclusion, it appears that selected equations from the literature and population-specific equations allow a satisfactory prediction of TBW from BIA in women with AN, but such predictions perform less well than those based on Wt alone.

REFERENCES


TOTAL BODY WATER IN ANOREXIA NERVOSA


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