# 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 ($D_2O$) 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 = height$^2$/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, $r^2$ 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 ($P \leq 0·001$). 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.* 1988*a*,*b*; Russell *et al.* 1994*a*,*b*). The composition of FFM of anorexic patients influences the efficacy of refeeding therapy and the prognosis of AN (Russell *et al.* 1994*a*,*b*). For example, Russell *et al.* (1994*a*) 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'

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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 ($\pm 1$ 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 amenorrhoeic. 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)/$Ht^2$ (m).

### *Total body water assessment*

TBW was measured by deuterium oxide ($D_2O$) dilution. A preliminary study aimed at establishing the equilibration time of $D_2O$ 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.* 1995*a*). Subjects had fasted for at least 8 h and voided the bladder before receiving orally a precisely weighed solution made up of $D_2O$ 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.* 1995*b*). 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 $\times$ 0·95, taking into account non-aqueous distribution of $D_2O$ (Heymsfield & Waki, 1991). The CV for duplicate measurements of $D_2O$ was $< 2{\cdot}0\%$. Body hydration (TBW%) was calculated as (TBW $\times$ 100)/Wt.

### *Bioelectrical impedance analysis*

The determination of bioelectrical impedance (Z) was made with a tetrapolar impedance plethysmograph (Human IM Scan, Dietosystem, 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 3 Ω at frequencies < 100 kHz and between 2 and 4 Ω 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 ($ZI_{50}$) by applying the formulas of Kushner *et al.* (1992) and at 100 kHz ($ZI_{100}$) 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 $P < 0{\cdot}05$. 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 ($P < 0{\cdot}0001$). As an absolute value,

Table 1. *Characteristics of patients with anorexia nervosa (AN) and age-matched controls*

(Mean values and standard deviations)

| | AN (*n* 19) | | Controls (*n* 27) | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| Age (years) | 22·1 | 4·9 | 24·3 | 4·0 |
| Wt (kg) | 39·5*** | 5·3 | 55·4 | 8·2 |
| Ht (m) | 1·605 | 0·059 | 1·636 | 0·059 |
| BMI (kg/m$^2$) | 15·3*** | 1·3 | 20·6 | 2·3 |
| TBW (litres) | 23·6*** | 3·0 | 30·3 | 4·0 |
| TBW% | 59·9*** | 2·4 | 55·0 | 4·2 |
| $Z_{50}$ (Ω) | 740*** | 78 | 600 | 56 |
| $Z_{100}$ (Ω) | 690*** | 73 | 558 | 51 |

TBW, total body water; TBW%, TBW standardized per kg body weight (body hydration); $Z_x$, bioelectrical impedance at a frequency of x kHz.

*** Mean values were significantly different from those for controls, $P < 0{\cdot}0001$ (ANOVA).

TBW was lower in anorexic than in control subjects. However, when standardized per kg Wt, TBW was higher in patients than controls ($P < 0{\cdot}0001$). Moreover, values of Z were higher in anorexic compared with control subjects ($P < 0{\cdot}0001$).

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; $P < 0{\cdot}0001$) while $ZI_{50}$ and $ZI_{100}$ explained 76 and 77% of its variance respectively (*n* 46; $P < 0{\cdot}0001$ 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 ($r^2 < 0{\cdot}70$, $P < 0{\cdot}0001$).

Values of TBW predicted by the formulas of Kushner *et al.* (1992), Deurenberg *et al.* (1993) and Segal *et al.* (1991) were highly correlated with those measured by $D_2O$ dilution (*n* 46), with values of *r* ranging between 0·874 (Kushner *et al.* (1991); ZI-based equation) and 0·917 (Segal *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 *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 *et al.* (1993) gave an accurate prediction of TBW in controls. The bias of the latter formula (Deurenberg *et al.* 1993) was similar to that we observed in other studies of healthy subjects (Battistini *et al.* 1995*a*; Borghi *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, SE of the estimate 1·6 litres, $P < 0{\cdot}0001$;

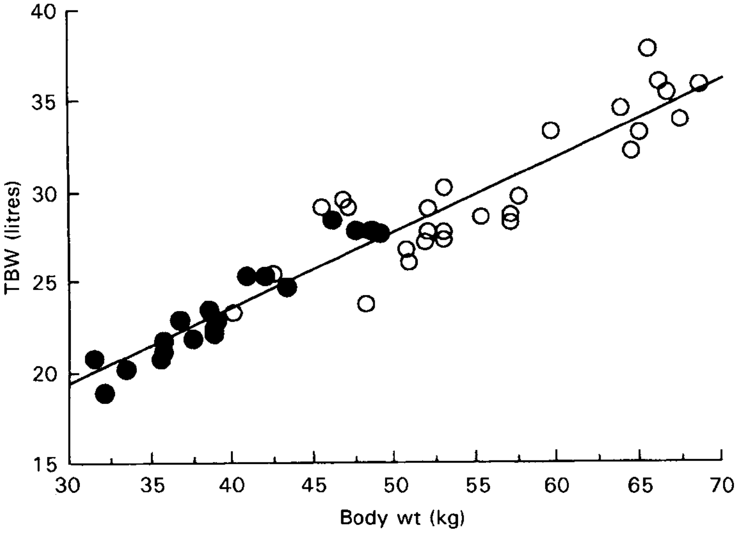


Fig. 1. Regression of total body water (TBW) *v.* weight (Wt) on a pooled sample (*n* 46) of anorexic women (●) and age-matched controls (○). TBW = 0·434 × Wt + 6·326; *r* 0·948, $P < 0{\cdot}0001$, SE of the estimate 1·6 litres, CV 5·7%.

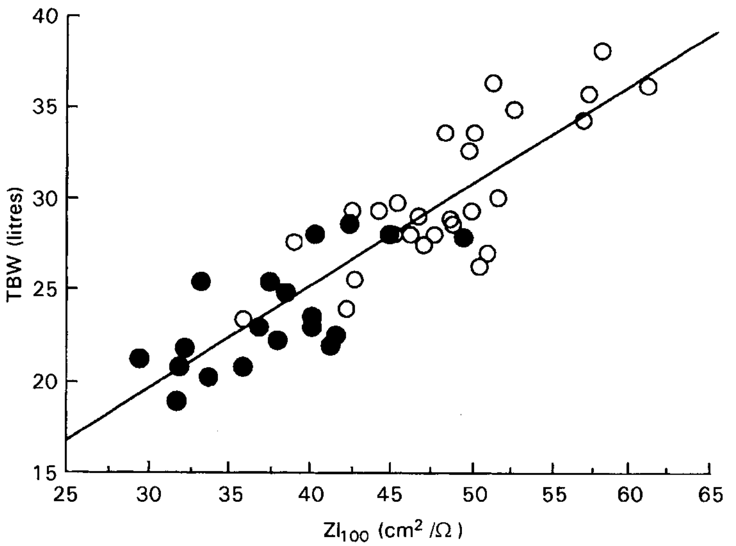


Fig. 2. Regression of total body water (TBW) *v.* impedance index at 100 kHz ($ZI_{100}$) on a pooled sample (*n* 46) of anorexic women (●) and age-matched controls (○). TBW = 0·563 × $ZI_{100}$ + 2·695; *r* 0·876, $P < 0.0001$, SE of the estimate 2·4 litres, CV 8·6 %.

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)

| | Bias† | | | | | |
|---|---|---|---|---|---|---|
| | All (*n* 46) | | Controls (*n* 27) | | Anorexic (*n* 19) | |
| Formula | Mean | SD | Mean | SD | Mean | SD |
| Segal *et al.* (1991) | 2·8*** | 2·0 | 2·9*** | 2·1 | 2·5** | 1·8 |
| Deurenberg *et al.* (1993) | 2·2* | 2·4 | 1·5 | 2·4 | 3·0**** | 2·1 |
| Kushner *et al.* (1992) ($ZI_{50}$) | 0·9 | 2·5 | 0·9 | 2·5 | 0·8 | 2·5 |
| Kushner *et al.* (1992) ($ZI_{50}$ and Wt) | −2·8*** | 2·3 | −3·2**** | 2·4 | −2·4** | 2·2 |
| Wt‡ | 0·0 | 0·2 | 0·1 | 0·2 | 0·0 | 0·3 |
| $ZI_{100}$‡ | 0·0 | 1·8 | −0·1 | 1·8 | 0·5 | 1·7 |
| $ZI_{100}$ and Wt‡ | 0·0 | 1·5 | 0·1 | 1·8 | −0·1 | 1·0 |

$ZI_x$, 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).

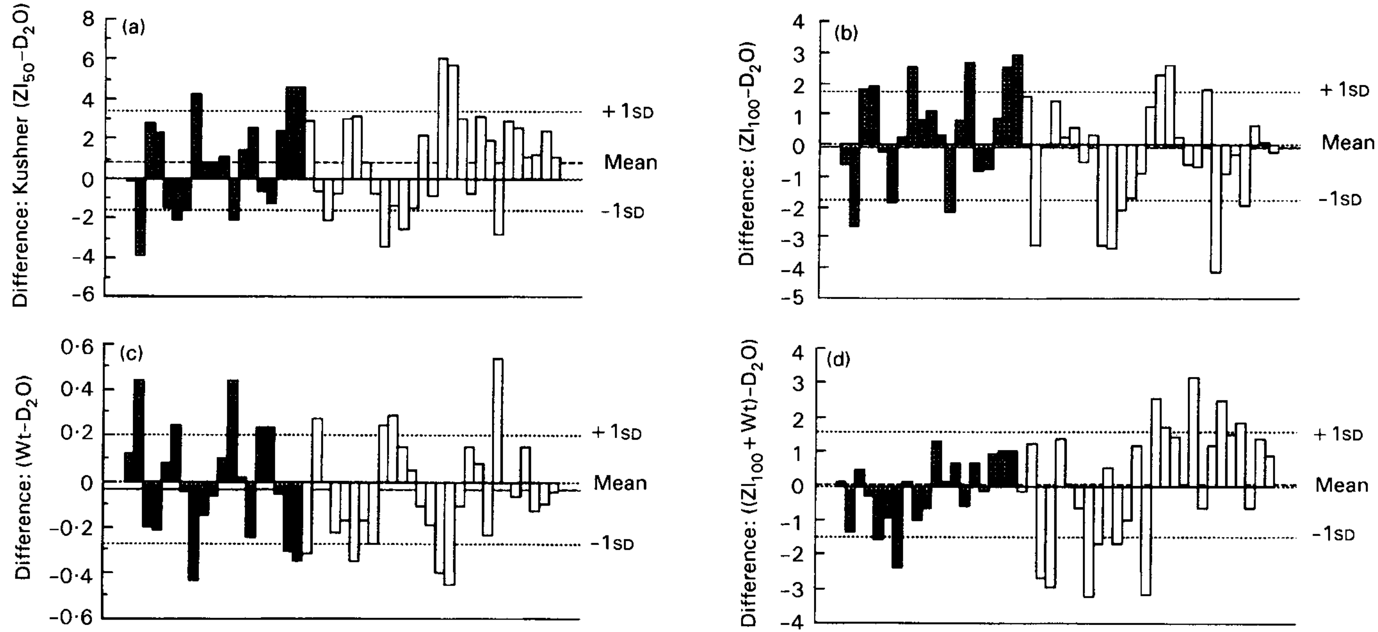


Fig. 3. Individual differences (litres) between the values of total body water measured by deuterium oxide ($D_2O$) dilution and those predicted by (a) Kushner's equation (based on the impedance index (ZI) at 50 kHz ($ZI_{50}$); Kushner *et al.* 1992), (b) ZI at 100 kHz ($ZI_{100}$), (c) weight (Wt) 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 $ZI_{100}$ (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.

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