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The prediction of total body water and extracellular water from bioelectric impedance in obese children

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Objectives: To assess the reliability of bioelectric impedance analysis (BIA) for predicting total body water (TBW) and extracellular water (ECW) in obese children.
Design: Comparison of five prediction models based on: (i) body weight (Wt), (ii) the impedance (Z) index (ZI = height^2/Z), (iii) the association of Wt and ZI, (iv) the body surface area (SA) to impedance ratio (SA:Z) and, (v) the body volume (V) to impedance ratio (V:Z).
Subjects: Thirty obese and 25 control children of 11.2 ± 1.8 y of age.
Measurements: TBW and ECW were assessed by deuterium and bromide dilution; Z was measured at frequencies of 5, 50 and 100 kHz.
Results: In controls, Wt explained 11% more variance of TBW than ZI (r^2 = 0.977, SEE = 0.9 l, CV = 3.8%) and the association of Wt and ZI improved the prediction of TBW only slightly (r^2 = 0.982, SEE = 0.8 l, CV = 3.5%). The SA:Z and V:Z indexes explained 6 and 33% less variance of TBW respectively as compared to Wt alone. In obese subjects, ZI explained 4% more variance of TBW than Wt (r^2 = 0.914, SEE = 1.8 l, CV = 6.4%) and the SA:Z ratio was the most accurate predictor of TBW (r^2 = 0.959, SEE = 1.2 l, CV = 4.4%). However, the increase in the explained variance of TBW associated to the use of the SA:Z ratio was of only 1% as compared to the association of ZI and Wt. The V:Z ratio explained 9% less of variance of TBW as compared to ZI. In both control and obese subjects, the association of Wt and ZI offered the best prediction of ECW (r^2 = 0.807, SEE = 1.564 l and r^2 = 0.826, SEE = 1.035 l, respectively). However, the values of CV were much higher in controls than in obese children (17.5% *vs* 8.4%) owing to their lower ECW and greater variability in ECW%. ZI was the most accurate predictor of TBW on the pooled sample (n = 55; r^2 = 0.910, SEE = 1.932 l, CV = 7.4%). However, it was a poor predictor of ECW on the same sample owing to its high CV (n = 55; r^2 = 0.866, SEE = 1.806 l, CV = 17.0%).
Conclusions: The body surface area to impedance ratio is the most accurate predictor of TBW in obese children but the association of ZI and Wt may be of more interest when BIA is used to estimate both TBW and ECW. The impedance index offers a good prediction of TBW but not of ECW in children with different levels of fatness.
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Descriptors: obesity; children; body composition; total body water; extracellular water; bioelectric impedance

Introduction

Bioelectric impedance analysis (BIA) is a simple and expedite method for the assessment of total body water (TBW) and extracellular water (ECW) (Heitmann, 1994). The prediction of TBW and ECW from BIA relies largely on the ECW to intracellular water (ICW) ratio (Deurenberg *et al*, 1989; Deurenberg *et al*, 1995). For this reason, subjects with an altered body water distribution between ECW and ICW may need population-specific equations in order to have an accurate prediction of body water compartments (Bedogni *et al*, 1996a; Bedogni *et al*, 1996b).

Whether obese subjects have an altered body water distribution has been the subject of some controversy until the recent work of Waki *et al* (1991). These Authors have convincingly shown that obese women have a reduced body hydration and an expanded ECW:ICW ratio in comparison to control women. More recently, we have shown that similar alterations in body water distribution occur in obese children (Battistini *et al*, 1995b). These findings suggest that standard methods for the assessment of body composition may require adjustments for use in obese subjects. BIA is among these methods since it relies heavily on body water distribution.

The prediction of TBW and ECW from BIA is commonly based on the impedance index (ZI), namely the ratio between squared height (Ht) and body impedance (Z) (Heitmann, 1994). The inclusion of body weight (Wt) with ZI among the predictor variables usually improves the accuracy of the prediction (Deurenberg, 1994). In a previous study on obese children, we found that the ratio between surface area (SA) and Z offered a more accurate prediction of TBW than the association of ZI and Wt (Battistini *et al*, 1992). We suggested that the predictive power of the SA:Z index could be explained by its sensitivity to changes in body electrical conductivity which occur with obesity. Theoretically, the ratio between body volume (V) and Z may offer an even more accurate prediction of TBW and possibly ECW owing to its known

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sensitivity to changes in body electrical conductivity (Lofgren, 1951; Nyboer, 1970).

The present study aimed therefore at assessing the accuracy of five different models (Wt, ZI, ZI and Wt, SA:Z, and V:Z) for the prediction of TBW and ECW in obese children.

Materials and methods

Subjects

Thirty obese and 25 control children of similar age (11.2 ± 1.8, range: 8.0–14.1 y) and sex were studied. Obesity was diagnosed on the basis of a relative weight for age (RW) > 120% and of a relative weight for height > 90th percentile (Paige, 1985; Battistini *et al*, 1992). In all cases, informed consent had been obtained from parents. The study protocol had been approved from the Ethical Committee at Torvergata University.

Anthropometry

Wt, Ht, triceps skinfold (TSF) and hip circumference (HC) were measured following the *Anthropometric Standardization Reference Manual* (Lohman *et al*, 1988). Relative weight (RW) was calculated as [(measured weight/ideal weight) × 100]. Values of ideal weight and TSF were obtained from the NCHS growth-charts; the same charts were used to evaluate the weight for height relationships (Frisancho, 1990). Body surface area (SA) was calculated from the formula of Du-Bois and Du-Bois (Du-Bois and Du Bois, 1916; Battistini *et al*, 1992)

$$SA(cm^2) = Wt^{0.425}(Kg) \times Ht^{0.725}(cm) + 71.84$$

Body volume (V) was calculated from HC and Ht using the following equation

$$V(cm^3) = [HC(cm)/(2 \times \pi)]^2 \times Ht(cm)$$

This formula approximates the body to a cylinder of circumference HC and length H (Geigy Scientific Tables, 1982).

TBW and ECW assessment

TBW and ECW were measured by deuterium oxide (D_2O) and bromide (Br) dilution, respectively. Subjects had fasted for at least eight hours and voided the bladder before receiving orally a precisely weighed solution made up of D_2O, NaBr and drinkable water. We had previously shown that D_2O and Br reach the equilibrium in the plasma of obese children between 2.5 and 3.0 h after their administration (Battistini *et al*, 1992; Battistini *et al*, 1995b). This time is comparable to that observed in control children. Therefore, plasma samples were collected before the administration of this solution and 3.5 h later in both control and obese children (Battistini *et al*, 1992; Battistini *et al*, 1994). D_2O concentration was measured by FT-IR spectrophotometry according to the method of Lukaski and Johnson (1985). TBW was calculated as deuterium dilution space × 0.95, taking into account non-aqueous distribution oF D_2O. Br concentration was measured by HPLC according to the method of Wong *et al* (1989). The final concentration of Br was below one tenth of the value regarded as toxic (6 mM) (Goodman and Gillman, 1970). ECW was calculated as bromide dilution space × 0.90 × 0.95, taking into account non-extracellular distribution of bromide and Donnan's effect, respectively. Body hydration (TBW%) was calculated as TBW standardized per kg of Wt. ECW% was calculated as ECW standardized per l of TBW.

BIA

Z was measured with a tetrapolar impedance plethysmograph (Human IM Scan, Dietosystem, Milano, Italy) at frequencies of 5, 50 and 100 kHz, as described in detail by Segal *et al* (1991). The Z-based indexes were calculated as follows

$$ZI(cm^2/\Omega) = Ht^2/Z$$

$$SA : Z(cm^2/\Omega) = SA/Z$$

$$V : Z(cm^3/\Omega) = V/Z$$

Statistics

Statistical analysis was performed on an Apple Macintosh computer using the Statview 4.5 and SuperAnova 1.1 software packages (Abacus Concepts, Berkeley, California, USA). Differences in body composition between controls and obese subjects were evaluated by one-way ANOVA coupled to Scheffe's *s*-test. Partial correlation coefficients were calculated to identify the frequencies at which ZI, SA:Z and V:Z were significantly correlated with TBW after correcting for ECW and *vice versa*. This method is described in detail by Deurenberg *et al* (1995). Linear and multiple regressions were used to predict TBW and ECW from Wt and the Z-based indexes in both obese and control subjects. Values of r^2, SEE and CV [(SEE/TBW or ECW by dilution) × 100] were used to assess the accuracy of the different models. Differences between measured and predicted values of TBW and ECW within groups were evaluated by paired *t*-tests. The same differences were evaluated by one-way ANOVA when the equations generated on controls were applied to obese subjects. Regression coefficients of the equations were also compared by ANCOVA using obesity as a covariate (0 for controls and 1 for obese children) (Norgan, 1995). Statistical significance was set to a value of $P < 0.05$. Values are given as mean ± s.d.

Results

The characteristics of control and obese children are given in Table 1.

Wt, RW and TSF were significantly higher in obese than in control children ($P < 0.0001$). Moreover, values of TSF were always over the 90th percentile for age in obese children, confirming their excess of fat-mass. At all frequencies, Z was significantly lower in obese than in control subjects ($P < 0.0001$). As an absolute amount, TBW and ECW were higher in obese than in control subjects ($P < 0.01$ and $P < 0.005$, respectively). However, when TBW and ECW were expressed as a relative amount, TBW% was lower ($P < 0.0001$) and ECW% higher ($P < 0.005$) in obese than in control children. Accordingly, the ECW:ICW ratio was higher in obese than in control subjects ($P < 0.0001$).

ZI, SA:Z and V:Z were highly correlated with TBW and ECW at all frequencies in both obese and control subjects (data not shown). After partial correlation analysis, however, these indexes were found to be significantly correlated ($P < 0.05$) with TBW only at frequencies of 50 and 100 kHz ($r \geq 0.61$ for ZI, $r \geq 0.64$ for SA:Z and $r \geq 0.51$ for V:Z at 50 kHz; $r = 0.62$ for ZI, $r \geq 0.64$ for SA:Z and

Table 1 Characteristics of control and obese children (mean ± s.d.)

	Controls ($n=25$)	*Obese* ($n=30$)
Sex (M:F)	13/12	16/14
Age (y)	11.0 ± 1.8	10.5 ± 1.5
Wt (Kg)	40.7 ± 11.3	56.0 ± 11.0***
Ht (cm)	149.1 ± 12.1	144.7 ± 10.6
RW (%)	97.9 ± 25.8	154.3 ± 18.5***
TSF (mm)	12.1 ± 5.2	27.7 ± 4.7***
Z5 (Ω)	775 ± 85	638 ± 61***
Z50 (Ω)	684 ± 67	545 ± 32***
Z100 (Ω)	650 ± 65	515 ± 35***
TBW (l)	23.5 ± 6.0	28.3 ± 6.3*
ECW (l)	8.9 ± 3.6	12.2 ± 3.0**
TBW% (%)	58.1 ± 2.3	50.5 ± 3.7***
ECW% (%)	37.0 ± 7.2	43.2 ± 2.6**
ECW : ICW	0.60 ± 0.18	0.77 ± 0.08***

* $P<0.01$, ** $P<0.005$, *** $P<0.0001$ *vs* controls.
Abbreviations: Wt = weight; Ht = height; RW = relative weight; TSF = triceps skinfold; Z_x = bioelectric impedance at a frequency of x kHz; TBW = total body water; ECW = extracellular water; TBW% = TBW standardized per Kg of weight; ECW% = ECW standardized per l of TBW; ECW : ICW = extra- to intra-cellular water ratio.

$r \geq 0.50$ for V:Z at 100 kHz). After the same procedure, these indexes appeared to be significantly correlated ($P<0.05$) with ECW only at a frequency of 5 kHz ($r \geq 0.52$ for ZI, $r \geq 0.53$ for SA:Z and $r \geq 0.44$ for V:Z). Values of Z at 100 and 5 kHz were therefore used for the prediction of TBW and ECW from the Z-based parameters.

The equations obtained by regressing TBW and ECW *vs* Wt and the Z-base indexes are given in Table 2.

In controls, Wt explained 11% more variance of TBW than ZI and the association of ZI and Wt improved the prediction of TBW only slightly. The SA:Z and V:Z indexes explained 6 and 33% less variance of TBW respectively as compared to Wt alone. In obese children, ZI explained 4% more variance of TBW than Wt. The inclusion of Wt with ZI into the regression model was able to explain an additional 4% of the variance of TBW. The SA:Z index offered the best prediction of TBW but the increase in the explained variance of TBW was of only 1% as compared to the association of ZI and Wt. The V:Z index explained 21% more variance of TBW in obese than in control children but it was the less accurate of all predictors. Values of CV associated to the prediction of TBW by weight and Z-based indexes were generally good and comparable in both control and obese children (Table 2).

In both control and obese subjects, Wt and ZI explained a similar variance of ECW (78 *vs* 75% and 74 *vs* 75%, respectively). As compared to ZI, the association of ZI and Wt explained an additional 6 and 8% of the variance of ECW in control and obese children, respectively. The SA:Z and V:Z indexes did not improve the prediction of ECW as compared to the association of Wt and ZI. However, the values of CV associated to the prediction of ECW from Wt and from the Z-based parameters were much higher in control than in obese children (Table 2). To explain this difference, it should be considered that: (i) the absolute amount of ECW was lower in control than in obese children (Table 1), (ii) the CV of ECW% was 3.3 times higher in controls than in obese subjects (Table 1) and, (iii) the residuals of the various regressions were more strongly correlated to ECW% in controls than in obese subjects [for example $r^2=0.682$ ($P<0.0001$) *vs* 0.321 ($P<0.05$) for Wt and $r^2=0.546$ ($P<0.0001$) *vs* 0.423 ($P<0.005$) for ZI_5].

The residuals of TBW predicted by ZI and Wt were not correlated with body water distribution, as determined by ECW%, in both control and obese children (P = ns). However, the residuals of ECW predicted by the same variables were significantly correlated to ECW% in both groups ($r^2=0.66$ in controls and $r^2=0.60$ in obese children, with $P<0.0001$). Again, this correlation was higher in controls for their greater variability in ECW%.

Formulae developed on controls were applied to obese subjects. Differences between values of TBW and ECW measured by dilution and predicted by the control-generated formulae are given in Table 3.

TBW was significantly underestimated by the SA:Z and V:Z models ($P<0.05$ and $P<0.01$, respectively) and ECW by the V:Z model ($P<0.01$) generated on controls. These results were in agreement with those obtained at ANCOVA (Table 3). While this would theoretically justify the inclusion of obese and control subjects in a single sample to predict TBW and ECW from Wt, ZI and the association of ZI and Wt, only the predictor with the lowest bias should be chosen for practical applications. By weighing the accuracy achieved by the control-generated equa-

Table 2 Prediction equations obtained by regressing total body water and extracellular water measured by dilution *vs* body weight and the impedance-based predictors

	Controls						*Obese*					
	a_1	a_2	b	r^{2*}	*SEE (l)***	*CV (%)*°	a_1	a_2	b	r^{2*}	*SEE (l)***	*CV (%)*°
TBW_{Wt}	0.526	—	1.920	0.977	0.9	3.8	0.521	—	−0.960	0.872	2.2	7.8
TBW_{ZI}[a]	0.716	—	−1.265	0.873	2.1	9.0	0.726	—	−1.440	0.914	1.8	6.4
TBW_{Wt+ZI}[a]	0.436 (Wt)	0.142 (ZI)	0.713	0.982	0.8	3.5	0.224 (Wt)	0.455 (ZI)	−2.965	0.948	1.4	5.1
$TBW_{SA:Z}$[a]	1.160	—	−0.101	0.915	1.7	7.4	1.138	—	−4.171	0.959	1.2	4.4
$TBW_{V:Z}$[a]	0.004	—	9.123	0.648	3.5	15.0	0.003	—	9.430	0.862	2.3	8.1
ECW_{Wt}	0.275	—	−2.435	0.782	1.6	18.2	0.241	—	−1.366	0.735	1.2	10.1
ECW_{ZI}[b]	0.450	—	−4.327	0.750	1.7	19.5	0.383	—	−0.586	0.750	1.2	9.8
ECW_{Wt+ZI}[b]	0.172 (Wt)	0.190 (Z)	−3.781	0.807	1.6	17.6	0.166 (Wt)	0.156 (ZI)	−2.340	0.826	1.0	8.5
$ECW_{SA:Z}$[b]	0.722	—	−3.589	0.767	1.7	18.8	0.597	—	−1.667	0.778	1.1	9.3
$ECW_{V:Z}$[b]	0.003	—	0.757	0.609	2.2	24.3	0.002	—	3.544	0.662	1.4	11.5

Bioelectric impedance measured at frequencies of [a]100 and [b]5 kHz.
* $P<0.0001$ for all values of r^2.
** P = ns (Student's paired t-test) for all predicted *vs* measured values.
° CV calculated as [SEE/(TBW or ECW by dilution) × 100].
Abbreviations: a = slope(s), b = intercept, TBW = total body water; ECW = extracellular water; Wt = bodyweight; ZI = impedance index; SA:Z = body surface area to impedance ratio; V:Z = body volume to impedance ratio (see text for details).

Table 3 Bias (mean ± s.d., in litres) associated to the prediction of total body water (TBW) and extracellular water (ECW) in obese children by using formulae developed on controls

	$TBW^{a,c}$ (l)	$ECW^{b,c}$ (l)
Wt	−3.1 ± 2.1	−0.9 ± 1.3
ZI	0.2 ± 1.8	1.5 ± 1.6
Wt + ZI	−2.7 ± 1.8	−0.1 ± 1.1
SA : Z	−4.7 ± 1.2*,***	−1.0 ± 1.5
V : Z	−5.3 ± 2,8**,***	−3.6 ± 2.3**,***

Bioelectric impedance measured at frequencies of [a]100 and [b]5 kHz.
[c]Bias calculated as (value by dilution − value by BIA).
* $P < 0.05$ and ** $P < 0.01$ (ANOVA) vs value obtained by dilution.
*** $P < 0.05$ (ANCOVA) for the regression coefficients of control vs obese children by using obesity status as a covariate (0 for controls and 1 for children).
Abbreviationss: Wt = body weight; ZI = impedance index; SA : Z = body surface area to impedance ratio; V : Z = body volume to impedance ratio (see text for details).

Table 4 Slopes (a) and intercepts (b) of the equations obtained by regressing total body water (TBW) and extracellular water (ECW) vs the impedance index (ZI) on all the study sample ($n = 55$). Also given are the values of r^2, SEE and of CV associated to the predictions

	a	b	r^2*	SEE (l)**	CV (%)***
TBW_{ZI}[a]	0.726	−1.524	0.910	1.9	7.4
ECW_{ZI}[b]	0.460	−3.944	0.866	1.8	17.0

Bioelectric impedance measured at frequencies of [a]100 and [b]5 kHz.
* $P < 0.0001$ for all values of r^2.
** P = ns (Student's paired t-test) for all predicted vs measured values.
*** CV calculated as [SEE/(TBW or ECW by dilution) × 100].

tions for predicting TBW and ECW in obese subjects, it appears that ZI is such a predictor. For this reason, equations were developed on all the sample ($n = 55$) to predict TBW and ECW from ZI (Table 4). The associated CV was good for TBW (7.4%) but not for ECW (17.0%).

Discussion

In this study, obese children had a reduced TBW% and an increased ECW:ICW ratio as compared to control subjects. Possible explanations and clinical implications of a similarly altered body water distribution in obese children have been discussed in detail elsewhere (Battistini *et al*, 1995b).

In controls, Wt was a better predictor of TBW than ZI. This is not surprising since a close correlation exists between Wt and TBW in healthy subjects (Kushner *et al*, 1992). Moreover, the predictive power of Wt with respect to TBW is likely to be enhanced in an homogenous sample such as that employed in the present study (Kushner, 1992). The use of Wt as a predictor of TBW left however an unexplained variance of 13% in obese as compared to a value of 2% in control children. This suggests that the physiological relationship between Wt and TBW may be altered in obese children and that factors other than Wt may be involved in the control of body water in obese subjects. This may be of pathophysiological importance since the altered water homeostasis of obese subjects is likely to play a role in the development of oedema and hypertension (Waki *et al*, 1991). In obese subjects, ZI is a better predictor of TBW than Wt. This can be attributed to the high sensitivity of body impedance for distinguishing between fat (that is low conductive) and fat-free (that is highly conductive) tissues (Deurenberg, 1994). On the contrary, Wt does not accurately reflect body composition in obese subjects (Forbes, 1993). While an increase of 4% in the explained variance of TBW may seem low to justify the use of ZI over that of Wt for the prediction of TBW, it is possible that the use of frequencies > 100 kHz will allow a better prediction of TBW from ZI in obese children (Deurenberg, 1994). In obese subjects, the use of Wt, Ht and Z in the form of the SA:Z ratio offered a better prediction of TBW than their simple association as ZI + Wt. This confirms that the SA:Z ratio is an accurate predictor of TBW in obese children (Battistini *et al*, 1992). The accuracy of the SA:Z ratio is to be attributed in part to the close relationship which exists between SA and TBW in obese subjects (Hume and Weyers, 1971).

The association of Wt and ZI offered the best prediction of ECW in both control and obese subjects. However, the values of CV associated to the use of this and of the other predictors were much higher in controls than in obese subjects. This difference was clearly influenced by the lower ECW and by the greater variability in ECW% of the former. While these data raise some doubts about the accuracy of BIA for predicting ECW in children of normal weight, it should be pointed out that the lowest frequency at which BIA was performed in this study was one of 5 kHz. Since there is increasing evidence that frequencies < 5 kHz (for example 1 kHz) allow a better prediction of ECW (Deurenberg *et al*, 1993; Battistini *et al*, 1995a; Deurenberg *et al*, 1995), one cannot exclude that the accuracy of BIA may be greater when Z is measured at these lower frequencies. In every case, our study suggests that the BIA method may be useful for assessing ECW in obese children.

The SA:Z index was not superior to the association of ZI and Wt for the prediction of ECW in obese subjects. This finding, together with the previous one of a minimal increase in the accuracy of the prediction of TBW, suggests that the association of ZI and Wt may be of more interest when BIA is used to predict both TBW and ECW in obese children. In spite of its theoretical superiority (Lofgren, 1951; Nyboer, 1970), the V:Z index gave the less accurate predictions of TBW and ECW in both obese and control subjects. The low accuracy of the V:Z index for the prediction of TBW is in agreement with the findings of Danford *et al* (1992) in a sample of young (5–9 y) children and with those of De Lorenzo *et al* (1995) in a sample of obese women. Although the V:Z index explained substantial more variance of TBW in obese than in control subjects, it was the less accurate predictor of TBW and ECW. Thus, we found no advantage of using a volume model for the prediction of TBW and ECW from BIA in children.

Changes in body hydration and water distribution are known to affect the accuracy of the BIA method (Deurenberg *et al*, 1989; Deurenberg *et al*, 1995). Our obese children had a lower TBW% and an higher ECW% as compared to controls and ZI allowed a reasonably good prediction of TBW but not of ECW on the pooled sample. Our study confirms therefore that BIA is sensitive to changes in body water distribution and that it offers a more accurate prediction of ECW in groups with the lower variability in ECW% (Borghi *et al*, 1996). It should nonetheless be noted that all of the given equations need to be validated on external samples of children before being employed in clinical practice.

In summary, BIA allows an accurate assessment of TBW and ECW in obese children. While the SA:Z ratio is the most accurate predictor of TBW in these children, the association of Wt and ZI, which allows a good prediction of both TBW and ECW, appears more useful for on-field use of BIA. The impedance index offers a reasonably good prediction of TBW but not of ECW in children with different levels of fatness. Further studies should be performed to establish if the use of frequencies < 5 kHz will allow a better prediction of ECW from BIA in children.

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