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Development of Anthropometry-Based Equations for the Estimation of the Total Body Water in Koreans

For developing race-specific anthropometry-based total body water (TBW) equations, we measured TBW using bioelectrical impedance analysis (TBW_{BIA}) in 2,943 healthy Korean adults. Among them, 2,223 were used as a reference group. Two equations (TBW_{K1} and TBW_{K2}) were developed based on age, sex, height, and body weight. The adjusted R^2 was 0.908 for TBW_{K1} and 0.910 for TBW_{K2}. The remaining 720 subjects were used for the validation of our results. Watson (TBW_W) and Hume-Weyers (TBW_H) formulas were also used. In men, TBW_{BIA} showed the highest correlation with TBW_H, followed by TBW_{K1}, TBW_{K2} and TBW_W. TBW_{K1} and TBW_{K2} showed the lower root mean square errors (RMSE) and mean prediction errors (ME) than TBW_W and TBW_H. On the Bland-Altman plot, the correlations between the differences and means were smaller for TBW_{K2} than for TBW_{K1}. On the contrary, TBW_{BIA} showed the highest correlation with TBW_W, followed by TBW_{K2}, TBW_{K1}, and TBW_H in females. RMSE was smallest in TBW_W, followed by TBW_{K2}, TBW_{K1} and TBW_H. ME was closest to zero for TBW_{K2}, followed by TBW_{K1}, TBW_W and TBW_H. The correlation coefficients between the means and differences were highest in TBW_W, and lowest in TBW_{K2}. In conclusion, TBW_{K2} provides better accuracy with a smaller bias than the TBW_W or TBW_H in males. TBW_{K2} shows a similar accuracy, but with a smaller bias than TBW_W in females.

Key Words : *Body Water; Electric Impedance; Anthropometry; Body Composition*

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INTRODUCTION

The measurement of total body water (TBW) is frequently performed to evaluate the body composition and nutritional status. The accurate measurement of TBW is difficult, and it requires isotopic dilution techniques. Therefore, several indirect equations for estimating the TBW using simple anthropometric variables are commonly employed. However, these equations are largely based on individuals of the western hemisphere.

The purpose of this study was to develop anthropometry-based TBW equations in Korean and to compare these equations with the other available TBW equations. Since it is difficult to perform isotopic dilution techniques on a large number of subjects, we used bioelectrical impedance analysis (BIA), which has been shown to accurately and reliably estimate TBW (1). Therefore, we first measured the TBW using BIA (TBW_{BIA}) in a large study population to develop an anthropometry-based TBW equation. Then to validate this equation, we analyzed the agreement between the TBW_{BIA} and the TBW derived from anthropometry-based equations in another control group.

MATERIALS AND METHODS

A total of 2,943 healthy adults were selected for this study from the 3,781 people visiting the Health Promotion Center (HPC) at Inha University Hospital (IUH) from May to December 2003. The exclusion criteria were as follows: age <18 yr, a serum creatinine >1.4 mg/dL, positive urine protein, subjects who complained of edema, those with an amputation or who had diabetes mellitus, congestive heart failure, chronic liver disease, or those subjects who did not allow BIA to be performed. Among them, 2,223 subjects were used for the development of equations. The remaining 720 subjects were used for the validation of equation. This study was approved by the ethical board of IUH.

After 8 hr of fasting, the subjects visited to the HPC at 9 a.m. Their height (Ht) and body weight (BW) were measured to the nearest 0.1 cm and 0.1 kg using a linear height scale and an electronic weight scale, respectively. The mean values of two measurements were used for data analysis.

BIA (Inbody 3.0, Biospace Co., Seoul, Korea) was performed by a well trained nursing staff. The equipment involves placing eight tactile electrodes on a patient in an upright posture. When the subject was standing on the sole electrodes and gripping the hand electrodes, the microprocessor was switched on and the impedance analyzer started to measure the segmental resistances of the right arm, left arm, trunk, right leg, and left leg at four frequencies (5, 50, 250 and 500 kHz), thus measuring a set of 20 segmental resistances for one individual. The mean values of two sets of BIA measurements were used for analysis. The repeat measured coefficient of variation for TBW was 0.29%, and the day-to-day coefficient of variation of TBW was 1.18%. The accuracy of the 8-point tactile-electrode impedance method on the measurement of TBW_{BIA} was validated on healthy subjects (2). The procedure was performed in 3 min or less and the TBW_{BIA} was automatically calculated from the BIA with equations installed in the instrument's program.

We chose the Watson (3) and Hume-Weyers (4) formulas to compare the accuracy of the newly developed equation:

Watson formula
Male: $TBW_W = 2.447 - (0.09156 \times age) + (0.1074 \times Ht) + (0.3362 \times BW)$
Female: $TBW_W = -2.097 + (0.1069 \times Ht) + (0.2466 \times BW)$

Hume-Weyers formula
Male: $TBW_H = (0.194786 \times Ht) + (0.296785 \times BW) - 14.012934$
Female: $TBW_H = (0.34454 \times Ht) + (0.183809 \times BW) - 35.270121$
Where age in years, Ht in cm, and the BW in kg.

Statistical analysis

The data were expressed as means ± SD. Linear regression analysis was performed to develop the anthropometry-based TBW equation. Stepwise selection was employed using entry and exit criteria of $p<0.01$. TBW_{BIA} was used as a dependent variable. Sex, age, Ht and BW were used as independent variables. Polynomial terms for continuous variables and multiplicative interaction terms were considered in the model building process. Pearson's correlation coefficient (r) was used to find the relationship between two variables. To analyze the differences in TBW_{BIA} and TBWs derived from anthropometry-based equations, one-way analysis of variance (ANOVA) was performed with using the Bonferroni method for the post-hoc test. To assess the agreement, Bland-Altman plots using the means and differences between TBW_{BIA} and calculated TBW were used (5). To quantitate the degrees of bias, we compared the correlation coefficients of the respective differences and means. The closer the correlation coefficient of Bland-Altman plot was to zero, the less the bias. Root mean square error (RMSE) and mean prediction error (ME) were also used. ME was also an indication of bias, but not of accuracy. The RMSE value was used as a measure of the goodness-of-fit of an equation. If there were more than one equation to fit the data, the one with the smallest RMSE value had the highest precision. The equations used for ME and RMSE are as follows:

$$ME = [\sum(TBW_{BIA} - \text{calculated TBW})]/n,$$

$$RMSE = \sqrt{\sum[(\text{calculated TBW} - TBW_{BIA})^2/n]}$$

A p value less than 0.05 was considered as statistically significant.

RESULTS

Development of anthropometry-based TBW equations

For the 2,223 subjects, the male to female ratio was 1.72:1, the mean age was 45.1 ± 10.9 yr, the mean BW was 64.3 ± 11.0 kg, the mean Ht was 164.9 ± 8.5 cm, and the mean TBW_{BIA} was 34.9 ± 6.6 L. The simple (TBW_{K1}) and complicated (TBW_{K2}) TBW equations based on the anthropometric variables were developed by linear regression analysis (Table 1). The adjusted R^2 was 0.908 for TBW_{K1} and 0.910 for TBW_{K2}.

Table 1. Linear regression equation for TBW_{BIA} in 2,223 subjects

Equation 1

Variable	Unstandardized Coefficients		Standardized Coefficients		p
	β	SE	β	t	
(Constant)	-9.710	1.395		-6.963	0.000
Sex	4.036	0.137	0.293	29.486	0.000
Age	-0.02606	0.004	-0.043	-6.164	0.000
Ht	0.113	0.009	0.144	12.381	0.000
BW	0.383	0.005	0.636	72.384	0.000

R	R^2	Adjusted R^2	SE of the estimate	F	p
0.953	0.908	0.908	2.0102	5477.193	0.000

$TBW_{K1} = -9.71 + 4.036 \times Sex - 0.02606 \times Age + 0.113 \times Ht + 0.383 \times BW$.

Equation 2

Variable	Unstandardized Coefficients		Standardized Coefficients		p
	β	SE	β	t	
(Constant)	1.485	1.126		1.319	0.187
BW × Ht	0.001518	0.000	0.509	9.47	0.000
Age^2	-0.0007872	0.000	-0.121	-3.353	0.001
BW	0.349	0.039	0.579	8.988	0.000
BW^2	-0.00199	0.000	-0.442	-7.685	0.000
Sex × BW	0.06611	0.002	0.34	29.788	0.000
Age × Ht	0.0002861	0.000	0.075	2.104	0.036

R	R^2	Adjusted R^2	SE of the estimate	F	p
0.954	0.910	0.910	1.9950	3713.436	0.000

$TBW_{K2} = 1.485 + 0.001518 \times BW \times Ht - 0.0007872 \times Age^2 + 0.349 \times BW - 0.00199 \times BW^2 + 0.06611 \times Sex \times BW + 0.0002861 \times Age \times Ht$.
Sex: male=1, female=0, Age: years, Ht: cm, BW: kg.

Validation of newly developed TBW equations

In another 720 control subjects, the male to female ratio was 1.28:1, the mean age was 47.0±11.1 yr, the mean BW was 63.6±10.5 kg, the mean Ht was 163.8±9.3 cm, and the mean TBW_{BIA} was 33.6±6.2 L. In males, TBW_{BIA} showed the highest correlation with TBW_{H} (r=0.951), followed by TBW_{K1} (r=0.945), TBW_{K2} (r=0.945) and TBW_{W} (r=0.937) (Table 2). There were no differences between the TBW_{BIA} and TBW_{K1} or TBW_{K2}. However, TBW_{W} and TBW_{H} were significantly larger than the TBW_{BIA}. There were significant differences between TBW_{W} and TBW_{K1} or TBW_{K2} and between the TBW_{H} and TBW_{K1}. In females, TBW_{BIA} showed the highest correlation with TBW_{W} (r=0.902), followed by TBW_{K2} (r=0.895), TBW_{K1} (r=0.890), and TBW_{H} (r=0.887). There were no differences between TBW_{BIA} and TBW_{W}, TBW_{K1} or TBW_{K2}. The TBW_{H} was significantly larger than the others.

In males, the TBW_{K1} and TBW_{K2} showed the lower RMSE (1.58, 1.58, 2.14, and 2.08 for TBW_{K1} TBW_{K2} and TBW_{W} TBW_{H}, respectively) and ME (0.526, 0.547, 1.426, and 1.362 for TBW_{K1} TBW_{K2} TBW_{W} and TBW_{H}, respectively) than the TBW_{W} and TBW_{H} (Table 3). On the Bland-Altman plot, the correlations between the difference and means were smallest for the TBW_{K2} (r= -0.192), followed by the TBW_{K1}, TBW_{W}, and TBW_{H} (Fig. 1A, C, E, G). In females, the RMSEs were smallest for the TBW_{W}, followed by the TBW_{K2}, TBW_{K1}, and TBW_{H} (1.49, 1.50, 1.62, and 1.70 for the TBW_{W}, TBW_{K2}, TBW_{K1} and TBW_{H}, respectively). The ME was closest to zero for the TBW_{K2}, followed by the TBW_{K1}, TBW_{W} and TBW_{H} (0.554, 0.556, 0.593, and 0.988 for the TBW_{K2}, TBW_{K1}, TBW_{W} and TBW_{H}, respectively). The correlation coefficients between the means and differences were highest for the TBW_{W} (r=-0.553), and lowest for the TBW_{K2} (r=0.057) (Fig. 1B, D, F, and H).

Table 2. Comparison and correlation coefficients of TBW_{BIA} with TBWs from anthropometry-based equation

	Male (n=404)	r	Female (n=316)	r
TBW_{BIA}	37.89±4.56		28.22±2.99	
TBW_{W}	39.32±3.96*,†	0.937	28.82±2.25	0.902
TBW_{H}	39.26±3.60*,‡	0.951	29.21±2.68*	0.887
TBW_{K1}	38.42±4.13	0.945	28.78±3.36	0.890
TBW_{K2}	38.44±4.28	0.945	28.78±3.07	0.895

Unit of number: Liter.
Statistical analysis by One-way ANOVA with post-hoc test with Bonferroni method and Pearson correlation.
*p=0.000 vs. TBW_{BIA}, †p=0.019 vs. TBW_{K1} and p=0.025, vs. TBW_{K2}, ‡p=0.04, vs. TBW_{K1}.

Table 3. Anthropometry-based TBW estimates relative to TBW_{BIA}

	RMSE	ME	Limit of agreement
Male			
TBW_{W}	2.14	1.426	-1.818~4.67
TBW_{H}	2.08	1.362	-1.826~4.55
TBW_{K1}	1.58	0.526	-2.47~3.522
TBW_{K2}	1.58	0.547	-2.429~3.523
Female			
TBW_{W}	1.49	0.593	-2.143~3.329
TBW_{H}	1.70	0.988	-1.774~3.75
TBW_{K1}	1.62	0.556	-2.5~3.612
TBW_{K2}	1.50	0.554	-2.234~3.342

RMSE, root mean square error; ME, mean prediction error.

DISCUSSION

In this study, we developed two anthropometry-based TBW

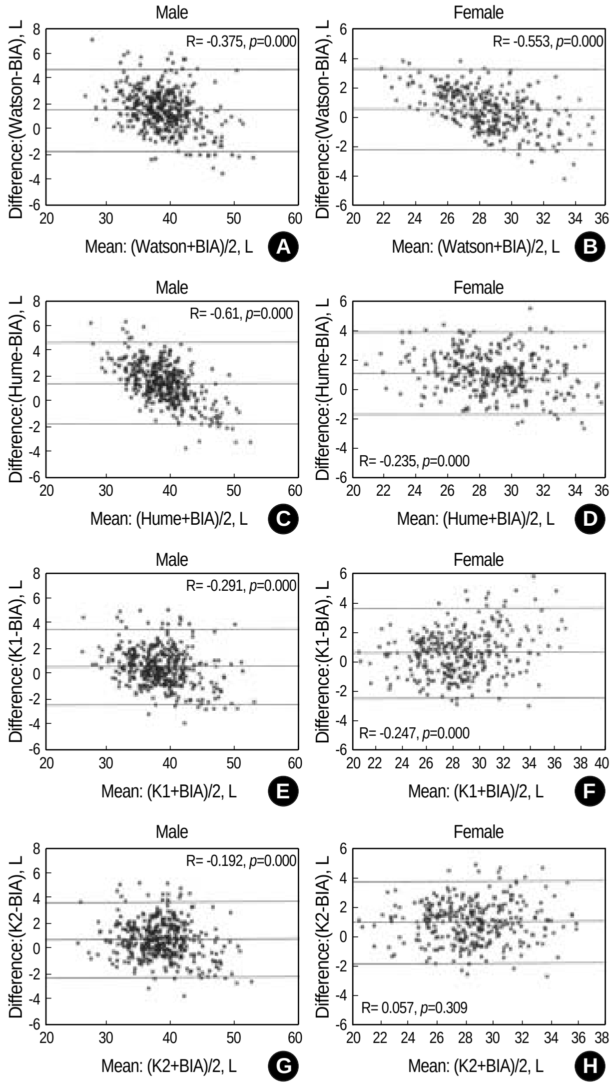

Fig. 1. Bland-Altman plot between anthropometry-based TBW and TBW_{BIA} according to gender and each equation. The three horizontal lines indicate the upper limit of agreement, the mean prediction error, and the lower limit of agreement.
BIA, TBW by BIA; Watson, TBW by Watson formula; Hume, TBW by Hume-Weyers formula; K1, TBW by K1 formula; K2, TBW by K2 formula.

equations (TBW_{K1} and TBW_{K2}) for Koreans using TBW_{BIA} as a reference. Among them, TBW_{K2} showed the highest precision and the smallest bias for males and a similar precision and the smallest bias for females compared to the TBWs derived from Watson or Hume-Weyers formulas.

Accurate estimation of the TBW is important in many pathophysiologic states, as the clinical symptoms and signs of volume dysregulation complicate a variety of medical and surgical conditions. Furthermore, the disposition of electrolytes, enteral and parenteral nutrition, and selected drugs largely depends on the size and distribution of the TBW space. As the majority of TBW resides in the skeletal muscle, TBW may also be used as estimates of somatic protein stores (6).

The need for an accurate measurement of the TBW is particularly important for dialysis patients, as it equates to the distribution volume of urea (V). In hemodialysis (HD) patients, urea is the substance that is most often monitored as a surrogate for measurement of dialysis adequacy (7). A dose of HD (prescribed or delivered) is best described as the fractional clearance of urea as a function of its distribution volume (Kt/V) (8). However, in the dialysis centers, it is not easy to measure TBW each time using an accurate method such as BIA. For convenience, the Kt/V is automatically calculated using a computerized program in which the TBW equations are installed by simply entering height, sex, the pre- and post-HD blood urea nitrogen concentration, the ultrafiltration amount and duration of HD. For the calculation of V, the Watson and Hume-Weyers formulas are generally recommended (9). However, these TBW equations were mainly derived from the age, gender, height and weight of a western population. These equations have not been validated in a Korean population, nor have their accuracies been compared with a race-specific formula. In this study, we found that the TBW equations derived from a western population showed greater bias than our formulas. They tended to overestimate the small TBWs and underestimate large TBWs. Compared to Caucasians, Koreans are smaller with lower body weights and lower values of TBW (10). Therefore, it is natural that systematic errors occur when applying the prediction formula from a reference population to another population under study. Several studies have pointed out that race-specific TBW equations should be used when applying them to another race with a different body build (11-13). Considering this background, TBW_{K2} may be helpful for assessing the nutritional status and dialysis adequacy more exactly for the Korean healthy control population and the Korean patients with end-stage renal disease.

In this study, TBW_{W} showed a lower RMSE value than the TBW_{K2} in females. Therefore, TBW_{W} might have a better accuracy than TBW_{K2}, at least in females. However, TBW_{W} showed a greater bias than TBW_{K2}, as shown in Fig. 1B, H. TBW_{K2} had a similar RMSE value and its ME was closer to zero than TBW_{W}. Furthermore, it had the least bias in females. Therefore, TBW_{K2} seemed to be more suitable for the estimation of the TBW in Korean females.

In this study, TBWs estimated from the Watson and Hume-Weyers formula showed overestimation in small TBWs and underestimation in large TBWs. The reason for this might be due to the characteristics of subjects when the Watson and Hume-Weyers formulas were derived. For the Watson formula, the mean TBW was between 36.7 and 44.1 L in males and between 31.4 and 33.2 L in females (3). For the Hume-Weyers formula, the mean TBW was between 35.3 and 46.2 L in males and between 30.2 and 39.8 L in females (4). Therefore, when the TBWs were out of those ranges, the TBWs estimated from the Watson and Hume-Weyer formula seemed to over- or under-estimate the real TBWs.

There are several limitations to this study. First, TBW was estimated using BIA rather than using deuterium oxide or another standard dilution method. However, any methods, even the gold standard methods, for the assessment of TBW are based upon assumptions that allow for some inherent errors. Furthermore, the gold standard methods are expensive, laborious and hard to apply to a large number of subjects, as in this study. BIA does have several advantages; it is easy to use, rapid, non-invasive, inexpensive and applicable at the bedside. Several studies have shown that TBW can accurately and reliably estimated by BIA in normal healthy subjects (1, 14, 15). We used segmental BIA by the eight-polar tactile electrode impedance method. Segmental BIA reduced the errors from whole body BIA estimation (16). The accuracy of the TBW assessment by this method has been validated in control subjects (2). Second, the subjects of this study were not randomly selected from nationwide regions. Therefore, the study subjects may not be representative of the entire Korean population. In spite of this problem, the number of study subjects was large enough to overcome this drawback. We also validated the accuracy of newly developed equations in another set of subjects. Third, for the males, the newly developed TBW equations (and even the TBW_{K2}) still showed weak correlation between the means and differences in the Bland-Altman plot. Thus, the TBW derived from TBW_{K2} might underestimate the real TBW in men with large BW. Fourth, this study was limited to the healthy subjects. Therefore, it should be validated for patients with the volume disorders such as acute renal failure, liver cirrhosis with ascites, ESRD, congestive heart failure, and nephrotic syndrome.

In summary, our race specific anthropometry-based equation provides superior or at least similar precision of TBW, compared to Watson or Hume-Weyers formula, in Korean subjects, with least bias. This equation may be useful for the estimation of TBW in a large number of subjects.

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