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Original Article

Assessment of total body water and lean body mass from anthropometry, Watson formula, creatinine kinetics, and body electrical impedance compared with antipyrine kinetics in peritoneal dialysis patients

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Abstract

Background. Indirect methods such as anthropometry (A), Watson formula (W), creatinine kinetics (CK), and body electrical impedance (BEI) are increasingly applied to determine total body water (TBW) and lean body mass (LBM) in dialysis patients. These methods share the disadvantage that they have been validated for healthy men only. We studied which of these four commonly applied methods can best be used routinely in CAPD patients.

Methods. TBW estimates obtained from A, W, CK, and BEI were compared with those obtained by a gold standard (antipyrine distribution volume, ADV) in eight CAPD patients. In addition, several BEI equations to derive lean body mass (LBM) were compared with LBM estimated by ADV in order to determine which equation is the most valuable for the assessment of LBM by BEI in CAPD patients.

Results. TBW as ADV was 41.4 ± 6.6 (mean $\pm$ SD) L. TBW estimated by W, A and CK underestimated ADV by a mean $\pm$ SD of 2.3 ± 13, 5 ± 8.4 and $12.3 \pm 10.9\%$ respectively. TBW as measured by BEI overestimated ADV by $2.5 \pm 8.8\%$. The correlation coefficients between ADV–TBW and TBW estimated by the indirect methods were $r = 0.88$ (A), $r = 0.87$ (BEI), $r = 0.82$ (CK), and 0.68 (W).

LBM estimated by ADV was 56.7 ± 8.9 (mean $\pm$ SD) kg; LBM by different BEI equations ranged from 49.9 ± 7 to 58.1 ± 10.7 kg.

The correlation coefficient between LBM by ADV and LBM according to the various BEI equations ranged from 0.81 to 0.93.

Conclusion. A and BEI: can be used to estimate TBW, but the considerable SD (or inaccuracy) makes individual predictions hazardous. Considering the correlation coefficients and difference between LBM by ADV and LBM according to different BEI equations, Deurenberg's formula can be advocated for use in the estimation of LBM by BEI.

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Introduction

In every nutritional survey of maintenance dialysis patients, protein and energy malnutrition and wasting are mentioned, affecting at least one-third of this population [1]. A large proportion of patients on chronic ambulatory peritoneal dialysis (CAPD) show signs of malnutrition, possibly due to losses of protein and decreasing dietary intake of protein and energy: for instance 41.6% of 224 CAPD patients from six centres in an international study on nutritional assessment [2]. No significant differences between the nutritional status of haemodialysis and CAPD patients have been found [3].

Malnutrition is associated with an increased morbidity [4]. The same holds true for Kt/V [5], a urea kinetic parameter of dialysis adequacy, which is a strong predictor of serum albumin concentration and hence a powerful predictor of death in CAPD [6]. Accurate determination of total body water in dialysis patients is important for assessment of fluid excess, for dialysis prescription by Kt/V, and for assessment of body composition or nutritional status. Calculation of total body water (TBW) or volume of distribution (V) as 0.6 times body weight is inaccurate, and determination of these variables by a tracer dilution method is laborious, invasive, and not well suited for routine patient care. Therefore, non-invasive and indirect methods such as anthropometry (A), Watson formula (W), creatinine kinetics (CK), and bioelectrical impedance (BEI) are increasingly applied for this purpose. In order to study which of these methods can routinely best be used for estimation of TBW and lean body mass in peritoneal dialysis patients, we compared estimations obtained by these methods with antipyrine distribution volume. The use of antipyrine in the measurement of total body water has been validated with deuterium oxide dilution both in normal subjects

and in subjects with an abnormal hydration status [7,8].

Since several equations have been used to derive LBM by BEI we also compared LBM estimated by ADV with LBM derived by different previously published BEI equations.

Subjects and methods

Eight patients, stable and on continuous peritoneal dialysis for more than 1 year, participated in the study after informed consent was obtained. End-stage renal disease was due to glomerulonephritis (2), nephrosclerosis (2), interstitial nephritis (1), haemolytic uraemic syndrome (1), adult polycystic kidney disease (1) and light-chain deposit disease (1), respectively. Mean ($\pm$ SD) endogenous creatinine clearance amounted to 3.8 ± 2.4 ml/min $\times 1.73$ m^2. Five patients were treated with continuous ambulatory peritoneal dialysis (CAPD), carrying out four to five 2-litre exchanges daily. Three patients were on continuous cyclic peritoneal dialysis (CCPD), using an automated cycler that provided four to five nocturnal 2-litre cycles and a single diurnal 2-litre cycle. The study protocol had been approved by the Ethical Committee of the Free University Hospital.

Measurement of total body water by calculation of antipyrine distribution volume (ADV) [7]: 1000 mg antipyrine was administered intravenously. Plasma samples were collected 2.5, 4 and 24 h after infusion. Plasma antipyrine levels were determined by high-pressure liquid chromatography [9]. Using pharmacokinetic methods the theoretical antipyrine concentration at $t = 0$ and the ADV was calculated. ADV was considered to be equal to TBW.

Anthropometry [10]: using a caliper, skinfold thicknesses at four sites (biceps, triceps, subscapular, and supra-iliac) were measured and translated into percent body fat [10]. The difference between body weight and fat mass was taken as lean body mass (LBM).

Watson formula [11]: taking age, height and weight into account for men, and weight and height for women, the Watson formula, a TBW prediction equation for adults, was applied to estimate TBW.

Creatinine kinetics [12]: LBM (kg) = (0.029 × production) + 7.38, whereas production = excretion + metabolic degradation. The components of creatinine excretion include dialytic removal and urinary excretion by remnant kidney function. Metabolic degradation = 0.38 × serum creatinine (mg/dl) × body weight (kg).

Bioelectrical impedance [13]: measurements were obtained with a tetrapolar electrode unit delivering 800 mA at 50 kHz (BIA 101, RJL Systems, Detroit, Michigan, USA) in a supine position. The sensor electrodes were placed over the bony aspects of the wrist and ipsilateral ankle [13]. Resistance values obtained were then used to calculate LBM using a software package provided by the manufacturer (RJL). In addition, four other bioelectrical impedance equations were applied to derive LBM (Table 1).

To enable comparison between the four methods and the different BEI equations, all predicted values were expressed as LBM (LBM = TBW and 0.73 [18]).

Statistical analysis

Data are expressed as mean $\pm$ SD. Wilcoxon's signed rank test was used to test the significance of difference

Table 1. Bioelectrical impedance equations used to derive lean body mass

RJL:
LBM = wt − (wt*(4.95/(1.1554−0.0841(wt*R)/ht^2) − 4.5)*100/100)
Lukaski [14]:
LBM = 0.734(ht^2/R) + 0.116(wt) + 0.096(Xc) + 0.878(Sex:F,0;M,l) − 4.03
Segal [15]:
< 20%BF
LBM = 0.00066360(ht^2) − 0.02117(R) + 0.62854(wt) − 0.12380(age) + 9.33285
> 20% BF
LBM = 0.00088850(ht^2) − 0.02999(R) + 0.42688(wt) − 0.07002(age) + 14.52435
Van Loan [16]:
LBM = 0.00085(ht^2) + 0.3767(wt) − 0.02375(R) − 0.1531(age) + 17.7868
Deurenberg [17]:
LBM = 0.698*10^{2}10^{2}ht^2/R + 3.5(Sex:F.0;M.1) + 9.4

Wt, weight in kg; ht, height in cm; R, resistance in ohms; Xc, reactance in ohms, BF = body fat.

between ADV and the other methods for assessment of body composition. Estimates of LBM obtained by each method were regressed (as dependent variables) against corresponding values obtained by antipyrine distribution volume (as independent variables), using Spearman's rank correlation test. The SD from zero was calculated by $\sqrt{[\text{mean (gold standard–other method})^2]}$. Bland and Alltman's procedure [19], in which the difference between two methods is compared to the mean result of the paired estimations, was used to test the relative validity of the prediction methods. A 0.05 level of significance was used in all statistical analyses.

Results

Patient characteristics are presented in Table 2. All patients had a normal length and weight compared to the Dutch population. The relationships between ADV and both TBW estimated by anthropometry and Watson formula are shown in Figure 1a. The regression line of ADV versus TBW–anthropometry is closer to the line of identity (correlation coefficient 0.88, $P < 0.005$) than that of ADV versus Watson formula–derived TBW ($r = 0.68$). In Figure 1b ADV is plotted

Table 2. Patient characteristics

Sex	Age (years)	Height (m)	Weight (kg)	Months on PD
M	65	1.68	68.8	36
M	64	1.93	82.0	18
M	73	1.74	96.6	12
M	62	1.75	63.4	26
M	53	1.68	65.8	14
F	64	1.70	74.1	23
F	54	1.73	82.0	21
F	61	1.74	71.8	14

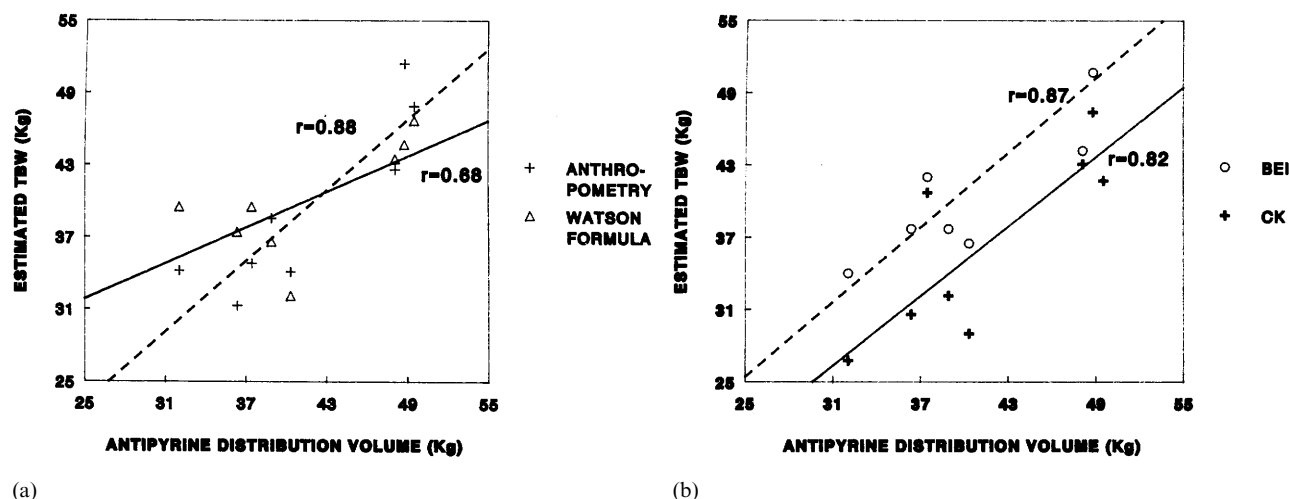(a)   (b)

Fig. 1a. Antipyrine distribution volume *versus* total body water (TBW) estimated by anthropometry (dotted line) or Watson formula.

Fig. 1b. Antipyrine distribution volume *versus* total body water (TBW) estimated by body electrical impedance (BEI; dotted line) or creatinine kinetics (CK).
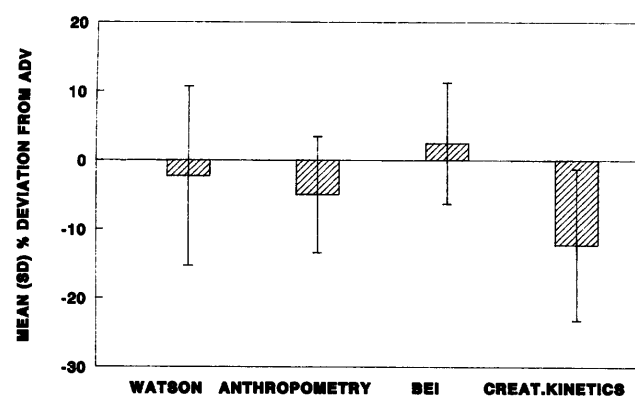

Fig. 2. Total body water estimations by Watson formula, anthropometry, body electrical impedance (BEI), and creatinine kinetics: mean ($\pm$ SD) percentage deviation from antipyrine distribution volume (ADV).

Table 3. LBM derived by different methods and several bioelectrical impedance (BEI) equations *versus* LBM estimated by antipyrine distribution volume (ADV)

	LBM estimate Mean $\pm$ SD (kg)	r (P value)	Mean difference (SD) between LBM by ADV and LBM by:
ADV	56.8 $\pm$ 8.9		
Watson (11)	54.8 $\pm$ 6.5	0.55 (0.147)	2.0 (6.2)
Anthropometry	53.9 $\pm$ 9.9	0.78 (0.037)	2.8 (4.4)
Creatinine kinetics	49.9 $\pm$ 10.5	0.76 (0.044)	6.9 (5.6)
BEI:			
RJL	58.1 $\pm$ 10.7	0.81 (0.031)	-1.4 (5.0)
Lukaski [14]	53.5 $\pm$ 11.3	0.93 (0.014)	3.2 (4.7)
Segal [15]	54.8 $\pm$ 10.7	0.88 (0.198)	1.9 (4.6)
Van Loan [16]	50.0 $\pm$ 7.1	0.88 (0.198)	6.7 (3.3)
Deurenberg [17]	54.7 $\pm$ 10.9	0.93 (0.014)	2.0 (4.6)

against TBW estimated by BEI and CK respectively. BEI-derived TBW showed the better correlation with ADV, generally overestimating ADV. A lower correlation was found between ADV and CK, generally underestimating ADV.

The mean percentage deviation of TBW estimated by the four methods studied from ADV is shown in Figure 2. W, A and CK underestimated ADV, whereas BEI overestimated ADV. The best estimations were obtained by A and BEI. All methods studied share the disadvantage of a large SD, making individual data difficult to interpret. The SD from zero for the difference in TBW estimated by W, A, BEI, and CK versus ADV was 6.5, 5.2, 5.1 and 8.8 1 respectively.

In a plot according to Bland and Alltman [19], the ADV method showed a 2.8 kg higher mean value of LBM than A, and a 1.4 kg lower mean value than BEI (Table 3). The 95% limits of agreement were calculated by the mean difference $\pm 2 \times$ SD, and for A and BEI

these amounted to -5.9 to 11.6 and -11.4 to 8.6 kg respectively.

Table 3 also reveals the results of a comparison of four previously published bioelectrical impedance equations to derive LBM. The correlation coefficients between LBM by ADV and LBM according to the equations ranged from 0.81 to 0.93. The differences between LBM by ADV and LBM according to the BEI equations ranged from -1.4 ± 5.0 to 6.8 ± 3.3 kg. The SD from zero for the difference in LBM estimated by the four BEI equations was 5.1 (RJL equation), 5.7 (Lukaski), 5.0 (Segal), 7.5 (Van Loan), and 5.0 (Deurenberg) respectively.

Discussion

Accurate determination of TBW is important not only for assessment of fluid excess and for dialysis prescription by Kt/V, but it is also an essential part of body

composition analysis. TBW is equal to the volume of water distributed in fat-free mass and is generally assumed to be fixed, i.e. 73% of fat-free mass [18].

In the era before deuterium oxide, antipyrine was the gold standard in the measurement of body water in humans, because its ease of analysis and non-toxicity [7]. Although it is still an open question which of the two spaces (of deuterium oxide and antipyrine, respectively) more closely agrees with total body water volume, each of the two methods may be used with the same reliability [20–22]. Both its neglible excretion and slow transformation make antipyrine attractive for assessing total body water [23]. The reduced clearance of antipyrine in ageing men [24] is not found in uraemic patients on regular peritoneal dialysis treatment [25] and comparison between the distribution volume of antipyrine and tritiated water space in haemodialysis patients has shown a good correlation, indicating that in dialysis patients antipyrine can be applied for an accurate determination of TBW [26].

TBW and LBM have been estimated in healthy individuals under steady-state conditions by anthropometric-derived formulas with the same relative accuracy as that provided from estimates based upon BEI measurements [27–29]. In dialysis patients, however, anthropometric measurements may not be sensitive enough to detect malnutrition established by total body nitrogen using neutron activation analysis [30]. Studying anthropometric norms in dialysis patients, Nelson *et al.* [31] found no major differences between patients and healthy persons except for non-diabetic female haemodialysis patients (significantly thinner than controls) and black diabetic female haemodialysis patients older than 55 years (lower triceps skinfold measurement than controls). In CAPD patients ($n=138$) triceps and subscapular skinfolds appeared not different from age-, sex- and race-matched healthy controls, whereas the mid-upper arm circumference was below the 50th percentile in 74% of the CAPD patients [31]. In haemodialysed diabetic patients a correlation of $r=0.82$ was observed between anthropometric and BEI determination of LBM [32]. More or less the same correlation coefficients between ADV and TBW anthropometry, and between ADV- and BEI-derived TBW, were found in our study of patients on peritoneal dialysis.

Watson's formula was derived from a selection of individual TBW volumes of 458 adult males and 265 adult females, obtained from dilution studies, together with their height, weight, and age [11]. There are, however, no data in the literature to validate Watson formula against deuterium oxide or antipyrine dilution for assessing TBW both in healthy subjects and in patients. Therefore, a comparison of our results obtained by the Watson formula and ADV with similar data is not possible. In a study of assessment of peritoneal dialysis adequacy, however, it was found, that Watson formula is less precise in estimating TBW than BEI, because BEI is less influenced by fat content in its quantitation of TBW [33]. This observation is in agreement with our results.

Bioelectrical impedance (BEI) is a non-invasive, safe, rapid and reproducible technique for assessing TBW and LBM, but the available technique needs more investigation in dialysis patients to expand its utility and validate its application [34,35]. In normal individuals BEI has been validated against deuterium oxide dilution [14,36–40], and against the hydrostatic densitometric method for measuring LBM [13–15,36,41,42]. However, determination of hydration state prior to assessment of LBM is preferable [42], and the accuracy of BEI has been challenged [43]. Validation studies of BEI in clinical conditions are few. Using deuterium oxyde dilution technique as the reference method, BEI appeared a useful measure for the assessment of TBW in elderly cancer patients [44], pregnancy [45], acromegalic patients [46], and patients with chronic obstructive pulmonary disease [47]. Furthermore, there was a good correlation between TBW as measured by BEI and the tritium dilution method in a group of renal patients including both haemodialysis and peritoneal dialysis patients ($r=0.90$) [48,49]. This is in agreement with our finding of a good relationship between BEI-derived TBW and ADV. Table 3 shows LBM derived by different bioelectrical impedance equations (shown in Table 1) versus LBM estimated by ADV. Deurenberg appeared to be the best equation, when the value of mean LBM, the correlation coefficient ($r=0.93$) and the mean difference ($\pm$ SD) between LBM by ADV and LBM by BEI are taken into account. LBM derived by BEI using Deurenberg's equation, however, underestimated ADV-derived LBM (and thus ADV-derived TBW, since $TBW = 0.73 \times LBM$). Underprediction of TBW by BEI has also been reported by Rallison *et al.* [50].

In a review article of methods for the assessment of human body composition it was stated, that when fat-free mass is estimated by creatinine excretion in normal individuals, error is high compared with reference values determined by densitometry [51]. Nevertheless, a new technique for estimating LBM from creatinine kinetics was developed [12]. In that study there was no validation against deuterium oxide dilution. However, LBM was also determined by BEI and anthropometric techniques. LBM values by creatinine kinetics correlated significantly with the other methods, but were lower. This is in agreement with our findings.

In the present study anthropometry and BEI emerged as the best predictors of TBW assessed by ADV. The combined use of both anthropometry and BEI has been shown to allow a proper assessment of body composition in patients on CAPD [52,53]. it must, however, be kept in mind that all skinfold measurements in our study were carried out by a single observer and that anthropometry is hampered by an interobserver variability, whereas BEI is not. With regard to application of BEI we previously reported that 'dry weight' (excluding both dehydration and overhydration) promotes the reliability of BEI [54]. This is supported not only by the large dependence of BEI on intracellular and extracellular water distribution [55], but also by possible cell overhydration in

CAPD patients [56]. De Lorenzo *et al.* [57] found that predialysis TBW as a percentage of LBM was much greater than the normal value of approximately 73% and they explained this by a relatively greater extracellular fluid volume, lowering the overall resistance. Thus, BEI may be less accurate for assessment of LBM than for TBW, since it assumes a fixed and normal water content per cell.

There is a theoretical difficulty when a method based on one set of assumptions is used to predict estimates obtained by another method, based on a different set of assumptions. For example this occurs when estimates of body composition obtained by the skinfolds and body mass index method, which are based on densitometry, are compared with estimates obtained from deuterium dilution. Variations in the water content of the fat-free mass will result in errors arising from densitometry and deuterium dilution that are approximately equal and opposite [28]. Especially in dialysis patients the proportion of water in the fat-free mass will vary. Unless measurements are performed at 'dry weight' the assumption that 73% of fat-free mass equals TBW may be wrong. Furthermore, discrepancies between the bedside methods and ADV may be due to biological differences between the test population used in this study and the original population used to validate the method (Watson formula, various BEI equations). The finding that Deurenberg's formula resulted in the best estimation of ADV-derived TBW may well be due to the fact that it was computed for a Dutch population, in addition to being the only equation not based upon weight.

Taking into consideration the limitations (equations utilized for computation incorporate constants derived from studies of non-uraemic individuals; anthropometry is operator-dependent; BEI is less accurate for assessment of LBM than for TBW), serial measurements of body composition variables in patients at 'dry weight' by anthropometry or BEI may prove useful to monitor the effect of nutritional intervention in dialysis patients.

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