

Limitations in Anthropometric Calculations of Total Body Water in Patients on Peritoneal Dialysis

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Abstract. Having an accurate estimation of total body water (TBW) is essential for the evaluation of dialysis efficacy in peritoneal dialysis (PD) patients. In this study, TBW volumes were measured by tritium dilution (TBW_{THO}) in 165 PD patients and compared with TBW calculations according to the Watson formulas. An alternative anthropometric formula based on the present PD population was also developed and validated in an independent sample of 29 PD patients. Furthermore, the relation between TBW_{THO} and body surface area (BSA) according to the formula of Gehan was analyzed. Body composition was assessed by a four-compartment model, based on measurements of TBW_{THO} and total body potassium. Mean values of TBW by the Watson formulas were almost identical to TBW_{THO}, and the correlation coefficient for the relationship of calculated to measured volumes was 0.89 ($P = 0.001$).

However, both anthropometric formulas—the Watson formulas as well as the new, alternative one—overestimated TBW in obese patients and *vice versa* in lean patients. Similarly, TBW was underestimated in patients who were overhydrated. The correlation coefficient between TBW_{THO} and BSA was 0.708 for males and 0.797 for females ($P = 0.0001$ for both). In obese patients, the relationship was even closer ($r = 0.924$ and 0.911 , respectively). In conclusion, anthropometric formulas to calculate TBW showed a considerable intraindividual variability compared with measured values. This was related to body composition features, such as degree of obesity and hydration. In contrast, BSA correlated closely to TBW in obese individuals. TBW as estimated by anthropometric formulas must be analyzed with caution, especially in the very obese or very lean patient.

Adequacy of dialysis, defined as clearance of small solutes or dose of dialysis, is a major issue in the nephrology community. In peritoneal dialysis (PD), urea and creatinine clearances both are used to assess the dose of dialysis. By tradition, various factors have been used to normalize these clearances for variations in body size. Creatinine clearance is standardized to body surface area (BSA), whereas for urea, the fractional clearance Kt/V is based on the distribution volume (V) for urea, which is equivalent to total body water (TBW).

There is no clear relationship between Kt/V and clinical outcome in PD patients (1–3). Furthermore, there is an increasing awareness that the Kt/V value is difficult to interpret in the very obese or the very lean dialysis patient (4–6).

To evaluate small solute clearance adequately, a correct measurement of the body water compartment is necessary. In clinical practice, TBW generally has been estimated by indirect methods using anthropometric formulas or by assuming that V is a fixed fraction of the body weight (7,8).

The first purpose of this study was to assess the accuracy of an established anthropometric method to estimate TBW—the

Watson formulas (7)—by comparing them with the TBW measured by an isotope dilution method. Second, we tried to identify patient groups in which current methods to estimate TBW would give misleading information. Third, because the Watson formulas initially were derived from patients who were free from conditions that might affect the water metabolism, we also developed alternative anthropometric equations, based on the present PD population. Finally, the relation between BSA and TBW was analyzed.

Materials and Methods

Patients

A total of 165 consecutive PD patients at the Department of Nephrology, Sahlgrenska University Hospital in Göteborg, Sweden, were included in the study. The majority of the patients were male, with a wide range of age and renal diagnoses (Table 1). All but five patients were Caucasian. The duration of PD varied from less than a month to up to 3 yr, with a mean value of 8 mo. In 90% of the patients, PD was the first dialysis modality when they reached end-stage renal disease. In most patients, several measurements of TBW by dilution technique had been performed (see below). Only one measurement, the “median” measurement, was used in the study. The TBW examinations were done as part of the routine follow-up, with the patients in stable clinical conditions.

Measurements

TBW was determined by isotope dilution of tritiated water (TBW_{THO}) (9). The patients were given 100 μ Ci (3.7 MBq) of THO orally. TBW was determined from plasma samples taken before and

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Table 1. Patient characteristics^a

Characteristics	All Patients (n = 165)	Males (n = 116)	Females (n = 49)
Age [yr; mean (±SD)]	57.5 (±14.4)	57.8 (±14.5)	56.7 (±14.4)
Duration of PD [mo; mean (±SD)]	8 (±8)	7 (±8)	10 (±10)
Primary renal disease (n)	124	86	38
Diabetic nephropathy (n)	32	25	7
Other renal diagnosis (n)	9	5	4

^a PD, peritoneal dialysis.

3 h after ingestion. The activity of plasma water was counted in a liquid scintillation counter. The coefficient of variation of a single TBW determination was 3.2% (9). As THO dilution may overestimate the TBW compartment as a result of equilibration with nonaqueous hydrogen atoms, a correction factor of 0.95 was applied (10).

Body weight (BW) was recorded on a digital scale to the nearest 0.1 kg with the patients dressed in light underwear. Body height (BH) was measured on a wall-mounted stadiometer with the patients standing upright without shoes. All measurements were obtained after the abdomen was drained of dialysis fluid.

TBW Calculations

Watson Formulas. TBW volumes obtained by dilution studies in adult males and females were used by Watson *et al.* (7) to develop prediction equations for TBW from anthropometric measurements for adults of any age (TBW_w). The equations that gave the best fit were:

$$\text{TBW (L)} = 2.447 - 0.09516 \text{ age (yr)} + 0.1074 \text{ height (cm)} + 0.3362 \text{ weight (kg) (male)}$$

$$\text{TBW (L)} = -2.097 + 0.1069 \text{ height (cm)} + 0.2466 \text{ weight (kg) (female)}$$

Body Surface Area

BSA was calculated according to Gehan and George (11), using the following formula:

$$\text{BSA} = 0.02350 \times \text{height (cm)}^{0.42246} \times \text{weight (kg)}^{0.51456}$$

Body Composition Analysis

Body fat (BF) and fat-free mass (FFM) were calculated according to a four-compartment model (9). In this model, BW is the sum of four compartments: fat-free extracellular solids (FFECS), body cell mass (BCM), extracellular water (ECW), and BF. Thus, FFM is composed of FFECS, ECW, and BCM. The input variables were total body potassium (TBK), TBW_{THO}, BW, height, and normal BW. BCM was calculated from TBK, measured in a whole-body counter (12). The normal BW for each patient was taken from Swedish and Norwegian population reference tables (13,14). As an index of obesity, BF/BW was used. For male patients, BF/BW > 25% was regarded as obesity, and for female patients BF/BW > 30%. Body hydration was expressed as TBW_{THO}/BW and TBW_{THO}/FFM.

Statistical Analyses

Standard statistics were used to describe the salient features of interest. Correlation between variables was assessed by linear regression. Calculated and measured values were compared by the Bland-

Altman method (15). A *P* value of less than 0.05 was considered statistically significant.

Results

Body Composition

The body composition characteristics of male and female patients are presented in Table 2. In these patients, varying degrees of obesity and body hydration were present. The ratio of TBW_{THO}/BW varied between 34 and 71.5%.

TBW, Measured and Calculated

TBW volumes are given in Table 3. The mean value of TBW according to the Watson formula (TBW_w) was almost identical to the mean value of the actual TBW measurement using THO.

When TBW_w was plotted against TBW_{THO}, a fairly strong correlation was found (*r* = 0.889, *P* = 0.0001), with a moderate degree of agreement (Figure 1). This is illustrated further in Figure 2, in which a Bland-Altman analysis has been performed (15). The mean difference between the methods was -0.383 L (SD, 3.391) with limits of agreement of -7.165 and +6.399 L. The Watson formulas overestimated small TBW volumes and underestimated large volumes. There was no significant correlation between intermethod TBW variation and BW.

Table 2. Body composition^a

Parameters	Males (n = 116)	Females (n = 49)
Body weight (kg)	74.5 (±12.0)	62.8 (±14.1)
BMI (kg/m ²)	24.0 (±3.4)	24.1 (±5.3)
TBK (mmol)	3314 (±651)	2349 (±421)
BSA (m ²)	1.9 (±0.19)	1.7 (±0.20)
BF/BW (%)	21.9 (±8.0)	29.2 (±10.0)
TBW/BW (%)	56 (±6)	50 (±7)
TBW/FFM (%)	71.6 (±1.6)	70.9 (±2.2)

^a Values are expressed as mean (±SD). BMI, body mass index, body weight/height²; TBK, total body potassium; BSA, body surface area; BF/BW, body fat related to body weight; TBW/BW, total body water related to body weight; TBW/FFM, total body water related to fat-free mass.

Table 3. Measured and calculated TBW^a

Parameters	All Patients (n = 165)	Males (n = 116)	Females (n = 49)
TBW _{THO} L	38.2 (±7.4)	41.3 (±5.9)	30.9 (±5.1)
TBW _w L	37.8 (±6.5)	40.9 (±4.8)	30.6 (±3.8)

^a Values are expressed as mean (±SD). TBW_{THO}, total body water measured by tritium dilution; TBW_w, total body water calculated according to the Watson formulas.

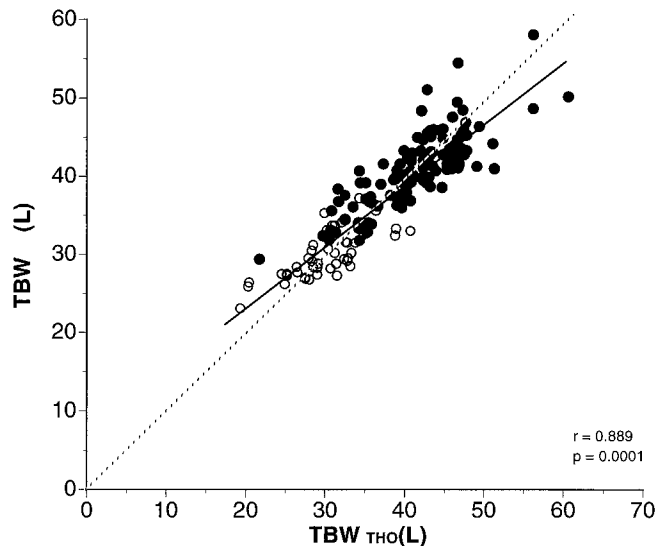


Figure 1. Calculated total body water (TBW) according to the Watson formulas in relation to TBW measured by tritium dilution. ○, female; ●, male.

Influence of Body Fat on Intermethod Differences

When the difference between TBW_w and TBW_{THO} is correlated to the index of obesity (BF/BW), it is evident that the Watson formula overestimated TBW in the obese patients (as defined in the Materials and Methods, Body Composition Analysis section) and *vice versa* in lean patients (Figure 3).

Influence of Hydration on Intermethod Differences

Figure 4 shows that when the difference between TBW_w and TBW_{THO} is related to the relative hydration of the body, *i.e.*, TBW_{THO}/BW, the Watson formula underestimated TBW in patients who were overhydrated and *vice versa*. The same results were obtained when body hydration was expressed as TBW_{THO}/FFM.

Prediction Equations of TBW Based on Present PD Population

Equations to predict TBW were derived from the THO measurements in the present patient population of 165 PD patients using the same approach as the Watson formulas. These equations are referred to as the “Sahlgrenska equations” (TBW_S). The ones that gave the best fit were as follows:

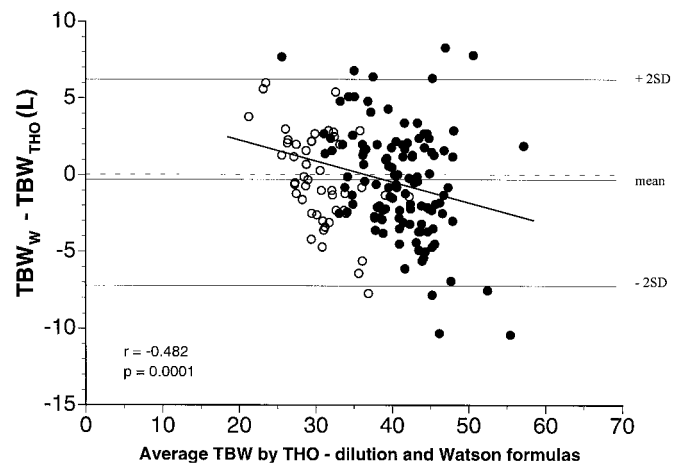


Figure 2. A Bland-Altman analysis of the difference between TBW calculated according to the Watson formulas and TBW measured by tritium dilution. ○, female; ●, male.

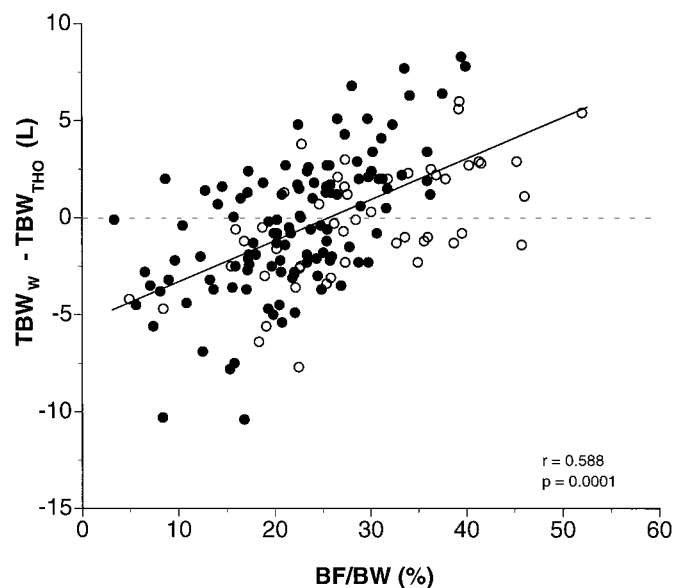


Figure 3. The difference between TBW calculated according to the Watson formulas and TBW measured by tritium dilution as a function of obesity, expressed as body fat in relation to body weight (BF/BW). ○, female; ●, male.

$$\text{TBW (L)} = -10.759 - 0.078 \text{ age (yr)} + 0.312 \text{ weight (kg)} + 0.192 \text{ height (cm)} \text{ (male)}$$

$$\text{TBW (L)} = -29.994 - 0.0004 \text{ age (yr)} + 0.214 \text{ weight (kg)} + 0.294 \text{ height (cm)} \text{ (female)}$$

$$\text{TBW (L)} = -42.879 - 0.033 \text{ age (yr)} + 0.274 \text{ weight (kg)} + 0.372 \text{ height (cm)} \text{ (all patients)}$$

The correlations between predicted and measured volumes were $r = 0.811$ (male patients), $r = 0.869$ (female patients), and $r = 0.89$ (all patients), respectively. Henceforth, the third equation, combined for both men and women, was validated in an independent sample of 29 PD patients, in which TBW_{THO} measurements had been performed (mean, 40.1 L; SD, 7.3).

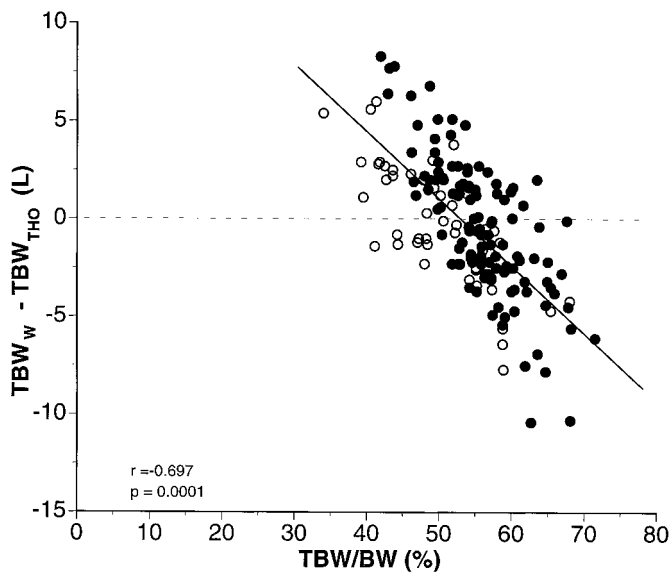


Figure 4. The difference between TBW calculated according to the Watson formulas and TBW measured by tritium dilution as a function of body hydration, expressed as TBW (measured by tritium dilution) in relation to BW (TBW/BW). ○, female; ●, male.

TBW_S (41.0 L; SD, 5.5) was strongly correlated to TBW_{THO} ($r = 0.835$, $P = 0.0001$). Mean TBW_S was not significantly different from TBW_{THO} (mean difference, 0.939; SD, 4.028). However, similar to the Watson formulas, the calculated values from the Sahlgrenska equation did not fit well to the measured values on the individual level but overestimated TBW in obese patients and underestimated TBW in lean or overhydrated patients (data and graphs not given).

Relation between BSA and TBW

As expected, there was a strong correlation between BSA and TBW_{THO} (male patients, $r = 0.708$; female patients, 0.797; $P = 0.0001$ for both). In obese patients, an even closer relationship was found (males, $r = 0.924$; females, $r = 0.911$).

Discussion

In the present study, TBW was measured by an acknowledged isotope dilution method in a large number of PD patients, and the results were compared with estimations of TBW from calculations based on anthropometric measurements, the commonly used Watson formulas. A considerable intermethod variability was found in a substantial proportion of the patients. The Watson formulas overestimated TBW in obese patients and underestimated TBW in overhydrated individuals. A revised anthropometric formula, based on the present patient population, did not increase the precision in comparison with the Watson formulas. In the obese patients, calculations of BSA seem to be more closely correlated to actual TBW.

All PD patients who had been analyzed by the tritium dilution method from 1993 to the end of 1998 were included. As this method is used in the regular follow-up at our clinic, very few of our PD patients during this time period were excluded from the study. Although the mean duration of PD at

the time of the THO measurement was relatively short, patients with PD treatment for up to 3 yr were included in the study because the median measurement, not the most recent, was chosen in patients who had had several dilution analyses. As a considerable percentage of the PD population is transferred to other treatment modalities within this period of time, the result of this study should be applicable to PD patients in general.

The THO and deuterium methods to measure TBW both are regarded as reference methods. Tritium dilution is advantageous in that the scintillation counting is robust and easily performed. However, a possible source of error (where the tracer is ingested and not injected) is that a delayed gastric emptying could give falsely high values of TBW as a result of incomplete equilibration.

A 5% correction for the isotope exchange is close to the theoretical maximum of hydrogen isotope exchange, calculated to be 5.22% (10). The exact correction factor is still under debate, and smaller differences between tritium space and TBW have been reported (16). The same is valid also for deuterium dilution. Arkouche *et al.* (17) performed dilution studies with both deuterium and ^{18}O . They found that deuterium overestimated ^{18}O space with 4.3%, a figure close to the 5% used in this study. The factor of 5% has also been applied in a recent study using THO dilution (18).

The method used to estimate LBM and BF in the present study may be regarded as “the second best.” Ideally, LBM should have been analyzed by dual energy x-ray absorptiometry, a method in which the LBM estimation is based on different assumptions than in the four-compartment method used in this study and a method that has independent sources of errors. The inability of dual energy x-ray absorptiometry to subdivide LBM into TBW and body cell mass is less important for this purpose.

The Watson equations have been obtained from 30 dilution studies that have been reported in the literature (7). The study participants were healthy volunteers and patients who had been hospitalized for “minor disorders.” However, patients who had conditions that could offset normal body hydration were not included in the calculations. Thus, the study populations differed in major respects from our target population, *i.e.*, the PD population. Therefore, the Sahlgrenska equations were developed as an attempt to find equations that could be better applicable to this patient category. The best fit to the TBW_{THO} data in our population of PD patients was an equation based on weight, height, and age. There was no additional benefit for including gender. However, these equations had the same limitations as those of Watson *et al.* It is obvious that both sets of equations fit at the group level but could not adequately predict TBW on an individual basis.

The formulas of Gehan and co-workers to predict BSA, published 1970, were derived from measurements in 401 subjects and correlated well with the approximations by du Bois and du Bois from 1916 (11,19,20). In a recent critical analysis of the accuracy of 15 existing BSA formulas, the one by Gehan and George turned out to have the highest degree of predictability (21).

When TBW is estimated as a fixed percentage of BW,

erroneous values will be obtained in a substantial number of PD patients. This was evident from the present study, in which body hydration varied from 34 to 71% in a population within a wide range of body size and body composition.

As stated above, the mean values of TBW were almost identical for both methods used in this study, but the variability between the methods was considerable. The same has been found in some of the previous smaller studies that have been published on this matter (17,22). However, in other studies that included various dilution methods, it was found that V derived by Watson overestimated (23) or underestimated (24,25) the body water compartment. In the study by Dahl *et al.* (25), this was obvious especially in patients with a higher degree of body hydration, which is in accordance with our own results. Arkouche *et al.*, however, found a good agreement between TBW volumes measured by deuterium dilution and TBW calculated from the Watson formulas (17).

There is no consistent view in the literature of the impact of obesity on TBW. Woodrow *et al.* (23) concluded in their study with deuterium dilution in 20 PD patients that the Watson formula overestimated V, and this was more apparent with increasing obesity, in agreement with the result in the present study. Wong *et al.* (24) found the opposite in their 20 PD patients, namely that the Watson formulas underestimated TBW compared with the deuterium dilution. This was emphasized in patients who were defined as “obese,” *i.e.*, BF/BW >25% (men) or >30% (women). When relating all inter-method differences to degree of obesity, they concluded that as body fat increases, deviations increase. Watson *et al.* (7) also concluded that extreme variations of body fat would affect the accuracy of the TBW prediction equations.

In the present study, *actual* body weight was used in all calculations, with the abdomen drained from dialysate. Although there is a constant effort to maintain the patients in optimal hydration, both over- and underhydrated patients would be present. Our study illustrates the typical clinical situation, in which the patient should be evaluated in the context of comorbidity and present nutritional status.

In previous studies, the hydration status has been evaluated in different ways. Wong *et al.* (24) concluded that their patients were overhydrated, because the hydration of FFM (calculated by a four-compartment method) was 76.6%. In contrast, Arkouche *et al.* (17) characterized their patients as being underhydrated, because the hydration of FFM (calculated by anthropometry) was found to be 69.7%. Finally, Woodrow *et al.* (23) estimated by clinical assessment that their patients were in “an ideal state of hydration.” The differences in their evaluations might well reflect the great difficulties in determining optimal hydration status. It should be noted that even in healthy individuals, ideal hydration is not easily defined and is less so in dialysis patients.

Our study illustrates the conclusions of Tzamaloukas *et al.* (26–30) that anthropometric equations that estimate TBW need to be adjusted to the degree of obesity, overhydration, and other co-factors. It is evident that the increase in body weight from obesity will contribute less to the TBW than weight increase from mere overhydration. No prediction equations

based on BW can distinguish between these two clinically different conditions.

Of particular interest for the clinician is that we found BSA to be more closely related to TBW in obese PD patients. This may be explained by the fact that in the formula for BSA, increased weight for height, caused by the accumulation of less hydrated obese tissue, results in a proportionally small increase of BSA. Therefore, formulas for BSA seem to be less sensitive for the changes in body composition that could occur in various populations, *e.g.*, dialysis patients (21). When creatinine clearance is normalized to BSA, it should therefore be less readily misinterpreted than Kt/V for any solute in this patient category. This is supported further by Hume and Weyers (8), who measured TBW by tritium dilution in 60 normohydrated patients and found an extremely good correlation between TBW_{THO} and BSA (*ad modum* du Bois and du Bois). Indeed, it could be suggested that creatinine clearance is a better estimate of the efficacy of dialysis than Kt/V_{urea}.

In conclusion, currently used formulas to calculate TBW showed a considerable intraindividual variability compared with actual measured TBW values, even when adapted to the specific PD population. The discrepancies were related to characteristics of body composition, particularly the degree of obesity and hydration, and resulted in erroneous estimations of the variable V in the Kt/V formula. An increased awareness of this problem will enhance our ability to interpret properly the various estimates of the delivered dose of dialysis. It also seems that in PD patients, creatinine clearance, normalized to BSA, is a less ambiguous approach to estimate the transperitoneal exchange.

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