To test the precision of estimates of body water and urea clearance in peritoneal dialysis (PD), we compared, in 925 PD patients who underwent formal urea kinetics studies, estimates of \( V \) and \( Kt/V \) urea obtained by the use of the Watson, Hume, and Sahlgrenska anthropometric formulas and two novel formulas, one (\( V_{\text{creat}} \)) computed using fat-free mass (FFM) estimated from creatinine kinetics as \( 0.73 \times \text{FFM}_{\text{creat}} \) and the other (\( V_{\text{BMI}} \)) calculated as \( 0.73 \times \text{FFM}_{\text{BMI}} \) where \( \text{FFM}_{\text{BMI}} \) was obtained by the Gallagher formula, which estimates body composition as a function of body mass index (BMI). Comparisons by twos were performed using the paired \( t \)-test and the Wilcoxon sign rank test with the Bonferroni correction for multiple (\( n = 10 \)) comparisons.

The results for \( V \) (liters) were Watson, 36.7 ± 7.1; Hume, 37.3 ± 7.3; Sahlgrenska, 36.8 ± 7.6; \( V_{\text{creat}} \) 32.2 ± 9.8; and \( V_{\text{BMI}} \) 37.2 ± 7.8. With the exception of \( V_{\text{BMI}} \) and \( V_{\text{Hume}} \) which did not differ, all other values differed (\( p < 0.001 \)) from one another regardless of whether a parametric or nonparametric comparison was performed.

The results for weekly total \( Kt/V \) urea were Watson, 2.05 ± 0.57; Hume, 2.03 ± 0.57; Sahlgrenska, 2.06 ± 0.59; from \( V_{\text{creat}} \) 2.42 ± 0.71; and from \( V_{\text{BMI}} \) 2.03 ± 0.58. All of those values differed from one another (\( p < 0.001 \)) by both methods of comparison. Using cut-off values (1.50, 1.75, and 2.00) as indices of adequate total weekly \( Kt/V \) urea, the discrepancies between any two estimates by the five studied formulas varied in the range 1.1% – 34.2%.

Despite numerically close mean values, estimates of \( V \) based on various anthropometric formulas differ substantially and cause substantial discrepancies in the classification of \( Kt/V \) urea as inadequate or adequate. This lack of precision, added to the known lack of accuracy of the estimates, confounds the interpretation of the clinical relevance of urea kinetic estimates in PD.

Key words
Body water, urea kinetics, adequacy of peritoneal dialysis

Introduction
The lack of association between peritoneal dialysis (PD) outcomes and urea kinetic studies (1) has shed doubts on the relevance of urea kinetics to the adequacy of PD (2,3). There is evidence that factors not accounted for by urea kinetics—for example, comorbidity (4)—have major impacts on the outcome of PD that could overshadow the potential effects of small-solute clearances. It has been suggested that minimal small-solute clearance values should be retained as a safety precaution to prevent under-dialysis (5).

One of the potential causes of the absence of clinical associations with urea kinetics is lack of accuracy and precision of the methods used to estimate \( Kt/V \) urea. The accuracy and precision of \( Kt/V \) urea estimates can be affected by sampling errors (\( Kt \)) and errors in estimates of \( V \). The precision of the methods for estimating \( V \) in clinical practice is the subject of this report.

Patients and methods
We used 24-hour urine and spent dialysate collections with blood sampling at the end of the collections to
analyze estimates of \( V \) and total (peritoneal plus renal) 
\( Kt/V \) urea in 925 patients (384 with diabetes) on con-
tinuous peritoneal dialysis for 7.3 ± 5.4 months (6).
We computed \( V \) by the Watson (7), Hume (8), and 
Sahlgrenska (9) anthropometric formulas and by two 
novel formulas, one (\( V_{BM1} \)) obtained from body mass 
index (BMI) by a modification of the Gallagher for-
maula (10), and the other (\( V_{creat} \)) obtained by a modi-
fication of the Keshaviah formula estimating fat-free 
mass (FFM) from creatinine kinetics (11).

We calculated \( V_{BM1} \) by modifying the Gallagher 
formula—which estimates body-fat percentage (%BF) 
in whites and African Americans as a function of BMI, 
sex, and age—as follows: If body weight = \( Wt \), 
\[\text{FFM BMI} = Wt - (\frac{\%BF}{100}) \times Wt, \] 
and \( V_{BM1} = 0.73 \times \text{FFM BMI} \) (12). The Gallagher formula was derived by 
comparing body-composition measurements by four-
compartment analysis to anthropometric measure-
ments and demographic information in a large number 
of normal subjects from North America. The final \( V_{BM1} \) 
formula was this:

\[ V_{BM1} = Wt \times (0.25915 + 6.1904 / \text{BMI}) - 0.0005767 \times Age + 0.11972 \times Sex - 0.000365 \times Sex \times Age - 0.2847 \times Sex / \text{BMI} \] \[1\]

where \( Wt \) is expressed in kilograms and \( Age \) in years, 
and \( Sex \) is 1 for men and 0 for women.

We calculated \( V_{creat} \) from the Keshaviah formula 
(11), estimating FFM from creatinine kinetics 
(\( V_{creat} \)) as follows: \( V_{creat} = 0.73 \times \text{FFM}_{creat} \). The 
final \( V_{creat} \) formula was this:

\[ V_{creat} = 5.2414 + 0.02117 \times (\text{Vol}_{Ur} \times \text{Creat}_{Ur} \times 10 \] 
+ \( \text{Vol}_{Dial} \times \text{Creat}_{Dial} \times 10 + 0.38 \times Wt \] 
\times \text{Creat}_{Ser} \) \[2\]

where urine volume (\( \text{Vol}_{Ur} \)) and dialysate drain vol-
ume (\( \text{Vol}_{Dial} \)) are expressed in liters per 24 hours; urine, 
dialysate, and serum creatinine concentration (\( \text{Creat}_{Ur}, \) 
\( \text{Creat}_{Dial}, \) and \( \text{Creat}_{Ser} \), respectively) are expressed in 
milligrams per deciliter; and body weight (\( Wt \)) is ex-
pressed in kilograms.

Both \( V_{BM1} \) and \( V_{creat} \) assume that the water con-
tent of FFM is 73%. That relationship holds true only for 
patients with normal hydration (13). In patients 
with overhydration, \( V_{Watson}, V_{Hume}, V_{Sahlgrenska} \) and 
\( V_{BM1} \) underestimate actual \( V \) because the water con-
tent exceeds 73% of FFM in that condition (12,14).

We compared various \( V \) and \( Kt/V \) urea values by 
twos using both the paired \( t \)-test and the Wilcoxon 
sign rank test with Bonferroni correction for multiple 
comparisons. Using the Bonferroni correction (\( n = 10 \), 
the highest \( p \) value for accepting a statistical differ-
ence as significant was 0.005 (0.05/10). To obtain an 
estimate of the disagreement of the classification of 
\( Kt/V \) urea as inadequate or adequate by the various 
estimates, we used three cut-off values (1.50, 1.75, 
and 2.00) of weekly total \( Kt/V \) urea to compute the 
number of measurements that did not agree. This last 
comparison was also carried out by twos.

To identify potential sources of discrepancies, we 
performed a series of 20 multiple linear regressions: 
10 for estimates of \( V \), and 10 for estimates of \( Kt/V \) 
urea. In each regression, the dependent variable was 
the difference between two estimates (for example 
\( V_{Watson} - V_{BM1} \)), and the candidate variables were sex, 
age, height, weight, BMI, duration of PD, and whether 
the patients had diabetes.

**Results**

For men (\( n = 552 \)), height was 172 ± 8 cm, weight 
was 75 ± 15 kg, and BMI was 25.5 ± 4.3 kg/m\(^2\). Cor-
responding values for women (\( n = 373 \)) were 158 ± 
9 cm, 65 ± 17 kg, and 25.9 ± 6.1 kg/m\(^2\). Table I shows 
the mean ± standard deviation (SD) of estimates of \( V \) 
and total (peritoneal plus renal) \( Kt/V \) urea. The nu-
derical differences between the mean values of \( V \) 
by the Watson, Hume, Sahlgrenska, and BMI formulas 
were only slight. For example, the difference between 
the largest and smallest \( V \) estimate (the mean Hume 
and mean Watson \( V \) values respectively) was, at 0.6 L, 
only 1.6% of the smallest \( V \) value (\( V_{Watson} \)). Similarly, 
the largest difference between mean weekly \( Kt/V \) urea 
estimates by the same four formulas was 0.03 weekly, 
or 1.5% of the smallest value. Estimates from creati-
nine kinetics were substantially smaller (for \( V \) ) and 
larger (for \( Kt/V \)) than those from each of the other 
formulas.

Despite the apparent closeness of the mean esti-
mates of \( V \) and \( Kt/V \) urea by the Watson, Hume, 
Sahlgrenska, and BMI formulas, statistical compari-
sions revealed significant differences. Only \( V_{Hume} \) and 
\( V_{BM1} \) did not differ by either paired \( t \)-test or Wilcoxon 
sign rank test. All other comparisons by twos, includ-
ing that between \( Kt/V_{Hume} \) and \( Kt/V_{BM1} \) showed sig-
nificant differences by both tests, with one exception: 
In the comparison between \( V_{Watson} \) and \( V_{Sahlgrenska} \), the
paired t-test showed a nonsignificant difference (mean difference: 0.085 ± 0.147 L; \( p = 0.037 \)), and the Wilcoxon sign rank test disclosed a highly significant difference (\( V_{\text{Watson}} > V_{\text{Sahlgrenska}} \) in 333 cases, and \( V_{\text{Sahlgrenska}} > V_{\text{Watson}} \) in 592 cases, \( p < 0.001 \)).

To test whether the differences observed in the estimates of \( Kt/V \) urea would affect the classification of dialysis adequacy, we computed the number of cases that would be classified as having adequate or inadequate urea clearance at three \( Kt/V \) urea cut-off values. Table II shows the comparison by twos. The discrepancies in the classification of \( Kt/V \) urea as adequate or inadequate seemed to increase, in general, with higher cut-off values, but tended to be small (from 1.1% to 6.4%) between the Watson, Hume, Sahlgrenska, and BMI estimates.

All 20 multiple linear regressions analyzing the differences between \( V \) or \( Kt/V \) urea estimates produced significant \( r^2 \) values. The factors that were identified as predictors of those differences included age (18 regressions), height (16 regressions), and sex and weight (14 regressions each).

**Discussion**

The main finding of this study is that, unlike the situation described in previous reports with substantially smaller numbers of observations (15), we found differences in even the mean values of estimates by various anthropometric formulas calculating \( V \) for urea kinetics. We also found that those differences led to misclassification of small-solute clearance adequacy in a small number of patients. Misclassification was more probable in patients who varied substantially from the mean in age, height, or weight. Sex was also a source of potential misclassification.

The lack of precision of the formulas studied, which can be attributed to the differences in the coefficients assigned by the formulas to determinants of body composition (age, sex, height, weight), compounds their potential errors from lack of accuracy. The standard error of the mean for each formula is in the order of several liters (7–10). If the small differences found in this study between the Watson, Hume, Sahlgrenska, and BMI estimates of \( V \) can produce the discrepancies shown in Table II, then their differences from actual body water, potentially in the order of several liters, should be expected to cause much larger discrepancies.

Another condition that confounds the analysis of urea kinetics in PD is lack of knowledge about how to handle the effect on \( V \) of overhydration. Because of findings that link large body size to survival in hemodialysis, it has been proposed that \( V \)—or any other size indicator—should not be treated as a passive reservoir, but as an index of metabolic activity. The argument could be made that, because edema is metabolically inert, it should not be part of \( V \) for urea kinetics. To test the likely result on urea kinetics of including in the calculation only the part of \( V \) that represents dry weight, we used creatinine kinetics to estimate \( V \), because of the suggestion that FFM estimated from creatinine kinetics represents a “dry weight” FFM (16). The disagreement between all other

**TABLE I** Estimates of body water (\( V \)) and dialysis adequacy (\( Kt/V \) urea)

<table>
<thead>
<tr>
<th>( V ) (L)</th>
<th>Watson</th>
<th>Hume</th>
<th>Sahlgrenska</th>
<th>BMI</th>
<th>creat</th>
</tr>
</thead>
<tbody>
<tr>
<td>36.7±7.1</td>
<td>37.3±7.3</td>
<td>36.8±7.6</td>
<td>37.2±7.8</td>
<td>32.2±7.8</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE II** Disagreement of classification of adequacy of \( Kt/V \) urea estimates by cut-off values

<table>
<thead>
<tr>
<th>( Kt/V ) Watson</th>
<th>1.50 Weekly</th>
<th>1.75 Weekly</th>
<th>2.00 Weekly</th>
</tr>
</thead>
<tbody>
<tr>
<td>( Kt/V ) Hume</td>
<td>27 (2.9)</td>
<td>53 (5.7)</td>
<td>59 (6.4)</td>
</tr>
<tr>
<td>( Kt/V ) Sahlgrenska</td>
<td>17 (1.8)</td>
<td>31 (3.4)</td>
<td>29 (3.1)</td>
</tr>
<tr>
<td>( Kt/V ) BMI</td>
<td>23 (2.5)</td>
<td>46 (5.0)</td>
<td>39 (4.2)</td>
</tr>
<tr>
<td>( Kt/V ) creat</td>
<td>105 (11.4)</td>
<td>233 (25.2)</td>
<td>303 (32.8)</td>
</tr>
</tbody>
</table>

| \( Kt/V \) Hume   | 10 (1.1)    | 36 (3.9)    | 46 (5.0)    |
| \( Kt/V \) Sahlgrenska | 16 (1.7)  | 43 (4.6)    | 48 (5.2)    |
| \( Kt/V \) BMI    | 110 (11.9)  | 256 (27.7)  | 316 (34.2)  |
| \( Kt/V \) creat  | 14 (1.5)    | 35 (3.8)    | 20 (2.2)    |
| \( Kt/V \) Sahlgrenska | 104 (11.2) | 242 (26.2)  | 298 (32.2)  |
| \( Kt/V \) BMI    | 114 (12.3)  | 253 (27.4)  | 296 (32.0)  |
estimates and the estimate using $V$ calculated from creatinine kinetics in the classification of adequacy based on $K_t/V$ urea was in the general order of 25% (Table II).

Conclusions

Current methods of estimating $V$ in clinical practice for urea kinetic analysis in PD are inaccurate and were found in the present study and in other studies (17) to lack precision. Evaluation of the relevance of urea kinetics in PD will have to await the development of more precise and accurate methods. Bioimpedance—which is simple and highly reproducible—offers promise. However, the accuracy of bioimpedance does not appear to have reached the desired level in PD patients so far (18).

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References


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