Correlation between Dt/V derived from ionic dialysance and blood-driven Kt/V of urea in African-American hemodialysis patients, based on body weight and ultrafiltration volume

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Abstract

Background: The Dt/V obtained by using ionic dialysance (D) as a surrogate for urea clearance (K) is a well-validated adjunct measure of hemodialysis adequacy, with a variable level of correlation with urea-based Kt/V. However, this correlation has not been examined based on patients’ body size and ultrafiltration (UF) volume during the dialysis session.

Methods: Simultaneous evaluations of online Dt/V and single-pool variable-volume urea Kt/V were made. Patients were categorized into three subgroups based on their weight (<60, 60–80 and ≥80 kg), body mass index (<25, 25–30 and >30 kg/m²) and UF volume (<1.5, 1.5–3 and >3 L). The correlation between Dt/V and Kt/V was evaluated for the entire cohort per dialysis session in each subgroup.

Results: Mean Kt/V was greater than the mean Dt/V (1.72 versus 1.50, P < 0.001), with an overall correlation r value of 0.602. This correlation was stronger in the medium weight group versus lower and higher weights. The correlation between Dt/V and Kt/V was inversely related to the UF volume (r = 0.698, 0.621 and 0.558 for those with UF volume of <1.5, 1.5–3.0 and >3 L, respectively). A total of 99.3% of patients with Dt/V of >1.2 also had Kt/V >1.2 and 9.5% of those with Dt/V <1.2 had their Kt/V <1.2.

Conclusions: There is a moderate degree of correlation between Dt/V and Kt/V in African-American hemodialysis patients, which is impacted by body size and UF volume. A Dt/V of >1.2 strongly predicts adequate dialysis as defined by Kt/V of >1.2.

Key words: adequacy, African American, Dt/V, hemodialysis, Kt/V
Introduction

Adequate delivery of hemodialysis dose as measured by the Kt/V derived from urea reduction is an important determinant of clinical outcomes in chronic hemodialysis patients [1, 2]. Currently, the Kt/V of urea is the preferred method for measuring the delivered dialysis dose [3]. The assessment of the Kt/V of urea is, therefore, mostly done on a once monthly basis with the implicit assumption that one hemodialysis session is representative of all other sessions.

The second-generation Daugirdas formula has been shown to have little systematic error and is now widely used to compute the Kt/V of urea [4, 5]. However, the need for pre- and post-dialysis collection of blood samples precludes its practical use in every dialysis session. However, the Kt/V assessed in one hemodialysis session does not account for potential inadequate dialysis doses that may be delivered during other sessions. Furthermore, incorrect sampling of post-dialysis urea is quite common and can result in erroneous conclusions regarding the delivered Kt/V [6].

The measurement of ion dialysis (D) and its use as a surrogate for urea clearance (K) has been suggested as an adjunct method of quantifying dialysis adequacy [7]. D can be calculated from conductivity measurement of the dialysate using probes at its inlet and outlet. With this technique, the inlet dialysate conductivity is transiently changed from baseline leading to a change in the outlet dialysate conductivity. The D is then calculated using the inlet and outlet conductivity values measured at two different points.

Since sodium (the main plasma ion) and urea have similar transfer characteristics across the dialysis membrane, the D is then used as a surrogate for K to calculate the Dt/V [7]. Unlike the Kt/V, measuring the Dt/V does not require blood sampling and can, therefore, be easily assessed during many hemodialysis sessions as needed at no additional cost. However, estimation of total body water (V) is needed to compute the Dt/V. Overestimation of V combined with underestimation of the K by D has led to underestimation of the delivered dialysis dose by Dt/V as compared with Kt/V [7]. The degree of correlation between the Dt/V and Kt/V has been variable and is dependent on the method used to estimate the V [7].

Available methods include percentages of dry weight [8, 9], the Watson’s anthropometric formula [8, 10–12], bioimpedance analysis [13], the single-pool variable-volume (SPVV) model [14–16] and direct dialysis quantification (DDQ) [16], all of which have been used to estimate the V in previous studies comparing the Dt/V with the Kt/V-urea. However, using pure percentages of body weight as estimates of V-urea has been shown to be inaccurate [17].

Despite the accuracy of the SPVV model to determine V (with subsequent use of D in place of manufacturer-provided K), it does not allow real-time comparison between Dt/V and Kt/V-urea [14]. On the other hand, bioimpedance methods are not widely available, while DDQ is quite a cumbersome method, making it unsuitable for routine clinical use [18].

We have, therefore, selected the Watson’s anthropometric formula to estimate the V, given its ease of applicability in routine clinical practice. However, the Watson’s formula has been shown to overestimate the V in hemodialysis patients. This error is more pronounced in Caucasians compared with African-Americans [19].

This interracial difference in the accuracy of anthropometrically estimated V may result in a different degree of correlation between Dt/V and Kt/V among different racial groups. In addition to race, the impact of body size and ultrafiltration (UF) volume (variables known to affect the V) on the degree of correlation between the Dt/V and Kt/V has not been extensively studied in the past. We investigated the correlation between Dt/V and Kt/V in an exclusive cohort of African-American chronic hemodialysis patients, looking for the impact of body size and UF volume on this correlation.

Materials and methods

Patients and dialysis characteristics

We included African-American patients aged 18–85 years with end-stage renal disease on standard thrice weekly chronic hemodialysis therapy for at least 6 months. Additional inclusion criteria included a stable, functioning arteriovenous access and satisfactory compliance with hemodialysis treatment. Patients with frequent intradialytic hypotension, history of systolic heart failure with ejection fraction <25%, dialysis catheter access and limb amputees were excluded. Both the Wayne State University Institutional Review Board and the DaVita Clinical Research Committee approved the study protocol. Informed consent was obtained from each study patient.

Baseline characteristics were recorded from all patients at inclusion. No changes were made to the patients’ routine dialysis prescription for the purpose of this study. The study was performed monthly for three consecutive months from August to October of 2012. Each study patient had one to three sessions of hemodialysis during which simultaneous evaluations of online Dt/V and SPVV urea Kt/V were made during a midweek hemodialysis session. All assessments were performed on the second dialysis treatment of the week to ensure that the interval between treatments was uniform and weight gains were not extreme. Dialysis treatments were performed using a Fresenius 2008 K machine equipped with the online clearance monitor (OCM) (Fresenius Medical Care North America, Lexington, MA, USA). The OCM method provides an automatic intradialytic measurement of the effective in vivo D, the total cleared blood volume Dt, the delivered dose of dialysis Dt/V and the plasma sodium concentration of the patient. It measures D six times throughout the dialysis session. We used Optiflux F180NR and F200NR single-use dialysers with blood flow rates of 400–600 mL/min and dialysate flow rates of 600–800 mL/min.

Patients were weighed at the beginning and end of each dialysis session. The actual dialysis time and net volume removed by UF were recorded as well. The patients were stratified into three pre-specified groups based on their weight (<60 kg, 60–80 kg and >80 kg), body mass index (BMI) (<25, 25–30 and >30 kg/m²) and UF volume (<1.5, 1.5–3 and >31 L).

Measurements, calculations and determination of dialysis dose

The serum urea blood samples were obtained in all patients just before the initiation of the treatment and immediately afterwards by the slow-flow method [20]. Serum blood urea nitrogen (BUN) concentrations were measured by the DaVita clinical laboratory. Dialysis adequacy was assessed monthly using the second-generation Daugirdas formula to calculate the single-pool Kt/V [4]. Simultaneous calculation of the Dt/V was performed for each corresponding dialysis session using the mean of six D measurements, the total dialysis time in minutes (t) and anthropometrically estimated V using the Watson formula [21].

The weight that we used for Watson equation was the estimated dry weight, which is a standard, relatively constant clinical parameter used in outpatient hemodialysis units.
Values of the single-pool Kt/V and the Dt/V were compared for the entire cohort and each of the mentioned pre-specified subgroups. We also calculated the Youden index [22] for selection of an optimal cutoff of Dt/V for accurate diagnosis of dialysis adequacy.

**Statistical analysis**

Data were encoded and tallied in SPSS version 20 (IBM Corp., Armonk, NY, USA). The delivered doses of dialysis determined by the Kt/V and Dt/V were expressed as mean ± standard deviation (SD). The Pearson or Spearman correlation coefficient was used for continuous data. For categorical data, we utilized Fisher’s exact tests and Pearson’s Chi-Square test. A P < 0.05 was considered to be significant. Analysis of the agreement between Kt/V and Dt/V was conducted using Bland–Altman plot method.

**Ethical standards**

Study was approved by the Institutional Review Board (IRB) of Wayne State University (IRB# 020912M1F).

**Results**

As shown in Figure 1, 160 chronic hemodialysis patients were screened, with 81 enrolled in the study. Simultaneous assessment of Kt/V and Dt/V was done on 60, 62 and 64 patients during a midweek hemodialysis session in the months of August, September and October of 2012, respectively. All the 81 enrolled study patients had simultaneous assessment of the Kt/V and Dt/V for a range of one to three dialysis sessions. A total of 186 measurements in 81 patients were available over the study period of 3 months.

Of the 81 patients enrolled, 36 (44.4%) were male while 45 (55.6%) were females. The mean age was 55.68 years [95% confidence interval (95% CI) 52.45–58.91; SD 14.6] with a range of 22–82 years. The mean weight was 83.2 kg (95% CI 76.96–89.49; SD 27.9) while the mean BMI was 28.43 kg/m² (95% CI 26.56–30.3; SD 8.2). UF volume ranged from 0 to 7.9 L with a mean of 2.74 L (95% CI 2.54–2.93; SD 1.4) (Table 1). The average dialysis session duration was 3–5 h with a mean of 4 h, depending on the individual patient.

Figure 2 shows the mean delivered dose of dialysis measured with Kt/V to be higher than that measured with Dt/V [Kt/V = 1.72 (1.68–1.76); Dt/V = 1.50 (1.46–1.53); P < 0.001], with an overall moderate positive correlation between the Kt/V and Dt/V (r = 0.602, P < 0.001). The degree of agreement between the two methodologies was examined using the Bland–Altman analysis (Figure 3), which was in keeping with the correlation between Kt/V and Dt/V as there is no proportional bias to the differences between Kt/V and Dt/V.

In the three subgroups based on the body weight, there was a better correlation between the Kt/V and Dt/V in the medium weight and BMI groups compared with those at the lower and higher ends (r = 0.581, 0.681 and 0.521 for those with weight <60 kg, 60–80 kg and ≥80 kg, respectively; r = 0.604, 0.653 and 0.545 for those with BMI of <25 kg/m², 25–30 kg/m² and >30 kg/m², respectively (Figure 4). However, we found the correlation between Kt/V and Dt/V to be inversely proportional to the UF volume based on the magnitude of UF (r = 0.698, 0.621 and 0.558 for sessions with UF volume <1.5, 1.5–3 and >31, respectively) (Figure 5).

Of the 144 dialysis treatment sessions in which patients had a Dt/V >1.2, 143 (99.3%) had Kt/V of >1.2. However, only 9.5% (4/42) of treatment sessions with Dt/V of <1.2 also had a Kt/V of <1.2. Of the 181 treatment sessions with Kt/V of >1.2, 143...
(79%) were associated with a Dt/V of >1.2. Four out of the five treatment sessions (80%) with Kt/V of <1.2 also had Dt/V of <1.2 (Table 2).

Youden’s index was calculated (Youden’s J = Sensitivity + Specificity – 1.091 with a 95% CI 0.006–0.140) and found to be 0.091.

Discussion

In the USA, African-American individuals carry a disproportionate higher burden of end-stage renal disease, comprising 32% of the end-stage renal disease population, while representing 13% of the general population. A large number of studies have established this increased risk for end-stage renal disease among blacks. There could be a large number of factors that contribute to this difference, genetic, anthropometric, socioeconomic, environmental, etc. These differences could account for the difference in various parameters like bone mineral metabolism and even dialysis clearance and overall survival on dialysis. Our patient population is predominantly African-American.

To our knowledge, this study is the first one comparing hemodialysis adequacy using ionic D (Dt/V) with the widely used Kt/V derived from second-generation Daugirdas formula in an exclusive cohort of African-American chronic hemodialysis patients. In the whole study group we report a moderate degree of correlation between the Dt/V and the Kt/V-urea with a mean Dt/V less than the mean Kt/V. This has already been well-demonstrated in numerous studies over the past two decades, [8, 11, 23–25]. This is possibly explained by the overestimation of V using the Watson’s formula [8, 13, 16, 19], as well as underestimation of K by D most likely caused by recirculation [26].

We found an overall moderate correlation between the Kt/V of urea and Dt/V ($r = 0.602$, $P < 0.001$, $n = 186$ hemodialysis sessions).

![Fig. 2. Correlation between Kt/V derived from second-generation Daugirdas formula (x-axis) and Dt/V from ionic D (y-axis) in all 81 patients.](image)

![Fig. 3. Bland-Altman analysis of the relation between Dt/V and Kt/V.](image)
overestimation of V observed in African-Americans compared with Caucasians when the Watson formula is used [17]. Over the past two decades Dt/V has been well-validated as a surrogate measure of hemodialysis adequacy. However, it is relation to body size and volume of UF in a given dialysis session has not been closely examined.

Since we used an anthropometric estimate of V, we prospectively divided our patients into three categories based on body weight and BMI to evaluate the impact of these two variables on the correlation between Kt/V-urea and Dt/V. We found a better correlation in the medium weight and BMI groups compared with those at the extremes of weight and BMI. This is probably explained by a better accuracy of anthropometrically estimated V in the medium weight and BMI groups compared with those at the extremes of body weight and BMI [28].

Therefore, interpretation of correlation Dt/V and Kt/V in patients with low and high BMI should be done cautiously.

We also evaluated the effect of UF volume on the correlation between the Kt/V and Dt/V by prospectively stratifying the hemodialysis sessions into three categories based on the UF volume: low (<1.5 L), medium (1.5–3.0 L) and high (>3.0 L). We demonstrated that the higher the UF volume, the poorer the correlation between the Kt/V and Dt/V. This is explained by the difference in the volume of distribution (Vd) of sodium and urea in the blood. The Vd of sodium in the blood is represented by plasma water while that of urea is by blood water. A more pronounced decrease in plasma water (Vd of sodium) relative to blood water (Vd of urea) with higher UF volume leads to a greater decrease in D with a relatively stable K which, in turn, results in a more prominent decrease in Dt/V with a relatively constant Kt/V and poorer correlation between the two [16, 29]. This is largely explained by the well-known Gibbs–Donnan equilibrium effect, which leads to attenuation of conductivity toward the second half of the dialysis session more pronounced with higher volumes of UF [25, 30, 31]. This is a quite significant finding in patients who require high UF volumes due to excessive inter-dialytic weight gain.

Finally, using the Kt/V-urea of at least 1.2 as a gold standard for adequate dialysis, we evaluated the ability of Dt/V to correctly classify dialysis sessions as adequate or inadequate. We found that a Dt/V of >1.2 almost always guarantees a Kt/V-urea of >1.2, and hence, adequate dialysis. On the other hand, a Dt/V <1.2 does not track well with inadequate dialysis. Thus, while a Dt/V >1.2 provides assurance regarding adequacy of dialysis, a Dt/V <1.2 only indicates the need for confirmation of adequacy by obtaining the Kt/V of urea.

Moreover, as Dt/V is a machine-driven test and does not involve sample processing or nursing time, detection of suboptimal clearance via conductivity method will allow earlier intervention including access recirculation in arteriovenous fistula with venous outflow stenosis. This will also allow timely adjustment of dialysis prescription in patients with deteriorating clearances.

Our study has several strengths. The sample size was larger than most previous similar studies. To our knowledge, this is the first study examining the correlation between SPVV Kt/V and D methods in the African-American chronic hemodialysis population as well as in subgroups of patients stratified on the
basis of body weight, BMI and UF volumes. We believe this is significant as the accuracy of anthropometric V estimates depend on factors such as race and body composition [19, 28].

The weaknesses of the study include reliance on the less accurate anthropometric estimation of V and the lack of a control racial group for direct comparison. Our patient population is predominantly African-American, making a Caucasian control group impossible. To our knowledge, this study is the first one comparing hemodialysis adequacy using ionic D (Dt/V) with the widely used Kt/V derived from second-generation Daugirdas formula in an exclusive cohort of African-American chronic hemodialysis patients. We believe this is a potential strength of our study.

Moreover, anthropometric methods are more convenient and practical for routine use in clinical settings compared with cumbersome approaches such as bio-impedance and DDQ. Although we did not have a control racial group, we were able to compare our findings with previous studies that primarily included Caucasian patient populations as indicated above.

We also understand that urea-based measures of Kt/V need proficient staff training on the correct steps to take prior to drawing the postdialysis BUN sample as it could be source of error. Our nurses are quite proficient and well trained in carrying out the blood-based measurement whether urea reduction ratio or Kt/V, which is a standard the Centers for Medicare & Medicaid Services requirement. They are periodically updated and retrained in these measurements.

### Table 2.
The ability of Dt/V to correctly classify hemodialysis sessions into adequate and inadequate using a reference value of Kt/V ≥1.2 as a gold standard to define adequate hemodialysis

| Dt/V category | Kt/V category | Total |
|---------------|---------------|-------|
| <1.2          |               |       |
| Count         | 4             | 1     | 5    |
| ≥1.2          |               |       |
| Count         | 38            | 143   | 186  |

| Diagnostics   | Value         | 95% CI          |
|---------------|---------------|-----------------|
| Accuracya     | 0.790         | 0.764–0.801     |
| MCRb          | 0.210         | 0.199–0.236     |
| Sensitivity   | 0.993         | 0.976–1.000     |
| Specificity   | 0.976         | 0.940–0.989     |
| PPV           | 0.800         | 0.776–0.896     |
| NPV           | 0.790         | 0.767–0.835     |
| Youden’s Jc   | 0.088         | 0.019–0.117     |
| NNTd          | 1.695         | 1.274–12.512    |
| NNDe          | 11.326        | 8.516–83.615    |

a Overall fraction correct = (a + d)/t; (often referred to simply as ‘Accuracy’).

b Misclassification rate = 1 – overall fraction correct.

Youden’s J = sensitivity + specificity – 1.

d Number needed to treat (NNT) = 1/absolute value of difference in proportions.

e Number needed to diagnose (NND) = 1/(Sensitivity – (1 – Specificity]) = 1/(Youden’s J).

PPV, positive predictive value; NPV, negative predictive value.

### Fig. 5. (A) Ultrafiltration volume ≤1.5 L, r = 0.698, P < 0.001, n = 33. (B) Ultrafiltration volume 1.51–3.0 L, r = 0.621, P < 0.001, n = 80. (C) Ultrafiltration volume >3 L, r = 0.558, P < 0.001, n = 69.
In the unit where our study was performed, 96% patients are of black ethnicity. Our study has very strict exclusion criteria so that dialysis clearance could not be affected; therefore, only 50% of the patients that were screened could be enrolled in the study.

This limitation can pose a problem in replicating the study or its use in practice. Larger studies involving multiethnic group will be needed to examine this further.

In conclusion, despite the fact that Dt/V tends to underestimate the Kt/V of urea, there still remains a moderate degree of correlation between Dt/V and Kt/V needs to be carefully addressed. The underestimation of Kt/V by the Dt/V may be less remarkable in African-American chronic hemodialysis patients. A Dt/V \( \geq 1.2 \) almost always indicates an adequate delivered dialysis dose while a Dt/V of \(<1.2\) is inconclusive. The Dt/V may be an acceptable adjunct for evaluation of dialysis adequacy but cannot substitute the standard method (Kt/V of urea).

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Conflict of interest statement

None declared.

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