# Estimation of Delivered Dialysis Dose by On-Line Monitoring of the Ultraviolet Absorbance in the Spent Dialysate

Fredrik Uhlin, BSc, Ivo Fridolin, MSc, Lars-Göran Lindberg, PhD, and Martin Magnusson, MD, PhD

 <u>Background:</u> Several methods are available to determine Kt/V, from predialysis and postdialysis blood samples to using on-line dialysate urea monitors or to ionic dialysance using a conductivity method. The aim of this study is to compare Kt/V calculated from the slope of the logarithmic on-line ultraviolet (UV) absorbance measurements, blood urea Kt/V, dialysate urea Kt/V, and Kt/V from the Urea Monitor 1000 (UM; Baxter Healthcare Corp, Deerfield, IL). <u>Methods:</u> Thirteen uremic patients on chronic thrice-weekly hemodialysis therapy were included in the study. The method uses absorption of UV radiation by means of a spectrophotometric set-up. Measurements were performed on-line with the spectrophotometer connected to the fluid outlet of the dialysis machine; all spent dialysate passed through a specially designed cuvette for optical single-wavelength measurements. UV absorbance measurements were compared with those calculated using blood urea and dialysate urea, and, in a subset of treatments, the UM. Results: Equilibrated Kt/V (eKt/V) obtained with UV absorbance (eKt/Va) was 1.19  $\pm$  0.23; blood urea (eKt/Vb), 1.30  $\pm$  0.20, and dialysate urea (eKt/Vd), 1.26  $\pm$  0.21, and Kt/V in a subset measured by the UM (UM Kt/V) was 1.24  $\pm$  0.18. The difference between eKt/Vb and eKt/Va was 0.10  $\pm$  0.11, showing a variation similar to the difference between eKt/Vb and eKt/Vd (0.03  $\pm$  0.10) and in a subset between eKt/Vb and UM Kt/V ( $-0.02 \pm 0.11$ ). Conclusion: The study suggests that urea Kt/V can be estimated by on-line measurement of UV absorption in the spent dialysate. Am J Kidney Dis 41:1026-1036. © 2003 by the National Kidney Foundation, Inc.

INDEX WORDS: Hemodialysis (HD); dialysis monitoring; dialysis dose; spectrophotometry; absorption; ultraviolet (UV); solute removal; spent dialysate; dialysis adequacy; dialysis efficiency; urea; Kt/V.

IALYSIS DOSE has been reported to have great significance for the outcome of dialysis treatment. Many studies have shown a relationship between dialysis dose, measured as Kt/V or urea reduction ratio (URR), and morbidity and mortality in hemodialysis (HD) patients. 1-9

Even if HD characteristics remain constant, it is difficult to attain a prescribed Kt/V because of great variability among different HD sessions (eg, variability in whole-body urea clearance). Also, in larger HD patients, difficulties can arise in achieving the goal Kt/V. Deviations in dialysis efficiency between different sessions also may be caused by, for example, changes in blood flow, access recirculation, treatment time, and decreased clearance of dialyzers. This, in turn,

may lead to inadequate dialysis treatment for patients. 6,12

Traditionally, dialysis adequacy is determined by calculating Kt/V from predialysis and postdialysis blood urea concentrations. However, urea removal can be significantly overestimated from immediate postdialysis concentrations because of compartment effects. 12-14 Laboratory errors also may lead to significant errors in the estimation of dialysis dose.6 Castro et al15 showed that the most accurate method to calculate equilibrated Kt/V (eKt/V) is to use a 30-minute postdialysis urea sample. However, this is often impractical in the clinical situation, and Kt/V has been estimated by measuring intradialytic urea concentrations 15,16 or using the rate-adjustment method. 17 A good correlation between intradialytic urea concentration measurements, rate equation calculations, and methods based on 30-minute postdialysis urea sampling has been reported.17

To overcome difficulties estimating Kt/V, an on-line monitoring system has been suggested as a more accurate method to achieve the treatment goal.<sup>6,8,10,18-20</sup> Different urea monitors are available to automatically measure urea concentrations in the spent dialysate.<sup>21-23</sup>

An alternative method has been developed that determines ionic dialysance assessed by temporarily increasing dialysate conductivity (so-

From the Department of Nephrology; and the Department of Biomedical Engineering, Linköping University, University Hospital, Linköping, Sweden.

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Address reprint requests to Fredrik Uhlin, BSc, Department of Nephrology, University Hospital, Linköping, S-581 85 Linköping, Sweden. E-mail: fredrik.uhlin@lio.se

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Table 1. Patient Data and Number of Treatments

Patient No.	Nephrological Diagnosis	Duration of HD (mon)	Glomerular Residual Function (Creatinine Clearance; mL/min)	No. of Study Sessions
1	Reflux nephropathy	13	. 0	7
2	Chronic uremia	16	0	. 6
3	Chronic pyelonephritis	42	0	. 15
4	Polycystic kidney disease	24	3	7
5	Diabetic nephropathy	50	0	14
6	Nephrosclerosis	10	9	7
7	Bilateral kidney cancer	25	0	4
8	Nephrosclerosis	13	8	.4
9	Status post cancer in urinary bladder	61	1	6
10	Nephrosclerosis	21	9	4
11	Diabetic nephropathy	65	11	3
12	Diabetic nephropathy	3	8	5
13-	Nephrosclerosis	41	. 0	2
		Mean 29.5 SD 20.2		Total 84

NOTE. Conversion factor for creatinine clearance from mL/min to mL/s is 0.0167.

dium concentration) in the dialysate inlet and measuring the change in conductivity at the dialysate outlet.<sup>24-26</sup>

It is known from high-performance liquid chromatography (HPLC) studies that many substances retained in uremic patients can be measured by ultraviolet (UV) absorption.<sup>27</sup> Such studies have shown differences in UV absorbance peaks between predialysis and postdialysis uremic serum, ultrafiltrate, or dialysate containing UV-absorbing small constituents and middle molecules. 27-35 HPLC peaks when screening UV-absorbing solutes in uremic serum separately<sup>27,34</sup> and total UV absorbance in serum that can be obtained as the cumulative and integrated peak height of all UV-absorbing HPLC peaks together<sup>36,37</sup> have been evaluated to obtain a dialysis ratio and extraction value. The ability to continuously monitor UV light transmittance of the dialysate using a 254-nm wavelength has been reported earlier. 38,39

Recently, a new technique for on-line monitoring of solutes in the spent dialysate using UV absorbance has been developed, enabling one to follow up a single HD session continuously and monitor deviations in dialysis efficiency. 40 Good correlations between UV absorbance and several small removed waste solutes, such as urea, creatinine, and uric acid, were found, indicating similar removal rates for these and UV-absorbing solutes that may enable the determination of K/V and Kt/V for urea.

This study compares delivered dialysis dose calculated from UV absorbance in the spent dialysate on-line and urea Kt/V calculated from urea in blood and dialysate and the Urea Monitor 1000 (UM; Baxter Healthcare Corp, Deerfield, IL).

## PATIENTS AND METHODS

This study was performed after approval of the protocol by the Ethics Committee of the Department of Nephrology, University Hospital of Linköping, Sweden. Informed consent was obtained from all participating patients.

Thirteen uremic patients (six women, seven men; mean age, 64.3 years; range, 21 to 81 years) on chronic thrice-weekly HD therapy were included in the study. Table 1 lists nephrological diagnoses, duration of HD therapy, glomerular residual function (creatinine clearance), and number of study sessions for each patient. Patients were monitored during dialysis treatment for 240 to 300 minutes.

Four different dialyzers were used: althane, with an effective membrane area of 1.8 m² (AF180; Ahltin Medical, Ronneby, Sweden; N = 47), polyamide S, 1.7 m² (Polyflux 17S; Gambro Lundia AB, Lund, Sweden; N = 12), and polysulfone dialyzers, 1.0 m² (N = 12) and 1.3 m² (N = 13; F50 and F6HPS, respectively; Fresenius Medical Care, Bad Homburg, Germany). Dialysate flow was 500 mL/min, and blood flow varied between 250 and 300 mL/min. In two sessions, using single-needle mode, average blood flow was 200 mL/min. Two types of machines were used: AK 200 (Gambro Lundia AB) and Fresenius 4008H (Fresenius Medical Care). The schematic clinical set-up of experiments is shown in Fig 1.

## The UM

An on-line dialysate monitor, the UM, with an accuracy of approximately ±5% was used to monitor dialysis dose

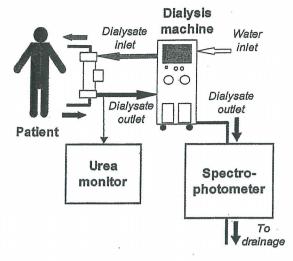


Fig 1. Schematic clinical set-up of experiments.

throughout a subset of sessions (N=40) using an althane dialyzer and 285-nm wavelength. A double exponential dialysate urea concentration time curve was obtained, providing on-line information on the two-pool Kt/V achieved throughout the treatment.<sup>21</sup> The UM was adjusted to measure urea every 5 minutes.

## **UV** Absorbance Monitoring

For determination of UV absorbance, a double-beam spectrophotometer (Uvikon 943; Kontron Instruments, Milan, Italy) with an accuracy of approximately  $\pm 1\%$  was used. Absorbance A of a solution, obtained by the spectrophotometer using the pure dialysate as the reference solution, was determined as follows:

$$A = \log \frac{I_r}{I_{r+s}} \tag{1}$$

where  $I_r$  is the intensity of transmitted light through the reference solution (pure dialysate) and  $I_{r+s}$  is the summated intensity of transmitted light through the reference solution containing the solutions under study (pure dialysate plus waste products from blood).

During on-line experiments, the spectrophotometer was connected to the fluid outlet of the dialysis machine, with all spent dialysate passing through the specially designed optical cuvette. The sampling frequency was set at two samples per minute. The obtained UV absorbance values were processed and presented on the computer screen by a personal computer incorporated in the spectrophotometer using Kontron software (Uvikon 943, version 7.0 for Windows; Kontron Instruments). Results from measurements using wavelengths of 280 nm (N = 25) and 285 nm (N = 59) are presented here.

## Sampling and Laboratory Analysis

Blood samples were drawn before the start of dialysis treatment  $(C_0)$  and immediately at the end of the treatment  $(C_0)$ . Dialysate samples were collected before dialysis (pure

dialysate), which was used as the reference solution, when the dialysis machine was prepared for starting and conductivity was stable and after 5, 15, 30, 60, 90, 120, 180, and 240 minutes (270 and 300 minutes if the treatment was >240 minutes). If a periodic self-test or alarm occurred during a time-tabled sampling, the sample was obtained instead after 1 to 3 minutes, depending on whether the UV-absorbance monitoring curve had been stabilized.

Urea concentrations were determined at the Clinical Chemistry Laboratory at Linköping University Hospital using standardized methods. Accuracy of the method for determination of urea in dialysate and blood was ±5%.

## Estimation of Dialysis Dose: Theory

A simple dialysate-side mass balance indicates that the dialysate outlet substance concentration  $C_{Do}$  is linearly related to the blood inlet substance concentration  $C_{Bi}$ . <sup>19,41</sup> For urea, a small solute that is transported over the dialyzer membrane mainly by diffusion, this relationship can be expressed as:

$$C_{Do} = \frac{K}{Q_{Di}} C_{Bi} \tag{2}$$

where  $Q_{Di}$  is the rate of dialysate flow into the dialyzer in milliliters per minute and K is dialyzer blood urea clearance in milliliters per minute. From the differential equation describing urea mass balance during dialysis, it can be determined that the average value of K/V may be approximated as the slope from the natural logarithm plot of urea blood or dialysate concentration ( $S_B$  or  $S_D$ ) versus time<sup>19</sup>:

$$Kt/V \approx -S_B * T \approx -S_D * T$$
 (3)

where T is dialysis session length in minutes and V is distribution volume of urea in the body in milliliters. To calculate Kt/V from on-line UV absorbance, the slope of blood and dialysate urea concentrations was replaced by the slope of UV absorbance (Sa) versus time  $(Kt/V \approx -Sa*T)$ . eKt/V according to the rate-adjustment method<sup>42</sup> was predicted from the rate of dialysis (K/V) and single-pool Kt/V (spKt/V) (see Appendix, Equation 10).

# Statistical Analysis

Results are expressed as mean ± SD. Samples obtained at times coinciding with self-tests or alarms of the dialysis machine were excluded. In addition, some sessions were excluded because of technical failure of the UM (3 of 40 sessions) or spectrophotometer (7 of 84 sessions). To be sure that deviating points during dialysis machine self-tests do not influence Sa values, those points were excluded. The obtained smoothed absorbance curve was used for Sa determination (Fig 2). Also, unrealistic Kt/V values marked "fit error" were excluded for the UM (2 of 40 sessions). Student's paired t-test (two tailed) and Levene test of homogeneity of variances were used to compare means for different methods and SD values, respectively. P less than 0.05 is considered significant. The different methods were compared using Bland-Altman<sup>43</sup> analysis. For the analysis, Statistica software (version 6.0, StatSoft, Inc, Tulsa, OK) was

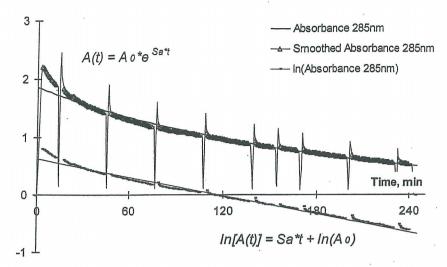


Fig 2. A typical on-line absorbance curve during a single HD treatment in which UV absorbance at 285-nm wavelength is plotted against time. Deviating points during the dialysis machine's self-tests were excluded, and Sa was obtained from the smoothed absorbance curve. A linear fitting curve from the logarithmic plot of the smoothed on-line absorbance is presented as:  $ln[A(t)] = Sa * t + ln(A_0)$ .

#### RESULTS

Figure 2 shows a typical on-line absorbance curve during a single HD treatment in which UV absorbance at 285-nm wavelength is plotted against time. UV absorbance drops and peaks during dialysis correspond to self-tests in the dialysis machine when the dialyzer is in bypass mode. The exponential fitting curve of the smoothed UV absorbance, A(t) = Ao \* exp(Sa \* t), is shown. The slope from the logarithmic plot of on-line absorbance values versus time, Sa, is presented. A linear fitting curve is presented as  $ln[A(t)] = Sa * t + ln(A_0)$  for the time-dependent plot.

Figure 3 shows mean eKt/V in all 84 treatments. Kt/V values were calculated using the second-generation Daugirdas formulas and the

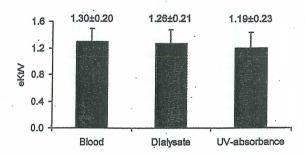


Fig 3. eKt/Vb from predialysis and postdialysis blood urea (N = 81) and eKt/V from the slope versus time, eKt/Vd (N = 84) and eKt/Va (N = 77).

rate-adjustment equation. Equation 8 to obtain spKt/V using blood urea (spKt/Vb; Appendix), and equation 9 to obtain spKt/V using dialysate urea (spKt/Vd) and UV absorbance (spKt/Va) using slopes  $S_D$  or  $S_D$  (280 or 285 nm) were used. eKt/V was calculated using equation 10 for all methods. The mean value given by Kt/V equilibrated using blood urea (eKt/Vb) was  $1.30 \pm 0.20$  (SD; N = 81); that equilibrated using dialysate urea (eKt/Vd),  $1.26 \pm 0.21$  (N = 84); and that equilibrated using UV absorbance (eKt/Va),  $1.19 \pm 0.23$  (N = 77). Higher values for eKt/Vb were obtained compared with eKt/Vd and eKt/Va (P < 0.05).

Figure 4 shows differences between individual values of eKt/Vb and eKt/Vd (Fig 4A) and eKt/Vb and eKt/Va (Fig 4B) plotted against eKt/Vb values. Mean value of the difference between eKt/Vb and eKt/Vd was  $0.026 \pm 0.097$  (N = 81; Fig 4A), and the difference between eKt/Vb and eKt/Va was  $0.102 \pm 0.114$  (N = 74; Fig 4B). The SD value for differences for dialy-sate urea and UV absorbance compared with blood urea showed no statistically significant difference (P < 0.05).

Figure 5 shows the standardized subset in which the UM was used. Mean values given by eKt/V or Kt/V measured by the UM (UM Kt/V) were (Fig 5): eKt/Vb,  $1.23 \pm 0.17$  (SD; N = 38); eKt/Vd,  $1.18 \pm 0.15$  (N = 40); UM Kt/V,  $1.24 \pm 0.15$  (N = 40); UM Kt/V (M = 40); UM K

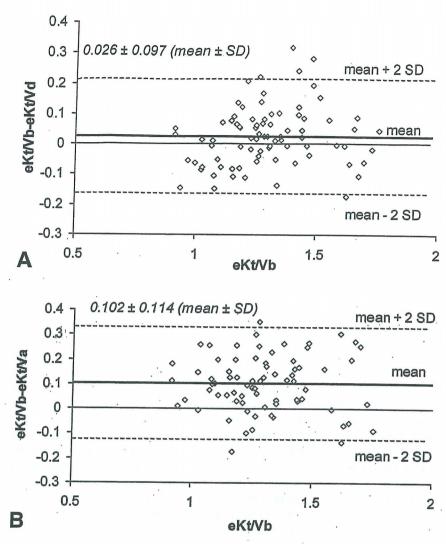


Fig 4. Differences between (A) eKt/Vb and eKt/Vd (N = 81) and (B) eKt/Vb and eKt/Va (N = 74) plotted against eKt/Vb.

0.18 (N = 35); and eKt/Va, 1.16  $\pm$  0.18 (N = 37). Mean eKt/Vb was not different from UM Kt/V and was higher compared with eKt/Vd and eKt/Va (P < 0.05), similar to the total material.

Figure 6 shows differences as mean  $\pm$  SD for eKt/V or UM Kt/V compared with eKt/Vb plotted against eKt/Vb values. Figure 6A shows differences between eKt/Vb and eKt/Vd of 0.040  $\pm$  0.115 (N = 38). The difference for UM Kt/V was  $-0.017 \pm 0.105$  (N = 34; Fig 6B); and between eKt/Vb and eKt/Va, 0.070  $\pm$  0.102 (N = 35; Fig 6C). The SD of the difference between eKt/Vb and eKt/Va was not significantly different compared with other differences (P < 0.05). This indicates that the SD value of

difference for eKt/Va is of the same order as for the other methods.

## DISCUSSION

The results presented show the potential to estimate dialysis dose in terms of Kt/V by applying the UV technique. Values for eKt/Vb as a reference method had higher values than eKt/Vd and eKt/Va (Figs 3 and 5) and showed almost the same value as UM Kt/V in a subset (Fig 5). Differences in Kt/V values between different methods (blood and dialysate urea, UM, and UV methods) were of the same magnitude (Figs 4 and 6).

One possible reason for the higher values for

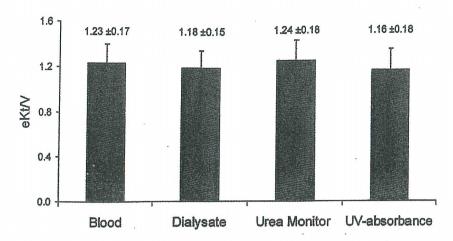


Fig 5. eKt/V for the subset of sessions, eKt/Vb (N = 38), eKt/Vd (N = 40), eKt/Va (N = 37), and UM Kt/V (N = 35).

eKt/Vb is that the first blood urea sample value, obtained before the start of the treatment, is higher than the initial dialysate urea or UV absorbance values determined after the start of the treatment. At the same time, this could be explained by preliminary data from in vitro dialysis using spent hemofiltrate and with a fixed V and t, indicating that K determined from UV absorbance is approximately 10% less than that for urea (data not shown). Many HPLC studies<sup>27-35</sup> have shown UV-absorbing solutes that were removed by HD and were of higher molecular weight than urea. The lower mean Kt/V value of the UV method may be explained by lower clearance of these UV-absorbing higher molecular-weight solutes compared with that of urea. In practice, this difference can be eliminated by adjusting the mean difference between blood and UV-absorbance Kt/V values.

The smallest difference regarding mean Kt/V was obtained between blood urea and the UM (Fig 5). Good agreement between mean eKt/V and UM Kt/V also has been shown earlier.<sup>44</sup>

The SD of the difference for dialysate urea, UM, and on-line UV absorbance compared with blood urea was not statistically significantly different when eKt/V was calculated using the second-generation Daugirdas formula (Figs 4 and 6). The same trend was obtained in the entire material because the calculated SD for differences in Kt/V values in the larger group (Fig 4) is similar to the SD for differences in the smaller subset (Fig 6). Even if urea concentration is measured in blood or spent dialysate, whereas the UV method measures all UV-absorbing com-

pounds in spent dialysate, the assumption that UV-absorbing solutes are removed in a similar manner compared with urea seems to be valid in this material. This also is confirmed by very good correlations between several small-molecular-weight waste products and UV absorbance<sup>40</sup> and similar concentration changes during dialysis for several azotemic markers (eg, urea, creatinine, uric acid, and pseudouridine), as reported earlier.<sup>34,39</sup>

Furthermore, it seems that UV-absorbing solutes can be subject to similar corrections regarding distribution volume and intercompartmental equilibration rates, similar to urea, although probably not having exactly the same distribution and equilibration intercompartmental rates in the body as urea. A similar equation that uses blood and dialysate urea slopes to calculate Kt/V and corrects for urea generation and ultrafiltration has been proposed by Garred et al<sup>19</sup> and can be an alternative way to correct Kt/V. A trend similar to eKt/V also was obtained when fixed-volume spKt/V was estimated using different methods, assuming negligible urea generation and ultrafiltraton rate (data not shown).

Another non-urea-based method that estimates urea Kt/V from ionic dialysance has been reported to have a random nonsystematic error of approximately 6% to 11% (SD) for Kt/V, depending on how urea distribution volume is calculated and if ionic dialysance is corrected for cardiopulmonary recirculation. The accuracy of the UV method described in this study shows a nonsystematic error of approximately 9% (100% \* SD of the difference/mean), which

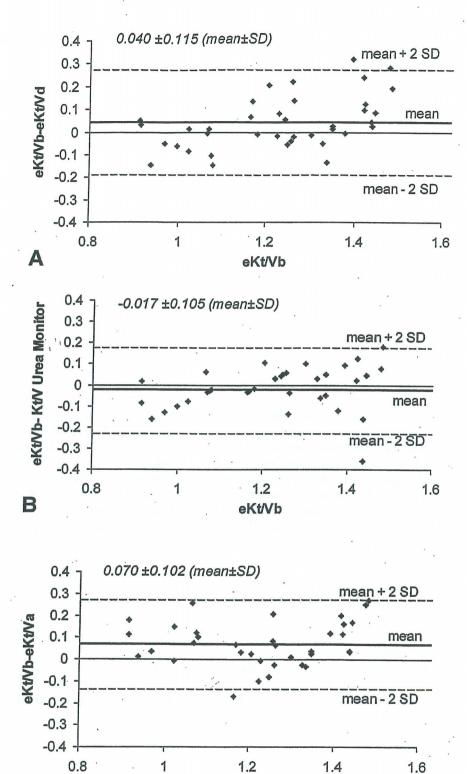


Fig 6. Differences between (A) eKt/Vb and eKt/Vd (N = 38), (B) eKt/Vb and UM Kt/V (N = 34), and (C) eKt/Vb and eKt/Va (N = 35) plotted against eKt/Vb.

eKt/Vb

is similar to errors of the other methods described. A way to further minimize the SD for differences between the blood urea and UV methods probably is to apply appropriate calibration (eg, patient or session related).<sup>46</sup>

Nevertheless, it still seems difficult to achieve a low SD, even using standard methods, because different urea-based methods (blood, dialysate, UM) show relatively high discrepancies despite expected high accuracy on urea concentration determination (accuracy of laboratory and UM, ±5%). This indicates that HD is a complicated clinical treatment in which the measurement situation is cumbersome. Various differences, lower and higher than obtained in this study, in both Kt/V and mean Kt/V, depending on methods used for comparison with UM (eg, variable-volume single-pool model, modified direct-dialysate quantification) and different clinical settings have been published. 17,21,41,47-52

Figure 2 shows a typical on-line UV-absorbance curve in flowing dialysate at a fixed wavelength (285 nm) versus time during a single HD session, showing the exponential decrease in UV-absorbing solutes during the dialysis treatment. The absorbance drops occur for the period of the dialysis machine's self-tests when the dialysator is in bypass mode (dialysate does not pass the dialysator). Figure 2 also shows the potential to follow up a single HD session continuously and monitor deviations in dialysator performance by using UV absorbance. An apparent UV-absorbance response to changes in blood flow for different flow value manipulations has been shown.40 Sampling frequency was set at two samples per minute during this experiment to restrict the amount of collected data. Considering that all events during HD are relatively slow, sampling frequency is not a limiting factor when using the UV method.

Such on-line monitoring methods as the UM, the presented UV method, and others using many samples during the dialysis treatment ensure that estimated Kt/V is less sensitive to measurement errors compared with manual dialysate sampling. The sampling procedure based on single samples, such as predialysis and postdialysis urea sample in blood, can have a great influence on the calculation of Kt/V.<sup>53-55</sup> However, the UM rejects unstable points not fit with the expected exponential decay.<sup>41</sup> Despite ensuring a good fit

in Kt/V values compared with the blood-urea method, the UM method cannot show all time traces of the treatment and the potential to record the time trace or other information in more unstable sessions technically is cumbersome. Conversely, the UV technique has the ability to follow up each dialysis treatment continuously because of the very high sampling frequency, allowing monitoring of any deviations on-line and presentation of data in an appropriate way on a screen. The method offers the ability to create a database in which valuable information about each dialysis treatment can be saved and analyzed afterward. The application could be especially suitable for following up patients during home HD. This information can be useful as a source for analyzing and revising treatment quality and existing standards and methods to ensure treatment quality and patient welfare.

To summarize, this study indicates that elimination of such a small-molecular-weight waste product as urea can be assessed by the UV technique. As a consequence, this makes it possible to determine K/V and calculate Kt/V, even when the technique does not measure urea itself. A relationship between Kt/Vurea (or URR) and mortality and morbidity has been shown in uremic patients, 1-9,56,57 although urea is considered nontoxic.58,59 With the UV method, it may be possible to measure the elimination of other toxic or nontoxic substances retained in uremic patients, with potential clinical significance. The common medications that patients were treated with seemed not to influence UV absorbance,46 but should be investigated further, as well as interference from the other solutes. To enhance clinical applicability of the UV method, interesting studies in the future would be UV measurements in a larger patient group calculating parameters other than Kt/V (eg, protein catabolic rate and total removed urea). To gain more knowledge about mechanisms behind the UV technique, in vitro studies should be performed.

In conclusion, this study suggests that delivered dialysis dose in terms of Kt/V can be estimated by monitoring UV absorbance in the spent dialysate on-line. Values for eKt/Vb were higher than those calculated from the dialysate urea and UV methods. Differences in Kt/V between different methods (blood and dialysate urea, UM, and UV method) were of the same order. UV-

absorbance measurements will help ensure dialysis quality by evaluating the delivery of the prescribed treatment dose and immediately identifying and being alert for deviations in dialysis treatment. This gives the potential for an individual approach to follow up and plan each dialysis treatment, giving feedback to nursing staff during and after interventions. Hopefully, the UV method adds a new technique and method to the wide discussion about quality and adequacy of the dialysis.

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### **APPENDIX**

Calculation of Kt/V

From the differential equation describing urea mass balance during a dialysis session, it can be determined that the average value for K/V during a session may be approximated as the slope from the natural logarithm plot of urea concentration in blood versus time,  $S_{\rm B}$ . Thus:

$$Kt/V \approx -S_B T$$
 (4)

where T is dialysis session length in minutes and V is distribution volume of urea in the body in milliliters. This equation would hold strictly if urea obeys fixed volume and single-pool kinetics and no urea is generated during the session. <sup>60</sup> According to Equation 2,  $S_B$  may be replaced by the slope from the natural logarithmic plot of urea concentration in spent dialysate versus time,  $S_D$ :

$$Kt/V \approx -S_D T$$
 (5)

Assuming that urea is distributed in a single-pool volume in the body, urea generation rate and ultrafiltration are negligible during the session, and the ratio K/V remains constant during the dialysis session, the following equation holds<sup>61,62</sup>:

$$Kt/V = -\ln \frac{C_t}{C_0} \tag{6}$$

According to Equations 4 and 5, we obtain from Equation 6:

$$\frac{C_t}{C_0} = \exp\left(-Kt/V\right) = \exp\left(S_B T\right) = \exp(S_D T) \tag{7}$$

if the slopes are used instead of blood urea concentrations and the previously mentioned assumptions are fulfilled. The single-pool volume Kt/V for blood, spKt/Vb, can be calculated according to the second-generation Daugirdas formula<sup>42</sup>.

$$spKt/Vb = -\ln\left(\frac{C_t}{C_0} - 0.008 \frac{T}{60}\right) + \left(4 - 3.5 \frac{C_t}{C_0}\right) \frac{UF}{W}$$
(8)

where UF is total ultrafiltration in kilograms and W is patient dry body weight in kilograms.

Using dialysate slope values according to Equation 8, the monocompartmental equation can be written as:

$$spKt/Vd = -\ln\left(\exp(S_D T) - 0.008 \frac{T}{60}\right) + (4 - 3.5 \exp(S_D T)) \frac{UF}{W}$$
 (9)

eKt/V according to the rate-adjustment method<sup>42</sup> is predicted from the rate of dialysis (K/V) and spKt/V as:

$$eKt/V = spKt/V - \frac{0.6}{(T/60)} spKt/V + 0.03$$
 (10)

The rate-adjustment method predicts that urea rebound is related to the rate of dialysis or dialysis efficiency.<sup>17</sup>

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