Supplemental Materials

Calculations for the two formulations of stdKt/V_{urea}

Two values for the adequacy parameter standard Kt/V_{urea} (stdKt/V_{urea}) were obtained to assess differences in the weight assigned to residual function in assessing dialysis adequacy. adequacy.[1] The first of these is denominated the "2015 KDOQI stdKt/V_{urea}." It is the stdKt/V_{urea} value provided by Solute-Solver and incorporates the increased weight assigned to residual function in the 2015 guideline. The second of these is denominated the "Original stdKt/V_{urea}." This value represents the value for stdKt/V_{urea} originally defined by Gotch[2] and incorporated in the 2006 KDOQI Guideline.[3] The original definition of stdKt/V_{urea} required calculation of a theoretical continuous urea clearance which would result in a constant urea concentration equal to the average pre-treatment urea concentration achieved by dialysis for a given urea generation rate. A stdKt/V_{urea} was then calculated as the continuous clearance multiplied by 10,080 (the number of minutes in a week) divided by the volume of distribution for urea. For the present study, the Original stdKt/V_{urea} value was calculated from the 2015 KDOQI stdKt/V_{urea} using equations provided in the 2015 Update of the KDOQI Hemodialysis Guideline[4] and in Daugirdas et al.[5]:

$$\text{Original stdKt/V}_{urea} = \text{2015 KDOQI stdKt/V}_{urea} - \left(\frac{K_{ru} \cdot 10{,}080}{V_{urea}} \cdot \left(1 - \left(\frac{0.947}{spKt/V + 1.62} + 0.4 \right) \right) \right)$$

where K_{ru} is the residual urea clearance and V_{urea} and spKt/V are the values for urea's volume of distribution and the single pool Kt/V_{urea} provided by Solute-Solver.

Values for the 2015 KDOQI stdKt/V_{urea} were similar in the two groups (2X: 2.53±0.53 vs. 3X: 2.41±0.14). Values for Original stdKt/V_{urea} which provides a measure of the combined dialytic and residual clearance required to achieve the same pre-treatment values for plasma urea concentration were also similar in the two groups (2X: 2.25±0.39 vs. 3X: 2.41±0.14). In the

2X weekly patients, however, the 2015 KDOQI stdKt/V_{urea} values were significantly higher than the Original stdKt/V_{urea} values (2.53±0.53 vs. 2.25±0.39, $p<0.01$), reflecting the increased weight given to residual clearance in the 2015 update of the guidelines.

Differences in time required to provide adequacy twice weekly treatment using the two formulations of stdKt/V_{urea}

The treatment times required for each of two weekly sessions to achieve a stdKt/V_{urea} of 2.2 using the 2015 KDOQI and Original formulations of stdKt/V_{urea} were obtained by modeling and illustrated in Supplemental Figure 1. Model inputs were the dialytic clearance, generation rate, two-compartment volume of distribution, and inter-compartmental clearance values for urea and the treatment time and daily fluid gain. From these inputs, the model first calculated the stdKt/V_{urea} achieved in a patient on a 3X weekly regimen with no residual function. The model then calculated the treatment times required in a 2X weekly regimen as a function of K_{ru} to provide the same stdKt/V_{urea}. Values for the input parameters used to make the figure are provided in its legend.

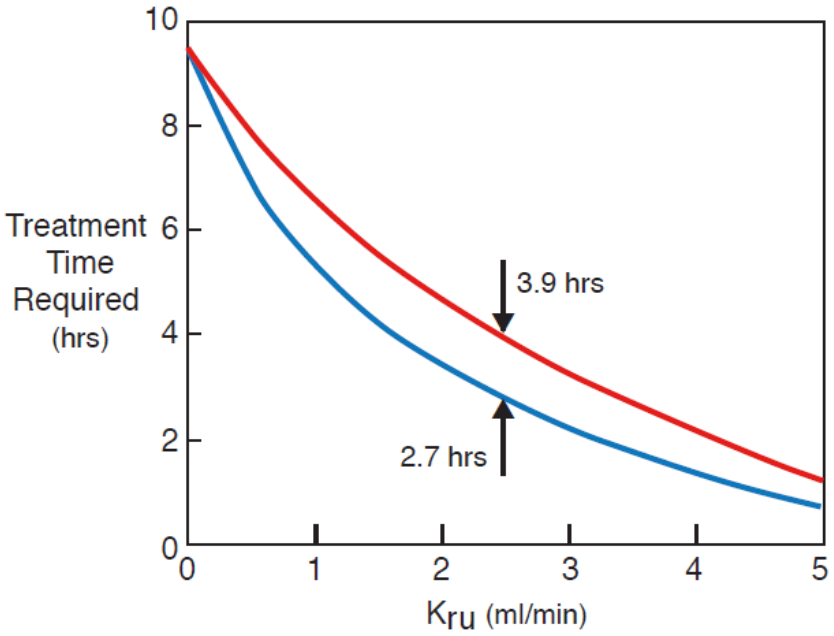
Supplemental Table 1

Solute Clearances Relative to the Glomerular Filtration Rate

	2X Weekly				Controls (n=9, fasting)	
	$K_{r,total}$ (ml/min)	$K_{r,total}$ / rGFR	$K_{r,free}$ (ml/min)	$K_{r,free}$ / rGFR	$K_{r,total}$ / eGFR	$K_{r,free}$ / eGFR
Urea	2.8 ± 1.5	0.75 ± 0.14	-	-	0.65 ± 0.14	-
HIPP	14 ± 8	5.2 ± 3.4	54 ± 52	13 ± 8	4.5 ± 0.7	17 ± 5
PAG	9.6 ± 8.0	2.9 ± 1.7	13 ± 12	3.2 ± 1.7[a]	3.6 ± 0.6	4.9 ± 1.3
IS	1.7 ± 1.4	0.45 ± 0.26	37 ± 45	9.0 ± 6.4[a]	0.54 ± 0.16	26 ± 10
PCS	0.71 ± 0.58	0.19 ± 0.09	18 ± 20	2.1 ± 1.6[a]	0.22 ± 0.08	13 ± 5

HIPP, hippurate; PAG, phenylacetylglutamine; IS, indoxyl sulfate; PCS, p-cresol sulfate. $K_{r,total}$, residual solute clearance calculated using the total plasma solute concentration; rGFR, estimated residual glomerular filtration rate calculated as the mean of the residual urea and creatinine clearances; $Kr_{,free}$, residual solute clearance calculated using the plasma free solute concentration; eGFR, estimated glomerular filtration rate calculated using the CKD-Epi formula. The control group included 9 subjects with normal renal function (CKD-Epi eGFR 107±14 ml/min/1.73m^2; creatinine clearance 148±35 ml/min/1.73m^2) who provided a 3-hour urine collection and a blood sample following an overnight fast for a previously published study.[6] Creatinine was measured using HPLC as previously described by Yue-dong[7] in the 2X Weekly patients and by the clinical laboratory for the Controls. In the 2X weekly group, the $K_{r,total}$ could not be calculated for HIPP in two patients and for PAG in one patient because post-treatment plasma concentrations fell below assay range. In the control group, the $K_{r,free}$ could not be calculated for PCS in one subject and for HIPP in one subject because the plasma free concentrations fell below the assay range and the $K_{r,total}$ could not be calculated for HIPP in one subject because the total plasma concentration fell below assay range.

[a] $p < 0.05$, values in the 2X patients versus corresponding values in the controls.



Supplemental Figure 1. Treatment time required per session of a 2X weekly regimen as a function of K_{ru} to achieve the stdKt/V_{urea} 2.2 using the 2015 KDOQI and the Original formulations of stdKt/V_{urea}. The treatment times required per session for a 2X weekly hemodialysis regimen to provide a stdKt/V_{urea} of 2.2 are plotted as a function of the residual kidney urea clearance K_{ru}. The blue line depicts treatment times required by the formulation of stdKt/V_{urea} included in the 2015 Update of the KDOQI Guideline for Hemodialysis Adequacy.[4] The red line depicts the treatment times required to provide the same stdKt/V_{urea} using the original formulation of stdKt/V_{urea} as described by Gotch[2] which requires that the same average pretreatment urea concentration be achieved at each level of Kru. The figure depicts treatment times required for a hypothetical patient with a two-compartment urea volume of distribution of 30 liters, an inter-compartmental urea clearance of 482 ml/min, a fluid gain of 1 liter/day removed by dialysis, and dialysis treatment providing a urea clearance of 247 ml/min. These values are the average values for the 2X weekly patients in the current study. The urea clearance was not adjusted for differences in the ultrafiltration rate. The solid arrows mark the treatment times required for a 2X weekly regimen with K_{ru} 2.5 ml/min using the 2015 KDOQI

stdKt/V_{urea} (2.7 hours) and the Original stdKt/V_{urea} (3.9 hours). The fractional reduction in time by the 2015 KDOQI Guideline is similar across a range of values for the dialytic clearance and volume of distribution of urea.

Supplemental Material References

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