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ORIGINAL ARTICLE

Residual renal function in incremental haemodialysis

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ABSTRACT

Background. Equivalent renal clearance (EKR) and standard clearance (stdK) are continuous-equivalent measures of urea clearance and include residual renal function (RRF), if calculated appropriately. RRF is qualitatively better than dialysis with equivalent urea clearance. Instructions for calculating stdKt/V (stdK scaled by urea distribution volume) and its target value (2.3) are presented in the Kidney Disease Outcomes Quality Initiative (KDOQI) 2015 guidelines. EKR targets have not been defined in the current guidelines.

Methods. The stdKt/V in the presence of RRF was calculated with the classic double-pool urea kinetic model and with the Daugirdas modification, which accentuates the renal contribution. The EKR/V (EKR scaled by urea distribution volume) was calculated with nominal and adjusted renal clearance (renal urea clearance multiplied by a weighting factor). New prescriptions with different continuous clearance targets were generated by a computer program.

Results. The contribution of RRF can be weighted flexibly in EKR/V by adjusting the renal clearance value. A new therapeutic index, EKR/V_a (adjusted total EKR/V), was introduced. In 62 incremental dialysis sessions of 16 patients with a renal urea clearance (K_r) of over 1 mL/min, the Daugirdas stdKt/V was, on average, 7.5% higher than classic stdK/V and adjusted EKR/V was 14.4% higher than unadjusted EKR/V.

Conclusions. The stdKt/V is not an optimal descriptor of haemodialysis urea clearance. With EKR/V, the role of RRF can be evaluated more sensibly. Using adjusted EKR/V as the target permits less frequent incremental dialysis.

Keywords: equivalent continuous clearance, incremental haemodialysis, residual renal function, stdKt/V, urea kinetics

INTRODUCTION

Guidelines for intermittent haemodialysis dosing are based on urea kinetics [1, 2]. Different dialysis schedules can be compared using the continuous-equivalent urea clearances—standard urea clearance (stdK) and equivalent renal urea clearance (EKR), commonly scaled by the urea distribution volume (*V*):

$$\mathrm{stdK/V = G/PAC/V} \tag{1}$$

$$\mathrm{EKR/V = G/TAC/V} \tag{2}$$

The most convenient unit for stdK/V and EKR/V is per week. The dimensionless variable stdKt/V = weekly stdK/V. *G*, *V*, the predialysis concentration (PAC) and the time-averaged concentration (TAC) are derived from the double-pool urea kinetic model (UKM), which includes the renal urea clearance. EKR/V is always greater than stdK/V. Current European and American guidelines have no recommendations on the EKR.

Residual renal function (RRF) is qualitatively better than dialysis with equal urea clearance. The clinical significance of RRF can be expressed in different ways. In the new Solute Solver 'What if' module (version 1.17, 9 June 2017), Daugirdas has adopted a new method to calculate stdKt/V_{urea} in incremental haemodialysis [3]. This method has been used also in the original Solute Solver since 15 December 2015 (e.g. version 2.08, 17 October 2017) [4]. The fractional renal urea clearance K_{rf} is added

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to dialysis stdKt/V_d, which results in a higher total stdKt/V than modelling with K_r. The classic method has been used in earlier versions of the Solute Solver (e.g. version 1.97, 2 July 2010). The background of the new approach has been described by Daugirdas *et al.* [5–7] and it has been incorporated into the Kidney Disease Outcomes Quality Initiative (KDOQI) 2015 guidelines [2] with a target value of 2.3.

The new method has been used in the Frequent Hemodialysis Network (FHN) trials [8, 9] and also by Casino and Basile [10], who have suggested adjusting the target as an alternative to modifying the measuring method. They propose that an EKR_{c35} of 12 mL/min/35 L (EKR/V=3.46/week) is an adequate continuous-equivalent dialysis urea clearance in anuric patients and that no dialysis is needed with a K_r of 6 mL/min/35 L (K_{rf} 1.73/week).

Casino and Basile [10] obviously mean that total EKR/V should be equal to the adjusted target [Equations (4) and (8); for an explanation of the variables, see Abbreviations and variables in Appendix]. So K_r is weighted by a factor of 2 compared with dialysis:

$$\text{Adjusted target} = \text{target } EKR_{c35} - K_{rc35} \tag{3}$$

$$EKR_{dc35} + K_{rc35} = \text{adjusted target} \tag{4}$$

$$EKR_{dc35} = \text{adjusted target } EKR_{c35} - 2 * K_{rc35} \tag{5}$$

$$\text{Adjusted target} = EKR_{dc35} + 2 * K_{rc35} \tag{6}$$

In EKR/V units,

$$\text{Adjusted target} = \text{target EKR/V} - K_{rf} \tag{7}$$

$$EKR/V_d + K_{rf} = \text{adjusted target} \tag{8}$$

$$EKR/V_d = \text{adjusted target} - 2 * K_{rf} \tag{9}$$

$$\text{Adjusted target} = EKR/V_d + 2 * K_{rf} \tag{10}$$

The aim of this study is to compare, by computer simulations, different methods of assessing the contribution of renal urea clearance to total continuous-equivalent urea clearance.

MATERIALS AND METHODS

Patients

A study based on the same group of 33 patients with 205 dialysis sessions was published previously [11]. Five of the sessions, in which all targets could not be achieved (due to a Q_b lower limit of 50 mL/min), were excluded from this study.

Computations

If t_d, K_d, K_r, UF, V, G and the schedule or frequency are known, the resulting average PAC, dialysis time TAC_d, interval time TAC_i, whole-cycle TAC_c, EKR/V and stdK/V can be computed. Dialyser *in vivo* K_0A can be calculated from Q_b, Q_d and the online ionic dialysance using the Michaels equation.

Tables 1 and 2 present the treatment data of a fictitious patient. The numbers in the 'Classic' and 'Without RRF' columns were computed with a program adapted from the Solute Solver 'What if' module using the same Runge–Kutta procedure [4], but with a symmetric schedule and the classic stdK/V calculation method including K_d and K_r.

A total of 200 new prescriptions, fulfilling a set of limits and targets, were generated automatically with an optimizing program. G and V were computed from the actual modelling sessions with a double-pool UKM program adapted from the Solute Solver, with three plasma urea samples, interdialysis urine collection and K_d from ionic dialysance. Q_b, Q_d and t_d were computed by numeric solution of the UKM equations. The program begins with minimum fr, t_d, Q_b and Q_d, preferentially increases Q_b and t_d and only increases the frequency as a last option.

In this material, the stdK/V target of 2.30/week corresponded to an average EKR/V value of 3.23/week and the EKR/V target of 3.20/week to an average stdK/V value of 2.21/week. A stdK/V value of 2.20/week and an EKR/V value of 3.20/week were chosen as optimization targets in the present study. All limits and targets used in generating the optimized prescriptions are listed in Table 3. In this study, clearances are water values, in the earlier work plasma values [11].

For incremental dialysis, the K_r adjusting coefficient (AC) and adjusted total EKR/V (EKR/V_a) are defined. If the RRF is believed to be qualitatively better than dialysis with equal urea clearance, a value >1 is given to the coefficient. Casino and Basile suggested a new EKR/V target (Equation 25) and a new variable Adjusted EKR/V (Equation 26):

$$\text{New EKR/V target} = \text{minimum EKR/V} - (AC - 1) * K_{rf} \tag{25}$$

$$\text{Adjusted EKR/V} = \text{modelled EKR/V} + (AC - 1) * K_{rf} \tag{26}$$

It turned out that Equation (24) resulted in values equal to those obtained with the combination of Equations (25) and (26), which may be obvious also from Equation (10). Equation (24) is easier to understand than the original Casino and Basile target-adjusting method and analogous to Daugirdas's stdKt/V from Equation (19). EKR/V_d was calculated according to Equations (11), (20) and (21). EKR/V_a is compared to the EKR/V target and is a therapeutic index, not a formally correct urea clearance measure.

The HDOptimizer demonstration program (http://www.verkkomunuainen.net/optimize.html) automatically generates haemodialysis prescriptions that fulfil 12 limits and targets. It is not intended to be used to treat patients, only to demonstrate the principles.

RESULTS

Actual dialysis sessions

Table 4 describes the actual dialysis sessions with substantial RRF and demonstrates the effects of K_r adjusting and the Daugirdas' method on the ECC values.

Daugirdas's stdK/V

The example in Table 1 clarifies the calculations. The input parameters are arbitrary, except the renal fractional clearance K_{rf} calculated from the renal clearance K_r and the distribution volume V [Equation (14)].

The total urea removal rate calculated from the input values of K_d and K_r equals the modelled generation rate G. In the 'Without RRF' columns are presented the treatment times required to achieve ECC values equal to those with RRF. With the conventional three times per week schedule without RRF, ECC values are within the guidelines' lower limits but are increased by RRF to a level difficult to achieve without RRF.

In Table 1 (with quite high K_r), Daugirdas's stdKt/V with RRF (in the second 'Daugirdas' column) is 12.5% higher than the modelled classic one (3.25 versus 2.89). The difference between

Table 1. An example of ECC calculation

	Classic		Daugirdas		Without RRF		
Input parameters							
Treatment frequency or schedule, per week	3.0	3.0	135[a]	135[a]	3.0	3.0	3.0
Treatment time, min	240	240	240	240	**612**	**451**	**340**
Dialyser clearance, mL/min	200	200	200	200	200	200	200
Renal clearance, mL/min	0.0	**4.0**	0.0	**4.0**	0.0	0.0	0.0
Renal fractional clearance, per week	0.00	1.12	0.00	1.12	0.0	0.0	0.0
Ultrafiltration, L	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Distribution volume, L	36.0	36.0	36.0	36.0	36.0	36.0	36.0
Generation rate, μmol/min	200	200	200	200	200	200	200
Output parameters							
nPCR, g/kg/day	1.01	1.01	1.01	1.01	1.01	1.01	1.01
PAC, mmol/L	26.3	19.3	23.4	17.1	17.2	19.3	21.9
TAC_c, mmol/L	17.5	13.2	17.7	13.4	8.9	10.8	13.2
TAC_d, mmol/L	14.0	10.3			5.5	7.5	9.9
TAC_i, mmol/L	17.8	13.4			9.6	11.3	13.6
Average removal rate by kidneys, μmol/min	0.0	52.9			0.0	0.0	0.0
Average removal rate by dialysis, μmol/min	199.9	147.1			200.0	200.0	200.0
Average total removal rate (sum), μmol/min	199.9	200.0			200.0	200.0	200.0
Renal contribution to urea removal, %	0.0	26.5			0.0	0.0	0.0
EKR, mL/min	11.4	15.1	11.3	15.0	22.5	18.5	15.1
EKR/V, per week	3.21	**4.25**	3.16	4.19	6.32	5.20	**4.25**
EKR/V_d, per week	3.20	3.12			6.31	5.18	4.23
EKR/V_r, per week	0.00	1.12			0.00	0.00	0.00
EKR/V_t (sum), per week	3.20	4.24			6.31	5.18	4.23
Renal contribution to EKR/V, %	0.0	26.5			0.0	0.0	0.0
stdK, mL/min	7.6	10.3	7.6	11.6	11.6	10.3	9.1
stdK/V, per week	2.12	**2.89**	2.13	**3.25**	**3.25**	**2.89**	2.55
$stdK/V_d$, per week	2.12	2.13	2.13	2.13	3.25	2.89	2.55
$stdK/V_r$, per week	0.00	0.77			0.00	0.00	0.00
$stdK/V_t$ (sum), per week	2.12	2.90			3.25	2.89	2.55
Renal contribution to stdK/V, %	0.0	26.5			0.0	0.0	0.0

[a]Mon-Wed-Fri schedule with blood samples drawn on Wednesday. Compare especially the bold numbers.

the classic and Daugirdas's stdK/V is observed only in sessions with RRF.

Adjusted EKR/V

Table 2 shows an example of EKR/V calculations with AC of 2.0. The EKR/V_a target can be achieved with two sessions per week. TAC, PAC and renal contribution are higher than without K_r adjusting.

The AC has no effect if its value is 1 or if $K_r = 0$. It affects only EKR/V_a, not Daugirdas's stdK/V. In incremental dialysis, EKR/V_a can be used as the main target to produce schedules resembling those used by Casino and Basile; stdK/V can be disregarded by setting a low minimum total stdK/V in the program. Emphasizing the clinical value of RRF by using an AC >1 inevitably increases urea concentrations (Table 5). The correct value of the AC is not known. It could, of course, be used also in modifying Daugirdas's stdK/V.

The competition between the kidneys and dialysis for blood urea can be seen in Table 2; urea removal by the kidneys increases when the dialysis time or frequency decrease. With adjusted K_r, the concentrations are considerably higher, close to those without RRF, and unadjusted total EKR/V is lower.

Comparison of the methods

In Daugirdas's stdK/V, 100% of K_{rf} is added to the modelled (compressed) dialysis stdK/V [Equation (19)], whereas in the Casino and Basile method, the weighted K_{rf} is added to the modelled dialysis EKR/V [Equation (24)]. In the original Casino and Basile approach, the therapeutic value of renal function is assumed to be exactly 2-fold compared to haemodialysis with equal urea clearance. Figure 1 shows the correlation between the results by the two methods.

In actual sessions with $K_r > 1$ mL/min, using an AC of 2.0 resulted in 14.4% higher EKR/V than without adjusting and 7.5% higher stdKt/V with the Daugirdas method compared with the classic stdK/V (Table 4). The patients were seemingly 'overdialysed' according to the current guidelines.

Tables 5 and 6 present data from optimized prescriptions. Optimizing with unadjusted EKR/V of 3.20/week as the only target in incremental dialysis results in higher clearances and lower concentrations, with lower resource consumption (time and frequency), than using classic stdK/V of 2.20/week (Table 5). With adjusted EKR/V as the only target, all values show a lower dialysis dose and higher weight given to RRF, compared with Daugirdas's stdKt/V.

Tables 5 and 6 show that optimizing with an adjusted EKR/V target of 3.20/week allows lower weekly treatment times and frequencies than Daugirdas's stdKt/V of 2.20. Casino and Basile have applied successfully once-per-week incremental dialysis. Their method with a K_r adjusting coefficient of 2.0 used in this study gives more weight to RRF and results in lower consumption of dialysis resources compared with the Daugirdas stdKt/V method.

Table 2. An example of adjusting EKR/V with a K_r adjusting coefficient of 2.0

	With nominal K_r		With adjusted K_r	
Input parameters				
Treatment frequency, per week	3.0	3.0	**3.0**	**2.0**
Treatment time, min	240	240	**145**	**237**
Dialyser clearance, mL/min	200	200	200	200
Renal clearance, mL/min	0.0	**4.0**	**4.0**	**4.0**
Renal fractional clearance, per week	0.00	1.12	1.12	1.12
Ultrafiltration, L	0.1	0.1	0.1	0.1
Distribution volume, L	36.0	36.0	36.0	36.0
Generation rate, μmol/min	200	200	200	200
K_r adjusting coefficient	**1.0**	**1.0**	**2.0**	**2.0**
Output parameters				
nPCR, g/kg/day	1.01	1.01	1.01	1.01
PAC, mmol/L	26.3	19.3	23.3	25.8
TAC_c, mmol/L	17.5	13.2	17.9	17.9
TAC_d, mmol/L	14.0	10.3	14.9	13.7
TAC_i, mmol/L	17.8	13.4	18.1	18.1
Average removal rate by kidneys, μmol/min	0.0	52.9	71.6	71.5
Average removal rate by dialysis, μmol/min	199.9	147.1	128.3	128.4
Average total removal rate (sum), μmol/min	199.9	200.0	199.9	199.9
Renal contribution to urea removal, %	0.0	26.5	35.8	35.8
EKR, mL/min	11.4	15.1	11.2	11.2
EKR/V, per week	3.21	**4.25**	3.14	3.14
EKR/V_d, per week	3.20	3.12	2.01	2.01
EKR/V_r, per week	0.00	1.12	1.12	1.12
EKR/V_t (sum), per week	3.20	4.24	3.13	3.13
Renal contribution to EKR/V, %	0.0	26.4	35.8	35.8
Adjusted EKR/V, per week	3.20	5.36	**4.25**	**4.25**
stdK/V, per week	2.12	2.89	2.40	2.17
$stdK/V_d$, per week	2.12	2.13	1.54	1.39
$stdK/V_r$, per week	0.00	0.77	0.86	0.78
$stdK/V_t$ (sum), per week	2.12	2.90	2.40	2.17
Renal contribution to stdK/V, %	0.0	26.5	35.8	35.9
Daugirdas's stdK/V, per week	2.12	3.25	2.66	2.51

Compare especially the bold numbers.

Table 3. Limits and targets for optimized prescriptions

	Minimum	Maximum
fr, per week	1	7
t_d, min	240	300
Q_b, mL/min	50	300
Q_d, mL/min	300	800
K_0A, mL/min	800	800
stdK/V, per week	2.20	
EKR/V, per week	3.20	
PAC, mmol/L		30.0
TAC, mmol/L		20.0

In the optimization program, all limits and targets, except minimum blood flow, can be set freely.

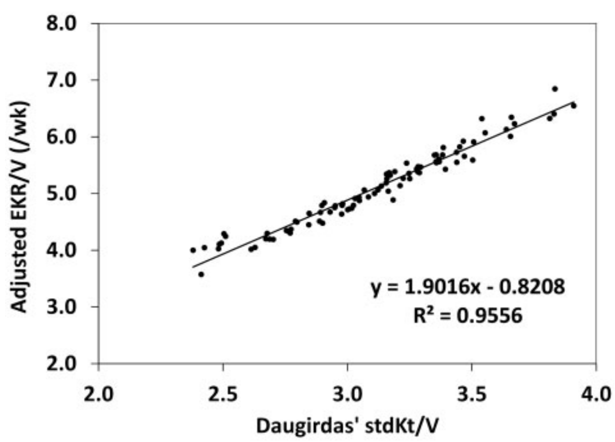

FIGURE 1: Correlation of Daugirdas's modified total stdKt/V and adjusted (with K_r adjusting coefficient of 2.0) total EKR/V in 89 actual haemodialysis sessions with RRF.

Figure 2, based on Equations (11) and (12), shows that the renal contribution to total urea removal can be >50% when an adjusted EKR/V of 3.20/week is used as the target in incremental dialysis. A Daugirdas stdK/V of 2.20/week gives slightly less value to RRF.

These results are based on computer simulations, not on empirical measurements from patients. In the simulations, the 'patients' are 'dialysed' optimally with an *in vivo* K_0A of 800 mL/min to exact targets.

DISCUSSION

The equation stdK = G/PAC [5, 12, 13] is a conventional clearance equation and its units may be, for example, mL/s, mL/min, L/h or L/wk. When G/PAC is divided by V, we get G/PAC/V = stdK/V [Equation (1)]. Where does 't' come from? The most convenient unit of stdK/V and EKR/V is per week. There exist in the literature several variations of the term 'stdKt/V'. Sometimes stdKt/V has been confused with session Kt/V or weekly Kt/V, as in the abstract of reference [8]. EKR/V or EKRt/V have not been widely used in the literature, therefore we have an opportunity to select the correct term and unit. For comparison with EKR/V, the other variable should have the same format. Here, stdK/V and stdKt/V are used as synonyms.

The differences in concentrations between the 'Classic' and 'Daugirdas' columns in Table 1 are due mainly to differences between the 'frequency' and 'schedule' input modes. The small differences in the third or fourth number of corresponding values are caused by inaccuracy of the multiple sequential iterations in their computation.

Table 4. Average values of actual dialysis sessions where K_r is >1.0 mL/min

Patients	16
Sessions	62
	Mean (SD)
Renal urea clearance, mL/min	2.2 (0.9)
Urea distribution volume, L	34.9 (6.6)
Urea generation rate, μmol/min	202 (69)
Treatment frequency, per week	2.94 (0.27)
Treatment time, min	300 (62)
Total dialyser clearance, mL/min	205 (15)
Ultrafiltration, L	2.6 (1.2)
Classic EKR/V, per week	4.59 (0.66)
Adjusted EKR/V[a], per week	5.23 (0.70)
Difference, %	14.4 (5.7)
Classic stdK/V, per week	2.97 (0.33)
Daugirdas's stdK/V, per week	3.19 (0.36)
Difference, %	7.5 (2.5)

[a]With K_r adjusting coefficient of 2.0.

In pursuing a universal equivalent continuous clearance, PAC was used as the denominator in stdKt/V, instead of the formally more correct TAC_c, to get values close to those in continuous ambulatory peritoneal dialysis (CAPD) [6, 12, 14]. stdK/V is related to the peak concentration hypothesis [15]. In the classic stdK/V, compression of K_r (as well as K_d) is due mainly to the 'wrong' denominator, but the calculation method—subtracting ECC values computed with $K_r = 0$ from corresponding total values—causes 'compression' of K_r also in EKR/V. In this article and in the HDOptimizer program, the dialysis contribution to stdK/V and EKR/V is calculated by Equations (11), (16), (20) and (21). EKR is usually lower in CAPD than in intermittent haemodialysis.

The original Gotch [13] and Leypoldt [16, 17] equations do not include RRF. The idea of adding uncompressed K_{rf} to compressed stdK/V_d to emphasize the clinical significance of RRF is formally questionable.

G/PAC/V (stdK/V) and G/TAC_c/V (EKR/V) are different descriptors of dialysis dosing, each with its own individual characteristics, value ranges and targets [18]. stdK/V is more sensitive to RRF [19] and treatment frequency [20] than EKR/V, but less sensitive to poor spacing (asymmetry of the schedule) [21]. In the example in Table 1, without RRF, 372 min (6.2 h; 155%) longer treatment time is required to achieve equal stdK/V as with RRF when using the Daugirdas calculation and 212 min (3.5 h; 88%) longer with classic stdK/V, but only 100 min (1.7 h; 42%) longer to control EKR/V. The essential questions are how to weight RRF and which of the following is more important in terms of outcome—PAC or TAC, peak or average concentration. It was

Table 5. Average values of optimized prescriptions with four different targets in 62 sessions where K_r is >1 mL/min (mean 2.2 mL/min, mean fractional clearance 0.64/week)

Target	Classic EKR/V, 3.20/week	Adjusted[a] EKR/V, 3.20/week	Classic stdK/V, 2.20/week	Daugirdas's stdK/V, 2.20/week
Dialysis EKR/V, per week	2.56	1.92	2.47	2.15
Classic EKR/V, per week	**3.20**	2.56	3.11	2.79
Adjusted EKR/V[a], per week	3.84	**3.20**	3.75	3.43
Dialysis stdK/V, per week	1.78	1.41	1.74	1.56
Classic stdK/V, per week	2.22	1.89	**2.20**	2.03
Daugirdas's stdK/V, per week	2.42	2.05	2.38	**2.20**
TAC, mmol/L	16.7	21.0	17.2	19.2
PAC, mmol/L	24.0	28.4	24.2	26.3
Treatment time, h/week	9.7	8.5	10.1	9.3
Treatment frequency, per week	2.3	2.1	2.4	2.3

[a]With K_r adjustment coefficient of 2.0. Treatment time 240–300 min, blood flow 50–300 mL/min, dialysate flow 300–800 mL/min, dialyser *in vivo* K_0A 800 mL/min. In each target column, the other targets have been disregarded. Compare especially the bold values.

Table 6. Treatment frequency distribution of 200 optimized prescriptions with four different targets

Frequency, /week	Classic EKR/V, 3.20/week	Adjusted[a] EKR/V, 3.20/week	Classic stdKt/V, 2.20/week	Daugirdas's stdKt/V, 2.20/week
1.0		6		1
2.0	69	73	42	52
3.0	130	120	157	146
3.5	1	1	1	1

[a]With K_r adjustment coefficient 2.0. Treatment time 240–300 min, blood flow 50–300 mL/min, dialysate flow 300–800 mL/min, dialyser *in vivo* K_0A 800 mL/min. In each target column, the other targets have been disregarded.

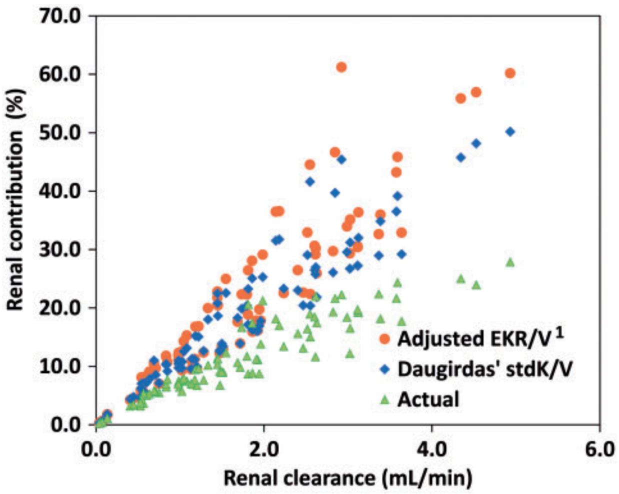

FIGURE 2: Renal contribution to total urea removal in 89 actual and simulated haemodialysis sessions with RRF. Adjusted EKR/V and Daugirdas's stdK/V values are from optimized prescriptions, with the corresponding parameter as the only target (3.20/week and 2.20/week, respectively). [1]With K_r adjusting coefficient 2.0.

recently shown in a small population that survival correlated significantly with EKR/V but not with stdK/V [22].

The KDOQI 2015 guidelines recommend the Daugirdas method to adjust stdKt/V upwards, but it is unclear by which method the target (2.3) has been determined. In the presence of RRF, stdKt/V values computed with the Daugirdas modification are not comparable to those from early versions of the Solute Solver. To avoid confusion, the new '100%' variable must not be called stdKt/V; it is a new index used in the FHN trials [8, 9], but probably with no impact on their results.

EKR/V_a is an index where the renal urea clearance can be weighted flexibly by the AC; the EKR/V target is held unchanged and is compared to EKR/V_a. In the Daugirdas method, K_{rf} is added to the modelled dialysis stdK/V_d [Equation (19)], whereas in the K_r adjusting method, K_{rf} is replaced in EKR/V_a by the adjusted K_{rf} [Equation (24)].

The stdK/V concept is distorted due to an attempt to combine CAPD, the peak concentration hypothesis and haemodialysis urea kinetics by using a wrong denominator. Differences between outcomes in CAPD and intermittent haemodialysis can be explained by factors other than urea clearance, for example, patient selection, intermittency of haemodialysis and differences in membrane permeability to uraemic toxins. The measuring method should not be modified with a view to obtaining the desired results.

In intermittent haemodialysis, treatment time and frequency, convection, fluid removal and RRF all affect the outcome, in addition to urea clearance. Haemodialysis dosing cannot be described by only one number. In the FHN trial [8], dialyser clearance was equal in both groups, but weekly treatment time and stdKt/V were significantly higher in the frequent haemodialysis group. Therefore it remains obscure whether the better outcome was due to higher frequency or longer weekly treatment time or higher urea clearance.

stdK/V and its modifications are calculated therapeutic or prognostic indexes, not measures of urea clearance. It is more appropriate to include K_r as clinically undervalued—but uncompressed in EKR/V—than to totally disregard it. If the goal is to reduce dialysis, adjusted EKR/V is more suitable for that purpose than Daugirdas's stdK/V. It will be harder to meet the Daugirdas stdKt/V target of 2.20/week than the adjusted EKR/V target of 3.20/week with once- or twice-weekly incremental dialysis. There are no empirical data to show how RRF should be weighted or what the effects of reducing the treatment intensity on outcomes in incremental dialysis are.

CONCLUSIONS

The relationships EKR/V = G/TAC/V and stdK/V = G/PAC/V hold, even in the presence of RRF, if K_r is appropriately included in the calculation of G and V. EKR/V is a formally correct physical measure of total urea clearance—one component of haemodialysis dosing—and not a prognostic index. The significance of RRF may be handled by adjusting the weight of renal clearance without changing the EKR/V target.

AUTHORS' CONTRIBUTIONS

A.V. is the only author and is responsible for the whole article.

CONFLICT OF INTEREST STATEMENT

None declared.

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Appendix

Abbreviations and variables

HD	haemodialysis
CAPD	continuous ambulatory peritoneal dialysis
KDOQI	Kidney Disease Outcomes Quality Initiative
ECC	equivalent continuous clearance
UKM	urea kinetic model
V	total postdialysis urea distribution volume (L)
G	urea generation rate (μmol/min)
fr	treatment frequency (sessions per week)
t_d	dialysis session duration (min)
t_i	interval time between sessions (min)
Q_b	blood flow (mL/min)
Q_d	dialysate flow (mL/min)
K_d	total dialyser urea clearance (mL/min)
K_r	renal urea clearance (mL/min)
K_{rc35}	renal urea clearance normalized to 35 L body water (mL/min/35 L)
K_{rf}	renal fractional urea clearance (/wk)
E_d	average urea removal rate by dialysis (μmol/min)
E_r	average urea removal rate by the kidneys (μmol/min)
E_t	average total urea removal rate (μmol/min)
TAC_d	time-averaged plasma water urea concentration during dialysis (mmol/L)
TAC_i	time-averaged plasma water urea concentration during the interval (mmol/L)
TAC_c	time-averaged plasma water urea concentration of the whole dialysis cycle (mmol/L)
PAC	average predialysis plasma water urea concentration (mmol/L)
stdK	standard urea clearance (mL/min)
$stdK/V_t$	total stdK/V (/wk)
$stdK/V_d$	dialysis contribution to $stdK/V_t$ (/wk)
stdK/Vr	renal contribution to stdK/Vt (/wk)
$stdKt/V_{Dau}$	Daugirdas' total stdKt/V
EKR	equivalent renal urea clearance (mL/min)
EKR_c	normalized EKR (mL/min/35 L or mL/min/40 L)
EKR_d	dialysis EKR (mL/min)
EKR_{c35}	EKR normalized to 35 L urea distribution volume (mL/min/35 L)
EKR_{dc35}	dialysis EKRc35 (mL/min/35 L)
EKR/V_t	total EKR/V (/wk)
EKR/V_d	dialysis contribution to EKR/V_t (/wk)
EKR/V_r	renal contribution to EKR/V_t (/wk)
EKR/V_a	adjusted total EKR/V (/wk)
K_0A	dialyser mass-area coefficient (mL/min)
AC	K_r Adjusting Coefficient

Equations

$$E_d = K_d * TAC_d * t_d * fr/10080 \quad (11)$$

$$E_r = K_r * TAC_c \quad (12)$$

$$E_t = E_d + E_r \quad (13)$$

$$K_{rf} = K_r/V/1000 * 10080 \quad (14)$$

$$TAC_c = (t_d * TAC_d + t_i * TAC_i)/(t_d + t_i) \quad (15)$$

$$stdK/V_d = E_d/PAC/V/1000 * 10080 \quad (16)$$

$$stdK/V_r = E_r/PAC/V/1000 * 10080 \quad (17)$$

$$stdK/V_t = stdK/V_d + stdK/V_r \quad (18)$$

$$stdK/V_{Dau} = stdK/V_d + K_{rf} \quad (19)$$

$$EKR_d = E_d/TAC_c \quad (20)$$

$$EKR/V_d = EKR_d/V/1000 * 10080 \quad (21)$$

$$EKR/V_r = K_{rf} \quad (22)$$

$$EKR/V_t = EKR/V_d + K_{rf} \quad (23)$$

$$EKR/V_a = EKR/V_d + AC * K_{rf,} \quad (24)$$

One week is 10080 minutes. TAC_d and TAC_i are derived from the double-pool concentration profile. In metabolic equilibrium, the average generation rate $G = E_t$.