- 24. Sacks HS, Fain JN. Human epicardial adipose tissue: a review. Am Heart J 2007; 153: 907–917
- 25. Stenvinkel P, Heimburger O, Paultre F *et al.* Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney Int 1999; 55: 1899–1911
- Dey D, Nakazato R, Li D *et al*. Epicardial and thoracic fat—noninvasive measurement and clinical implications. Cardiovas Diagn Ther 2012; 2: 85–93
- 27. Nakazato R, Rajani R, Cheng VY *et al.* Weight change modulates epicardial fat burden: a 4-year serial study with non-contrast computed tomography. Atherosclerosis 2012; 220: 139–144
- 28. Alexopoulos N, Melek BH, Arepalli CD *et al.* Effect of intensive versus moderate lipid-lowering therapy on epicardial adipose tissue in hyperlipidemic postmenopausal women: a substudy of the BELLES (Beyond Endorsed Lipid Lowering with EBT Scanning) trial. J Am Coll Cardiol 2013; 61: 1956–1961
- 29. Wu YW, Kao HL, Huang CL et al. The effects of 3-month atorvastatin therapy on arterial inflammation, calcification,

abdominal adipose tissue and circulating biomarkers. Eur J Nucl Med Mol Imaging 2012; 39: 399–407

- 30. Abe M, Matsuda M, Kobayashi H *et al.* Effects of statins on adipose tissue inflammation: their inhibitory effect on MyD88independent IRF3/IFN-beta pathway in macrophages. Arterioscler Thromb Vasc Biol 2008; 28: 871–877
- Dong L, Kerwin WS, Chen H *et al.* Carotid artery atherosclerosis: effect of intensive lipid therapy on the *vasa vasorum*—evaluation by using dynamic contrast-enhanced MR imaging. Radiology 2011; 260: 224–231
- 32. Baigent C, Landray MJ, Reith C *et al*. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet 2011; 377: 2181–2192

Received for publication: 1.3.2013; Accepted in revised form: 29.4.2013

Nephrol Dial Transplant (2013) 28: 2595–2603 doi: 10.1093/ndt/gft255

Impact of targeting *K*t instead of *K*t/*V*

Francisco Maduell¹, Rosa Ramos², Inés Palomares², Alejandro Martín-Malo³, Manolo Molina⁴, Jesús Bustamante⁵, Rafael Pérez-García⁶, Aileen Grassmann⁷ and José Ignacio Merello² on behalf of the ORD group

Correspondence and offprint requests to: Francisco Maduell; E-mail: fmaduell@clinic.ub.es

ABSTRACT

Background. Patients must receive an adequate dialysis dose in each hemodialysis (HD) session. Ionic dialysance (ID)

¹Department of Nephrology and Renal Transplantation, Hospital Clínic, University of Barcelona, Barcelona, Spain,
²NephroCare Medical Management, Fresenius Medical Care, Madrid, Spain,
³Nephrology Department, Hospital Universitario Reina Sofía, Córdoba, Spain,
⁴Nephrology Department, Hospital Universitario Santa Lucía. Cartagena, Murcia, Spain,
⁵Nephrology Department, Hospital Clínico Universitario de Valladolid, Valladolid, Spain,

⁶Nephrology Department, Hospital Universitario Infanta Leonor, Madrid, Spain and

⁷Medical Board EMEALA, Fresenius Medical Care, Waltham, MA, USA

Keywords: adequacy, dialysis dose, ionic dialysance, *K*t, online monitoring

enables the dialysis dose to be monitored in each session. The aim of this study was to compare the achievement of Kt versus eKt/V values and to analyse the main impediments to reaching the dialysis dose.

Methods. Of 5316 patients from 54 Fresenius Medical Care centers in Spain undergoing their usual HD regime, 3275 received ID and were included in the study.

Results. The minimum prescribed dose of eKt/V was reached in 91.2% of the patients, while the minimum recommended dose of *K*t was reached in only 66.8%. Patients not receiving the minimum *K*t dose were older, had spent 7 months less on dialysis, had a dialysis duration of 6 min less, had 5.7 kg more of body weight and Q_b was 47 mL/min lower. The target *K*t was not reached by 62% of patients with catheters and by 37% of women. With each quintile increase of body weight, eKt/Vdecreased and *K*t increased. Of patients with a body weight >80 kg, 1.4%, mostly men, reached the target *K*t but not prescribed eKt/V.

Conclusions. The impact of monitoring the dose with Kt instead of Kt/V is that identifies 25.8% of patients who did not reach the minimum Kt while achieving Kt/V. The main impediments to achieving an adequate dialysis dose were catheter use, female sex, advanced age, greater body weight, shorter dialysis time and lower Qb.

INTRODUCTION

ORIGINAL ARTICLE

Traditionally, dialysis dose recommendations are based on monthly analytical determinations, although these determinations are often carried out bimonthly or quarterly. The National Kidney Foundation's haemodialysis (HD) practice guidelines (DOQI) recommend a minimum Kt/V of 1.2 and/ or an urea reduction ratio (URR) of 65%. Multiple factors can influence the efficacy of each HD session and consequently, control systems have been created to quantify the dose received by the patient in each session and in real time. Currently, various monitoring systems have incorporated sensors, called online clearance monitoring (OCM) or Diascan, which noninvasively measures the effective ionic dialysance (ID), equivalent to urea clearance (K), by using the machine's own conductivity probes. These sensors enable the dialysis dose to be calculated without additional workload, analytical determinations or cost [1-3].

Systematic determination of K by ID multiplied by the duration of the HD treatment session (T_d or t) allows Kt to be obtained, a real measure of dialysis dose, expressed in liters. Kt offers the advantages that both K and t are real and are measured by the monitor. When Kt/V is used, V must be introduced and therefore, a value based on anthropometric formulas (age, gender, body weight and height) or other methods (bioimpedance) must be introduced, hampering evaluation and standardization of Kt/V [4, 5].

In 1999, Lowrie *et al.* [6] proposed *K*t as a marker of dialysis dose and mortality. These authors observed a *J*-shaped survival curve when they distributed the patients into quintiles from the smallest to the highest URR, while the curve descended with *K*t for the same patients [7]. A minimal effective *K*t of 40–45 L for women or 45–50 L for men was recommended. In 2005, the minimum *K*t dose was individualized according to the body surface area (BSA) [8] and was validated in a further study [9]. The ORD (Optimizing Results in Dialysis) Research initiative began in 2010 with the aim of improving HD patient outcomes by elucidating patient characteristics and practising care in Spain [10].

The aim of this study was to compare the achievement of a minimum target *K*t and $eKt/V \ge 1.2$, and to explore the factors influencing delivery of an adequate dialysis dose, based on a clinical database from the Spanish Fresenius Medical Care dialysis centers [11].

PATIENTS AND METHODS

In this cross-sectional study, the EuCliD database was analyzed and 54 FMC centers in Spain were included. Of 5316 patients, 3275 (61%) were receiving ID and were included in this study. We compiled all data during 1 month. We recorded their survival status (active, transplanted, transferred, death and others) 1 year later.

The patients were dialyzed with 4008S or 5008 (Fresenius) monitors, equipped with OCM sensors. This device noninvasively measures the effective ID, which is equivalent to urea clearance, using two conductivity probes. A mathematical model consisting of a quadratic equation with two unknown variables, applied to the two dialysate conductivity measures at the inlet and at the outlet of the dialyzer, identifies the effective ID corrected for ultrafiltration and vascular access recirculation.

The prescription of dialysis dose aimed to achieve a minimum Kt/V. In accordance with clinical guidelines [12–14], the minimum target of eKt/V was defined as \geq 1.2. eKt/V was calculated in the same month by routine mid-week blood analysis of pre- and post-dialysis urea, according to the two-compartment Daugirdas formula. We analyzed the extent to which the minimal individualized target Kt and the minimum target eKt/V were achieved.

The minimum target *K*t was calculated for each patient evaluating target *K*t values in terms of BSA based on the analysis of patient survival time tested before in previous studies to determine which best fit the empirical data. The best fit form was a simple algebraic expression that produces a curve increasing with the BSA, such that target *K*t increases more rapidly at low BSA than at high BSA. As a result of this curve, we obtained the *K*t target value from a formula that shows target *K*t in terms of the calculated BSA [8, 9]: minimum target *K*t in liters = 1/[0.0069 + (0.0237/BSA)], with BSA in m² = weight^{0.425} × height^{0.725} × 0.007184, with weight (post-dialysis dry body weight) in kilograms and height in centimeter. Dialysis dose prescriptions aimed to achieve a minimum *K*t/*V* although *K*t was retrospectively analyzed.

The *K*t (between 10 and 14 readings per patient) was assessed at each dialysis session for 1 month to calculate the monthly average received. Achievement of the individual minimum *K*t dialysis dose was defined as a mean delivered *K*t equal to or greater than this target *K*t.

The analysis was performed with the SPSS computer program, version 19. Qualitative variables are shown as percentages and quantitative variables as mean \pm standard

deviation. Student's *t*-test, the Mann–Whitney *U*-test or ANOVA were used to compare quantitative variables, in accordance with the categories and types of normal or nonparametric distribution. The chi-squared test was used for qualitative variables. A value of P < 0.05 was considered to be statistically significant. Multivariate logistic regression analysis was performed to identify factors predicting the achievement of the minimum target *K*t and/or *eKt/V*. Confidence intervals were calculated at 95%.

RESULTS

A total of 43584 ID sessions, 43% conventional HD and 57% online hemodiafiltration, were analyzed in the 3275 patients during the monitoring period. Blood samples for eKt/V analysis were obtained once during the study for each patient.

The mean age was 67.3 ± 15 years, the mean length of time on an HD program was 45.8 ± 41 months and 63% of all patients were male. The mean body height was 162.1 ± 10 cm, the mean BSA was 1.77 ± 0.27 m² and the mean anthropometric Watson volume was 35.5 ± 7.5 L, The etiology of chronic renal failure was diabetes mellitus in 18.7%, nephroangiosclerosis in 13.5%, glomerulonephritis in 10.5%, chronic tubulointerstitial nephropathy in 10.1%, polycystic kidney disease in 7.8%, systemic disease in 3.3%, urological causes in 1.5% and unknown in 34.5%. Each patient received the HD treatment with helixone filters (1.4–1.8 m²). T_d was 236 ± 15 min, blood flow rate (Qb) was 388 ± 40 mL/min, dialysate flow rate (Q_d) was 513 ± 10 mL/min, and body weight was 69.0 ± 15 kg. Vascular access was through an autologous arteriovenous fistula (AVF) in 2266 patients (69.2%), prosthetic arteriovenous fistula (PTFE) in 134 (4.1%) and venous central catheters (CVCs) in 875 (26.7%).

A mean eKt/V of 1.57 ± 0.32 was obtained. The minimum eKt/V target dose of 1.2, which was the initial prescription goal, was achieved in 91.2% of the patients (Figure 1).

When the minimum recommended *Kt* dialysis dose was 49.3 ± 4.06 L, the mean delivered *Kt* was 52.6 ± 8.80 L. The minimum *Kt* dose was achieved in 66.8% of the patients (Figure 1). The difference between the actual liters of *Kt* received and the minimum prescribed liters of *Kt* ranged from -39 to +30 liters, expressed in deciles (Figure 2).

The main differences in dialysis parameters between patients achieving and not achieving the minimum *K*t dose are shown in Table 1. The determining factors were older age, less time on the dialysis program, shorter sessions and lower Qb. Body weight was also a differentiating factor, with patients reaching target values having a mean of 67.1 ± 14 kg and patients not achieving these values having a mean of 72.8 ± 15 kg.







FIGURE 2: Differences between the *K*t administered and the minimum prescribed *K*t (distribution by deciles of liters of *K*t received; *n* = 3275).

	Kt achieved n = 2189 (66.8%)	<i>K</i> t not achieved <i>n</i> = 1086 (33.2%)	P-value
eKt/V	1.657 ± 0.30	1.399 ± 0.34	0.000
Kt target (L)	48.9 ± 4	50.3 ± 4	0.000
Kt (L)	56.8 ± 6	44.0 ± 7	0.000
Age (years)	66.6 ± 15	69.1 ± 13	0.000
Months in HD	48.2 ± 43	41.2 ± 37	0.000
$T_{\rm d}$ (min)	238.1 ± 10	231.8 ± 19	0.000
Q _b (mL/min)	405 ± 47	352 ± 83	0.000
Q _d (mL/min)	512 ± 62	514 ± 64	NS
Filter area (m ²)	1.43 ± 0.11	1.44 ± 0.13	0.007
K _O A urea (mL/min)	1002 ± 86	1011 ± 99	0.006
Post-HD weight (kg)	67.1 ± 14	72.8 ± 15	0.000
Height (cm)	162.2 ± 10	162.1 ± 10	NS
BSA (m ²)	1.75 ± 0.21	1.83 ± 0.21	0.006
Vol. Dist. Urea Watson (L)	35.05 ± 6.19	36.30 ± 6.35	NS

Table1. Differencesbetweenpatientsachieving or not Kt adjusted to the BSA

Analysis of body weight and division of the population into quintiles of body weight showed an inverse relation between eKt/V and body weight. However, this relation was direct between *K*t and body weight (Figure 3). The degree of eKt/V and *K*t achievement gradually reduced as body weight increased, the only exception being patients in the lowest quintile of body weight, who were less likely to achieve the minimum *K*t dose than were patients in the quintile immediately above.

The minimum *K*t dose was reached in fewer women (63%) than men (69%), even though the value was lower (45.58 ± 4.0 in women versus 50.37 ± 3.7 in men; P < 0.001). Table 2 examines gender differences for the prescribed dialysis parameters. Compared with men, women were older, had a shorter T_d , lower Q_b and Q_d , and had a lower body weight.

The type of vascular access had a clear influence on the dialysis dose. The minimum dose was less frequently achieved in patients dialyzed with a CVC (38%) than in those dialyzed with an AVF and PTFE (77%), even though the minimum

prescription of *K*t and the body weight were lower (Table 3). Patients with a CVC were older and had a lower Qb.

To analyze the discrepancies between eKt/V and Kt, we compared the 2142 (65.4%) patients who achieved both criteria with those who achieved only one of the criteria or neither of them (Table 4). In 845 patients (25.8%), the target eKt/V was achieved but not the target Kt. In these patients, body weight was significantly higher and Kt was lower. In this group, there was also a significantly higher percentage of women (45.6 versus 36%), T_d was 5 min shorter and Q_b was 49 mL/min lower. Catheter use was also significantly higher (48 versus 15%). After logistic regression and risk analysis in the groups of patients not achieving the minimum Kt, we observed that older age, higher body weight and catheter as vascular access represent a risk of not accomplishing the Kt target. In contrast, prolonging the length of the HD session increased the probability of reaching target Kt (Table 5).

Kt, but not eKt/V, was achieved in 47 patients (1.4%). Importantly, this small group mainly consisted of men (93.4%) with a higher body weight (increase of 19.2 kg). Compared with patients who achieved both criteria (Table 4), in this group, dialysis duration and Qb were similar, but Q_d was slightly higher. The percentage of patients with a CVC was only 8.5%. The logistic regression analysis showed that women achieved an eKt/V target value four times more than men. Higher body weight increases the risk of not raising eKt/V objectives. In contrast, longer dialysis time increased the probability of reaching the minimum eKt/V target (Table 5).

Neither eKt/V nor Kt was achieved in 7.35%. In this group, CVCs were used in more than half (57.7%), body weight was 11.6 kg higher, 24% were women and T_d and Q_b were lower (Table 4). Logistic regression showed that body weight reduced the possibility of reaching both eKt/V and Kt. Catheter use reduced the probability of reaching both eKt/V and Kt by 58%, while the dialysis duration improved the probability of reaching target levels% (Table 5).

Downloaded from https://academic.oup.com/ndt/article/28/10/2595/1808268 by Biblioteca Universitaria.Facultad de Medicina user on 13 December 202'

One year follow-up after the end of the study reveals 9% mortality in *K*t accomplishment patients versus 11% in eKt/V accomplishment patients, but we will need deeper survival analysis to relate morbidity and mortality to *K*t or eKt/V accomplishment.

DISCUSSION

This study describes the impact of the use of *K*t instead of *K*t/*V*. The differences in other methods lie in dose determination, expression of *K*t in liters and exhaustive monitoring of all dialysis sessions. Compared with the usual analytical recommendations for eKt/V, the greatest challenge is that a third of the patients did not achieve the minimum *K*t dose, while only 9% of patients failed to reach the target eKt/V. This study allowed us to analyze the characteristics of the patients not achieving the minimum target eKt/V or *K*t, or both, compared with those that reached both minimum dialysis doses. The determining factors for under-dialysis were CVC use, female sex and higher body weight. Individualizing the dialysis parameters (essentially T_d and Q_b) to the patient characteristics







FIGURE 3: Percentage of patients achieving *K*t or eKt/V target dose according to weight quintile n = 3275).

Table 2. Influence of gend	er over HD doses and dialysis	parameters	
	Men <i>n</i> = 2066 (63.1%)	Women <i>n</i> = 1209 (36.9%)	P-value
eKt/V target	1.2	1.2	
eKt/V achieved	1.50 ± 0.29	1.71 ± 0.01	0.000
% Pt. <i>eKtV</i> achieved	1149 (95%)	1838 (89%)	0.000
Kt target (L)	50.37 ± 3.71	45.58 ± 4.03	0.000
<i>K</i> t achieved (L)	53.98 ± 8.70	50.30 ± 8.43	0.000
% Pt. <i>K</i> t achieved	1422 (69%)	767 (63%)	0.001
Age (Years)	66.39 ± 15.02	69.02 ± 14.24	0.000
Months in HD	44.04 ± 39.36	49.08 ± 43.8	0.000
<i>T</i> _d (min)	237.61 ± 13.46	233.55 ± 14.48	0.002
Q_b (mL/min)	394.84 ± 71.93	376.35 ± 52.78	0.000
Q _d (mL/min)	516.28 67.95	506.98 46.29	0.000
Filter area (m ²)	1.44 ± 0.13	1.41 ± 0.076	0.000
K _O A urea (mL/min)	1015 ± 102	990 ± 62	0.000
Post-HD weight (kg)	71.83 ± 13.73	65.11 ± 14.55	0.000
Height (cm)	166.6 ± 9.0	154.5 ± 7.7	0.000
BSA (m ²)	1.83 ± 0.20	1.6 ± 0.21	0.000
Vol. Dist. Urea Watson (L)	38.39 ± 5.51	30.46 ± 3.91	0.000

(mainly gender, body weight and vascular access) is required to ensure the appropriate dialysis dose.

Current dialysis dose recommendations are based on monthly analytical determinations, although these determinations are often carried out bimonthly or quarterly. The National Kidney Foundation's HD practice guidelines (DOQI) recommend a minimum Kt/V of 1.2 and/or an URR of 65%. However, these guidelines recommend a Kt/V of 1.3 and a URR of 70% to ensure that these minimum requirements are reached [13]. The same recommendations can also

1.8

1.6

1.4

1.2

1

56

Table 3. Impact of vascula	ar access on dialysis dose and HD j	parameters	
	AVF or PTFE <i>n</i> = 2398 (73.3%)	Catheter <i>n</i> = 877 (26.7%)	P-value
eKt/V	1.60 ± 0.30	1.51 ± 0.38	0.000
<i>K</i> t target(L)	49.62 ± 4.01	48.56 ± 4.09	0.000
<i>K</i> t achieved (L)	54.92 ± 7.83	46.23 ± 8.07	0.000
% Pt. <i>K</i> t achieved	1851 (77%)	331(38%)	0.000
Age (years)	66.19 ± 14.92	70.66 ± 13.90	0.000
Months in HD	46.56 ± 40.92	44.28 ± 42	0.024
$T_{\rm d}$ (min)	236.56 ± 12.71	234.84 ± 16.98	NS
Q _b (mL/min)	406.42 ± 44.30	337.11 ± 86.60	0.000
Q _d (mL/min)	513.12 ± 61.87	512.36 ± 59.38	NS
Filter area (m ²)	1.43 ± 0.11	1.43 ± 0.11	NS
K _O A urea (mL/min)	1005 ± 90	1007 ± 93	NS
Post-HD weight (kg)	70.06 ± 14.33	67.37 ± 14.33	0.000
Height (cm)	163.3 ± 10	158.9 ± 10	0.000
BSA (m ²)	1.79 ± 0.22	1.73 ± 0.22	0.000
Vol. Dist. Urea Watson (L)	36.12 ± 6.33	33.66 ± 5.74	0.000

be Gui of t are cula (3 t thai fact con ceiv mo dos

be found in the European Guidelines [15], the Canadian Guidelines [16], the UK Guidelines [17] and the Guidelines of the Spanish Society of Nephrology [14]. If determinations are only carried out monthly, bimonthly or quarterly to calculate the dialysis dose, the results of these 4, 6 or 12 readings (3 to 7% of the sessions) will be extrapolated to everything that occurs in the 156 annual sessions. Because multiple factors can influence dialytic efficacy in each HD session, control systems have been developed to quantify the dose received by the patient in each session and in real time. Most monitors have incorporated ID, which allows the dialysis dose to be calculated in all sessions, without involving additional workload, analytical determinations or cost. Consequently, many dialysis units have already abandoned preand post-dialysis urea determinations. However, a post-dialysis monthly blood sample is recommended to calculate other parameters of the urea kinetic model, such as the protein catabolic rate, as well as to adequately monitor electrolytes and bicarbonates.

Using *K*t offers several advantages. Both *K* and t are realtime monitor readings, which cannot be manipulated by the user and can be used in all dialysis sessions at no additional cost. The *J*-shaped survival curve, which occurs when patients are distributed into quintiles according to the URR or Kt/V[7], is avoided (patients who appear to be receiving a higher dialysis dose when the Kt/V or URR is measured could be considered as under dialysis if *K*t is considered). The initial 1999 recommendations were made according to gender [6] and were individualized in 2005 according to the BSA [8]. These indications were validated [9]; a *K*t of between 4 and 7 L less than the prescribed dose increases mortality by 10%, between 7 and 11 L less would lead to a 25% increase and \geq 11 L less would increase mortality by over 30%. In this study, we found that the recommended dose was achieved in 91% of patients when classical eKt/V prescriptions were used, while only 67% did so if *K*t alone was used.

Various studies that have used ID in HD and that have expressed ID as Kt/V have concluded that Kt/V readings through ID differ from analytical readings, although the correlation between both procedures is good [18, 19], being equal to that in hemodiafiltration [20], which demonstrates variability between the methods used. To obtain Kt/V, V must be introduced, an inaccurate value, which can be obtained by anthropometrical equations such as Watson's, by calculating the measured Kt divided by the analytical Kt/V or by bioimpedanciometry [21]. Kt/V determined by ID is normally underestimated compared with Kt/V calculated by the second-generation Daugirdas formula obtained by analysis [18, 19, 22, 23].

Several studies have shown that the general Kt/V recommendations could lead to underdialysis in women. In a later analysis in the HEMO study, increasing the dialysis dose in a subgroup of women reduced mortality by 19% [24]. The same conclusion was observed by Port et al. [25] in 74120 patients in the USA and in 10 816 patients in seven countries taking part in the DOPPS study. Based on these studies, Spanish guidelines [14] now recommend that women should receive a Kt/V dose >1.6. As shown by our results, achieving eKtV is influenced by gender, women being the group achieving the highest eKt/V. However, when Kt is chosen as the dialysis dose indicator, this difference disappears (Table 5). We found that achievement of Kt recommendations was 6% lower in women, especially in women who reached the target eKt/V but not the target Kt. This could be an explanation for higher under-dialysis in women.

Table 4.	Comparison between	<i>Kt/Ve</i> and <i>Kt</i> compliant	patients versus th	ose eKt/V, Kt or both	non-
complia	nt patients				

	Achieved eKt/V Achieved Kt n = 2142 (65.4%)	Achieved <i>eK</i> t/ <i>V</i> not achieved <i>K</i> t <i>n</i> = 845 (25.8%)	P-value	Not achieved eKt/V Achieved Kt n = 47 (1.43%)	P-value	Not achieved eKt/V not achieved Kt n = 241 (7.35%)	P-value
eKt/V	1.68 ± 0.27	1.51 ± 0.26	0.000	1.12 ± 0.80	0.000	1.00 ± 0.26	0.000
Kt target (L)	48.74 ± 3.89	49.83 ± 4.07	0.000	54.01 ± 3.26	0.000	51.90 ± 4.01	0.000
Kt achieved (L)	56.80 ± 6.29	44.53 ± 6.07	0.000	58.93 ± 5.24	NS	42.16 ± 8.03	0.000
Gender (% Fem)	36%	45.6%	0.000	6.4%	0.000	23.7%	0.000
Age (years)	66.81 ± 15.2	69.92 ± 13.2	0.000	58.61 ± 15.6	0.001	66.15 ± 13.9	NS
Months in HD	48.6 ± 3.60	43.2 ± 37.2	0.003	29.16 ± 23.88	0.008	33.72 ± 33.96	0.000
$T_{\rm d}$ (min)	238.07 ± 9.8	233.40 ± 15.6	0.000	241.8 ± 38.8	NS	226.1 ± 28.4	0.000
$Q_{\rm b}$ (mL/min)	406 ± 47	357 ± 88	0.000	403 ± 47	NS	336 ± 59	0.000
$Q_{\rm d}$ (mL/min)	512 ± 60	512 ± 58	NS	542 ± 100	0.027	524 ± 82	0.047
Filter area (m ²)	1.42 ± 0.11	1.43 ± 0.12	NS	1.42 ± 0.11	0.003	1.46 ± 0.18	0.001
KOA urea (mL/min)	1001.2 ± 84.0	1006.8 ± 92.51	NS	1049 ± 133.79	0.002	1006.8 ± 92.5	0.000
Post-HD weight (kg)	67.06 ± 13.4	71.62 ± 14.6	0.000	86.29 ± 14.2	0.000	78.68 ± 15.6	0.000
AV (% catheter)	15.3%	48%	0.000	8.5%	0.000	57.7%	0.000
Height (cm)	162.0 ± 10.3	161.0 ± 9.7	NS	169 .9 ± 11.7	0.000	165.7 ± 10.6	0.000
BSA (m ²)	1.74 ± 0.20	1.80 ± 0.22	0.000	2.03 ± 0.20	0.000	1.92 ± 0.22	0.000
V Watson (L)	34.85 ± 6.05	35.42 ± 6.03	NS	43.77 ± 6.54	0.000	39.38 ± 6.50	0.000

Spalding et al. [26] reports that Kt/V could underestimate the dose in women, as well as in small men, highlighting the importance of the patient's body weight and the inverse behavior with the dose expressed as Kt/V or Kt. Based on the argument that there are various physiological variables scaled allometrically with respect to body size in the animal kingdom, Singer and Morton's group [27, 28] emphasize that both the glomerular filtration rate and the basal metabolic rate in mammals are scaled according to body weight with an almost identical exponent. Therefore, increasing the dialysis dose in those patients with a lower body weight should be considered. Our results support this explanation, target Kt was not achieved in a higher percentage of patients in the lowest body weight quintile, although these patients received the highest Kt/V. In contrast, the small group of patients (<2% and mainly men over 85 kg) who reached the minimum Kt but not the minimum Kt/Vshould be considered as receiving a correct dose.

Finally, the risk of under-dialysis increased in patients with CVCs. In European countries, the use of tunneled CVC has

gradually increased as a permanent form of vascular access [29]. Although the blood flow (Qb) obtained with tunnelled catheters is increasingly higher, the dialysis doses reached remain even lower than those obtained by native AVFs or vascular prostheses. Due to the high variability of doses between HD sessions when using a catheter, the ideal solution would be to generalize monitor use with ID and incorporate Kt determination into each session to guarantee an adequate minimum dose. According to a previous study [30], when monitors are not available for monitoring Kt, the HD time should be increased, on average, by 30 min if a catheter is used in the normal position and by 60 min if the catheter is in an inverted position. In the present study, only 38% of the patients with a CVC reached the minimum Kt. Similarly, of the patients who did not reach Kt but did reach tKt/V or did not reach either, those with CVCs represented 48 and 58%, respectively. The use of the ID also allows an estimation of access recirculation through the ID/blood flow rate ratio [31, 32].

E	
T	
C	
H	
H	
2	
A	
~	
H	
Z	
9	
2	
0	

	Kt non-accomplishment		<i>eK</i> t/V non-accomplishment		Kt and eKt/V non-accomplishment	lishment
	OR (IC 95%)	P-value	OR (IC 95%)	P-value	OR (IC 95%)	P-value
Age (years)	1.01 (1.003-1.018)	0.003	0.98 (0.979-0.999)	0.036	NS	NS
Gender male (Ref:Fem)	NS	NS	3.70 (2.595-5.300)	0.000	3.60 (2.45–5.28)	0.000
Time in HD (years)	NS	NS	0.93 (0.882-0.980)	0.007	0.94(0.88-0.99)	0.041
Q _b (mL/min)	0.97 (0.968-0.974)	0.000	0.98 (0.977-0.983)	0.000	0.97 (0.97–0.99) (0.97	0.000
Catheter (Ref: FAVi)	1.66 (1.297–2.127)	0.000	NS	NS	1.58 (1.05–2.38)	0.028
HD session time	0.93 (0.929-0.945)	0.000	0.95 (0.942-0.958)	0.000	0.94 (0.93–0.95)	0.000
Post-HD weight (kg)	1.08 (1.073-1.090)	0.000	1.08 (1.069–1.092)	0.000	1.07 (1.06–1.09)	0.000
Parameters predicting Kt and/or eKt/V Non-accomplishment ($N = 3275$) Logistic regression adjusted to: age, gender, time in HD, Q _b , vascular acce	t/V Non-accomplishment ($N = 327$ gender, time in HD, Q _b , vascular ac	'5). ccess, effective time H	275). access, effective time HD session and post-HD weight. NS, Non-significant differences.	S, Non-significant diff	erences.	

In 2008, Daugirdas et al. [33, 34] proposed rescaling standard Kt/V to BSA as an alternative to Kt/V or stdKt/V which might allow better quantification of dialysis for both men and women. To calculate the surface area, normalized stdKt/V is needed to have pre- and post-urea, spKt/V, eKt/V, stdKt/V, anthropometric V formula, BSA, adequate ratio delivered stdKt/ V and S-normalized minimum target stdKt/V. In 2010, Basile et al. [35] compared alternative methods for scaling the dialysis dose instead of V (W^{0.67}, BSA, resting energy expenditure, high metabolic rate organ mass, liver size and bioelectrical resistance). The implementation of this methodology has not been incorporated into clinical practice probably because of the difficulty in understanding and making the appropriate calculations. However, the use of *K*t seems easy because it is provided directly by the monitor and only it is needed to check if minimum target Kt is reached. Nowaday, the only current reference is the study of Lowrie et al. with recommendations to set minimum Kt adjusted to BSA [8], which are different for different BSA in a non-linear relationship.

Like all treatments, the dialysis dose should be adequately prescribed. Achieving a minimum dialysis dose is the responsibility of nephrologists and is an area that could be improved. Because age, gender and comorbidity cannot be changed, prescription should be adjusted to the dialysis parameters and treatment should be adapted to ensure that the prescribed schedule is received by the patient and inadequate treatment is avoided.

In conclusion, the advantage of monitoring the dose with Kt instead Kt/V is that this method identifies 25.8% of patients who did not reach the minimum Kt while achieving Kt/V. This difference is particularly evident in women, in patients with a low body weight, and in those with venous central catheters. The routine use of Kt is recommended in all patients who are routinely dialyzed with ID monitors. Although there is still a lack of scientific evidence on the use of Kt, now seems the right time to prepare for a change. The percentage of HD machines providing Kt has increased in the last few years and could probably reach nearly 100% in the next few years. Therefore, the time is ripe for studies such as our own to rethink dose monitoring and for prospective studies to define and validate the minimum Kt recommendations.

CONFLICT OF INTEREST STATEMENT

R.R., I.P., A.G. and J.I.M. are employees of Fresenius Medical Care. None of the other authors have any financial or proprietary interest in the devices or products used in this study.

REFERENCES

1. Peticlerc T, Goux N, Reynier AL *et al*. A model for noninvasive estimation of in vivo dialyzer performances and patient's conductivity during hemodialysis. Int J Artif Organs 1993; 16: 585–591

- 2. Steil H, Kaufman AM, Morris AT *et al.* In vivo verification of an automatic non invasive system for real time K_t evaluation. ASAIO 1993; 39: M348–M352
- Peticlerc T, Bene B, Jacobs C *et al.* Non-invasive monitoring of effective dialysis dose delivered to the haemodialysis patient. Nephrol Dial Transplant 1995; 10: 212–216
- Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 1980; 33: 27–39
- 5. Ilstrup K, Hanson G, Shapiro W *et al.* Examining the foundations of urea kinetics. Trans Am Soc Artif Organs 1985; 31: 164–168
- Lowrie EG, Chertow GM, Lew NL *et al.* The urea {clearance x dialysis time} product (*K*_t) as an outcome-based measure of he-modialysis dose. Kidney Int 1999; 56: 729–737
- Chertow GM, Owen WF, Lazarus JM *et al.* Exploring the reverse J-shaped curve between urea reduction ratio and mortality. Kidney Int 1999; 56: 1872–1878
- Lowrie EG, Li Z, Ofsthun NJ *et al.* The online measurement of hemodialysis dose (*K*_t): Clinical outcome as a function of body surface area. Kidney Int 2005; 68: 1344–1354
- 9. Lowrie EG, Li Z, Ofsthun NJ *et al.* Evaluating a new method to judge dialysis treatment using online measurements of ionic clearance. Kidney Int 2006; 70: 211–217
- Aljama P. ORD Work and Initiative Group ('Optimising Results in Dialysis'). Nefrología 2012; 32: 701–703
- Marcelli D, Moscardó V, Steil H *et al.* Data Management and Quality Assurance for Dialysis Network. Contrib Nephrol. 2002; 137: 293–299
- 12. Held PJ, Port FK, Wolfe RA *et al*. The dose of hemodialysis and patient mortality. Kidney Int 1996; 50: 550–556
- NKF-DOQI Hemodialysis Adequacy Work Group Membership. Guidelines for hemodialysis adequacy. Am J Kidney Dis 1997; 30: S22–S63
- Maduell F, García M, Alcázar R. Dosificación y adecuación del tratamiento dialítico. Guías SEN: Guías de Centros de hemodiálisis. Nefrología 2006; 26: 15–21
- European Best Practice Guidelines for Haemodialysis. Nephrol Dial Transplant 2002; 17: 17–21
- The Canadian Society of Nephrology. Clinical practice guidelines the delivery of haemodialysis. J Am Soc Nephrol 1999; 10: S306–S310
- The Renal Association. Recommended standards for haemodialysis. Royal College of Physicians of London. Treatment of adult patients with renal failure. Recommended standards and audit measure 1997; 17–29
- Maduell F, Navarro V, García H *et al.* Results of monitoring the dose of hemodialysis in real time at every treatment session. Nefrología 1999; 19: 532–537
- Teruel JL, Fernández Lucas M, Marcen R *et al.* Estimation of the K_t/V with a ionic dialysance monitor. Nefrología 2001; 21: 78–83

- Maduell F, Puchades MJ, Navarro V *et al.* Monitoring hemodialysis dose with ionic dialysance in on-line hemodiafiltration. Nefrología 2005; 25: 521–526
- 21. Teruel JL, Álvarez Rancel LE, Fernández Lucas M *et al.* Control of the dialysis dose by ionic dialysance and bioimpedance. Nefrología 2007; 27: 68–73
- 22. Moret K, Beerenhout CH, van den Wall Bake AW *et al.* Ionic dialysance and the assessment of K_t/V : the influence of different estimates of V on method agreement. Nephrol Dial Transplant 2007; 22: 2276–2282
- Lindley EJ, Chamney PW, Wuepper A *et al.* A comparison of methods for determining urea distribution volume for routine use in on-line monitoring of haemodialysis adequacy. Nephrol Dial Transplant 2009; 24: 211–216
- 24. Depner T, Daugirdas J, Greene T *et al.* Hemodialysis (HEMO) Study Group: Dialysis dose and the effect of gender and body sike on outcome in the HEMO Study. Kidney Int 2004; 65: 1386–1394
- Port FK, Wolfe RA, Hulbert-Shearon TE *et al.* High dialysis dose is associated with lower mortality among woman but not among men. Am J Kidney Dis 2004; 43: 1014–1023
- 26. Spalding EM, Chandna SM, Davenport A *et al.* K_t/V underestimates the hemodialysis dose in women and small men. Kidney Int 2008; 74: 348–355
- Singer MA, Morton AR. Mouse to elephant: Biological scaling and K_t/V. Am J Kidney Dis 2000; 35: 306–309
- Singer MA. Of mice and men and elephant: Metabolic rate sets glomerular filtration rate. Am J Kidney Dis 2001; 37: 164–178
- 29. Pisoni RL, Young EW, Dykstra DM *et al.* Vascular access use in Europe and the United States: results from the DOPPS. Kidney Int 2002; 61: 305–316
- Maduell F, Vera M, Arias M *et al.* How much should dialysis time be increased when catheters are used? Nefrología 2008; 28: 577–580
- Mohan S, Madhrira M, Mujtaba M *et al.* Effective Ionic dialysance/blood flow rate ratio: an indicator of access recirculation in arteriovenous fistulae. ASAIO J 2010; 56: 427–433
- 32. Tan J, Mohan S, Herbert L *et al*. Identifying hemodialysis catheter recirculation using effective ionic dialysance. ASAIO J 2012; 58: 522–525
- 33. Daugirdas JT, Depner TA, Kuhlmann MK *et al.* Surface-areanormalized K_t/V : A method of rescaling dialysis dose to body surface area-implications for different-size patients by gender. Semin Dial 2008; 21: 415–421
- Ramirez SPB, Kapke A, Port FK *et al.* Dialysis dose scaled to body surface area and size-adjusted, sex-specific patient mortality. Clin J Am Soc Nephrol 2012; 7: 1977–1987
- Basile C, Vernaglione L, Lomonte C et al. Comparison of alternative methods for scaling dialysis dose. Nephrol Dial Transplant 2010; 25: 1232–1239

Received for publication: 23.1.2013; Accepted in revised form: 3.4.2013