

ORIGINAL ARTICLE

Individualizing Kt by sex and body surface area: implications for survival in hemodialysis patients

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ABSTRACT

Background. The administration of an adequate dialysis dose is a critical aspect for ensuring the effectiveness of hemodialysis (HD) treatment and improving survival. Kt is a key indicator to evaluate the dose, with two targets: based on sex (Kt-Sx) and body surface area (Kt-BSA).

Methods. This retrospective study (2022–23) was conducted across 15 HD centers analyzed 1829 prevalent patients and 317 842 HD sessions.

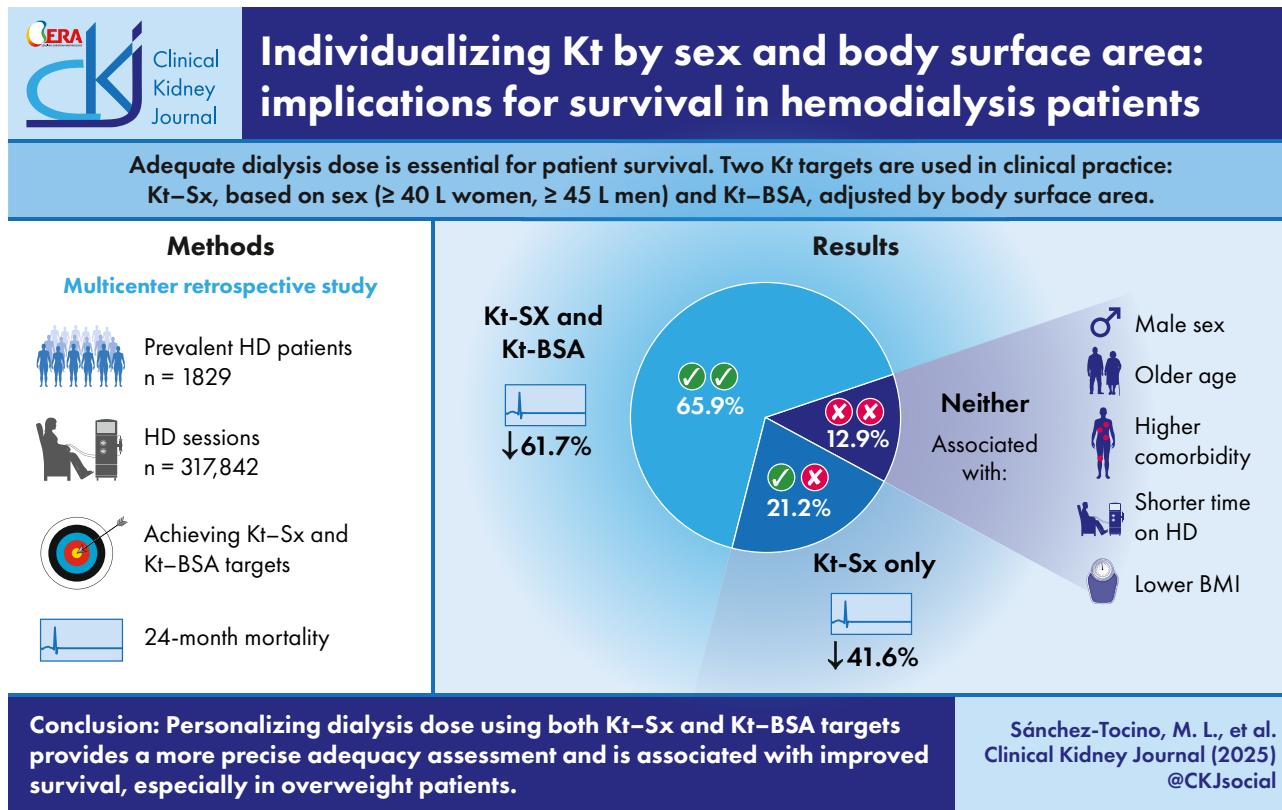
Results. It was found that 65.9% met both Kt targets, 21.2% met only Kt-Sx and 12.9% met neither. Failure to meet both of the targets was associated with being male, older age, shorter time on HD, higher comorbidity, low body mass index, use of a catheter, shorter sessions, conventional HD, low flow rates and small membranes. Meeting at least the Kt-Sx target was associated with a 41.6% reduction in 24-month mortality risk, and an even more favorable association was observed when both targets were met, reducing the risk by 61.7%.

Conclusions. These findings highlight the importance of personalizing dialysis considering both sex and BSA, particularly in overweight or obese patients, to improve survival.

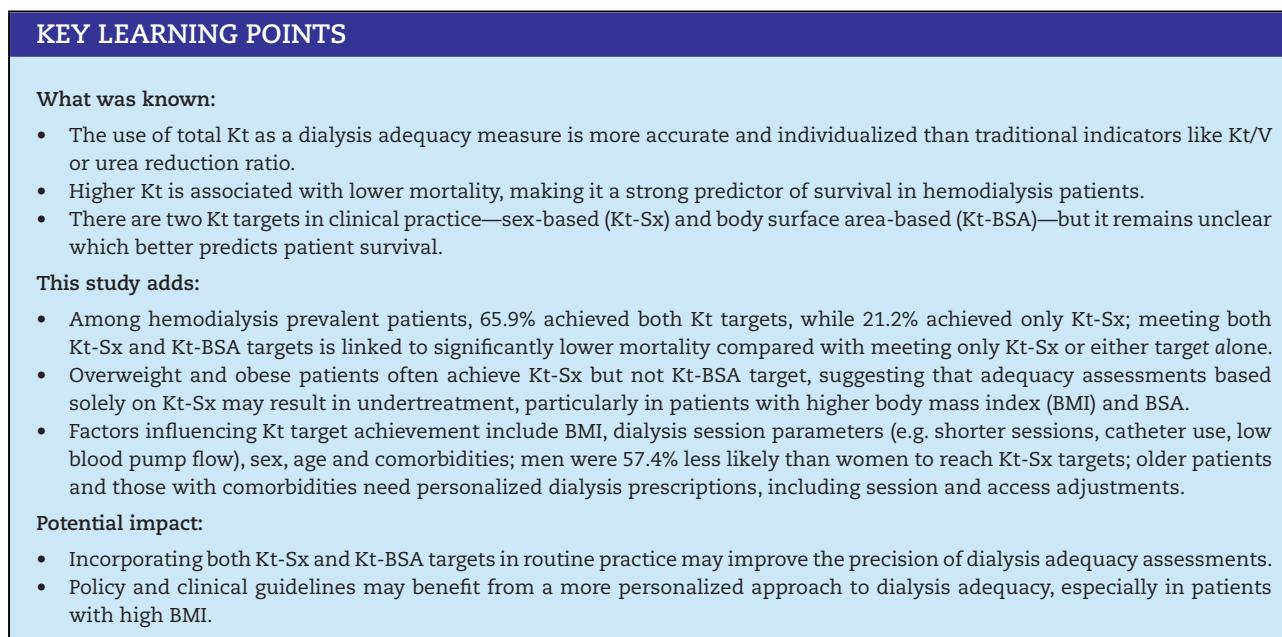
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GRAPHICAL ABSTRACT



Keywords: body mass index, body surface area-based Kt, dialysis adequacy, dialysis dose, sex-based Kt



INTRODUCTION

The administration of an adequate dialysis dose is a critical aspect for ensuring the effectiveness of treatment and improving survival in hemodialysis (HD) patients. Traditionally, parameters such as the urea reduction ratio (URR) and Kt/V have been used to measure the quality of HD. However, Kt has become a more specific and reliable indicator for assessing the adequacy of the administered dialysis dose [1–3], as, unlike Kt/V, Kt is not influenced by the distribution volume [4, 5]. An inverse relationship between Kt and mortality has been observed, such that higher Kt is continuously associated with lower mortality. This behavior contrasts with URR, whose relationship with mortality follows a “J-shaped” curve [6].

The use of Kt as an indicator of dialysis dose and its impact on mortality is not a recent concept [7–9]. Its use as a measure of dialysis adequacy is more demanding than other parameters and is associated with improved survival. Moreover, real-time measurement during each HD session allows for immediate adjustments, making it the preferred marker to assess dialysis effectiveness by more accurately reflecting individual variations and changes over time [10].

In clinical practice, there are two Kt targets: sex-based Kt (Kt-Sx) and body surface area-based Kt (Kt-BSA). The first, proposed by Lowrie et al. in 1999 [7], suggests that a minimum Kt of 40 L for women and 45 L for men correlates with reduced mortality in HD patients. This is the most commonly used target [10]. However, later research suggested that individualizing Kt based on BSA could optimize clinical outcomes in patients of the same sex [8, 9].

Although it is widely accepted that achieving an adequate dialysis dose is essential, the question arises as to which dialysis dose indicator is most suitable for patient survival: Kt-Sx or Kt-BSA? And for which patients? The aim of this study was to analyze how meeting both, one or neither of the Kt targets influences mortality, as well as to identify the factors that prevent reaching these targets in treatment.

MATERIALS AND METHODS

Study design

This was a retrospective observational study conducted over a 2-year period, from January 2022 to December 2023.

Population

A cohort of prevalent patients undergoing chronic HD from 15 centers of the Fundación Renal Española was included, comprising 4 hospital-based units and 11 outpatient units. The analysis included all patients over 18 years of age who had been undergoing HD for >3 months at the selected centers during the study period. Patients with <3 months of treatment and sessions lasting <120 min or >300 min were excluded.

Variables

Variables related to patient characteristics, dialysis sessions and dialysis efficacy parameters were analyzed using two databases (“Patients” and “Sessions”) extracted from electronic health records. Patient-related variables included: age (years), sex, time on HD (months), comorbidity assessed by the Charlson Comorbidity Index, etiology of chronic kidney disease (diabetic, vascular, interstitial nephritis, glomerulonephritis, polycystic kid-

ney disease, undetermined, other), length of follow-up in the study (from enrollment to the end of observation or discharge; months), date of discharge from the unit and reason for discharge (transplantation, transfer, death, clinical improvement or switch to peritoneal dialysis). Anthropometric variables included: body mass index (BMI), and body surface area (m²).

Session-related variables included: type of vascular access (native/prosthetic arteriovenous fistula or catheter), dialysis modality (conventional HD, online HDF), session duration (min), dialyzer size (mm), dialysate flow rate (mL/min), average blood flow during dialysis (mL/min) and use of automated dialysate flow (with or without autowheel).

Dialysis efficacy parameters analyzed were: Kt measured by the dialysis monitor, total cleared volume (liters), and replacement volume administered in convective therapies (liters).

Definition of dialysis adequacy objectives

The target values used to compare the average Kt achieved in each patient's dialysis sessions were as follows:

- Kt-Sx: a minimum of 40 L for women and 45 L for men [8, 9].
- Individualized Kt target based on BSA (Kt-BSA): calculated using the formula $1/[0.0069 + (0.0237/BSA)]$, where BSA is the body surface area estimated using the Dubois and Dubois formula ($m^2 = \text{weight}^{0.425} \times \text{height}^{0.725} \times 0.007184$) [11]; Kt relative to BSA is considered optimal when it is greater than or equal to the value established in the reference tables [8].

Ethics

The study was approved by the Research Ethics Committee of the Área de Salud de Salamanca (PI 2025 01 1808) and complied with the ethical principles of the Declaration of Helsinki (Fortaleza, Brazil, 2013), the recommendations of the World Health Organization, the professional code of ethics and Spanish legislation. Data were collected in a pseudonymized manner to ensure the privacy of patients undergoing HD during the study period.

Statistical analysis

Quantitative variables were expressed as mean and standard deviation or as median and interquartile range, depending on whether the distribution was normal. Qualitative variables were presented as absolute frequencies and percentages. To analyze the association between qualitative variables across different groups, the Chi-square test was used. For comparisons involving more than two groups, analysis of variance was applied. When variables did not follow a normal distribution, comparisons were conducted using the Kruskal-Wallis test.

The association between achieving the Kt target (sex, BSA or both) and BMI was assessed using logistic regression and restricted cubic splines. For fitting the restricted cubic splines, three knots were placed at fixed percentiles (10th, 50th and 90th). The reference point (odds ratio = 1.00) was set at the median BMI.

Mortality analysis was performed using Kaplan-Meier estimates and Cox proportional hazards regression. The relative mortality risk obtained from Cox regression models was adjusted for sex, age, BMI, diabetes and vascular access type. Covariate selection for the multivariable models was guided by a directed acyclic graph (DAG) (Supplementary Appendix Fig. A1), which identified age, sex, BMI, comorbidity and vascular access

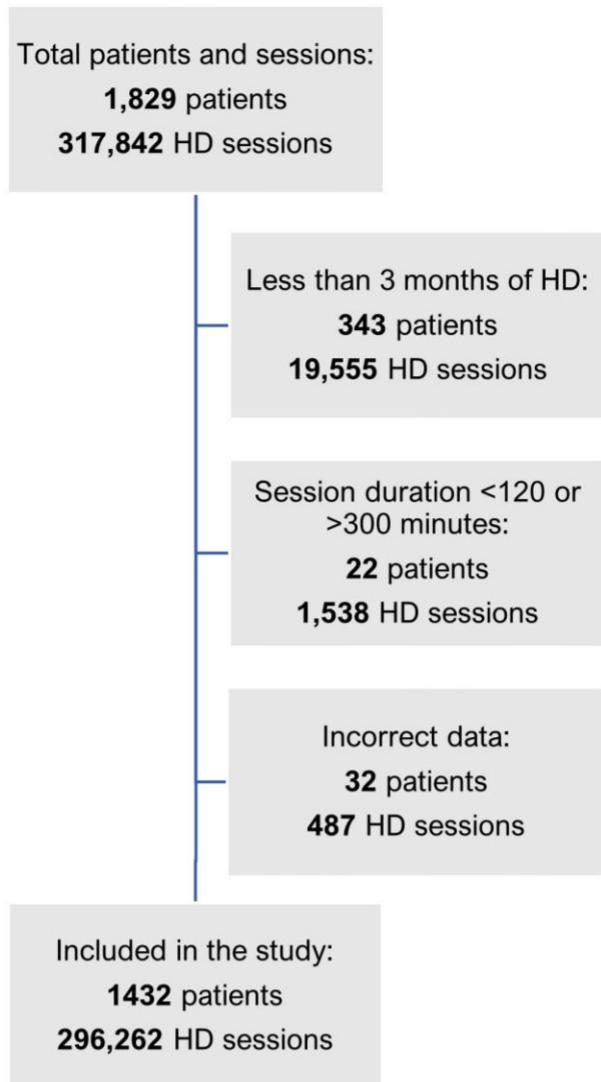


Figure 1: Flow diagram of patients and sessions included in the study.

as potential confounders. To avoid redundancy due to the inclusion of age and end-stage renal disease within the Charlson Index, we used diabetes as a clinically relevant comorbidity proxy in the Cox models. Statistical analyses were conducted using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA) and R for Windows version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria), with RStudio version 2024.12.1 Build 563. A significance level of .05 was considered for all tests.

RESULTS

A total of 1432 prevalent patients and 296 262 HD sessions meeting the inclusion criteria were analyzed (Fig. 1). The mean age was 67.8 ± 14.7 years, 64.9% (930) were male and the mean HD duration was 60.6 ± 70.4 (3.0–530.0) months. Diabetes mellitus was the most common cause of chronic kidney disease (421; 29.4%), and the mean Charlson comorbidity index was 8.1 ± 3.2 . An arteriovenous fistula (AVF) was used in 187 577 (63.4%) sessions, and a central venous catheter in 108 446 (36.6%). All demographic, patient and session characteristics are summarized in Supplementary Appendix Tables A1 and A2.

Table 1: Dialytic efficacy data.

	Total, n = 296 262 (100%)
Cleared volume (L), n = 296 040	79.4 ± 12.7
Substitution volume in online HDF (L), n = 178 516	23.2 ± 14.3
Kt measured on monitor, n = 296 262	52.1 ± 9.7

Data are presented as mean \pm standard deviation.
 Substitution volume in online HDF refers to the volume of replacement fluid administered during convective therapies.
 HDF, hemodiafiltration.

Dialytic efficacy and Kt target achievement

The mean Kt measured on the monitor was 52.1 ± 9.7 (Table 1). Of all patients, 943 (65.9%) achieved both defined Kt targets, and 184 (12.9%) did not achieve any (Table 2). Regarding patients who only achieved one of the targets, 303 (21.2%) met only the Kt-Sx, and 2 patients (0.1%) met only the Kt-BSA and not the Kt-Sx. These latter patients were excluded from the analysis of achieving one target versus both or none.

Patient characteristics related to Kt target achievement

Men were less likely to achieve Kt targets: 14.8% of men versus 9.4% of women did not achieve either target, while 64.4% of men versus 68.7% of women achieved both targets ($P = .014$). Older age was associated with a lower likelihood of achieving targets (mean age 72.3 ± 12.6 years for those who achieved none, 67.7 ± 14.3 years for those who achieved one and 66.9 ± 15.1 years for those who achieved both; $P < .001$), as was higher comorbidity (mean Charlson Comorbidity Index score 9.4 ± 3.2 , 8.5 ± 3.3 , and 7.7 ± 3.1 , respectively; $P < .001$). Conversely, longer time on dialysis was associated with a higher likelihood of achieving targets (median time: 23.7 months for none, 33.3 months for one and 45 months for both; $P < .001$).

Patients with higher BSA were more likely to achieve only the Kt-Sx target (mean BSA: 1.9 ± 0.2 m^2 for those achieving only Kt-Sx, compared with 1.7 ± 0.2 m^2 for those achieving both and 1.7 ± 0.3 m^2 for those achieving none; $P < .001$). Similarly, overweight/obese patients with a BMI above the median were more likely to achieve the Kt-Sx target, but not the Kt-BSA target (mean BMI: 28.2 ± 5.4 kg/m^2 for those achieving only Kt-Sx, vs 25.4 ± 5.1 kg/m^2 for both and 24.7 ± 4.9 kg/m^2 for none; $P < .001$) (Fig. 2A).

Logistic regression with restricted cubic splines showed an almost linear relationship between higher BMI and a greater likelihood of achieving the Kt-Sx target, suggesting a steady increase in probability with increasing BMI (Fig. 2B). For achieving both Kt-Sx and Kt-BSA targets, the relationship with BMI was inverse, with a steeper decline up to the median (BMI = $25.3 \text{ kg}/\text{m}^2$), followed by a plateau, indicating that higher BMI was associated with a lower likelihood of achieving both targets, though the effect was less pronounced beyond the median (Fig. 2C) (Table 2A).

Characteristics of sessions related to Kt target compliance

The probability of not achieving any Kt target was associated with the use of a catheter as vascular access (26.6% vs 10.8% with AVF did not achieve any target, and 53.8% vs 72.6% with

Table 2: Achievement of objectives in relation to (A) patient characteristics and (B) session characteristics.

(A) Patient characteristics				
Total patients n = 1432 (100%)	Achieve Kt-Sx and/or Kt-BSA			P-value
	None, 184 (12.9%)	Only Kt-Sx, 303 (21.2%)	Both, 943 (65.9%)	
Sex, n = 1430 (n, %)				
Men	137 (14.8)	193 (20.8)	598 (64.4)	.014
Women	47 (9.4)	110 (21.9)	345 (68.7)	
Age, n = 1430 (mean \pm SD)	72.3 \pm 12.6	67.7 \pm 14.3	66.9 \pm 15.1	<.001
Time on HD, n = 1430 [median (IQR)]	23.7 (9.4–45.4)	33.3 (14.8–58.9)	45.0 (23.1–79.8)	<.001
Charlson, n = 1045 (mean \pm SD)	9.4 \pm 3.2	8.5 \pm 3.3	7.7 \pm 3.1	<.001
BMI, n = 1430 (mean \pm SD)	24.7 \pm 4.9	28.2 \pm 5.4	25.4 \pm 5.1	<.001
BSA, n = 1430 (mean \pm SD)	1.7 \pm 0.3	1.9 \pm 0.2	1.7 \pm 0.2	<.001
(B) Session characteristics				
Total sessions n = 296 262 (100%)	Achieve Kt-Sx and/or Kt-BSA			P-value
	None, 48 935 (16.5%)	Only Kt-Sx, 52 371 (17.7%)	Both, 194 400 (65.9%)	
Vascular access, n = 295 467 (n, %)				
Native/prosthetic AVF	20 152 (10.8)	31 207 (16.7)	136 053 (72.6)	<.01
Catheter	28 751 (26.6)	21 146 (19.6)	58 158 (53.8)	
Session time, n = 295 706 (mean \pm SD)	196.7 \pm 30.2	219.4 \pm 20.2	227.8 \pm 15.9	<.001
HD type, n = 295 691 (n, %)				
Conventional	31 474 (26.6)	24 706 (20.9)	62 096 (52.5)	<.001
HDF	17 455 (9.8)	27 660 (15.6)	132 300 (74.6)	
Qb, n = 295 651 (mean \pm SD)	343.1 \pm 40.9	355.4 \pm 38.4	364.7 \pm 36.8	<.001
Autoflow, n = 295 706 (n, %)				
Yes	30 982 (19.8)	26 955 (17.2)	98 640 (63.0)	<.001
No	17 953 (12.9)	25 416 (18.3)	95 760 (68.8)	
Membrane surface area, n = 295 019 (n, %)				
Small 1.4–1.7	14 527 (33.2)	7645 (17.5)	21 537 (49.3)	<.001
Medium 1.8–2.1	30 430 (14.3)	35 389 (16.7)	146 427 (69.0)	
Large 2.2–2.5	3917 (10.0)	9080 (23.2)	26 067 (66.7)	

HDF, hemodiafiltration; IQR, interquartile range; Qb, blood flow rate; SD, standard deviation.

AVF achieved both targets; $P < .001$, conventional HD (26.6% vs 9.8% in HDF did not achieve any target, and 52.5% vs 74.6% in HDF achieved both targets; $P < .001$), use of dialysate autoflow (19.8% vs 12.9% without autoflow did not achieve any target, and 63.0% vs 68.8% without autoflow achieved both targets; $P < .001$) and smaller membrane surface areas (33.2% with small membrane, 14.3% with medium membrane, and 10.0% with large membrane did not reach any target; compared with 49.3% with small membrane, 69.0% with medium membrane, and 66.7% with large membrane achieved both targets; $P < .001$). Shorter sessions were associated with lower compliance to the targets (mean of 196.7 ± 30.2 min for those not achieving any target, 219.4 ± 20.2 for those achieving one, and 227.8 ± 15.9 for those achieving both; $P < .001$), as were lower blood pump flows (mean of 343.1 ± 40.9 mL/min for those not achieving any target, 355.4 ± 38.4 for those achieving one, and 364.7 ± 36.8 for those achieving both; $P < .001$) (Table 2B).

Survival analysis in relation to Kt target achievement

During the study period, a total of 205 patients (14%) died. Patients who achieved both Kt targets showed higher 24-month survival (88.7%) compared to those who achieved only one target (Kt-Sx) (84.5%) or none (75.5%) (log-rank 32.1; $P < .001$) (Fig. 3A). Unadjusted Cox regression results indicated that achieving both targets or only one (Kt-Sx) was significantly associated with lower 24-month mortality, with a 61.7% reduction (HR 0.383; 95%

CI 0.270–0.542; $P < .001$) and a 41.6% reduction (HR 0.584; 95% CI 0.388–0.879; $P = .010$), respectively, compared to not achieving any targets. In the multivariable analysis adjusted for sex, age, BMI, diabetes, and vascular access, only achievement of both targets remained independently associated with lower mortality risk (HR 0.514; 95% CI 0.355–0.745; $P < .001$), while the association for achieving only Kt-Sx lost statistical significance (HR 0.830; 95% CI 0.540–1.275; $P = .394$) (Table 3, Fig. 3B). Among covariates, increasing age was associated with a 4.2% increase in mortality risk (HR 1.042; 95% CI 1.029–1.055; $P < .001$), whereas higher BMI was associated with a 7.5% reduction (HR 0.925; 95% CI 0.894–0.957; $P < .001$). Sex, diabetes and type of vascular access did not show an independent effect on mortality.

DISCUSSION

This study highlights the importance of personalizing adequacy targets through Kt (Kt-Sx and Kt-BSA) and dialysis prescription as a potential approach to optimise treatment efficacy and improve survival. Among the HD prevalent patients studied, 65.9% achieved both Kt targets, while 21.2% achieved only Kt-Sx but not the body surface area-adjusted target. Previous studies suggest that achieving the Kt-BSA is generally less frequent, as it represents a more demanding criterion [12]. In our analysis, achieving both Kt targets (Kt-Sx and Kt-BSA) was associated with a 61.7% reduction in mortality risk, whereas achieving only Kt-Sx but not Kt-BSA was associated with a 41.6% reduction. After

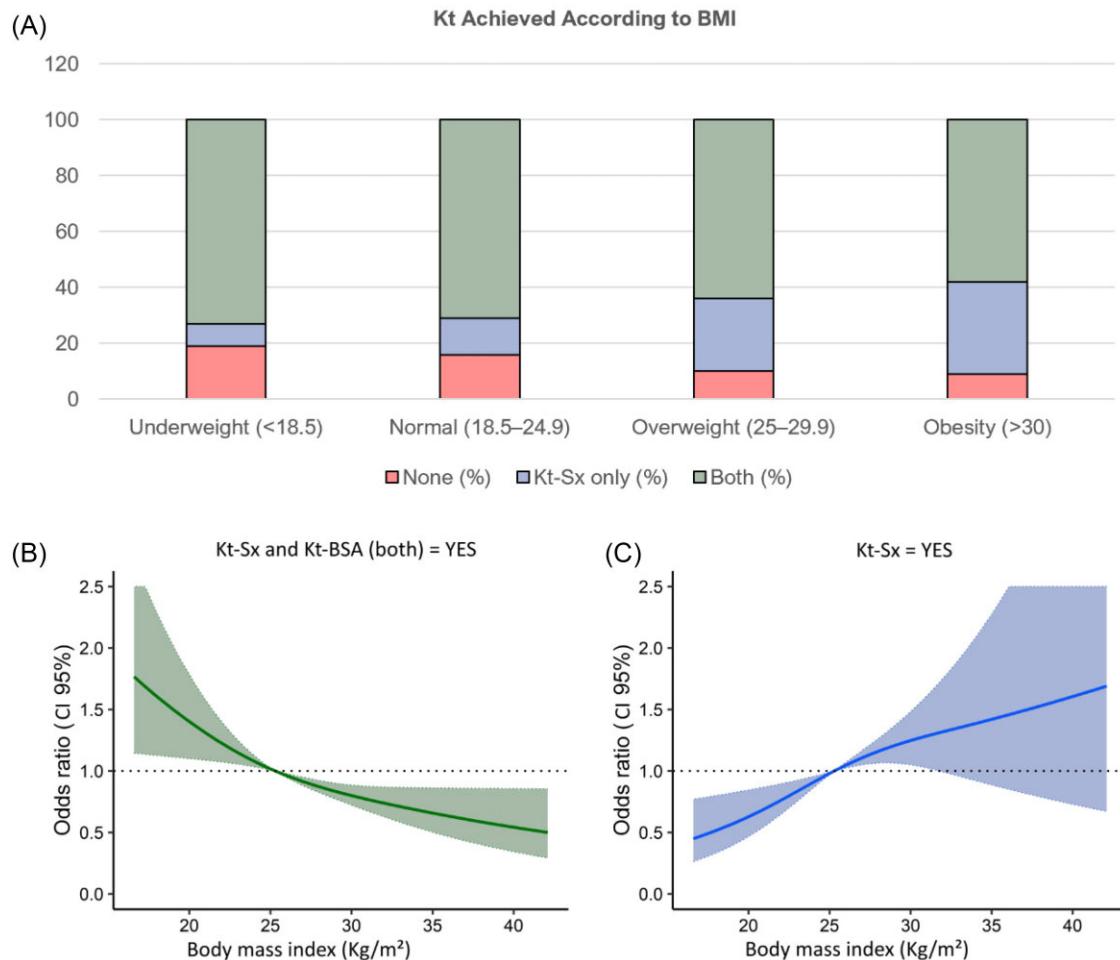


Figure 2: Kt compliance by BMI. (A) Bar chart of Kt compliance by BMI. (B) Probability of achieving Kt-Sx using logistic regression and cubic splines. (C) Probability of achieving both Kt-Sx and Kt-BSA using logistic regression and cubic splines.

multivariable adjustment, only the achievement of both Kt targets remained independently associated with lower mortality risk, while the association for achieving only Kt-Sx lost statistical significance, suggesting that Kt-Sx alone may not be sufficient.

Determining the optimal dialysis dose remains a controversial topic. A higher dialysis dose has consistently been associated with improved survival, regardless of the indicator used [13]. In this study, as expected, prevalent patients who did not achieve either of the Kt targets had a higher mortality risk compared to those who achieved at least one. However, the adjusted analysis demonstrated that only patients who achieved both Kt targets maintained a clear survival advantage, while those who reached Kt-Sx but not Kt-BSA did not. These findings suggest that focusing solely on the Kt-Sx target may not be sufficient and could have implications for prevalent patient survival. Several studies have shown that the Kt-BSA target is more stringent and provides a more individualized assessment of HD dose adequacy [14, 15]. Adjusting the dose based on body surface area, which depends more on height than on weight, may reduce errors related to weight loss or fluid retention [16].

In addition, BMI had a significant impact on achieving Kt targets. Overweight and obese patients, as well as those with higher BSA, were more likely to fail to achieve the BSA-adjusted target, even if they met the sex-based target. Conversely, patients with

low BMI were more likely to fail to achieve the sex-adjusted Kt target but not the Kt-BSA target, although this group accounted for only 0.1% of the sample.

Overweight and obesity represent a “paradox” in HD [17]. While in the general population excess weight is associated with higher mortality and increased risk of chronic kidney disease, in HD patients it may have a protective effect [18–20]. However, this condition also presents challenges in achieving optimal dialysis targets [20]. As shown in the present study, patients with higher BMI are less likely to receive adequate dialysis, which also impacts their survival [21]. These findings support the need to individualise therapy according to BMI, taking into account the more demanding target in each case.

In addition to BMI, factors influencing the achievement of one or both Kt targets include both modifiable dialysis session parameters related to dialysis prescription, as well as non-modifiable factors such as sex, age and comorbidities. Regarding sex, men were 57.4% less likely than women to achieve at least the Kt-Sx target. This may be due to the lower proportion of fat and higher proportion of muscle mass in men, which results in a higher dialyzable volume [22].

In terms of age and comorbidity, older patients less frequently reached the Kt target. Patients over 65 years of age tend to experience more adverse symptoms during HD due to age-related fragility and physiological factors such as the loss of lean

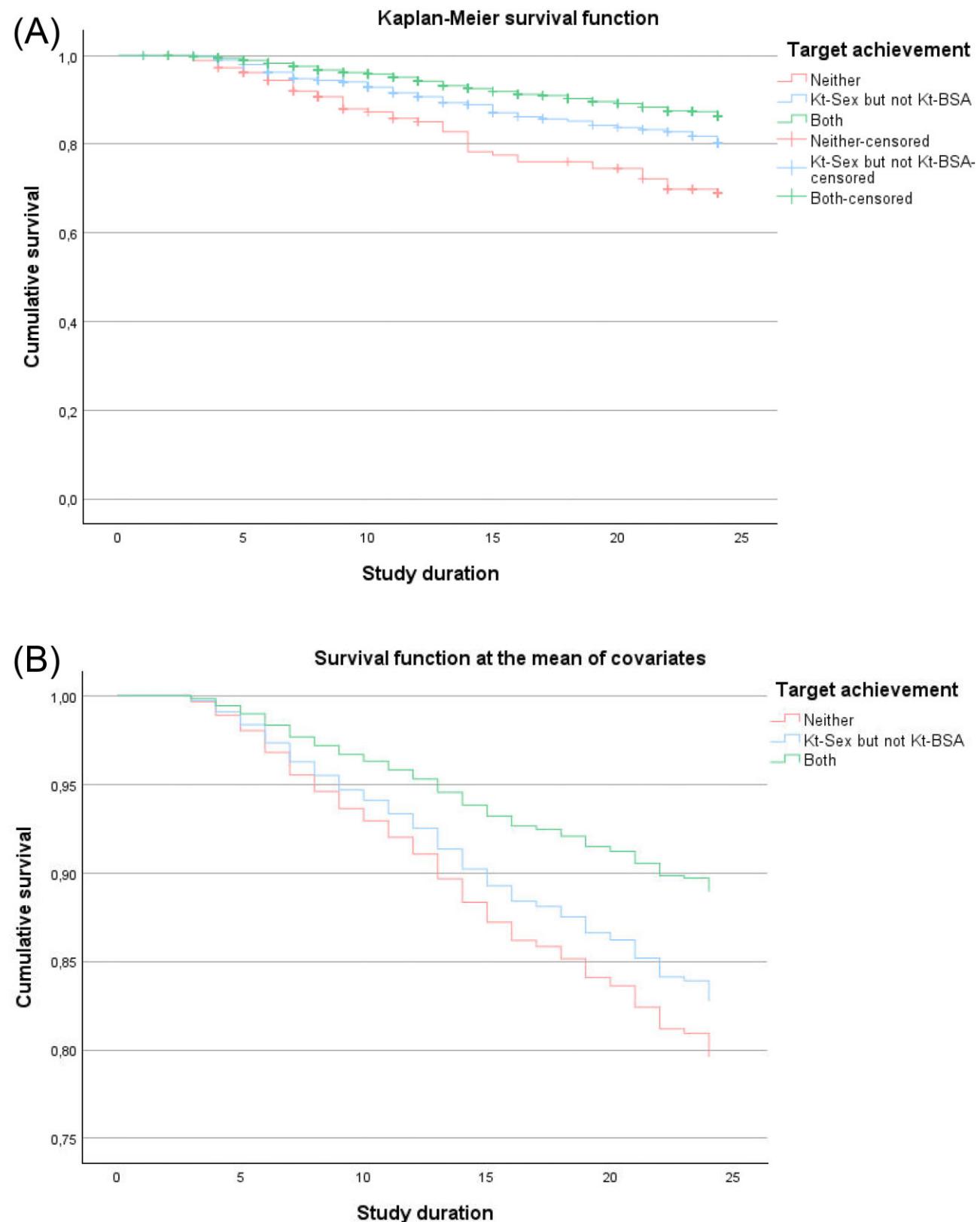


Figure 3: Mortality analysis based on achievement of Kt targets using Kaplan-Meier estimates (A) and Cox proportional hazards regression adjusted for age, sex, BMI, diabetes and vascular access (B).

Table 3: Cox regression analysis for mortality risk according to Kt target achievement.

Exposure (Kt targets)	Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI) ^a	P-value
None (reference)	1.00		1.00	
Only Kt-Sx (not Kt-BSA)	0.584 (0.388–0.879)	.010	0.830 (0.540–1.275)	.394
Both Kt-Sx + Kt-BSA	0.383 (0.270–0.542)	<.001	0.514 (0.355–0.745)	<.001
Covariates (adjusted model)				
Sex			0.936 (0.694–1.262)	.663
Age			1.042 (1.029–1.055)	<.001
BMI			0.925 (0.894–0.957)	<.001
Diabetes			1.311 (0.970–1.773)	.079
Vascular access			0.743 (0.551–1.001)	.051

^aAdjusted for sex, age, BMI, diabetes and vascular access type.

body mass and reduced total body volume [23]. Regarding comorbidities, this may be attributed to increased hemodynamic instability, intolerance to ultrafiltration volume, and a higher risk of intra- and post-dialysis complications in this group of patients [24]. Both factors suggest that elderly and comorbid patients may require more tailored dialysis prescriptions (e.g. reduced session time, frequency adjustments, etc.), which should be addressed in future studies.

Time on HD also influences goal achievement, as patients who start dialysis often maintain residual diuresis, which is not considered in Kt goals. They may receive shorter or less frequent sessions (incremental HD) for progressive adaptation and maintenance of residual kidney function [25]. Additionally, complications at this stage, such as intradialytic hypotension, volume overload or malnutrition, could affect treatment efficacy [26].

Regarding dialysis session prescription, the main factors that hindered achieving an adequate dialysis dose were the use of a catheter as vascular access, short HD sessions (<200 min), conventional HD instead of HDF, low blood pump flows (<350 mL/min), use of auto-flow and small dialyzer membranes. These results are consistent with the literature indicating that the dialysis dose depends on factors such as dialyzer surface area, blood pump flow rate, session duration and the type of vascular access [27, 28]. Moreover, in the case of HDF, it significantly reduces both all-cause and cardiovascular mortality compared with conventional HD [29–31].

Although the utility of measuring Kt-Sx and Kt-BSA remains a subject of debate [16, 32], it is essential to emphasize the need to individualize dialysis targets based on patient characteristics. Our findings suggest that Kt-BSA is a more demanding indicator of dialysis dose with potential relevance to survival, making its measurement particularly important in obese patients or those with a high BMI. Further studies are needed to explore individualized dialysis prescription strategies that could help support achieving these targets in such prevalent patient populations.

This study has limitations inherent to retrospective, registry-based designs, including the lack of prospective validation and potential incomplete data on patients and sessions. First, the inclusion of prevalent patients with widely different dialysis vintages (from recently initiated to long-term treatments) may introduce survivor bias, since only those who survived long enough to be included were analyzed. Consequently, the results mainly apply to stable HD populations rather than incident patients. Second, the calculation of mean Kt over the follow-up period may carry a potential risk of immortal time bias, as only patients who survived long enough contributed multiple sessions. Third, unmeasured variables such as other organ failures, inflammatory status, nutritional factors or differences in treatment prescription could also have influenced both Kt achievement and survival outcomes. Finally, as the mean follow-up was

relatively short (18 months), the study may not capture longer-term effects on mortality. These aspects should be considered when interpreting the associations observed.

Future studies should include incident cohorts to more accurately assess the impact of Kt on mortality from therapy initiation. Future research should also explore sex-based differences more deeply and assess whether body surface area adjustment modifies the relationship between dialysis dose, sex/gender, and mortality. The role of age and comorbidities in optimizing dialysis for older adults also warrants investigation.

Among the strengths are the large sample size and high number of sessions, which enhance data representativeness in HD. Moreover, the 2-year follow-up reduces bias and reinforces the reliability of the results.

In conclusion, adjusting dialysis dose based solely on sex may not be sufficient; it could be crucial to correct Kt by body surface area, especially in overweight or obese patients, to improve clinical outcomes and survival.

SUPPLEMENTARY DATA

Supplementary data are available at [Clinical Kidney Journal](https://doi.org/10.1093/ckj/sfz369) online.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

None declared.

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