

## Calculation of Kt/V in haemodialysis: a comparison between the formulas

Cálculo de Kt/V em hemodiálise: comparação entre fórmulas

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### ABSTRACT

**Introduction:** The quality of delivered dialysis can be measured by the Kt/V ratio, which can be calculated in various ways. **Objective:** To compare the Kt/V ratio obtained with the formulas of Lowrie (L) and Daugirdas (D) with the results measured by an Online Clearance Monitor (OCM). **Method:** Observational, cross-sectional study of 59 patients on hemodialysis (HD). Data were collected in the same dialysis session (predialysis and postdialysis urea) and Kt/V was calculated by the OCM of the Fresenius 4008S machine (Fresenius Medical Care AG, Bad Homburg, Germany). **Results:** A total of 95 sessions were assessed, with a predominance of males 56% (33), and a sample mean age of 57 + 14 years. Hypertension (42%; n = 25), diabetes (12%; n = 7) and glomerulonephritides (8%; n = 5) were the most frequent causes of chronic kidney disease (CKD). Mean Kt/V values obtained with the L and D formulas and the OCM were 1.31, 1.41 and 1.32, respectively. Comparison between the L and D formulas showed a statistically significant difference (p = 0.008), with a Pearson's correlation of 0.950. The difference between the D formula and the OCM was also significant (p = 0.011 and r = 0.346), probably due to convective loss, estimated by the D formula but not by the OCM and L formula. The difference between the L formula and the OCM was not significant (p = 0.999 and r = 0.577). **Conclusion:** These data suggest that the OCM can be used as a guide to the real-time adjustment of the dialysis dose.

**Keywords:** Dialysis. Renal Insufficiency, Chronic. Quality Control.

### RESUMO

**Introdução:** A qualidade da diálise oferecida aos pacientes em diálise pode ser mensurada pelo Kt/V, o qual pode ser calculado de diversas maneiras. **Objetivo:** Comparar os resultados de Kt/V obtidos por meio das fórmulas de Lowrie (L) e de Daugirdas (D) com os resultados mensurados pelo monitor de *clearance online* – *Online Clearance Monitor* (OCM). **Método:** Estudo observacional transversal com 59 pacientes em hemodiálise (HD). Os dados foram coletados na mesma sessão de diálise: (ureia pré-diálise e pós-diálise) e o resultado de Kt/V foi obtido pelo OCM da máquina Fresenius 4008S (Fresenius Medical Care AG, Bad Homburg, Alemanha). **Resultado:** Foram analisadas 95 sessões, em que prevaleceu o sexo masculino, 56% (33), com idade média de 57 + 14 anos. A hipertensão arterial com 42% (25), diabetes com 12% (7) e glomerulonefrite com 8% (5) foram as causas mais frequentes da doença renal crônica (DRC). O Kt/V médio obtido pela fórmula de L, de D e pelo OCM foi de 1,31; 1,41 e 1,32, respectivamente. A comparação entre as fórmulas de L e D mostra que há diferença estatística p = 0,008 com a correlação de Pearson de 0,950. Entre D e OCM a diferença também é significativa: p = 0,011 e r = 0,346, provavelmente devido a perda convectiva, avaliada pela equação de D e não observadas por OCM e L. A comparação entre L e OCM não foi significativa p = 0,999 e r = 0,577. **Conclusão:** Os dados sugerem que o OCM pode ser utilizado como um norteador para ajuste da dose de diálise em tempo real.

**Palavras-chave:** Diálise. Insuficiência Renal Crônica. Controle de Qualidade.

## INTRODUCTION

The incidence and prevalence of chronic kidney disease (CKD) have increased at an alarming rate.<sup>1</sup>

Because several studies have demonstrated a correlation between hemodialysis (HD) dose and morbidity and mortality, the former must be measured in order to estimate whether CKD patients on HD are being adequately treated. Although symptoms and signs are important indicators, they are not sensitive or specific enough to precisely monitor the HD dose.<sup>2</sup>

The following formulas have been used to quantify the dose of dialysis: urea reduction ratio (URR), Kt/V single pool (spKt/V) and equilibrated Kt/V (eKt/V). In the Kt/V ratio, the dialyzer urea clearance (K) is multiplied by dialysis time (t), the product being then divided by the patient's urea distribution volume (V). K depends on dialyzer size, blood flow rate and dialysate flow. Although t normally ranges between 3 and 4 hours (180-240 minutes per dialysis session), it can be adjusted. The patient's urea distribution volume (V) corresponds to approximately 50% of body weight, and may be more precisely estimated with an anthropometric equation which considers gender, age, height and weight (Watson's equation, for example).<sup>3,4</sup>

The adequate standard HD dose is estimated for patients undergoing three sessions a week. Dialysis adequacy is set by the *National Kidney Foundation Disease Outcomes Quality Initiative* (NKF-DOQI) guidelines, which recommend that spKt/V should be kept over 1.2.<sup>2</sup>

A DOQI-approved method for Kt/V calculation is Daugirdas's formula (1996):  $spKt/V = -\ln(R - 0.008 \times t) + (4 - 3.5 \times R) \times 0.55 \times UF/V$ , in which R is predialysis urea/postdialysis urea, t is dialysis time in hours, -ln is the negative natural logarithm, UF is weight loss in kilograms and V is the anthropometric urea distribution volume in liters, which may be calculated with Watson's equation or simply estimated as  $0.55 \times$  postdialysis weight.<sup>3,4</sup> Another option is to use Lowrie's formula (1983):  $Kt/V = \ln$  predialysis urea/postdialysis urea.<sup>5</sup>

NKF-DOQI and Brazilian guidelines have recommended that the dialysis dose should be controlled, with blood samples, at least once a month.<sup>2</sup> However, there are now dialysis machines that provide on-line real-time monitoring of dialysis efficiency, by showing Kt/V on the screen. On-line clearance monitors (OCMs) measure the difference of conductivity between the dialysis fluid entering

and leaving the dialyzer, through the difference of electrolyte concentration. This measurement is used to calculate the ionic dialysant, which is very close to effective urea clearance, as long as dialysant flow, blood flow and blood electrolyte composition are kept constant during measurement time. This method, which is easy to use and has low cost, is based on the assumption that sodium clearance equals urea clearance.<sup>2,6</sup>

This non-invasive method for Kt/V determination is unlikely to substitute for routine blood sampling, although OCMs provide an opportunity for monitoring unstable patients, chiefly in relation to dialysis quality, through verification of the Kt/V at the end of each dialysis session, with prompt problem identification and early resolution.<sup>7</sup>

Therefore, the purpose of this study was to compare Kt/V results obtained with Lowrie's formula (L Kt/V) with those obtained with Daugirdas's formula (D Kt/V), and the latter with OCM-measured results (OCM Kt/V).

## METHOD

This was an observational, quantitative study undertaken at the Hemodialysis Unit of the Hospital São Lucas of the Pontifícia Universidade Católica do Rio Grande do Sul (HSL-PUC/RS), Brazil.

The sample was composed of all CKD patients on HD at the unit. Patients under 18 years of age were excluded from the study.

Data were collected from laboratory exams and Kt/V results obtained from the Fresenius 4008S HD machines (Fresenius Medical Care AG, Bad Homburg, Germany) equipped with an OCM, on the same day blood sampling occurred. The standard dialysate flow, in all machines, was 500 ml/min. Each patient underwent two blood samplings, which were performed on the second dialysis session of the first week of the month, for two weeks.

Blood sampling occurred at two time-points: in the first minute of dialysis a blood sample was obtained from the arterial line of the extracorporeal system (predialysis sample); the second sample was obtained soon after the prescribed dialysis time was completed. Blood pump flow was reduced to less than 100 ml/min, for two minutes, according to the unit's protocol. Only then was the sample obtained from the arterial line (postdialysis sample).

In order to calculate the Kt/V, the following data were collected: dry weight, weight gain

between sessions, height, age, sex, blood flow and hematocrit.

We used descriptive statistics and categorical data, described as frequencies and percentages. Continuous variables were described as means and standard deviations when there was a normal distribution. Comparison between the formulas was made through variance analysis (ANOVA), with identification of the differences through Bonferroni's test, with significance set at  $p < 0.05$ . The *Statistical Package for the Social Sciences version 17.0 (SPSS) program was used for the statistical calculations.*

The study was approved by the Ethics Committee of the HSL-PUC/RS (protocol 10/05098).

## RESULTS

We assessed 95 HD sessions of a total of 59 patients, 95% of the sessions lasting 4 hours.

The clinical and demographic variables of the sample are presented in Table 1. Table 2 shows the distribution of the patients according to their underlying disease.

ANOVA between the formulas showed a statistically significant difference ( $p = 0.003$ ). Mean L Kt/V, obtained through blood samples, was 1.31 ( $\pm 0.24$ ). Mean second-generation D Kt/V was 1.41 ( $\pm 0.26$ ). Although there was a significant difference between these results ( $p = 0.008$ ), the formulas had a good Pearson's correlation of 0.950 ( $p < 0.000$ ).

Mean second-generation D Kt/V, obtained through blood samples, was 1.41 ( $\pm 0.26$ ). Mean non-invasive OCM Kt/V was 1.32 ( $\pm 0.30$ ). Comparison between D Kt/V and OCM Kt/V showed a statistically relevant significance ( $p = 0.011$ ) and a low Pearson's correlation of 0.346 ( $p < 0.001$ ).

Comparison between L Kt/V and OCM Kt/V did not show statistical significance ( $p = 0.999$ ) and had an adequate Pearson's correlation of 0.577.

## DISCUSSION

In this study there was a predominance of men (56% of the sample), a result which, along the mean age, is similar to that of other studies.<sup>8</sup> Our results are in agreement with the 2010 census undertaken by the Brazilian Nephrology Society, which showed that 57% of the Brazilian population on HD is composed of men, the male sex being a risk factor for CKD. In addition, 35.2% of

the dialysis population have hypertension as their main underlying disease, followed by diabetes mellitus in 27.5% of the cases.<sup>1,9</sup>

Our study also showed hypertension as the main underlying disease (42%), followed by diabetes mellitus (12%), glomerulonephritides (8%) and polycystic kidney disease (7%). A previous study undertaken in the south of Brazil found hypertension as the underlying disease in 36.7% of all CKD cases, with diabetic nephropathy accounting for 31.4%.<sup>8</sup>

In this study, mean hematocrit was 32.9%, which is equivalent to a hemoglobin concentration of 11g/dl, slightly under what is recommended in the literature. Another study undertaken in Porto Alegre, at another dialysis unit, showed hematocrit values very close to ours (mean 33.5%).<sup>10</sup> Notwithstanding, the UK Renal Association guidelines recommend that hemoglobin should

**Table 1** CLINICAL AND DEMOGRAPHIC VARIABLES OF THE STUDY SAMPLE (n = 59)

Variable	Summary
Male sex (n)%	33 (56)
Age (years)	57 $\pm$ 14
Mean weight gain between dialysis sessions (kg)	2.4 $\pm$ 1.0
Dry weight (kg)	69.2 $\pm$ 15.4
Height (m)	1.6 $\pm$ 0.9
Blood flow (ml/min)	293.7 $\pm$ 28.4
Dialysate flow (ml/min)	500
Dialysis time (h)	3.9 $\pm$ 0.3
Hematocrit (%)	32.9 $\pm$ 4.9

Source: Data collected by the researcher.

Note: The data are presented as means  $\pm$  standard deviations, frequencies, absolute numbers and percentages.

**Table 2** UNDERLYING DISEASES OF THE STUDY PATIENTS (n = 59)

Underlying disease	n (%)
Hypertension	25 (42)
Diabetes mellitus	7 (12)
Glomerulonephritides	5 (8)
Polycystic kidneys	4 (7)
Other diseases	11 (19)
Not reported	7 (12)

Source: data collected by the researcher.

Note: The data are presented in absolute numbers and percentages.

be kept between 10 and 12 g/dL in CKD patients stages 4 and 5, with the use of stimulants of erythropoiesis.<sup>11</sup>

Research has demonstrated that weight gain over 2.5 kg was associated with increases of both systolic and diastolic predialysis blood pressure.<sup>12</sup> Our patients had a mean interdialytic weight gain of 2.4 kg ( $\pm 1.03$ ).

Dialysis dose is a good marker of dialysis quality. It is thus essential to know the actual dialysis dose that is being delivered at each session.<sup>2</sup> According to the DOQI guidelines, the minimum value recommended for three sessions a week is a Kt/V over 1.2.<sup>2</sup>

Our Kt/V results are, on average, in accordance with what is advised, being 1.31 ( $\pm 0.24$ ) for Lowrie, 1.41 ( $\pm 0.35$ ) for Daugirdas and 1.32 ( $\pm 0.29$ ) for OCM. There was a significant difference between the D Kt/V and L Kt/V and OCM Kt/V.

A Spanish study observed that concordance between D Kt/V and Kt/V obtained with other formulas varies. Because Daugirdas formula overestimates Kt/V in comparison with Lowrie's, the authors proposed a 1997 K/DOQI criterion, according to which dialysis is considered adequate when D Kt/V is 1.2 or above and L Kt/V is 1.0 or above.<sup>6</sup>

This probably occurs because Daugirdas's formula includes convective loss, that is the weight difference divided by the distribution volume.<sup>3</sup> On the other hand Lowrie's formula and the OCM assess diffusive loss only. The weak correlation between the OCM and Daugirdas's formula may be accounted for by the different types of transport. OCM Kt/V is diffusive while D Kt/V is convective. Lowrie's formula and OCM have good correlation, possibly due to the same transport mechanism (diffusive) they assess.

Another Spanish study compared OCM Kt/V and D Kt/V (second generation), but in hemodiafiltration sessions of chronic patients. There was good correlation ( $r = 0,952$ ), with mean OCM Kt/V of  $1.49 + 0.54/\text{session}$  and D Kt/V of  $1.74 + 0.58/\text{session}$ .<sup>13</sup> The difference we found, in comparison with the Spanish study, may be attributed to hemofiltration, which has greater convective loss, partially determined by dialysate flow (800 ml/min), ultrafiltrate, blood flow and procedure time.<sup>13</sup> In our study, the dialysate flow was 500 ml/min, and only hemodialysis sessions were assessed.

Kt/V is very important for the assessment of dialysis quality and adequacy. Each formula has its own relevant characteristics, Lowrie's formula being simple,

easily understood and readily acceptable. Although more complex, Daugirdas's formula is widely used, as it includes individualized information such as height, weight and blood flow. These data are also included in the OCM measurements, but with the added bonus of providing real-time Kt/V values, which allow prompt interventions to increase Kt/V should the need arise.

## CONCLUSION

The data suggest a statistically significant difference between the results obtained with Daugirdas's formula and those obtained with Lowrie's formula and the OCM.

Our study demonstrated that although these formulas may lead to different results, there is good correlation between them. The important goal is not to compare results from different formulas or identify the best one, but set a standard for the formula in use. We confirmed that OCM is a practical instrument for daily use, to complement the other formulas, helping to adequate the dialysis dose delivered to reach excellent patient's benefit. It should be highlighted, however, that the patient's clinical picture is above any formula and should be the ultimate guide to dialysis adequacy.

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