Determination of Dialysis Dose
- *A Clinical Comparison of Methods* -

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Introduction and Objectives

Within the dialysis community quality standards have been debated extensively; the European Best Practice Guidelines recommended as minimum treatment dose an equilibrated Kt/V = 1.2 [1]. In clinical practice this minimum threshold value is not achieved for each and every patient. [2,3]

Clinical practice guidelines such as NKF-K/DOQI or European Best Practice Guidelines recommend regular measurements of the delivered haemodialysis dose ***Kt/V*** using a validated method. Nowadays, automatic on-line measurements are available, as alternatives to the conventional method with blood samples, adjacent laboratory analysis of urea concentrations and subsequent calculation.

Methods

The clinical trial was designed as prospective, observational, international, multi-centre study to compare three different methods of dialysis dose assessment in clinical routine: ***Kt/V*Dau**, ***Kt/V*OCM**, and ***Kt/V*BCM**.

The dialysis dose measured via blood samples, laboratory analysis of the urea concentration and application of Daugirdas' formula is evaluated in this study as standard method (***Kt/V*Dau**).

The dialysis dose measured via automatic **O**n-line **C**learance **M**onitor (OCM) with anthropometric estimate (Watson) of the urea distribution volume ***V*** is the second method determined in this study (***Kt/V*OCM**).

For a more accurate ***Kt/V*** measured by OCM the urea distribution volume ***V*** is additionally measured by the **B**ody **C**omposition **M**onitor (BCM, Fresenius Medical Care) instead of being only estimated: This is the third method to determine dialysis dose (***Kt/V*BCM**).

In this study these 3 different methods to determine dialysis dose were simultaneously applied in each patient. The trial was planned as a study with all eligible patients of each study centre, thus a nearly complete cross-section of those patients, who comply with the selection criteria.

Results

18 European dialysis centres participated in this prospective clinical trial. 1606 patients on haemodialysis (HD) or on-line-HDF (oHDF) were screened whether eligible for the study, 1089 patients were enrolled, and 1076 patients had full data set and were analyzed, see Fig. 1.

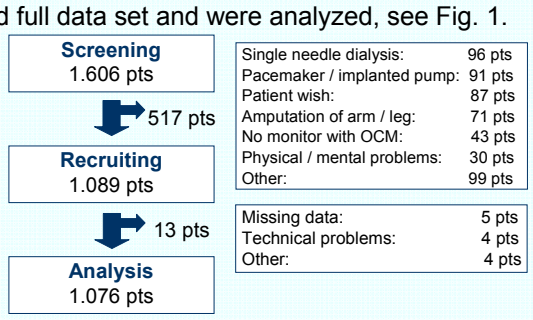

Fig. 1
Patient flow chart. Single needle HD was excluded due to OCM, pacemaker / implanted pumps / large amputations due to BCM. Patients with physical or mental problems were not recruited. All patients fulfilling inclusion criteria were informed, volunteers with signed informed consent were recruited.

In the analysis cohort 38 % of the patients were treated by HD and 62 % by oHDF, for patient characteristics see Table 1: The mean values for oHDF in comparison to HD show lower age (-5.4 years), more males (+3.5 %), slightly higher BMI (+0.1 kg/m²) and more anuric patients (+15 %).

Table 1
Patient characteristics of the analysis cohort (N=1076); data expressed as number, mean value ± standard deviation or percentage.

Characteristics	Units	All Patients (N=1076)	Patients on HD (N=407)	Patients on oHDF (N=669)
Age	years	66.0 ± 13.9	69.3 ± 13.2	63.9 ± 13.9
Sex	%: male female	57.0 / 43.0	54.5 / 45.5	58.4 / 41.6
Body mass index	kg/m²	26.1 ± 5.2	26.0 ± 5.1	26.1 ± 5.2
Residual renal function*	%: low medium high	30 / 25 / 45	21 / 22 / 57	36 / 26 / 38

*low: < 100 ml/day, 100 ml/day ≤ medium ≤ 500 ml/day, high: > 500 ml/day

For treatment data see Table 2: The mean values for oHDF in comparison to HD show longer treatment duration (+26 min), more processed blood (+15 L), slightly higher pre- and post-dialytic body weight (+1.6 kg and +1.2 kg) and higher ultrafiltration volume (+0.6 L).

Table 2
Treatment data of the analysis cohort (N=1076); data expressed as mean value ± standard deviation.

Treatment data	Units	All Patients (N=1076)	Patients on HD (N=407)	Patients on oHDF (N=669)
Dialysis duration	h	4.35 ± 0.47	4.18 ± 0.46	4.44 ± 0.45
Pre-dialytic weight	kg	76.5 ± 16.9	75.5 ± 16.6	77.1 ± 17.1
Post-dialytic weight	kg	74.6 ± 16.6	73.9 ± 16.3	75.1 ± 16.8
Ultrafiltration volume	L	2.34 ± 1.21	1.97 ± 1.19	2.57 ± 1.17
Volume of processed blood	L	82.7 ± 19.3	73.4 ± 18.4	88.4 ± 17.5

As already observed by others[4] the mean urea distribution volume was larger if anthropometrically estimated than if measured (-1.7 L), see Table 3. The mean dialysis doses were higher for oHDF in comparison to HD, independently from the determination method (***Kt/V*Dau**: +0.36, ***Kt/V*OCM**: +0.28, ***Kt/V*BCM**: +0.33).

Table 3
Urea distribution volume ***V*** and dialysis dose ***Kt/V*** in the analysis cohort (N=1076); data expressed as mean value ± standard deviation.

Dialysis dose data	Units	All Patients (N=1076)	Patients on HD (N=407)	Patients on oHDF (N=669)
V_{Watson}	L	37.5 ± 7.0	36.8 ± 7.0	37.9 ± 7.1
V_{BCM}	L	35.8 ± 7.5	35.3 ± 7.3	36.0 ± 7.6
Kt/V_{Dau}	-	1.74 ± 0.45	1.51 ± 0.40	1.87 ± 0.43
Kt/V_{OCM}	-	1.47 ± 0.34	1.30 ± 0.30	1.58 ± 0.32
Kt/V_{BCM}	-	1.65 ± 0.42	1.44 ± 0.37	1.77 ± 0.40

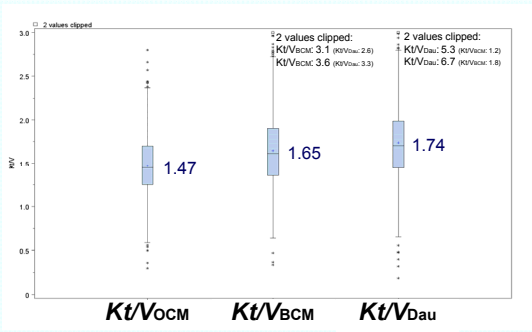

Fig. 2
Box and whisker plot of dialysis dose in the analysis population (1076 patients):
Dialysis dose measured by **O**n-line **C**learance **M**onitor with estimated urea distribution volume ***V*Watson** (***Kt/V*OCM**), dialysis dose determined by on-line clearance monitor with measured urea distribution volume ***V*BCM** (***Kt/V*BCM**), .and conventional dialysis dose with blood samples, urea concentration determination and Daugirdas' formula (***Kt/V*Dau**).

In the analysis cohort dialysis dose was measured as ***Kt/V*OCM** = 1.47 ± 0.34, ***Kt/V*BCM** = 1.65 ± 0.42, and ***Kt/V*Dau** = 1.74 ± 0.45, see Fig. 2. On average, ***Kt/V*OCM** resulted in 16 % lower values compared to ***Kt/V*Dau**, whereas ***Kt/V*BCM** was 5 % lower than ***Kt/V*Dau**. Outliers were incidentally observed for ***Kt/V*Dau** due to falsely high urea reduction ratio >95% (possible measurement or laboratory errors), whereas OCM based dose measurements ***Kt/V*OCM** and ***Kt/V*BCM** delivered realistic values. Correlation between ***Kt/V*Dau** (without outliers) and ***Kt/V*OCM** was 0.81, and 0.82 between ***Kt/V*Dau** (without outliers) and ***Kt/V*BCM**, see also Fig. 3.

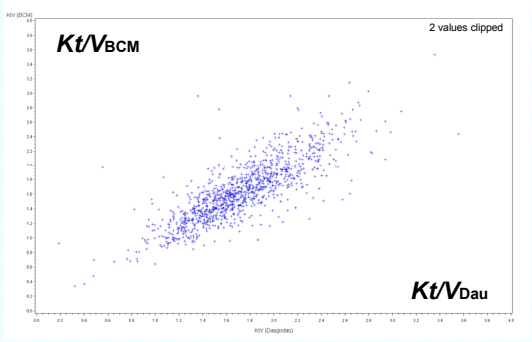

Fig. 3
Dialysis dose in the analysis population (1076 patients): Dialysis dose determined by on-line clearance monitor with measured urea distribution volume V (***Kt/V*BCM**) compared to the conventional dialysis dose with blood samples, urea concentration determination and Daugirdas' formula (***Kt/V*Dau**).

Comparison between ***Kt/V*Dau** and ***Kt/V*BCM** shows acceptable agreement over the whole range, independent of Kt/V, see Fig. 4.

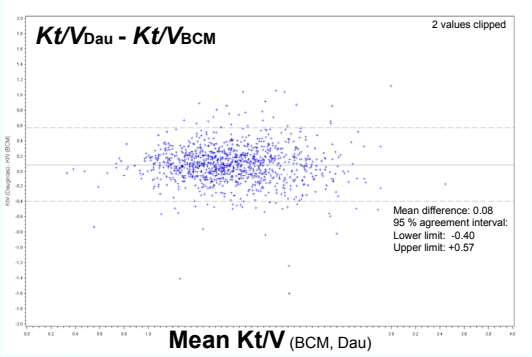

Fig. 4
Bland-Altman plot of dialysis dose in the analysis population (1076 patients): Comparison of dialysis dose measured by on-line clearance monitor with measured urea distribution volume ***V*BCM** (***Kt/V*BCM**) and conventional dialysis dose with blood samples, urea concentration determination and Daugirdas' formula (***Kt/V*Dau**).

Discussion

Methods to quantify dialysis dose based on blood sampling are critical concerning proper timing, compliance with recommended methods, and are known for occasional mistakes in handling, storage or transport of the samples or in laboratory errors of measuring urea.[5-10] The second generation Daugirdas' formula was modelled in 1993 from 500 HD sessions with a total error in an acceptable 5% range throughout the investigated range of dialysis doses (0.7<***Kt/V***<2.1).[5] We observed that the conventional method ***Kt/V*Dau** based on blood sampling was occasionally prone to outliers, whereas the automated dialysis dose determinations ***Kt/V*OCM** and ***Kt/V*BCM** delivered plausible values.

Although the On-line Clearance Monitor accurately measures urea clearance ***K*** and effective dialysis duration ***t***[11], for the dialysis dose ***Kt/V*** an accurate urea distribution volume ***V*** is mandatory. The anthropometric Watson formula was derived from 723 adults obtained from dilution studies,[12] it is applied as default value in the dialysis monitor 4008 and 5008. Meanwhile, this anthropometric estimate was suggested to overestimate the total body water of HD patients. [4,13-17]

The accuracy of BCM to determine total body water was evaluated earlier in more than 1,000 healthy individuals against available gold standard reference methods (e.g. bromide, deuterium, dual-energy X-ray absorptiometry, air displacement plethysmography, clinical assessment), and agreement with clinical assessment of fluid status was demonstrated in several hundred patients.[18,19] In our study the BCM measurement delivered with 35.8 L a mean urea distribution volume ***V*** that was 1.7 L lower than the estimate derived from the Watson formula. Due to this lower urea distribution volume the dialysis dose ***Kt/V*BCM** (with all parameters ***K***, ***t***, and ***V*** measured) was higher than the dialysis dose ***Kt/V*OCM** (with only ***K*** and ***t*** measured, and ***V*** estimated according to Watson) and closer to ***Kt/V*Dau**.

Conclusions

Due to the automated procedure the on-line clearance measurement with the Watson estimate of the urea distribution volume ***Kt/V*OCM** was easiest to use, but the difference to the conventional method was larger; the automatic on-line clearance measurement with the urea distribution volume measured by Body Composition Monitor ***Kt/V*BCM** had a higher correlation to the conventional method.

REFERENCES
1 European Best Practice Guidelines for Haemodialysis (part 1). Nephrol Dial Transplant 2002; 17 (suppl 7): S16-31.
2 Coyne D, Delmez J, Spence G, et al. Impaired delivery of hemodialysis prescriptions: an analysis of causes and an approach to evaluation. J Am Soc Nephrol. 1997 Aug;8(8):1315-8.
3 Priess M, Benz RL. Quantifying the role of factors that limit attainment of K/DOQI urea reduction ratio dialytic goal. Clin Nephrol. 2006 Aug;66(2):98-102.
4 Kloppenburg W, Stegeman C, de Jong P, et al. Anthropometry-based equations overestimate the urea distribution volume in hemodialysis patients. Kidney Int. 2001 Mar;59(3):1165-74.
5 Daugirdas J. Second generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. J Am Soc Nephrol 1993; 4: 1205-1213.
6 Lindsay R, Stemby J. Future directions in dialysis quantification. Semin Dial. 2001 Jul-Aug;14(4):300-7.
7 Geddes C, Traynor J, Walbaum D, et al. A new method of post-dialysis blood urea sampling: the 'stop dialysate flow' method. Nephrol Dial Transplant. 2000 Apr;15(4):517-23.
8 Wallin O, Söderberg J, Van Guelpen B, et al. Preanalytical venous blood sampling practices demand improvement- a survey of test-request management, test-tube labelling and information search procedures. Clin Chim Acta. 2008 May;391(1-2):91-7.
9 Jensen E, Stahl M, Brandslund I, et al. Stability of heparin blood samples during transport based on defined pre-analytical quality goals. Clin Chem Lab Med. 2008;46(2):225-34.
10 Beto J, Bansal V, Ing T, et al. Variation in blood sample collection for determination of hemodialysis adequacy. Council on Renal Nutrition National Research Question Collaborative Study Group. Am J Kidney Dis. 1998 Jan;31(1):135-41.
11 Kuhlmann U, Goldau R, Samadi N, et al. Accuracy and safety of on-line clearance monitoring based on conductivity variation. Nephrol Dial Transplant 2001; 16: 1053-8
12 Watson P, Watson I, Batt R. Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr. 1980 Jan;33(1):27-39.
13 Wuepper A, Tattersall J, Kraemer M, et al., Determination of urea distribution volume for Kt/V assessed by conductivity monitoring. Kidney Int 2003; 64: 2262-2271.
14 Ikizler T, Sezer M, Filakoll P, et al. Urea space and total body water measurements by stable isotopes in patients with acute renal failure. Kidney Int. 2004 Feb;65(2):725-32.
15 Tzamaloukas A, Murata G, Vandejagt D, et al. Body composition evaluation in peritoneal dialysis patients using anthropometric formulas estimating body water. Adv Perit Dial. 2003;19:212-6.
16 Daugirdas J, Greene T, Depner T, et al. Anthropometrically estimated total body water volumes are larger than modeled urea volume in chronic hemodialysis patients: effects of age, race, and gender. Kidney Int. 2003 Sep;64(3):1108-19.
17 Lindley E, Charmey P, 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 Jan;24(1):211-6. Epub 2008 Aug 12.
18 Moissl U, Wabel P, Charmey P, et al. Body fluid volume determination via body composition spectroscopy in health and disease. Physiol Meas. 2006 Sep;27(9):921-33. Epub 2006 Jul 25.
19 Wabel P, Charmey P, Moissl U, et al. Importance of whole-body bioimpedance spectroscopy for the management of fluid balance. Blood Purif. 2009;27(1):75-80. Epub 2009 Jan 23.

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