ONLINE KT/V (UREA) MONITORING IN MAINTENANCE HEMODIALYSIS PATIENTS, SINGLE CENTER EXPERIENCE.

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ABSTRACT:

Introduction: *Dialysis adequacy is an important factor affecting overall morbidity and mortality in patients on maintenance hemodialysis, The Urea reduction Rate (URR) measures the change between pre-dialysis and post-dialysis serum urea levels. Single pool Urea clearance index (Kt/V) was developed to include both the volume of distribution of urea and the time of effective dialysis session in the equation of determining dialysis adequacy; recently online volume monitoring and hence online Kt/V (urea) were incorporated in the dialysis machines to facilitate measurement of dialysis adequacy.*

Aim of The Work: *evaluate the relation between On-line Kt/V_{Urea} and the conventional adequacy measurement method Urea Reduction ratio (URR).*

Methods: *208 patients on maintenance Hemodialysis at Dubai Hospital –Dubai Heath Authority, for at least 3 months and followed up for 4 months were included.*

Results and Discussion: *108 Patients were male (52%) and 100 females (48%), age (Mean±SD) 59±18.6 years old, and Duration on dialysis (Mean±SD) 51.2±21 months. We found a statistically significant correlation between the online Kt/V and the measured one. R-square 0.209 and P-value 0.002, which was independent of the other covariates included in the model. ROC analysis showed the online value of online Kt/V in comparison to the standard measured URR at different URR cut-off values, at URR > 60%, the overall model accuracy 83% with area under the curve AUC (95%CI) 0.873(0.805-0.942) P-value < 0.001. With higher URR > 70%, the overall model accuracy improved to 87.4% with area under the curve AUC (95%CI) 0.913(0.875-0.951) P-value < 0.001.*

Conclusion*: Our results confirm the hypothesis that the online Kt/V Urea function incorporated in many recent dialysis machines is a sensitive indicator of dialysis adequacy delivered during hemodialysis sessions.*

Keywords: *Hemodialysis, online adequacy, urea reduction rate, Online Kt/V, single pool Kt/V_{Urea}*

INTRODUCTION:

Dialysis adequacy has an important role in reducing cardiovascular events and the overall morbidity and mortality in patients on maintenance hemodialysis, which has been proved in multiple trials [(1-3)].

Adequacy of dialysis is vital for the overall outcome of patients on maintenance hemodialysis and has been linked to mortality

and morbidity. KDOQI clinical practice guideline for hemodialysis adequacy recommends a target single pool Kt/V of ≥1.4 per hemodialysis session for patients treated thrice weekly, with a minimum delivered of single pool Kt/V ≥ 1.2 per hemodialysis session. In addition, KDIGO Clinical Practice Guidelines for AKI recommend delivery of Kt/V > 1.3 on a thrice-weekly dialysis schedule, corresponding to a hemodialysis delivery with a URR > 0.69 three times per week [4&5]. Multiple methods are used to measure dialysis adequacy and progressive development with new options added to dialysis machines. For patients on regular hemodialysis, the adequacy was measured with Urea as the clearance marker. Urea reduction Rate (URR) measures the change between the pre-dialysis and post-dialysis serum urea level; however, this formula ignored the volume removed during the dialysis session and was less accurate [6]. Single pool Urea clearance index (Kt/V) developed to include both the volume of distribution of urea and the time of effective dialysis session in the equation of determining dialysis adequacy; however, multiple blood sampling and special sampling techniques are required to generate accurate results [7&8]. Single pool Kt/V_{Urea} calculated using second generation logarithmic (Daugirdas) equation: ***Kt/V=-ln (R-0.008 x t)+(4−3.5 x R) x 0.55 x UF/Vurea.*** Where R is the ratio of post-dialysis BUN, (BUN-post) divided by pre-dialysis BUN (BUN-pre), t is the dialysis session duration in hours, UF is the ultrafiltration volume in liters, and V-urea is the estimated volume of distribution of urea [9&10&11].

An online monitoring system for dialysis dose calculations has been incorporated in recent dialysis machines and has been tested not only to measure the total delivered dose during a hemodialysis session but also to evaluate the clearance process during dialysis and give immediate feedback to online adjustments. This timely dose adjustment made it possible to provide consistently adequate dialysis doses to hemodialysis patients. Online calculation of Kt/V_{urea} from conductivity or UV-absorbance measurements in the dialysate is incorporated in hemodialysis monitors and makes it possible to estimate the dialysis dose without the need for blood or dialysate samples [12&13&14]

AIM OF THE WORK:

Our study aims to confirm the relationship between the online clearance monitoring of adequacy (online Kt/V) feature built-in new dialysis machines (online Kt/V) and the conventional blood samples adequacy measurement method Urea Reduction ratio (URR). Also, to determine the accuracy and efficiency of online clearance monitoring and feasibility of use as adequacy marker with reduction of blood sampling, thus, reducing the burden on dialysis unit and laboratory staff and reducing the overall dialysis cost.

METHODS:

208 patients on maintenance Hemodialysis at Dubai Hospital –Dubai Heath Authority for at least 3 months before the start of the study and followed up for 4 consecutive months, were included. Data collected included age, gender, vascular access, number of sessions per week, session duration, dialyzer type (high or low flux), and modality of dialysis (Hemodialysis or hemodiafiltration). Data were tabulated and analyzed using SPSS 26 statistical software, with significance level (0.05) and statistical power (95%). Student T-test & Annova F-test for comparison between continuous variables and Chi-square test for comparison between categorical variables were used. Pearson correlation and linear regression analysis for correlation between adequacies measured by dialysis machine (online Kt/V) and urea reduction ratio. Also, a multivariate logistic regression model for individual factors

influences the correlation with a multivariate model including vascular access, dialysis modality, number of weekly dialysis sessions, duration of the session, blood flow rate, dialysate flow rate, and type of dialyzer used to determine confounders that might affect the relation between online Kt/V and URR.

Receiver operating curve (ROC) analysis for evaluation of the predictive value of online Kt/V (urea) as a monitor of Urea clearance and dialysis adequacy against standard Urea reduction rate at different cut-off values.

Ethical consideration:

The study was approved by the institutional Ethics Committee of (Dubai Scientific Research Ethics Committee, of Dubai Health Authority) (Approval No: DSREC-12/2016_09).

RESULTS AND DISCUSSION:

208 patients who matched the inclusion criteria were included. This includes 108 male (52%) and 100 female (48%), age (Mean±SD) 59±18.6 years old, Duration on dialysis (Mean±SD) 51.2±21 months, vascular access was arteriovenous fistula in 102 (49%) and permanent hemodialysis catheter in 105 (51%), dialysis modality was mainly conventional Hemodialysis in 193(88%) and Hemodiafiltration in 25 (12%). The dialyzer used was high flux dialyzer in 56 (26.9%) and low flux dialyzer in 152 (73.1%), while dialysate flow rate (Mean±SD) 530.5±54.8ml/min and blood flow rate (Mean±SD) 261±51.6 ml/min. Most patients completed their 4-hour schedule 160 (76.9%), compared to those who have a mean dialysis session duration of less than 4 hours 48 (23.1%). 189 patients (90.9%) were on thrice weekly dialysis schedule, and the majority have been on dialysis for 12-60 months 116 (55%), 52(25%) for more than 60 months and only 40 (19.2%) on dialysis for less than 12 months.

4 readings of online Kt/V reported over 4 consecutive months on midweek sessions of the same date of monthly laboratory investigations, and the average for different study parameters tabulated in Table (1) was used in further analysis. We found a statistically significant correlation between online Kt/V and the measured URR as shown in Figure (1) with an ***R-square of 0.209 and P-value of 0.002***. Which was independent of the other covariates included in the model age, duration of dialysis, number of sessions per week, vascular access, blood and dialysate flow, dialysis modality, and the type of dialyzer used. As illustrated in Table (2) and Figure (3), the ROC analysis showed the predictive value of online Kt/V in comparison to the standard measured URR at different URR cut-off values. At URR > 60%, the overall model accuracy of 83% with area under the curve AUC (95%CI) 0.873(0.805-0.942), *P*-value < 0.001. With higher URR > 70%, the overall model accuracy improved to 87.4% with area under the curve AUC (95%CI) 0.913(0.875-0.951) *P* < 0.001.

Table 1: Online Kt/V and Measured Urea Reduction Rate Relation to Different Study Parameters

		n (%)	MEASURED URR (average of 4 readings)	online KT/V (average of 4 readings)
			Mean±SD	Mean±SD
Age Groups	Less Than 40 Years Old	27(13)	66.5±5.9	1.3±0.2
	40 - 60 Years Old	63(30.3)	66.7±5.7	1.2±0.2
	60 - 80years Old	99(47.6)	66.1±5.2	1.1±0.2
	More Than 80 Years Old	19(9.1)	64.7±5.3	1.1±0.1
Duration on Dialysis Groups	12 Months or Less	40(19.2)	65.4±3.8	1.1±0.1
	12-60 Months	116(55.7)	65.2±5.2	1.2±0.2
	More Than 60 Months	52(25)	67.2±5.3	1.2±0.2

Vascular Access	AVF/AVG	102(49)	66.9±5.5	1.2±0.2
	Permenant Cathter	106(51)	64.7±5.1	1.1±0.2
Modality of Dialysis	Hd	193(88)	65.6±5.2	1.2±0.2
	Hdf	25(12)	67.2±6.3	1.3±0.2
Sessions/Week Groups	Less Than 3 Sessions /Week	16(7.7)	65.6±5.3	1.1±0.2
	3 Sessions /Week	189(90.9)	65.9±5.4	1.2±0.2
	More Than 3 Sessions /Week	3(1.4)	66±5.2	1.3±0.3
Session Duration Groups	Less Than 4 Hours	48(23.1)	63.5±5.1	1.1±0.1
	4 Hours	160(76.9)	67.3±5.9	1.3±0.2
Blood Flow Group	Less Than 250 Ml/Min	62(29.8)	64.6±5.6	1.1±0.1
	≥ 250 Ml/Min	146(70.2)	66.7±5.9	1.30.2
Dialysate Flow Group	500 Ml/Min	204(98.1)	64.8±5.3	1.2±0.2
	More Than 500ml/Min	4(1.9)	65.6±5.8	1.3±0.2
Dialyzer	Low-Flux Dialyzer	152(73.1)	65.5±5.2	1.1±0.2
	High-Flux Dialyzer	56(26.9)	66.4±5.9	1.2±0.2

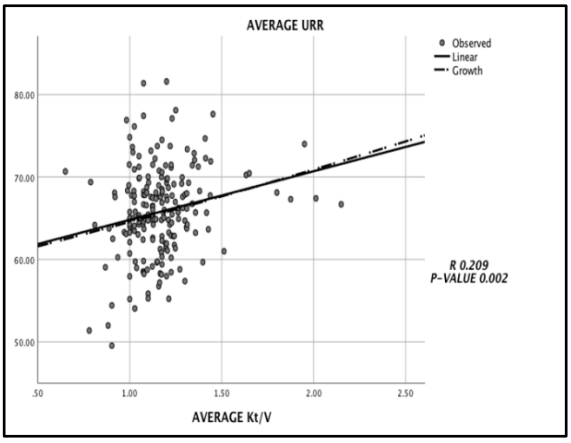

Figure 1: Correlation between Online Machine Kt/V and Measured Urea Reduction Ratio

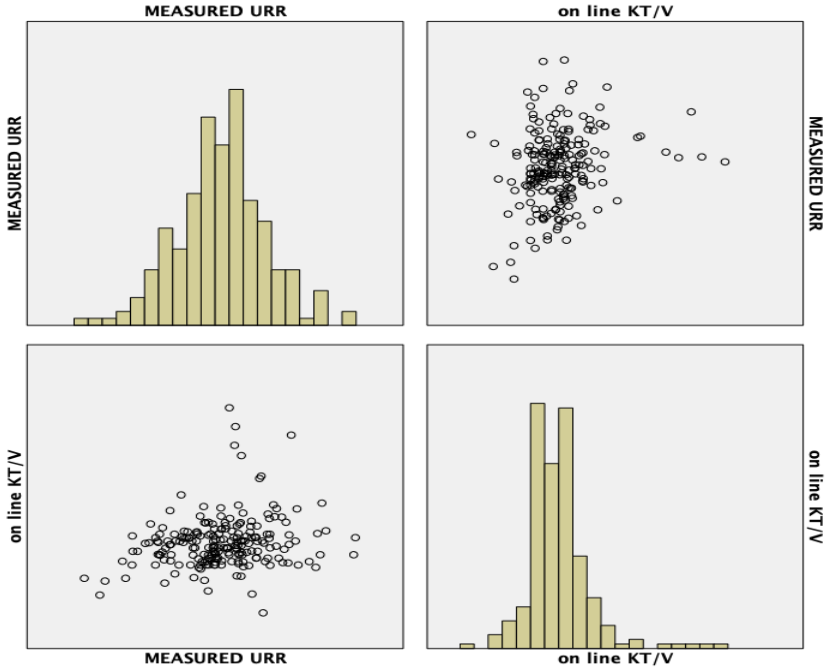

Figure 2A: Online Kt/V and URR Relation in All Subgroups

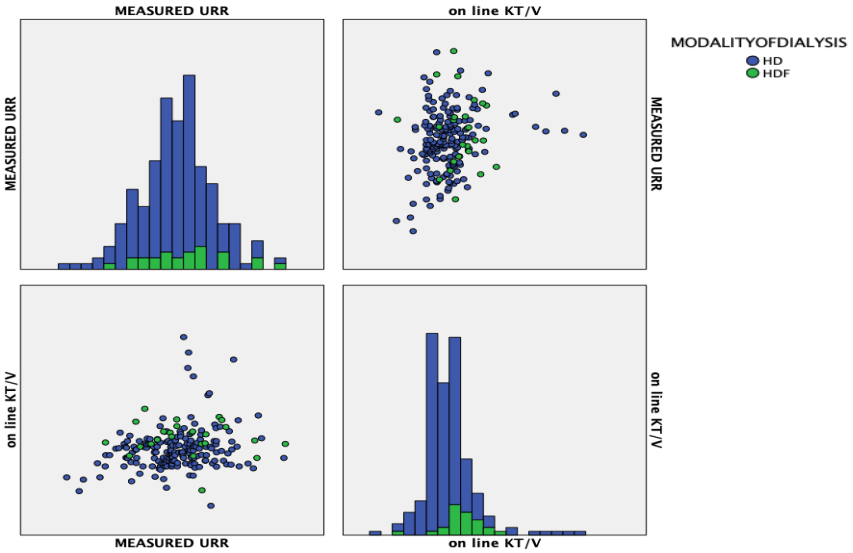

Figure 3B: Online Kt/V AND URR relation with dialysis modality

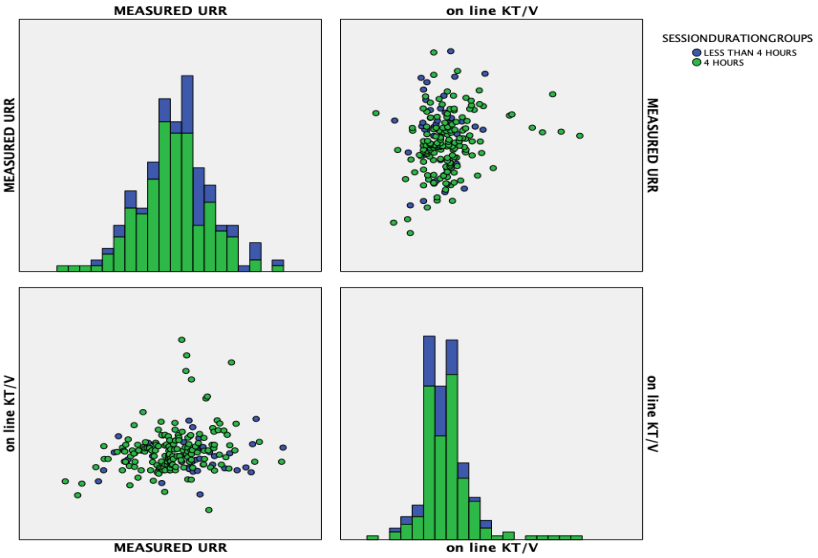

Figure 2C: Online Kt/V & URR And Relation to Dialysis Session Duration

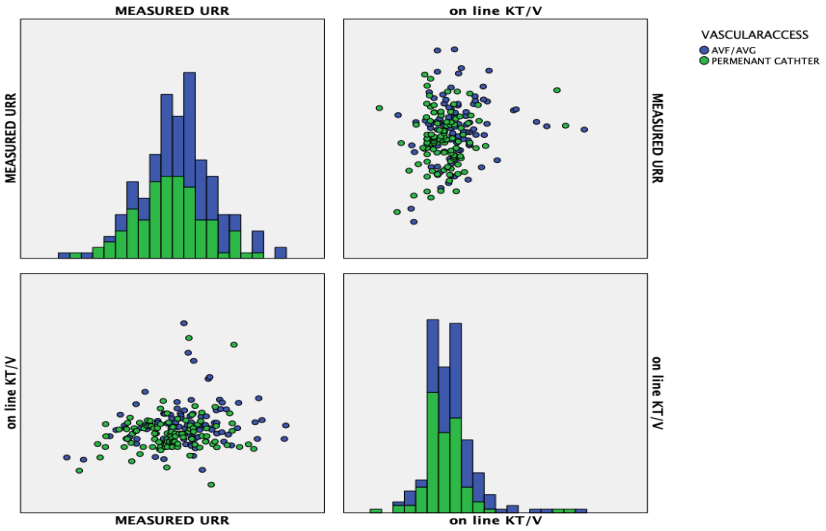

Figure 2D: Online Kt/V & URR And Relation to Vascular Access

Table 2: Roc Analysis of Predictive Value of On-Line Kt/V Against Standard Measured URR

URR Level	Positive	Negative	AUC	95% Confidence Interval		P-VALUE
				Lower Bound	Upper Bound	
URR>60	184	24	0.873	0.805	0.942	<0.001
URR>70	41	167	0.913	0.875	0.951	<0.001
Larger values of the test result variable (Online KT/V) indicate stronger evidence for a positive actual state.						
a. Under the nonparametric assumption						
b. Null hypothesis: true area = 0.5						

AUC: Area Under the Curve

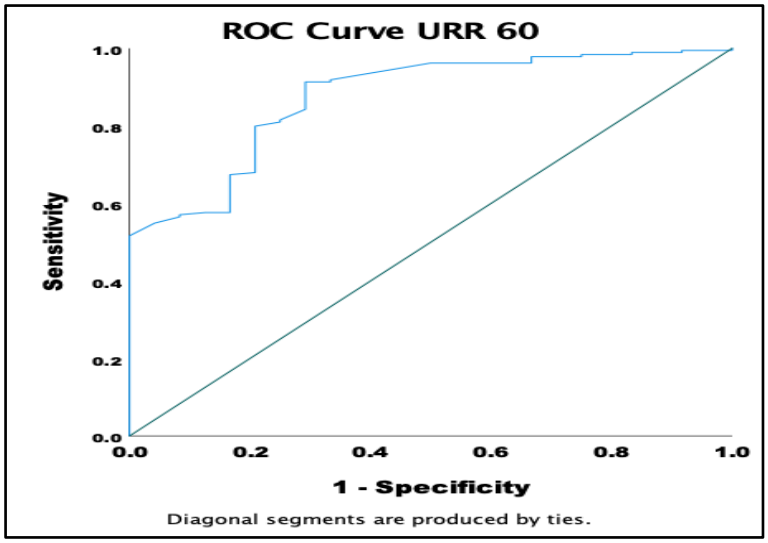

Figure 4A: Roc Curve for Predictive Value of Online Kt/V at Different URR Cut-Off Values >60%

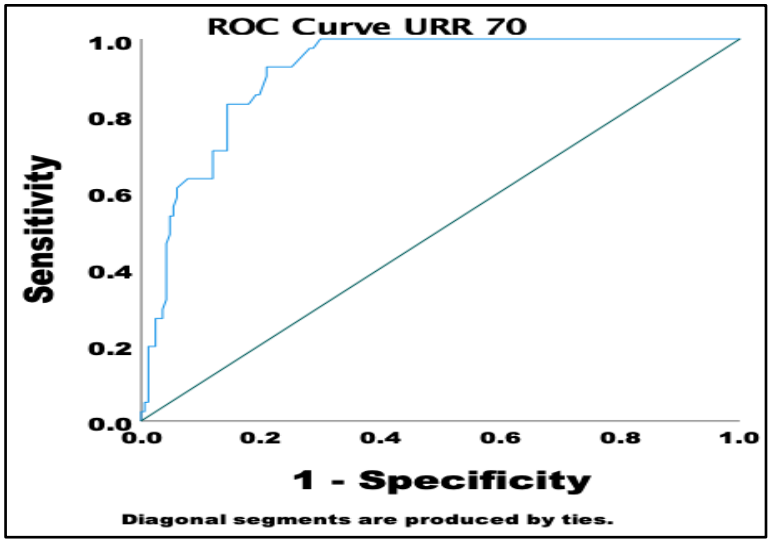

Figure 5B: Roc Curve for Predictive Value of Online Kt/V at Different URR Cut-Off Values >70%

In Figure (4) and Table (3) comparing the proportion of categories of online Kt/V to categories of measured URR, we found a significantly higher proportion of patients whose online Kt/V > 1.4 had measured URR >70% (66.7%) *P-value < 0.001*. On the other hand, the higher proportion of patients who online Kt/V < 1 had their measured URR less than 60% (63.2%) *P < 0.001*.

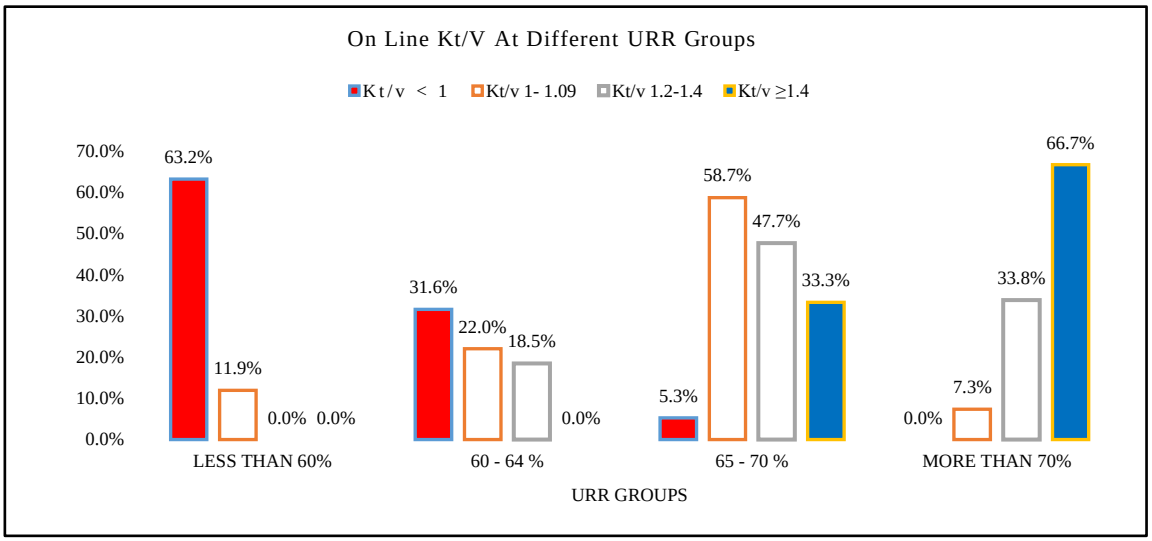

Figure 6: Online Kt/V Levels at Different URR Groups (% From X Axis Category URR Category)

Table 3: Online Kt/V at Different Measured URR Groups

Online Kt/V Groups	URR Groups								P-Value
	Less Than 60%		60 - 64 %		65 - 70 %		More Than 70%		
	N	%	N	%	N	%	N	%	
Kt/v < 1	12	63.2%	6	31.6%	1	5.3%	0	0.0%	<0.001
Kt/v 1- 1.09	13	11.9%	24	22.0%	64	58.7%	8	7.3%	0.020
Kt/v 1.2-1.4	0	0.0%	12	18.5%	31	47.7%	22	33.8%	0.040
Kt/v ≥1.4	0	0.0%	0	0.0%	5	33.3%	10	66.7%	<0.001

Our results go by previously published literature that studied the sensitivity of online monitoring of adequacy option, online blood volume monitoring, and online Kt/V_{Urea} incorporated in many dialysis monitors in timely detection of Urea clearance, thus any needed intervention decisions can be done at the bedside, hence ensuring delivery of adequate dialysis sessions while improving the overall outcome of patients on dialysis [15&16&17].

Conclusion:

Our results confirm the hypothesis that the online Kt/V (urea) function incorporated in many recent dialysis machines is a significantly sensitive indicator of dialysis adequacy delivered during hemodialysis sessions and can reduce the burden of repeated blood sampling, laboratory cost, and staff timing which can be directed towards other aspects of patient care. Further studies are needed with a large scale of patients and a wider scope of parameter measures to prove the benefits of progressive development in dialysis machines both in providing cost-effective and efficient hemodialysis treatment. Large-scale studies with a higher number of patients needed before online adequacy monitoring can substitute the costly monthly laboratory evaluation currently practiced.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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قياس كفاءة إزالة اليوريا خلال جلسة الديلزة الدموية Online Kt/V (Urea) في مرضى الفشل الكلوي المزمن تجربة مركز واحد

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مقدمة: تعد كفاية غسيل الكلى عاملاً مهمًا يؤثر على المراضة والوفيات الإجمالية لدى المرضى الذين يعانون من الفشل الكلوي المزمن والمعالجين بالديلزة الدموية ، ويقيس معدل خفض اليوريا (URR) التغيير بين مستويات ما قبل الديلزة ومستويات اليوريا في مصل ما بعد الديلزة . تم وضع مؤشر إزالة اليوريا لمجموعة واحدة (Single pool Kt/V) ليشمل كلاً من حجم توزيع اليوريا ووقت جلسة غسيل الكلى الفعالة في معادلة تحديد كفاية غسيل الكلى ؛ تم مؤخرًا دمج مراقبة الحجم الكلي للدم المتعرض للديلزة Blood volume monitoring وبالتالي online (Kt/V) urea كفاءة إزالة اليوريا خلال جلسة الديلزة في آلات غسيل الكلى لتسهيل قياس كفاءة جلسات الديلزة الدموية للكلي .

هدف الدراسة: تقييم العلاقة بين قياس كفاءة جلسات الديلزة الدموية للكلي المدمجة بماكينات الديلزة online (Kt/V) urea وطريقة قياس الكفاية التقليدية نسبة خفض اليوريا (URR).

الطرق: تم تضمين 208 مرضى يعانون من غسيل الكلى في مستشفى دبي - هيئة صحة دبي، لمدة 3 أشهر على الأقل وتمت متابعتهم لمدة 4 أشهر.

النتائج والمناقشة: كان 108 مرضى من الذكور (52٪) و 100 أنثى (48٪)، والعمر (المتوسط ± SD) 59 ± 18.6 عامًا، ومدة غسيل الكلى (المتوسط ± SD) 51.2 ± 21 شهرًا. وجدنا علاقة ذات دلالة إحصائية بين Kt/V عبر الإنترنت ومعدل خفض اليوريا المقاس . R-square 0.209 و P-value 0.002، والتي كانت مستقلة عن المتغيرات الأخرى المدرجة في النموذج. أظهر تحليل ROC القيمة الإلكترونية لـ Kt/V عبر الإنترنت مقارنة بـ URR القياسي المقاس بقيم قطع URR مختلفة، عند URR 60% >، 83% دقة النموذج الإجمالية مع مساحة تحت المنحنى > P-value (0,805-0,942) 0,873 (95% CI) AUC 0,001. مع ارتفاع ٪70 > URR، تحسنت دقة النموذج الإجمالي إلى 87.4٪ مع مساحة تحت منحنى 0.913 (95٪ CI) AUC P-value < 0.001 (0.875-0.951).

الاستنتاج: تؤكد نتائجنا الفرضية القائلة بأن قياس online Kt/V Urea المدمجة في العديد من آلات غسيل الكلى الحديثة هي مؤشر حساس لكفاية الديلزة الدموية الذي يتم تقديمه أثناء جلسات الديلزة الدموية الكلى.