Assessment of hemodialysis adequacy in patients with chronic kidney disease in the hemodialysis unit at Tanta University Hospital in Egypt

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Background and objectives

Worldwide, hemodialysis (HD) constitutes the most common form of renal replacement therapy and many studies have shown strong correlation between HD dose and clinical outcome measured by Kt/V.

This study was conducted to evaluate HD adequacy in patients with end-stage renal disease to identify the prevalence and causes of inadequate HD and the impact of HD adequacy on patient outcomes.

Patients and methods

This cross-sectional study was conducted on 100 patients in the HD unit at Tanta University Hospital. All patients gave their consent and were informed about the study purpose. Data were collected using a reliable questionnaire (including clinical, demographic, dialysis, laboratory, and radiological data). SpKt/V was used to assess the adequacy of HD. Statistical analysis was carried out for all collected data using SPSS 18. Statistical significance was determined at a P-value less than 0.05.

Results

The results revealed inadequate HD dose in 60% of the study population. The results also showed that, with increasing time and frequency of dialysis, blood flow rates, low recirculation percentages, reduction of intradialytic complaints, and well-functioning vascular access are associated with better HD adequacy. Our findings clearly showed a strong positive correlation between dialysis dose and Hb level, serum albumin level, normalized protein catabolic rate, and physical health.

Conclusion

A significant percentage of patients had inadequate HD. HD adequacy was influenced by several factors such as duration and frequency of the dialysis session, patients' complaints, and well-functioning vascular access.

Keywords:

adequacy, hemodialysis, outcomes, vascular access

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Introduction

End-stage renal disease (ESRD) causes irreversible, severe kidney failure for which patients require treatment with dialysis or kidney transplantation to survive [1]. It is a major outcome of chronic kidney disease (CKD), with an important effect on the quality of life (QOL) and health resource utilization. In addition to its costs, a large number of patients die from cardiovascular diseases before the initiation of renal replacement therapy [2].

Hemodialysis (HD) is one of the main modalities of renal replacement therapy [3].

Even though HD treatment is successful in ameliorating many of the clinical manifestations of ESRD and in postponing otherwise imminent death, HD patients still have higher mortality and hospitalization rates, as well as lower QOL, compared with the general population [4].

The concept of quality, adequacy, or appropriateness of HD, which was introduced in the 1970s, implies that dialysis should enable patients to have a normal QOL, as well as allow solid clinical tolerance with minimal problems during the dialysis and interdialysis periods [5].

Quantification of the dialysis dose is essential to the management of chronic HD treatment because the adequacy of the dose has a profound effect on patient morbidity and mortality [6].

The aim of this work was to evaluate HD adequacy in patients with ESRD who were being maintained on regular HD in the hemodialysis unit at Tanta

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Patients and methods

This study was carried out on 100 stable patients with ESRD undergoing regular HD for more than 6 months. No patient dropped out of the study.

Inclusion criteria

Patients on regular HD for 6 months (at least) by means of an arterio-venous fistula (AVF) in the hemodialysis unit at Tanta University Hospital were eligible for inclusion in the study.

Exclusion criteria

- (1) Patients who were not on regular HD.
- (2) Patients using central venous catheters or arterio-venous grafts.
- (a) The patients were divided into two groups according to Kt/V values.
- (b) Group I: This group included patients with Kt/V of at least 1.2 who were considered to have adequate dialysis dose.
- (c) Group II: This group included patients with Kt/V less than 1.2 who were considered to have inadequate dialysis dose.
- (d) All patients in this study were subjected to full history taking, complete physical examination, and laboratory investigations including blood urea nitrogen (BUN) (before dialysis and after dialysis), serum albumin, and hemoglobin (Hb) level. Urea reduction ratio (URR) was calculated using the following formula [7]:

$$\label{eq:urrange} \text{URR} = \!\! \left(\frac{\left(\text{PredialysisBUN} - \text{postdialysisBUN} \right)}{\text{PredialysisBUN}} \right) \!\!.$$

Kt/V was calculated using the second-generation Daugirdas formula [8]:

Single-pool Kt/V = -In
$$(R -0.008 \times t) + (4 -3.5 \times R) \times \text{UF/}W$$
,

where In represents the natural logarithm; R is the ratio of postdialysis to predialysis BUN; t is the length of a dialysis session in hours; UF is the ultrafiltration volume in liters; and W is the patient's postdialysis weight in kilograms. Online medical calculators were used.

Vascular access recirculation was calculated using the formula [9]:

Recirculation(%) =
$$\left(\left\lceil \frac{S - A}{S - V} \right\rceil \right) \times 100$$
.

In the above formula S, A, and V refer to the systemic urea concentrations in the peripheral blood, blood entering the arterial line, and postdialyzer venous circuit, respectively.

Normalized protein catabolic rate (nPCR) was calculated using the formula:

$$nPCR = (0.0136 \times F) + 0.251,$$

where F is equal to Kt/V ×([predialysis BUN + postdialysis BUN] \div 2) [10].

HD prescription was revised to detect the following:

- (1) Blood flow rate (BFR).
- (2) Ultrafiltration volume (UF volume).
- (3) Effective surface area of the dialyzer.
- (4) Venous pressure.

Assessment of health-related quality of life

A QOL questionnaire, a brief version of the World Health Organization QOL (WHOQOL-BREF) (The WHOQOL Group, 1996), which is a well-documented scoring system that has been used as a QOL tool for the general population as well as for patients on maintenanceHD, was submitted to every patient and a self-assessment of QOL was then measured by WHOQOL-BREF. For patients who could not read or write Arabic, the questionnaire was administered by me with the assistance of an interpreter. The four domains of the WHOQOL-BREF are the following.

Domain 1 (physical health): assesses activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility, pain and discomfort, sleep and rest, and work capacity.

Domain 2 (psychological health): assesses body image and appearance, negative feelings, positive feelings, self-esteem, spirituality, religion, personal beliefs, thinking, learning, memory, and concentration.

Domain 3 (social relationships): covers personal relationships, social support, and sexual activity.

Domain 4 (environment): assesses financial resources, freedom, physical safety and security, health and social care (accessibility and quality), home environment, opportunities for acquiring new information and skills,

participation in and opportunities for recreation and leisure activities, physical environment (pollution, noise, traffic, and climate), and transport.

The raw score of each domain was then converted to a standardized score of 0-100 to maintain uniformity in the scores. Higher scores indicate better QOL of the patients. The QOL index of each domain and its correlation with dialysis dose (Kt/V) were assessed.

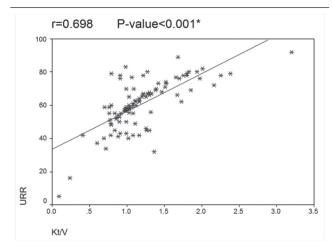
Results

There were 40 patients in group I and 60 patients in group II. Our results demonstrated that all patients in group I (Kt/V ≥ 1.2) had URR of at least 65% and all patients in group II (Kt/V < 1.2) had URR less than 65%. The correlation between dialysis dose (Kt/V) and URR was statistically significant (P < 0.01) (Figure 1).

Female patients showed a better clearance rate (46.5%) compared with male patients (35.1%). Percentage differences for Kt/V values among male and female patients were statistically insignificant (P = 0.429). In the current study, the mean ± SD age of the study population was 53.04 ± 14.7. Difference in clearance rates among the various age groups was statistically insignificant (P = 0.103). The highest clearance rates were observed in the age group 31-45 years, which represents around 15% of the study population.

A strong association between higher clearance rates and increased dialysis duration of each session (4 h; 78.9%), frequency of dialysis per week (three times/ week; 46.8%), and BFR (>300 ml/min; 63.3%) was noted and differences for both variables were statistically significant (P = 0.001, 0.012, and 0.003,respectively) (Tables 1-3).

Figure 1



Correlation between Kt/V and URR. URR, urea reduction ratio.

Kt/V values and effective surface area of the dialyzer

Our study population was placed on two different membrane size filters (1.3 and 1.6 m²). When these two groups were compared with regard to their clearance rates, 70% of those who were on 1.6 m² had a Kt/V value of at least 1.2 compared with only 32.5% of those who were on 1.3 m². Differences in the clearance rates were statistically significant (P = 0.005) (Table 4).

Low recirculation resulted in better dialysis adequacy $(0-10\%; 72\% \text{ with } \text{Kt/V} \ge 1.2) \text{ (Table 5)}.$

Our findings with respect to ultrafiltration rate and clearance showed a clear trend of improvement in Kt/V values with increased ultrafiltration rate (within limits). This was evident from the findings of Kt/V values of at least 1.2 with frequencies of 16.7, 33.3, 35.9, and 64% among those with UFs of 1-0, 1.1-2,

Table 1 Comparison between Kt/V values with respect to BFRs

BFR		n (%)		χ²-	test
(ml/min)	Group I	Group II	Total	χ²	<i>P</i> -value
200–250	5 (20.00)	20 (80.00)	25 (25.00)	11.343	0.003*
251-300	16 (35.56)	29 (64.44)	45 (45.00)		
More than 300	19 (63.33)	11 (36.67)	30 (30.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

BFRs, blood flow rates; *P value < 0.05 (statistically significant).

Table 2 Comparison between Kt/V values with respect to duration of dialysis session

Dialysis/h		n (%)	χ²-test		
	Group I	Group II	Total	χ^2	<i>P</i> -value
2.5	0 (0.00)	1 (100.00)	1 (1.00)	17.286	0.001*
3	3 (16.67)	15 (83.33)	18 (18.00)		
3.5	22 (35.48)	40 (64.52)	62 (62.00)		
4	15 (78.95)	4 (21.05)	19 (19.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

^{*}P value < 0.05 (statistically significant).

Table 3 Comparison between Kt/V values with respect to frequency of sessions/week

Dialysis		χ²-test			
session/weeks	Group I	Group II	Total	χ^2	P-value
Twice	4 (17.39)	19 (82.61)	23 (23.00)	6.362	0.012
Thrice	36 (46.75)	41 (53.25)	77 (77.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

Table 4 Comparison between Kt/V values in respect of dialyzer's surface area

Dialyzer		n (%)		χ².	-test
effective surface area	Group I	Group II	Total	χ^2	P-value
1.3 m ²	26 (32.50)	54 (67.50)	80 (80.00)	7.878	0.005*
1.6 m ²	14 (70.00)	6 (30.00)	20 (20.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

^{*}P value < 0.05 (statistically significant).

2.1-3, and 3.1-4 l/dialysis session, respectively. However, decrease in clearance rate was noted in patients with UF volume greater than 4 l as only 22.2% of them showed Kt/V values of at least 1.2. Differences in the clearance rates were statistically insignificant (P = 0.056) (Table 6).

Diabetic nephropathy was the most common cause of ESRD and represented 30% of our study population with a clearance rate of 30% (Kt/V \geq 1.2). Hypertension was represented by 28% of the study population. The results also showed that 60% of the study population was dialyzed with radiocephalic fistulas and 38.3% of them had a Kt/V value of at least 1.2. Better clearance rates were found in association with absence of patient complaints and vascular access complications. The results also showed strong positive relationship between dialysis dose and Hb (mean Hb = 10.66 ± 2.15) g/dl, serum albumin (mean albumin = 4.32 ± (0.79) g/dl, nPCR (mean nPCR = 0.91 ± 0.27) g/kg/day, and scoring of physical domain of WHOQOL-BREF (physical health).

In the current study, hypotension was found to be the most frequent complaint during dialysis treatments. The results showed that 23% of the study population complained of hypotension and 39% had a Kt/V value of at least 1.2. Cramps were reported by 8%, whereas 19% of the patients reported a complaint of dizziness. Dizziness was found to be the second most frequent complaint during dialysis treatments and patients in this group had the lowest clearance rate (36.84%; Kt/V ≥ 1.2).

Differences in Kt/V values among these different complications during the dialysis session were statistically insignificant (P = 0.997) (Tables 7 and 8).

Discussion

Over the past 10 years, published data indicated that survival of dialysis patients is strongly associated with the delivered dialysis dose [11]. Improvements in survival rates at higher dialysis doses were reported for all major causes of mortality including coronary heart disease, other cardiac diseases such as stroke, and infection. This observation is compatible with the hypothesis that low doses of dialysis may promote atherosclerosis, infection, malnutrition, and failure to thrive [12].

At present, the HD dose is quantified by the parameter Kt/V, which measures urea removal during treatment; a single-pool Kt/V of 1.2 is considered an adequate dose [13]. The primary data from the National Cooperative Dialysis Study (NCDC) showed that Kt/V less than 0.8 was associated with a relatively high rate of patient morbidity, whereas Kt/V values between 1.0 and 1.2 were associated with better outcome [6].

As regards dialysis adequacy, analysis of the results of the present study revealed that around 60% of the study population had Kt/V values less than 1.2, indicating that patients were receiving an inadequate HD dose.

These results were in agreement with similar findings from other developing countries such as Brazil, Nigeria, Nepal, Pakistan, and Iran (about 55-65% of patients had a Kt/V less than 1.2) [14]. In contrast, the results

Table 5 Comparison between Kt/V values with respect to percentage of AR

Recirculation		n (%)			χ²-test	
(%)	Group I	Group II	Total	χ²	<i>P</i> -value	
0–10	36 (72.00)	14 (28.00)	50 (50.00)	43.556	<0.001*	
11–20	4 (13.33)	26 (86.67)	30 (30.00)			
21–30	0 (0.00)	15 (100.00)	15 (15.00)			
More than 30	0 (0.00)	5 (100.00)	5 (5.00)			
Total	40 (40.00)	60 (60.00)	100 (100.00)			

^{*}P value < 0.05 (statistically significant).

Table 6 Comparison between Kt/V values with respect to UF volume/session

Volume of		χ²-test			
UF/session (I)	Group I	Group II	Total	χ^2	P-value
0–1	1 (16.67)	5 (83.33)	6 (6.00)	9.209	0.056
1.1–2	7 (33.33)	14 (66.67)	21 (21.00)		
2.1–3	14 (35.90)	25 (64.10)	39 (39.00)		
3.1-4	16 (64.00)	9 (36.00)	25 (25.00)		
>4	2 (22.22)	7 (77.78)	9 (9.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

UF, ultrafiltration volume.

Table 7 Comparison between Kt/V values with respect to vascular access (types of AVFs)

Type of current AVF	n (%)			χ²-test	
	Group I	Group II	Total	${\chi^2}$	<i>P</i> -value
Radiocephalic	23 (38.33)	37 (61.67)	60 (60.00)	1.042	0.594
Brachiocephalic	14 (46.67)	16 (53.33)	30 (30.00)		
Transbrachiobasilic	3 (30.00)	7 (70.00)	10 (10.00)		
Total	40 (40.00)	60 (60.00)	100 (100.00)		

AVFs. arterio-venous fistula.

Table 8 Correlationsbetween dialysis dose (Kt/V) and other variables

Correlations	K	t/V
	r	<i>P</i> -value
Hb	0.491	0.000
Albumin	0.380	0.000
nPCR	0.888	0.000
Physical domain	0.303	0.002
Psychological domain	-0.165	0.100
Social domain	-0.029	0.776
Environmental domain	0.097	0.338
SBP	0.099	0.327
DBP	0.151	0.134
URR	0.698	0.000

DBP, diastolic blood pressure; Hb, hemoglobin; nPCR, normalized protein catabolic rate; SBP, systolic blood pressure; URR, urea reduction ratio.

of the present study were in disagreement with those reported from developed countries such as the USA, as, according to the 2007 annual report, over 90% of patients had a Kt/V greater than 1.2 [15].

As regards the relationship between Kt/V and URR, the results of the present study revealed that all patients with spKt/V at least 1.2 had URR of at least 65% (statistically significant positive correlation between Kt/V and URR; *P* < 0.001).

These results were in agreement with the study by Afshar et al. [16], who found a statistically strong correlation between URR and eKt/V (P < 0.001).

In contrast, our results were in disagreement with the study by Oreo and Hamburger [17], who reported a poor correlation between URR and Kt/V in 942 patients when both values were measured simultaneously.

As regards the BFR, analysis of the results of the present study revealed that increased BFRs were associated with increased rate of clearance. This is clear from the findings of Kt/V values of at least 1.2 (200-250 ml/min, 20%; 251-300 ml/min, 35.6%; more than 300 ml/min, 63.3%). Difference in clearance rates among the various groups of BFRs was statistically significant (P = 0.003). These results were in agreement with the study by Kim et al. [18], Borzou et al. [19], Ward [20], and Port et al. [21]. In contrast, our results were in disagreement with those of Ghali and Malik [22]; there was no significant effect of increasing BFR on HD adequacy. They attributed their results to the effect of other factors affecting dialysis adequacy, such as malnutrition, anemia, short time of dialysis session, premature cessation of sessions of HD, infection, inadequate blood flow from vascular access, hypotension episodes, technical reasons, and the design of the study and the sample

As regards the duration of HD sessions, analysis of the results of the present study revealed that clearance was strongly associated with increased duration of the dialysis process. Difference in clearance rates among the various duration periods was statistically significant (P = 0.001). These results were in agreement with the study by Stewart et al. [23], who showed that time still had a profound effect on dialysis adequacy, indicating the importance of ensuring that patients remain on dialysis for the full time prescribed. Even 5 min makes a big difference. For each 5 min that a treatment is shortened, the patient loses significant dialysis time when reviewed cumulatively over time [15].

As regards dialysis frequency, analysis of the results of the present study revealed improvement in clearance rates with increased dialysis frequency per week. Differences in clearance rates were statistically significant (P = 0.012). The findings in this respect were consistent with previous reports that linked improvements in clearance rates with frequency of dialysis [24].

As regards UF volume, analysis of the results of the present study revealed a clear trend of improvements in Kt/V values with increased UF rate (within limits, as decrease in clearance rate was noted in patients with UF volume >41). However, differences in the clearance rates among different groups were statistically insignificant (P = 0.056). Few studies have examined the direct association of UF rate on long-term outcomes in HD patients. The Netherlands Cooperative Study on the adequacy of dialysis recently reported the association between excessive ultrafiltration and mortality, independent of the delivered Kt/V urea [25].

As regards the effective surface area of the dialyzer, analysis of the results of the present study revealed improvements in Kt/V values with increased dialyzer surface area. Differences in clearance rates were statistically significant (P = 0.005). These results were in agreement with previous reports on membrane size and clearance rates by Stivelman et al. [26] and Pascual et al. [27]. The use of larger surface area dialyzers permits high rates of urea clearance to be achieved, offering the advantage of improving blood purification by removing higher-molecular-weight and middle-molecular-weight solutes [27].

As regards access recirculation (AR), analysis of the results of the present study revealed that low recirculation percentage would result in better dialysis adequacy. Differences in Kt/V values among these

recirculation groups were statistically significant (P < 0.001).

These results were in agreement with those of Santoro [28], who concluded that the form of needle insertion and the distance between the needles should be considered a part of the process of recirculation reduction, with the classical form presenting the lowest percentages of AR and with unidirectional needles providing satisfactory results as long as the distance between them is 5 cm or more.

Diabetic and hypertensive nephropathy are the leading underlying etiologies of ESRD [29]. Diabetes is the leading cause of ESRD in developed countries and accounts for 45% of prevalent kidney failure, up from 18% in 1980 [30]. According to Afifi et al. [31], the prevalence of diabetic nephropathy among ESRD patients in Egypt increased from 8.9% in 1996 to 24.5% in 2003. The data of the present study in this respect are consistent with the worldwide percentage for the etiology of ESRD.

Hypotension is one of the most common medical complications seen during HD. Multiple factors are associated with intradialytic hypotension, such as excessive ultrafiltration, anemia, antihypertensive medications, cardiac disease, and errors in estimation of patient's dry weight [32].

In the current study, hypotension was found to be the most frequent complaint during dialysis treatments. The results showed that 23% of the study population complained of hypotension. These results were in agreement with those of Sherman [33].

In the present study, arteriovenous fistulas (AVFs) were the vascular access used in all study patients as patients with AVGs and central venous catheters (CVCs) were previously excluded. Analysis of the results of the present study revealed that the majority of patients (60%) were dialyzed using radiocephalic fistulas. These results were in agreement with the 2006 update of KDOQI guidelines, which consider the most distal site possible to permit the maximum number of future possibilities for access; therefore, the radiocephalic fistula is the first choice of access. Our results also showed that patients who were dialyzed with a brachiocephalic fistula had the highest clearance rate (46.67% of them showed a Kt/V \geq 1.2) in comparison with the other two groups. These results might be because the brachiocephalic fistula had the higher BFR and was easier to cannulate in comparison with radiocephalic and brachiobasilic fistulas. However, differences in clearance rates among the different types of AVFs were statistically insignificant (P = 0.594).

The mean Hb level was 10.66 ± 2.15 g/dl in the study patients. This value is lower than the recommended DOQI guidelines, which recommend an Hb of 11–12 g/l. The mean Hb in our study population was lower, compared with that of other countries: mean Hb levels were 12 g/dl in Sweden; 11.6-11.7 g/dl in the USA, Spain, Belgium, and Canada; and 11.1-11.5 g/dl in Australia, New Zealand, Germany, Italy, UK, and France [34]. The factors responsible for the low Hb levels in our patients, compared with the DOQI guidelines and those of other countries, are the following: blood loss, lack of consistent supplies of erythropoietin, and insufficient dialysis dose. There is good evidence that dialysis adequacy results in better control of anemia and other parameters that correlate with dialysis adequacy, such as hypertension and patients' nutritional status [35].

As regards the dialysis dose (Kt/V) and serum albumin, our results revealed that the positive correlation between dialysis dose (Kt/V) and serum albumin was statistically significant (P < 0.001).

These results were in agreement with those of Ahmad et al. [36], who showed a strong positive correlation between serum albumin and dialysis adequacy, as expressed by Kt/V. This finding also suggests that patients undergoing chronic HD adjust their protein intake automatically according to the dose of HD delivered, probably because of an improvement in appetite as a result of the disappearance of uremic symptoms from the digestive system (e.g. nausea, anorexia, and vomiting).

As regards the dialysis dose (Kt/V) and nPCR, the analysis of our results revealed that the positive correlation between dialysis dose (Kt/V) and nPCR was statistically significant (P < 0.001).

These results were in agreement with those of Lindsay and Spanner [37], who showed that any attempt to increase the protein intake in patients undergoing HD was unsuccessful if any previous increases in the amount of prescribed HD were not established first. They also found a linear positive correlation between Kt/V and nPCR.

As regards the dialysis dose (Kt/V) and scoring of the four domains of WHOQOL-BREF, analysis of the results of the present study revealed that the positive correlation between dialysis dose (Kt/V) and scores of the physical domain of WHOQOL-BREF was statistically significant (P < 0.001), whereas there was no correlation between dialysis dose (Kt/V) and psychological domain score (P = 0.100), social domain score (P = 0.776), and environmental domain score

(P = 0.338) of WHOQOL-BREF. These results were in agreement with those of Manns et al. [38], who found that increase in dialysis dose was associated with a better QOL, and in agreement with those of Benz et al. [39], who found that increase in dialysis dose was associated with a decrease in the number of awakenings at night.

As regards dialysis dose (Kt/V) and blood pressure (systolic blood pressure and diastolic blood pressure) analysis of the results of the present study revealed that there was no correlation between dialysis dose (Kt/V) and blood pressure [neither systolic (P = 0.327) nor diastolic (P = 0.134)].

These results were in agreement with the study by McGregor et al. [40], who did not ascertain any correlation between Kt/V and blood pressure, and with the study by Rahman et al. [41], who found strong correlation between blood pressure and interdialytic weight gain. In contrast, the results of the present study were in disagreement with the results of Panagoutsos et al. [35], who found a reduction in blood pressure with an increase in dialysis dose, suggesting that increased dialysis dose was more effective in blood pressure control. Others have also reported similar findings with corresponding increase in dialysis dose [42].

In summary, the findings of the present study clearly showed that with increasing time and frequency of dialysis, BFRs, low recirculation percentages, reduction of intradialytic complaints, and well-functioning vascular access were associated with better dialysis adequacy.

We recommend the following: individualizing the HD prescription based on monthly assessment of single-pool Kt/V would be beneficial and practical in providing safe and cost-effective HD treatment. To ensure that ESRD patients treated with chronic HD receive adequate treatment, the delivered dose of HD needs to be measured monthly. HD centers should have a continuous quality improvement and patient review system in place that recognizes patients who are receiving suboptimal dialysis adequacy, identify the cause, and rectify it if possible, and assess whether targets are achieved in accordance with DOQI guidelines in an effort to achieve improved long-term outcomes in patients on chronic HD.

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Conflicts of interest

There are no conflicts of interest.

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