



Cohort Study

Chronic hemodialysis: Evaluation of dialysis adequacy and mortality[☆]Ziba Aghsaiefard^a, Abolfazl Zendeheel^{b,c}, Reza Alizadeh^{d,*}, Azardokht Salehnasab^e^a Department of Internal Medicine, School of Medicine, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran^b Geriatrics Department, Ziaei Hospital, Tehran University of Medical Sciences, Tehran, Iran^c Family Medicine Department, Ziaei Hospital, Tehran University of Medical Sciences, Tehran, Iran^d Department of Anesthesiology and Intensive Care, School of Medicine, AJA University of Medical Sciences, Tehran, Iran^e Student Research Committee, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Objective: Dialysis efficacy is one of the important issues in patients undergoing hemodialysis. This study aimed to determine the adequacy of dialysis with mortality and hospital admissions in patients undergoing hemodialysis. **Methods:** This retrospective cohort study was conducted on patients who underwent dialysis. Dialysis adequacy was measured based on the Kt/V criterion. Age, sex, disease etiology, duration of dialysis, and access dialysis were evaluated.

Results: 128 patients with a mean age of 61.48 ± 13.36 years were included in the study. 8 patients had a history of kidney transplantation. The mean dialysis time in the patients was 4.30 ± 3.39 years. The mean Kt/V in the patients was 1.40 ± 1.8 years. Of the 128 patients, 53 were hospitalized for cardiac or renal reasons. The number of fatalities was 9 cases out of 128. The cause of death in all the cases was heart problems. There was a statistically significant correlation between the adequacy of dialysis in terms of Kt/V and mortality, but it was not associated with hospitalization.

Conclusion: Inadequate dialysis in terms of Kt/V is likely to increase the rate of mortality among dialysis patients.

1. Introduction

Dialysis efficacy is one of the important issues in patients undergoing hemodialysis. Various studies show that the better the dialysis is, the lower the uremic complications and the morbidity and mortality of the patients is reduced. A periodic review of dialysis efficacy by dialysis clinics is recommended [1,2]. Measuring blood urea samples and clinical symptoms alone cannot be indicative of the efficacy of dialysis. Typically, URR and Kt/V are commonly used to evaluate the efficacy and adequacy of dialysis [2–4].

Using Kt/V with URR is preferable because it shows urea removal more precisely. Kt/V is obtained using the following parameters: urea clearance (K), treatment duration (t), and volume of urea distribution (V). The filter clearance is determined by the manufacturer (K in the formula), and the duration (t in the formulation) of the dialysis is directly related to the adequacy of dialysis [5]. Dialysis adequacy is indicated by clear filter, longer the duration of dialysis and the amount of urea removed [6]. The importance of performing the appropriate dose

and timing of dialysis on the health status of the patient has been studied and proven in many studies to the extent that it can directly affect the survival rate of the patients [7,8]. Even in some studies, the relationship between Kt/V and mortality has been reported, indicating an increase in survival rates in patients with high Kt/V [9].

At present, cardiovascular disease and inadequate dialysis are the main causes of morbidity and mortality in hemodialysis patients [10, 11]. Studies have been carried out to estimate dialysis adequacy in Iranian population, and most patients are seen to not reach desirable level of dialysis. Kt/V > 1.2 is regarded as the minimum acceptable dialysis quality by Iranian Ministry of health, which is lower than those accepted in European countries and America. This makes reaching adequate dialysis quality in Iranian population difficult when compared with other population where acceptable Kt/V levels are greater than 1.2 [1]. Various studies have been carried out in Iran that indicates the inefficacy of dialysis in Iranian patients [12,13]. 87% of dialysis patients in Abadan (12%), 96.7% in Bushehr (13%) and 80.6% of patients in Arak have with reported with inadequate dialysis [14–16]. One, three

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and five year survival rate in Khuzestan among nondiabetic hemodialysis patients has been seen to be 98.7%, 73.8% and 58.9%, respectively [17]. However, mortality has not been studied as a primary outcome of dialysis inadequacy.

The aim of this study was to determine the adequacy of dialysis with mortality and hospital admissions in patients undergoing hemodialysis.

2. Materials and methods

This retrospective cohort study was conducted on all the patients referred to (XXX) from 2014 to 2020. These patients were non-anemic and were aged above 18 years. Required information was extracted from the medical records of the patients and entered into the form.

The number of admissions (due to renal problems) and the death of patients (due to renal and cardiovascular problems) was extracted and calculated as the outcomes. The minimum follow-up time for patients was two years. Age, sex, disease etiology, duration of dialysis, and access dialysis were other variables that were studied in this study. The cause of the patient's death was obtained from death certificate issued by a medical doctor (known and expected cases) or a forensic expert (autopsy cases).

Dialysis adequacy was measured based on the Kt/V (urea clearance) criterion. The criteria for urea clearance, dialysis time and body volume are used. The calculation of Kt/V was done from the following formula:

$$Kt/V = -\ln(R-0.03) + [(4-3.5 R) \times (UF \div W)]$$

Where, UF is the filtration volume in liters, W is the patient's weight after dialysis in kilograms, and R is the BUN ratio after dialysis before dialysis.

Patient tests were recorded within three months of starting dialysis and continued until the end of the second year. The mean values obtained were recorded as target values for each patient. In the event of a patient's death, the time was recorded in less than two years after starting hemodialysis. Hospital admissions were recorded for each patient until the last follow-up time.

After completing the forms, the data were entered into SPSS v20 for analysis. Quantitative variables were presented with normal distribution

of Mean \pm SD and qualitative variables were presented using frequency (in percentage). P-value < 0.05 was considered to be statistically significant. The relationship between Kt/V level and mortality rate and frequency of hospitalization in different causes due to cardiac causes were analyzed by independent sample test for age, sex, diabetes mellitus and duration of dialysis.

The study was approved by the committee of research ethics of (XXX).

Unique identifying number is: researchregistry7199.

The methods are stated in accordance with STROCSS 2021 guidelines [18].

3. Results

Of 128 patients included in the study, 73 men (57%) and 55 women (43%) were included in the study with the mean age of 61.48 ± 13.36 years (18–89 years). 8 (6.3%) patients had a previous history of kidney transplantation. Type of dialysis access was used in 73 patients (57%) fistula and in 55 patients (43%) Permcat. The mean dialysis time in the patients was 4.30 ± 3.39 years (1–16 years). Of the 128 patients (41.4%), 53 were hospitalized for cardiac (no evidence of underlying cardiac disease) or renal reasons. 8 patients (6.3%) had a previous history of kidney transplantation.

Fatality was reported in 9 (7%) cases. The cause of death in all cases was heart problems. The mean Kt/V in the patients was 1.40 ± 1.8 (0.81–1.91 years) (Fig. 1). 1.2–1.4 being normal Kt/V, 45 (35.2%) patients were in the normal range and 83 (64.8%) were outside the normal range.

The mortality rate in the group Kt/V < 1.2 was 30.8%, in the group 1.2–1.4 was 0% and in the group 1.4 < Kt/V was 7%.

The most common cause of renal failure in patients with chronic hemodialysis was diabetes (Table 1).

There was a statistically significant correlation between dialysis adequacy in terms of Kt/V and mortality in chronic hemodialysis patients ($p = 0.001$) (Table 2). There was a statistically significant correlation between dialysis adequacy in terms of Kt/V and mortality in chronic hemodialysis patients in men and women (Table 3), age group

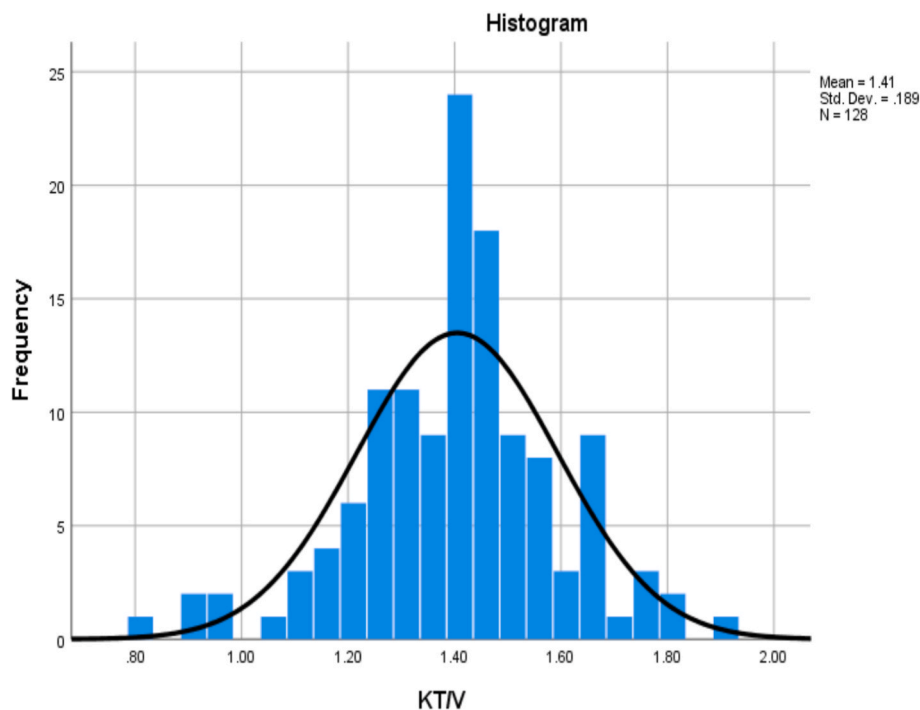


Fig. 1. Histogram diagram of the frequency distribution of patients in terms of Kt/V.

Table 1
Distribution of causes of kidney failure in chronic hemodialysis patients by mortality.

Causes of Kidney Failure	Alive		Dead	
	Number	Percent	Number	Percent
Diabetes	56	1/47	5	6/55
Hypertension	27	7/22	0	0/0
Polycystic kidney	2	7/1	0	0/0
Glomerulonephritis	2	7/1	0	0/0
Congenital kidney stone	2	7/1	0	0/0
Kidney infection	3	5/2	0	0/0
Lupus	2	7/1	0	0/0
Trauma	1	8/0	0	0/0
Nephrotic Syndrome	0	0/0	0	0/0
Unknown	0	0/0	1	1/11
Total	3	2/20	3	3/33
	119	100	9	100

Table 2
Distribution of the relationship between dialysis adequacy and mortality in chronic hemodialysis patients.

dialysis adequacy in terms of Kt/V	Dead		Alive		P-value
	Number	%	Number	%	
1.2>	4	44.4	9	7.6	0.001
1.2-1.4	0	0.0	45	37.8	
1.4<	5	55.6	65	54.6	
Total	53	100	119	100	

Chi-Square Test was used. The statistical value of P < 0.05 is significant.

Table 3
Distribution of the relationship between dialysis adequacy and mortality in chronic hemodialysis patients by gender.

Gender	dialysis adequacy in terms of Kt/V	Dead		Alive		p-value
		Number	%	Number	%	
Male (n = 73)	1.2>	1	100.0	6	8.3	0.008
	1.2-1.4	0	0.0	31	43.1	
	1.4<	0	0.0	35	48.6	
Female (n = 55)	1.2>	3	37.5	4	8.3	0.030
	1.2-1.4	0	0.0	14	29.2	
	1.4<	5	62.5	30	62.5	

Chi-Square Test was used. The statistical value of P < 0.05 is significant.

more than 65 years old (Table 4), patients with a history of dialysis of 6 years or more (Table 5), use of fistulas and premixes (Table 6). Among patients with Kt/V < 1.2, 8 (15.1%) had history of hospitalization, those with Kt/V 1.2-1.4 18 (34%) and those with Kt/V > 1.4 27 (50.9%) had

Table 4
Distribution of the relationship between dialysis adequacy and mortality in chronic hemodialysis patients by age of patients.

Age group	dialysis adequacy in terms of Kt/V	Dead		Alive		p-value
		Number	%	Number	%	
45>yr (n = 12)	1.2>	0	0.0	6	8.3	0.580
	1.2-1.4	0	0.0	31	43.1	
	1.4<	1	100.0	35	48.6	
45-55yr (n = 24)	1.2>	1	100.0	4	8.3	0.126
	1.2-1.4	0	0.0	14	29.2	
	1.4<	0	0.0	30	62.5	
55-65yr (n = 40)	1.2>	1	100.0	3	7.9	0.133
	1.2-1.4	0	0.0	12	31.6	
	1.4<	0	0.0	23	60.5	
≥65yr (n = 52)	1.2>	2	40.0	3	6.4	0.03
	1.2-1.4	0	0.0	16	34.0	
	1.4<	3	60.0	28	59.6	

Chi-Square Test was used. The statistical value of P < 0.05 is significant.

Table 5
Distribution of the relationship between dialysis adequacy and mortality in chronic hemodialysis patients by duration of dialysis.

Duration of dialysis	dialysis adequacy in terms of Kt/V	Dead		Alive		p-value
		Number	%	Number	%	
2>yr (n = 23)	1.2>	1	4.3	1	4.3	1.00
	1.2-1.4	10	43.5	10	43.5	
	1.4<	12	52.2	12	52.2	
2-4yr (n = 52)	1.2>	2	28.6	3	6.7	0.052
	1.2-1.4	0	0.0	19	42.2	
	1.4<	5	71.4	23	51.1	
4-6yr (n = 18)	1.2>	1	100.0	3	17.6	0.133
	1.2-1.4	0	0.0	5	29.5	
	1.4<	0	0.0	9	52.9	
≥6yr (n = 35)	1.2>	1	100.0	2	5.9	0.004
	1.2-1.4	0	0.0	11	32.3	
	1.4<	0	0.0	21	61.8	

Table 6
Distribution of the relationship between dialysis adequacy and mortality in chronic hemodialysis patients in terms of dialysis access.

Type of dialysis access	dialysis adequacy in terms of Kt/V	Dead		Alive		p-value
		Number	%	Number	%	
Fistula (n = 73)	1.2>	2	40.0	4	5.9	0.015
	1.2-1.4	0	0.0	25	36.8	
	1.4<	3	60.0	39	57.4	
Permcath (n = 55)	1.2>	2	50.0	5	9.8	0.043
	1.2-1.4	0	0.0	20	39.2	
	1.4<	2	50.0	26	51.0	

Chi-Square Test was used. The statistical value of P < 0.05 is significant.

history of hospitalization. There was no such correlation in terms of hospital admissions, p = 0.29.

4. Discussion

In this study, 41.4% of patients were hospitalized for cardiac and renal reasons (dialysis failure). There was no significant correlation between the adequacy of dialysis and the number of hospitalized patients (p = 0.295). Similar results were obtained in evaluating the adequacy of dialysis with hospitalization in terms of underlying variables such as age, sex, duration of dialysis and type of vascular access. The findings showed that there was a significant correlation between the adequacy of dialysis and mortality (p = 0.001). There was no mortality in the normal Kt/V group (1.2-1.4) and about 45% of the patients died in group Kt/V < 1.2 and 55% in Kt/V 1.4 or more. Furthermore, diabetes was reported in 55.6% patients, however, the cause of renal failure was not statistically significant. In the study by Chandrashekar et al., there was no statistically significant difference between the diabetic and non-diabetic patients in terms of mortality rate (RR = 1.01, p = 0.803) [19]. It has been shown that, despite advances in the technology of dialysis machines and drug treatments, the mortality rate of dialysis patients in India is still high [20,21]. The study included 96 patients with two years follow up and a history of at least 3 months of hemodialysis (8-12 h per week). Of 96 patients, 19 patients died with an 19.8% mortality due to ischemic heart disease. However, in the present study, despite the higher number of patients, during the similar period, 7% (9 out of 128) died of cardiac and renal reasons.

A number of studies have indicated that dialysis insufficiency is one of the independent parameters associated with increasing mortality [22, 23]. In the study by Chandrashekar et al., the efficacy of dialysis was correlated with mortality of the patients, and the researchers concluded that dialysis adequacy is negatively associated with mortality. Djukanovi'c et al. [19] reported that deaths in patients with incomplete dialysis (Kt/V < 1.2) were higher and it was concluded that Kt/V can be

considered as an independent predictor to determine the patient's death time.

In our study, it was found that 60% of the patients died in the age group of 65 and older had Kt/V above 1.4. On the other hand, similar was observed in patients with dialysis duration 6 years and older, such that all of these patients had Kt/V less than 1.2. In other words, it can be concluded that patients with age 65 years or more and with the dialysis duration of 6 years are at greater risk of mortality as a result of inadequate dialysis. These patients are likely to have lesser tolerance than other groups to abnormal Kt/V, and therefore they should be more carefully evaluated for their urea clearance. Given the relatively low proportion of deaths in the present study, more meticulous conclusions are required.

In Japan, the guidelines have suggested that the minimum Kt/V in patients with chronic hemodialysis of three dialysis sessions per week is higher than 1.2. Considering this, Japan has increased the life span of dialysis patients compared to other countries. Kimata and colleagues examined the association between Kt/V and overall mortality of patients on the basis of gender Japan [24]. In 5784 hemodialysis patients (from 1999 to 2011) with a minimum dialysis period of one year and receiving three dialysis sessions per week, it was shown that low Kt/V is associated with increased mortality. The findings showed that the prevalence of low Kt/V in men was 27–37% and in women 10–15%. The findings showed that Kt/V related mortality was higher in women (12/1 - 00/1: 95% CI, 06/1 = HR).

Various studies suggest increased dialysis levels are beneficial for patients, but excessive dialysis may also be associated with increased mortality [25]. Abdulla et al. found that Kt/V higher than 1.68 is associated with increased mortality. The patients with the low body mass index received the high levels of dialysis, leading to significant reduction in serum creatinine levels. Accompanying this issue with malnutrition could have subjected them to higher mortality.

Confirming the low Kt/V ratio with increased mortality can indicate that modifying therapeutic interventions can greatly enhance survival in dialysis patients. Consideration of factors such as the age of patients and the history of dialysis can be effective foreseeing the outcomes. The study adds to the pre-existing knowledge that inadequacy of dialysis leads to increased mortality amongst hemodialysis patient however larger sample size is required to assess the true effect.

5. Conclusion

The findings of the study showed that there was no significant correlation between the dialysis adequacy and hospitalization, but it was significant correlated to mortality. This association was evaluated based on the age and duration of dialysis, indicating that the age group over 65 years and those with a history of dialysis over 6 years with abnormal Kt/V are at greater risk. Patients with dialysis adequacy of 1.2–1.4 had 0% mortality, indicating the significance of dialysis adequacy on survival years.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Sources of funding

No funding was secured for this study.

Author contribution

Dr. Ziba Aghsaeifard: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Azardokht Salehnasab and Dr. Abolfazl Zendehdel: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr.Reza Alizadeh: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Registration of research studies

1. Name of the registry: N/a
2. Unique Identifying number or registration ID: IR.TUMS.MEDICINE.REC.1397.028
3. Hyperlink to the registration (must be publicly accessible): <https://ethics.research.ac.ir/ProposalCertificateEn.php?id=12841&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true>.

Guarantor

Ziba Aghsaeifard.

Consent

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by research center fund and deployed accordingly.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103541>.

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