Original Article

Sleep and Quality of Life in Relation to Dialysis Adequacy in Chronic Kidney Disease Patients Undergoing Hemodialysis

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Abstract

Background: Adequate clearance contributes to improving the quality of life and sleep of patients with End-Stage Chronic Kidney Disease (CKD). The aim of the study was to investigate the correlation between dialysis adequacy, sleep quality and quality of life in patients undergoing a chronic hemodialysis program.
Methodology: The study was conducted among 352 patients with CKD. Quality of life was assessed using the kidney disease and Quality of Life (KDQOL-SF™) questionnaire, and sleep quality with the Pittsburgh questionnaire. Hematological indices were also taken to calculate the adequacy of clearance and their correlation with their quality of life as well as with sleep.
Results: The Kt/V ratio was greater in patients who had better sleep quality and was associated with patients' quality of life and all of its dimensions. 82.7% of patients had poor sleep quality. Good sleep quality was positively associated with both physical and mental health scales as well as physical and cognitive functioning, vitality, social and emotional role, while overall quality of life was negatively associated with poor sleep quality. MDRD creatinine clearance was negatively associated with the physical health scale, while no significant correlation was observed between the mental health scale and global quality of life and MDRD creatinine clearance or CKD-EPI
Conclusions: The quality of sleep was correlated with the quality of life of the patients. Providing adequate dialysis significantly contributes to improving and maintaining the level of quality of life and sleep as a key component of the quality of life of CKD patients undergoing hemodialysis and consequently in the reduced morbidity and mortality of these patients.

Key-words: Chronic Kidney Disease, Dialysis, Adequacy of clearance, Quality of Life, Sleep

Introduction

In recent years, chronic kidney disease (CKD) has evolved into a major public health problem both as a direct cause of global morbidity and mortality and as an important risk factor for cardiovascular diseases (Fradelos, 2018). On a global scale, the incidence of the disease is estimated between 8-16% (Zyga, 2017). In the US, current estimates suggest that 37 million people, or about 15% of adults, have CKD, many of whom (about 9 in 10 people) don't know it.

CKD is slightly more common in women (14%) than men (12%).

It occurs more often in people older than 65 years (in 38% of people) than in people younger than 45-64 years (12%) and 18-44 years old (6%), but the possibility of its development into chronic renal failure end-stage disease is greater in younger individuals (≤65 years) with CKD (Centers for Disease Control and Prevention, 2021).

The increased cost burden of replacement therapies and care for patients with end-stage renal disease significantly affects the patient's quality of life. The public health cost of replacement therapy interventions (hemodialysis, peritoneal dialysis, kidney transplant) exceeds 2.5 million and is projected to double to 5.4 million by 2030. In addition, accessibility barriers exist in many countries in treatment due to the lack of renal replacement services. An indicative estimate is that 2.3-7.1 million adults have died prematurely due to lack of access to treatment (Bikbov et al., 2020).

Hemodialysis has been found to affect patients' sleep quality. In one study the majority (54%) of patients were found to have pathological somnolence (mean sleep latency <5 minutes) with the sleep latency being related to urea. When conventional hemodialysis was converted to nocturnal hemodialysis, there was a significant reduction in blood urea nitrogen and sleep apnea severity (Hanly et al., 2003). The uremic syndrome can exacerbate sleep disturbances in patients with end-stage renal disease by accumulation of uremic toxins, volume overload, or both (Söreide et al., 1991). In 46 dialysis patients in Canada, it was found that 76% of the study population had poor sleep. Poor physical function in chronic hemodialysis patients was associated with sleep disturbance, after controlling for inflammation and dialysis adequacy (Sabbagh et al., 2008).

Hemodialysis has been reported to affect patients' quality of life. In a study in Egypt, the subscales of the physical dimension were found to score below the mean of 50, suggesting that these patients suffer from poor physical performance. Social functioning and role limitation due to mental functioning were scored above 50, while general mental health was scored almost 100 representing the maximum score (Hasan et al., 2021). A descriptive study found a significant relationship between dialysis adequacy and quality of life (Kalender & Tosun, 2014).

Aim: The aim of the present study was to investigate the degree of effect of adequate clearance on sleep and quality of life in patients with Chronic Kidney Disease.

Methodology

Study population: he study population consisted of a total of 352 adults with end-stage chronic kidney disease undergoing a three-week dialysis program.

Data collection tools: Quality of life was assessed with the KDQoL. The tool consists of 24 questions and composes 20 dimensions of quality of life. It is a special quality of life assessment tool for kidney disease patients. It has been translated into Greek and weighted to the Greek population. The questionnaire is available for free in the Greek language from http://www.rand.org/health/surveys_tools/kdqol.html. Sleep quality was assessed with the Greek version of the Pittsburgh Sleep Quality Index (PSQI). Clearance efficiency was calculated by the Kt/V ratio.

Data Collection: Data collection was done through a face-to-face structured interview process between January 2021 and April 2021.

Ethics: In the present study, the anonymity of the sample was respected and permission was obtained from the ethic committee (36914/23-06-2021).

Statistical analysis: Mean values and standard deviations (Standard Deviation=SD) were used to describe the quantitative variables. Absolute (N) and relative (%) frequencies were used to describe qualitative variables. To compare the quality of life and health of the participants between the various factors, either the t-test or the analysis of variance by one factor (one way ANOVA) was used. Linear regression analysis was used to find independent factors related to the quality of life and health assessment scales from which dependence coefficients (β) and their standard errors (standard errors=SE) were derived.

Demographic and clinical data of the participants were used as independent variables. Statistical significance was set at 0.05. The statistical program SPSS22.0 was used for the analysis.

Results

The sample consists of 350 patients with a mean age of 66.41±10.03 years. Patient demographics are presented in Table 1.

The mean Body Mass Index was calculated to be 26.40±4.52 with 42.3% of the participants being within normal levels. 66.3% were non-smokers and 81.7% did not exercise. Smokers smoked 13.8±8.9 cigarettes per day and exercised 2.5±6.2 hours. The median MDRD creatinine clearance was 5.74, while the median CKD-EPI creatinine clearance was 5.39. 58.3% of patients had uric acid values within normal limits. Table 2 shows the characteristics and habits of the patients regarding kidney disease.

The mean value of the KT/V ratio was 1.24±0.10. Values were significantly lower in cases where sleep quality was poor (1.23±0.09 vs. 1.30±0.09, $p<0.001$). Higher values in KT/V were associated with significantly higher values in all dimensions of the KDQOL scale, with the exception of the dimensions 'Encouragement by dialysis staff' and 'Patient satisfaction' which were not found to be significantly related to KT/V (table 4).

Totally, 82.7% of patients had poor sleep quality, while 17.8% of patients had good sleep quality. Higher scores on the quality-of-life scale were found to have dialysis team stimuli (85.8±20.5), patient satisfaction (74.7±25.8), disease symptoms (63.9±25) and cognitive functioning (62.6±26.9).

Table 1. Patient demographics

		N	%
Gender	Male	223	63.7
	Female	127	36.3
Education level	Illiterate	50	14.3
	Primary	125	35.7
	Secondary	150	42.9
	Postgraduate	25	7.1
Family status	Single	56	16.0
	Married	197	56.3
	Divorced	37	10.6
	Window	60	17.1
Children		265	75.7
Occupation	Retired	244	69.7
	Driver	13	3.7
	Farmer	27	7.7
	Household	29	8.3
	Engineer	22	6.3
	Craftsman	12	3.4
	Private employee	1	0.3
	Public/State employee	2	0.6
Work status	Full time	54	15.4

	Part time	29	8.3
	Student	1	0.3
	Household	18	5.1
	Retired	236	67.4
	Unemployed	12	3.4
Monthly income	<500€	88	25.1
	500-1.000€	150	42.9
	1001-1.500€	89	25.4
	1.501-2.000€	16	4.6
	>2.000€	7	2.0
Residence region	Urban area	159	45.4
	Rural area	191	54.6
Smoking		118	33.7
Exercise		64	18.3
Type of exercise	Running	10	14.5
	Walking	54	78.3
	Swimming	5	7.2

Table 2. Patient characteristics and habits related to kidney disease.

		N	%
Primary disease	Diabetic nephropathy	80	22.9
	Glomerulonephritis	46	13.1
	Arterial hypertension	68	19.4
	Polycystic kidney disease	39	11.1
	Unknown cause	84	24.0
	Other causes	33	9.4
Years on hemodialysis, Mean (SD), median		5.10 (4.50)	4.0 (2.0 – 7.0)
Age at start of hemodialysis. Mean (SD), median		61.46 (15.0)	62.5 (53.0 – 72.0)
How do you get to the Dialysis Center?	Car (patient drives)	138	39.4
	Public transport	22	6.3
	Ambulance	18	5.1
	Car (relatives drive)	98	28.0

	Taxi	73	20.9
	Other	1	0.3

Table 3. shows the values of the dimensions of the patients' quality of life.

	Mean	SD
Functional capacity	41.89	31.60
Physical aspects	29.73	40.95
Pain	48.69	28.06
General health state	34.27	22.59
Vitality	44.13	23.39
Social aspects	50.0	25.46
Emotional aspects	40.76	46.96
Mental health	48.49	22.93
Summary physical health scale	34.0	10.17
Summary mental health Scale	39.05	11.10
Symptoms/Problems	63.93	25.0
Effects of CKD in the daily life	41.0	27.47
Overload imposed for CKD	44.29	26.72
Work condition	43.60	37.09
Cognitive function	62.59	26.87
Social interaction	56.57	20.14
Sexual function	33.13	34.21
Sleep	55.64	17.36
Dialysis team stimuli	85.82	20.50
Patient satisfaction	74.71	25.76

Table 4. Correlation coefficients of KT/V with dimensions of the KDQOL scale.

	r	P
Functional capacity	0.39	**<0.001**
Physical aspects	0.30	**<0.001**
Pain	0.29	**<0.001**
General health state	0.21	**<0.001**
Vitality	0.32	**<0.001**

Social aspects	0.27	**<0.001**
Emotional aspects	0.18	**0.001**
Mental health	0.22	**<0.001**
Summary physical health scale	0.42	**<0.001**
Summary mental health Scale	0.19	**<0.001**
Symptoms/Problems	0.32	**<0.001**
Effects of CKD in the daily life	0.26	**<0.001**
Overload imposed for CKD	0.25	**<0.001**
Work condition	0.30	**0.006**
Cognitive function	0.24	**<0.001**
Social interaction	0.23	**<0.001**
Sexual function	0.33	**<0.001**
Sleep	0.23	**<0.001**
Dialysis team stimuli	-0.04	0.502
Patient satisfaction	-0.01	0.826

Discussion

The present study included 350 patients with a mean age of 66.4 years, most of whom were male, married, with secondary education, retired and living in a rural area. Two-thirds of the sample were non-smokers and the majority did not exercise. The median time on dialysis was 4 years and the median age at initiation of dialysis was 62.5 years. 82.7% of patients had poor sleep quality, while participants had moderate quality of life, both overall and in all individual dimensions.

Although many questionnaires are available to assess quality of life, the KDQOL-SF is the most commonly used. It has many advantages over other tools. It has been tested in a number of people with kidney disease, has a general and specific component for the evaluation of chronic kidney disease, and can be used in hemodialysis and peritoneal dialysis patients with questions about sexual function (Hays et al., 1997).

In many studies, a strong correlation between dialysis dose and clinical outcome has been described. Adequacy of hemodialysis is now recognized as a strong predictor of morbidity and mortality in patients with end-stage renal disease undergoing regular hemodialysis (Port et al., 2002).

Dialysis adequacy and optimal dose can be assessed using a variety of techniques and methods, including the Kt/v ratio, which is the most common and preferred method for numerically expressing dose and/or dialysis adequacy (Taal et al., 2011). A minimum Kt/V value of 1.2, with a frequency of 3 hemodialysis

sessions per week, has been suggested as an acceptable goal, recommendations strongly supported by the HEMO research (Eknoyan et al., 2002).

In the present study the mean value of KT/V was 1.24±0.10 units, which means that the clearance adequacy of the patients was within the target. The Kt/v ratio determined by simulating the kinetics of a single urea concentration is the most common and preferred method for numerically expressing dose and/or dialysis adequacy because it is more specific and accurate (Kuhlmann et al., 2019).

In the present study the KT/V ratio was greater in patients with better sleep quality and was associated with patients' quality of life and all of its dimensions. In a corresponding study the mean Kt/V was 1.06 ± 0.05, where only 39.1% of all patients achieved the Kt/V target (Adas et al., 2014).

Other studies have found similar findings. A study conducted in Iran found the mean Kt/V to be 1.17 ± 0.4, where in 56.7% of patients the value of the Kt/V ratio was less than 1.2 (Amini et al., 2011). In a study conducted in Sri Lanka, only 28.2% of dialysis sessions had a Kt/V value ≥ 1.2 (Rodrigo et al., 2010). In Europe, the mean delivered dialysis dose as measured by the Kt/V ratio ranged from 1.28 to 1.50 (Hecking et al., 2004).

Adequacy of hemodialysis also has beneficial effects on the quality of life of hemodialysis patients. A greater value of the Kt/V ratio has been associated with an improved score in the physical dimension of quality of life, but not in the mental and renal dimensions (Hasan et al., 2021).

In a Canadian study hemodialysis adequacy was associated with improved quality of life in 4 of 11 dimensions of kidney disease, 6 of 8 dimensions of the SF-36 questionnaire, and the visual analog scale EQ-5D (Manns et al., 2002). Also, hemodialysis adequacy has been associated with the emotional role of the SF-36 Quality of Life Scale (Kalender & Tosun, 2014).

In the present study the body dimension subscales were positively correlated with increasing Kt/V ratio. A similar correlation was found for the subscales of the psychological dimension of quality of life. These results are in accordance with the literature (Kalender & Tosun, 2014; Manns et al., 2002).

This association may be attributed to repeated doctor-patient interactions, which may have increased patients' interest in the concept of quality of life. This may encourage physicians to pay more attention to the psychological aspects of the patient when reassessing quality of life. Several studies have examined the association between dialysis adequacy (using the Kt/V ratio) and health-related quality of life. Some showed no significant correlation, while some showed different results (Ayoub & Hijjazi, 2013; Merkus et al., 1997).

In the present study, scores on all three subscales of the physical dimension were below average, indicating poor physical functioning in these patients. It is a fact that in end-stage renal disease, the physical dimension is more affected mainly due to the physical inactivity of the patients. Physical activity is related to physical characteristics of the patient, such as body mass index.

Obese patients and those who do not exercise have been reported to be physically inactive and have a poorer quality of life. In these patients, physical exercise has improved their health-related quality of life (García-Martínez et al., 2020).

Another reason why the patients in the present study have a low physical quality of life is the weakness they feel. Frailty is a clinical syndrome associated with age or any condition that contributes to the reduction of the physiological capacity of multiple organ systems. Frailty in hemodialysis patients has been reported as a factor that reduces patients' quality of life (Adame Perez et al., 2019; Nixon et al., 2020).

Frailty has an impact not only on the physical dimension of quality of life, but also on the mental one (Lee et al., 2015).

The psychological dimension of quality of life includes social functioning, role limitations resulting from psychological functioning, and general mental health. In the present study, the mental health score was moderate to poor. The mental state of dialysis patients is closely related to social status, which is expected to change significantly due to their illness and their inability to work and obtain adequate financial security.

As a result, these patients lose their self-esteem and feel disabled. In addition, hemodialysis itself can cause mood and sleep disturbances that can

lead to greater psychological distress, further burdening health professionals, physicians and nurses, working in hemodialysis units (Czyżewski et al., 2014; Mapes et al. al., 2004).

Hemodialysis patients suffer from depressive thoughts, lack of positive thoughts, anxiety and a sense of self-isolation, which results from physical inactivity. Hemodialysis patients experience anxiety about disease progression, initiation of dialysis, long wait for transplant or transplant outcome, and awareness of impending death. Both anxiety and depression are associated with poor outcomes in dialysis patients and are predictors of reduced quality of life (Palmer et al., 2013).

Dialysis patients enter a vicious cycle. On the one hand they experience depression which reduces their quality of life and on the other hand poor health-related quality of life leads to greater depression (Wyld et al., 2019). In the present study patients scored moderately on the physical dimension of quality of life, indicating that these patients have a low functional status, contributing in turn to a low mental quality of life (Gutiérrez-Peredo et al., 2020).

Good sleep is crucial for people's good health. In the literature, various rates of sleep disorders in dialysis patients have been reported, ranging from 57.1% to 90.86% (Abassi et al., 2016; Chang & Yang, 2011; Mehrabi et al., 2017; Sadeghi et al. al., 2010). In a Canadian study, it was found that the majority of hemodialysis patients had pathological sleepiness.

Sleep latency was associated with urea. When the type of hemodialysis was changed to nocturnal hemodialysis, urea nitrogen and sleep apnea severity were significantly reduced (Hanly et al., 2003). Another study reported that two-thirds of dialysis patients had poor sleep. In the same study and consistent with the results of the present study, poor physical functioning was associated with sleep disturbance (Sabbagh et al., 2008).

Thus, in the present study the quality of sleep was correlated with the quality of life of the patients. The better quality of sleep the patients had, the better their quality of life. Also, it was found that the quality of sleep is related to physical activity and specifically the patients who did physical exercise had a better quality of sleep and therefore a better quality of life.

One study showed the beneficial effect of endurance exercise, a non-pharmacological strategy, in improving total sleep time, sleep latency, night awakenings and sleep efficiency in hemodialysis patients. In the same study, endurance exercise was found to enhance the redox and inflammatory profile in these patients, likely as a result of increased NO bioavailability and decreased asymmetric dimethylarginine (ADMA) concentration (Corrêa et al., 2020).

Physical activity and increased energy expenditure have been reported to improve sleep quality in hemodialysis patients (Cho et al., 2018). One study found that resistance exercise reduced body fat and improved glycemic homeostasis and sleep quality in this population (Sakkas et al., 2008). A possible explanation for this response, at least in part, would be an exercise-induced increase in a facilitator of glucose uptake, NO (Sylow et al., 2017).

Limitations: The present study has some limitations. Assessing dialysis adequacy alone is a limitation because it is not done in a single way. Also, the quality of life is subjective for each patient and in literature there is heterogeneity of the tools used to assess it.

Conclusions: Adequacy of clearance of the patients included in the present study was within the target according to international guidelines. Patients with better quality of sleep and better quality of life, both overall and in its individual dimensions, had greater clearance adequacy. Furthermore, the patients' quality of life was found to be moderate to poor with poor physical functioning and moderate to poor mental health. Men, younger patients, patients with a higher level of education, those with better sleep quality and those who exercised had an increased quality of life.

Also, physical exercise had better sleep quality and better quality of life. Younger patients had better sleep quality. Patients who exercised had better quality of life, and this is because patients who exercised did not suffer from musculoskeletal problems, which are responsible for lower quality of life.

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