ORIGINAL RESEARCH

The relationship between spirometric parameters and hemodialysis adequacy in hemodialysis patients

Feyzi Gokosmanoglu[1], Ceyhun Varim[1], Hakan Cinemre[1], Yasemin Kaya[2], Gulsah Baycelebi[3]

[1]Department of Internal Medicine, Faculty of Medicine, Sakarya University, Turkey;
[2]Department of Internal Medicine, Faculty of Medicine, Ordu University, Turkey;
[3]Department of Internal Medicine, Ordu Unye State Hospital, Ordu, Tukey.

Corresponding author: Ceyhun Varim, MD;
Address: Adnan Menderes caddesi, Saglik Sokak, No. 195-54000, Adapazari/Sakarya, Turkey;
Telephone: +902642552106; E-mail: ceyhunvarim@yahoo.com

Abstract

Aim: In our study we aimed to investigate the relationship between spirometric parameters and Kt/V, which is an indicator of dialysis adequacy.
Methods: The study was conducted at four centers in Turkey using Kt/V values in evaluating hemodialysis adequacy. Subjects included 71 patients 18 years old and above who had been receiving hemodialysis treatment for at least six months. Patients' Kt/V values were calculated. Spirometric parameters of FEV_1, FVC, FEV_1/FVC, PE, and FEF_{25-75} were measured in all patients. Relationships between these parameters and URR, serum electrolytes, serum creatinine, blood urea nitrogen, and hemoglobin were assessed.
Results: Factors potentially affecting patients' spirometric parameters of FEV_1, FVC, FEV_1/FVC, PEF, and FEF_{25-75} were examined by using cascading multiple linear regression analysis method. The highest variance (R^2) model for FVC was determined as having two components, age and Kt/V. For the FEV_1, a three-factored model was formed, and age and Kt/V were determined to be independent predictor indicators. Regarding the PEF value, Kt/V and age were found to be independent predictors for the four-component model.
Conclusion: Our findings indicate that age and dialysis adequacy (Kt/V) constitute statistically significant independent predictors for spirometric parameters in hemodialysis patients.

Keywords: dialysis adequacy, hemodialysis, spirometric parameters.

Introduction

Chronic renal failure (CRF) is a chronic and progressive disease. A decrease in glomerular filtration rate (GFR) continues with deterioration of kidneys metabolic-endocrine functions and impairment of fluid-solid balance regulation.When creatinine clearance falls below 5-10 ml/minute/1.73 m^2, end stage renal failure is indicated and patients require renal replacement treatments, such as hemodialysis, peritoneal dialysis and renal transplantation. The most used renal replacement treatment is hemodialysis (HD). Studies have found that effective hemodialysis decreases morbidity and mortality. Pulmonary complications are frequently seen in these patients due to inadequate dialysis or because patients do not obey fluid restrictions. Pulmonary edema, pleural effusion, fibrosis, calcification, pulmonary hypertension, and/or hemosiderosis may occur in patients diagnosed with CRF (1). Also, bronchitis, interstitial fibrosis, and hyperemia are often detected in these patients in autopsy (postmortem) examinations (2). The most frequently seen complications are clinical or subclinical pulmonary edema and pleural effusion. When creatinine clearance falls below 50 ml/minute/ 1.73 m^2, fluid retention starts in the body, and due to excessive fluid uptake, pulmonary capillary pressure increases. Uremic toxins impair pulmonary capillary permeability and as a result pulmonary edema occurs. Also, cardiac disorders in uremic patients contribute to pulmonary edema and pleural effusion (2).

Getting efficient HD is dependent on several factors. Some of these factors include dialysis adequacy (Kt/V), patients' nutritional status, existing comorbid diseases, degree of anemia, social-economical state, patients' compliance, adequate bloodstream and the type of membrane used in hemodialysis. The most used indicators of dialysis adequacy are measurements of urea clearance in each HD session. For this purpose, urea reduction rate (URR) and Kt/V are calculated. It has been demonstrated that when Kt/V increases, morbidity and mortality rates significantly decrease (3).

Nowadays, after clinical inspection and lung graphics (X-ray), spirometric tests become one of the basic investigation methods in diagnosis, treatment and monitoring of diseases. With these tests, we can evaluate pulmonary functions in an objective and quantitative manner. There are few studies investigating the relationship between Kt/V adequacy and respiratory functions in hemodialysis patients. In our study we aimed to investigate the relationship between spirometric tests and Kt/V value, which is an indicator of dialysis adequacy.

Methods

The study was conducted at four centers in Turkey using Kt/V values in evaluating hemodialysis adequacy. Subjects included 71 patients who were 18 years old and above and who had been undergoing dialysis treatment for at least six months. Exclusion criteria included any pathological findings of respiratory or circulatory system in the anamnesis or physical examination, having a rheumatic disease, chronic lung disease or cerebrovascular disease, hemoglobin <7 gr/dlt, or ejection fraction <40%. Patients were undergoing dialysis twice or three times a week. Effective surface area changed between 1-2.2 m^2 according to the patient's body surface area (1 m^2/m^2 body surface area), FX class high flux hemodialyzer (FX 50, FX60, FX80) standard heparinization, and with Fresenius 4008-B trademark hemodialysis machines at a blood flow of 250-400 ml/minutes and a dialysate pump rate 300-700 ml/minutes, from arteriovenous fistula.

According to the NFK-DOQ criteria (4), blood samples were taken via arterial needles before starting dialysis procedure and applying heparin or serum in order to establish pre-dialysis urea values. To establish post-dialysis urea values, we decreased the pump rate of hemodialysis machine to 50 ml/ minute for a period of 15 seconds. At the end of this period, we took blood from the nearest blood collection port on the hemodialysis set and finished the dialysis procedure. Blood samples were taken in the middle session of the week from patients undergoing dialysis three times a week, and at the beginning session of the week from patients undergoing dialysis twice a week. We calculated the Kt/V values of patients who were included to the study twice a month for a total of 12 times. Kt/V value was calculated with Daugirdas-2 formula [Kt/V= -1n (R-0.008 t) + (4-3.5×R) × UF/KVA] (3). The arithmetic average of these Kt/V values was decided as patients Kt/V value. Normal Kt/V value was decided as $\geq$1.2 according to National Kidney Foundation - Dialysis Outcomes Quality Initiative criteria because there is a consensus on $\geq$1.2. URR, which shows the reduction rate of urea in one dialysis session, was calculated as URR=100-(1-BUN post-dialysis/BUN pre-dialysis). It is suggested that minimum target URR value should be 0.65 (4).

Creatinine, total calcium (Ca^{+2}), phosphate (P), albumin, uric acid, hemoglobin (Hgb), iron (Fe^{+3}) and total iron binding capacity (TIBC), ferritin, and cholesterol were also assessed from the serum samples. Patients underwent spirometric tests after hemodialysis, after becoming clinically stabile. The spirometry test was performed using a spirometric V plus spirometric device, with the patients sitting at a 90º sitting-up position. Patients were all previously informed about the tests. Spirometric tests were performed with at least three technically acceptable methods approved by the American Thoracic Society criteria (5). The highest values obtained from three different curves were taken into the study. Forced vital capacity (FVC), forced expiratory volume at first second (FEV_1), FEV_1/FVC, forced expiratory flow rate (FEF_{25-75}), and peak flow rate were evaluated among spirometric parameters.

Statistical analysis

The basic and definitive data were defined as mean and standard deviation, in those showing a normal distribution and, median and a low-high interval, in those not showing a normal distribution. For group comparisons, Student's t-test and the non-parametric Mann-Whitney U-test were used. Multiple cascading regression analysis was used while searching for factors that affected spirometric parameters. Predictors having the highest variance (R^2) were introduced into the regression analysis. All P-values were calculated as double-sided. SPSS 16.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

Results

There were 39 males (54.9%) and 32 females (45.1%), for a total of 71 hemodialysis patients in this study. The mean age was 54.9±13.4 years (range: 20-82 years) and the disease follow-up period was rather skewed with a median of 57 months (range: 6-216 months). The demographic characteristics, laboratory parameters and primary diseases of the patients are shown in Table 1.

Because Kt/V values were inadequate (Kt/V<1.2) for seven patients, we could not make a group comparison. There were 15 patients whom URR were not enough (<65%). Factors potentially affecting FEV_1, FVC, FEV_1/FVC, PEF and FEF_{25-75} as spirometric parameters, were searched by forming multiple cascading linear regression analysis models. In regression analysis, predictor factors supplying the highest R^2 were, respectively, Kt/V, age and hemoglobin for FEV_1; Kt/V and age for FVC; and Kt/V, age, hemoglobin and calcium levels for PEF. A regression model containing these factors was formed. For FVC, the two component model including age and Kt/V had the highest variance (R^2). Regression equation was as follows: FVC = 5.79 – (0.039*age) – (0.864*Kt/V). Remarkably, age and Kt/V were found to be statistically significant independent predictors (Table 2). The parameters showed normal distribution. A normal probability graphic of FVC values is shown in Figure 1.

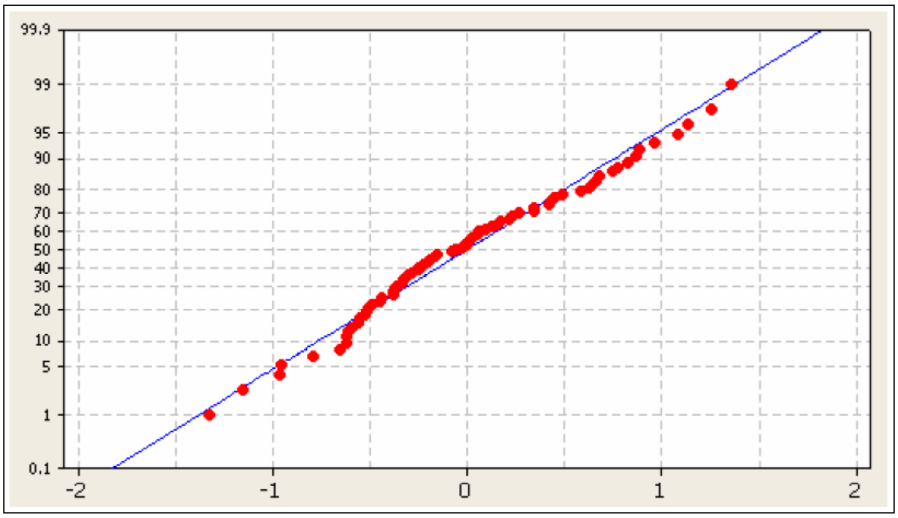
Table 1. Properties of hemodialysis patients

Demographic properties	Mean ± SD	Median
Patients' age (years)	54.86±13.4	54
Dialysis period (months)	57.14±51.6	57
Males (number)	39	
Females (number)	32	
BMI (kg/m^2)	26.74±4.3	26
Causes of chronic renal failure (numbers)		
Diabetic nephropathy	28	
Hypertensive nephropathy	14	
Glomerulonephritis	7	
Policystic kidney disease	6	
Urological diseases	5	
Pregnancy and complications	3	
FMF – Amyloidosis	2	
Other	6	
Laboratory Results		
Serum Albumin	3.87±0.5	3.8
Hemoglobin	11.2±1.4	11.2
Urea	146.9±38.7	146.9
Creatinine	6.96±2	6.9
Potassium	5.11±0.7	5.1
Calcium	8.4±0.7	8.4
Phosphate	4.9±1.4	4.9
Parathormone	284.6±356	284
Ferritin	1172.2±447	1172
Transferrin saturation (%)	35	
Total cholesterol	165±50	165
Working Parameters		
URR	67.57±10	67
Kt/V	1.4±0.2	1.4
FVC	2.35±0.9	2.3
FEV1	1.94±0.7	1.9
FEV_1/FEV	82.88±9.7	82.8
FEF_{25-75}	2.12±1	2.1
PEF	291.1±121	291

Table 2. Regression analysis: FVC and age, Kt/V

Predictors	Coefficient	T	P
Age	-0.039	8	<0.001
Kt/V	-0.864	-2.47	0.016
	S=0.764	R^2=32.3%	

Figure 1. Normal probability graph of FVC

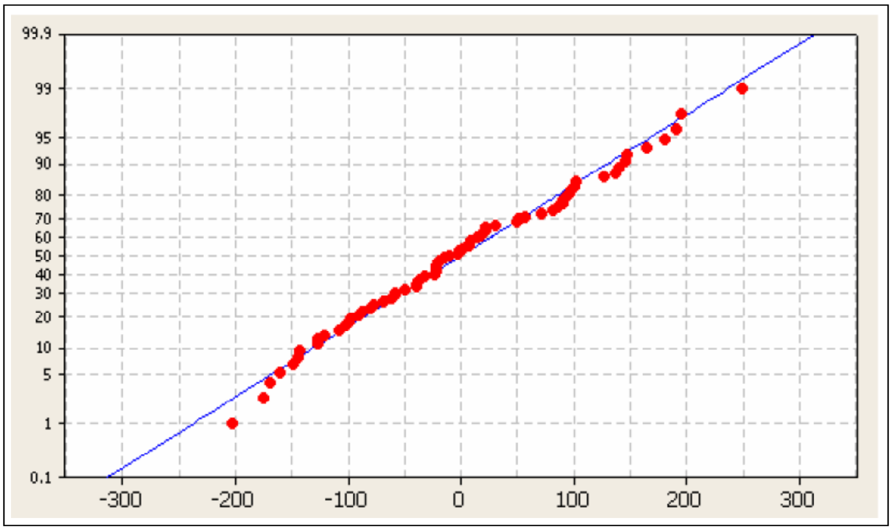


For the FEV_1, a triple model consisting of age, Kt/V and hemoglobin had the highest R^2 value. Regression equation was as follows: $FEV_1 = 4.13 – (0.031*age) – (0.627*Kt/V) + (0.042*Hgb)$. Age and Kt/V values were statistically significant among these three parameters as shown in Table 3. Parameters showed a normal distribution. The normal probability of FEV_1 value is shown in Figure 2.

Table 3. Regression analysis: FEV_1 and age, Kt/V, Hemoglobine

Predictors	Coefficient	T	P
Age	-0.031	0.0056	<0.001
Kt/V	-0.627	0.276	0.027
Hgb	0.042	0.048	0.388
	S=10.5	R^2=34.7%	

Figure 2. Normal distribution of FEV_1

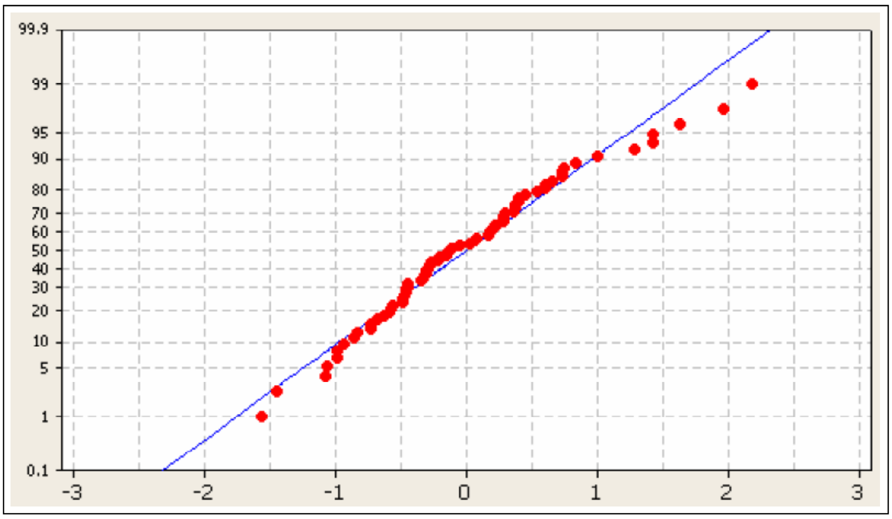


For the PEF, a tetra model consisting of age, Kt/V, Hgb and Ca^{+2} had the highest R^2. Regression equation was as follows: PEF = 430 – (4.6*age) – (130.5*Kt/V) + (9.3*Hgb) + (23.8*Ca^{+2}). Among these, only age and Kt/V values were statistically significant as presented in Table 4. Parameters showed normal distribution. A normal probability graph of PEF value is shown in Figure 3.

Table 4. Regression analysis: PEF and age, Kt/V, Hgb, Ca^{+2}

Predictors	Coefficient	T	P
Age	-4.6	-4.74	0.000
Kt/V	-130.5	-2.69	0.009
Hgb	9.3	1.09	0.28
Ca^{+2}	23.8	1.46	0.15
	S=10.5	R^2=22.9%	

Figure 3. Normal distribution of PEF



The highest R^2 value of the regression analysis, which was formed by calculating FEV_1/FVC values, was 34.2%. Age, Kt/V and ferritin levels were accepted as the best indicators.

Discussion

We observed 71 patients regularly undergoing hemodialysis for chronic renal failure, and found that age and Kt/V values are independent predictors for FVC, FEV_1 and PEF, ferritin and Kt/V values are independent predictors for FEV_1/FVC percentages. The significance values are in the order of PEF> FVC> FEV_1.

There may be pathological changes without respiratory symptoms or findings in the lungs of uremic CRF patients undergoing hemodialysis. Respiratory system complications in chronic renal failure patients, having regular hemodialysis treatment, are well studied. However, the affect of hemodialysis on pulmonary function is less known (6).

Reduction in lung diffusion capacity, decrease in tidal volume with restrictive type pulmonary disease, and interstitial edema are the most frequent of these pathologies (7). Research involving PEF measurements has showed that 75% of hemodialysis patients have a restrictive type of pulmonary diseases. Also, it has been reported that restrictive type pulmonary diseases are most seen in hemodialysis, peritoneal dialysis and renal transplant patients (8). In the results of our study, the highest relationship with Kt/V was detected as the values of PEF.

There are two ways of respiratory function loss in CRF patients who do not have primary pulmonary diseases. Firstly, long-term interstitial and alveolar edema causes fibrosis in CRF patients. The basic property of dialysis is that it removes body's volume overload and excess fluid from the lungs. Kovelis et al. showed in their study that there was a statistically significant increase in FVC values and statistically insignificant increase in FEV1 values at the first week of dialysis, in patients undergoing dialysis for the first time (9).

In addition, we showed in our study that there is a significant relationship between dialysis adequacy indicators and respiratory parameters also in patients undergoing dialysis for a long time. Kovelis et al. showed that the most important factor playing a part in the increase of FVC is the reduction of body weight by removing excess fluid through dialysis (9). Despite this fact, in another study no relationship was detected between improvement in spirometric parameters and weight loss and laboratory indexes after dialysis (10). The second factor related to impairment in respiratory functions is when patients' blood has an allergic reaction with the dialysate membrane and an inflammatory response occurs. This condition may be eliminated with an increase in respiratory distress after dialysis session. None of the patients in our study reported an increase in respiratory distress.

It has been shown in previous studies that hemodialysis corrects spirometric parameters (11), improves exercise toleration and increases the quality of life (12). Compared with healthy people, CRF patients in our study had significantly lower spirometric values. Furthermore, patients' symptoms significantly decreased after dialysis. However, in some other studies no effects of dialysis on spirometric parameters could be found (13). Also, no significant difference between spirometric parameters, as measured at the beginning, middle, and end of the dialysis, could be detected (14). This condition can be explained as the minimal alveolar edema at the pulmonary tissue of the patients undergoing hemodialysis may correct symptoms but make no change in spirometric parameters. In our study, there is a relationship between Kt/V and spirometric parameters and the significance degree is PEF> FVC > FEV_1.

In another study, it was found that patients who were on a long-term hemodialysis program showed a significant decrease of the FVC following five years' treatment and none of the recorded spirometric parameters improved significantly one-hour after hemodialysis compared to the pre-hemodialysis period. They also found out that, although changes in spirometry observed in the population getting hemodialysis treatment have a reversible character during the first years of renal replacement therapy, after five years these changes become irreversible (6). In our study, we searched dialysis adequacy and found out that long-term efficient dialysis may be the cause of the significant relationship between respiratory parameters and dialysis adequacy. The dialysis adequacy rate was 90% in our patients and the inadequate dialysis rate was 10%. In those studies, because dialysis adequacy and spirometric parameters were not compared, inadequate dialysis may have been the cause of the ineffectiveness of hemodialysis on respiratory function improvement or inadequate dialysis itself may be a major cause of respiratory function deterioration. Most studies have shown significant improvements in respiratory symptoms at the end of the dialysis (12-14).

One study compared patients undergoing hemodialysis with bicarbonate and acetate dialysate and found that improvement in spirometric parameters was only significant in patients undergoing hemodialysis with bicarbonate. All spirometric parameters showed significant increases in the bicarbonate group, except FEV_1/FVC ratio (10). In our study, we used bicarbonate dialysate in all patients and found that the relationship between dialysis adequacy and increase in spirometric parameters such as PEF, FVC, FEV_1 was statistically significant. However, similar to a previous study (10), no increases in FEV_1/FVC and FEF_{25-75} were observed in our study and predictor factors could not be detected.

In conclusion, in our study, age and dialysis adequacy (Kt/V) were found to be the most significant indicators among the respiratory functions' parameters in hemodialysis patients. It is known that Kt/V affects morbidity and mortality of hemodialysis patients to a high degree. Respiratory distress in hemodialysis patients or deterioration of spirometric parameters can show that clearance with dialysis is inadequate. We expect that dialysis adequacy will reduce the loss of pulmonary capacity and thus increase the survival rate of patients.

Conflicts of interest: None declared.

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