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Original Article

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Outcome and Risk Factors for Mortality in Peritoneal Dialysis Patients: 22 Years of Experience in a Turkish Center

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ABSTRACT

Background: European peritoneal dialysis populations have identified and reported mortality and morbidity risk factors. However, no reports are pointing out the factors affecting the outcomes of these patients during more than 2 decades of follow-up in Türkiye. This single-center study aims to evaluate patient mortality and peritonitis rates and estimate confounding factors affecting patient mortality over 22 years.

Methods: Adult patients who underwent peritoneal dialysis at our center between December 1994 and December 2016 were enrolled in this retrospective cohort study. The primary outcome of the present study was mortality, and the secondary outcomes were technical failure and peritonitis.

Results: Two hundred fifty patients were included in this study. The patients were followed up for a median of 39.5 months (range 17-71). Forty-eight (19.2%) patients died. Survival rates at 5, 10, and 15 years were 86.8% (217/250), 64.6% (86/133), and 41.1% (30/73), respectively. The prevalence of diabetes mellitus [14 (29.2%) vs. 20 (9.9%); $P < .001$] and cardiovascular disease [16 (33.3%) vs. 24 (11.9%); $P < 0.001$] were significantly higher in the deceased group compared to the survival group. Cardiovascular disease was the leading cause of death [26 (54.1%)]. Age (hazard ratio (HR) 1.06; 95% CI, 1.04-1.09; $P < .001$), male sex (HR 2.07; 95% CI, 1.10-3.90; $P = .024$), and transfer to peritoneal dialysis due to vascular access problems (HR 3.91; 95% CI, 1.90-8.07; $P < .001$) were associated with mortality in multivariate analysis. Also, catheter exit-site infection, peritonitis rate, catheter removal, and technical complications were similar between the groups. The peritonitis rate was 0.2 episodes per patient per year.

Conclusion: The mortality rate of the patient population in our center was similar to Europe and the United States. Cardiovascular diseases and diabetes are the leading causes of death in Turkish peritoneal dialysis patients, as in other populations.

Keywords: Chronic kidney diseases, peritoneal dialysis, mortality

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INTRODUCTION

Kidney replacement therapies are essential for the end-stage kidney disease (ESKD) patient's survival. Hemodialysis (HD) is the leading kidney replacement treatment, but more than 150,000 patients are under peritoneal dialysis (PD) worldwide.[1] According to the Turkish Society of Nephrology, the prevalence of PD was reported as 4.1%.[2]

Several conditions, including uremic toxins, peritoneal catheters, and dialysis solutions, may prompt cardiovascular disease in PD patients.[3,4] Also, demographic data (e.g., older patients, body mass index (BMI) <18 kg/m^2) and comorbid diseases (e.g., cardiovascular diseases and diabetes mellitus) have been documented as risk factors for mortality in these patients. In addition, several European PD populations have identified and

reported risk factors for mortality and morbidity.[5] However, there were no reports in Türkiye that pointed to factors influencing the outcome of these patients during more than 2 decades of follow-up. This single-center study aims to evaluate patient mortality and peritonitis rates and estimate confounding factors affecting patient mortality over twenty-two years.

MATERIAL AND METHODS

Patient Characteristics

Adult patients undergoing PD at our center between December 1994 and December 2016 were enrolled in this retrospective cohort study. Patients with more than 3 months of clinical follow-up under PD were included in the analysis. Patients lost to follow-up were excluded (Figure 1).

The demographic, clinical, and laboratory results were collected from the hospital data and analyzed retrospectively. Age at the initiation of PD, gender, primary kidney disease, history of kidney replacement therapy, comorbidity, previous peritonitis episodes, Kt/V, and creatinine clearance values were obtained. Coronary artery disease, cerebrovascular disease, and peripheral arterial disease are defined as cardiovascular diseases. Adequacy of dialysis was assessed annually through measurement of weekly Kt/V for urea and weekly creatinine clearance using standard methods. Mean values of Kt/V urea and creatinine clearance during follow-up were recorded for each patient. The study obtained approval from the Medical Ethics Committee of Istanbul University Faculty of Medicine on February 26, 2016, with protocol number 2016/269. Informed consent was obtained from the study participants.

Study Outcomes

The primary outcome of the present study was mortality during follow-up in PD patients. The secondary outcomes were PD technical failure and peritonitis in PD patients.

MAIN POINTS

- The present study analyzed 22 years of experience with 250 peritoneal dialysis patients with a follow-up of 4 years at a large university hospital. The mortality rate of the peritoneal dialysis population at our center was similar to Europe and the United States.
- Patients transferred to peritoneal dialysis due to vascular access problems have a higher mortality rate than those who choose it themselves. Choosing peritoneal dialysis before vascular access problems in hemodialysis patients may reduce mortality rates.
- There were no differences between the survival and nonsurvival groups in body mass index and first-, fifth-, and tenth-year weight differences.
- The peritonitis rate was 0.2 episodes per patient per year. The peritonitis rate of our center is below the target of the International Society of Peritoneal Dialysis.

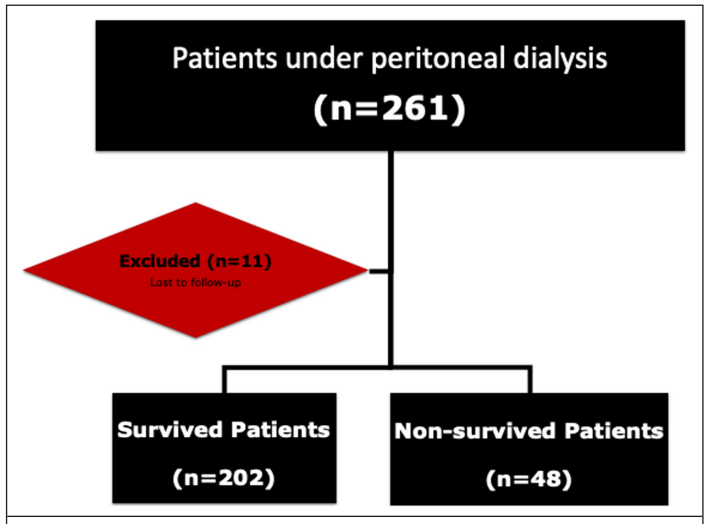

Figure 1. Flowchart of the patients in the study.

Statistical Analysis

Patients were categorized as survivors and deceased. All variables were analyzed according to the groups. Gender, etiology of chronic kidney disease, comorbid diseases, kidney replacement history, complications, and reasons for PD choice were presented as numbers and percentages. Body mass index, weight, follow-up period, peritoneal creatinine, urea clearance, and residual clearance (with nonnormal distribution) were specified with medians and interquartile ranges. Chi-square and Fisher's exact tests were used for categorical variables, and the Mann–Whitney *U*-test was used for quantitative variables with a non-normal distribution.

Cox regression analysis was used to determine potential confounders and mortality. Known risk factors (age, sex, cardiovascular diseases, diabetes mellitus) and significant variables between groups (reason for PD choice, prior kidney replacement history) were entered into the univariate analysis. A multivariate analysis was calculated by using confounders obtained from univariate analysis. Any collinearity was not detected, and effect modifiers were not added in the Cox regression analysis. Hazard ratios and the corresponding 95% CIs refer to the increase per unit in a continuous variable. A *P*-value of less than .05 is considered significant.

RESULTS

Two hundred and fifty patients (54.4% males) were enrolled in this study. Of them, 34.8% of the patients reached ESKD due to chronic glomerulonephritis, and 10.4% (n = 26) had diabetic nephropathy. Thirty-four patients (13.6%) had diabetes mellitus, 40 (10.4%) had cardiovascular diseases, and 7 patients (2.8%) had a history of malignancy. The prevalence of diabetes mellitus [14 (29.2%) vs. 20 (9.9%); $P < .001$] and cardiovascular diseases [16 (33.3%) vs. 24 (11.9%); $P < .001$) was significantly higher in the deceased group compared to the surviving group. Table 1 shows the demographic characteristics of patients.

Table 1. Demographic Data of Patients According to Mortality

	All Patients (n = 250)	Surviving Patients (n = 202)	Deceased Patients (n = 48)	*P*
Age (years)	53 (41-62)	50 (38-60)	68 (56-78)	**<.001**
Gender n, (%)				
Male	136 (54.4)	104 (51.5)	32 (66.7)	.06
Female	114 (45.6)	98 (48.5)	16 (33.3)	
Etiology of CKD n, (%)				
Chronic glomerulonephritis	87 (34.8)	84 (41.6)	3 (6.2)	**<.001**
Diabetic nephropathy	26 (10.6)	13 (6.4)	13 (27.1)	**<.001**
Hypertensive nephrosclerosis	24 (9.6)	15 (7.4)	9 (18.8)	**.016**
Polycystic kidney disease	18 (7.2)	16 (7.9)	2 (4.2)	.54
CAKUT	36 (14.8)	26 (12.9)	10 (20.8)	.16
Unknown	53 (21.2)	45 (22.3)	8 (16.7)	.39
Other	6 (2.4)	3 (1.5)	3 (6.2)	.09
Comorbid disease n, (%)				
Diabetes mellitus	34 (13.6)	20 (9.9)	14 (29.2)	**<.001**
CVD	40 (10.4)	24 (11.9)	16 (33.3)	**<.001**
Malignancy	7 (2.8)	5 (2.5)	2 (4.2)	.62
Prior kidney replacement history n, (%)				
Initially PD	111 (44.4)	98 (48.5)	13 (27.1)	**.007**
Switched to PD from HD	116 (46.4)	86 (42.6)	30 (62.5)	**.013**
Switched to PD from TX	41 (16.4)	34 (16.8)	7 (14.6)	.87
BMI (kg/m^2)	23.5 (20.7-26.5)	23 (20.4-26.1)	24.9 (21.9-28.1)	.94
First-year weight difference	2.15 (-0.28-4.78)	2 (0-4.9)	2.4 (-1.5-4.25)	.94
Fifth-year weight difference	2 (0-8.2)	2.3 (0-8.6)	1.5 (-0.7-5.6)	.26
Tenth-year weight difference	3.3 (-0.2-7.8)	3.3 (-0.3-8)	2.5 (1-4)	.19

P-values were obtained by comparing living and deceased patients, and values below .05 are shown in bold. Variables are demonstrated as median (interquartile range 25-75) or number (percentages).
BMI, Body Mass Index; CAKUT, congenital anomalies of the kidney and urinary tract; CKD, chronic kidney disease; CVD, cardiovascular disease; HD, hemodialysis; PD, peritoneal dialysis; TX, transplantation.

Patients were followed with a median duration of 39.5 months (interquartile range (IQR) 25-75, 17-71). One Hundred and eleven patients (44.4%) had started PD first, and 116 (46.4%) had switched from HD to PD. Also, the number of initial PD patients in the surviving group was significantly higher than the deceased patients [98 (48.5%) vs. 13 (27.1%); *P* = .007], and the number of patients were transferred from HD to PD was lower in the surviving group compared to the other group [86 (42.6%) vs. 30 (62.5%); *P* = .013) (Figure 2). There were no differences between the surviving and deceased groups in BMI, first-, fifth-, and tenth-year weight differences.

During the follow-up period, 48 patients died. The 5, 10, and 15-year survival rates were 86.8% (217/250), 64.6% (86/133), and 41.1% (30/73), respectively. Cardiovascular disease was the leading cause of death [26 (54.2%)]. In addition, eight died (16.7%) of sepsis, 6 (12.5%) of the unknown, 3 (6.3%) of malignancy, and 5 (10.4%) of other causes. Patients transferred to PD due to vascular access problems have a higher mortality rate than those who choose PD themselves (42.8% vs. 16.2%; *P* = .01). The study parameters of the patients by mortality are shown in Table 2. Also, 15-year survival patients with high peritoneal membrane permeability had a significantly higher survival rate than patients with low peritoneal membrane permeability (83% vs. 29%; *P* < .001).

Catheter exit-site infection, peritonitis rate, catheter removal, technical complications, and weekly total Kt/V urea were similar between the groups. The most common reason for catheter removal was peritonitis (n = 38). The peritonitis rate was 0.2 episodes per patient per year. The most common cause (n = 115, 47.6%) was culture-negative peritonitis, followed by alpha-hemolytic (n = 19, 7.6%), methicillin-sensitive *Staphylococcus aureus* (n = 14, 5.3%), and nonhemolytic streptococci (n = 9, 3.6%). Study parameters of patients according to peritoneal membrane permeability groups are shown in Table 3.

Although age (hazard ratio (HR) = 1.06; 95% CI, 1.04-1.08; *P* < .001), male sex (HR = 2.19; 95% CI, 1.20-4.00; *P* = .011), cardiovascular disease (HR = 2.53; 95% CI, 1.33-4.81; *P* = .004), and diabetes mellitus (HR = 2.53; 95% CI, 1.36-4.72; *P* = .004), transfer to PD due to vascular access problem (HR = 3.27; 95% CI, 1.70-6.32; *P* < .001) were independently associated with mortality in univariate Cox regression analysis, age (HR = 1.06; 95% CI, 1.04-1.09; *P* < .001), male sex (HR = 2.07; 95% CI, 1.10-3.90; *P* = .024), and transfer to PD due to vascular access problems (HR = 3.91;

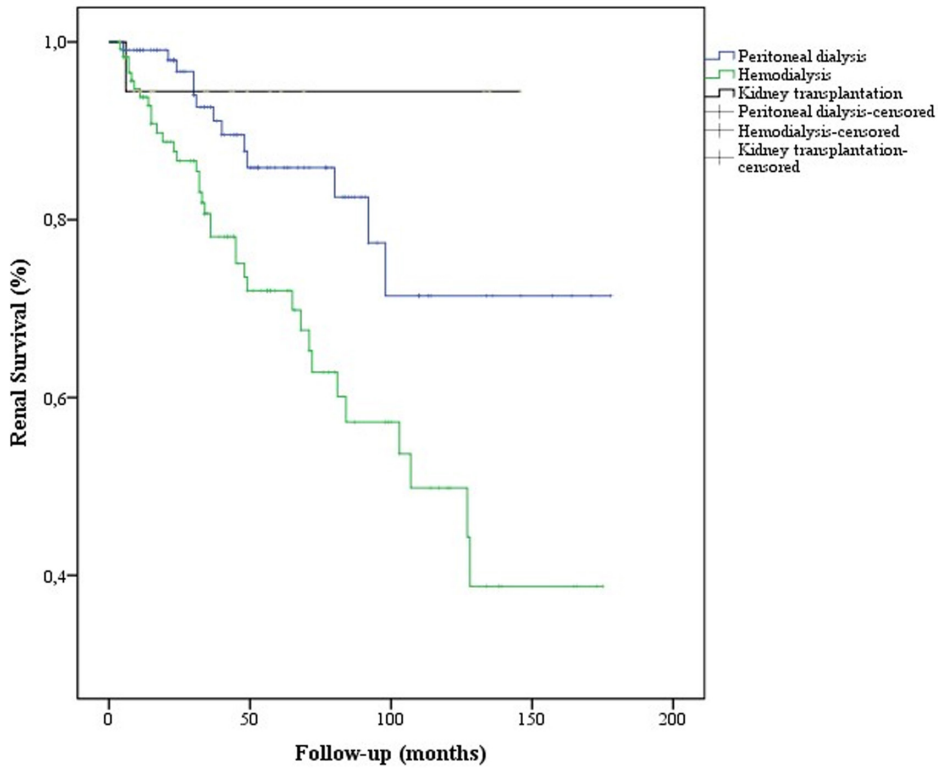

Figure 2. Effect of initial kidney replacement method on patients' survival.

95% CI, 1.90-8.07; $P < .001$) were associated with mortality in multivariate Cox regression analysis. Mortality-associated variables are demonstrated in Table 4.

DISCUSSION

The present study analyzed 22 years of experience of 250 PD patients at a large university hospital with a median follow-up

Table 2. Study Parameters of Patients According to Mortality

	All Patients (n = 250)	Surviving Patients (n = 202)	Deceased Patients (n = 48)	*P*
Follow-up period (months)	39.5 (17-71)	42 (17-72.3)	33.5 (17.5-67.3)	**.09**
Complications n, (%)				
Technical complication	95 (38)	79 (39.1)	16 (33.3)	.55
Peritonitis rate (episodes/patient-year)	0.2 (0-0.6)	0.2 (0-0.5)	0.4 (0-1)	.35
Catheter removal	29 (11.6)	26 (12.9)	3 (6.3)	.31
Catheter exit site infection	53 (21.2)	45 (22.3)	8 (16.7)	.43
Reason for PD choice n, (%)				
Own request	222 (88.8)	186 (92.1)	36 (75)	**<.001**
Vascular access problems	28 (11.2)	16 (7.9)	12 (25)	
Measurements obtained from the peritoneal equilibration test				
Peritoneal Kt/V urea	2.1 (1.9-2.4)	2.1 (1.9-2.4)	2.1 (1.9-2.4)	.11
Peritoneal CCr (L/week/1.73 m^2)	60 (51.5-71.6)	60.1 (51.5-71.3)	57.9 (50.5-73.2)	.94
Residual clearance (mL/min)	0 (0-1.8)	0 (0-1.95)	0 (0-1.04)	**.042**
Survival rate n, (%)				
Fifth year	217/250 (86.8)			
Tenth year	86/133 (64.6)			
Fifteenth year	30/73 (41.1)			

P-values were obtained by comparing living and deceased patients, and values below .05 are shown in bold. Variables are demonstrated as median (interquartile range 25-75) or number (percentages).
CCr, creatinine clearance; PD, peritoneal dialysis.

Table 3. Comparison of Clinical Parameters According to the Peritoneal Membrane Permeability

	Low Average (n = 91)	High Average (n = 95)	High (n = 30)	*P*
Follow-up period (months)	36 (21-57)*	40 (16-78)	72 (48-134)*	**<.001**
Complications n, (%)				
Technical complications	28 (31)	41 (43.1)	16 (53.3)	.36
Peritonitis rate (episodes/patient-year)	0.3 (0-0.6)	0.2 (0-0.6)	0.3 (0.1-0.7)	.31
Catheter removal	6 (6.6)	15 (15.8)	5 (16.7)	.25
Catheter exit infection	21 (23.1)	29 (30.5)	13 (43.3)	.21
Reason for PD choice n, (%)				
Own request	76 (87.9)	84 (88.4)	28 (93.3)	.70
Vascular access problems	11 (12.1)	11 (11.6)	2 (6.7)	
PD modality n, (%)				
CAPD	61 (67)	61 (64.2)	20 (66.7)	.92
APD	30 (33)	34 (35.8)	10 (33.3)	
Measurements obtained from the peritoneal equilibration test				
Peritoneal Kt/V urea	2.1 (1.9-2.4)	2.1 (1.9-2.4)	2.2 (1.9-2.5)	.72
Peritoneal CCr (L/week/1.73 m^2)	54 (46-69)*	61 (53-71)	69 (60-76)*	**<.001**
Residual clearance (mL/min)	0 (0-2.4)	0 (0-1.4)	0 (0-1.9)	.57
Survival rate n, (%)				
Fifth year	77/91 (88)	83/95 (87)	29/30 (97)	.22
Tenth year	29/45 (64)	35/54 (65)	19/21 (91)	.07
Fifteenth year	7/24 (29)	11/31 (36)	10/12 (83)	**.005**

P-values were obtained by comparing the low, low average, high average, and high groups, and values below .05 are shown in bold. Variables are demonstrated as median (interquartile range 25-75) or number (percentages).
APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; CCr, creatinine clearance; PD, peritoneal dialysis.
*In the post hoc analysis, a significant difference was found between the low average and high group (*P* < .001).

Table 4. Factors Associated with Mortality According to the Cox Regression Analysis.

	Univariate Analysis			Multivariate Analysis		
	Hazard Ratio	CI	*P*	Hazard Ratio	CI	*P*
Age	**1.06**	**1.04-1.08**	**<.001**	**1.06**	**1.04-1.09**	**<.001**
Male sex	**2.19**	**1.20-4.00**	**.011**	**2.07**	**1.10-3.90**	**.024**
CVD	**2.53**	**1.33-4.81**	**.004**	**1.08**	**0.52-2.25**	**.85**
Diabetes mellitus	**2.53**	**1.36-4.72**	**.004**	**1.15**	**0.57-2.29**	**.70**
Reason for PD choice (Vascular access problems vs. own request)	**3.27**	**1.70-6.32**	**<.001**	**3.91**	**1.90-8.07**	**<.001**
Prior kidney replacement history	1.24	0.70-2.20	.47			

Values identified as significiant in the Cox regression analysis are presented in bold.
CVD, cardiovascular disease; PD, peritoneal dialysis.

of 39.5 months. The 5, 10, and 15-year survival rates were 86.8% (217/250), 64.6% (86/133), and 41.1% (30/73), respectively. Also, kidney transplantation provides a survival benefit compared to dialysis in initial replacement therapy. In a previous study from Türkiye, the fifth and tenth year survival rates were described as 68.8% and 40.7%, respectively.[6] A previous report from ANZDATA found that 3-year patient survival was 65%-73%.[7] Our survival rates are better than these reports; however, ANZDATA data was obtained from an older database, and the developments in PD treatment can explain this condition (Table 5).

Table 5. Comparison of Patient Survival Outcomes Under Peritoneal Dialysis

	United States[13]	ANZDATA[7]	Europe[14]	Our Center
Patient surviving for 3 years	53.8%	65%-73%	50%	86.8% (5 years)
Technical failure for 3 years		38%		

Some articles have reported that high peritoneal membrane permeability is associated with an increased risk of death in the patient population due to increased protein loss with decreased fluid and minor solute removal.[8] On the other hand, this argument has not been proven yet.[9] In our data set, patients with high peritoneal membrane permeability had a significantly higher survival rate than patients with low peritoneal membrane permeability. However, these results should be confirmed by multicenter studies with a large cohort since the groups were not homogeneous in our single-center study.

According to the US and European Registry Reports, the most common cause of ESKD in PD patients is diabetes mellitus, accounting for approximately 30% of all etiologies.[10,11] In our study, chronic glomerulonephritis was the most common cause of ESKD, followed by congenital anomalies of the kidney and urinary tract and diabetes mellitus. However, patients with diabetic nephropathy had a worse prognosis than nondiabetic patients, similar to previous registry reports.

In our study, the frequency of cardiovascular disease and diabetes mellitus was higher in the deceased group than in the survived group. However, multiple regression analyses showed that age and transfer to PD due to vascular access problems were associated with mortality. This result was associated with the relatively low number of diabetic and cardiovascular patients.

The peritonitis rate of our center is below the International Society of Peritoneal Dialysis[12] target of peritonitis rate at risk, which does not exceed 0.4 episodes per year. Our study found that a history of peritonitis was a predictor of mortality. The reasonable rates of peritonitis in this study can be explained by a single-center study in which patients were monitored regularly. Also, it can be associated with improving patient education, according to the guidelines.

Our study had some limitations. First, this study had a retrospective design, and data collection was not part of a formal prospective study in which all designable parameters were collected. Second, single-center study results may not apply to the other centers. However, the data are fair and can be checked easily in a single-center study.

The mortality rate of the patient population at our center was similar to Europe and the United States. Cardiovascular diseases and diabetes are the leading causes of death in Turkish PD patients, as in other populations.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Committee Approval: The study obtained approval from the Medical Ethics Committee of Istanbul University Faculty of Medicine on February 26, 2016, with protocol number 2016/269.

Informed Consent: Informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Y.C., A.T., S.B.; Design – Y.C., A.T., S.B.; Supervision – A.T., S.B.; Resources – E.D., Y.C.; Materials – E.D., Y.C.; Data Collection and/or Processing – E.D., Y.C., Y.G., F.S.S., U.M.; Analysis and/or Interpretation – E.D., Y.C.; Literature Search – E.D., Y.C.; Writing Manuscript – E.D., Y.C.; Critical Review – E.D., Y.C., Y.G., F.S.S., U.M., A.T., S.B.

Declaration of Interests: The authors have no conflict of interest to declare.

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