











# The Impact of Peritonitis on Clinical Outcomes of PD Patients: A Single Center Experience

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## Abstract

**Objective:** The aim of the present study was to investigate peritonitis episodes and causative agents in patients undergoing peritoneal dialysis (PD), to examine the effects of peritonitis on technical and patient survival, and to determine whether the number of peritonitis episodes and causative agents was a risk factor or not.

**Materials and Methods:** The medical records of 387 patients who started PD between January 2001 and January 2015 were evaluated retrospectively. Patients without peritonitis (Group 1 (n=123 patients)) and with detected peritonitis (Group 2 (n=243 patients)) were divided into two groups. Group 2 patients were subdivided according to the number of peritonitis (Group 2a 1 episode and Group 2b  $\geq 2$  episodes). Sociodemographic data and clinical courses were compared, and the reasons for PD withdrawal were obtained between the groups. Survival analysis was performed, and the effects of peritonitis on mortality were investigated.

**Results:** A total of 427 peritonitis episodes were detected. The most common organism was *Staphylococcus aureus* (36%). The leading cause of death was cardiovascular disease in Group 1, whereas it was infection in Group 2a and Group 2b. Technique survival and mortality rates were similar among the groups. Risk factors for patient survival were history of peritonitis more than once and history of catheter exit site/tunnel infection. History of catheter exit site/tunnel infection was the only risk factor for technique survival.

**Conclusion:** Our study has shown that even though the causes for mortality were different, mortality rates, and technique survival were similar between the two main groups. Infectious complications may affect patient and technical survival.

**Keywords:** Peritoneal dialysis, peritonitis, clinical outcomes

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## INTRODUCTION

Peritoneal dialysis (PD) has been a common choice of renal replacement therapy for end-stage renal disease (ESRD). Although developments in catheter designs, such as initiation of Y connection and dual bags, identification of risk factors, such as nasal carriage, and administration of prophylactic antibiotics while catheter insertion, have resulted in a notable decrease in peritonitis incidence, the infection remains as a significant complication in PD patients. The main cause of peritoneal catheter loss and discontinuation of PD therapy is infection (1-3).

Studies have demonstrated that peritonitis is the leading cause of technique failure for PD patients, but peritonitis rates vary depending on the patient population (4, 5). Severe, recurrent, prolonged peritonitis causes changes in the peritoneal membrane structure and leads to functional alterations and eventually membrane failure. Peritonitis is a major cause of conversion to hemodialysis especially in prolonged circumstances (6-8).

The association between prolonged, recurrent peritonitis episodes and mortality in patients with PD is not clearly understood. Peritonitis is one of the leading eti-



ologies of death directly or indirectly in approximately 16% of PD patients. Peritonitis episodes directly affect mortality in low rates, detected <5% according to most of the studies (8-12). This rate of mortality depends greatly on the causative microorganism and is highest for fungal peritonitis, followed by those due to Gram-negative bacteria (13-16).

The aim of the present study was to investigate peritonitis episodes and causative agents in patients undergoing PD, to examine the effects of peritonitis on technical and patient survivals, and to determine whether the number of peritonitis episodes and causative agents was a risk factor or not.

## MATERIALS AND METHODS

The medical records of consecutive 387 PD patients in our PD unit who began PD therapy between January 2001 and January 2015 were evaluated retrospectively. A total of 21 patients were excluded from the study. Exclusion criteria were recovering renal function, absence of dialysis requirement anymore, aged <18 years old, missing data (coming from another city for the first PD control to us but unavailable after this time), being followed by other PD units. The remaining 366 patients' data were enrolled in the study.

All patients performed PD with a double cuffed, straight Tenckhoff catheter. PD catheters were inserted by Seldinger method in our unit. Surgical technique was used if patients were obese, or Seldinger method was unsuccessful. Antibiotic prophylaxis (at least 1 h prior to the procedure with intravenous cefazolin 1 g vial) was administered to all patients prior to catheterization. After insertion, patients were educated, and approximately 2-3 weeks later, continuous ambulatory peritoneal dialysis or automatic peritoneal dialysis (APD) was started.

Age, gender, educational level, sociodemographic characteristics, the availability of someone to administer PD (e.g., their

family or healthcare workers), and the nature of the use of PD (patient preference or a compulsory choice) were investigated in depth using patient records. We noted whether the patient had previously received hemodialysis, and if so, the history of the hemodialysis treatment was recorded. The etiology of the ESRD and the presence of comorbid systemic diseases, such as hypertension, cardiovascular disease (CVD), cerebrovascular events, and malignancy, were recorded.

Clinical data, such as systolic and diastolic blood pressure measurements, daily urine volumes, daily mean ultrafiltration (UF) amounts, and cardiothoracic indices, were recorded for all patients at the beginning and at the end of the study. Laboratory data, such as serum urea, creatinine, calcium, phosphorus, albumin, intact parathyroid hormone, hemoglobin, ferritin values, and transferrin saturation, were recorded at the initiation of PD treatment and the last visit.

During the follow-up period, infectious complications (peritonitis and catheter exit site/tunnel infections), and culture results were recorded. Patients were classified as having peritonitis if they fulfilled at least two of the following criteria: (1) presence of clinical symptoms (pain, fever, and cloudy dialysate); (2) presence of >100 leukocytes/mm<sup>3</sup> dialysate, with at least 50% polymorphonuclear neutrophils; and (3) positive culture or Gram stain. Culture of the dialysate has been performed as recommended by the International Society for Peritoneal Dialysis (ISPD) (3). Presence of local tenderness, redness, purulent drainage, and/or positive culture from the catheter exit site was categorized as tunnel infection. Exit site drainage cultures were obtained together with dialysate fluid cultures in case of suspicion for catheter exit site/tunnel infection.

We initiate empirical antibiotic therapy as soon as possible after appropriate microbiological specimens have been obtained in our PD unit. Vancomycin (intraperitoneal) 15-30 mg/kg ev-

**Table 1.** Demographic data of the groups

	Group 1 (n=123)	Group 2a (n=112)	Group 2b (n=131)	p
Gender (M/F)	60/63	53/59	62/69	0.96
Age (years)	46±17.5	48.5±16.9	42.8±14.9	0.025
Patients with HD history (n)	21	24	23	0.40
Mean HD period (months)	33.5±27	33.1±44.1	26.2±33.3	0.749
Mean PD follow-up period (months)	27.4±25.9	41.3±35.2	57.8±36	<0.001
Mean APD period (months)	21.3±20.9	25.9±29.2	37.2±28.6	0.034
Treatment modality (CAPD) (n)	94	85	85	0.52
PD choice (compulsory patients) (n)	31	28	20	0.06
Familial support (assisted PD) (%)	19	27	17	0.41
Presence of diabetes mellitus (%)	24	26	23	0.62

ery 5 days and ciprofloxacin 250 mg twice a day are the most commonly used empirical antibiotic treatments, and therapy is also observed according to culture antibiogram results. We remove PD catheter in various situations, such as no clinical response within 5 days despite appropriate antibiotic therapy, patients with sustained high dialysis effluent whole blood cell counts, and patients with fungal peritonitis. We initiate mupirocin ointment in patients with any discharge from the catheter exit site and redness around the catheter after the microbiological specimens are obtained. We start oral or parenteral fluconazole therapy according to clinical severity for patients with prolonged peritonitis and/or catheter withdrawal.

Patients were divided into two groups according to the presence of peritonitis infection. Patients without any peritonitis episode during the follow-up period were defined as Group 1, whereas patients with at least one peritonitis episode were defined as Group 2. Group 2 patients were divided into two groups according to the number of peritonitis episodes as patients with one episode consisted of Group 2a and those with two or more episodes consisted of Group 2b.

Sociodemographic data and clinical courses were compared, and the reasons for PD withdrawal were obtained between the groups. Survival analysis of all patients was performed, and the effects of peritonitis on mortality were investigated.

**Table 2.** Clinical and laboratory data of the groups at initial and last visits

		Group 1 (n=123)	Group 2a (n=112)	Group 2b (n=131)	p
Systolic blood pressure (mm Hg)	Initial visit	117±28	122.6±31.5	117.6±25.4	0.243
	Last visit	113±31	119.7±30.8	110.9±26.7	0.078
Diastolic blood pressure (mm Hg)	Initial visit	72.5±16	76.8±17.7	75.9±16	0.121
	Last visit	71.9±18.4	74.5±16.2	69.9±16.3	0.133
Cardiothoracic index	Initial visit	0.47±0.06	0.48±0.06	0.46±0.05	0.147
	Last visit	0.47±0.06	0.48±0.05	0.47±0.06	0.55
Urine volume (mL/day)	Initial visit	425±505	397±448	401±505	0.898
	Last visit	197±339	184±371	95±237	0.033
Ultrafiltration (mL/day)	Initial visit	984±464.5	988±477	1030±435	0.698
	Last visit	1132±567	1091±525	1052±525	0.54
Kt/V	Initial visit	2.19±0.7	3.0±0.7	2.07±0.7	0.309
	Last visit	2.46±0.8	2.48±0.9	2.65±0.9	0.546
Creatinine (mg/dL)	Initial visit	8.83±3.1	8.7±3.3	8.8±2.9	0.967
	Last visit	9.39±2.9	8.5±3.1	8.7±2.6	0.069
Calcium	Initial visit	8.97±0.96	9±1.01	8.98±1.03	0.581
	Last visit	9.06±1.1	8.9±0.98	9±0.97	0.499
Phosphorus	Initial visit	5.2±1.8	5.2±1.99	4.9±1.5	0.594
	Last visit	4.7±1.6	4.8±1.8	4.32±1.2	0.057
Parathormone	Initial visit	379±513	305±364	353±366	0.421
	Last visit	397±482	407±359	474±463	0.375
Albumin	Initial visit	3.6±0.7	3.7±0.7	3.7±0.6	0.299
	Last visit	3.6±0.7	3.5±0.7	3.5±0.7	0.248
Hemoglobin	Initial visit	10.6±1.9	10.6±1.7	10.5±1.8	0.892
	Last visit	11.2±1.9	11.1±1.8	11.3±2.4	0.819
Ferritin	Initial visit	424.9±413	465±533	434±358	0.781
	Last visit	375±391	403±477	424±355	0.697

This retrospective study was prepared in accordance with the Declaration of Helsinki.

**Statistical Analysis**

Statistical Package for the Social Sciences version 15.0 (SPSS Inc.; Chicago, IL, USA) was used for analysis. Mann-Whitney U test was used for nonparametric variables. One-way ANOVA test was used for analyzing clinical and biochemical parameters. Post hoc Tukey test was performed if one-way ANOVA test was found as statistically significant. Patient and technique survival rates were calculated by Kaplan–Meier test, and outcomes were

compared by the log rank test. Risk factors and calculated hazard ratio for patient mortality were also analyzed by backward logistic regression of the Cox proportional hazards method. Parametric variables were presented as mean±standard deviations. A p value <0.05 was considered statistically significant.

**RESULTS**

A total of 366 patients who have started PD between 2001 and 2015 were evaluated. One hundred ninety-one patients were female. The mean age of the patients was 45.6±16.6 years, and the mean follow-up time was 42.6±35 months. Of the 366 patients,

**Table 3.** Distribution of peritonitis and catheter exit site/tunnel infection agents among the groups

	Group 1 (n=123)		Group 2a (n=112)		Group 2b (n=131)	
	Peritonitis	CASTI	Peritonitis	CASTI	Peritonitis	CASTI
MRSA	0	4	18	14	84	36
MSSA	0	15	34	38	134	55
<i>Pseudomonas</i> species	0	0	3	5	10	20
<i>Escherichia coli</i>	0	1	8	1	25	2
<i>Enterobacter</i> species	0	0	3	0	17	0
Diphtheroid bacilli	0	0	0	0	8	0
Culture negative	0	3	24	9	91	14
<i>Streptococcus</i> species	0	2	4	1	27	2
<i>Klebsiella pneumoniae</i>	0	0	6	1	9	2
<i>Staphylococcus epidermidis</i>	0	0	5	0	2	0
<i>Acinetobacter</i>	0	0	3	0	7	0
Fungal organisms	0	0	4	0	17	0

MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*; CASTI: catheter exit site/tunnel infection

**Table 4.** Causes HD transferring and mortality

		Group 1	Group 2a	Group 2b
Causes of mortality	Peritonitis/sepsis	–	18	32
	Cardiovascular	20	12	16
	Malnutrition	3	1	4
	Dialysis inadequacy	1	1	9
	Unknown causes	4	3	3
HD transferring	Peritonitis/sepsis	–	24	31
	Cardiovascular	5	4	6
	Malnutrition	3	2	2
	Dialysis	17	7	10
	Patient wish	4	1	1

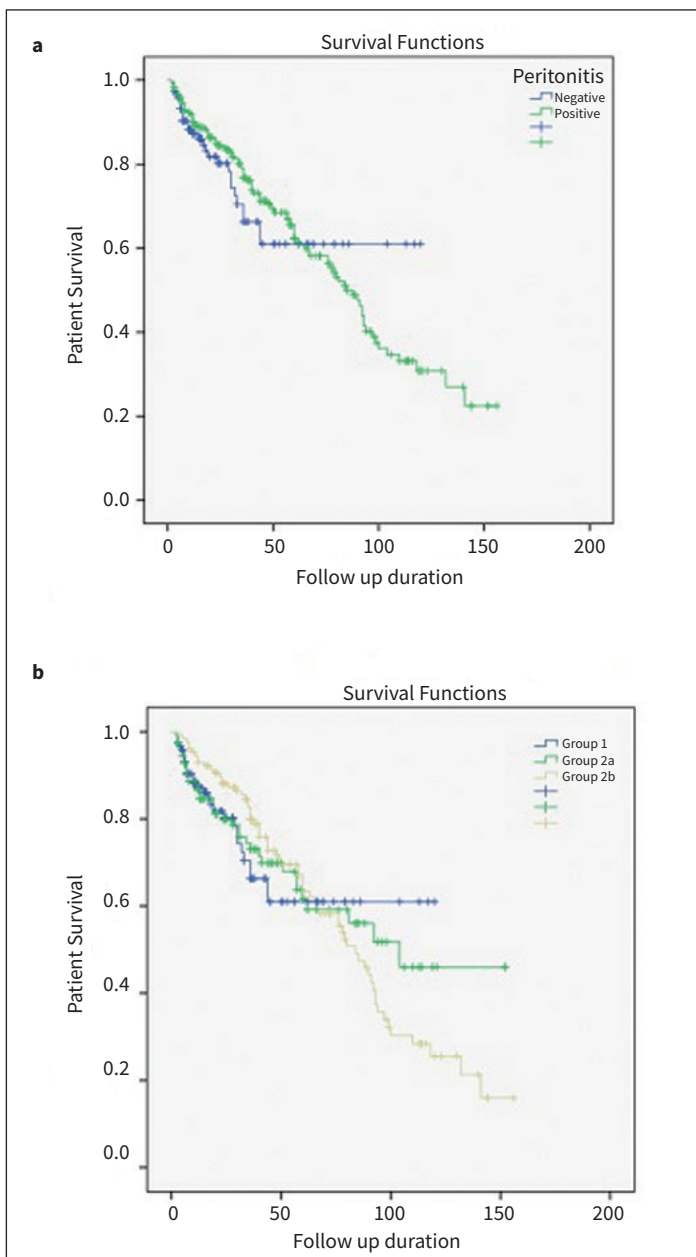
123 patients consisted of Group 1 with no peritonitis episode, and 243 patients consisted of Group 2 with at least one peritonitis episode. Patients were divided into two groups in Group 2, 112 patients with one peritonitis episode consisted of Group 2a and the remaining 131 patients consisted of Group 2b with at least two peritonitis episodes. Table 1 shows the demographic data of the groups.

The mean PD treatment period was found as statistically significant ( $p < 0.001$ ). Group 2b patients were significantly younger than Group 2a in post hoc analysis ( $p = 0.025$ ). Follow-up time in Group 1 was significantly shorter than that in Group 2a and

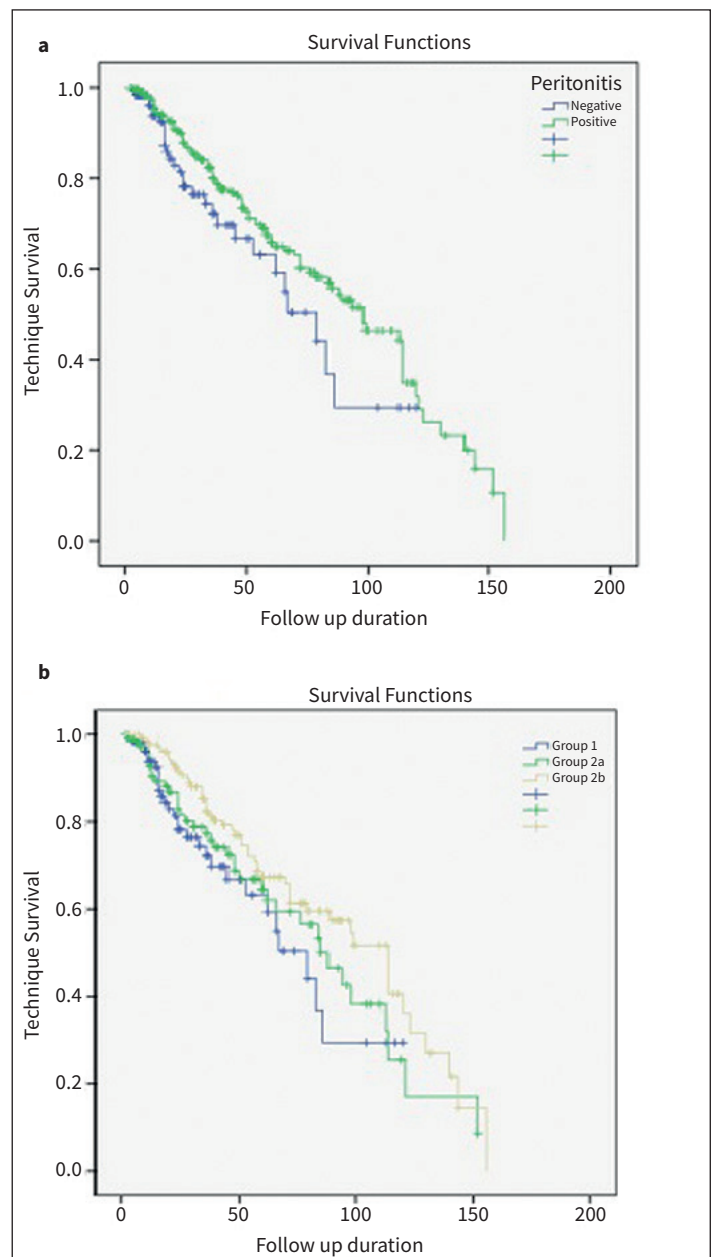
Group 2b ( $p = 0.004$  and  $< 0.001$ , respectively). Follow-up time was also statistically shorter in Group 2a than in Group 2b ( $p < 0.001$ ). The APD treatment period was significantly longer in Group 2b patients than in Group 1 patients ( $p = 0.034$ ).

Statistical analysis for the presence of past hemodialysis history, nature of PD preference, presence of anyone to perform PD, treatment modality, and rate of patients with diabetes was all similar among the three groups (Table 1).

Table 2 shows the initial and last visit clinical and laboratory data of the three groups. At the time of the initiation of treat-



**Figure 1. a, b.** Survival analysis of patients with and without peritonitis history (a), Survival analysis of the subgroups (b).



**Figure 2. a, b.** Technique survival analysis of the patients with and without peritonitis history (a), Tecnique survival analysis of the subgroups (b).

ment, blood pressure levels, daily urine volumes, UF volumes, and laboratory parameters were similar between the groups. Last visit daily urine volumes were significantly lower in Group 2b than in Group 1 ( $p=0.033$ ).

A total of 427 peritonitis episodes were observed in Group 2b; 36 patients had relapsing peritonitis, whereas 19 had recurrent peritonitis. The most common organism causing peritonitis was *Staphylococcus aureus*, cultured in 36% of the episodes. Table 3 shows the causative agents for peritonitis and catheter exit site/tunnel infections.

During the follow-up period, 28 patients died, 32 patients had kidney transplantation, and 29 patients were transferred to hemodialysis (HD) from Group 1. Thirty-five patients died, 17 patients had kidney transplantation, and 38 patients were transferred to HD in Group 2a. Sixty-four patients died, 8 patients had transplantation, and 50 patients were transferred to HD in Groups 2b. Death rates were higher in patients who had more than two peritonitis.

The leading cause of death was CVD in Group 1, whereas it was infection (peritonitis and/or sepsis) in Group 2a and Group 2b ( $p<0.001$ ). In patients with at least one peritonitis episode (Group 2a and Group 2b), 50 patients died due to peritonitis and/or sepsis. Fungal organisms were detected in 9 (18%) of these patients (2 in Group 2a and 7 in Group 2b patients), and *Enterobacter* species were cultured in eight patients (1 in Group 2a and 7 in Group 2b).

Peritonitis and/or sepsis were the major causes for transfer to HD in Group 2, whereas dialysis inadequacy was the leading cause in Group 1 ( $p<0.001$ ). Table 4 shows the causes of mortality and reasons for transfer to HD.

Survival was similar between Group 1 and Group 2 (Figure 1a) (log rank=0.80). The mean survival time for patients in Group 1 was  $82.1\pm 6.0$  months. The mean survival rates for years 1, 2, 3, and 5 were 87.2%, 80.2%, 66.3%, and 61.3%, respectively. The mean survival time for Group 2a was  $94.1\pm 7.5$  months. The mean survival rates for years 1, 2, 3, and 5 were 86.7%, 79.9%, 73%, and 61.6%, respectively. The mean survival time for Group 2b was  $84\pm 5.0$  months. The mean survival rates for years 1, 2, 3, and 5 were 93%, 87.2%, 78.9%, and 63.4%, respectively. Survival was similar among the groups (Figure 1b) (log rank=0.850). History of two or more peritonitis episodes ( $p=0.004$ , RR=0.483, CI: 0.294-0.795) and catheter exit site/tunnel infection ( $p=0.027$ , RR=0.836, CI: 0.713-0.98) was found to be an independent risk factor for patient survival in Cox regression analysis.

Technique survival was similar between Group 1 and Group 2 (Figure 2a) (log rank=0.08). The mean technique survival times were  $76.5\pm 6.7$  months in Group 1,  $93.8\pm 7.7$  months in Group 2a, and  $82.2\pm 4.9$  months in Group 2b. The mean technique survival rates for years 1, 2, 3, and 5 were 93.8%, 80.7%, 74.5%, and

65.2% for Group 1, 93.7%, 83.8%, 78.2%, and 66.5% for Group 2a, and 94.4%, 87%, 72.4%, and 58% for Group 2b, respectively. Technique survival was similar for the three groups (Figure 2b) (log rank=0.440). History of catheter exit site/tunnel infection was the only independent risk factor determining technique survival in Cox regression analysis ( $p=0.006$ , RR=0.805, CI: 0.689-0.939).

## DISCUSSION

Our study has shown that even though the causes for mortality were different, mortality rates were similar between the two main groups. Risk factors for patient survival were history of peritonitis more than once and history of catheter exit site/tunnel infection. The major cause of mortality was cardiovascular reasons in patients without peritonitis, whereas it was peritonitis and/or sepsis in patients with peritonitis history. Technique survival was similar between Group 1 and Group 2. Independent risk factor for technique survival was history of catheter exit site/tunnel infection. The most frequent cause of transfer to HD was dialysis inadequacy in Group 1, whereas it was peritonitis and/or sepsis in Group 2.

There are conflicting results about survival rates in studies with PD population (17-19). Age, race, genetic factors, sociodemographic variables, such as HD history, presence of comorbid diseases, such as diabetes mellitus and CVD, malnutrition, and reduced residual renal function have been shown as factors affecting mortality in previous studies (20-25). We have found higher mortality rates in patients with two or more peritonitis than in other patients. PD follow-up time was longer in these patients, and residual renal function loss (daily urine volume) was inevitably more as it can be expected. Gram-negative organisms were isolated more frequently in this group. These factors may be the reasons for higher mortality rates in this population.

Previous studies identified peritonitis as an independent risk factor for patient and technique survivals in PD patients (10, 26-28). The impact of peritonitis changed substantially due to the decrease in the peritonitis rates through the use of the double-bag or Y-set (29). Furthermore, the number of effective peritonitis treatments increased after the widespread application of the ISPD guidelines (3, 30). However, recently, several studies reported no influence of peritonitis on mortality in PD patients (6, 31). Similarly, peritonitis was not associated with poor outcomes in elderly PD patients (32). Consistent with recent studies, in our study, peritonitis history (one episode or more) was not associated with patient survival. However, having a history of two or more peritonitis and catheter exit site/tunnel infection was found to be a poor predictor of patient survival in our study.

Mortality in patients without peritonitis history was mostly due to cardiac reasons, whereas peritonitis and/or sepsis were the leading causes in patients with peritonitis history. CVD is prevalent in chronic kidney disease (CKD). It is the most frequent cause of death in these patients, accounting for approximately

50% of all causes (33). The most important causes of death were infections (61%) and cardiovascular events (39%) in the CKD population from a Far Eastern country (34). We also found that the most frequent causes of death were infections (peritonitis and/or sepsis) and cardiovascular events in a 10-year survey from our PD unit (35).

In a similar Turkish cohort, initial serum albumin level, obesity, and longer PD duration were found as risk factors for peritonitis (36). In addition, some other studies revealed that advanced age, presence of comorbidities, such as diabetes mellitus, and absence of RRF were found to be independently associated with patient and/or technique survival (37-39). Many studies reported that peritonitis has been identified as an independent risk factor for technique failure in PD (10, 32, 40). Exit site and catheter tunnel infections are the major known predisposing factors for PD-related peritonitis (41). Peritonitis associated with concurrent catheter exit site/tunnel infection is more likely to proceed to catheter loss (42). Technique survival rates were found to be similar between patients with and without peritonitis history in our study. Catheter exit site/tunnel infection but not peritonitis was found to be a risk factor for technique survival. Similarity of patient and technique survivals between the groups may explain the shorter follow-up period and more common CVD in Group 1.

The most important limitation of our study is the retrospective design of a single center experience. In addition, the effect of PD modality on patient and technique survival has not been examined in depth. Time to develop peritonitis has not been determined so the impact of early peritonitis on mortality was not included to our analyses.

## CONCLUSION

Mortality and technique survival rates were similar between patients with and without peritonitis. History of two or more peritonitis and catheter exit site/tunnel infections was defined to be an independent risk factor for patient survival. The presence of catheter exit site/tunnel infection history was associated with technique survival. Peritonitis and/or sepsis were the leading causes of mortality in patients with peritonitis history, whereas cardiac reasons were the most common reason for mortality in patients without peritonitis history.

**Ethics Committee Approval:** The study was prepared in accordance with the Declaration of Helsinki.

**Informed Consent:** Informed consent is not necessary due to the retrospective nature of this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – Z.A.U.; Design - Z.A.U., Y.K., T.B, T.S, A.Ü.; Supervision -Y.K., T.B., E.A., T.S., A.S.; Resources – Z.A.U., Y.K., T.B., E.A., T.S., A.S. ; Materials – Z.A.U., F.Ç.B., A.K., T.S., E.A.; Data Collection and/or Processing - Z.A.U., F.Ç.B.; Analysis and/or Interpretation

– Z.A.U., F.Ç.B., A.S., M.S; Literature Search – A.S., A.K., M.S., N.B.H.; Writing Manuscript – Z.A.U., A.K., N.B.H., M.S.; Critical Review – Z.A.U., N.B.H., A.Ü.

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