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Characteristics and Survival Results of Peritoneal Dialysis Patients Suffering from COVID-19 in Turkey: A Multicenter National Study

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Keywords
Coronavirus disease-19 · Peritoneal dialysis · Mortality · Outcome · Complications

Abstract
Introduction: We aimed to study the characteristics of peritoneal dialysis (PD) patients with coronavirus disease-19 (COVID-19), determine the short-term mortality and other medical complications, and delineate the factors associated with COVID-19 outcome. ***Methods:*** In this multicenter national study, we included PD patients with confirmed COVID-19 from 27 centers. The baseline demographic, clinical, laboratory, and radiological data and outcomes at the end of the first month were recorded. ***Results:*** We enrolled 142 COVID-19 patients (median age: 52 years). 58.2% of patients had mild disease at diagnosis. Lung involvement was detected in 60.8% of patients. Eighty-three (58.4%) patients were hospitalized, 31 (21.8%) patients were admitted to intensive care unit and 24 needed mechanical ventilation. Fifteen (10.5%) patients were switched to hemodialysis and hemodiafiltration was performed for four (2.8%) patients. Persisting pulmonary symptoms ($n = 27$), lower respiratory system infection ($n = 12$), rehospitalization for any reason ($n = 24$), malnutrition ($n = 6$), hypervolemia ($n = 13$), peritonitis ($n = 7$), ultrafiltration failure ($n = 7$), and in PD modality change ($n = 8$) were reported in survivors. Twenty-six patients (18.31%) died in the first month of diagnosis. The non-survivor group was older, comorbidities were more prevalent. Fever, dyspnea, cough, serious-vital disease at presentation, bilateral pulmonary involvement, and pleural effusion were more frequent among non-survivors. Age (OR: 1.102; 95% CI: 1.032–1.117; p: 0.004), moderate-severe clinical disease at presentation (OR: 26.825; 95% CI: 4.578–157.172; $p < 0.001$), and baseline CRP (OR: 1.008; 95% CI; 1,000–1.016; p: 0.040) were associated with first-month mortality in multivariate analysis. ***Discussion/Conclusions:*** Early mortality rate and medical complications are quite high in PD patients with COVID-19. Age, clinical severity of COVID-19, and baseline CRP level are the independent parameters associated with mortality.

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Introduction

With the declaration of the pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization in March 2020, many changes occurred about the clinical practices and attitudes about health care. There have been many papers reporting the increased mortality in elderly patients and those with comorbidities like hypertension, cardiovascular disease, pulmonary disease, diabetes, and chronic kidney disease (CKD) [1]. Patients with stage-5 CKD with multiple comorbidities and advanced age have increased mortality due to coronavirus disease-19 (COVID-19) as well as dialysis patients [2].

Therefore, prevention from COVID-19 has become of prime importance. Home-based therapies of end-stage renal disease (ESRD), namely peritoneal dialysis (PD) and home hemodialysis (HD) gained more popularity with the onset of the pandemic considering the HD centers, which are potentially opposite to the policy of social distancing [3]. PD patients, which account for 11% of the global dialysis population [4], have the advantage of keeping themselves from health center-related transmission of COVID-19. Hence, case studies of PD patients with COVID-19 are scarce and include very few patients.

A Chinese study conducted in Wuhan examined 695 dialysis patients with COVID-19 during the early phase of the pandemic. Thirty-two HD and 4 PD patients had the infection. PD patients had a lower rate of infection (1.8%) compared to HD patients (7.2%) (RR = 4.07) [5].

Another study from Wuhan stated that only 8 of 818 PD patients were diagnosed to have COVID-19, a rate which was close to that of the general population [6].

Several risk factors for severe disease and mortality in the general population have been reported in the literature, and data is growing up. A cohort study from New York analyzed more than 5,000 COVID-19 patients and showed that advanced age and CKD are important risk factors [7]. This was supported by the study of Williamson et al. [8] who analyzed the health records of about 17 million people. They reported that patients with a glomerular filtration rate <30 mL/min/1.73 m^2 and organ transplantation are at high risk [8]. Dialysis patients seem to have an increased risk of mortality that may be due to the presence of risk factors described up to now in the literature. A large study from Turkey analyzed 1,210 patients with COVID-19 and found that intensive care unit (ICU) admission and the mortality rate were higher in patients with CKD and HD patients compared to those without kidney disease [9]. Another study from Turkey analyzed 879 CKD and control patients, 68.8% of them were more than 65 years of age and found out that severe-critical disease, ICU admission, and in-hospital mortality were found to be more frequent in the older group regardless of demographic parameters, comorbidities, clinical, and laboratory data on presentation [10].

Although existing data suggest an increased mortality rate, data about the course of COVID-19 in PD patients, its short and long-term effects on the patient and technique survival are limited. Moreover, specific factors associated with increased risk of death have not been clearly defined yet. Therefore, we aimed to study the characteristics of PD patients with COVID-19, determine the short-term mortality and other medical complications, and delineate the factors associated with COVID-19 outcome.

Materials and Methods

This national multicenter study was planned and designed with the unconditional support of the Turkish Society of Nephrology. The Ethics Committee of Health Sciences University, Istanbul Haseki Training and Research Hospital, approved this study (No: 256–2020). The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2008. This retrospective study cohort followed the report "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)" [11].

We created an electronic web-based database to collect data of patients on PD therapy for at least 3 months. The diagnosis and treatment of COVID-19 patients were governed by the "National COVID-19 Diagnosis and Treatment" guideline [12].

Population and Setting

The study included all PD patients who had confirmed SARS-CoV-2 infection based on positive reverse transcriptase-polymerase chain reaction (RT-PCR) testing of a nasopharyngeal swab recorded in this database from the attending PD centers. Patients with dialysis duration less than 3 months, those with incomplete outcome data, SARS-CoV-2 RT-PCR negative patients, and patients with readmissions were excluded from the study. The time period of the study was between March 2020 at which the first case was detected in our country and June 2021.

The database included data regarding age, gender, smoking status, the primary cause of CKD, the duration of PD therapy. Comorbidities; namely hypertension (HT), diabetes mellitus (DM), ischemic heart disease (IHD), heart failure (HF), chronic obstructive pulmonary disease, cerebrovascular disease, chronic liver disease, autoimmune/inflammatory diseases, and malignancy were recorded. The medications (angiotensin-converting enzyme-ACE-inhibitors, angiotensin receptor blockers-ARB-, calcium channel blockers, beta blockers, any other antihypertensive drugs, insulin, oral antidiabetics, statins, antiaggregants, and anticoagulants) of the patients were also recorded to the database.

The clinical and laboratory data and data about PD treatment at the last visit before the diagnosis of COVID-19 and the data at the time of diagnosis were recorded. The weight, height, systolic, and diastolic blood pressures were noted. The PD modality (continuous ambulatory peritoneal dialysis-CAPD-, continuous cyclic peritoneal dialysis-CCPD-, and nocturnal intermittent peritoneal dialysis-NIPD), daily dialysis solution volume used, the daily amount of ultrafiltration, the number of exchanges, daily urine volume, total Kt/V, dialyzate Kt/V, and dialyzate/plasma creatinine ratio at the fourth hour of peritoneal equilibrium test were recorded. Regarding laboratory analysis; urea, creatinine, sodium, potassium, calcium, phosphorus, parathyroid hormone, aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), albumin, ferritin, C-reactive protein (CRP), hemoglobin levels and leukocyte, neutrophil, lymphocyte, and platelet counts were recorded.

Measurements and Definitions

The date of diagnosis of COVID-19, the possible source of the infection, the interval between the onset of the symptoms and the diagnosis, the complaints on presentation, the clinical picture of the patients at presentation (asymptomatic patient, mild disease or moderate-severe disease, severe-vital disease), computerized tomography (CT) findings (normal, solitary lesion, multiple unilateral lesions, or multiple bilateral lesions), oxygen saturation, other laboratory findings (fibrinogen, D-dimer and procalcitonin levels were recorded besides the above-listed parameters), medications given for COVID-19, and the place of treatment (inpatient or outpatient) were noted. Asymptomatic patients were diagnosed during screening in the absence of any symptoms. Patients with symptoms like fever and cough without dyspnea were named to have mild disease, even with abnormal CT findings. Those with the moderate-severe disease had dyspnea, necessitating oxygen therapy, and bed rest besides other symptoms. Patients who had hypoxia (oxygen saturation less than 90% despite oxygen support) or hemodynamic disorders requiring ICU follow-up were classified as serious-vital disease.

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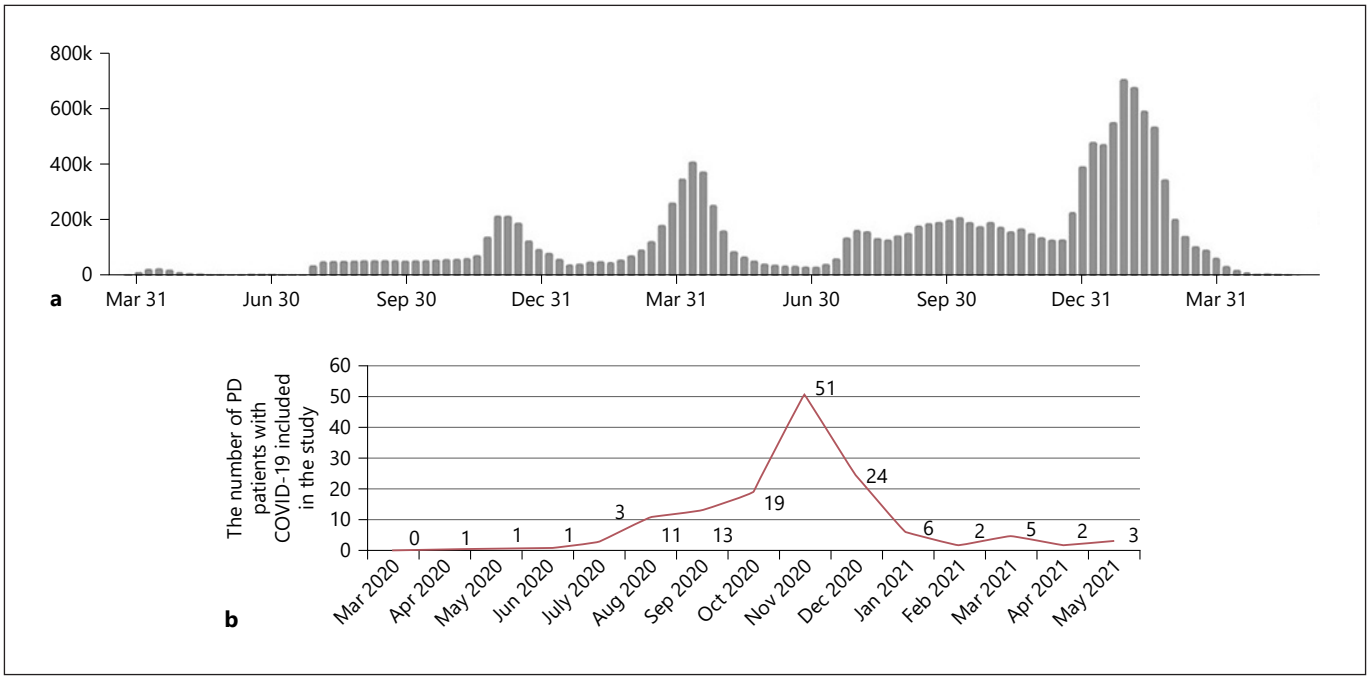

Fig. 1. The total number of cases in our country declared by the World Health Organization (**a**) and the distribution of the number of patients diagnosed to have COVID-19 within the study period (**b**) [13].

Follow-Up and Outcome

The need for transfer to ICU, non-invasive mechanical ventilation, intubation, extracorporeal therapies (extracorporeal membrane oxygenation-ECMO-, hemofiltration or hemodiafiltration), the total length of hospitalization, and duration of ICU stay were recorded in hospitalized patients. The complications during the hospital stay including leucopenia (<3,500/mm^3), lymphopenia (<1,200/mm^3), anemia (hemoglobin<10 g/dL), thrombocytopenia (<150,000/mm^3), at least two times increase in LDH, AST, and ferritin levels, cytokine storm and acute respiratory distress syndrome (ARDS), symptomatic hypotension, shock, secondary bacterial infection, thromboembolic events, and any change in the PD treatment were noted. The outcomes were recorded at the 1st month regarding both mortality (primary endpoint) and other medical conditions like presence of persistent pulmonary symptoms, hospitalization for any cause, respiratory infections, thromboembolic events, malnutrition, hypervolemia, peritonitis, ultrafiltration failure, and need for change in PD regime (secondary endpoints) were recorded as well as laboratory data.

Statistical Analyses

IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. We decided the normality of variables using visual methods (histograms and probability plots) and Kolmogorov-Smirnov tests. Categorical variables were presented numbers and percentages, and numeric variables were presented median and interquartile ranges (25–75%) for descriptive statistics. We used the χ^2 test for two or multiple group comparisons of categorical variables. Independent *t*-test or Mann-Whitney U test was used as appropriate in the comparison of numerical variables. A multivariate analysis model with binary logistic regression analyses (with "enter method"), including parameters significantly related to mortality in univariate analyses, was conducted to assess the independent parameters related to first-month mortality. $p < 0.05$ was accepted as the level of significance.

Results

Demographic and Baseline Characteristics

We enrolled a total of 142 RT-PCR positive COVID-19 patients from 27 centers nationwide. The distribution of the number of patients diagnosed to have COVID-19 during the study period as well as the total number of cases in our country declared by the World Health Organization is presented in Figure 1 [13].

59.8% of the patients were female. The median age was 52 years (IQR: 42–61). Eight patients (5.7%) were active smokers, 36 patients (25.7%) were ex-smokers and 96 patients (68.6%) were non-smokers. The demographic data, the primary cause of kidney disease, comorbidities, medications, data related to the PD regime, and baseline laboratory tests are presented in Table 1. The most common comorbidities were diabetes mellitus, hypertension, and ischemic heart disease. The most frequent primary kidney disease was nephrosclerosis, followed by diabetic ne-

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Table 1. Demographic data, comorbidities, PD modality, data related to PD, and laboratory findings at the last control before COVID-19 presented comparatively according to the survival

	Total (n = 142)	Survivors (n = 116)	Non-survivors (n = 26)	p value
Age, years*, median (IQR)	52 (42–61)	50 (41–58)	64 (60–71)	**<0.001**
Gender, *n* (%)				
Male	57/142 (40.1)	45/116 (38.8)	12/26 (46.2)	0.489
Female	85/142 (59.9)	71/116 (61.2)	14/26 (53.8)	
Co-morbidites, *n* (%)				
Diabetes mellitus*	41/142 (28.9)	28/116 (24.1)	13/26 (50.0)	0.009
Hypertension	113/142 (79.6)	91/116 (78.4)	22/26 (84.6)	0.481
COPD*	9/142 (6.3)	4/116 (3.4)	5/26 (19.2)	0.003
Ischemic heart disease*	28/142 (19.7)	17/116 (14.7)	11/26 (42.3)	0.001
Heart failure*	19/142 (13.4)	10/116 (8.6)	9/26 (34.6)	<0.001
Cerebrovascular disease	9/142 (6.3)	6/116 (5.2)	3/26 (11.5)	0.229
Malignancy	3/142 (2.1)	3/116 (2.6)	0/26 (0.0)	0.407
Autoimmune/autoinflammatory diseases	6/142 (4.2)	6/116 (5.2)	0/26 (0.0)	0.236
Medications, *n* (%)				
ACE inhibitors	25/142 (17.6)	20/116 (17.2)	5/26 (19.2)	0.810
Angiotensin receptor blockers	37/142 (26.1)	29/116 (25.0)	8/26 (30.8)	0.545
Calcium channel blockers	80/142 (56.3)	69/116 (59.5)	11/26 (42.3)	0.111
Beta blockers	66/142 (46.5)	54/116 (46.5)	12/26 (46.1)	0.971
Other antihypertensives	32/142 (22.5)	25/116 (21.5)	7/26 (26.9)	0.554
Insulin	28/142 (19.7)	21/116 (18.1)	7/26 (26.9)	0.307
Oral antidiabetics	8/142 (5.6)	6/116 (5.2)	2/26 (7.7)	0.614
Statins*	17/142 (12.0)	10/116 (8.6)	7/26 (26.9)	**0.009**
Antiaggregants	53/142 (37.3)	42/116 (36.2)	11/26 42.3)	0.561
Anticoagulants	8/142 (5.6)	8/116 (6.9)	0/26 (0.0)	0.168
Primary kidney disease, *n* (%)				
Primary glomerular disease	16/142 (11.3)	15/116 (12.9)	1/26 (3.8)	0.185
Diabetic nephropathy	36/142 (25.4)	26/116 (22.4)	10/26 (38.5)	0.089
Nephrosclerosis	41/142 (28.9)	30/116 (25.9)	11/26 (42.3)	0.094
Polycystic kidney disease	12/142 (8.5)	10/116 (8.6)	2/26 (7.7)	0.878
Others*	37/142 (26.1)	35/116 (30.2)	2/26 (7.7)	**0.018**
Smoking status, *n* (%)				
Non-smoker	96/139 (68.6)	82/116 (71.3)	14/25 (56.0)	0.195
Active smoker	8/140 (5.7)	5/116 (4.3)	3/25 (12.0)	
Ex-smoker	36/140 (25.7)	28/116 (24.3)	8/25 (32.0)	
PD modality*, *n* (%)				
CCPD	17/142 (12.0)	13/116 (11.2)	4/26 (15.4)	0.152
NIPD	27/142 (19.0)	26/116 (22.4)	1/26 (3.8)	
CADP	98/142 (69.0)	77/116 (66.4)	21/26 (80.8)	
Body mass index, kg/m^2, median (IQR)	25.3 (23.4–29.0)	25.2 (23.4–28.8)	26.6 (23.8–29.6)	0.472
Weight, kg, median (IQR)	69.8 (62.5–78.0)	69.6 (62.0–77.0)	71.6 (63.0–80.0)	0.507
Systolic BP, mm Hg, median (IQR)	130 (120–145)	130 (120–150)	132 (120–140)	0.504
Diastolic BP, mm Hg, median (IQR)	80 (71–90)	80 (74–90)	80 (70–85)	0.076
Data related to PD, median (IQR)				
Dialyzate volume, L/day	8.0 (7.2–9.5)	8.0 (7.4–9.5)	8.0 (6.0–8.0)	0.749
Ultrafiltration, mL/day	1,200 (775–1,500)	1,100 (700–1,500)	1,200 (1,000–1,500)	0.188
Number of exchanges, /day	4 (4-4)	4 (4-4)	4 (4-4)	0.184
Kt/V (total)	2.1 (1.9–2.5)	2.11 (1.8–2.5)	2.1 (1.9–2.4)	0.750
Kt/V (dialysate)	1.8 (1.4–2.0)	1.8 (1.4–2.0)	1.8 (1.6–2.1)	0.826
Dialysate/Plasma creatinine (4th hour)	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.66 (0.6–0.7)	0.124
Urine volume, mL/day*	600 (130–1,000)	775 (200–1,150)	225 (100–725)	**0.044**
Laboratory data, median (IQR)				
Urea, mg/dL	96 (69–122)	98 (74–124)	91 (69–120)	0.552
Creatinine, mg/dL	7.7 (5.9–9.9)	7.9 (6.3–10.1)	6.5 (4.6–9.0)	0.637

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Table 1 (continued)

	Total (n = 142)	Survivors (n = 116)	Non-survivors (n = 26)	p value
Sodium, mmol/L	137 (134–139)	137 (134–139)	136.5 (133.5–138)	0.443
Potassium, mmol/L	4.5 (4–5)	4.5 (4–5)	4.2 (3.7–4.9)	0.208
Calcium, mg/L	8.9 (8.5–9.2)	9.0 (8.5–9.2)	8.9 (8.4–9.9)	0.559
Phosphorus, mg/L	4.9 (4.2–5.6)	4.9 (4.2–5.6)	5.0 (4.1–5.9)	0.928
PTH, pg/mL	333 (223–637)	330 (217–625)	352 (238–715)	0.760
AST, U/L	13.0 (11.0–20.0)	12.0 (10.0–18.5)	17.0 (13.0–25.0)	0.736
ALT, U/L	14.0 (10.0–19.0)	14.0 (10.0–18.0)	15.0 (11.0–25.0)	0.095
LDH, U/L	202 (166–250)	205 (167–239)	191 (149–290)	0.965
Albumin, g/dL	3.6 (3.3–3.9)	3.6 (3.3–4.0)	3.6 (3.3–3.8)	0.407
Ferritin, ng/mL	265 (159–482)	271 (159–496)	240 (167–425)	0.522
CRP, mg/L	6.0 (3.0–12.4)	4.5 (2.0–12.9)	8.8 (6.0–10.6)	0.472
Hemoglobin, g/dL	10.9 (9.6–12.0)	10.9 (9.7–12.0)	11.0 (9.5–12.2)	0.453
Leukocyte, /mm^3	7,365 (5,700–8,815)	7,355 (5,740–8,775)	7,630 (5,155–8,900)	0.801
Neutrophil, /mm^3	4,630 (3,530–6,080)	4,630 (3,530–5,600)	5,335 (3,430–6,700)	0.147
Lymphocyte, /mm^3	1,640 (1,200–2,170)	1,640 (1,200–2,200)	1,625 (1,215–1,890)	0.128
Platelet, ×1,000/mm^3	251 (194–322)	248 (194–314)	265 (181–357)	0.066

IQR, Interquartile range; COPD, Chronic obstructive pulmonary disease; ACE, Angiotensin-converting enzyme; CCPD, Continuous cyclic peritoneal dialysis; NIPD, Nocturnal intermittent peritoneal dialysis; CAPD, Continuous ambulatory peritoneal dialysis; BP, blood pressure; PTH, Parathyroid hormone; AST, Aspartate transaminase; ALT, Alanine transaminase; LDH, Lactate dehydrogenase; CRP, C-reactive protein.
* $p < 0.05$ between survivors and non-survivors.

phropathy. The majority (69%) of patients were on CAPD program, while others followed an automated peritoneal dialysis (APD) program. The median systolic and diastolic blood pressures at the last visit before COVID-19 and at the first month were 130 (120–145) and 80 (71–90) mm Hg at the last visit before infection and 130 (120–140) and 80 (75–90) mm Hg at the first month.

The Data regarding COVID-19

Table 2 presents data about the diagnosis and clinical findings during COVID-19. Ninety-two patients had a history of a family member who was also PCR positive. Thirteen patients were diagnosed during screening while asymptomatic. The possible source of infection was mostly family-house contacts. The median duration between the first symptom and the diagnosis was 3 (2–5) days. The most common symptom was cough, followed by fever and sore throat. Most of the patients had mild disease at the time of diagnosis. 66.7% of patients had CT examination and findings of lung involvement were detected in 60.8% of them.

The most common finding on CT was bilateral multiple lesions with ground-glass appearance (Table 2, online suppl. Table; for all online suppl. material, see www.karger.com/doi/10.1159/000526909). Oxygen saturation at the time of diagnosis was normal (>95%) in 19 patients, 90–95% in 27 patients, and below 90% in 33 patients. This data could not be reached for 63 patients. Eighty-three patients were hospitalized while the remainder 59 patients were followed as outpatients. The treatment methods used for the treatment of COVID-19 were favipiravir (119 patients), glucocorticoids (48 patients), macrolide antibiotics (28 patients), hydroxychloroquine (15 patients), tocilizumab (5 patients), lopinavir-ritonavir (4 patients), anakinra/canakinumab (3 patients), oseltamivir (3 patients), convalescent plasma (2 patients), and apheresis/immune adsorption (2 patients). No change was made regarding PD regime during infection in 52 patients. The number of exchanges was changed in 5 patients, PD modality (APD or CAPD) was changed in 6 patients, 15 patients were switched to hemodialysis and hemodiafiltration was performed for 4 patients. This data was missing for 60 patients. Thirty-one patients were transferred to ICU. Among them, 24 patients needed mechanical ventilation. ECMO was performed for 3 patients and eight patients had hemodiafiltration. The median duration of stay in ICU was6 (4–9.5) days, and the median duration of total hospitalization was 9 (7–15) days. The problems observed during hospitalization were lymphopenia (n = 59), anemia (n = 51), more than two times increase in ferritin levels (n = 44), more than 2 times increase in LDH level (n = 30), secondary bacterial infec-

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Table 2. The data related to COVID-19

	Total (n = 142)	Survivor (n = 116)	Non-survivor (n = 26)
The possible source of infection, *n* (%)			
Unknown	34/141 (24.1)	26/115 (22.6)	8/26 (30.9)
Family-house contacts	86/140 (61.0)	71/115 (61.7)	15/26 (57.7)
Health institution	8/140 (5.7)	7/115 (6.1)	1/26 (3.8)
Social activities	13/141 (9.2)	11/115 (9.6)	2/26 (7.7)
Positive family history of COVID-19	92/121 (76.0)	75/101 (74.3)	17/20 (85.0)
Diagnosis with testing while asymptomatic	13/136 (9.5)	13/113 (11.5)	0/26 (0.0)
Symptoms, *n* (%)			
Fever*	84/141 (59.6)	64/115 (55.7)	20/26 (76.9)
Dyspnea*	66/140 (47.1)	42/114 (36.8)	24/26 (92.3)
Cough*	92/142 (64.8)	70/116 (60.3)	22/26 (84.6)
Sore throat	70/141 (49.6)	54/115 (47.0)	16/26 (61.5)
Diarrhea	20/140 (14.3)	14/114 (12.3)	6/26 (23.1)
Loss of smell sensation	39/135 (28.9)	32/112 (28.6)	7/23 (30.4)
Loss of taste sensation	45/134 (33.6)	38//111 (34.2)	7/23 (30.4)
The clinical picture at the time of diagnosis, *n* (%)			
Asymptomatic disease*	14/142 (9.9)	14/116 (12.1)	0/26 (0.0)
Mild disease*	75/142 (52.8)	73/116 (62.9)	2/26 (7.7)
Moderate-severe disease	34/142 (23.9)	25/116 (21.6)	9/26 (34.6)
Serious-vital disease*	19/142 (13.4)	4/116 (3.4)	15/26 (57.7)
Findings of pneumonia on CT*	73 (60.8)	51 (53.1)	22 (91.1)
CT findings*, *n* (%)			
Normal	15/89 (16.9)	14 (20.9)	1 (4.5)
Solitary lesion	11/89 (12.4)	10 (14.9)	1 (4.5)
Unilateral multiple lesions	8/89 (9.0)	6 (9.0)	2 (9.1)
Bilateral multiple lesions	55/89 (61.8)	37 (55.2)	18 (81.8)
Ground glass appearance	76/95 (80.0)	55/70 (78.6)	21/25 (84.0)
Unilateral pleural effusion*	9/87 (10.3)	3/62 (4.8)	6/25 (24.0)
Bilateral pleural effusion*	14/87 (16.1)	6/62 (9.7)	8/25 (32.0)
Laboratory data at the time of diagnosis, median (IQR)			
Creatinine, mg/dL	8.1 (6.0–11.3)	8.13 (6.37–11.3)	7.37 (4.58–10.97)
Sodium, mmol/L	135 (131–138)	135 (131–138)	133 (131–136)
Potassium, mmol/L	4.3 (3.9–4.9)	4.3 (4.0–4.8)	4.1 (3.5–5.0)
Calcium, mg/dL	8.5 (7.9–9.0)	8.5 (7.9–9.0)	8.4 (7.7–9.6)
Phosphorus, mg/dL	4.9 (4.1–5.7)	4.9 (4.0–5.6)	4.8 (4.4–6.0)
AST, U/L*	18.0 (11.5–27.0)	17.0 (11.0–25.0)	21.0 (12.0–39.0)
ALT, U/L	15.0 (10.0–24.0)	15.0 (10.0–21.5)	15.5 (10.0–27.0)
LDH, U/L*	274 (214–333)	273 (206–322)	279 (242–563)
Albumin, g/dL	3.2 (2.86–3.7)	3.25 (2.9–3.7)	3.2 (2.7–3.7)
Ferritin, ng/mL	536 (222–980)	536 (202–866)	667 (367–1,277)
Fibrinogen, mg/dL	482 (320–646)	476 (333–632)	560 (56–706)
D-dimer, µg/L	500 (57–1,030)	533 (70–1,000)	371 (45–1,190)
Procalcitonin, ng/mL	1.2 (0.4–9.3)	1.1 (0.3–11.0)	2.0 (11.2–7.6)
CRP, mg/L*	41.0 (6.4–90.0)	22.3 (5.0–60.0)	96.0 (68.7–152.0)
Hemoglobin, g/dL	10.45 (9.2–11.9)	10.2 (9.1–11.8)	11.1 (9.8–12.5)
Leukocyte, /mm^3*	6,400 (4,600–9,300)	6,170 (4,490–8,400)	9,630 (4,980–12,420)
Neutrophil, /mm^3*	4,240 (2,540–5,960)	4,220 (2,410–5,600)	7,425 (3,290–10,540
Lymphocyte, /mm^3	1,000 (700–1,600)	1,050 (750–1,700)	800 (630–1,190)

AST, Aspartate transaminase; ALT, Alanine transaminase; LDH, Lactate dehydrogenase; CRP, C-reactive protein. * $p < 0.05$ between survivors and non-survivors.

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Table 3. The result of binary logistic regression analysis of the parameters related to first-month mortality

	OR	95% CI for OR		*p* value
		lower	upper	
Age (year)	1.080	1.005	1.161	0.035
Gender (male vs. female)	1.600	0.408	6.283	0.500
Diabetes mellitus	2.834	0.631	12.737	0.174
Heart failure	2.150	0.521	8.875	0.290
PD modality (APD vs. CAPD)	1.390	0.320	6.038	0.660
Clinical picture at presentation (moderate-severe disease vs. asymptomatic or mild disease)	29.59	4.42	197.78	<0.001
CRP (mg/L)	1.009	1.001	1.018	0.036
AST (U/L)	1.029	0.994	1.065	0.110

The model did not include chronic obstructive pulmonary disease, residual urine, and LDH due to lack of data. In addition, leukocytes and neutrophils were not included in the model because they showed a high correlation with CRP. APD, Automated peritoneal dialysis; CAPD, Continuous ambulatory peritoneal dialysis; CRP, C-reactive protein; AST, Aspartate transaminase.

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tions (n = 28, one was peritonitis), shock/severe hypotension (n = 24), more than two times increase in AST level (n = 21), thrombocytopenia (n = 20), cytokine storm/adult respiratory distress syndrome (n = 17), leucopenia (n = 16), and thromboembolic event (n = 1) with decreasing frequency.

Outcomes at First Month and Characteristics of Survivor and Non-Survivor Patients

During the 1 month of follow-up, 26 patients (18.31%) died. These patients were compared with the survivors (Table 1, Table 2 and online Suppl. Table). The non-survivor group was older. Diabetes mellitus, hypertension, chronic obstructive pulmonary disease, ischemic heart disease, and heart failure were more prevalent in the non-survivor group. The medications that the patients used were similar except statins more commonly used by non-survivors. Primary kidney disease, smoking status, blood pressures, and body mass indexes of the groups were not different. CAPD was more frequent in the non-survivor group, while NIPD was more frequently used in the survivor group. PD regime and Kt/V values were similar, while daily urine volume was less in the non-survivor group. No significant difference was detected between these groups regarding laboratory parameters measured at the last visit before COVID-19 (Table 1).

None of the non-survivors' O_2 saturation at the time of hospitalization was normal. 96.2% of the ICU-admitted patients and 91.7% of mechanically ventilated patients died. All deaths were among hospitalized patients, and none of the patients who were treated as outpatients died.

Fever, dyspnea, and cough as symptoms and serious-vital disease at presentation, bilateral pulmonary involvement, and pleural effusion detected by CT were more frequent in the non-survivors (Table 2). They had higher AST, LDH, and CRP levels, leukocyte, and neutrophil counts (Table 2). Oseltamivir, macrolide antibiotics, glucocorticoids, and lopinavir-ritonavir were more frequently used for the treatment of non-survivors (online Suppl. Table). Oxygen saturation at presentation was lower, switch to hemodialysis more frequently needed and all in-hospital events were more common among non-survivors, including leucopenia, lymphopenia, thrombocytopenia, increase in AST, ALT, LDH, and ferritin levels, cytokine storm, ARDS, and secondary bacterial infections (online Suppl. Table). The clinical outcomes other than death were analyzed for the survivor patients. Among them, 27 had persisting pulmonary symptoms, 12 had lower respiratory system infection, and 24 patients were hospitalized for any reason. The other clinical outcomes were malnutrition (n = 6), hypervolemia (n = 13), peritonitis (n = 7), ultrafiltration failure (n = 7), and change in PD modality (n = 8). In the binary logistic regression analysis, age (OR: 1.102; 95% CI: 1.032–1.117; p: 0.004), moderate-severe clinical disease at the time of presentation (OR: 26.825; 95% CI: 4.578–157.172; $p < 0.001$), and CRP levels (OR: 1.008; 95%CI; 1,000–1.016; p: 0.040) were the independent parameters associated with increased first-month mortality (Table 3).

Discussion

In this multicenter nationwide study, the characteristics and first-month survival and complications of a large group of patients with COVID-19 were examined and

very important data were obtained. We found 1-month mortality of 18.31%. In addition, the patient's age, the severity of clinical presentation, and CRP level at admission were independent parameters associated with this death. In addition, we observed that the complications such as persisting pulmonary symptoms, lower respiratory tract infection, hospitalization for any reason, malnutrition, hypervolemia, peritonitis, ultrafiltration failure, and the need for change in PD modality continued in patients in the first month. The mortality data of PD patients with COVID-19 is quite limited. Although they involve a small number of patients, the mortality rate was reported as 25% (2/8) [14], 9% (1/11) [15]. Another study reported a mortality rate of 27.3% in a population of both PD and HD patients [16].

It is understood from the current literature that bad outcomes after COVID-19 are associated with increasing age, chronic kidney disease, being dialysis-dependent, or transplanted [7–9]. PD patients comprise a special subpopulation of patients with dialysis-dependent CKD. Data about the outcomes of PD patients are scarce during the pandemic. This may be related to their knowledge about the hygiene rules and the use of face masks. Besides, and more importantly, frequent hospital visits are not needed for them leading to better isolation ability. Therefore, we aimed to study the characteristics of PD patients with COVID-19 and determine the outcome.

There are 3,292 PD patients in our country according to the registry reports [17]. So, 142 patients registered in our study comprise 4.3% of PD patients. But this number does not represent the exact one because not all PD centers in our country provided data for the study. Besides, PCR negative patients were not included. A Chinese study from Wuhan reported that 32 HD and 4 PD patients had the infection among the 695 patients [5]. Another multicenter study from Wuhan studied 818 patients between January 1, 2020, and April 12, 2020 [6]. Eight patients were detected to have COVID-19 (2.44/1,000 person-months) and the infection rate was similar to the general population in that city. Home dialysis methods hypothetically protect from community-acquired infections. Perl et al. [18] reported that 34 patients had COVID-19 among 3,622 home dialysis (2,853 PD and 769 home HD) patients, while 207 of 9,890 center HD patients had the infection. These similar rates may be interpreted as a consequence of careful infection prevention and control measures in HD centers compared to the earlier periods of the pandemic.

We can see in our study that lung involvement determined by CT, hypoxia, need for hospitalization, in-hospital events, and admission to ICU are quite often in these patients and the mortality rate is 18.31%. There are few reports about the mortality rate of PD patients with COVID-19 in the literature. In a study from Stockholm region, 4 PD patients were recorded to be hospitalized for COVID-19 and one of them (73 years old) died and the other 3 patients survived [19]. Another study from New York reported 11 PD patients with COVID-19 of them, 2 died, and 3 needed mechanical ventilation [20]. A Chinese study from Wuhan examined dialysis patients with COVID-19 regarding mortality during the early phase of the pandemic. Among the 695 patients, 32 HD and 4 PD patients had the infection. Thirty-four dialysis patients died during the study period, and 15 of them were due to COVID-19. The mortality rate was higher compared to the same periods in 2018 and 2019 [5].

The median age of patients in our study was 52 years. This was lower than the age reported in the study by Tortonese et al. [16] who reported the clinical characteristics and outcome of 44 dialysis patients (both HD and PD patients) with COVID-19 in Paris. The median age was 61 years in that study.

The most common symptoms were cough, followed by fever and sore throat. These were fever and chills (79.5%) followed by anorexia and weight loss (59.1%), cough (43.2%), shortness of breath (29.5%), and diarrhea (13.6%) in the study by Tortonese et al. [16]. In the study by Ghonimi et al. [15] including HD and PD patients, the most common symptoms were fever, cough, and dyspnea. Diarrhea was more frequent in PD patients in this study. We detected lung involvement in 60.8% of patients. 72% of patients were detected to have lung involvement in another study [18] and severe radiological involvement was detected in 31.7% of patients involved in the study conducted in Paris [16]. Eighty-three patients (58.5%) were hospitalized and 31 patients were transferred to ICU (21.8%) in our study. These rates are higher than in the general population.

PD patients continue their dialysis regime after the diagnosis of COVID-19 usually. But, there may be a need for transfer to HD or change in the PD recipe during COVID-19 due to volume status and changes in the transport characteristics of patients that may be seen potentially in other infections. Jiang et al. [6] stated that 1 patient had HD due to volume overload, and one had peritonitis. Otherwise, PD was continued. Eleven patients had their PD protocol changed during COVID-19 and 19 patients needed HD or hemodiafiltration during the hospital stay in our study. We also observed an increased rate of peritonitis, ultrafiltration failure, and hypervolemia during

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the first month of diagnosis and a considerable number of patients needed a change in PD modality. The long-term outcome results about the PD treatment would be commented on with further studies.

In the study by Jiang et al. [6], in which 8 PD patients were detected to have COVID-19 (2.44/1,000 person-months), the median Kt/V, UF amount, and residual urine were found to be lower in COVID-19 patients. At the end of the study period, 2 patients died (one due to cerebrovascular bleeding one due to myocardial infarction) and six were discharged. The median duration of hospitalization (35 days) was higher compared with the general population in Wuhan [14].

Increased mortality rate detected in PD patients with COVID-19 may be speculated to be due to increased age, multiple comorbidities, and volume overload that are frequently seen in them. Ghonimi et al. [15] compared the outcomes of HD and PD patients with COVID-19 in Qatar. Seventy-six of 1,064 dialysis patients (65 HD and 11 PD patients) had COVID-19 during the study period. Admission to ICU, patients with ARDS and the need for mechanical ventilation was recorded in 25%, 18.4%, and 17.1% of patients, respectively. Eleven HD (15%) and 1 PD (9%) patient died. Age, heart failure, COPD, atrial fibrillation, low oxygen saturation, ICU admission, need for mechanical ventilation, and inotropes were more frequent among patients who died. Only ICU admission was found to be related to increased mortality in multivariate analysis. But, this mortality data mainly belongs to HD patients. The only PD patient who died was reported to have fungal peritonitis.

In the study from Paris [16] in which the mortality rate was 27.3%, mortality was higher in patients with oxygen requirements and those transferred to ICU. Cough, thrombocytopenia, LDH>2xnormal, and CRP >175 mg/L were associated with death.

In the study by Jager et al. [21], the 28-day death rate was 25.0% in PD patients and 23.8% in HD patients. Advanced age, male gender, and hypertension were related to increased mortality.

Our study has provided more clear results about the factors related to mortality with the high number of patients involved. Increasing age, severe clinical picture at the time of presentation, and elevated CRP levels were associated with increased mortality.

Limitations

Being a multicenter study, the clinical practices and technical feasibilities would change from one to another center and lack of complete standardization may affect the outcome. Besides, the treatment of COVID-19 patients who do not need hospitalization is governed by the teams of Ministry of Health. Moreover, these treatments were extremely varied, because in practice, COVID-19 treatments were directed according to the continuously updated guide of the Ministry of Health, so we did not expect to be the center level difference. But, our patient count was not too much to allow the detailed sub-analysis of these treatments. Another shortcoming in our study is the inability to distinguish cause-effect relationship in response to treatments, since the treatments given to severe cases differs from those given to mild-moderate cases.

In conclusion, the early mortality rate is quite high, and other medical complications are frequent over the first month of the diagnosis of COVID-19. Age, clinical severity of COVID-19, and baseline CRP level are the independent parameters associated with mortality. PD treatment can be continued safely in most patients, but PD-related complications are frequent among PD patients with COVID-19.

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Statement of Ethics

The Ethics Committee of Health Sciences University, Istanbul Haseki Training and Research Hospital, approved this study (No: 256-2020). The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2008. This retrospective study cohort followed the report Strengthening the Reporting of Observational Studies in Epidemiology. Informed consent was not required as this is a retrospective study and this was confirmed by the above mentioned committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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