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Original Article

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Outcomes of Peritoneal Dialysis after Kidney Transplant Failure: A Single-Center Experience*

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ABSTRACT

Objective: Despite advancements in graft survival, the kidney allograft failure is increasingly leading to the initiation of dialysis. While studies indicate no significant differences in survival among dialysis modalities, there are concerns about negative clinical outcomes associated with peritoneal dialysis (PD) in this population.

Methods: This retrospective study analyzed 19 patients who initiated PD following kidney transplant failure (PD-postTx) from January 2010 to June 2022, comparing them with 70 transplant-naive patients who began PD during the same time-frame (PD-noTx group). Acomparison of residual diuresis, episodes of peritonitis, time on PD therapy, and patient survival was performed between 2 groups.

Results: The PD-postTx group was younger and less likely to have diabetes than the PD-noTx group. Compared to PD-noTx patients, PD-postTx patients had more peritonitis episodes (35.7% vs. 68.4%, $P = .011$) and significant decline in urine volume at the end of the first year ($P = .002$). Residual kidney function (RKF) reduced the risk of peritonitis (OR 0.262, 95%CI 0.105-0.653; $P = .040$). -PD-postTx patients had a higher probability of transfer to hemodialysis. Three and 5-year PD survival were 81.7%, 65.4%, and 98.5%, 91.9% in PD-postTx and PD-noTx groups, respectively ($P = .015$). Multiple analysis showed a trend toward PD discontinuation in previously transplanted patients (HR 2.772, 95%CI 0.899-8.543; $P = .076$). Patient survival rates were comparable in both groups.

Conclusion: A prior history of transplantation poses a risk for PD discontinuation and peritonitis; but not for mortality in PD patients. The preservation of RKF may significantly contribute to the protection of peritonitis and the improvement of time on PD therapy.

Keywords: Kidney transplantation, peritoneal dialysis, peritoneal dialysis discontinuation, peritonitis, time on peritoneal dialysis, transplant failure

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INTRODUCTION

Long-term kidney allograft survival has consistently improved over the decades.[1] However, with the rising total number of kidney transplants (KTx), the management of patients following KTx failure has become essential. In the United States, 11% of candidates waitlisted for transplantation had a prior transplant, while 10% of patients who received a transplant had a history of previous transplantation.[2] This underscores the significant burden of allograft failure in the end-stage kidney disease (ESKD) population. Preemptive transplantation is the optimal treatment for individuals with kidney failure; nonetheless, the proportion of transplants following failed allografts has declined over time.[3] Approximately, 1-2% of transplant recipients return to dialysis by the end of the first-year post-transplantation.[2,4] Therefore,

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the optimal transition process, including modality counseling, should be managed with attention to transplant-related risk factors.

Kidney allograft failure leads to a 3-fold increase in mortality risk compared to patients who have a functioning transplant.[5] Nevertheless, overall patient survival rates are similar across different dialysis modalities following allograft failure.[6-8] Peritoneal dialysis (PD) is less favored compared to hemodialysis (HD) following KTx failure (3-18%).[6,7,9,10] However, evidence indicates that advanced age and comorbidities are the primary risk factors influencing outcomes, irrespective of the dialysis method employed.[7,10] Both dialysis methods provide comparable outcomes following KTx failure, making PD a viable option for these patients. Studies examining mortality, PD discontinuation, and peritonitis rates in PD patients with KTx failure vs. transplant-naive individuals have revealed inconsistent findings.[9,11-13] This study assessed outcomes in patients who initiated PD following KTx failure and those who are transplant naive, addressing the limited data available in the literature.

MATERIAL AND METHODS

Study Population

Patients who initiated PD at our center between January 2010 and June 2022 were evaluated retrospectively. The exclusion criteria included individuals under 18 years of age, those who had undergone PD for less than 6 months, patients who received more than 2 months of HD prior to PD, and individuals with a history of multiple organ transplants. Following the exclusion criteria, patients were categorized into 2 groups according to their prior KTx history: (1) 19 patients who initiated PD after kidney allograft loss (PD-postTx) and (2) 70 patients who had not received a KTx (PD-noTx).

Clinical and demographic data of patients, including age, gender, comorbidities, PD modality, and age at PD initiation, were collected from patient files. Diuresis volume was assessed based on 24-hour urine collection during the initial month of PD, at the end of the first year, and at the last follow-up visit. Loss of residual kidney function (RKF) was defined as anuria, marked by diuresis of less than 100 mL in 24 hours. The definition of immunosuppression included the prescription of prednisone at a dosage of 5 mg/day or higher and/or the administration of a calcineurin inhibitor or an antiproliferative agent. PD discontinuation was defined as transition to HD. PD–associated peritonitis was diagnosed when 2 or more of the following criteria were met: (1) consistent clinical features, (2) effluent white cell count exceeding 100/mm^3 with neutrophils comprising over 50% of the total cell count, and (3) positive effluent culture.[14] The clinical outcomes regarding diuresis volume, peritonitis, PD discontinuation, and mortality were documented until December 2024. The outcomes were evaluated by comparing patients in PD-postTx and PD-noTx groups.

The study protocol was approved by the Ethical Committee of Ankara University (Approval No: İ08-539-22, Date: 05.10.2022) and was conducted in accordance with the Declaration of Helsinki. Informed consent has not been obtained due to the retrospective design of the study.

Statistical Analysis

The variables are presented as the mean ± SD, median (minimum-maximum), or percentage (%). Comparisons between PD-postTx and PD-noTx were made using the paired student's *t*-test, Mann–Whitney *U* test, chi-square test, or Fisher's test as appropriate. Logistic regression was employed to analyze factors associated with episodes of peritonitis. Variables exhibiting a *P*-value less than .10 from univariate analyses were included as potential factors in the regression model. The final model was established using a forward stepwise elimination approach (Forward LR), with odds ratios (OR), 95% confidence intervals (CI), and Wald statistics calculated for each variable. Time on PD therapy was evaluated through Kaplan-Meier survival analysis, supplemented by the Log-Rank test. Univariate Cox analysis was employed to identify parameters affecting transfer to HD within the entire cohort. A multiple Cox regression analysis was performed to determine hazard ratios (HRs) for independent risk factors.

The statistical analysis utilized IBM Statistical Package for Social Sciences version 30.0 software (IBM SPSS Corp.; Armonk, NY, USA). A *P*-value below .05 is considered statistically significant.

MAIN POINTS

- Patients initiating PD following kidney transplant failure has an elevated risk of PD discontinuation and peritonitis relative to those without a transplantation history.
- Residual kidney function declines more rapidly in patients with a transplantation history and was predictive for peritonitis episodes irrespective of immunosuppression status.
- To achieve favorable outcomes in patients initiated PD after kidney allograft failure, complications, and comorbidities must be carefully managed and treatment must be tailored according to transplant-related factors.

RESULTS

Patient Characteristics

The demographic and clinical data of the 2 groups are presented in Table 1. The mean age at PD initiation was 47 years and patients at PD-postTx group were significantly younger (38.3 ± 12.4 vs. 48.9 ± 16.4, respectively; *P* = .004). In terms of gender, weight, PD mode, and the etiology of ESKD, the groups were comparable. Diabetes was more common in the PD-noTx group than in the PD-postTx group (5.3% vs. 28.6%, respectively; *P* = .060).

Table 1. Demographic and Clinical Data of Peritoneal Dialysis Patients, According to Transplantation Status

Parameters	PD-postTx (n = 19, 21.3%)	PD-noTx (n = 70, 78.7%)	*P*	Total (n = 89, 100.0%)
Female, n (%)gender	7 (36.8)	36 (51.4)	.259	43 (48.3)
Age, years	43.2 ± 12.6	52.7 ± 16.1	**.020**	52.6 ± 15.8
ESKD etiology, n (%)			.091	
Hypertension	5 (26.3)	21 (30.0)		22 (24.7)
Diabetic kidney disease	1 (5.3)	17 (24.3)		22 (24.7)
Glomerulonephritis	4 (21.1)	13 (18.6)		17 (19.1)
Unknown	4 (21.1)	8 (11.4)		12 (13.5)
Other	5 (26.3)	11 (15.7)		16 (18.0)
Diabetes mellitus	1 (5.3)	20 (28.6)	.060	21 (23.9)
Weight, kg	67.0 ± 14.0	71.2 ± 15.4	.305	70.3 ± 15.2
Immunosuppression, n (%)	10 (52.6)	2 (2.9)	**<.001**	12 (13.5)
PD characteristics				
Age at PD initiation, years	38.3 ± 12.4	48.9 ± 16.4	**.004**	46.6 ± 16.2
PD modality, n (%)			.052	
CAPD	15 (78.9)	38 (54.3)		53 (59.6)
APD	4 (21.1)	32 (45.7)		36 (40.4)
Initial diuresis, mL (n = 81)	1520.6 ± 1038.3	1622.8 ± 1032.3	.716	1602.6 ± 1028.2
First year diuresis, mL	293.7 ± 112.1	1108.9 ± 77.6	**<.001**	953.6 ± 685.8
First year PET, n (%)			**.046**	
Low (0.34-0.49)	0 (0.0)	15 (21.4)		15 (16.8)
Low average (0.50-0.64)	8 (42.1)	30 (42.9)		38 (42.7)
High average (0.65-0.80)	6 (31.6)	22 (31.4)		28 (31.5)
High (0.81-1.03)	5 (26.3)	3 (4.3)		8 (9.0)
Outcomes				
Time on PD therapy, months	60.0 (range:29-194)	63.0 (range:28-206)	.575	61.0 (28-206)
With residual kidney function, n (%)	4 (21.1)	52 (74.3)	**<.001**	56 (62.9)
Patients with peritonitis				
at least 1 episode	13 (68.4)	25 (35.7)	**.011**	38 (42.7)
≥2 episodes, n (%)	8 (42.1)	14 (20.0)	.070	22, (24.7)
Transfer to HD, n (%)	7 (36.8)	8 (11.4)	**.015**	15 (16.9)
Death, n (%)	5 (26.3)	17 (24.3)	1.000	22 (24.7)

The values are described as the mean ± SD, median (minimum-maximum) or number (%). Values appears in bold if *P*-value was significant (below .05). APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ESKD, end stage kidney disease; HD, hemodialysis; kg, kilograms; PD, peritoneal dialysis; PET, peritoneal equilibration test; Tx, transplantation.

In PD-postTx group, the follow-up with a functioning graft was 117.4 ± 87.2 months. Four patients had undergone preemptive KTx and median dialysis vintage before KTx was 4.5 (0-132) months in PD-postTx group. Patients were transplanted at mean age of 28 years, 78.9% from living donor. Among the patients, 6 experienced biopsy-proven rejection, comprising 3 cases of T-cell–mediated rejection, 1 case of mixed rejection, 1 borderline rejection, and 1 case of chronic active T-cell–mediated rejection. Patients diagnosed with acute rejection (n = 5) and recurrent glomerulonephritis (n = 1) were administered additional immunosuppression, which includes anti-thymocyte globulin, steroids, and plasmapheresis based on their diagnosis; however, PD was initiated no sooner than 6 months following these interventions. The causes of graft loss in the cohort were chronic allograft nephropathy in 12 patients (63.2%), acute rejection in 4 patients (21.1%), chronic active rejection in 1 patient (5.3%), malignancy in 1 patient (5.3%), and recurrent glomerulonephritis in 1 patient (5.3%). The mean time on PD and total dialysis vintage was similar in PD-postTx and PD-noTx groups (*P* = .575 and *P* = .163, respectively). Five (26.3%) patients in the PD-postTx group administered 5 mg/day of prednisone after transplant failure, and 5 (26.3%) patients received prednisone plus a calcineurin inhibitor or azathioprine. Two patients (2.9%) in the PD-noTx group received 5 mg/day of prednisone

for extrarenal manifestations of sistemic lupus erythematosus and vasculitis.

Peritonitis and Other Complications

Peritonitis and other PD-associated complications, such as exit-site infection, tunnel infection, and catheter malfunction, were more common in PD-postTx group compared with PD-noTx group (73.7% vs. 37.1%, respectively; *P* = .039). Thirteen patients (68.4%) from the PD-postTx group encountered at least one episode of peritonitis, in contrast to 25 patients (35.7%) in the PD-noTx group (*P* = .011). The PD-postTx group exhibited a greater incidence of peritonitis than the PD-noTx group (0.33 vs. 0.13 episodes per patient per year, respectively). Among culture positive peritonitis episodes, the highest prevalence was *Staphylococcus aureus* (34.8%), followed by coagulase-negative *Staphylococcus* (13.0%), other gram-positive Cocci (21.7%), gram-negative Bacilli (26.2%), and fungi (4.3%). The evaluation of patients who experienced at least 1 episode of peritonitis revealed a higher prevalence among younger PD initiation (*P* = .033), individuals with no history of diabetes mellitus (*P* = .028), those with a longer PD duration (*P* = .018), patients with KTx history (*P* = .011), and among patients with no residual diuresis (*P* = .004). In the multivariate model, the presence of RKF was independently preventive for peritonitis (OR 0.262, 95% CI 0.105-0.653; *P* = .040) and KTx history was not a risk factor (*P* = .209).

Initial diuresis volume was similar between PD-postTx and PD-noTx groups (*P* = .716). However, the decline in the diuresis volume was much greater in the PD-postTx group at the end of the first year (*P* = .002) (Figure 1A) and no difference was observed in the PD-postTx group concerning immunosupression usage (*P* = .513) (Figure 1B). At the end of approximately 5 years of follow-up, 4 patients (21.1%) in PD-postTx, and 52 (74.3%) in PD-noTx group had RKF (*P* < .001).

Final Outcomes

Fifteen patients (16.9%) were transferred to HD during the follow-up. The causes of PD discontinuation were dialysis inadequacy and/or ultrafiltration failure (n = 6, 40.0%), peritonitis (n = 4, 26.7%), catheter disfunction (n = 2, 13.3%), patient's preference or psychosocial causes (n = 2, 13.3%), and diaphragmatic leak (n = 1, 6.7%). Patients who were transferred to HD had at least 1 peritonitis episode (73.3% vs. 36.5%, *P* = .009). Three and 5-year PD survivals in patients who had 3 or more peritonitis episodes or not were 90.9%, 72.7%, 95.9%, 79.7%, respectively (*P* = .076) (Figure 2A). Patients with transplantation history experienced a higher rate of PD discontinuation compared with transplant-naive patients (36.8% vs. 11.4%). Three and 5-year PD survivals in PD-postTx and PD-noTx group were 81.7%, 65.4%, and 98.5%, 91.9%, respectively (*P* = .015) (Figure 2B). In multiple analysis, a trend toward a higher risk for PD discontinuation in patients with a history of KTx was observed (HR 2.772, 95% CI 0.899-8.543; *P* = .076). Mortality rate was similar between the groups (PD-postTx 26.3% vs. PD-noTx 24.3%).

DISCUSSION

The current research demonstrated that patients initiating PD following KTx failure had an elevated risk of PD discontinuation and peritonitis relative to those without a transplantation history. However; the 2 groups exhibited no difference in patient survival. An increased number of peritonitis episodes and KTx failure was associated with a trend indicating a higher risk for PD discontinuation.

A previous study in Turkiye assessed 34 PD patients with a history of failed KTx and compared them to 82 PD patients without prior transplantation.[15] Duman et al[15] demonstrated that previous KTx did not negatively impact patient survival and time on PD therapy; nonetheless, it was linked to a higher occurrence

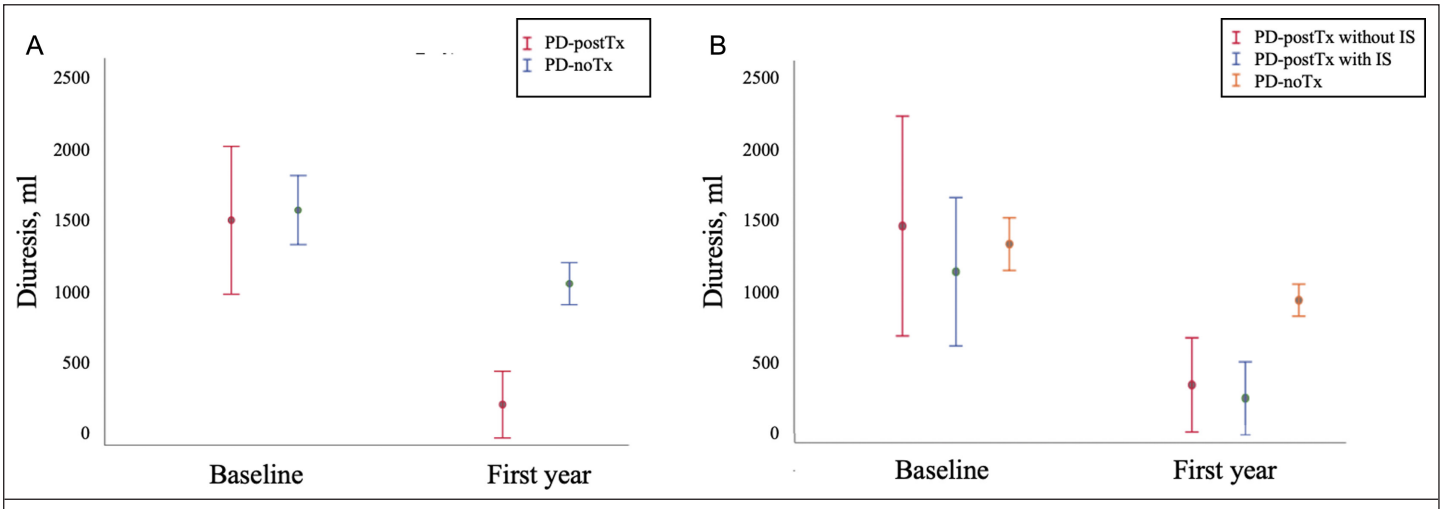


Figure 1. Diuresis volume at baseline, and at the end of the first year of peritoneal dialysis. (A) According to transplantation history status, decline in diuresis volume PD-postTx 1321.9 ± 882.2 mL vs. PD-noTx 528.0 ± 891.0 mL; *P* = .002. (B) According to immunosupression status, decline in diuresis volume PD-postTx without IS 1492.8 ± 915.3 mL, PD-postTx with IS 1188.9 ± 886.3 mL vs. PD-noTx 528.0 ± 891.0 mL; Group 1-2 *P* = .512; Group 1-3 *P* = .008; Group 2-3 *P* = .040. Symbols and lines represent the mean and SD of the mean. IS, immunosupression; PD, peritoneal dialysis; Tx, transplantation.

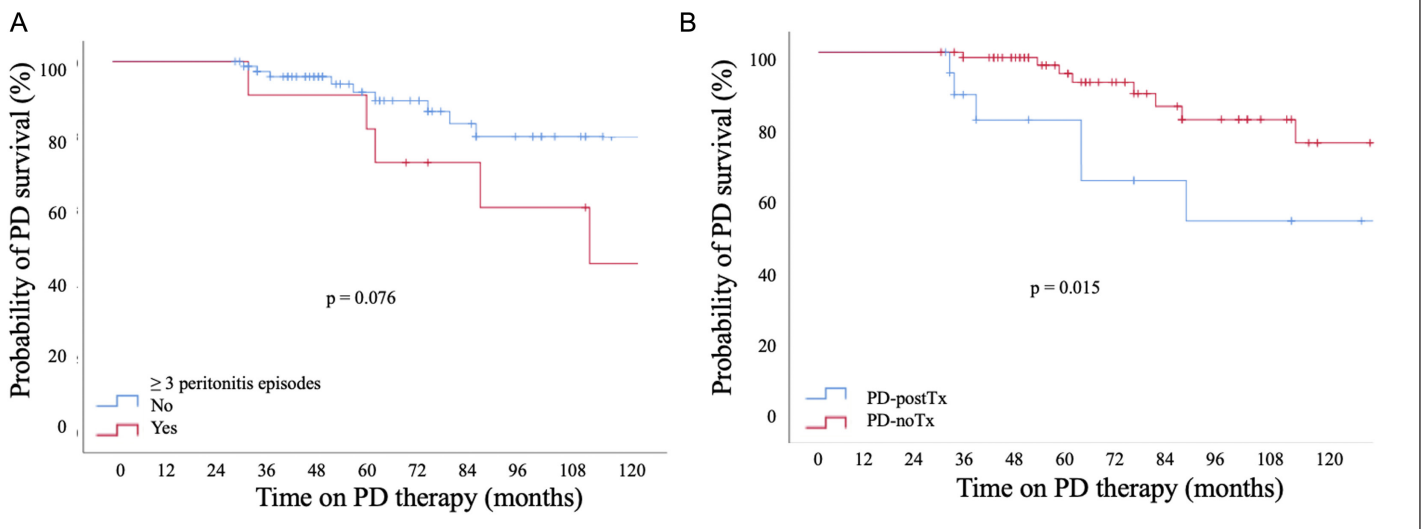


Figure 2. Kaplan-Meier plot showing PD survival. (A) According to experience of ≥3 peritonitis episodes. (B) According to transplantation history status. IS, immunosupression; PD, peritoneal dialysis; Tx, transplantation.

of peritonitis episodes. The survival rates of the technique at 1, 3, and 5 years were 83%, 77%, and 60% for the transplantation group, and 91%, 64%, and 48% for the no-transplantation group, respectively. Our study found that the time on PD therapy in the PD-postTx group were similar to those reported by Duman et al.; however, the survival rates in the tranplant-naive group were markedly superior.

Some small studies indicated adverse outcomes in patients with failed transplantation.[12,13,16] Nonetheless, further research revealed contrary findings. In comparison to 13 638 transplant-naive patients, 309 individuals returning to PD after failed KTx in Australia and New Zealand from 1991 to 2004 were younger and exhibited a lower incidence of diabetes mellitus, as in this study.[11] The rates of mortality, death-censored PD discontinuation, and peritonitis-free survival were comparable between the 2 groups. A study comparing patients who began PD after failed KTx with case-matched groups of transplant-naive patients starting on PD, as well as patients transitioned from HD to PD, found similar survival rates.[17] Transplantation rates were lower among patients who began PD following failed KTx compared to those with no transplantation history, yet comparable to rates of patients transferred to PD from HD. The French Language Peritoneal Dialysis Registry reported one of the largest cohorts in this population.[9] In a study of 328 patients who returned to PD following prior KTx, patient survival and peritonitis rates were comparable to those of 656 matched transplant-naive patients initiating PD over the same timeframe. However, the former group exhibited a greater incidence of PD discontinuation and had reduced access to a new transplantation. Two-years PD survival was 59% in the transplantation group and 77.7% in the control group. Prior KTx failure and episodes of peritonitis during PD treatment were significantly predictive of PD discontinuation. A meta-analysis of 12 retrospective observational studies, including these studies, indicated that patients who began PD following KTx failure did not exhibit an elevated risk of mortality, PD discontinuation, or peritonitis in comparison to transplant-naive individuals.[18]

This study reported that while PD discontinuation rates were elevated in patients with a KTx history compared to PD patients with no transplantation history, time on PD therapy were superior to those reported in prior studies.[9,15] This variation may arise from the evolution of practice approaches over different time periods and also highlights the importance of center activity in technical success, as demonstrated by Mujias et al.[17] Furthermore, although the adverse impacts of diabetes are well-documented on time on PD therapy, our control group with higher diabetes prevelance exhibited enhanced time on PD therapy compared to PD-postTx group. It should also be noted that the dialysis vintage before KTx may also affect the outcomes. The evidence suggests that instead of establishing a causal relationship between transplantation history and time on PD therapy, a comprehensive evaluation of the factors affecting time on PD therapy in this patient population, which is likely to include fast peritoneal solute transfer rate, is necessary.[19]

The predominant cause of technical failure identified in the previous studies was peritonitis.[17] In this study, the primary reason for transitioning to HD was dialysis inadequacy and/or ultrafiltration failure. The decline of RKF may correlate with PD discontinuation in both individuals with or without a transplantation history.[20] The rate of decline in RKF was observed to be more rapid in patients with failed KTx who initiated PD compared to those who had never undergone transplantation.[21,22] Even though some studies claimed that immunosuppression might prevent residual diuresis without elevating the risk of peritonitis and mortality,[23,24] our research indicates a reduction

in diuresis among patients with a transplantation history, irrespective of immunosuppression status. Furthermore, the increased risk of infectious complications, including peritonitis, attributed to immunosuppression requires careful consideration regarding the continuation or cessation of immunosuppression after transplant failure.[25,26] The fact that all patients in the PD-postTx group without immunosuppression experienced at least one peritonitis episode in this study, indicating the importance of evaluating risk factors of peritonitis other than immunosuppression. Residuel kidney function, which was identified as a protective factor against peritonitis and observed to decline more rapidly in patients with a transplantation history in the cohort, may play a crucial role in mitigating peritonitis and enhancing time on PD therapy.[27] It is essential to assess the effectiveness of multiple strategies proposed for patients undergoing PD to preserve RKF, including the blockade of the renin-angiotensin-aldosterone system, prevention of hypotensive episodes and hypertension, minimization of high ultrafiltration, reduction of dialysate glucose exposure, utilization of icodextrin solutions, implementation of incremental PD, and avoidance of contrast agents and nonsteroidal anti-inflammatory drugs, specifically in the context of kidney allograft failure cohort.[28]

The assessment of urine output, management of immunosuppressive therapy, and extended follow-up after the initiation of PD in patients represent notable strengths of this study. This research has several limitations. The study's limited sample size and retrospective design might permit for residual confounding. The assessment of the data are limited by the small patient sample and should not be generalized to the broader population. The differences in diabetes prevalence, and age between the groups necessitate cautious interpretation of the results.

In conclusion, this study indicates that patients experiencing kidney allograft loss are at an elevated risk of PD discontinuation, particularly those who have lost RKF. Dialysis modality selection after kidney allograft failure requires consideration of individualized patient factors, which can also enhance medical care. Patients with kidney allograft failure can achieve favorable outcomes with PD through careful management of complications and comorbidities.

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

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Ankara University (Approval No: İ08-539-22, Date: 05.10.2022).

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