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Overview of peritoneal dialysis outcomes in Northern Cyprus: a nation based study

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ABSTRACT

Aim: Peritoneal dialysis (PD) is the more preferred renal replacement therapy (RRT) option for most patients with end-stage renal disease (ESRD) who can not achieve a kidney transplantation. By an enhanced national PD program, more patients may have a chance to take the advantage of this treatment option. In this study, we aim to investigate whether PD is preferred as the first dialysis treatment modality in Northern Cyprus and reveal the outcomes in order to improve the further PD program.

Material and Method: Peritoneal dialysis patients aged above 18 years who were followed between 2003-2021 in Northern Cyprus were investigated retrospectively. Demographic data, primary kidney diseases, comorbidities and previous RRT modalities were analysed. Episode(s) of peritonitis, total duration on PD therapy, switch to kidney transplantation or HD, and mortality rate were evaluated. Outcomes of elderly (≥ 65 years) and diabetic patients who were dropped out from PD were found out.

Results: A total of 123 patients aged 18-83 years were included in the study. Forty percent of 123 PD patients initiated RRT with PD. The median time was found 1 month in the rest of the patients to transfer PD from other modalities. Renal transplantation was performed in 16.8% of patients during follow-up whereas 34.7% were transferred to HD after 41 months. Inadequate dialysis (40.7%), PD-related infections (29.6%), ultrafiltration insufficiency (18.5%), mechanical complications (11.1%) were the most common causes of switching from PD to HD. The duration of being under PD therapy was 36.5 months for 46 patients who died under PD therapy. Cardiovascular events (50%) and various infections (%35) were the leading causes of mortality. A total of 48 (43.2%) PD patients had at least one episode of peritonitis. Total duration on PD treatment, PD rate as initial RRT modality, the prevalence of hypertension and diabetes mellitus (DM), peritonitis rate, and use of automated PD were not significantly different between elderly (n=34) and adult individuals (18-65 years). The duration of being under PD therapy was longer for males than females (p=0.044) and the duration of PD therapy was similar in the dropped out patients with or without DM (p=0.205).

Conclusion: A significant amount of patients received HD before initiation of PD (60%). Age is not be considered as a challenging barrier for PD initiation in Northern Cyprus. Precautions to prevent the development of peritonitis may contribute to extend the total duration of PD treatment.

Keywords: End-stage renal disease, peritoneal dialysis, renal replacement therapy

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INTRODUCTION

The prevalence of patients with end-stage renal disease (ESRD) undergoing renal replacement therapies (RRTs) is increasing worldwide (1). Although transplantation is the best option among RRTs, there is a shortage of organ donors, and thus most of the patients with ESRD have to be put on either hemodialysis (HD) or peritoneal dialysis (PD) while on a waiting list for transplantation (2). Epidemiology of ESRD and treatment options for these patients should be considered in the health system projections of each country.

Patients should be well informed about different treatment modalities in the predialysis period. Besides the medical factors, patients' preferences, expectancy, and needs should be considered for a better quality of life (3). Modality conversion may sometimes be required during the follow-up. Although the proportion of patients on HD is much more than patients on PD, the pattern of choice may be different among countries and regions (4).

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Analysis of the PD registry of each country may help to improve the national PD program –to determine medical expenses, and demand for health care professionals, to allocate health care resources fairly. With the national PD program, more patients may have a chance to take advantage of this treatment option. Mortality and morbidity data may allow us to take necessary precautions. This may give us a chance to overcome barriers and build a strong PD program to improve health outcomes. In order to contribute to the development of the PD program in Northern Cyprus, we planned to assess our national PD registry as a first step. In this study, we aim to investigate whether PD is preferred as the first dialysis treatment modality in Northern Cyprus and to evaluate the duration of being under PD therapy, and outcomes in order to improve the PD program.

MATERIAL AND METHOD

The study was approved by Dr. Burhan Nalbantoğlu State Hospital Ethics Committee (Date: 5.11.2021, Decision number: 55/21). All procedures were performed in accordance with the principles stated in the Declaration of Helsinki. We evaluated all 125 adult PD patients (> 18 years) who were followed in Northern Cyprus from the year 2003 to 2021. Two missing PD patients were excluded due to moving to another country within 3 months following the onset of the PD therapy. There was a single team who was responsible for follow-up PD patients in the country.

Demographic data, primary kidney diseases, and comorbidities including diabetes mellitus (DM), hypertension, heart failure, peripheral vascular disease, cerebrovascular disease, liver disease, peptic ulcer, malignancy, acquired immunodeficiency syndrome, a solid tumor, or hematological malignancy were noted. Charlson's comorbidity index was calculated for each participant. Previous RRT histories of the patients were screened retrospectively to determine whether PD was the initial RRT modality or not. Duration of time spent on other RRT modalities before initiation of PD was found out. Data of initial peritoneal equilibrium test results and switch to automated PD were collected. The proportion of patients who had peritonitis was determined.

The primary endpoint of this study was PD dropout. PD dropout was defined as the termination of PD therapy and resulted in switching to another RRT (renal transplantation or HD) or mortality. Causes of switching from PD to HD were analyzed. We evaluated patient survival and described the causes of mortality. Peritoneal dialysis duration was calculated for each participant who dropped out from PD. The dropout rates of 1, 2, and 5 years following the onset of the PD initiation were found out. Peritoneal dialysis duration and a dropout rate of 1 and after 5 years of PD initiation were compared between female and male PD patients.

Elderly patients who initiated PD at age ≥65 were compared with adult individuals in terms of initial RRT modality, time passed to initiate PD after first RRT, use of automated PD. Peritoneal dialysis duration, peritonitis rate, use of automated PD, the prevalence of hypertension, diabetes, Charlson's comorbidity index, and outcomes were evaluated for elderly and adult patients who were dropped out from PD. The dropout rates of 1 and 5 years were evaluated for elderly and adult individuals.

Initial RRT modalities, the duration of being under PD therapy, peritonitis rate, use of APD, the prevalence of hypertension, Charlson comorbidity index, and a dropout rate of 1 and 5 years were compared between PD patients with and without DM.

Statistical Analysis

We used the Statistical Program for Social Science (SPSS) version 15 for Windows. Normality tests were performed to identify whether variables were in the normal distribution. Descriptive statistics are presented as mean±standart deviation, median, minimum and maximum values. Categorical values are described as percentages. Student's t-test or Mann-Whitney U test was used for the mean comparison of two groups. Chi-square statistics were used to compare two categorical variables. Binary logistic regression was performed to evaluate the impact of peritonitis on the drop out rate of PD. p value lower than 0.05 was considered statistically significant.

RESULTS

A total of 123 patients aged 18-83 years were included in the study. Twenty-five patients were actively on PD therapy, 2 moved to another country on PD therapy, and 96 dropped out from PD. A greater number of male than female patients received PD (73% vs 27%). Unknown etiology (32.5%) and DM (29.3%) were the most common etiological factors for renal diseases in these patients (**Table**). Peritoneal dialysis was the initial RRT modality for 40% of patients (**Figure 1**). The median time was found 1 month for the patients to transfer PD from other modalities. Automated PD was used by 58 (53.2%) patients.

Table. Demographic and clinical features of peritoneal dialysis patients	
Gender, female/male, n (%)	33/90 (27/73)
Age initiated peritoneal dialysis*	59 (18-83)
Time passed to initiate peritoneal dialysis after first renal replacement therapy, months*	1 (0-328)
Diabetes mellitus prevalence, n (%)	53 (43.4)
Hypertention prevalence, n (%)	104 (87.4)
Primary kidney disease, n (%)	
Diabetes mellitus	36 (29.3)
Glomerulonephritides	17 (13.8)
Hypertension	7 (5.7)
Tubulointerstitial disease	4 (3.3)
Policystic kidney disease	8 (6.5)
Other	10 (8.1)
Unknown	40 (32.5)
Charlson comorbidity index*	5 (2-9)
Initial peritoneal equilibrium test category, n (%)	
Low transporter	3 (3.5)
Low-average transporter	23 (27.1)
High-average transporter	42 (49.4)
High transporter	17 (20)
Patients experienced peritonitis, n (%)	48 (43.2)
Use of automated peritoneal dialysis, n (%)	58 (53.2)
*median (minimum-maximum)	

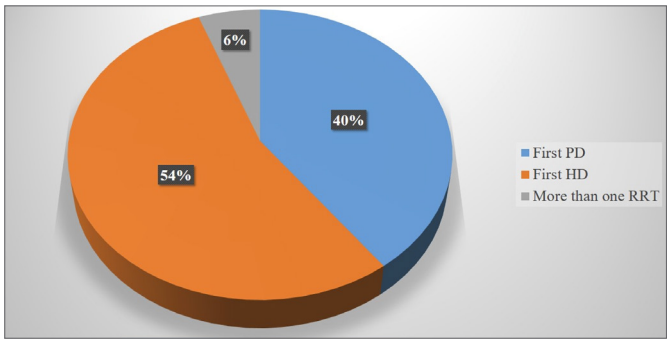

Figure 1. Distrubition of patients according to first renal replacement therapies
*PD; peritoneal dialysis, HD; hemodialysis, RRT; renal replacement therapy

Sixteen (16.8%) patients had renal transplantation during follow-up. Thirty-three patients (34.7%) were switched to HD. Median transfer time to HD was 41 months (1-122 months). Dropout rate to HD was 9.5% in 2019, 4.2% in 2020 and 4.0% in 2021. Inadequacy dialysis and PD-related infections were the most common causes of switching from PD to HD (**Figure 2**). A total of 48 (43.2%) PD patients had at least one episode of peritonitis. Peritonitis was found as an important factor affecting the dropout rate of PD (p<0.0001).

Forty-six (48.4%) patients died on PD therapy at the age of 67±11. Average time spent under PD was found 36.5 months (1-150 months) for these patients. Mortality rates for last three years were evaluated and it was 13.6% in 2019, 14.8% in 2020, and 17.2% in 2021. Cardiovascular events (50%) and various infections (%35) were the leading causes of mortality.

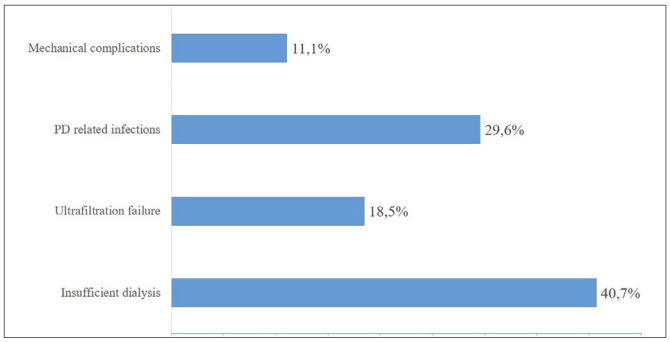

Figure 2. Causes of transfer from peritoneal dialysis to hemodialysis
*PD; peritoneal dialysis

The duration of being under PD therapy was 36 (1-150) months in patients who dropped out from PD. 18.9% (18/95) of dropouts occurred within 1 year of PD initiation, whereas 66.3% (63/95) occured after 2 years and 28.4% (27/95) after 5 years of PD initiation.

Gender

Total duration on PD treatment was longer in males (n=67) then females (n=28) (41 [1-150] vs 21 [3-120] months, p=0.044). Thirty-two percent (9/28) of female patients dropped out within the first year of PD whereas only 13% (9/67) of male patients dropped out of PD within the same period (p=0.034). The dropout number of female and male patients after 5 years of the onset of the PD was similar (6/28 F, 21/67 M, p>0.05).

Elderly and Adult Patients

Elderly patients, who initated PD at aged ≥65, consisted 32.5% (40/123) of all PD patients. Initial RRT modality was PD in 32.5% (13/40) of elderly patients and 43.4% (36/83) of adult patients (p>0.05). Time passed to initiate PD after first RRT was similar between elderly (n=40) and adult patients (n=83) (1.5 [0-328] vs 1[0-164] months, p>0.05). Elderly patients used automated PD more commonly than adult individuals (67% [24/36] vs 47% [34/73], p=0.048).

The duration of being under PD therapy was 34.5 (1-150) months for elderly (n=34) and 38 (1-139) months for adult individuals (n=61) who were dropped out from PD (p>0.05). Peritonitis was similar in elderly and adult patients who were dropped out from PD (16/31 vs 27/54, p>0.05). The use of automated PD was not significantly different between elderly and adult patients who were dropped out from PD (19/30 vs 28/53, p>0.05 for all). Prevalence of hypertension (27/33 vs 56/60, p>0.05) and DM (19/34 vs 26/62, p>0.05) were similar between the two groups. The comorbidity index was found significantly higher in the elderly group than adult individuals who were dropped out (5.85±1.48 vs 4±1.59, p<0.0001). The dropout rate within 1 year of PD was similar for elderly and adult individuals (8/34 vs 10/61, p>0.05). The dropout rate of PD at 5 years was similar for elderly and adult individuals (8/34 vs 19/61, p>0.05).

Diabetic and Non-diabetic Patients

A total of 53 PD patients out of 123 (43.4%) had DM. Diabetic patients who chose PD as the initial RRT modality were not significantly different than non-diabetic patients (n=24/53 vs 25/69, p>0.05).

Patients who dropped out from PD were grouped as diabetic (45/96, 46.9%) and non-diabetic patients (51/96, 53.1%). Peritoneal dialysis duration was 31 (1-139) months for patients with DM and 43 (2-150) months for patients without DM (p>0.05). The prevalence of peritonitis was similar in the two groups (21/39 vs 22/46, p>0.05). The use of APD was similar for patients with and without DM (18/36 vs 29/47, p>0.05). Hypertension was more prevalent in patients with DM than patients without DM (43/44 vs 40/49, p=0.012). The comorbidity index was significantly higher in patients with DM than patients without DM (5.93±1.34 vs 3.48±1.25, p<0.0001). The dropout rate within 1 year of PD onset was similar for diabetic and nondiabetic individuals (7/45 vs 11/50, p>0.05). The dropout rate after 5 years of PD initiation was similar for individuals with and without DM (9/45 vs 18/50, p>0.05).

DISCUSSION

Our present results show that a significant amount of patients required HD before initiation of PD in Northern Cyprus. This was higher than the rates reported in previous studies from other countries (5). Late admission of patients to the nephrology department, delay in predialysis education, less use of urgent PD may be some of the possible explanations for this observation. In this study, we found that patients aged ≥ 65 years had similar results to adults, and diabetic patients had similar outcomes to non-diabetic patients. Therefore, age and DM should not be considered as challenging barriers for PD.

PD has the advantage of being home-based therapy away from the hospital, with social distancing without need for transportation which becomes more important nowadays due to the COVID-19 pandemic (6). Peritoneal dialysis offers patients the opportunity to dialysis with relative protection of residual kidney function and no need for vascular access site. Clinical outcomes and survival were as good as HD (7-9). A more flexible schedule of PD may provide greater patient freedom like more opportunities to travel, and social rehabilitation, and may deliver improved quality of life (4,8,10,11). Reduced early graft dysfunction following transplantation was reported in PD patients (12). Besides all these potential benefits, PD is also accepted as a cost-effective RRT method (13).

Despite all its advantages, the use of PD is lower than HD in most parts of the world (4,7,11,14). Similarly, PD is less likely preferred RRT modality in Northern Cyprus. We need to clarify the reasons why PD is not widely used. There may be factors related to patient, health care team, and health care system (4). Patients may be inadequately educated on modality choice and they may feel fear that leads to reluctance in accepting PD (15). Problems faced arranging catheter insertion and catheter dysfunction as an early technique failure are important challenges (7). Patient education and training may be time-consuming, and a lack of motivation of the health care team may be some of the underlying factors (15). Reimbursement schemes and government policies may be also responsible for the wide variation in the use of PD between countries (4).

Patients with ESRD should have the opportunity to access various treatment options (14). Predialysis patients should be educated timely about the dialysis modalities and encouraged to make a choice that is most suited to their lifestyles (4,7,16). Enough time should be spent discussing treatment modalities and effective educational programs may include sessions with family members (16). Catheter placement, patient training, and continued support may be some of the other factors on which we need to focus (7). A dedicated staff who will participate in the education and training PD programs is essential. The health care team should help patients to feel confident to dialyze. Appropriate socio-economic circumstances and social support are also required, and home visits may support patient cooperation (7).

Patients may admit in late-stage requiring dialysis. Unplanned RRT initiation may lead patients to choose HD instead of PD. These patients are less likely to change their modality to PD. The feeling of improvement that patients feel after starting HD may lead to the perception that the current treatment is the best treatment. An urgent start PD program is an acceptable option and may reduce central venous catheter requirement for patients who prefer to be on PD (7,9). Incidences of catheter-related bloodstream infections and dialysis-related complications were reported lower in urgent-start PD than urgent-start HD via a central venous catheter (3). Patients who have already initiated HD therapy should also receive information about other RRT modalities. A significant number of these patients may transfer to PD in the first 6 months of therapy (16,17). We found that PD was the initial RRT modality only for 40% of patients, and it took approximately 1 month for others to initiate PD after the first RRT. Pulliam et al. reported 25%– 27% of PD patients were transferred from HD, and only 1%–2% had a failed allograft (18). This indicates that PD should be more encouraged as a first RRT modality in

our country. High prevalence of unknown etiology in our cohort may implicate late admission of the patients which may limit time for adequate education in the predialysis period. Urgent PD may also be less performed.

Dropout rate from PD to HD improved in last three years from 9.5% in 2019 to 4.0% in 2021 in Northern Cyprus. Strategies to improve PD technique survival may help to keep patients on PD and lead to higher-quality dialysis with better outcomes (4,7). High rates of technique failure may limit time spent on PD. Unfortunately, the majority of the patients discontinue PD within 2-3 years of commencement (7,11), and only a few patients are left on PD after 5 years of PD initiation (10,18). The longevity of PD still remains a concern (4). Catheter dysfunction, peritoneal or catheter-related infections, inadequacy dialysis, or ultrafiltration failure are among the common reasons for technique failure. Psychosocial barriers like a burden and patient preference are the other contributing factors (19,20). In our study majority of PD patients dropped out after 2 years of PD initiation. Peritoneal dialysis duration was 41 months for patients who dropped out from PD to HD, and insufficient dialysis and PD-related infections were the most common causes. We may need to give greater attention to prevent technique failure to make long-term PD possible. Mortality rate of PD patients was increased in last three years from 13.6% in 2019 to 17.2% in 2021 which might be attributed to COVID-19 pandemia. Cardiovascular events and infections are the leading causes of mortality in PD patients.

The predominance of male patients was noted in our study. There are conflicting reports about gender-specific differences in technique failure. Some trials reported lower technical failure rates in females compared to men (21,22) whereas no gender-specific differences were found in others (23,24). Different characteristics of the PD population like age, the need for sufficient numbers of caregivers might affect the results. Male and female patients may also have different coping skills (25). We found the duration of being under PD therapy was longer in males than females. The dropout rate of female patients was higher within the first year of PD onset, whereas the dropout rate after 5 years of PD onset was similar in the two groups.

The elderly are less likely to initiate RRT with PD than HD (26,27). However, PD may be a better option for the elderly rather than HD as hemodynamic instability and vascular access may be greater problems for this age group. Initiating RRT with PD rather than HD was found associated with better patient survival for the full 5 year follow-up period for patients aged above or below 65 years (4). Availability of assisted PD programs may be useful for some elderly patients who prefer to perform PD but need help (28). Our results supported that elderly patients have comparable outcomes to adult individuals. Elderly patients used automated PD more commonly than adult individuals in our study.

Diabetes is the most common cause of ESRD worldwide. Diabetic patients were less likely to receive PD as first RRT than nondiabetic patients in Europe (26,27,29). The presence of diabetic retinopathy and peripheral neuropathy, anxiety about poorer glycemic control, and increased risk for peritonitis may be the underlying reasons (29). Transfer to HD may be more common in diabetic PD patients (25). However, our study revealed that a significant amount of PD patients in Northern Cyprus had DM, and number of diabetic patients who chose PD as the initial RRT modality were not different than non-diabetic patients. Despite the greater prevalence of comorbidities, the duration of being under PD therapy and dropout rate were similar in patients with and without DM. Peritonitis rate was not different as well. All these results encourage the use of PD in diabetic patients. The difference in results may be due to the heterogeneity of patients with DM.

The limitations of the study are as follow. First, psychosocial factors could not be evaluated among the dropout causes due to the retrospective design of the study. Second, data about predialysis education, nephrology care before the start of dialysis, and the presence of caregivers were not included. Third, as this is a nation-based study, results may not be entirely generalized.

CONCLUSION

A significant amount of patients required HD before initiation of PD. Early admission of patients to the nephrology department and timely initiation of education programs may contribute to decreasing the need for HD before PD. As elderly patients had similar results with adult individuals, age is not be considered as a challenging barrier for PD. Precautions to prevent the development of peritonitis may contribute to extend the total duration of PD treatment. Region-specific issues related to using PD need to be described to improve the outcomes of PD patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by Dr. Burhan Nalbantoğlu State Hospital Ethics Committee (Date: 5.11.2021, Decision number: 55/21).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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