Predictors of Patient Survival in Continuous Ambulatory Peritoneal Dialysis

10-Year Experience in 2 Major Centers in Tehran

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Introduction. Many factors have been proposed to be associated with higher mortality in patients on continuous ambulatory peritoneal dialysis (CAPD). However, the relative importance of these factors may differ among patients with different characteristics. We evaluated survival of patients on CAPD and its influencing factors in Iran.

Materials and Methods. We enrolled 282 patients on CAPD between 1996 and 2006 at 2 major CAPD centers in Tehran. Patient survival was investigated during this period. Demographic characteristics, laboratory data, dialysis adequacy parameters, residual renal function, peritoneal transport characteristics, and nutritional status were assessed as potential predictors of the outcome.

Results. The mean duration of follow-up was 18.4 ± 14.5 months. Sixty patients (21%) died during the studied period. In univariate analysis, age, body mass index, history and duration of hemodialysis before CAPD, diabetes mellitus, blood pressure, patient selection criteria, edema, peritonitis, renal residual function, urine volume, dialysis adequacy, and serum levels of cholesterol, triglyceride, intact parathyroid hormone, calcium, and albumin were predictors of patient survival. Multivariate analysis demonstrated that old age, diabetes mellitus, prior hemodialysis longer than 7 months, low serum albumin, calcium, trigelyceride, and parathyroid hormone levels independently predicted mortality, while the use of angiotensin-converting enzyme inhibitors was associated with a better survival.

Conclusions. This study showed that older patients on CAPD and diabetics are at a higher risk of mortality. On the other hand, nutritional and metabolic factors are other predictors of mortality. Especial concern should be applied to good nutrition and treatment of comorbidities in these patients.

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INTRODUCTION

The number of patients with end-stage renal disease (ESRD) is increasing in the world due to aging populations, longer life expectancy of patients, increasing access to renal replacement therapies, and higher incidence of diabetes mellitus and hypertension.[1] Dialysis prevents death of uremia; however, survival of these patients is still

a major concern. Although several reports have shown patients on peritoneal dialysis (PD) have better survival than patients on hemodialysis in the first 2 years on dialysis, still their mortality is high.[4,5] Cardiovascular disease remains a major cause of death in about 30% to 50% of patients with ESRD.[1] The reasons for mortality in patients with PD may be due to many factors including old age, comorbid diseases, malnutrition, low-residual kidney function, and high peritoneal transport.[1-6] The Canada-USA (CANUSA) study group showed that the relative risk of death increased with decreased removal of small solutes and serum albumin.[7] In some studies, however, association of mortality and solute transport has not been confirmed.[8,9] The relative impact of risk factors may differ between patients with different characteristics.

After establishment of continuous ambulatory PD (CAPD) program in 1996 in Iran, the number of patients on CAPD has been increasing over the time. At present, up to 1500 patients with ESRD (3%) are treating by CAPD in Iran. The purpose of this study was to evaluate patient survival in CAPD in 2 major CAPD centers in Iran and its related factors.

MATERIALS AND METHODS

Patients

We enrolled 282 adult patients on CAPD in 2 major CAPD centers (Dr Shariati Hospital and Shafa PD center) in Tehran, Iran. Patients older than 18 years who had been on CAPD for at least 3 months were enrolled the study. These patients had been on CAPD between1996 and 2006. In February 2006 we reviewed demographic data, laboratory data, dialysis adequacy parameters, residual renal function (RRF), peritoneal transport characteristics, and nutritional status from patients' charts. Dialysis adequacy parameters, including creatinine clearance and Kt/V, peritoneal equilibration test (PET), and normalized protein catabolic rate (NPCR) had been calculated with the PD Adequest 2.0 for Windows program (Baxter Healthcare Co, Deerfield, Illinois, USA).

The negative selection criteria for CAPD included vascular access problems and/or cardiovascular diseases in patients who were not eligible for hemodialysis or kidney transplantation. The end point of the study was patients' death and transfer to hemodialysis program, kidney transplantation, or end of the study (considered as censored data).

Biochemical Analyses

Laboratory data including hemoglobin, serum creatinine, blood urea nitrogen, serum calcium, phosphorus, intact parathyroid hormone, lipid profile, and serum albumin were collected. Development of peritonitis episodes and other infections were accessed as reported in the patients' charts. Data related to peritoneum, ultrafiltration, and solute clearance were as follows: weekly total Kt/V and weekly total creatinine clearance were calculated based on the analyses of a 24-hour collection of dialysis solution and urine. The RRF was estimated by the assessment of the mean of renal creatinine and urea clearances. The PET was performed with a standard 4-hour dwell period using 2.25% glucose concentration for a 2-L volume exchange. Finally, calculation of dialysis adequacy, RRF, and PET characteristics were done by the PD Adequest 2.0 for Windows program (Baxter Healthcare Co, Deerfield, Illinois, USA).

Nutrition and Medications

The nutritional status of the patients was assessed by calculation of NPCR and serum albumin. History of taking calcium carbonate, calcitriol, folic acid, intravenous iron, erythropoietin, statin, and antihypertensive drugs (beta blockers, calcium channel blockers, and angiotensin-converting enzyme [ACE] inhibitors and angiotensin receptor blockers) during the follow-up period were recorded.

Statistical Analyses

The SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA) was used for statistical analyses. Univariate and multivariate Cox regression analysis was used to identify the factors which predict patient survival by categorization of continuous variables to get higher hazard ratio. Actuarial patient survival rates were determined by the Kaplan-Meier method. In technique survival analysis, event was transferring to hemodialysis and the others considered as censored. Continuous data were presented as mean ± standard deviation. A difference was considered significant when the *P* value was less than .05.

RESULTS

A total of 282 patients with a mean age of 50.7 ± 16.0 years (range, 14 to 82 years) were included in the study. Of the patients, 157 (55.7%) were candidate for CAPD based on positive selection criteria and 118 (41.8%), based on negative selection criteria. One hundred and forty patients (49.6%) had a history of prior hemodialysis before starting PD. Table 1 outlines characteristics of the patients.

The mean duration of follow-up was 18.4 ± 14.5 months (range, 1 to 104 months). At the end of study, 60 patients (21.3%) died. Among survived patients, 124 (44.0%) were active on CAPD. Table 2 summarizes the final status of the patients. Causes of drop-out from CAPD program were peritonitis in 38 (37%), mechanical problems in 9 (14%), membrane failure in 6 (9%), tunnel infection in 1 (2%), patient's preference in 2 (3%), and others in 10 patients (15%).

Table 1. Characteristics of Patients on Continuous Ambulatory Peritoneal Dialysis*

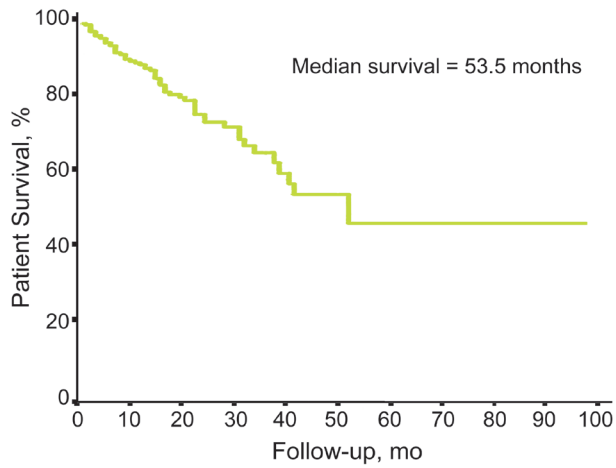
Characteristic	Value
Number of patients	282
Age, y	50.7 ± 16.0
Males	150 (53.2)
Body mass index, kg/m^2	23.8 ± 4.1
Diabetes mellitus	93 (32.9)
Hypertension	28 (9.9)
Comorbidities	76 (29.6)
IHD	71 (25.2)
CHF	46 (16.3)
CVA	12 (4.2)
Patient selection	
Positive	157 (55.7)
Negative	118 (41.8)
Not determined	7 (2.5)
Systolic BP, mm Hg	136.0 ± 23.7
Diastolic BP, mm Hg	81.0 ± 13.7
Serum albumin, mg/dL	3.6 ± 0.5
NPCR, g/kg/d	0.78 ± 0.2
Peritonitis, per patient/y	0.63
Total Kt/V	2.1 ± 0.6
Creatinine clearance, L/wk/1.73 m^2	80.4 ± 28.8
Urine volume, mL/d	741 ± 611
Ultrafiltration, mL/d	906 ± 534
RRF, mL/min	3.3 ± 3.0
PET	
Low	10 (3)
Low average	77 (21)
High average	166 (46)
High	106 (30)

*Values in parentheses are percents. IHD indicates ischemic heart disease; CHF, congestive heart failure; CVA, cerebrovascular accident; BP, blood pressure; NPCR, normalized protein catabolic rate; RRF, residual renal function; and PET, peritoneal equilibration test.

Table 2. Final Status of Patients on Continuous Ambulatory Peritoneal Dialysis

Status	Patient (%)
Still on peritoneal dialysis	124 (44.0)
Died	60 (21.3)
Transferred to hemodialysis	63 (22.3)
Received a kidney transplant	29 (10.3)
Improved kidney function	6 (2.1)

Patient survival at 1, 2, 3, 4, and 5 years was 88%, 74%, 65%, 54%, and 46%, respectively (Figure). Technique survival at these years was 88%, 72%, 56%, 39%, and 32%, respectively. The most common cause of death was cardiovascular diseases (53%), followed by infections (12%), others (25%), and unknown (10%). The mean interval between initiation of dialysis and death was 14.7 ± 12.3 months (range, 1 to 53 months). The correlation between different variables and patient survival in a univariate Cox regression model is shown in Table 3; older age, presence of diabetes mellitus, comorbidities, history of prior 7-month or longer hemdialysis, negative patient selection, high body mass index, systolic blood pressure less than 100 mm Hg, diastolic blood pressure less than 65 mm Hg, presence of moderate to severe edema, history of peritonitis more than 2 episodes per year, no RRF, low urine volume, total creatinine clearance less than 55 L/wk/1.73 m^2, Kt/V less than 1.8, low serum albumin level, and NPCR were associated with higher mortality. Despite the role of peritonitis, exit site infection and tunnel



Survival of patients on continuous ambulatory peritoneal dialysis.

Table 3. Predictors of Mortality on Univariate Analysis*

Variable	*P*
Age ≥ 45 y	< .001
Body mass index ≥ 20	.03
Diabetes mellitus	.03
Comorbidity	< .001
History of prior hemodialysis	.008
Prior hemodialysis ≥ 7 mo	< .001
Negative patient selection	< .001
Systolic BP < 100 mm Hg	.02
Diastolic BP < 65 mm Hg	.002
Edema	.002
Peritonitis > 2 episodes/y	.007
RRF	.03
TCC < 55 L/wk/1.73 m^2	.02
Kt/V < 1.8	.046
Serum creatinine < 6 mg/dL	.001
Urine volume < 250 mL/d	.02
Serum albumin < 3.5 mg/dL	< .001
NPCR < 0.8	.01
Serum calcium < 8.5 mg/dL	.008
iPTH ≤ 35 ng/L	< .001
Serum cholesterol < 180 mg/dL	< .001
Serum triglyceride < 130 mg/dL	.02

*BP indicates blood pressure; RRF, residual renal function; TCC, total creatinine clearance; NPCR, normalized protein catabolic rate; and iPTH, intact parathyroid hormone.

infection had no significant correlation with patient survival. Mortality of patients with urine volume less than 250 mL/d was 2 times higher than those with higher urine volumes. No RRF increased the mortality 2-fold, as well.

In multivariate analysis, age, diabetes mellitus, duration of prior hemodialysis, serum albumin, ACE inhibitors, intact parathyroid hormone level, serum triglyceride level, and serum calcium level predicted mortality (Table 4). Cox regression analysis on different age groups showed that mortality of patients older than 45 years was 25 times more than that of patients younger than 45 years. The use of calcium carbonate, calcitriol, folic acid, intravenous iron, erythropoietin, and all antihypertensive drugs were associated with better survival. However, multivariate Cox regression analysis showed that only the use of ACE inhibitors was associated with better survival (P = .04; odds ratio, 2.09).

DISCUSSION

In this study, the impact of different factors on survival of patients on CAPD was evaluated. In general, patient survival in our study was comparable to that reported from other countries.[6,10] On the other hand, technique survival was lower than that in western countries.[6,10] The mean age of the patients (50.7 years) was high and also diabetes mellitus was frequent (33%) as a cause of ESRD. Age and diabetes mellitus are associated with different cardiovascular events and could adversely affect survival of patients on dialysis.[1-6,10,14] Our results were consistent with other studies. Death rates of diabetic patients on CAPD were higher than nondiabetics. In fact, diabetes mellitus per se is an independent risk factor affecting long-term survival of patients on PD.[4-6] In diabetic patients on long-term PD, structural and functional changes of the peritoneal membrane occur, which are caused mainly by increased levels of advanced glycation endproducts.[5] Nearly, half of the patients were candidate for CAPD based on negative selection. This shows that CAPD was considered for patients who had vascular access problem, cardiovascular diseases, or contraindication for kidney transplantation. History of hemodialysis before PD in 51% of patients confirms this state. This is the first study which evaluated the correlation between patient selection and patient survival and it showed that patients with negative selection had lower survival.

Table 4. Independent Predictors of Patient Survival (Cox Multivariate Analysis)

Variable	Hazard Ratio (95% CI)	*P*
Age ≥ 45 y	25.6 (4.4 to 148.5)	.001
Serum albumin < 3.5 mg/dL	3.0 (1.0 to 9.2)	.049
Diabetes mellitus	4.4 (1.3 to 14.4)	.01
Prior hemodialysis > 7 mo	4.7 (1.4 to 13.9)	.01
Parathyroid hormone ≤ 35 ng/L	12.9 (2.8 to 59.5)	.001
Serum calcium < 8.5 mg/dL	12.7 (2.5 to 64.9)	.002
Serum trigelyceride < 130 mg/dL	5.1 (1.4 to 18.2)	.01
No ACE inhibitor	6.4 (1.8 to 22.0)	.003

Serum albumin and NPCR were among predictors of mortality in our patients. In about 80% of the patients, NPCR was less than the standard, which shows most of them suffering from malnutrition. Hypoalbuminemia (< 3.5 mg/dL) was also frequent in about 40% of the patient. In multivariate analysis, there was correlation between hypoalbuminemia and mortality. Low serum albumin may reflect the poor nutritional status of the patients. Several studies have shown that low serum albumin is a predictor of mortality.[7,11-13] Especial concern should be applied to nutrition of these patients, which could be associated with decrease in mortality rate of these patients. Total creatinine clearance (80.4 L/wk/1.73 m^2) and total Kt/V (2.1) were approximate to the recommended doses. Peritoneal equilibrium tests results showed that most of the patients were among high and high average groups. This study did not show any association between solute transport and mortality, which is consistent with the study of Paniagua and colleagues.[8]

The RRF had a significant correlation with patient survival which has been confirmed in many studies. In fact, preservation of RRF is associated with a survival benefit and decrease in morbidity.[14,15] It is necessary to work on strategies which preserve RRF. Peritonitis was the most common cause of PD termination in 37% of alive patients. In fact, peritonitis rate was high in our patients which has been decreased recently by new systems and paying more attention to patient education. Among laboratory findings, parathyroid hormone was an independent predictor of patient survival. Mortality of the patients with lower parathyroid hormone levels was higher. We speculate that a low parathyroid hormone level may be a sign of adynamic bone disease and a higher risk of cardiovascular diseases and mortality.[17] In this study, serum total calcium (not ionized calcium) was measured, and low serum calcium could be related to low serum albumin and increased mortality. Low serum triglyceride concentration was also associated with higher mortality. We could not explain this association, although low serum triglyceride can reflect the poor nutritional status of these patients.

CONCLUSIONS

We found that older age, presence of diabetes mellitus, low serum albumin, calcium, triglyceride, and intact parathyroid hormone levels, and the use of ACE inhibitors independently predicted mortality of patients on CAPD during an 18-month follow-up period. In conclusion, this study suggests that good patient selection, prevention of peritonitis episodes, treatment of comorbidities, and improving nutritional status decrease morbidity and mortality of patients on CAPD.

CONFLICT OF INTEREST

None declared.

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