

Enrollment Fluid Status Is Independently Associated with Long-Term Survival of Peritoneal Dialysis Patients

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Fluid overload is a common complication in peritoneal dialysis (PD) patients. The prognostic importance of enrollment fluid status in long-term PD patients remains to be investigated. The objective of the present study was to investigate the prognostic importance of enrollment fluid status in the long-term survival of PD patients. We enrolled 53 PD patients (mean age: 53 years) from November 2000 to February 2006. On enrollment, demographic, clinical, and biochemical data were recorded. Bioelectrical impedance analysis (BIA) was used to determine the fluid status of PD patients, including extracellular water (ECW), intracellular water (ICW), and total body water (TBW). Fluid status was corrected for body surface area (BSA): ECW–BSA, ICW–BSA, and TBW–BSA respectively. Patients were followed to January 2008. The ECW–BSA correlated negatively with albumin, a marker of nutrition ($r = -0.53$, $p < 0.0001$). The ICW/ECW ratio ($r = 0.36$, $p = 0.018$) correlated directly and the ECW/TBW ratio ($r = -0.36$, $p = 0.019$) correlated negatively with creatinine. Patients who survived during the study period had a significantly lower ECW–BSA (8.29 L/m^2 vs. 9.91 L/m^2 , $p = 0.001$) than did those who did not survive. Patients with enrollment ECW–BSA below 9 L/m^2 had a significantly better 7-year cumulative survival (Kaplan–Meier) than did patients with a ECW–BSA of 9 L/m^2 or more ($p = 0.019$). Using multivariate Cox regression analysis, adjusting for age, race, diabetes, human immunodeficiency virus (HIV) status, and months on dialysis at enrollment, ECW–BSA was a significant independent predictor of mortality (relative risk: 1.50; $p = 0.03$). In conclusion, ECW–BSA was a significant independent predictor of long-term survival in PD patients.

Key words

Extracellular water, intracellular water, bioimpedance analysis, mortality

Introduction

Despite improvements in dialysis technology and survival rate over the past decade, the current mortality rate of peritoneal dialysis (PD) patients remains high. According to the 2007 report from the U.S. Renal Data System, the annual mortality for PD patients was 179 per 1000 patient–years (1). Identification of various risk factors and aggressive risk factor modification are important strategies to improve outcomes in these patients. The clinical outcome of PD patients is influenced by many factors—among them, age, race, diabetes status, nutrition status, solute transport status, adequacy, and the presence of inflammation and other comorbid conditions (2–6).

Fluid overload is a common complication in PD patients, and particularly in long-term PD patients (7). In PD patients, fluid status has been reported to be significantly related to diastolic blood pressure (DBP) and eccentric left ventricular hypertrophy (LVH) (8). Fluid overload is closely associated with the development of hypertension in these patients (9). Malnutrition is a strong risk factor for mortality in PD patients (10). Improved fluid status is associated with improvement in nutrition status, and deterioration in fluid status is associated with the development of malnutrition (11). Fluid overload may be an important factor contributing to high mortality in PD patients.

Previous studies showed that, in PD patients, total sodium and fluid removal was a predictor of 3-year survival (12) and baseline ultrafiltration was a significant predictor of 2-year survival (13). The prognostic importance of enrollment fluid status (such as extracellular fluid) in long-term PD patients has not been investigated. Bioelectrical impedance analysis (BIA)

has been well established as a method of measuring body composition and fluid status in PD patients (14,15). In the present study, we used BIA to examine the relationship of enrollment fluid status to long-term survival of PD patients followed for 7 years.

Patients and methods

Our study enrolled 53 PD patients (mean age: 53 years; 53% women; 68% African American) treated at the Avram Center for Kidney Diseases in the Long Island College Hospital from November 2000 to February 2006. Demographic, clinical, and biochemical data were recorded on enrollment. Patients were followed to January 2008.

The BIA measurements were conducted using an impedance plethysmograph (800 mA, 50 kHz). Electrical impedance, resistance, and reactance were measured for the study patients, and body composition parameters, including fluid status [extracellular water (ECW), intracellular water (ICW), total body water (TBW)] were determined using Cyprus version 1.0 (BIA-101: RJL/Akern Systems, Clinton Township, MI, U.S.A.). Fluid status values were normalized to body surface area (BSA), which was derived from body weight and height using standard equations.

Statistical analysis

Continuous variables are reported as mean \pm standard deviation. Correlations are reported either as a Pearson correlation coefficient or a Spearman rank correlation coefficient. Observed survival was computed by the Kaplan–Meier method. Independent predictors of survival were determined by Cox regression analysis. Calculations were performed using SPSS for Windows, version 12.0.1 (SPSS, Chicago, IL, U.S.A.).

Results

At enrollment, mean ECW–BSA was 9.21 ± 1.57 L/m² (range: 6.48–14 L/m²), ICW–BSA was 12.0 ± 2.11 L/m² (range: 8.58–17.6 L/m²), TBW–BSA was 21.2 ± 2.74 L/m² (range: 17.1–30 L/m²), and albumin and creatinine were 3.77 ± 0.61 g/dL (range: 2.1–5.3 g/dL) and 12 ± 4 mg/dL (range: 2.6–20.5 mg/dL) respectively.

Table I shows the relationship of age and markers of nutrition with fluid status and fluid distribution index. Age correlated negatively with ICW–BSA ($r = -0.28$, $p = 0.04$) and ICW/ECW ratio ($r = -0.39$, $p = 0.004$), and positively with ECW/TBW ratio ($r = 0.39$, $p = 0.004$). Serum albumin correlated negatively with ECW–BSA ($r = -0.53$, $p < 0.0001$) and ECW/TBW ratio ($r = -0.43$, $p = 0.004$), and positively with ICW/ECW ratio ($r = 0.40$, $p = 0.007$). Serum creatinine correlated directly with ICW/ECW ratio ($r = 0.36$, $p = 0.018$) and negatively with ECW/TBW ratio ($r = -0.36$, $p = 0.019$). During the study period 21 patients (40%) died. The patients who survived during the study period had a significantly lower ECW–BSA than did those who did not survive (8.29 L/m² vs. 9.91 L/m², $p = 0.001$). Patients were allocated to one of two groups based on ECW–BSA value: less than 9 L/m² or 9 L/m² or more. After more than 7 years of observation, the cumulative observed survival of PD patients with an enrollment ECW–BSA below 9 L/m² was significantly better than that of patients with an ECW–BSA of 9 L/m² or more ($p = 0.019$, Figure 1).

Independent predictors of patient survival were determined using a multivariate Cox regression analysis that adjusts for other variables known to influence survival. In this model, ECW–BSA (relative risk: 1.50; $p = 0.03$) and months on dialysis at enrollment (relative risk: 1.014; $p = 0.011$) were significant independent

TABLE I Correlations of age and markers of nutrition with fluid status in peritoneal dialysis patients

Variable	Age (years)		Albumin (g/dL)		Creatinine (mg/dL)	
	r Value	p Value	r Value	p Value	r Value	p Value
ECW–BSA (L/m ²)	0.09	0.54	-0.53	<0.0001	0.06	0.70
ICW–BSA (L/m ²)	-0.28	0.04	0.08	0.60	0.24	0.11
TBW–BSA (L/m ²)	-0.17	0.23	-0.24	0.11	0.22	0.14
ECW/TBW	0.39	0.004	-0.43	0.004	-0.36	0.019
ICW/ECW	-0.39	0.004	0.40	0.007	0.36	0.018

ECW–BSA = extracellular water volume normalized for body surface area in square meters; ICW–BSA = intracellular water volume normalized for body surface area in square meters; TBW–BSA = total body water volume normalized for body surface area in square meters.

predictors of mortality risk. For every liter increase in ECW–BSA at enrollment, mortality risk increased by 50% (Table II).

Discussion

The major finding in our study was that the volume of ECW determined by BIA at enrollment, corrected for BSA (ECW–BSA), was a significant independent predictor of all-cause mortality in long-term PD patients. Interestingly, in our study, the values obtained by BIA for ECW (16.8 L vs. 18.3 L by the deuterium method and 16.2 L by multi-frequency BIA), ECW–BSA (9.21 L/m² vs. 9.4 L/m² by the deuterium method), and TBW

(38.9 L vs. 38.3 L by the deuterium method) are very close to those reported by other authors (16,17). Higher levels of ECW–BSA at enrollment were associated with increased all-cause mortality in our PD patients followed for more than 7 years. We are not aware of any other published report in the literature concerning the association of enrollment ECW volume with long-term (7-year) survival in PD patients. We obtained similar results with enrollment ECW not normalized to BSA (data not shown).

The literature contains few published reports regarding the effect of volume status on outcome in PD patients. Fluid status has been reported to be significantly related to DBP and LVH in PD patients (8). Ates *et al.* (12) reported that removal of sodium and fluid is a predictor of mortality in PD patients followed for 3 years. According to a 2-year European multicenter prospective outcome study, baseline ultrafiltration was significantly associated with survival in PD patients (13). Recently, body fluid distribution assessed by the extracellular-to-intracellular fluid ratio has been reported to be an independent predictor of 3-year survival in PD patients (18).

Another important observation in the present study was the presence of significant correlations between serum albumin, creatinine, and fluid status values and fluid distribution index in PD patients (Table I). Inverse correlation of albumin with ECW–BSA and ECW/TBW ratio may indicate dilutional hypoalbuminemia from extracellular volume expansion or increased albumin concentration from extracellular volume decrease. Hypoalbuminemia may also result from a poor nutrition status in PD patients.

Association between fluid status and nutrition status has been reported in PD patients (11). Serum creatinine is an indicator of somatic protein status. The ICW volume reflects water content in the body

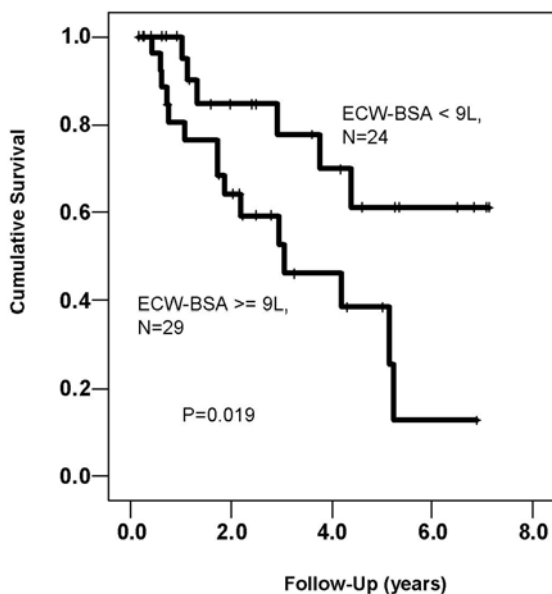


FIGURE 1 Observed survival by extracellular water volume normalized for body surface area (ECW–BSA) in peritoneal dialysis patients at enrollment.

TABLE II Independent predictors of mortality in peritoneal dialysis patients by multivariate Cox regression analysis

Variable	Relative risk	p Value
Age in years	1.03	0.20
Race (African American vs. others)	1.04	0.97
Diabetes (with vs. without)	1.79	0.36
HIV positivity (yes vs. no)	4.39	0.04
Months on dialysis at enrollment	1.014	0.01
ECW–BSA	1.50	0.03

ECW–BSA = extracellular water volume in liters normalized for body surface area in square meters.

cell mass (19). A decreased ICW may indicate loss of intracellular proteins caused by protein–energy malnutrition. Negative correlation of serum creatinine with ECW/TBW ratio and positive correlation with ICW/ECW ratio further confirm the association between nutrition status and fluid status in PD patients.

Our data agree with a previously published report that the ECW/TBW ratio is inversely correlated with albumin and creatinine, markers of nutrition (11). We and others have previously reported the importance of the nutrition markers albumin and creatinine as predictors of mortality in PD patients (2,6,10).

Conclusions

Our study showed that enrollment ECW–BSA volume is a strong independent predictor of 7-year survival in PD patients. Our study demonstrates the prognostic importance of ECW determined by the BIA method in long-term PD patients. Markers of nutrition are associated with fluid status in PD patients. Further studies need to be done to determine whether interventions to improve fluid status will increase survival in these patients.

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