Tohoku J. Exp. Med., 2014, **233**, 295-300

Residual Urinary Volume Is a Predictor of Overhydration in Patients on Peritoneal Dialysis

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Fluid overload is linked to hypertension and cardiovascular diseases in patients on peritoneal dialysis (PD). It is important to monitor the residual urinary volume in patients with end-stage renal disease (ESRD). In fact, fluid overload and residual urinary volume have been considered the risk factors of mortality in ESRD patients on PD. However, the relationship between residual urinary volume and fluid overload was still controversial. Therefore, the objective of this cross-sectional study was to evaluate the association between residual urinary volume and the volume status of PD patients. Body composition was measured using a portable multifrequency whole-body bioimpedance assessment. Relative overhydration was defined when the ratio of overhydration to extracellular water was > 0.15. We examined 75 patients, with a mean age of 50.7 years and mean body mass index of 23.5 kg/m^2. Dialysis vintage was 46.5 months. The patients were divided into the anuric group (n = 30; urine output ≤ 100 mL/day) and the group of urine output > 100 mL/day (n = 45). The anuric group showed higher degree of relative overhydration compared to the patients with the urine output of > 100 mL/day (p = 0.020). In a multivariable linear regression analysis, anuria, diabetes, and serum albumin level were independently associated with relative overhydration. In conclusion, volume status should be closely monitored in anuric patients, and the preservation of residual urinary volume is one of important goals to maintain volume status in PD patients.

Keywords: bioelectrical impedance; body composition; body fluid; peritoneal dialysis; residual urinary volume
Tohoku J. Exp. Med., 2014 August, **233** (4), 295-300.

Introduction

Fluid status and volume homeostasis are important in patients on peritoneal dialysis (PD) since fluid overload has been linked to mortality in patients on this dialysis modality (Wizemann et al. 2009; Paniagua et al. 2010; Van Biesen et al. 2011). Close attention to volume status management facilitates blood pressure control and stabilization of left ventricular mass in long-term dialysis patients (Gunal et al. 2003; Hiramatsu et al. 2007). However, the assessment of volume status is relatively crude and lacks a reliable objective tool. Clinical assessments include absence of edema and good blood pressure control. The various objective methods are cardiothoracic ratio, assessment of jugular venous pressure, inferior vena cava (IVC) diameter, and biomarkers such as brain/atrial natriuretic peptide or N-terminal prohormone of brain natriuretic peptide (Woodrow and Ronco 2012). Direct measurement of extracellular water (ECW) and total body water (TBW) by dilution methods is the gold standard method, but these techniques are laborious and expensive (Woodrow 2007). Multifrequency bioimpedance is a different method to assess body composition and volume status (Cox-Reijven et al. 2001). The Body Composition Monitor (BCM) is a noninvasive, easy, and relatively inexpensive method and has recently been validated (Moissl et al. 2006; Wabel et al. 2009; Devolder et al. 2010; Van Biesen et al. 2011).

The development of fluid overload in PD patients has multifactorial causes, such as excessive salt and fluid intake, cardiac disease, insufficient use of hypertonic exchange, and membrane failure. Residual renal function is a powerful predictor of outcome in PD patients (Bargman et al. 2001), and is usually considered to play an important role in maintaining fluid balance (Venkataraman and Nolph 2000; Pecoits-Filho et al. 2004). However, Cheng et al. (2006) showed that residual renal function may be not as important as expected in maintaining good volume status. Moreover, other studies have reported that ECW expansion is associated with reduced urine output (UO) (Davenport et al. 2011b). Therefore, the objective of the present study

Received April 1, 2014; revised and accepted July 15, 2014. Published online August 22, 2014; doi: 10.1620/tjem.233.295.
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was to evaluate the association between residual urinary volume and the volume status of PD patients.

Methods

Subjects

We performed a cross-sectional, observational, single-center study in patients with PD. All stable patients undergoing PD for at least 3 months were screened for eligibility. Patients were excluded if they had an implanted electronic medical device, any kind of metal implant or artificial joints, amputations, were pregnant, or were in a period of lactation. A total of 75 patients were enrolled in the study.

All patients provided written informed consent, and the study protocol was approved by the ethics committee of the institutional review board of Gachon University Gil Medical Center.

Methods

Baseline information at enrollment included age, sex, height, weight, the cause of end-stage renal disease (ESRD), and dialysis information. Blood pressure was measured at the hospital when the patients visited hospital for measuring body composition. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Biochemical parameters were measured using standard laboratory techniques, and included blood urea nitrogen (BUN), creatinine, albumin, alkaline phosphatase, and total cholesterol.

Body composition was measured by a portable multifrequency whole-body bioimpedance assessment using the BCM (Fresenius Medical Care, Bad Hombug, Germany). Electrodes were attached to one hand and one foot on the same side, after the patient had been in the recumbent position for at least 5 minutes. The patient cable was then connected. After measurements, data such as overhydration (OH), ECW, intracellular water (ICW), and TBW were determined. BCM assessments were performed with a full abdomen. Relative OH (ROH) was defined when the ratio of OH to ECW was > 0.15 (Wizemann et al. 2009).

The daily glucose exposure was calculated as the product of the volume and the glucose concentration for all the daily exchanges. For example, for an individual who was using 4 × 2 L exchanges (2 × 1.36%, and 2 × 2.27%), there would be 54.4 + 90.8 = 145.2 g of glucose per day.

Modified peritoneal equilibration test (PET) using a 3.86% glucose solution was performed, and the dialysate-to-plasma ratio for creatinine was calculated. Renal and peritoneal Kt/V values were calculated using urea clearances from a 24-hour collection of urine and dialysate effluent. Urea distribution volume was calculated using the Watson equation (Watson et al. 1980). Total Kt/V was calculated as the sum of renal and peritoneal Kt/V. Glomerular filtration rate was calculated as the average of 24-hour urinary creatinine clearance and urea clearance (Nolph et al. 1993), and was normalized for body surface area obtained by the Du Bois and Du Bois equation (Du Bois and Du Bois 1989).

Statistical analysis

Continuous variables were expressed as the mean and standard deviation for the number of observations, and categorical variables were expressed as numbers with percentages. Categorical variables were compared with the χ^2 test or Fisher's exact test, and continuous variables were compared with a Student's *t*-test. Univariate regression was performed to determine correlations between ROH and other variables. A multivariate linear regression analysis was performed with ROH as the target variable, to identify factors that were independently associated with OH. Variables were selected for entry in the model selection procedure either because of a univariate regression results of $p < 0.05$ or biological plausibility. Values of $p < 0.05$ were considered statistically significant. The data analysis was conducted using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Demographic data of the study population are shown in Table 1. Of the 75 patients, mean age was 50.7 ± 13.0 years, 67% were male, and mean BMI was 23.5 ± 3.5 kg/m^2. Dialysis vintage was 46.5 ± 37.9 (median; 38.0) months. The causes of ESRD were diabetes in 30 patients (40%), which was followed by glomerulonephritis in 14 (19%), hypertension in 5 (7%), renal tuberculosis in 1 (1%), and unknown causes in 25 (33%). The frequencies of anuric patients according to the causes of ESRD were 11 patients (37%) with diabetes, 6 (43%) with glomerulonephritis, 1 (20%) with hypertension, 1 (100%) with renal tuberculosis and 11 (44%) with unknown causes.

The patients were divided into two groups based on residual urinary volume: the anuric group with UO ≤ 100 mL/day, and the group with UO > 100 mL/day. There were 30 (40%) and 45 (60%) patients in the anuric group and the UO > 100 mL/day group, respectively. Comparisons of various parameters between the groups are shown in Table 2. The anuric group had a greater ultrafiltration volume and less residual urinary volume and residual renal function, compared to the patients with UO > 100 mL/day. The anuric group also had a higher creatinine level and glucose exposure level than the UO > 100 mL/day group. Systolic and diastolic blood pressure did not differ between the groups, but the anuric group took more numbers of antihypertensive medications. Between the groups, age, sex, BMI, and albumin did not differ significantly.

A comparison of bioimpedance parameters between

Table 1. Demographic characteristics of the study populations.

Variable	Mean ± S.D. (n = 75)
Age (years)	50.7 ± 13.0
Sex (n, %)	
Male	50 (67%)
Female	25 (33%)
Body mass index (kg/m^2)	23.5 ± 3.5
Dialysis vintage (months)	46.5 ± 37.9
The causes of end-stage renal disease (n, %)	
Diabetes	30 (40%)
Glomerulonephritis	14 (19%)
Hypertension	5 (7%)
Renal tuberculosis	1 (1%)
Unknown	25 (33%)

Table 2. Baseline characteristics according to residual urinary volume.

	Total (n = 75)	UO > 100 mL/day (n = 45)	Anuria (n = 30)	P
Age (years)	50.7 ± 13.0	52.0 ± 14.0	48.6 ± 11.3	0.269
Sex (Male)	50 (67%)	29 (64%)	21 (70%)	0.803
Body mass index (kg/m^2)	23.5 ± 3.5	23.6 ± 3.3	23.4 ± 4.0	0.803
Diabetes (n, %)	32 (43%)	19 (42%)	13 (43%)	1.000
Systolic blood pressure (mmHg)	141.4 ± 21.0	142.4 ± 18.6	140.0 ± 24.5	0.633
Diastolic blood pressure (mmHg)	77.8 ± 12.0	78.3 ± 10.6	77.2 ± 14.0	0.694
Numbers of antihypertensive medications	4.8 ± 3.1	4.2 ± 2.8	5.7 ± 3.4	0.049
Diuretics (n, %)	38 (51%)	29 (64%)	9 (30%)	0.005
Cardiothoracic ratio (%)	47.7 ± 6.2	46.6 ± 5.6	49.5 ± 6.7	0.052
Albumin (g/dL)	3.6 ± 0.4	3.7 ± 0.4	3.6 ± 0.4	0.241
Alkaline phosphatase (U/L)	106.8 ± 78.8	103.6 ± 86.1	111.4 ± 67.7	0.678
Blood urea nitrogen (mg/dL)	55.0 ± 17.9	53.7 ± 19.9	56.9 ± 14.6	0.458
Creatinine (mg/dL)	10.8 ± 3.9	9.7 ± 3.8	12.6 ± 3.4	0.001
Total cholesterol (mg/dL)	165.5 ± 30.7	163.5 ± 27.1	168.4 ± 35.6	0.503
PD modality (n, %)				0.879
Continuous ambulatory PD	67 (89%)	40 (89%)	27 (90%)	
Continuous cycling PD	8 (11%)	5 (11%)	3 (10%)	
Icodextrin (n, %)	14 (19%)	7 (16%)	7 (23%)	0.546
Glucose exposure (g/day)	140.3 ± 38.4	128.1 ± 22.6	161.6 ± 47.0	< 0.001
Transporter (n, %)				0.916
Fast	9 (12%)	6 (13%)	3 (10%)	
Fast average	25 (33%)	16 (36%)	9 (30%)	
Slow average	36 (48%)	20 (44%)	16 (53.3%)	
Slow	5 (7%)	3 (7%)	2 (6.7%)	
D/P Creatinine	0.64 ± 0.12	0.64 ± 0.11	0.65 ± 0.13	0.555
Ultrafiltration (mL/day)	1,239 ± 846	924 ± 675	1,713 ± 865	< 0.001
Total weekly urea clearance (Kt/V)	2.14 ± 0.54	2.31 ± 0.55	1.88 ± 0.41	< 0.001
Residual urinary volume (mL/day)	438.1 ± 498.1	725.8 ± 453.0	6.7 ± 25.4	< 0.001
Residual renal function (mL/min/1.73 m^2)	1.59 ± 1.95	2.66 ± 1.88	0.02 ± 0.07	< 0.001
Bioimpedance parameters				
Absolute OH (L)	2.5 ± 2.1	1.9 ± 0.6	3.3 ± 2.5	0.006
Relative OH	0.138 ± 0.102	0.115 ± 0.091	0.173 ± 0.108	0.020
Total body water (L)	37.4 ± 7.7	36.4 ± 7.7	38.8 ± 7.7	0.189
ECW (L)	17.3 ± 3.2	16.7 ± 2.8	18.2 ± 3.7	0.050
ICW (L)	20.1 ± 5.0	19.7 ± 5.4	20.6 ± 4.5	0.447
ECW/ICW	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.580
Lean tissue mass (kg)	42.2 ± 11.9	39.8 ±11.4	45.6 ± 11.9	0.046

PD, peritoneal dialysis; D/P, dialysate-to-plasma ratio; OH, overhydration; ECW, extracellular water; ICW, intracellular water.

the anuric and UO > 100 mL/day groups is shown in Table 2. The anuric group had higher ROH than the UO > 100 mL/day group (0.173 ± 0.108 vs. 0.115 ± 0.091, p = 0.020) (Fig. 1).

The univariate analysis showed that there was a positive relationship between ROH and each of diabetes, anuria, ECW, and ECW/ICW. There was a negative correlation between ROH and serum albumin. There was no association between residual renal function and ROH (Table 3). In the multivariable linear regression analysis, anuria (β coefficient = 0.207, p = 0.033), diabetes (β coefficient = 0.215, p = 0.026), and serum albumin level (β coefficient = −0.535, p < 0.001) were independently significant parameters associating with ROH (Table 4).

Discussion

We demonstrated that residual urinary volume in PD patients was inversely related with ROH, which represented hydration status as well as the extent of edema. Anuric patients had higher degree of volume overload than the

patients with UO > 100 mL/day. We also showed that diabetes and hypoalbuminemia were associated with volume overload. ROH was measured by multifrequency bioimpedance, a simple, safe, and inexpensive method to measure different water compartments of the human body.

We showed that residual urinary volume was associated with volume OH. A recent study also demonstrated that ECW expansion is associated with reduced UO (Davenport et al. 2011b). Our data are in agreement with that study, although the parameters of volume index were different. Hypervolemia is prevalent in PD patients, and PD patients with residual renal function have an advantage in reaching fluid balance because residual renal function contributes to fluid and sodium removal. However, Cheng et al. (2006) reported that residual renal function and residual urinary volume are not as important as expected in maintaining good volume status. These results might be due to the health belief among patients with higher residual renal function that they could be more liberal with salt and fluid intake. Davies et al. (2003) observed that residual renal function tends to be better preserved in patients with better volume homeostasis who are receiving icodextrin as compared with hypervolemic patients receiving hypertonic glucose. Their study suggests that hypervolumic status per se is not protective of long-term preservation of residual renal function. On the contrary, Konings et al. (2003) showed that patients with a reduction in extracellular volumes associated with icodextrin have a faster decrease in their UO and residual renal function. However, in their study, the patients were euvolemic, and the baseline levels of residual renal function were substantially higher than those in the study of Davies et al. (2003).

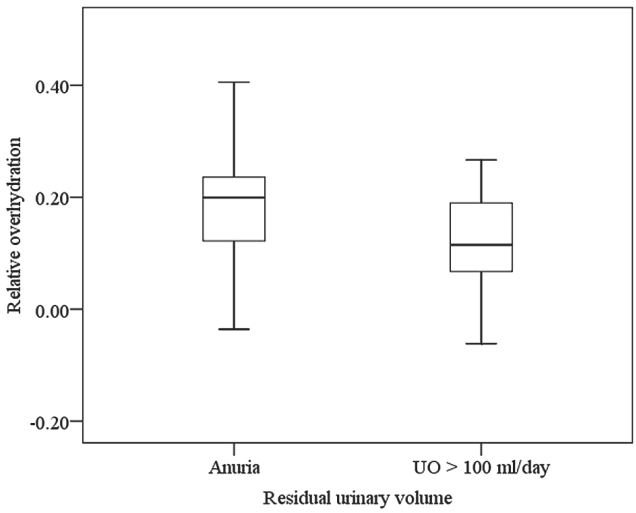

Fig. 1. Relationship between residual urinary volume and relative overhydration (ROH). The anuric group had more ROH than the UO > 100 mL/day group ($p = 0.020$).

We found that diabetes was associated with fluid overload. Diabetic dialysis patients have greater interdialytic weight gain than nondiabetic hemodialysis patients (Davenport 2009) and diabetic PD patients have more fluid

Table 3. Association of relative overhydration with clinical variables by univariate linear regression analyses.

Variables	Standardized coefficients	*P*
Age (years)	−0.020	0.866
Sex (Male)	−0.037	0.756
Body mass index (kg/m^2)	−0.204	0.079
Diabetes	0.236	0.041
Systolic blood pressure (mmHg)	0.057	0.630
Diuretics	−0.082	0.483
Albumin (g/dL)	−0.56	< 0.001
Creatinine (mg/dL)	−0.184	0.114
Total cholesterol (mg/dL)	−0.085	0.466
Anuria (≤ 100 mL/day)	0.269	0.020
Residual renal function (mL/min/1.73 m^2)	−0.177	0.131
Use of icodextrin	0.017	0.888
D/P Creatinine	0.152	0.195
Ultrafiltration (mL/day)	0.154	0.186
Total Kt/V	−0.001	0.994
Total body water (L)	−0.055	0.638
ECW (L)	0.307	0.007
ECW/ICW	0.744	< 0.001
Lean tissue mass (kg)	−0.087	0.479
Fat (kg)	−0.068	0.592

D/P, dialysate-to-plasma ratio; ECW, extracellular water; ICW, intracellular water.

Table 4. Association of relative overhydration with clinical variables by multiple linear regression analyses.

Variables	β coefficient	t	P
Age (years)	−0.007	−0.073	0.942
Male	−0.031	−0.334	0.739
Diabetes	0.215	2.277	0.026
Systolic blood pressure (mmHg)	0.161	1.659	0.102
Anuria (≤ 100 mL/day)	0.207	2.182	0.033
Albumin (g/dL)	−0.535	−5.682	< 0.001

overload than nondiabetic patients (Watson et al. 1980; Higgins et al. 1989; Van Biesen et al. 2011). Diabetic patients have also increased thirst (Davies 2003). The higher blood sugar levels in diabetic patients could lead to reduced net ultrafiltration by reducing the peritoneal to blood glucose osmotic gradient, with consequent increased reliance on PD solutions with higher glucose content (Konings et al. 2003). Restricting salt and water intake may help reduce the use of hypertonic glucose solution and thus facilitate blood glucose control in diabetic patients undergoing PD (Watson et al. 1980). Insulin therapy per se may potentially lead to increased food and sodium intake by increasing carbohydrate intake.

We showed that albumin was related to fluid status. Previous studies have revealed that there is a negative correlation between albumin and OH (Davison et al. 2009; Davenport et al. 2011a; Van Biesen et al. 2011). Lower albumin levels may result from extracellular dilution in OH status. Cigarran et al. (2007) found that a decrease of 0.1 g/dL in serum albumin was associated with a 330-mL increase in ECW. However, it is impossible to determine whether low albumin is a consequence or a cause of OH. Hypoalbuminemia may be caused by chronic inflammation and malnutrition. The patients with hypoalbuminemia should alert the clinician to potential overload.

Although multiple factors play a role in hypertension, it has been well known that hypertension is associated with fluid overload in dialysis patients (Wizemann et al. 2009). The use of OH provided by BCM improved the results of volume control and hypertension management in PD patients (Luo et al. 2011). However, there was no relationship between fluid status and blood pressure in our study. The reason was because the anuric group took more numbers of antihypertensive medications than the UO > 100 mL/day group. In addition, the anuric group had a greater ultrafiltration volume than the UO > 100 mL/day group, but the anuric group was exposed to significantly more hypertonic glucose than the UO > 100 mL/day group.

The limitation of our study is that it is a modest-sized and observational study, making it impossible to draw conclusions regarding cause and effect in the statistical associations observed. Second, BCM was performed once with each patient in our study. Repeated measurement of BCM might be helpful to minimize in-patient or inter-patient variation.

In conclusion, anuria, low serum albumin levels and diabetes were independently associated with OH, as determined by bioelectric impedance analysis in patients on PD. The prevention of fluid overload in dialysis patients, which is linked to hypertension and cardiovascular disease, should be a major goal. We propose that volume status should be closely monitored in anuric PD patients and the preservation of residual urinary volume is important to maintain volume status in PD patients.

Acknowledgments

This work was supported by intramural grant of Gachon University Gil Medical Center for 2011.

Conflict of Interest

The authors declare no conflict of interest.

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