

Brain Natriuretic Peptide and Impedance Cardiography to Assess Volume Status in Peritoneal Dialysis Patients

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Assessment of volume status in patients with end-stage renal disease has long been a problem. Objective tools for estimating dry weight are necessary. The present study was designed to determine if better assessment of volume status could be achieved by measuring brain natriuretic peptide (BNP) and thoracic fluid content (TFC) by bioimpedance.

We prospectively surveyed 51 medically stable peritoneal dialysis (PD) patients during their routine visits to our PD facility. There were no exclusion criteria. Clinical volume status was assessed by the attending nephrologist as hypovolemic, euvolemic, or hypervolemic. Once the clinical assessment was complete, plasma BNP concentration was measured. The TFC was determined by bioimpedance cardiography measured in the supine position.

Of 51 patients, 19 (37.3%) were considered hypervolemic, 30 (58.8%) euvolemic, and 3 (5.9%) hypovolemic by clinical assessment. As defined by systolic blood pressure ≥ 130 mmHg or diastolic pressure ≥ 80 mmHg (or both), 57% were hypertensive. The hypovolemic group was excluded from the statistical analysis because of the small sample size. Logistic regression analysis did not show a significant correlation between clinical assessment of volume and BNP ($p = 0.76$) or TFC ($p = 0.39$).

Our data demonstrate the limitations of BNP and thoracic impedance in helping with the clinical evaluation of volume status in a cohort of chronic PD patients.

Key words

BNP, cardiac impedance, CAPD, hypertension, hemodynamics

Introduction

According to the U.S. Renal Data System 2006 annual report, cardiovascular disease and cerebrovascular accidents are the most prevalent causes of morbidity and mortality in dialysis patients (1). Hypertension, which is commonly observed in dialysis patients, is a major risk factor for the foregoing conditions (2–5). Studies in the past have suggested that at least 80% of all hypertension in dialysis patients is attributable to chronic hypervolemia (3).

Hypertension is common in peritoneal dialysis (PD) patients. Some studies have suggested that PD patients tend to have chronic fluid overload that is responsible in part for poor blood pressure (BP) control. This situation is particularly true for continuous ambulatory PD (CAPD) patients as duration of therapy increases, with accompanying declines in residual renal function and permeability changes in the peritoneal membrane (4,5). Appropriate volume control has been found to be critically important for the achievement of adequate BP control in PD patients (3).

One of the challenges faced by nephrologists caring for end-stage renal disease patients is the clinical assessment of volume (CAV). Most PD treatments incorporate a prescription for fluid removal targeted to the patient's dry weight, which is clinically estimated. Clinical assessment of dry weight is inexact because of the difficulty of determining the actual hydration status of an individual patient (4,5). Chronic fluid overload, which is frequently found in PD patients, is associated with poor BP control, left ventricular hypertrophy, and cardiac dysfunction, all of which are independent predictors of cardiovascular

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mortality (2–5). Conversely, hypovolemic patients may suffer from symptoms of volume depletion that may result in decreases in BP and negative effects on residual renal function.

Several different techniques have been used to derive a more accurate method of assessing dry weight, but none of those techniques is generally accepted and used. The purpose of the present study was to evaluate the use of brain natriuretic peptide (BNP) levels and thoracic fluid content (TFC) measured by means of cardiac bioimpedance (ICG), to help in the assessment of volume status in a cohort of patients maintained on long-term PD therapy.

Patients and methods

New Haven CAPD is a free standing PD unit located in an urban area. The organization and structure of the unit have been described previously (6).

All of the patients from the New Haven CAPD unit were invited to participate in the present study. Medically stable patients who had been on PD for at least 3 months and who had not experienced acute medical problems in the preceding 4 weeks were eligible. Approximately 75% of those invited agreed to take part in the investigation. Between January and April of 2005, we prospectively surveyed 51 adults on continuous cycling PD. The protocol conformed to the ethical guidelines of our institution.

All patients were studied during their routine monthly visit to the CAPD unit. Volume status was clinically evaluated by the attending nephrologist as hypovolemic, euvolemic, or hypervolemic based on clinical data derived from the patient's interview and physical examination. Each patient's medications, anthropometric and hemodynamic data, dialysis prescription, and cardiovascular risk factors were noted and recorded.

Once the clinical assessment was complete, blood samples for BNP were collected in tubes containing ethylenediamine tetraacetic acid. Blood was drawn with the patient in the semi-recumbent position. Plasma concentrations of BNP were determined by AxSYM BNP radioimmunoassay (Abbott Laboratories, Abbott Park, IL, U.S.A.).

The ICG data was obtained by a trained nurse using the BioZ ICG Monitor (CardioDynamics, San Diego, CA, U.S.A.). This equipment uses four dual electrodes applied to opposite sides of the neck at a level between the ears and clavicles and another two on either side of the chest following the mid-axillary

line at the level of the xiphoid process. The ICG data was collected with the patient in the supine position, having rested for 5 minutes before measurement. Because TFC can detect intravascular and extravascular fluid changes, the ICG-derived TFC was used to evaluate volume status (7).

Statistical analyses were performed using the Stata 8.2 statistical computer program (StataCorp LP, College Station, TX, U.S.A.). Results are expressed as mean \pm standard deviation. Relationships between numeric variables were assessed by the Pearson correlation coefficient, and categorical variables by the Spearman rank correlation. Logistic regression analysis was used to calculate odds ratios and to examine the probability that BNP and TFC could impact the CAV. Multiple regression analysis was used to evaluate the combined influence of plasma BNP concentrations and cardiac impedance parameters on the CAV. Values of $p < 0.05$ were considered statistically significant. Agreement of the CAV with BNP and TFC was reviewed by the receiver operating characteristic (ROC) curve.

Results

Table I shows the demographic, anthropometric, and hemodynamic characteristics of the study population. Of the 51 patients, 19 (37.3%) were considered hypervolemic, 30 (58.8%) euvolemic, and 3 (5.9%) hypovolemic by clinical assessment. The hypovolemic group was excluded from the statistical analysis because of the small sample size.

Hypertension was defined as a systolic BP (SBP) \geq 130 mmHg or diastolic BP (DBP) \geq 80 mmHg (or both). The current Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease suggest a BP target of less than 130/80 mmHg in chronic kidney disease patients. In our study population, 57% of the patients were hypertensive.

Mean BNP was 477.4 ± 732.1 pg/mL in the euvolemic group as compared with 665.2 ± 992.1 pg/mL in the hypervolemic group. This difference was not statistically significant ($p = 0.48$). The correlation between CAV and BNP was poor ($p = 0.64$, Figure 1).

Mean TFC was 32.1 ± 5.7 kOhm/m² in the euvolemic group as compared with 32.9 ± 7.8 kOhm/m² in the hypervolemic group (normal range: 30 – 50 kOhm/m² in men and 21 – 37 kOhm/m² in women). This

difference was not statistically significant ($p = 0.72$). The correlation between CAV and TFC was poor ($p = 0.89$, Figure 1).

We examined the correlation between the TFC and BNP levels from the euvoletic and hypervolemic groups; no significant relationship was observed between those variables in either group ($p = 0.10$).

TABLE I Demographic, anthropometric, and hemodynamic data, cardiovascular comorbidity, and risk factors

Age (years) ^a	56±16.2
Men/women	25/26
Duration of dialysis (years) ^a	2.6±3.6
Systolic blood pressure (mmHg) ^a	136.9±18.1
Diastolic blood pressure (mmHg) ^a	77.8±12.7
Mean arterial pressure (mmHg) ^a	97.2±18.4
Heart rate (beats per minute) ^a	65.9±13.1
Past medical history (%)	
Coronary artery disease	25.5
Peripheral vascular disease	11.8
Congestive heart failure	7.8
Diabetes mellitus	37.3
Hypertension	88
Renal artery stenosis	3.9
Antihypertensive therapy (%)	
None	19.6
Monotherapy	25.5
Combination therapy	54.9
Charlson comorbidity index ^a	5±2.4

^a Mean ± standard deviation.

Logistic regression analysis between the CAV and BNP and TFC revealed no significant correlations between those variables (Table II). The area under the ROC curve was 0.55 for BNP [95% confidence interval (CI): 0.35 to 0.74] and 0.54 for TFC (95% CI: 0.35 to 0.74), as shown in Figure 2.

Multiple regression analysis revealed a limited association between the CAV, TFC, BNP, and several other clinical parameters such as SBP, DBP, and mean arterial pressure (Table III).

Levels of BNP were analyzed using a logistic model at various reference values. Levels of BNP failed to adequately correlate with the CAV at 100 pg/mL ($p = 0.72$), 300 pg/mL ($p = 0.94$), 400 pg/mL ($p = 0.49$), 500 pg/mL ($p = 0.46$), 600 pg/mL ($p = 0.87$), and 900 pg/mL ($p = 0.77$).

Discussion

Some authors have suggested that BNP levels could be a useful tool to assess volume status in dialysis patients (8,9). Increased circulating levels of BNP are commonly seen in hemodialysis (HD) patients, and these elevated levels have been associated with left ventricular dysfunction and hypertrophy (8–10), decreased survival, and higher rates of cardiovascular events (11,12). Similar findings have been reported in CAPD patients (13). Plasma BNP levels in CAPD patients are elevated as compared with levels in the

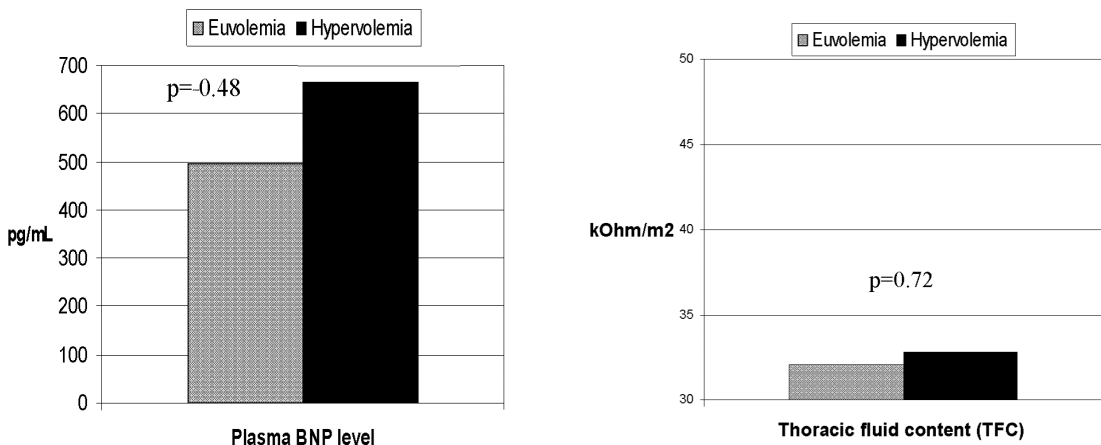


FIGURE 1 Mean values of brain natriuretic peptide (BNP) and thoracic fluid content (TFC) in euvoletic and hypervolemic patients. Mean BNP was 477.4 ± 732.1 pg/mL in euvoletic patients and 665.2 ± 992.1 pg/mL in hypervolemic patients. Mean TFC level was 32.1 ± 5.7 kOhm/m² in euvoletic patients and 32.8 ± 7.8 kOhm/m² in hypervolemic patients.

TABLE II Logistic regression analysis between clinical volume assessment, brain natriuretic peptide (BNP), and thoracic fluid content (TFC)

	Odds ratio	Standard error	Clinical volume assessment		
			z	p>[z]	95% confidence interval
BNP	0.9998358	0.0005284	-0.31	0.756	0.9988007 to 1.000872
TFC	1.05	0.0596613	0.86	0.391	0.9393424 to 1.173694

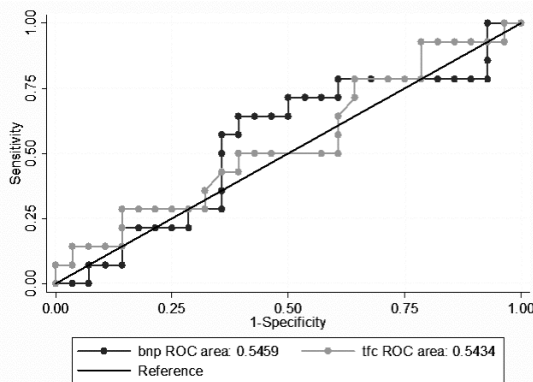


FIGURE 2 Receiver operating characteristic (ROC) curve for brain natriuretic peptide (bnp) and thoracic fluid content (tfc).

general population; however, levels in CAPD patients are significantly lower than those in HD patients, suggesting that extracellular volume expansion is less in CAPD patients (11,13,14). Studies have indicated that plasma BNP levels decrease significantly after a HD session, implying that volume overload is an important stimulus for BNP secretion (15). Thus, BNP levels have been suggested to be a useful tool for volume assessment in HD patients.

We hypothesized that BNP levels would be a useful tool to assess volume status in PD patients. The assay is easy to perform and widely available, making the use of this marker a viable option.

We observed a broad range of BNP levels, with considerable overlap between euvoletic and hypervolemic patients, suggesting that BNP measurements would be of limited usefulness. Our statistical analysis failed to prove any benefit of this biochemical marker to the CAV. Add to that the inability of BNP to detect underhydration (14), and it becomes clear that BNP is an inadequate volume assessment tool. The limited usefulness of BNP measurements

has been implied in other studies of PD (16) and HD patients (14,15).

The high plasma concentration of BNP in dialysis patients seems to be multifactorial, being affected by extracellular volume expansion, concomitant heart disease, and decreased renal clearance (9). No consensus has yet been reached concerning the definition of “normal” BNP concentration in PD patients. The issue requires further investigation.

The ICG is a noninvasive, simple-to-operate, and compact device that has the ability to measure hemodynamic parameters such as cardiac output, cardiac index, SBP, DBP, mean arterial pressure, systemic vascular resistance index, and TFC. The use of ICG has been extensively documented in patients with heart failure (17,18) and hypertension (7,19). Several studies comparing ICG with invasive methods have validated ICG hemodynamic data in stable outpatients (18,7). The standard ICG hemodynamic parameter used to assess fluid status is TFC. Variations in TFC have been shown to be directly proportional to intravascular and extravascular changes (7,20). Using TFC, volume changes in response to diuretics have been detected in patients with heart failure (21).

Studies with ICG in dialysis patients have been limited mainly to patients maintained on HD. The TFC is able to detect HD-induced volume changes during the course of a HD session (22,23). Hemodynamic data from ICG is also highly reproducible in HD patients (22).

The present study is the first to use ICG as an adjunct tool for volume status assessment in PD patients. Our data demonstrated poor correlation between TFC and the CAV. This observation held true whether TFC was analyzed independently or in conjunction with BNP levels.

The poor performance of TFC in our study may possibly be related to the abnormal body fluid composition seen in PD patients. Several investigators have suggested that, because of the effect of gravity,

TABLE III Multiple regression analysis between clinical volume assessment, natriuretic peptide (BNP), thoracic fluid content (TFC), and several clinical variables

	Coefficient	Standard error	Clinical volume assessment		
			z	p> [z]	95% confidence interval
BNP	-0.000438	0.0006353	-0.69	0.491	-0.0016832 to 0.0008071
TFC	-0.052804	0.0601806	0.88	0.380	-0.0651478 to 0.1707559
Age	-0.00064	0.028766	-0.02	0.982	-0.570204 to 0.0557404
CCI	0.1412582	0.1591505	0.89	0.375	-0.1706711 to 0.4531875
SBP	-0.0012845	0.0237081	-0.05	0.957	-0.0477515 to 0.0451826
DBP	0.038301	0.0346351	1.11	0.269	-0.0295825 to 0.1061845

CCI = Charlson comorbidity index; SBP = systolic blood pressure; DBP = diastolic blood pressure.

the legs of dialysis patients have more excess fluid than do the arms and the trunk (24,25). The estimation of thoracic fluid volume is further complicated by the heterogeneous distribution of the electric current in this body segment (25). For these reasons, some authors have reported that regional bioimpedance in compartments such as the leg may be a more sensitive way to assess fluid changes (24,25).

Conclusions

The present study showed poor correlation of the CAV with BNP and with ICG-derived TFC. These findings suggest that BNP levels and TFC measurements have limited usefulness in the evaluation of volume status in PD patients.

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