Cardiovascular mortality remains the commonest cause of death for peritoneal dialysis patients. As such, preventing persistent hypervolemia is important. On the other hand, hypovolemia may potentially risk episodes of acute kidney injury and loss of residual renal function, a major determinant of peritoneal dialysis technique survival. Bioimpedance has developed from a single-frequency research tool to a multi-frequency bioelectrical impedance analysis readily available in the clinic and capable of measuring extracellular, intracellular, and total body water. Similarly, natriuretic peptides released from the heart because of myocardial stretch and increased intracardiac volume have also been variously reported to be helpful in assessing volume status in peritoneal dialysis patients. The question then arises whether these newer technologies and biomarkers have supplanted the time-honored clinical assessment of hydration status or whether they are merely adjuncts that aid the experienced clinician.

Key words
Bioimpedance, brain natriuretic peptides

Introduction
After peritonitis (1), loss of ultrafiltration with volume overload is the next most common cause of enforced modality change for peritoneal dialysis (PD) patients. Thus, it is important to be able to detect volume excess early to allow for appropriate changes to the PD prescription and for re-evaluation so that if extracellular fluid accumulation cannot be controlled, timely transfer to hemodialysis can be organized.

All patients starting PD should receive counseling about dietary sodium restriction to limit thirst and daily weight gain, which helps to minimize the use of hypertonic glucose exchanges. Although some patients have the classic triad of clinical signs of extracellular volume overload (pitting peripheral edema, raised jugular venous pressure, and pulmonary rales), many hypertensive PD patients—although they may have some minor peripheral edema—have no other clinical signs suggestive of extracellular volume expansion. The lack of clinical signs is a result both of the limitations of clinical examination in detecting extracellular volume expansion (2) and of the mechanisms of sodium balance, which comprise both the classical osmotic sodium balance (sodium accumulation associated with water retention) and the non-osmotic sodium balance (when sodium switches for potassium in muscle and binds to negatively-charged tissue interstitial matrix proteoglycans without any change in body water) (3). On the other hand, the presence of peripheral leg edema may not reflect generalized extracellular fluid overload. Localized edema may form because inflammatory conditions are causing increased endothelial permeability or because venous or lymphatic drainage are being obstructed. Edema may also be a result of the combination of physical inactivity and dependent posture.

Aids to clinical assessment could, on the one hand, potentially help to prevent chronic volume overload in PD patients (4) with its consequent adverse cardiovascular outcomes, and on the other, to identify patients becoming hypovolemic, thus preventing repeated episodes of acute kidney injury and accelerated loss of residual renal function (5).
Discussion

Does bioimpedance have a role in fluid volume assessments?

Bioimpedance is resistance to a flow of electrical current through body tissues, and it is determined by the ionic conductance of tissue fluid on one hand and the dielectric properties of tissue interfaces on the other. Resistance to flow depends both on the length of the electrical pathway and on the cross-sectional area. The use of alternating current and a number of increasing frequencies induces a stepwise recruitment of conduction through various body compartments, which enables calculation of those various body compartments (6).

Bioimpedance is reported as a series of measurements of resistance and reactance, the latter being the ability of a tissue to retain an electrical field like a capacitor, because of the lipid-rich cell membrane bilayer. Tissues vary in their resistance and reactance depending on water and cell content—for example, blood and adipose tissue. At low frequencies, the extracellular fluid compartment is the primary conducting pathway, but at the highest frequencies, loss of cell membrane capacitance allows for conduction through both the extracellular and intracellular compartments, thus allowing for measurement of intracellular (ICW), extracellular (ECW), and total body water (TBW). The measured impedance is the sum of both the capacitive reactance attributable to cell membranes and other tissue interfaces, and the resistance of both ICW and ECW. The phase angle is the difference between the external applied electrical current and the measured voltage, which is attributable to the capacitive reactance of the cell membranes. The phase angle is therefore a direct measure of capacitance and important in establishing ICW volumes. Several studies have shown that, in both healthy subjects and dialysis patients, TBW measured by bioelectrical impedance analysis (BIA) is as accurate as that obtained by dilution methods using D\textsubscript{2}O (7,8). 

Bioimpedance is affected by the length of the electrical circuit, typically from hand to foot electrodes, and the body cross-sectional area. For single measurements, then, the question of how best to standardize results arises. Although some researchers have corrected for patient height and body surface area, most have adopted the ECW/TBW ratio (8,9). In addition, because of differences in body composition between the sexes and during aging, manufacturers of bioimpedance devices have developed corrections to the basic Cole–Cole equations (6) to allow for some of the differences. However, it is also apparent that body composition varies with the presence of type 2 diabetes (10) and with ethnicity (11). One way of overcoming some of these confounders is to take serial measurements over time. By plotting impedance vector lengths and phase angles at a single electrical frequency, changes in volume can be tracked without having to determine the absolute ICW or ECW (Figure 1). In contrast, multiple-frequency (MF)–BIA allows for measurement of ICW and ECW.

Most of the resistance to electrical flow occurs during passage in the arms and legs, and therefore whether bioimpedance measurements should be made with the peritoneal cavity empty or full has been a matter of debate. From a practical standpoint, it is easier to make measurements with dialysate instilled rather than having to drain it, take the measurements, and then instill fresh dialysate. Studies using whole-body devices with single hand and foot electrodes have not observed a difference, but those using MF-BIA devices with paired hand and foot electrodes that allow for the measurement of separate compartmental

![Figure 1](image_url)

**Figure 1** A single-frequency bioimpedance nomogram plotting resistance against reactance for a female patient shows that changes in the peritoneal dialysis prescription designed to increase ultrafiltration losses led to an improvement in volume control. Normal confidence limits (50%, 75%, and 95%) are shown. Protein–energy wasting leads to loss of intracellular water and reduced reactance. Bioimpedance can therefore be used to assess nutrition status.
volumes have shown differences (12). Therefore, for reliability, bioimpedance measurements should be made with the peritoneal dialysate drained.

Most MF-BIA studies have shown that, regardless of modality, PD patients—although clinically thought to be euvoletic—generally had an increased ECW/TBW ratio, particularly in the legs and trunk (13). Patients with increased ECW/TBW did not have greater ultrafiltration volumes during a standard transport test using a 22.7 g/L dialysate (14) or greater residual urine output (15). Indeed, the increased ECW/TBW was the result of a combination of ECW expansion and ICW loss, partly attributable to increased vascular permeability and albumin leakage (16) secondary to inflammation and comorbidity (17,18). Those physiologic conditions explain why apparently volume-overloaded PD patients may not have increased urine output or an increased ultrafiltration response to hypertonic glucose dialysate. As such, in most MF-BIA studies, single MF-BIA measurements have not been reported to improve patient management above and beyond simple clinical examination of the patients for volume assessment.

A MF-BIA test may provide an accurate assessment of ECW and ICW, but it cannot reliably determine the effective circulating plasma volume and, therefore, the intravascular volume status. However, serial measurements are more useful both for assessing trends in volume status and the effect of changes in the PD prescription (Figure 1) and also for assessing changes in body composition over time to allow for earlier detection of patients with protein–energy wasting (19). On the other hand, MF-BIA can detect patients with underhydration and increased risk of hypovolemia potentially leading to episodes of acute kidney injury that can cause premature loss of residual renal function.

Bioimpedance assessments rely on passing electrical currents through the body and therefore cannot be made in all patients—for example, those fitted with cardiac pacemakers and defibrillators. Similarly, whole-body bioimpedance analysis cannot be performed in amputees, although segmental measurements are possible.

Do natriuretic peptides aid volume assessment in PD patients?
Atrial natriuretic peptide is released by distension of the atria, and that finding led to the introduction of natriuretic peptides into cardiology practice as an adjunct to clinical examination to aid in the diagnosis of heart failure. More recently, brain natriuretic peptide (BNP) has replaced atrial natriuretic peptide in the diagnosis of heart failure (20). Brain natriuretic peptide, released by the ventricles, has a longer half-life than atrial natriuretic peptide, and is not affected by PD exchanges (21). Many studies have reported that BNP is a major risk factor for cardiovascular mortality (22), although there is debate concerning the value of a single BNP measurement, because BNP has variously been associated with left ventricular systolic dysfunction, left ventricular mass, volume overload, and inflammation (23,24).

The role of BNP in assessing volume status in PD patients remains unclear, with some reports failing to show any association with volume status (25), and others having shown that serial changes in MF-BIA–measured volume status are mirrored by changes in BNP (26). Certainly, overhydration and BNP are both major mortality risk factors for PD patients (27). Some of the differences reported by current studies may be related to differences in the patient groups studied in terms of pre-existing cardiovascular morbidity and hydration status. In addition, different natriuretic peptides were often measured. The pro-hormone pre-proBNP is cleaved into N-terminal proBNP, proBNP, and BNP, which is then cleaved into two different BNP peptide sequences, and there are differences in half-life between those peptides. Moreover, although BNP is predominantly enzymatically broken down by endothelial neutral peptidases, some BNP is filtered by the glomerulus and degraded by proximal tubular endopeptidases. Even though there is no strong association between residual renal function and serum natriuretic peptides (Figure 2), the study populations varied in residual renal function.

Although there is a MF-BIA reference range for normal healthy individuals (and by inference, ranges for healthy PD patients), there are no such normal values for natriuretic peptides. Whereas N-terminal proBNP concentrations above 150 pmol/L are supportive of cardiac failure in patients acutely admitted to the emergency department with cardiorespiratory symptoms, there is in the PD population no acknowledged cut-off point to delineate overhydration from normal hydration on one hand, and no lower cut-off value to alert the clinician to volume depletion on the other. Single natriuretic peptide results therefore have
to be interpreted together with the clinical examination, other relevant medical history, and the results of pertinent investigations. However, the trend in serial investigations may help to assess changes in PD prescription and changes in volume status over time (Figure 3).

**Summary**
Loss of residual renal function is a major predictor of forced modality change for PD patients. It is therefore important that PD patients do not become hypovolemic, thus risking episodes of acute kidney injury and premature loss of residual renal function. But on the other hand, persistent hypervolemia risks heart failure and increases the risk of cardiovascular death.

Clinical examination remains important in the assessment of the hydration status of PD patients. A MF-BIA test can be helpful in analyzing ECW, ICW, and TBW. But although an elevated ECW/TBW ratio may be associated with overhydration, the increased ECW may not be intravascular, instead being related to increased capillary permeability and interstitial fluid retention. Similarly, an increased ECW/TBW may be a result of loss of fat and muscle, with a reduced ICW because of protein–energy wasting, inflammation, and cancer cachexia. Similarly, although BNPs may reflect intravascular volume, they are also affected by pre-existing cardiac pathology, and no reference range has yet been established for PD patients. In this context, serial measurements of MF-BIA and BNPs may help to guide the response to changes in PD prescription and may aid in clinical assessment, but clinical evaluation remains the cornerstone of hydration status assessment in PD patients.

**Disclosures**
The author has no financial conflict of interest.

**References**
Bioimpedance or Natriuretic Peptides for Volume Assessment in PD?


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