



# Effect of volume indices of bioimpedance analysis on clinical outcomes, including left ventricular hypertrophy, in patients undergoing peritoneal dialysis

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Volume status is an important risk factor that affects morbidity and mortality in patients undergoing peritoneal dialysis (PD). Volume overload may lead to major cardiovascular complications, such as left ventricular hypertrophy (LVH). Proper monitoring and intervention in cases of volume overload are important for improving survival in patients that are undergoing PD. Multifrequency bioimpedance analysis (BIA) is a simple and accurate method of body composition analysis.

In the current issue of *Kidney Research and Clinical Practice*, Tangwonglert and Davenport [1] reported an analysis of the impact of fluid status on left ventricular mass (LVM) in patients undergoing PD. This study reinforces the importance of extracellular water (ECW) expansion rather than systolic or mean arterial blood pressure and the detrimental effect of the same on LVH. An equal regression in LVH along with a reduction in ECW volume has also been discussed. I want to discuss the effects of BIA volume indices on clinical outcomes, including LVH, in patients undergoing PD.

Hypoalbuminemia is an important determinant of tissue

overhydration (OH) and can be linked to inflammation or peritoneal protein loss in patients undergoing PD. The presence of excess fluid is not equivalent to expanded plasma volume; rather, it is associated with increased extravascular ECW accumulation in patients with hypoalbuminemia. Several factors, such as diabetes, sex, age, residual renal function (RRF), and modality of PD should be considered when interpreting the volume status in patients undergoing PD. Van Biesen et al. [2] observed a substantial volume overload in a cohort that was comprised of incident patients on PD, with patients with diabetes and males being affected more severely. Volume overload has been associated with mortality. In patients with diabetes undergoing PD, an increase in ECW volume was found to be secondary to increased vascular permeability and albumin transfer to interstitial tissues. Because RRF is an important determinant for PD success, there is a tendency in clinical practice to allow an increase in ECW volume in patients undergoing PD. The relationship between ECW/total body water (TBW) and RRF preservation remains in debate. McCafferty et al. [3] reported that the increments and decrements in ECW/TBW were not associated with changes in RRF.

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However, Kang et al. [4] reported that RRF at 1 year after PD initiation was higher in the initial low edema index (ECW/TBW) group than in the initial high edema index group, and that a baseline high edema index was associated with higher mortality among patients undergoing PD. With defining the time-averaged RRF (TA-RRF) as the mean RRF values at PD initiation and 1 year after PD initiation, the authors also reported that a high TA-RRF tertile was associated with a lower edema index at 1 year in patients undergoing PD [5].

Tangwonglert and Davenport [1] reported that in the group with LVM index (LVMI) reductions, none of the patients were initially treated with automated PD (APD). Rather, a greater number of patients with increased LVMI were initially treated with APD cyclers. This might be attributable to the differences in peritoneal sodium removal processes in different PD modalities and the types of peritoneal dialysates that were used. Adequate removal of water and sodium via dialysate might be important for preventing hypervolemia, especially in patients undergoing APD. The use of a low-sodium dialysate, icodextrin dialysate, and long-term exposure of dialysate could be helpful to mitigate sodium retention in patients undergoing APD. In most cases in this study, relatively sufficient sodium and fluid removal was facilitated by using icodextrin (80%) and a suitable long-term PD modality (both continuous ambulatory PD [CAPD] and continuous cycler PC [CCPD], 90%).

For more accurate measurement of BIA, patients are recommended to maintain an empty abdomen during the evaluation of body composition. The presence of peritoneal dialysates has been observed to lead to an increase in not only intracellular water, ECW, and TBW volume but also the edema index (ECW/TBW), leading to an underestimation of body fat mass [6]. The ECW/TBW ratio may increase in confounding conditions, such as muscle loss, diabetes, and hypoalbuminemia, and this ratio has been validated as a predictor of survival. The ECW/TBW ratio should be normalized based on sex and age. An ECW/TBW ratio of  $\geq 0.4$  was used to define OH, as suggested by the manufacturer (Biospace, Seoul, Korea). In this study, the mean ECW/TBW values during the first and second rounds of echocardiography were less than 0.4. Several studies have reported a negative correlation between ECW/TBW and clinical outcomes, including cardiovascular mortality. Shu et al. [7] reported that bioimpedance-assessed OH (ECW/TBW) is a predictor of

mortality and technique failure in patients undergoing PD. However, the correlation between volume control and RRF preservation in patients undergoing PD must be observed closely. Strict volume control for normalizing the ECW/TBW ratio in comorbid patients undergoing PD may lead to hypovolemia and RRF loss. Although the ECW/TBW ratio is most widely accepted as an index of hydration in patients undergoing PD, it does not indicate the degree of OH. The OH status is commonly defined by  $\text{OH/ECW} > 15\%$ , as described by Wizemann et al. [8] in a body composition monitor. Another recent study showed that chronic fluid overload strongly predicted the risk of death and transfer to hemodialysis in patients undergoing PD. The IPOD-PD (Initiative of Patient Outcomes in Dialysis-Peritoneal Dialysis) Study Group reported that a volume overload of  $>17.3\%$  was independently associated with a higher death risk than in cases with relative volume overload of  $\leq 17.3\%$  [2].

Tangwonglert and Davenport [1] reported on the relationship between ECW and LVM in patients undergoing PD. Regardless of whether the expansion in extracellular volume was suitable for RRF preservation, the hypervolemic effect on LVH might be an important determinant of clinical outcomes in patients undergoing PD. In this study, only the ECW/height ratio was independently associated with the percentage change in LVMI in a multivariable model; however, it was not associated with ECW/TBW or changes in systolic or mean arterial pressure, urine output, 24-hour PD ultrafiltration, or net sodium balance. A limited number of studies have reported on serial echocardiograms in PD patients. In a large-scale Korean study, Hong et al. [9] showed that strict volume control based on repeated measurements using bioimpedance spectroscopy was an independent predictor of left ventricular (LV) systolic function in non-anuric patients undergoing PD. However, they were not able to assess whether changes in LVM were related to changes in ECW. The Korean COMPASS (Control of Fluid Balance Guided by Body Composition Monitoring in Patients on Peritoneal Dialysis) study also did not reveal differences in clinical outcomes, including echocardiographic parameters, between the BIS-guided and control groups [10].

Patients with chronic kidney disease (CKD) exhibit several potential risk factors for LVH, as they are more likely to have hypertension, ECW volume expansion, and anemia. Nevertheless, owing to renin-angiotensin system activation and other disruptions in circulation, certain patients

remain hypertensive even though their ECW volume status is carefully monitored. Sustained volume overload or longstanding hypertension could be directly associated with eccentric or concentric LVH, respectively. Antihypertensive medications that are used, such as angiotensin II receptor blockers, could exert beneficial effects on LVH regression. In this study, less than 20% of patients undergoing PD were treated with renin-angiotensin blockers/receptors, and unexpectedly, the majority of patients showed concentric LVH. Ejection fraction (EF), which is measured using conventional echocardiography, is an insensitive parameter due to both intra- and interobserver variability. Furthermore, LVH and changes in LV structure in patients with CKD could lead to LV systolic dysfunction despite a normal EF. The prevalence of impaired LV global longitudinal strain (GLS) despite preserved left ventricular EF in predialysis patients and those undergoing dialysis is relatively high (32%). In this respect, LV GLS is effective for early detection of LV systolic dysfunction in patients with CKD with preserved EF. Although there is currently no consensus on hydration measurements using BIA, several cohort studies have shown that OH, as measured using the ECW/TBW or OH/ECW ratio, is strongly associated with a poor survival outcome in patients undergoing PD. However, the impact of ECW/height on LVH should be tested in carefully designed clinical trials.

### Conflicts of interest

The author has no conflicts of interest to declare.

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