Bioimpedance and echocardiography used interchangeably in volume comparison of dialysis patients

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Abstract
Background: Euvolemia is a major issue in chronic kidney disease. The present study compares cardiac condition and volume status in peritoneal dialysis (PD) and hemodialysis (HD) patients and points out importance of volume control.

Methods: From a single-center center, 81 PD and 89 HD patients were enrolled. Echocardiography and body composition analysis using bioimpedance spectroscopy (BIS) technique were performed. Overhydration (OH) and extracellular water (ECW) in liters and OH/ECW % were used as volume indices.

Results: Patients were younger (47.6±14.5 and 53.1±11.8 years, p<0.05), daily urine volume higher (1068±926 vs 290±444 ml, p <0.001) and dialysis vintage was shorter (30.1±18.6 vs 53.6±35.4 months, p<0.001), systolic blood pressure was lower (127.5±15.4 vs 140.3±18.9 mmHg, p<0.001) in PD than HD group respectively. Volume indices were (OH, OH/ECW %, ECW/height, ECW to Intracellular Water ratios (E/I) (p<0.05)) significantly higher in HD patients compared to PD patients. Over all 66 of 170 patients (39%) had OH/ECW % <5 and OH/ECW % ratio was positively correlated with Left atrium index (R2=0.105, p<0.05). Interventricular septum diameter and Left ventricular mass index (1.41±0.24 and 159.6±48.2 vs. 1.27±0.17 cm and 115.8±37 g/m2, p<0.001) were increased in HD than in PD group. After multivariate adjustment OH/ECW increased with: HD and diabetic patients. LVH increased with: HD group, OH/ECW (%) and SBP significantly.

Conclusion: Overhydration was more common among HD. Excess fluid may lead adverse effect in organ functions especially cardiac condition. This indicates that the current clinical and technical tools to achieve euvolemia are insufficient and that an additional tool, such as BIS, could be useful in the diagnosis of overhydration. Hippokratia 2012, 16, 4: 329-334

Key words: Bioimpedance, Hemodialysis, Hypervolemia, Left ventricular hypertrophy, Peritoneal dialysis

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Introduction
Cardiovascular events due to hypertension and related cardiac conditions have been the leading cause of mortality in all dialysis patients. Most studies revealed that hypertension persists despite antihypertensive drugs while left ventricular hypertrophy (LVH) does not decrease or even progresses throughout the dialysis vintage. Some authors believe that heart disease in dialysis is a natural event, suggesting that deterioration is inevitably linked to that procedure. Wang et al, demonstrated that increasing left ventricular mass is related to worse cardiovascular outcome in peritoneal dialysis (PD) patients.

On the contrary, other studies have shown that a strict volume control strategy decreases blood pressure (BP) without drugs, causes regression of LVH and prolongs survival. This suggests that volume control is neglected in most hemodialysis centers, despite the fact that treating physicians may consider that Dry Weight (DW) of their patients has been reached. There is no easily applicable method to determine extra cellular volume and consequently estimate DW. Thus DW has to be clinically defined by several indirect methods. In PD patients the assessment of volume status is relatively crude. Volume status is often assessed indirectly by measuring fluid removal, failing to take into account fluid balance by omission of dietary fluid intake.

Bio-impedance spectroscopy (BIS) represents a different approach to the assessment of fluid status and this analytic technique mainly uses electrical properties of biological cells and fluids. The Body Composition
Monitor (BCM, Fresenius Medical Care, Bad Homburg, Germany) is a bio-impedance spectroscopy device for clinical use, validated by isotope dilution methods\cite{10,11}, and reference body composition methods\cite{12,13}, and has been used in hemodialysis (HD)\cite{14,15} and PD\cite{16,17}.

We aimed here to compare hydration status, as measured with BCM, and echocardiography in PD and HD patients in a same center where much attention is paid for preserving residual renal function; consequently we wanted to focus on volume control in both dialysis modalities.

Material and methods

Patients

Eighty one continuous ambulatory peritoneal dialysis (CAPD) and 89 prevalent HD patients actively treated in a same center in Fresenius Medical Care facility were enrolled in the study at June 2009. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Patients who were older than 18-years, on maintenance bicarbonate HD scheduled thrice weekly (12 hours/week) and incident patients undergoing CAPD for at least 6 months willing to participate in the study with a written informed consent, were included. Exclusion criteria were the presence of pacemaker or defibrillator, artificial joints, pin or amputation, being scheduled for living donor renal transplantation, presence of serious life-limiting co-morbid situations, like malignancy, uncontrollable infection, end-stage cardiac, pulmonary, or hepatic disease, pregnancy or lactating and patients on automated PD.

Systolic and diastolic blood pressure were measured at the time of BIS investigation and presented as the mean of at least three measurements. We used mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) for analyses.

The following variables: age, sex, body mass index (BMI), history of diabetes and vascular events to include cardiovascular, peripheral vascular, cerebrovascular recorded and from patient charts, hemoglobin, serum albumin, calcium, phosphorus, urea, creatinine, sodium and potassium, were obtained.

Measurement of overhydration

BIS was measured in all PD patients with empty abdomen, and midweek interdialytic day in HD patients. Total body electrical impedance to an alternate current (0.2 mA) with fifty different frequencies (5-1000 KHz) were assessed using a multifrequency analyzer (Body Composition Monitor, Fresenius Medical Care, Bad Homburg, Deutschland GmbH). Four electrodes were placed on the right hand and foot or on the side contra lateral to the arteriovenous fistula, of the supine patients. Two electrodes were dorsally placed on the right hand in the metacarlo-phalangeal articulations and in the carpus, respectively, 5 cm apart. The pair on the foot was located in the metatarso-philangeal and in the ankle articulation, 6 cm apart. Results of measurements included that of overhydration, total body water, extracellular water, intracellular water, body mass index, nutrition index and impedance index, lean tissue index, fat tissue index, and body cell mass. BIS uses physiological modeling and mixture equations (Cole–Cole plot and Hanai formulae) to first determine the electrical resistance of extracellular water (ECW) and intracellular water (ICW) and then calculate the volumes of these respective compartments. This is essential for identification of overhydration (OH) – the BCM uses the BIS technique\cite{18}.

The BCM expresses the body weight in terms of lean tissue mass (LTM – mainly muscle), adipose tissue mass (ATM – mainly fat) and OH. Each of these compartments has a specific composition and contains a known quantity of water per mass of tissue. OH is almost 100% extracellular water, whereas the water of LTM and ATM consist of differing proportion of extracellular and intracellular water in addition to solid components.

Healthy individuals are considered to be “normally hydrated” and therefore have virtually no overhydration. These individuals may be characterized in terms of ATM and LTM only. However, in pathological conditions the presence of excess fluid that has to be taken into consideration. Excess fluid represents an expansion of only the extracellular water, whereas ICW remains unchanged. The excess fluid may reside within adipose tissue or lean tissue raising the hydration of the respective tissue above the “normal” values (e.g. edema). Alternatively, excess fluid may simply appear as a distinct compartment without altering the hydration of the major tissues (e.g., ascites, pleural effusion). As the extracellular hydration of LTM and ATM is known, the expected “normal” volume of ECW of these tissues can be calculated. The difference between “normal” ECW and measured ECW is the excess fluid, OH.

Reference ranges are available for overhydration (OH), lean tissue index (LTI), fat tissue index (FTI) and extracellular/intracellular (E/I) ratio. The reference ranges are defined by a reference population of 1000 healthy subjects between 18 and 75 years with a body mass index between 18 - 32 kg/m\(^2\). The reference ranges are defined by the 10th and 90th percentiles of the reference population and are specific to age and gender\cite{19}. These ranges simplify identification of abnormal conditions by comparing a patient’s data to the reference population.

Echocardiography:

Echocardiographic measurements done at the time of BIS investigation by one cardiologist, who is not aware of the patients’ BCM results, using a Philips Envisor C. M-mode, two dimensional Doppler recordings are simultaneously obtained with electrocardiography according to the recommendation of the American Society of Echocardiography. Comprehensive echocardiographic examination\cite{20,21} included assessment of left ventricular systolic and diastolic functions, left ventricular mass and measurement of left atrial volumes. The following measurements were taken: left atrium diameter (LAD),
left ventricular end-diastolic (LVEDD) and end-systolic diameters (LVEDS), right ventricular end-diastolic diameter, thickness of the posterior wall and the interventricular septum. LVM was calculated following the equation described by Devereux and Reichek: $LVM = 1.04 \times [(IVS + LVDd + PWT) - (LVDd)] - 136$ (g). Left ventricular mass index (LVMI) was calculated by dividing LVM by body surface area; LV hypertrophy was defined as LVMI $\geq 131$ g/m$^2$ in males and $\geq 113$ g/m$^2$ in females. LAD was adjusted for height.

Statistical analysis

Statistical analysis was performed with SPSS 18.0 software (SPSS, Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentages. Continuous variables were compared using Pearson’s Chi-square test or Fisher Exact Chi-square test. Forward stepwise logistic regression used for comparing patients compared to PD patients (p<0.05), (Table 2).

Results

In total, 81 PD and 89 HD patients were analyzed. Patients were younger in PD than HD (47.6±14.5 and 53.1±11.8 years respectively) (p<0.05).

Daily urine volume higher (1068±926 vs. 290±444 ml, p<0.001) and dialysis vintage is shorter (30.1±18.6 vs 53.6±35.4 months p<0.001) in PD than HD.

Systolic blood pressure was lower in PD compared to HD patients (127.5±15.4 vs. 140.3±18.9 mmHg, p<0.001). However there was no difference in diastolic blood pressure.

Hematocrit and biochemical parameters were similar between groups except Urea which is higher in PD than HD groups (125.5±26.9 to 109.7±31.4 mg/dl, p <0.001). The relevant demographic, clinical, and biochemical variables are listed in Table 1.

Overall 66 of 170 patients (39%) have OH/ECW % <5. Overhydration was more pronounced in HD patients compared to PD patients (1.72±1.88 vs 1.09±1.53 L) (p<0.05). Relative OH (OH/ECW %) (9.17±9.11 vs 6.20±8.96), the ratio of ECW to height (10.42±1.62 vs 9.93±1.45 L/m), extracellular to Intracellular Water Ratio (E/I) (0.92±0.12 vs 0.87±0.11) were all higher in HD patients compared to PD (p<0.05), (Table 2).

Interventricular septum diameter and Left ventricular mass index were significantly increased in HD than PD (1.41±0.24 and 159.6±48.2 vs 1.27±0.17 cm and 115.8±37 g/m$^2$, p<0.001), (Table 3).

OH/ECW % ratio was positively correlated with LAi ($R^2=0.105$, p<0.05), (Figure 1).

After multivariable adjustment OH/ECW increased with HD relative to PD and in Diabetic patients (Table 4).

After multivariable adjustment of age, gender, presence of diabetes, cardiovascular disease history, smoking, dialysis vintage and residual renal volume we found that LVH risk increased with HD relative to PD, OH/ECW and SBP significantly (Table 5).

Discussion

Due to its continuous nature that potentially allows for a steady state and the avoidance of fluctuating volume status, PD has historically been considered superior to HD with respect to maintaining adequate volume control among patients with end-stage renal disease. Despite this advantage, many patients on PD are hypertensive and volume overloaded. This is most frequently due to a preventable or treatable process.

However, from a literature review, it is clear that reported volume status in PD patients varies widely and that the way PD and HD and are practiced in single centers might thus be more important than the modality per se.

Biesens et al, conducted a study comparing both modalities in a center did not find a difference in hydration or body composition between PD and HD patients; although, as could be expected, overhydration was virtually zero after HD. It is not clear, however, whether volemia in HD should be considered before or after HD.

Up to now, due to bio-physical reasons, bio-impedance spectroscopy was considered not to measure sequestered fluid in the trunk. Therefore, presence or absence of PD fluid in the abdomen thought to have no influence the readings of hydration status. Biesen at al measured BCM assessments with full abdomen but it is recently demonstrated that measurement with an empty abdomen, better reflects overhydration and is related to echocardiographic parameters so in present study BIS was measured in all PD patients with empty abdomen.

Traditional CV risk factors, however, play a central role in chronic kidney disease (CKD). Hypertension, often together with diabetes, is today the first cause of CKD. In present study also diabetes was the most common cause of end stage renal disease (ESRD) approximately 1 in 5 were diabetics in PD and HD group. Hypertension plays a major role in cardiac damage in CKD via LVH induction. As in other populations, in CKD patients the presence of LVH is predictive of a worse CV prognosis.

In present study SBP and LVMI were lower in PD than HD patients. Among patients with ESRD, nearly more than 70% have LVH. A study by Stack and Sarnak evaluated 2,257 patients with ESRD at the start of dialysis. Mean age was 58 years, and mean glomerular filtration rate (GFR) estimated by Modification of Diet in Renal Disease (MDRD) Study equation was <8 ml/min. Among different covariates, hypertension, diabetes, tobacco use, low serum albumin and higher calcium and parathyroid hormone were the factors independently associated with LVH. After 2 years of follow-up, the presence of LVH was associated with lower survival. Increasingly greater prevalence of LVH with declining renal function, and, as expected, the prevalence of LVH was >70% in patients with stage 5 CKD. After multiple regression analysis, the variables independently associated with LVMI were GFR, hemoglobin, diastolic BP and age.
### Table 1: Clinical and laboratory measurements in Hemodialysis versus Peritoneal Dialysis patients.

<table>
<thead>
<tr>
<th></th>
<th>PD (n=81)</th>
<th>HD (n=89)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.6±14.5</td>
<td>53.1±11.8</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Sex % (male)</td>
<td>44 (54.3)</td>
<td>54 (60.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.6±8.5</td>
<td>164.6±9.2</td>
<td>NS</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>70.7±13.8</td>
<td>73.6±12.7</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.1±5.2</td>
<td>27.2±4.6</td>
<td>NS</td>
</tr>
<tr>
<td>DM (%)</td>
<td>16 (21.1)</td>
<td>19 (21.3)</td>
<td>NS</td>
</tr>
<tr>
<td>CVD (%)</td>
<td>6 (8)</td>
<td>15 (17.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Diuresis (ml/day)</td>
<td>1068±926</td>
<td>290±444</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis vintage (months)</td>
<td>30.1±18.6(7.8-101.8)</td>
<td>53.6±35.4(6.7-199.8)</td>
<td>0.001</td>
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<tr>
<td>SBP (mmHg)</td>
<td>127.5±15.4</td>
<td>140.3±18.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77.7±11.1</td>
<td>76.5±6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>11.3±1.8</td>
<td>11.7±1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Htc (%)</td>
<td>33.1±5.0</td>
<td>33.9±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Albumine (g/dl)</td>
<td>3.87±0.27</td>
<td>3.84±0.16</td>
<td>NS</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>9.38±0.85</td>
<td>9.13±0.76</td>
<td>NS</td>
</tr>
<tr>
<td>P (mg/dl)</td>
<td>4.75±1.08</td>
<td>5.05±1.47</td>
<td>NS</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>109.7±31.4</td>
<td>125.5±26.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>7.69±3.12</td>
<td>7.92±1.88</td>
<td>NS</td>
</tr>
<tr>
<td>Na (meq/L)</td>
<td>137.7±3.6</td>
<td>137.4±2.5</td>
<td>NS</td>
</tr>
<tr>
<td>K (meq/L)</td>
<td>4.66±0.59</td>
<td>4.82±0.61</td>
<td>NS</td>
</tr>
</tbody>
</table>

*BSA: Body surface area, BW: Body weight, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, DM: Diabetes mellitus, CVD: Cardiovascular disease, NS: Non statistically significant.*

### Table 2: Body Composition Monitor parameters in Hemodialysis versus Peritoneal Dialysis patients.

<table>
<thead>
<tr>
<th></th>
<th>PD (n=81)</th>
<th>HD (n=89)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OH (L)</td>
<td>1.09±1.53</td>
<td>1.72±1.88</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>OH/ECW %</td>
<td>6.20±8.96</td>
<td>9.17±9.11</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>ECW/Height</td>
<td>9.93±1.45</td>
<td>10.42±1.62</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>TBW (L)</td>
<td>35.5±6.16</td>
<td>36.00±6.48</td>
<td>NS</td>
</tr>
<tr>
<td>ECW (L)</td>
<td>16.41±2.88</td>
<td>17.20±3.18</td>
<td>NS</td>
</tr>
<tr>
<td>ICW (L)</td>
<td>19.11±3.69</td>
<td>18.81±3.73</td>
<td>NS</td>
</tr>
<tr>
<td>E/I</td>
<td>0.87±0.11</td>
<td>0.92±0.12</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>LTI (kg/m²)</td>
<td>14.26±2.45</td>
<td>13.93±2.97</td>
<td>NS</td>
</tr>
<tr>
<td>FTI (kg/m²)</td>
<td>11.74±5.72</td>
<td>12.70±6.01</td>
<td>NS</td>
</tr>
</tbody>
</table>


### Table 3: Echocardiographic parameters in Hemodialysis versus Peritoneal Dialysis patients.

<table>
<thead>
<tr>
<th></th>
<th>PD (n=81)</th>
<th>HD (n=89)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVDd (cm)</td>
<td>2.36±0.35</td>
<td>2.71±0.32</td>
<td>0.000</td>
</tr>
<tr>
<td>IVSd (cm)</td>
<td>1.27±0.17</td>
<td>1.41±0.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>205.8±73.0</td>
<td>281.1±87.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>115.8±37</td>
<td>159.6±48.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVH (%)</td>
<td>61.5</td>
<td>83.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA (mL)</td>
<td>3.81±0.66</td>
<td>3.96±0.47</td>
<td>NS</td>
</tr>
<tr>
<td>LAI (mL/m²)</td>
<td>2.17±0.35</td>
<td>2.25±0.31</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Values expressed as mean ± Standard deviation, RVDd: Right Ventricular Internal Dimension-Diastole. IVSd: Interventricular septum diameter, LVM: Left ventricular mass, LVMI: Left ventricular mass index, LVH: Left ventricular hypertrophy, LAI: Left atrial volume index. NS: Non statistically significant.*
In the present study overall LVH is 72.4% with more pronounced in HD group than PD group. Although the pathogenesis of LVH in CKD is considered to be multifactorial, hypertension, alterations of fluid and electrolyte balance and anemia are identified as the major determinants of LV growth in CKD and ESRD patients. From a hemodynamic view, LVH is primarily an adaptive remodeling process, compensating for an increase in cardiac work, which may be due to volume and/or pressure overload. This study revealed that LVH is more common in HD than PD patients together with SBP. This single-center study indicates that clinically relevant overhydration, as defined by BCM even in a center where much attention is paid to volume status, is very high. This indicates that the current clinical and technical tools available to help the clinician attempt to achieve euvoealma are insufficient and that an additional tool, such as BCM, can be useful in the diagnosis of overhydration as a practical and inexpensive method than other imaging techniques.

The main limitation of this study is its cross-sectional design, which enables associations but not cause and effect to be determined with certainty. The unequal distribution of age and dialysis vintage between the groups were not anticipated but were taken into account in the subsequent analysis.

In summary, HD patients are more overhydrated than PD patients. The excess fluid encourages ECW accumulation which may lead adverse effect in organ functions especially cardiac condition. The normalizing the volume status may have impact on intravascular volume, patient well-being, and residual renal function. The benefit of normalizing the volume status should be tested in carefully designed prospective randomized controlled clinical trials.

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