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Numerical expression of volume status using the bioimpedance ratio in continuous ambulatory peritoneal dialysis patients: A pilot study

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Background: Volume overload results in higher mortality rates in patients on continuous ambulatory peritoneal dialysis (CAPD). The ratio of bioimpedance (RBI) might be a helpful parameter in adjusting dry body weight in CAPD patients. This study examined whether it is possible to distinguish between non-hypervolemic status and hypervolemic status in CAPD patients by using only RBI.

Methods: RBI was calculated as follows: RBI = impedance at 50 kHz/impedance at 500 kHz. Based on the experts' judgements, a total of 64 CAPD patients were divided into two groups, a non-hypervolemic group and a hypervolemic group. The RBI was measured from right wrist to right ankle (rw-raRBI) by bioimpedance spectroscopy (BCM®, Fresenius Medical Care) before and after the peritosol was emptied. Other RBIs were measured from the right side of the anterior superior iliac spine to the ipsilateral ankle (rasis-raRBI) to control for the electro-physiological effects of peritoneal dialysate.

Results: The mean rw-raRBI of non-hypervolemic patients was higher than that of hypervolemic patients in the presence (1.141 ± 0.022 vs. 1.121 ± 0.021, $P < 0.001$) of a peritosol. Likewise, the mean rasis-raRBI of non-hypervolemic patients was higher than that of hypervolemic patients (presence of peritosol: 1.136 ± 0.026 vs. 1.109 ± 0.022, $P < 0.001$; absence of peritosol: 1.131 ± 0.022 vs. 1.107 ± 0.022, $P < 0.001$).

Conclusion: The volume status of CAPD patients was able to be simply expressed by RBI. Therefore, this study suggests that when patients cannot be analyzed using BCM, RBI could be an alternative.

Keywords: Bioimpedance, Hypervolemia, Peritoneal dialysis

Introduction

Euvolemia is an important predictor of outcome in continuous ambulatory peritoneal dialysis (CAPD) patients [1,2], as volume overload is related to cardiac dysfunction [3], pulmonary and peripheral edema [4], and increasing mortality [5]. Volume status is usually based solely on clinical observations such as blood pressure, peripheral pitting edema, and findings of cardiomegaly and/or pulmonary edema in chest X-ray [6,7]. However, these findings do not always estimate the correct volume status [8,9].

Bioimpedance spectroscopy is used to estimate volume status in CAPD patients, by measuring the impedance (Z) at various frequencies [2,10]. A Body Composition Monitor (BCM®; Fresenius Medical Care, Bad Homburg, Germany) measures bioimpedance at multi-frequencies

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over a range from 5 to 1,000 kHz. At low frequencies, the current cannot cross the cell membrane and will only flow through extra-cellular compartments; at high frequencies, the current can flow through both intra- and extra-cellular compartments. Extra-cellular water (ECW) includes blood plasma, interstitial water, and over-hydrated water. Total body water (TBW) is the sum of ECW and intra-cellular water (ICW). The BCM software can calculate and display the amounts of ECW, ICW, TBW, and over-hydration (OH), where OH is the amount of ECW excess expected for a normal subject [11].

Although validation studies to estimate the volume status by BCM have been performed [11], such measurements do not completely reflect the race, sex, age, or body size of the subjects; they also do not reflect the presence of electrically interruptible devices, third-space fluid retention, or subjects with amputations. Cha et al [12] reported that bioimpedance analysis (BIA) had important limitations for quantifying the fluid compartment in which sequestration of fluid in the trunk region frequently occurred.

In clinical practice, there is a need for a numerical index suggesting the correct volume status to adjust individual dry body weight (DBW) in CAPD patients regardless of patient characteristics. Park et al [7] reported that the ratio of bioimpedance at the right leg (rl-RBI = impedance at 50 kHz [Z50]/impedance at 500 kHz [Z500]) could be used as an objective index for determining DBW in new hemodialysis patients. Our current study examined whether we could distinguish euvolemia from hypervolemia with only RBI without software for BCM in CAPD patients.

Methods

Bioimpedance was measured by BCM at multi-frequencies from 5 to 1,000 kHz in 64 CAPD patients between January 2014 and September 2015 at Asan Medical Center in Seoul, Korea. Subjects were placed in a supine position, and the BCM's two-point tactile electrode was placed on the right wrist and right ankle, after the subjects emptied their peritoneal cavity. The amounts of OH, ECW and TBW were calculated by on-board software of the BCM device along with the patients' individual data such as age, sex, height, and weight with empty peritoneal cavity.

All patients were divided into two groups, a non-hypervolemic group and a hypervolemic group. The hypervolemic group contained patients with clinical evidence of pre-tibial pitting edema (PTPE), hypertension, cardiomegaly, and/or pulmonary edema on chest X-ray.

Clinical volume status of CAPD patients was assessed by three medical staff (two nephrologists and a nurse) from the dialysis center at Asan Medical Center. CAPD patients were separated into the hypervolemic group and the non-hypervolemic group by the agreement of two or more of these experts.

We attached an electrode to each patient's right wrist and ipsilateral ankle, and all 64 patients' RBIs were calculated as the ratio of measured Z50 and Z500. In order to avoid the electro-physiologic effects of peritoneal dialysate before and after drainage of peritosol, the electrode attachment sites were changed from right wrist and right ankle (rw-raRBI) to right anterior superior iliac spine and right ankle (rasis-raRBI).

The study was approved by the Institutional Review Board (IRB) of Asan Medical Center (No. 2016-0346). Since the current study was a retrospective observational study, the IRB waived the need for written consent from the patients.

Statistical methods

Clinical variables and measured values via BCM were summarized as the mean ± standard deviation or the median (first quartile, third quartile). Clinical variables and volumes calculated by BCM, rw-raRBI, and rasis-raRBI were compared between the two groups by parametrical or non-parametrical analysis. All statistical analyses were carried out using IBM SPSS Statistics version 20.0 (IBM Co., Armonk, NY, USA). Statistical tests were two-sided, and $P < 0.05$ was considered significant.

Results

The comparisons of the baseline characteristics between the non-hypervolemic group and hypervolemic group are summarized in Table 1. PTPE and systolic blood pressure were more severe and higher, respectively, in the hypervolemic group than in the non-hypervolemic group. The amounts of OH and ECW and the ratios of ECW/TBW and OH/ECW calculated by the BCM software were significantly higher in the hypervolemic group than in the non-hypervolemic group (Table 2).

Ham et al [13] and Wizemann et al [14] suggested OH/ECW > 7% and > 15% as criteria for volume overload, respectively. The distribution of subjects according to OH/ECW was significantly similar to the distribution according to evidence of clinical hypervolemia. The distributions of patients with volume overload under criteria of OH, OH/ECW, and clinically assessed volume status are presented in Table 3. The rw-raRBI of CAPD patients that were clinically non-hypervolemic was higher than that of hypervolemic patients in the presence of peritoneal dialysate (1.141 ± 0.022 vs. 1.121 ± 0.021, $P < 0.001$) and in its absence (1.141 ± 0.023 vs. 1.121 ± 0.021, $P < 0.001$). The rasis-raRBI in non-hypervolemic CAPD patients was also higher than that of hypervolemic patients with peritosol (1.136 ± 0.026 vs.1.109 ± 0.022, $P < 0.001$) and without peritosol (1.131 ± 0.022 vs. 1.107 ± 0.022, $P < 0.001$) (Table 4).

Table 5 shows that difference between rw-raRBI and rasis-raRBI was statistically significant in all four conditions (non-hypervolemia with peritosol: 1.141 ± 0.022 vs.1.136 ± 0.026, $P = 0.021$; non-hypervolemia without peritosol: 1.141 ± 0.023 vs.1.131 ± 0.022, $P = 0.023$; hypervolemia with peritosol: 1.121 ± 0.021 vs. 1.109 ± 0.022, $P < 0.001$;

Table 1. Comparison of baseline characteristics between the non-hypervolemic group and the hypervolemic group

Characteristic	Non-hypervolemia (n = 43)	Hypervolemia (n = 21)	*P* value
Sex, male	16 (37.2)	12 (57.1)	0.215
Age (yr)	49.5 ± 14.25	47.1 ± 15.14	0.562
Cause of ESRD			
Diabetes mellitus	7 (16.3)	9 (42.9)	0.112
Hypertension	13 (30.2)	3 (14.3)	
Glomerulus nephritis	10 (23.2)	3 (14.3)	
Others	13 (30.2)	6 (28.6)	
Duration of CAPD (mo)	67.4 (43.6, 83.2)	62.6 (15.7, 88.2)	0.663
Height (cm)	162.2 ± 8.21	163.5 ± 11.48	0.588
Weight without peritosol (kg)	61.0 (53.5, 68.5)	67.4 (51.5, 79.0)	0.169
Systolic BP (mmHg)	141 (119, 150)	160 (154, 165)	< 0.001
Diastolic BP (mmHg)	79.4 ± 13.14	85.2 ± 11.21	0.084
Heart rate (beat/min)	76.5 ± 11.94	77.7 ± 10.26	0.700
Hemoglobin (g/dL)	9.72 ± 1.74	9.98 ± 1.42	0.555
Albumin (g/dL)	3.6 (3.4, 3.8)	3.5 (3.3, 3.8)	0.620
Pretibial pitting edema	–: 43 (100)	+: 21 (100)	< 0.001

Data are presented as number (%), mean ± standard deviation, or median (first quartile, third quartile).

BP, blood pressure; CAPD, continuous ambulatory peritoneal dialysis; ESRD, end-stage renal disease.

Table 2. Comparison of calculated volumes and ratios by BCM® between the non-hypervolemic group and the hypervolemic group after drainage of peritosol

Variable	Non-hypervolemia (n = 43)	Hypervolemia (n = 21)	*P* value
OH (L)	0.8 (0.3, 1.7)	3.8 (3.0, 4.1)	< 0.001
ECW (L)	13.9 (12.4, 16.7)	17.6 (13.7, 20.8)	0.015
ECW/TBW	0.46 ± 0.04	0.50 ± 0.03	< 0.001
OH/ECW	0.07 ± 0.08	0.22 ± 0.09	< 0.001

Data are presented as median (first quartile, third quartile) or mean ± standard deviation.

BCM®, Fresenius Medical Care, Bad Homburg, Germany.

ECW, extra-cellular water; OH, over-hydration; TBW, total body water.

Table 3. Relationships between OH, OH/ECW by BCM® and clinically assessed volume status

Variable	Clinical assessment		*P* value
	Non-hypervolemia (n = 43)	Hypervolemia (n = 21)	
OH			0.060
≤ 0 L (n = 9)	9 (20.9)	0 (0)	
> 0 L (n = 55)	34 (79.1)	21 (100)	
OH/ECW			< 0.001
≤ 7% (n = 24)	23 (53.5)	1 (4.8)	
> 7% (n = 40)	20 (46.5)	20 (95.2)	
OH/ECW			< 0.001
≤ 15% (n = 39)	35 (81.4)	4 (19.0)	
> 15% (n = 25)	8 (18.6)	17 (81.0)	

Data are presented as number (%).

BCM®, Fresenius Medical Care, Bad Homburg, Germany.

ECW, extra-cellular water; OH, over-hydration.

Table 4. Comparison of ratio of bioimpedance (RBI) in accordance with clinically assessed volume status

RBI	Non-hypervolemia (n = 43)	Hypervolemia (n = 21)	*P* value
rw-ra			
Dialysate (+)	1.141 ± 0.022	1.121 ± 0.021	< 0.001
Dialysate (–)	1.141 ± 0.023	1.121 ± 0.021	< 0.001
rasis-ra			
Dialysate (+)	1.136 ± 0.026	1.109 ± 0.022	< 0.001
Dialysate (–)	1.131 ± 0.022	1.107 ± 0.022	< 0.001

Data are presented as mean ± standard deviation.

rw-ra, right wrist to right ankle; rasis-ra, right anterior superior iliac supine to right ankle.

Table 5. Relationship between the clinical volume status and the ratio of bioimpedance (RBI) according to the presence of peritosol and the measuring sites

RBI	Non-hypervolemia (n = 43)		*P* value	Hypervolemia (n = 21)		*P* value
	Dialysate (+)	Dialysate (–)		Dialysate (+)	Dialysate (–)	
rw-ra	1.141 ± 0.022	1.141 ± 0.023	0.621	1.121 ± 0.021	1.121 ± 0.021	0.520
rasis-ra	1.136 ± 0.026	1.131 ± 0.022	0.505	1.109 ± 0.022	1.107 ± 0.022	0.821
P value	0.021	0.023		< 0.001	< 0.001	

Data are presented as mean ± standard deviation

rw-ra, right wrist to right ankle; rasis-ra, right anterior superior iliac supine to right ankle.

hypervolemia without peritosol: 1.121 ± 0.021 vs. 1.107 ± 0.022, $P < 0.001$). However, regardless of measured sites and presence or absence of peritoneal dialysate, RBIs did not show any difference between groups (rw-raRBI in non-hypervolemia: 1.141 ± 0.022 vs. 1.141 ± 0.023, $P = 0.621$; rw-raRBI in hypervolemia: 1.121 ± 0.021 vs. 1.121 ± 0.021, $P = 0.520$; rasis-raRBI in non-hypervolemia: 1.136 ± 0.026 vs. 1.131 ± 0.022, $P = 0.505$; rasis-raRBI in hypervolemia: 1.109 ± 0.022 vs. 1.107 ± 0.022, $P = 0.821$).

Discussion

BCM is a well-known device to measure amount of volume overload. However, RBI could also be used to distinguish hypervolemic patients from non-hypervolemic patients. Although the software on the BCM required multiple frequencies from 5 to 1,000 kHz, individual patient data in the specific model, and data in the standardized population, RBI at 50 and 500 kHz did not require a model or any data for a standardized population or any patient information for its calculation. Although RBI cannot quantitatively estimate the degree of volume overload, unlike the OH of BCM, it has the potential for development, such as miniaturization of the device, simplified instructions, and high portability in clinical practice. If many studies of RBI are performed, a target range of RBI reflecting non-hypervolemia can be determined. This pilot study confirmed the possibility that RBI could be a novel numerical index for estimation of volume status in CAPD patients.

Considering that higher survival rates have been associated with more suitable removal of fluid by peritoneal dialysis [15], and that greater amounts of excess body fluid were found to be related to higher mortality in CAPD patients [16], an optimal volume status is expected to be associated with better survival in CAPD patients.

Although peritoneal dialysis has the advantage of effective control of excessive body fluid and hypertension compared to hemodialysis [17], peritoneal dialysis patients tend to have more excess body fluid than hemodialysis patients [18]. This excessive body fluid is an appropriate explanation for the high cardiovascular mortality rate in peritoneal dialysis patients. Accurate determination of adequate body fluid status might decrease cardiovascular mortality rates, but over-strict body fluid control could decrease the patient's residual renal function [19].

Although the estimation of volume status using deuterium and tritium is the gold standard [20], it is not cost-effective in clinical practice. Physical and radiological examinations are frequently used to estimate volume status, but they are semi-quantitative and subjective methods that are not suitable to identify optimal DBW in CAPD patients. By contrast, BCM is an available device that objectively and reproducibly measures body weight- or height-normalized OH.

Cha et al [12] have reported that BIA had important limitations when quantifying fluid compartments in the sequestration of fluid in the trunk. Hence, we created another parameter of bioimpedance, between the right anterior superior iliac spine and right ankle, to avoid the effects of peritoneal dialysate and compared rasis-raRBI with rw-raRBI. However, an rw-raRBI difference between with peritosol and without peritosol were not observed in either the hypervolemic group (1.121 ± 0.021 vs. 1.121 ± 0.021, $P = 0.520$) or the non-hypervolemic group (1.141 ± 0.022 vs. 1.141 ± 0.023, $P = 0.621$) (Table 5). This might have resulted from the relatively small amount of peritoneal dialysate retained compared to ECW or TBW.

In a healthy population without cardiovascular, renal, hepatic, or endocrine disease, the ratio of ECW to TBW will be maintained within a specific narrow range. In our current study series, both RBIs were significantly higher in the non-hypervolemic group than in the hypervolemic group. This suggests that RBI can be used as an index of volume overload. However, we found significant differences between rasis-raRBI and rw-raRBI in all four conditions (Table 5). This suggests the importance of location when measuring bioimpedance. It is necessary to obtain target ranges of RBI according to specific measurement sites.

RBI can be easily applied to patients with a pacemaker, which could interrupt flow of current, or with amputated extremities onto which it is impossible to attach leads. However, measurable segments and the standard value of each segment should be studied in large-scale prospective studies.

When we attached leads to the right anterior superior iliac spine and right ankle, the OH, ECW, and TBW amounts calculated by BCM were incorrect and unacceptable as most patients' TBW was higher than their body weight and/or OH was higher than ECW. This resulted from the BCM recognizes the human body as one-cylinder. BCM can only calculate the impedance between the wrist and the ankle.

There were several limitations to this study. It was a single-center study with a small study population and no control group. In future studies, more data on RBI for all extremities will enable the estimation of volume status and avoidance of electrical interference in patients with implantable cardioverter defibrillators [21]. Another large-scale study is needed to overcome these limitations.

In conclusion, our study showed that RBI could be a novel numerical index for estimating the volume status in CAPD patients. For calculating RBI, there is no need for information such as age, sex, height, and weight, which are essential for use of BCM. Therefore, an RBI spectroscope could be smaller, less expensive, and more convenient to use than BCM. In addition, in patients who cannot be tested with BCM, RBI could be an alternative by calculating other segments of the body.

Conflicts of interest

All authors have no conflicts of interest to declare.

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