ORIGINAL ARTICLE

Bioimpedance spectroscopy method to determine hypervolemia in maintenance hemodialysis patients

Merhametsiz O[1], Oguz EG[1], Yayar O[1], Bektan B[2], Canbakan B[1], Ayli D[1]

[1]Department of Nephrology, Diskapi Yildirim Beyazit Training and Research Hospital
[2]Department of Internal Medicine, Ankara Numune Training and Research Hospital
Ankara, Turkey

Abstract

Background: Hypervolemia is a major risk factor for hypertension leading to cardiovascular diseases and also a frequent problem in maintenance hemodialysis (MHD) patients. Fluid overload (FO) can be determined by bioimpedance spectroscopy (BIS) which is a new, practical, and non-invasive method. We tried to determine FO by BIS in MHD patients and find out the relationship between FO and clinical features.

Material and Methods: We studied 100 MHD patients aged between 20 and 85 years and undergoing hemodialysis three times weekly for minimum one year. By using BIS, we estimated FO and extracellular water (ECW). The patients who exhibited a FO/ECW ratio >15% were considered as FO.

Results: Twenty-nine (29.0%) patients had a FO/ECW ratio >15%. In the overhydrated group, the mean pre-hemodialysis systolic blood pressure was 153.3 ± 20.0 mmHg and the mean diastolic blood pressure was 89.1 ± 8.5 mmHg. These were significantly higher than in the non-overhydrated group (113.5 ± 14.5 and 71.0 ± 8.8, p <0.001). FO was significantly correlated with systolic and diastolic blood pressures (r =0.63, p <0.001 and r =0.59, p <0.001). The patients were divided into two groups, i.e. those with cardiothoracic index (CTI) of >0.5 and those with CTI of ≤0.5. The median FO/ECW ratio was 0.11 L in the former group and 0.08 L in the latter group with a significant difference (p =0.006).

Conclusions: Hypervolemia is associated with high blood pressure and left ventricular hypertrophy that should be treated effectively to prevent cardiovascular diseases in MHD patients. BIS is useful to assess hydration status in MHD patients. Hippokratia 2015; 19 (4): 324-331.

Keywords: Bioimpedance spectroscopy, hemodialysis, hypervolemia, hypertension, overhydration

Corresponding Author: Ebru Gok Oguz, Department of Nephrology, Diskapi Yildirim Beyazit Education and Research Hospital, 3210, Ankara, Turkey, tel: +905063148406, fax: +903123116351, e-mail: ebrugokoguz@hotmail.com

Introduction

Cardiovascular disorders and hypertension are the leading causes of mortality in maintenance hemodialysis (MHD) patients[1]. Hypervolemia is a specific contributor to arterial hypertension among these patients. Volume status can be evaluated with the cardiothoracic index (CTI) based on telecardiography and with the diameter of the left atrium, the thickness of the left ventricular wall, and the diameter of the inferior vena cava based on transthoracic echocardiography in addition to clinical signs[2]. In recent years, bioimpedance spectroscopy (BIS) has attracted attention as it is easy to use, reliable and non-invasive. This method, during which electric currents in low frequencies are transmitted through the human body, was first used in 1969 to measure the total fluid volume of the body. Volume and composition of the body fluids are determined based on conduction features of tissues. Tissues containing fluids and electrolytes are more conductive and fluid volume of these tissues can be measured by BIS; however, fluid volume of fat tissue, bones and spaces containing air cannot be measured with this method[3].

In this study, we aimed to investigate the potential clinical and biochemical parameters which could influence hypervolemia evaluated by BIS in maintenance MHD patients. The study was also directed towards showing that BIS, which is simple, inexpensive, non-invasive and quick to use, could be employed in clinical practice.

Material and Methods

Study population

This is a retrospective study. It was performed on hemodialysis patients in a private hemodialysis (HD) center (Ankara Life) between 1 and 31 October in 2013. One hundred and thirty patients, older than 18 years of age and having a four-hour hemodialysis session three times weekly for minimum one year, were examined for eligibility for this study. Patients with coronary artery stents, implanted defibrillators and cardiac pacemakers, and those who underwent extremity amputation and/or had metal prosthesis and artificial joints were excluded.

Pregnancy, lactation, acute/chronic infection, malignancy, severe cardiac, pulmonary or hepatic failures were also defined as exclusion criteria. Thirty patients were excluded and a total of 100 MHD patients (55 males/45 females) were included in the study. The study protocol was implemented in accordance with the Declaration of Helsinki Protocol and approved by Ankara Numune Education and Research Hospital Scientific Ethical Committee (approval number: 696-2013, 4/12/2013).

Study design

We collected data about demographic features (age, gender, height, weight, body mass index, and body surface area), clinical features (presence of diabetes, antihypertensive medication use, duration of HD, systolic and diastolic blood pressures before and after HD, and mean arterial blood pressure), results of BIS (extracellular water, total body water, excess extracellular water, fat tissue mass, and lean tissue mass), results of recent laboratory investigations (equilibrated Kt/V, URR, albumin, total calcium, phosphorus, parathormone, ferritin, transferrin saturation, C-reactive protein (CRP) and haemoglobin), and CTI based on telecardiography. Biochemical analyses were made with the MODULAR P 800 (Roche Diagnostics, Mannheim, Germany) and hemogram was measured with the XE 2100 (Roche Diagnostic, Japan).

Measurements made with body composition monitor (BCM) before and after dialysis in the midweek, and systolic and diastolic blood pressures measured with sphygmomanometer were used. Weight was measured with the same standard scale before and after HD, and height was measured with the same stadiometer in all the patients. Body mass index (BMI) was calculated by the following formula: Weight /Height^2 (kg/m^2).

Body surface area (BSA) was calculated with DuBois formula (weight $^{0.425}$ x Height $^{0.725}$) x 0.007184 and expressed in m^2. Mean arterial pressure (MAP) was calculated by the following formula: diastolic blood pressure (DBP) + [systolic blood pressure (SBP) – DBP]/3.

CTI was based on measurements obtained with BCM and posterior-anterior pulmonary x-rays taken when the x-ray tube was 180 cm away from the chest, and the ratio cardiac diameter/chest diameter was used. CTI >0.5 suggested cardiomegaly.

Bioimpedance

BCM (Fresenius Medical Care D GmbH, Germany) was used to perform BIS, to measure fluid status and body composition. We used BIS values obtained before dialysis in the midweek. Measurements were made when the patients were lying on their back with their arms and legs were slightly abducted. We used a total of four electrodes, of which two were placed 1cm proximal to metacarpophalangeal joints on dorsal sides of the hands and two were placed 1cm proximal to metatarsophalangeal joints on dorsal sides of the feet. The electrodes were placed on the arms without venous routes used for HD. After data about age, weight and height were recorded, it took 1-4 minutes to complete BIS measurements for each patient. The electrodes were not removed until the measurements were completed. Meanwhile, the patients were not allowed to eat or drink. The measurements were made before HM in all the patients. We used in the study the values recorded for extracellular water (ECW), total body water (TBW), fluid overload (FO), lean tissue mass (LTM), and fat tissue mass (FTM). FO values obtained through BIS and the FO/ECW ratio calculated later were used to evaluate hydration status. In light of the literature[4], a FO/ECW ratio >15% was accepted as FO. Fat tissue and lean tissue were evaluated with fat tissue index (FTI) and lean tissue index (LTI) respectively. Fat tissue index was calculated as fat tissue mass/height^2 and LTI was calculated as lean tissue mass/height^2.

Statistical analyses

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) version 20 (SPSS, Chicago, IL, USA). Distributions of variables were evaluated by the Kolmogorov-Smirnov test. Continuous data are presented as mean ± standard deviation or median and minimum-maximum values depending on their distribution. For two group comparisons, the Student's t-test was used for variables that met parametric test conditions and the Mann-Whitney U-test for the others. Categorical data are presented as frequencies and percentages; χ^2 test and Fisher's exact tests were used when appropriate. Independent predictors for overhydration and CTI >0.5 were determined by logistic regression analyses. Cut-off values for the independent predictors were calculated with ROC curve analysis and Youden's Index. $p < 0.05$ was accepted as significant for all statistical analyses.

Results

Demographic features and laboratory results of the study sample and patients with FO

The study included a total of 100 patients, of whom 55 were male (55.0%), and 45 were female (45.0%). The mean age of the patients was 58.8 ± 15.1 years. Of all the patients included, 29 (29.0%) were found to have FO. A higher rate of the male patients had overhydration (79.3 vs. 45.1, p =0.002). The patients with FO had a higher BMI (27.0 ± 5.2 vs. 22.5 ± 3.4, p <0.001) (Table 1).

SBP and DBP decreased after dialysis (SBP: 132.4 ± 20.4 vs. 109.3 ± 13.9; DBP: 80.0 ± 9.8 vs. 68.6 ± 8.6, p <0.001). Decreases in SBP and DBP were more remarkable in the patients with FO (SBP: 39.8 vs. 16.3; DBP: 18.1 vs. 8.5, p <0.001) (Figure 1a, Figure 1b). In the FO group, the mean pre-HD SBP was 153.3 ± 20.0 mmHg and the mean DBP was 89.1 ± 8.5 mmHg. They were significantly higher than in the non-FO group (113.5 ± 14.5 and 71.0 ± 8.8, p <0.001). FO was significantly correlated with systolic and diastolic blood pressures (r =0.63, p < 0.001 and r =0.59, p < 0.001).

The patients with FO (n =29) had significantly higher ECW and total body fluid (TBF) volumes (18.1 ± 3.8 vs. 14.7 ± 2.7 and 34.3 ± 6.7 vs. 30.1 ± 5.2 respectively; p

Table 1: Demographic features of the study sample that included in total 100 of whom 29 (29.0%) were found to have fluid overload.

Variables	All population (n=100)	FO		p
		Yes (n=29)	No (n=71)	
Age (years)	58.81 ± 15.1	55.62 ± 16.8	61.52 ± 14.1	0.076
Sex (male) n (%)	55 (55)	23 (79.3)	32 (45.1)	0.002
Height (m)	1.61 ± 0.09	1,64 ± 0,09	1.59 ± 0.09	0.035
Weight (kg)	66.85 ± 14.7	69.66 ± 14.8	59.95 ± 12.4	0.002
BMI (kg/m²)	25.67 ± 5.1	26.97 ± 5.2	22,46 ± 3.4	0.001
Body surface area (m²)	1,73 ± 0.2	1.67 ± 0.2	1,66 ± 5.2	0.064
HD duration (year)	8 (1-31)	8 (1-31)	5 (1-28)	0.181
Diabetes mellitus n (%)	28 (28)	7 (24.1)	21 (29.6)	0.633
Antihypertensive treatment	41 (41)	14 (48.3)	27 (38.0)	0.377
Vascular accsess n (%)				
Fistula	86 (86)	22 (75.9)	64 (90.1)	0.091
Catheter	13 (13)	6 (20.7)	7 (9.9)	
Graft	1 (1)	1 (3.4)		

FO: fluid overload, BMI: Body mass index, HD: hemodialysis, n: number, data are presented as mean ± standard deviation or number (percentage).

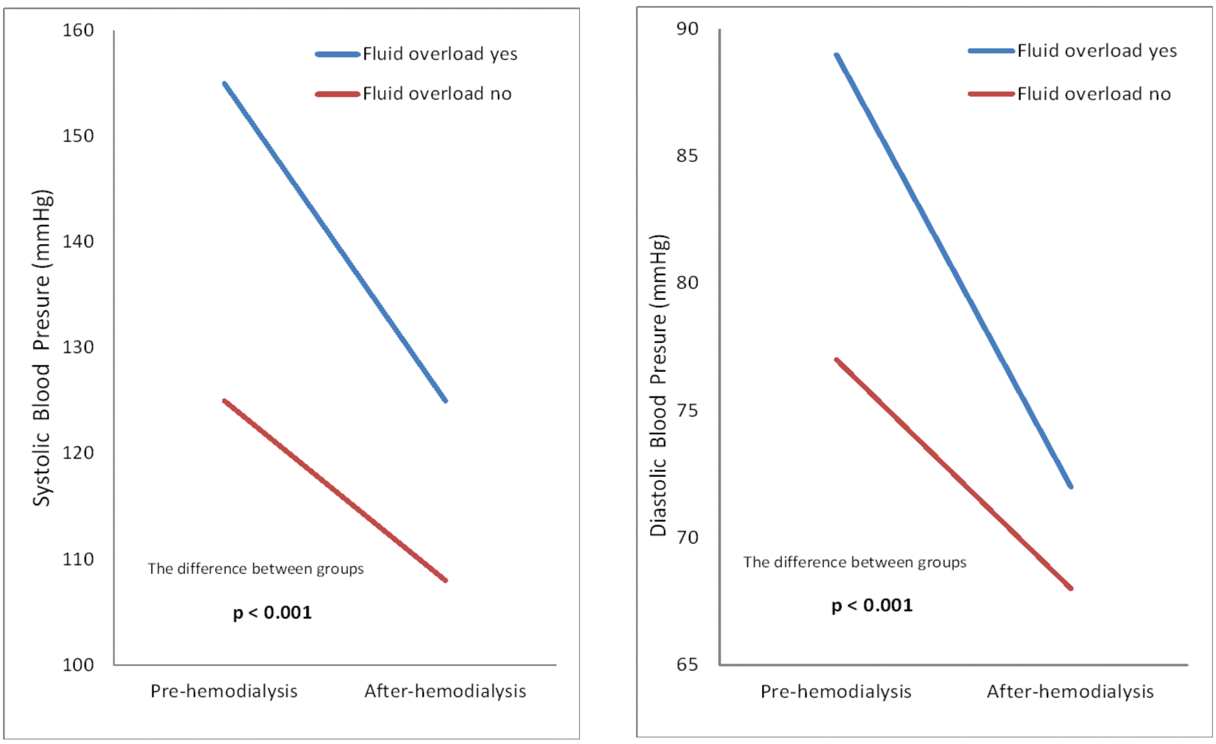

Figure 1: In the 29 of the total 100 maintenance hemodialysis patients, who were found to have fluid overload, the decreases in systolic blood pressure (SBP) and in diastolic blood pressure (DBP) after dialysis were more remarkable. **1a:** SBP: 39.8 vs. 16.3 mmHg; p <0.001. **1b:** DBP:18.1 vs. 8.5 mmHg; p <0.001.

<0.001, p =0.001). These patients also had significantly higher lean tissue mass (54.6 ± 12.9 vs. 44.5 ± 13.1, p =0.001), but significantly lower fat tissue mass (28.9 ± 10.1 vs. 38.3 ± 9.9, p =0.001). In addition, they had significantly higher median CRP (1.10 vs. 0.67, p =0.012). Fifty-five percent of all the patients had CTI >0.5. A significantly higher rate of the patients with overhydration had CTI >0.5 (75.9% vs. 46.5%, p=0.008). The patients with FO had a significantly higher FO/ECW (0.18 vs. 0.07), ECW/TBW (0.53 ± 0.07 vs. 0.49 ± 0.06, p =0.01) and ECW/height (11.0 ± 2.2 vs. 9.2 ± 1.5, p <0.001). They also had a significantly higher ECW/BSA (10.8 ± 2.3 vs.

8.45 ± 1.2, p <0.001) and LTI (20.1 ± 4.9 vs. 17.3 ± 4.6, p =0.009). FTI was significantly lower in these patients (11.0 ± 4.3 vs. 34.0 ± 5,0, p <0.001) (Table 2).

Independent Variables Predictive of FO

Risk factors found significant in the single factor analysis were analysed with multiple regression analysis. SBP (OR =1.156, p <0.001), CRP (OR =1.576, p =0.023), ECW/BSA (OR =3.776, p <0.001) and LTI (OR =1.110, p =0.021) before HD were independent risk factors which were predictive of FO. When effects of the risk factors in the multiple regression models were removed, overhydration was found to be affected most by ECW/BSA (Table 3).

Table 2: Laboratory results of the study sample that included in total 100 of whom 29 (29.0%) were found to have fluid overload.

Variables	All population	FO		p
		Yes (n=29)	No (n=71)	
ECW (L)	15.70 ± 3.4	18.08 ± 3.8	14.7±2.7	<0.001
TBW(L)	31.29 ± 5.9	34.29 ± 6.7	30.06 ± 5.2	0.001
FO (L)	1.43 (0.02-4.96)	3.02 (1.40-4.96)	1.12 (0.02-2.81)	<0.001
Lean tissue mass (kg)	47.37 ± 13.7	54.59 ± 12.9	44.53 ± 13.1	0.001
Fat tissue mass (kg)	35.63 ± 10.8	28.85 ± 10.1	38.31 ± 9.9	0.001
Equilibrated Kt/V	1.59 ± 0.3	1.60 ± 0.3	1.58 ± 0.2	0.741
URR (%)	78.41 ± 5.6	78.32 ± 6.6	78.45 ± 5.2	0.919
Transferrin saturation	24.9 (3.9-77.1)	25.35 (12.4-77.1)	24.8 (3.9-71.9)	0.562
Hemoglobine (g/dl)	11.6 ± 1,8	11.24 ± 2.5	11.75 ± 1.4	0.190
Ferritin (ng/ml)	589 (28-2103)	530 (28-2103)	623.5 (37-1618)	0.358
Total calcium (mg/dl)	9.24 ± 0.8	9.29 ± 0.9	9.22 ± 0.8	0.702
Phosphorus (mg/dl)	5.39 ± 1.5	5.10 ± 1.2	5.50 ± 1.6	0.230
Parathormone, (ng/l)	338.25 (10.55-1852)	290 (37.16-1218.8)	356.3 (10.55-1852)	0.729
Albumin (g/dl)	4.01 ± 0.4	3.96 ± 0.4	4.03 ± 0.4	0.461
CRP (mg/dl)	0.70 (0.02-16.13)	1.10 (0.11-16.13)	0.67 (0.02-8.30)	0.012
CTI increase n (%)	55 (55)	22 (75.9)	33 (46.5)	0.008
FO/ ECW	0.093 (0-0.27)	0.18 (0.08-0.27)	0.07 (0-0.22)	<0.001
ECW/TBW	0.50 ± 0.06	0.53 ± 0.07	0.49 ± 0.06	0.010
ECW/height (L/m)	9.71 ± 1.9	11.0 ± 2.2	9.2 ± 1.5	<0.001
ECW/BSA (L/m^2)	9.12 ± 1.9	10.75 ± 2.3	8.45 ± 1.2	<0.001
LTI (kg/m^2)	18.14 ± 4.8	20.10 ± 4.9	17.34 ± 4.6	0.009
FTI (kg/m^2)	14.10 ± 5.2	11.04 ± 4.3	15.34 ± 5.0	<0.001

FO: fluid overload, ECW: extracellular water, TBW: total body water, URR: urea reduction ratio, CRP: C-reactive protein, CTI: cardiothoracic index, BSA: body surface area, LTI: lean tissue index, FTI: fat tissue index, n: number, data are presented as mean ± standard deviation, median (minimum-maximum values) or number (percentage).

Table 3: Independent variables predictive of fluid overload. Risk factors found significant in the single factor analysis were analysed with multiple regression analysis and overhydration was found to be affected most by ECW/BSA (extracellular water/body surface area).

Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Sex	4.672 (1.697-12.863)	0.003		
BMI	1.253 (1.109-1.412)	<0.001		
Pre-HD SBP	1.116 (1.068-1.166)	<0.001	1.156 (1.079-1.238)	<0.001
Pre-HD DBP	1.239 (1.137-1.350)	<0.001		
CRP	1.195 (1.010-1.428)	0.015	1.576 (1.099-2.260)	0.023
Lean tissue	1.059 (1.021-1.098)	0.002		
Fat tissue	0.914 (0.871-0.960)	<0.001		
ECW/TBW	1.094 (1.013-1.183)	0.023		
ECW/Height	1.778 (1.318-2.398)	<0.001		
ECW/BSA	2.990 (1.747-5.119)	<0.001	3.766 (1.879-7.548)	<0.001
LTI	1.127 (1.025-1.240)	0.014	1.110 (1.020-1.180)	0.021
FTI	0.827 (0.744-0.919)	<0.001		

BMI: body mass index, Pre-HD: pre- hemodialysis, SBP: systolic blood pressure, DBP: diastolic blood pressure, CRP: C-reactive protein, ECW: extracellular water, TBW:total body water, BSA:body surface area, LTI: lean tissue index, FTI: fat tissue index, OR: odds ratio, CI: confidence interval.

Demographic Features and Laboratory Results in the Patients with CTI >0.5 and those with CTI ≤0.5

The patients with CTI >0.5 (n =47) were significantly older than those with CTI <0.5 (63.4 ± 11.9 vs. 57.0 ± 13.2, p =0.01) (Table 4). SBP, DBP and MAP after HD were significantly lower in the patients with CTI >0.5 than in those with CTI <0.5 [(SBP: 21.9 vs. 18.2; DBP: 13.2 vs. 10.1; MAP: 13.4 vs. 10.1; p <0.001)] (Figure 2a, Figure 2b, Figure 2c).

Median FO was 1.63 L in the patients with CTI >0.5 and 1.22 L in those with CTI <0.5 (p =0.017). A significantly higher rate of the patients with CTI >0.5 had FO (40.0% vs. 15.6%, p =0.008). The mean FO /ECW was 0.11 L in the patients with CTI >0.5 and 0.08 L in those with CTI <0.5 (p =0.006). There was not a significant difference in ECW/TBW, ECW/height, ECW/BSA, LTI and FTI between the patients with CTI >0.5 and those with CTI <0.5 (Table 5).

Table 4: Demographic features in the 47 patients with cardiothoracic index >0.5 and in the 53 with cardiothoracic index ≤0.5.

Variables	CTI >0.50 (n=47)	CTI ≤0.50 (n=53)	p
Age (years)	63.40 ± 11.9	56.95 ± 13.2	0.010
Sex (male) n (%)	34 (61.8)	21 (46.7)	0.130
Height (m)	1.62 ± 0.09	1.60 ± 0.09	0.341
Weight (kg)	67.37 ± 14.8	66.20 ± 14.7	0.868
BMI(kg/m²)	26.03 ± 5.5	25.37 ± 4.8	0.444
Body surface area (m²)	1.73 ± 0.2	1.72 ± 0.2	0.905
HD duration (year)	7 (1-31)	8 (1-23)	0.622
Diabetes mellitus n (%)	12 (21.8)	16 (35.6)	0.179
Antihypertensive treatment	23 (41.8)	18 (40.0)	0.995
Vascular accsess n (%)			
Fistula	49 (89.1)	37 (82.2)	0.24
Catheter	5 (9.1)	8 (17.8)	
Graft	1 (1.8)		

CTI: cardiothoracic index, BMI: body mass index, HD: hemodialysis, n: number, data are presented as mean ± standard deviation or number (percentage).

Table 5: Laboratory results in the 47 patients with cardiothoracic index >0.5 and in the 53 with cardiothoracic index ≤0.5.

Variables	CTI >0.50 (n=47)	CTI ≤0.50 (n=53)	p
ECW(L)	15.84 ± 3.4	15.50 ± 3.4	0.618
TBW (L)	31.36 ± 6.3	31.20 ± 5.6	0.897
FO (L)	1.63 (0.27-4.96)	1.22 (0.02-4.66)	0.017
Lean tissue (kg)	49.54 ± 12.4	44.55 ± 14.8	0.069
Fat tissue (kg)	34.35 ± 9.9	37.32 ± 11.7	0.173
Equilibrated Kt/V	1.58 ± 0.3	1.60 ± 0.3	0.813
URR (%)	78.25 ± 5.4	78.61 ± 5.9	0.754
Transferrin saturation	23.65 (3.89-77.09)	27.47 (6.04-59.22)	0.406
Hemoglobine (g/dl)	11.64 ± 1.65	11.55 ± 2.1	0.805
Ferritin (ng/ml)	570 (28-2103)	596 (37-1555)	0.304
Total calcium (mg/dl)	9.40 ± 0.8	9.34 ± 0.8	0.132
Phosphorus (mg/dl)	5.37 ± 1.5	5.40 ± 1.6	0.932
Parathormone (ng/l)	404.9 (10.55-1218)	273.86 (48.74-1852.4)	0.220
Albumin (g/dl)	3.98 ± 0,4	4.04 ± 0.4	0.460
CRP (mg/dl)	0.89 (0.02-16.13)	0.61 (0.02-6.11)	0.211
Overhydration n (%)	22 (40.0)	7 (15.6)	0.008
FO / ECW	0.11(0-0.16)	0.08(0-0.21)	0.006
ECW/TBW	0.51 ± 0.07	0.49 ± 0.05	0.319
ECW/Boy (L/m)	9.76 ± 1.9	9.66 ± 1.9	0.803
ECW/BSA (L/m²)	9.21 ± 1.9	9.00 ± 1.9	0602
LTI (kg/m²)	18.82 ± 4.2	17.31 ± 5.5	0.124
FTI (kg/m²)	13.42 ± 4.78	14.91 ± 5.6	0.155

CTI: cardiothoracic index, ECW: extracellular water, TBW: total body water, FO: fluid overload, URR: urea reduction ratio, CRP: C-reactive protein; BSA: body surface area, LTI: lean tissue index, FTI: fat tissue index, n: number, data are presented as mean ± standard deviation, median (minimum-maximum values) or number (percentage).

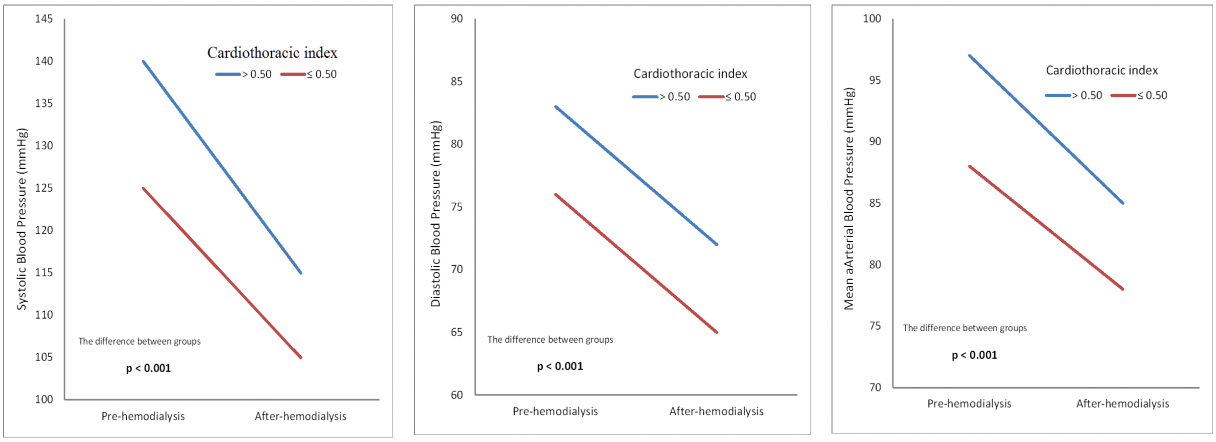

Figure 2: In the 47 of the total 100 maintenance hemodialysis patients, who were found to have cardiothoracic index (CTI) >0.5, the decreases in systolic blood pressure (SBP), diastolic blood pressure (DBP) and in mean arterial pressure (MAP) after dialysis were more remarkable. **2a:** SBP: 21.9 vs. 18.2 mmHg; p <0.001. **2b:** DBP: 13.2 vs. 10.1 mmHg; p <0.001. **2c:** MAP: 13.4 vs. 10.1 mmHg; p <0.001.

Independent Risk Factors Predictive of CTI >0.5

Multiple regression analysis of the risk factors found to be significant in the single factor logistic regression analysis was made. Age (OR =1.056, p =0.011) was predictive of CTI >0.5. FO (OR =4.340, p =0.015) and SBP (OR =1.041, p =0.006) and MAP before HM (OR =1.081, p =0.013) were also predictive of CTI >0.5. When effects of the risk factors in the multiple regression model were removed, the patients with FO were found to be 4.340 times more likely to have CTI >0.5 than those without FO (Table 6).

Discussion

In MHD patients it is of great importance to reduce volume loads and to achieve dry weight, in order to prevent cardiovascular complications. Dry weight is defined as the lowest weight which can be tolerated without development of hypovolemia symptoms during dialysis in HD patients[5]. Many studies have shown that dry weight, one of the most important indicators of sufficiency of HD, causes a considerable decrease in morbidity and mortality[6,7]. Ozdoğan et al in their study found that an interdialytic weight gain of 1% increases mortality by 22%. This underlines the importance of volume control in HD patients[8]. However, draining excess fluid leads to intradialytic and postdialytic complications and provokes acute ischemic events, which may cause organ damage[9,10]. Shoji et al in their two-year study on 1244 HD patients found that hypotension increased significantly the mortality in these patients[11]. Therefore, reliable methods which can determine volume status easily and accurately, are needed. At present, although dry weight is mostly determined based on clinical assessment, several other parameters can also be used. Measuring the diameter of the vena cava on echocardiography, monitoring relative blood volume, performing ultrasonography of the chest for pulmonary congestion and measuring atrial natriuretic peptide, cGMP, serum sodium, haematocrit, albumin, and renin-aldosterone concentrations can show differences in volume loads. However, the results of these tests can be misleading in the presence of cardiac valve disease, congestive heart disease, anaemia, and malnutrition. Moreover, some of the above methods are quite expensive and can be performed in few health centers. Another disadvantage is their inability to show overhydration quantitatively[12]. In recent years, in addition to clinical parameters which allow sensitive and objective evaluations, BIS has been extensively studied. This method allows determining features of hydration and fluid

Table 6: Independent risk factors predictive of cardiothoracic index >0.5. When effects of the risk factors are removed in the multiple regression model, the patients with fluid overload are found to be 4.340 times more likely to have cardiothoracic index >0.5 than those without.

Variables	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.043 (1.010-1.079)	0.013	1.056 (1.012-1.102)	0.011
Pre-HD SBP	1.052 (1.024-1.080)	<0.001	1.041 (1.012-1.072)	0.006
Pre-HD DBP	1.103 (1.047-1.163)	<0.001		
Pre-HD MAP	1.114 (1.054-1.177)	<0.001	1.081 (1.016-1.149)	0.013
Overhydration amount	1.609 (1.096-2.362)	0.015		
Overhydration presence	3.619 (1.372-9.547)	0.009	4.340 (1.559-12.084)	0.015
FO/ ECW	1.108 (1.032-1.190)	0.005		

Pre-HD: pre-hemodialysis, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: Mean arterial pressure, FO: fluid overload, ECW: extracellular water; OR: odds ratio, CI: confidence interval.

composition of the body by transmitting alternating currents in different frequencies through the body, by using conductive features of tissues and depending on decreases in voltages[3]. Cells act as an insulator and prevent conduction of currents at low frequencies, which shows ECW. However, they become conductive under the influence of currents at high frequencies, which can be transmitted in intracellular and extracellular fluids, which shows TBW. FO, i.e. excess extracellular water, is determined by comparing extracellular fluid volumes from patients with reference values from healthy controls[13]. In studies on HM patients, it was concluded that bioelectrical impedance analysis can be considered an objective criterion for maintaining dry weight and keeping blood pressure under control[14,15]. Wizemann et al in a study followed 269 HM patients for 3.5 years and made measurements with BCM. The researchers considered 15% as the cut-off value of FO/ECW ratio and found that mortality was remarkably high in hypervolemic patients when the cut-off value was over 15%[4]. In the present study, the patients with FO/ECW ratio >0.15 were considered hypervolemic, and 29% of the study sample were found to have FO.

Consistent with the literature, this study revealed that SBP, DBP and MAP were higher in the patients with hypervolemia determined with BIS than in those without hypervolemia. In addition, a significantly higher rate of the patients with hypervolemia had high CTI, indicator of left ventricular hypertrophy (LVH). This suggested that measurements with BIS were correlated with clinical findings and that BIS is a reliable method.

However, Maduell et al reported that BCM was not sensitive enough to show excess fluid less than three litres[16]. Since the patients in this study were assigned to the groups based on FO/ECO ratio, i.e. those with FO/ECW >15% and those with FO/ECW <15%, whether the quantity of the volume load affected the sensitivity of the method could not be evaluated.

In several studies, ECW/BSA has been used in normalization of FO measured with BIS[17]. In this study, ECW/BSA was found to be related to FO/ECW. This suggested that both ECW/BSA and FO/ECW could be used in normalization of BIS values. Liu et al started a study in 2012 and planned to include more than 1300 patients in 16 centers, to compare fluid management guided by BCM with that based on clinical findings, mortality and frequencies of cardiovascular and cerebrovascular events. The results of this comprehensive study have yet to be reported and will undoubtedly shed light on the issue[18].

The most frequent cardiovascular diseases are hypertension and resultant LVH. Chen et al in their study found that ECW was higher in hypertensive patients than in normotensive patients. They concluded that decreased ECW caused blood volume to retur n to normal in these patients[19]. Machek et al categorized patients into two groups, that is, those with FO/ECW >15% and those with FO/ECW ≤15%. They adjusted the volume so that FO/ECW would be 5-15% for one year. At the end of this one year in their study, blood pressure returned to normal in the patients with FO and their need for antihypertensive treatment decreased, and intradialytic complications disappeared after normal fluid volume was achieved in the patients with low hydration[20]. Ozkahya et al reported that rigorous control of fluid volume and restriction of sodium in oral diet reduced interdialytic weight gain, blood pressure, and the need for antihypertensive treatment. This allowed achieving desirable blood pressure results with HM alone without antihypertensive treatment[21]. Moissl et al in their study lasting for three months showed that fluid management guided by BIS brought about considerable improvements in blood pressures in HM patients. They reported that as the fluid volume decreased by 1 lt, predialysis SBP decreased by 9.9 mmHg[14]. Compatible with the literature, the present study showed that reductions in systolic and diastolic blood pressures after HD were more remarkable in the patients with hypervolemia, but that MAP did not differ.

LVH increases cardiovascular morbidity and mortality, and many studies have indicated a relation between regression of LVH and decreased mortality. Considering that mortality in patients with end-stage renal failure is 10-20 times higher than in the general population, regression of LVH becomes more important[22]. In a study by Ozkahya et al on HD patients, LVH was evaluated based on echocardiographic findings and CTI. It was shown to regress with restriction of salt and ultrafiltration without antihypertensive treatment[23]. In addition, Hür et al showed that evaluation of volume loads with BIS provided a better fluid management, which caused a decrease in blood pressure, in turn resulting in regression of LVH[24]. Consistent with the literature, the present study revealed that age, SBP, DBP, MAP, presence and degree of FO and FO/ECW before HD independently affected LVH. In a study by Seibert et al, blood pressure decreased, and LVH regressed in the patients undergoing HD in accordance with their dry weight based on BIS[25]. Since the present study did not have a prospective design, the relation between decreased volume load due to HD and CTI could not be investigated. However, the relation between hypervolemia and hypertension, and LVH in HD patients was revealed clearly. The obtained findings showed that presence of FO and SBP before HD were predictors of LVH.

Consistent with the results of a study reported in the literature[26], the present study showed hypervolemia at a higher rate among males. However, further studies with larger samples are needed to confirm the effect of gender on hypervolemia. In addition, a significantly higher rate of the patients with higher BMI had hypervolemia. In a similar study by Resic et al, hypervolemia was found to be more frequent in the patients with higher BMI, though it was not significant[27].

It is known that chronic kidney disease (CKD) is an inflammatory process and becomes more marked due to extracorporeal circulation and contribution of the membrane in patients on HD[28]. Several studies have revealed higher levels of CRP, an indicator of inflammation, in patients with CKD and those on dialysis than in the general population[29,30]. However, the relation between FO and CRP is not clear yet. In the current study, CRP levels were higher in the patients with overhydration than in those without FO and CRP on its own was found to be an effective risk factor in overhydration. A study by Ortega et al indicated that brain natriuretic peptide can be associated with CRP before dialysis[31]. Also, Garagarza et al in a study on 75 HD patients showed similar results to the present study[32] The current study revealed a relation between increased CRP and FO. It can be suggested that FO can contribute to mortality through increased inflammation in addition to hypertension and SBP in HD patients.

We found that volume status of HD patients could be determined with BIS. This method can be used routinely to show volume status of HD patients in the future. Since the study had a cross-sectional design, it was not possible to evaluate long-term effects of overhydration and strict volume control on the cardiovascular system. Therefore, further studies likely to reveal their long-term effects are required.

Conflict of interest

The authors declare no conflicts of interest related to the contents of this article.

References

1. Zareba W. Initiation of dialysis: Trigger or cause of cardiovascular events? Kidney Int. 2015; 88: 942-944.
2. Chazot C, Wabel P, Chamney P, Moissl U, Wieskotten S, Wizemann V. Importance of normohydration for the long-term survival of hemodialysis patients. Nephrol Dial Transplant. 2012; 27: 2404-2410.
3. Onofriescu M, Mardare NG, Segall L, Voroneanu L, Cuşai C, Hogaş S, et al. Randomized trial of bioelectrical impedance analysis versus clinical criteria for guiding ultrafiltration in hemodialysis patients: effects on blood pressure, hydration status, and arterial stiffness. Int Urol Nephrol. 2012; 44: 583-591.
4. Wizemann V, Wabel P, Chamney P, Zaluska W, Moissl U, Rode C, et al. The mortality risk of overhydration in hemodialysis patients. Nephrol Dial Transplant. 2009; 24: 1574-1579.
5. Yılmaz Z, Yıldırım Y, Aydın FY, Aydın E, Kadiroğlu AK, Yılmaz ME, et al. Evaluation of fluid status related parameters in hemodialysis and peritoneal dialysis patients: Clinical usefulness of bioimpedance analysis. Medicina (Kaunas). 2014; 50: 269-274.
6. Kimmel PL, Varela MP, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, et al. Interdialytic weight gain and survival in hemodialysis patients: effects of duration of ESRD and diabetes mellitus. Kidney Int. 2000; 57: 1141-1151.
7. Kalantar-Zadeh K, Regidor DL, Kovesdy CP, Wyck DV, Bunnapradist S, Horwich TB, et al. Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis. Circulation. 2009; 119: 671-679.
8. Ozdogan O, Kayikcioglu M, Asci G, Ozkahya M, Toz H, Sezis M, et al. Left atrial volume predicts mortality in low-risk dialysis population on long-term low-salt diet. Am Heart J. 2010; 159: 1089-1094.
9. Eldehni MT, McIntyre CW. Are there neurological consequences of recurrent intradialytic hypotension? Semin Dial. 2012; 25: 253-256.
10. Burton JO Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. Clin J Am Soc Nephrol. 2009: 4: 914-920.
11. Shoji T, Tsubakihara Y, Fujii M, Imai E. Hemodialysis-associated hypotension as an independent risk factor for two-year mortality in hemodialysis patients. Kidney Int. 2004; 66: 1212-1220.
12. Kraemer M, Rode C, Wizemann V. Detection limit of methods to assess fluid status in dialysis patients. Kidney Int. 2006; 69: 1609-1620.
13. Onofriescu M, Hogas S, Voroneanu L, Apetrii M, Nistor I, Kanbay M, et al. Bioimpedance-guided fluid management in maintenance hemodialysis: a pilot randomized controlled trial. Am J Kidney Dis. 2014; 64: 111-118.
14. Moissl U, Arias-Guillén M, Wabel P, Fontseré N, Carrera M, Campistol JM, et al. Bioimpedance-guided fluid management in hemodialysis patients. Clin J Am Soc Nephrol. 2013; 8: 1575-1582.
15. Mamat R, Kong NC, Ba'in A, Shah SA, Cader R, Wong V, et al. Assessment of body fluid status in hemodialysis patients using the body composition monitor measurement technique. J Clin Nurs. 2012; 21: 2879-2885.
16. Maduell F, Arias M, Massó E, Fontseré N, Carrera M, Vera M, et al. Sensitivity of blood volume monitoring for fluid status assessment in hemodialysis patients. Blood Purif. 2013; 35: 202-208.
17. Vasko R, Müller GA, Ratliff BB, Jung K, Gauczinski S, Koziolek MJ. Clinical judgment is the most important element in overhydration assessment of chronic hemodialysis patients. Clin Exp Nephrol. 2013; 17: 563-568.
18. Liu L, Long G, Ren J, Li J, Xu J, Lei J, et al. A randomized controlled trial of long term effect of BCM guided fluid management in MHD patients (BOCOMO study): rationales and study design. BMC Nephrol. 2012; 13: 120.
19. Chen YC, Chen HH, Yeh JC, Chen SY. Adjusting dry weight by extracellular volume and body composition in hemodialysis patients. Nephron. 2002; 92: 91-96.
20. Machek P, Jirka T, Moissl U, Chamney P, Wabel P. Guided optimization of fluid status in hemodialysis patients. Nephrol Dial Transplant. 2010; 25: 538-544.
21. Ozkahya M. Pharmacological and non-pharmacological treatment of hypertension in dialysis patients. Kidney Int Suppl (2011). 2013; 3: 380-382.
22. Zoccali C. Left ventricular mass index as an outcome measure in clinical trials in dialysis patients: a word of caution. Am J Nephrol. 2011; 33: 370-372.
23. Ozkahya M, Ok E, Cirit M, Aydin S, Akçiçek F, Başçi A, et al. Regression of left ventricular hypertrophy in hemodialysis patients by ultrafiltration and reduced salt intake without antihypertensive drugs. Nephrol Dial Transplant. 1998; 13: 1489-1493.
24. Hur E, Usta M, Toz H, Asci G, Wabel P, Kahvecioglu S, et al. Effect of fluid management guided by bioimpedance spectroscopy on cardiovascular parameters in hemodialysis patients: a randomized controlled trial. Am J Kidney Dis. 2013; 61: 957-965.
25. Seibert E, Müller SG, Fries P, Pattmöller J, Kuss O, Heine GH, et al. Calf bioimpedance spectroscopy for determination of dry weight in hemodialysis patients: effects on hypertension and left ventricular hypertrophy. Kidney Blood Press Res. 2013; 37: 58-67.
26. Van Biesen W, Williams JD, Covic AC, Fan S, Claes K, Lichodziejewska-Niemierko M, et al; EuroBCM Study Group. Fluid status in peritoneal dialysis patients: the European Body Composition Monitoring (EuroBCM) study cohort. PLoS One. 2011; 6: e17148.
27. Resić H, Ajanović S, Kukavica N, Masnić F, Corić A. Plasma levels of brain natriuretic peptides and cardiac troponin in hemodialysis patients. Bosn J Basic Med Sci. 2009; 9: 137-141.
28. Muslimovic A, Rasic S, Tulumovic D, Hasanspahic S, Rebic D. Inflammatory Markers and Procoagulants in Chronic Renal Disease Stages 1-4. Med Arch. 2015; 69: 307-310.
29. Liu SH, Li YJ, Wu HH, Lee CC, Lin CY, Weng CH, et al. High-sensitivity C-reactive protein predicts mortality and technique failure in peritonealdialysis patients. PLoS One. 2014; 9: e93063.
30. Hemayati R, Lesanpezeshki M, Seifi S. Association of dialysis adequacy with nutritional and inflammatory status in patients with chronic kidney failure. Saudi J Kidney Dis Transpl. 2015; 26: 1154-1160.
31. Ortega O, Gallar P, Muñoz M, Rodríguez I, Carreño A, Ortiz M, et al. Association between C-reactive protein levels and N-terminal pro-B-type natriuretic peptide in pre-dialysis patients. Nephron Clin Pract. 2004; 97: c125-c130.
32. Garagarza C, João-Matias P, Sousa-Guerreiro C, Amaral T, Aires I, Ferreira C, et al. Nutritional status and overhydration: can bioimpedance spectroscopy be useful in hemodialysis patients? Nefrologia. 2013; 33: 667-674.