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Assessment of volemia status using ultrasound examination of the *inferior vena cava* and spectroscopic bioimpedance in hemodialysis patients

Procena statusa volemije ultrazvučnim pregledom donje šuplje vene i spektroskopskom bioimpendancom kod bolesnika na hemodijalizi

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Abstract

Background/Aim. Hypervolemia is an important risk factor for the development of cardiovascular morbidity and mortality in patients treated with regular hemodialysis. There is still no reliable method for assessing the status of volemia in these patients. The aim of the study was to assess the status of volemia in patients treated with regular hemodialysis by measuring the parameters of the *inferior vena cava* (IVC) and bioimpedance. **Methods.** The effect of hemodialysis treatment on ultrasound parameters of the IVC, as well as on the parameters measured by bioimpedance, was examined before and after hemodialysis. The values of the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) were measured both before and after hemodialysis. Forty-five patients were involved in this non-interventional cross-section study, including the patients treated with standard bicarbonate dialysis. According to the interdialytic yield, the patients were divided into three groups: I (up to 2,000 mL), II (2,000–3,000 mL), and III (over 3,000 mL). **Results.** The values of the IVC parameters and the parameters measured with bioimpedance were significantly lower after treatment with hemodialysis ($p < 0.005$). The third group of patients had a significantly higher total fluid volume in the body compared to the group I, as well as a significantly greater volume of extracellular fluid ($p < 0.005$). The significantly lower values of NT-proBNP in all groups ($p < 0.005$) were detected after hemodialysis. After treatment with hemodialysis, a positive correlation was observed between the concentration of NT-proBNP in the serum and the extracellular/intracellular water ratio. However, the correlation between NT-proBNP concentration and total fluid measured by bioimpedance spectroscopy did not reach statistical significance. **Conclusion.** Measurement of the IVC ultrasound parameters and volemia parameters using bioimpedance significantly contributes to the assessment of the status of volemia. Nevertheless, it cannot be used as a separate parameter, only in combination with all other methods.

Key words:
plasma volume; renal dialysis; spectrophotometry; vena cava, inferior; ultrasonography.

Apstrakt

Uvod/Cilj. Hipervolemija je značajan faktor rizika od razvoja kardiovaskularnog morbiditeta i moratliteta kod bolesnika koji se leče redovnom hemodijalizom. Još uvek ne postoji suverena metoda za procenu statusa volemije kod tih bolesnika. Cilj istraživanja bio je da se merenjem parametara donje šuplje vene i merenjem bioimpedance proceni status volemije kod bolesnika koji se leče redovnom hemodijalizom. **Metode.** Ispitivan je uticaj tretmana hemodijalizom na ultrazvučne parametre donje šuplje vene, kao i na parametre merene spektroskopskom bioimpedancom (SB) pre i posle hemodijalize. Merene su i vrednosti N-terminalnog prohormona moždanog natriuretskog peptida (NT-proBNP) pre i posle hemodijalize. U neinterventnu studiju preseka bilo je uključeno 45 bolesnika koji se leče standardnom bikarbonatnom dijalizom. Prema intradijaliznom prinosu bolesnici su bili podeljeni u tri grupe: I (do 2 000 mL), II (2 000 – 3 000 mL), III (preko 3 000 mL). **Rezultati.**

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Vrednosti parametara donje šuplje vene i parametara izmerenih SB-om bili su značajno niži nakon tretmana hemodijalizom ($p < 0.005$). Treća grupa bolesnika imala je značajno veću ukupnu zapreminu tečnosti u organizmu pre hemodijalize u poređenju sa I grupom, kao i značajno veću zapreminu vanćelijske tečnosti ($p < 0{,}005$). Nakon hemodijalize detektovane su značajno niže vrednosti NT-proBNP-a u svim grupama ($p < 0{,}005$). Posle tretmana hemodijalizom, zabeležena je pozitivna korelacija između koncentracije NT-proBNP-a u serumu i odnosa ekstracelularne/intracelularne tečnosti; međutim korelacija između koncentracije NT-proBNP-a i ukupne tečnosti izmerene putem SB nije dostigla statističku značajnost. **Zaključak.** Merenje ultrazvučnih parametara donje šuplje vene i parametara volemije SB-om u značajnoj meri doprinosi proceni statusa volemije, ali se ne može koristiti kao odvojeni parametar, već u kombinaciji sa svim drugim metodama.

Ključne reči:
plazma, volumen; hemodijaliza; spektometrija; v. cava inferior; ultrasonografija.

Introduction

Hypervolemia is an important risk factor for the development of cardiovascular morbidity and mortality, as well as adverse outcomes in patients treated with regular hemodialysis [1]. The assessment of volemia status in these patients is performed by clinical examination, lung radiography, ultrasound examination of the lungs, inferior vena cava, and the heart, measurement of volemia using bioimpedance spectroscopy (BIS), and monitoring of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) in the serum [1].

The goals of hemodialysis are to eliminate excess fluid, achieve adequate dry weight and depuration of the organism from uremic toxins, and regulate electrolyte imbalance. Dry weight is the weight obtained at the end of a regular dialysis session, below which the patients will most likely develop symptomatic hypotension [2].

Symptomatic hypotension is associated with ultrafiltration rate during hemodialysis treatment and the rate at which the removal is performed. Inadequate dry weight assessment leads to chronic volume overload. Removing too much excess fluid (below the dry weight) causes hypovolemia and vertigo, headache, pain, and cramps in the muscles, and a decrease in perfusion of vital organs occurs. In cases where the elimination of fluid is not sufficient (weight above the dry weight), a chronic hypervolemic condition and complications occur, such as hypertension, left ventricular hypertrophy, diastolic dysfunction, congestive heart failure, and edema of the lungs [3].

Radiography of the heart and lungs is highly specific but with low sensitivity for the conditions of hypervolemia. The disadvantage of this diagnostic method is that it sometimes takes several hours for the radiographic changes of hypervolemia to occur. In addition, in 20% to 40% of patients, radiographic changes of hypervolemia are absent [4]. What is important when assessing the status of volemia is the echocardiographic examination of the heart to assess the structure and function of the left ventricle, as well as the disorder of left ventricular systolic and diastolic function. This examination may indicate the condition of hypervolemia, but it does not give us information that the patient is in normovolemia [5–7].

Ultrasound of the lungs is used to estimate the volume of fluid in the extravascular lung section and the severity of the degree of hypervolemia [8]. This method is useful in detecting pulmonary congestion, even before the manifested clinical picture, and it correlates well with systolic cardiac function. The disadvantage of this method is that it may not always correlate with hypervolemia [9].

The results of numerous studies indicate that hyper- or hypovolemia can be determined in a dialysis patient using ultrasound measurement of the diameter of the *inferior vena cava* (IVC) [10, 11]. However, the recommended values of the IVC diameter (IVCd) that would correlate with optimal body weight are not generally accepted because of individual variations, as well as due to significant subjectivity in the measurement. In their study, Munizt Pazeli et al. [12] concluded that ultrasound of the IVC could be performed by nephrologists who have little experience in ultrasound, and the findings were potentially useful for dry weight assessment in patients on dialysis. The IVCd, IVC index (IVCi), and IVC collapsibility index (IVCci) are measured using ultrasound examination of IVC. The normal diameter of the IVC is 15–20 mm, and it varies depending on the breathing cycle. In the inspirium, the diameter decreases and amounts to 0–15 mm, and in the expirium, it increases and amounts to 15–20 mm. The anterior-posterior diameter of the IVC was measured subxiphoidally at a distance of 2–3 cm from the right atrium during spontaneous breathing, forced inspiration, and forced expiration. The IVCi is the ratio of the IVCd and the body surface (BS) of the patient: IVCd/BS (mm/m^2). The normal IVCi is 8.0–11.5 mm/m^2 (euvolemia). The IVCi below 8 mm/m^2 indicates hypovolemia, and over 11.5 mm/m^2 is considered hypervolemia. In order to calculate the IVCci, it is necessary to measure its diameter in inspirium (IVCinsp) and expirium (IVCexp). The IVCci is calculated using the formula: IVCci = [(IVCexp- IVCinsp)/ IVCexp] × 100%. If the IVCci is 50% to 75%, we are talking about euvolemia, if it is below 50%, it is hypervolemia, and over 75%, it is hypovolemia [13, 14].

Additionally, the concentration of NT-proBNP in plasma, which has a significant prognostic value for cardiovascular mortality in hemodialysis patients, was used in assessing the status of volemia in these patients [15,16]. NT-proBNP is often increased in patients with chronic renal failure [17,18]. When examining patients with asymptomatic chronic renal failure who have not yet started dialysis treatments, an increased level of NT-proBNP was observed in more than half of the patients [18]. However, there is no clear cut-off in the literature for the concentration of NT-proBNP that would distinguish cardiac from renal failure (cut-off values range from 5,000 to 7,000 pg/mL). NT-proBNP is not only specific for hypervolemia but also for nutritional status, systolic and diastolic left ventricular dysfunction [19].

Precise assessment of the status of volemia in patients on dialysis also includes the analysis of BIS. Bioimpedance represents the total resistance of tissue and fluid to the flow of micro-amperage alternating current through the body [20]. Two methods work on the principle of BIS. One is the so-called "whole body BIS" where the electrodes are placed on the wrist and ankle on the same side of the body, and using appropriate mathematical and physiological tissue models, we obtain data on the total amount of water in the body (TBW) and the amount of water in tissue cells [20, 21]. The second method of BIS is a segmental BIS, which separately measures the amount of water in the extremities and the trunk. It can be done with eight electrodes; it is very precise, but the examination lasts for a longer time, and in practice, it has not shown an advantage in relation to the whole body BIS [22, 23].

A shift in the application of BIS to determine the condition of volemia in hemodialysis patients was provided by two studies published in 2009. These studies have shown that: 1) hypervolemia prior to dialysis treatment greater than 15% of normal extracellular fluid (approximately 2.5 L in an average person of 70 kg) correlated with a twice higher risk of fatal outcome during the 3.5 year follow-up period, compared to those patients in whom this predialysis hypervolemia was lower [24]; 2) reduction of this "critical" hypervolemia can improve arterial blood pressure values and reduce therapy in hemodialysis patients [25].

The aim of this study was to investigate the degree of association between the status of volemia assessed clinically (interdialytic yield), with IVC measurement, BIS, and determination of NT-proBNP, and the values of the parameters measured by BIS. Moreover, we determined the influence of hemodialysis treatment on the concentration of NT-proBNP in the serum of the patients. We also examined the influence of the degree of ultrafiltration on the values of the parameters of ultrasound examination of IVC, as well as the degree of correlation between NT-proBNP in the serum and the parameters of ultrasound examination of the inferior vena cava before and after hemodialysis.

Methods

Patients

A cross-sectional study (non-interventional study) included 45 patients treated with regular hemodialysis for more than three months. According to the rate of targeted ultrafiltration, the patients were divided into three groups. The first group consisted of patients with a yield of up to 2,000 mL (n = 14), the second group consisted of patients with a yield of 2,000 mL to 3,000 mL (n = 12), and the third group of patients had a yield of over 3,000 mL (n = 19). Patients were dialyzed using low-flux and high-flux synthetic dialyzers, 12 hrs a week, using a bicarbonate ultrapure hemodialysis solution, and the machines type Fresenius 4008, 508S and Gambro AKA20US and Gambro Artis. The study was conducted at the Center for Nephrology and Dialysis of the Clinical Center of Kragujevac with respect to the Helsinki Declaration and Good Clinical Practice.

Biochemical analyses

The following examination parameters were determined in all patients: complete blood count (CBC), the status of iron in the organism (serum iron concentration, transferrin saturation, serum ferritin concentration), parameters of secondary hyperparathyroidism (serum calcium concentration, serum phosphate concentration), solubility produc, serum alkaline phosphatase concentration, serum intact parathyroid hormone concentration), microinflammatory parameters (C-reactive protein), nutritional status parameters (concentration of total protein and serum albumin). The concentrations of NT-proBNP in the serum were assessed 15 min before the start of hemodialysis and 15 min after the shutdown of hemodialysis. The adequacy of hemodialysis was assessed on the basis of Kt/V index (dialysis dose, i.e., product of urea clearance during dialysis (K) and time of dialysis procedure (t) divided by urea distribution volume, V) and URR index (urea reduction ratio) [26]. Laboratory parameters were sampled in accordance with a laboratory test protocol for patients who were treated in the chronic hemodialysis program; there was no need for additional blood sampling.

BIS was performed by Body Composition Monitor (BCM) module (BCM; manufacturer Fresenius Medical Care, Software version: 3.2); the patient's hydration status was assessed 15 min before the start of hemodialysis and 15 min after the shutdown of hemodialysis. The electrodes were placed on the wrist of one hand and the foot on the same side of the body of the patient in a lying position. This BIS device uses a multi-frequency current range (50 different frequencies from 5 to 1,000 kHz) and provides data on the total body water (TBW), the extracellular fluid (ECF), the intracellular fluid (ICF), and the quantification of the excess volume of ECF. The results are displayed on the monitor after 2 min of measurement and stored on a card for each patient individually.

Ultrasound examination of the IVC

Ultrasound examination was performed on the LOGIQ P5 ultrasound apparatus using a 3.5 MHz probe.

The anterior-posterior diameter of the IVC (IVCd) was measured in its proximal during spontaneous breathing and during inspiration (IVCinsp) and expiration (IVCexp), 30 min before and after the shutdown of hemodialysis, subxyphoidally at a distance of 2–3 cm from the right atrium of the heart. Based on the measured IVC parameters, the IVCi and IVCci were determined.

Statistical analysis

The data were processed in the statistical software SPSS 20.0 for Windows (IBM SPSS Statistic for Windows, Version 20.0, USA). The results are presented as the mean ± standard deviation (SD) for numerical and the frequency for attribute data. The following tests were used for statistical analysis of the obtained data: the Kolmogorov-Smirnov test (estimation of the normality and distribution of data), the Student's *t*-test, the Mann-Whitney *U* test, the single-factor analysis of variance – ANOVA, the Kruskal-Walis test, the univariate and multivariate logistic regression analyses, the Spearman's and Pearson's correlation coefficient. The significance threshold was 0.05.

Results

Table 1 shows general patient data that include the analysis of demographic and clinical characteristics. The values of the measured biochemical parameters are also shown.

Figure 1 shows the percentage of patients according to the rate of ultrafiltration.

Table 1

General patient data including demographic and clinical characteristics (values of the measured biochemical parameters are also shown)

Variable	Values
Gender (female), n (%)	15 (33.7)
Age (years)	64.91 ± 10.82
Length of HD treatment (years)	7.02 ± 6.48
Body weight index (kg/m^2)	26.17 ± 4.80
Ultrafiltration (L/HD)	2.67 ± 1.19
Hypervolemia measured using BCM (L)	2.71 ± 1.35
Systolic arterial blood pressure before HD (mm Hg)	130.49 ± 18.47
Diastolic arterial blood pressure before HD (mm Hg)	77.75 ± 8.43
Medium arterial blood pressure before HD (mm Hg)	104.45 ± 12.81
Pulse arterial blood pressure before HD (mm Hg)	52.47 ± 13.76
Erythrocytes (x10^{12}/L)	3.27 ± 0.45
Leukocytes (x10^9/L)	6.54 ± 2.09
Hemoglobin (g/L)	101.89 ± 13.10
Sodium (mmol/L)	137.49 ± 2.98
Potassium (mmol/L)	5.33 ± 0.67
Magnesium (mmol/L)	1.22 ± 0.29
Calcium (mmol/L)	2.28 ± 0.80
Phosphorus (mmol/L)	1.33 ± 0.50
Iron (umol/L)	8.43 ± 3.14
TIBC (mmol/L)	33.6 ± 6.22
Ferritin (ng/mL)	794.40 ± 286.31
Transferrin saturation	0.23 ± 0.06
Uric acid (umol/L)	364.00 ± 52.74
Total protein (g/L)	63.33 ± 5.35
Albumins (g/L)	36.24 ± 4.76
CRP (mg/L)	6.98 ± 9.60
Parathormone (pg/mL)	261.64 ± 395.91
Urea (mmol/L)	20.78 ± 4.32
Creatinine (umol/L)	743.07 ± 206.46
URR index	63.31 ± 13.88
Kt/V	1.22 ± 0.61

HD – hemodialysis; BCM – Body Composition System; TIBC – total iron binding capacity; CRP – C-reactive protein; URR – urea reduction ratio; Kt/V – dialysis adequacy index (K = clearance of urea; t – duration of dialysis; V – total body water). All values are expressed as mean ± standard deviation, except gender given as number (percentage).

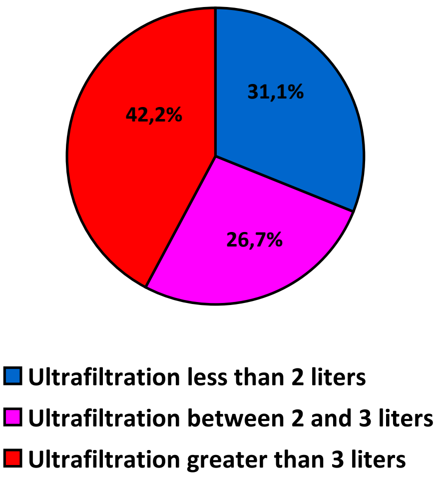

Fig. 1 – The percentage of patients according to the rate of ultrafiltration.

Influence of the rate of ultrafiltration on the examined parameters used to assess volemia

By comparing the mean values of ECF between the three groups, it was found that they were not equal. Namely, the third group (ultrafiltration greater than 3,000 mL) had significantly higher ECF values than the first group (p = 0.017) and the second group (p = 0.025). A statistically significant difference in comparison of TBW was recorded only between the first and the third group of patients (p = 0.046) (Table 2).

Mean values of extracellular fluid in examined patient groups

Statistically significant differences were not detected between the groups when the values of NT-proBNP, IVCd, IVCi, IVC insp, IVC exp, IVCci, and the ECF/ICF ratio were compared. The mean values of ECF are shown in Figure 2.

Table 2

Influence of the rate of ultrafiltration on the examined parameters used to assess volemia

Variable	Ultrafiltration (L) 0 – 2 (n = 14)	2 – 3 (n = 12)	> 3 (n = 19)	*p*
NT-proBNP (pg/mL)	5,188 (3,968–14,070)	7,536 (6,612 – 24,625)	11,949 (5,675–19,361)	0.309
IVCd (mm)	17.51 ± 3.47	18.73 ± 3.51	17.75 ± 3.09	0.615
IVCi (mm)	9.4 ± 1.84	10.70 ± 2.22	9.17 ± 1.71	0.119
IVCinsp (mm)	1.1 ± 0.38	1.17 ± 0.41	1.26 ± 0.38	0.681
IVCexp (mm)	2.25 ± 0.45	2.36 ± 0.41	2.93 ± 3.17	0.608
IVC collapsibility	50.02 ± 11.53	51.34 ± 11.41	45.0 ± 10.07	0.238
ICF (L)	17.90 (17.10–9.00)	15.05 (12.55–18.60)	18.80 (16.60–21.00)	0.105
ECF (L)	17.65 (16.30–18.80)	16.65 (15.25–19.40)	19.80 (18.35–21.60)	*0.020*
OH (L)	2.24 ± 1.08	2.8 ± 1.55	2.97 ± 1.37	0.282
TBW (L)	35.60 (34.10–38.10)	30.75 (27.80–38.15)	38.90 (35.15–42.60)	0.046
ECF/ICF index	1.0 ± 0.12	1.08 ± 0.18	1.08 ± 0.14	0.299

NT-proBNP – N-terminal prohormone of brain natriuretic peptide; OH – hypervolemia; TBW – total body water; IVC – *inferior vena cava*; d – diameter; i – index; insp – inspirium; exp – expirium; ICF – intracellular fluid; ECF – extracellular fluid.
Values are given as median (25th percentile – 75th percentile) or mean value ± standard deviation.

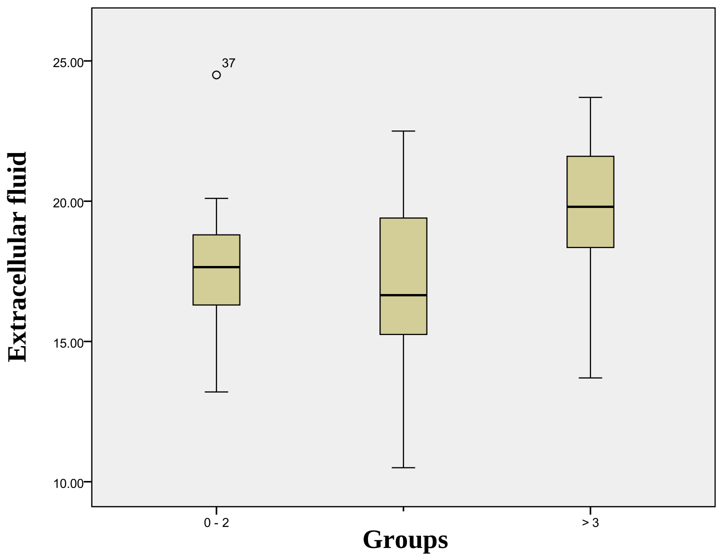

Fig. 2 – Mean values of extracellular fluid in examined patient groups formed according to the rate of ultrafiltration (in liters).

Comparison of the examined parameters before and after hemodialysis

The values of laboratory findings, ultrasound (IVCd, IVCi, IVCci), and volemia parameters used to assess the clinical condition of patients were statistically significantly lower after hemodialysis, except in the measurement of IVC values (*p* = 0.990). The values of IVCci 30 min after hemodialysis were statistically significantly higher compared to the values of this parameter before hemodialysis (48.15 ± 11.38 *vs* 55.45 ± 15.07, respectively; *p* = 0.008). This result suggests that the patients switched from the state of hypervolemia to the state of euvolemia after hemodialysis. This was corroborated by the result of weight changes before and after hemodialysis. The results of these comparisons are given in Table 3.

The degree of correlation of serum NT-proBNP values with other before-hemodialysis parameters

A positive correlation was detected between serum NT-proBNP with ultrasound parameters VCId, VCIi, VCIinsp, VCIexp, VCIci, and changes in body weight. NT-proBNP was also positively correlated with the ECF/ICF index and weight change. Persons with higher values of NT-proBNP lose more body fluid. NT-proBNP was in a negative correlation with the VCI collapsibility index, which means that higher NT-proBNP values are in correlation with a lower VCI collapsibility index. That is, the patients in hypervolemia have a high NT-proBNP and low VCI collapsibility index (Table 4).

The degree of correlation of serum NT-proBNP values with other parameters after hemodialysis

Correlations of NT-proBNP with ultrasound parameters and volemia condition parameters after dialysis are shown in Table 5.

It can be seen that after hemodialysis, NT-proBNP was positively correlated with volemia, body weight, and ECF/ICF index. However, a negative correlation was recorded between NT-proBNP and IVCci, which was on the border of statistical significance (*p* = 0.060).

Table 3

Comparison of the examined parameters before and after hemodialysis

Variable	Before hemodialysis	After hemodialysis	*p*
NT-proBNP (pg/mL)	12.982 ± 10.865	8.837 ± 9.355	< 0.0005
IVCd (mm)	18.07 ± 3.35	14.70 ± 4.29	< 0.0005
IVCi (mm)	9.61 ± 1.97	7.10 ± 2.85	< 0.0005
IVCinsp (mm)	1.20 ± 0.39	0.87 ± 0.34	< 0.0005
IVCexp (mm)	2.60 ± 2.15	2.03 ± 0.59	0.002
IVC collapsibility	48.15 ± 11.38	55.45 ± 15.07	0.008
ICF (L)	18.30 ± 4.41	18.21 ± 4.02	0.990
ECF (L)	18.65 ± 3.74	16.51 ± 3.36	< 0.0005
OH (L)	2.71 ± 1.35	0.27 ± 1.38	< 0.0005
TBW (L)	36.65 ± 6.88	34.30 ± 6.21	< 0.0005
ECF/ICF index	1.06 ± 0.15	0.90 ± 0.20	< 0.0005
Body weight (kg)	76.53 ± 15.18	73.08 ± 14.88	0.0001

Explanations for abbreviations are given below Table 2.
Values are given as mean value ± standard deviation.

Table 4

The degree of correlation of serum NT-proBNP values with other parameters before hemodialysis

Variable 1	Variable 2	R	*p*
NT-proBNP	VCId	0.471	0.001
NT-proBNP	VDIi	0.369	0.018
NT-proBNP	VCIinsp	0.484	0.001
NT-proBNP	VCIexp	0.393	0.008
NT-proBNP	VCI collapsibility	-0.400	0.006
NT-proBNP	ICF	-0.182	0.236
NT-proBNP	ECF	0.261	0.084
NT-proBNP	OH	0.452	0.002
NT-proBNP	TBW	0.084	0.584
NT-proBNP	ECF/ICF	0.499	< 0.0005
NT-proBNP	Ultrafiltration	0.230	0.134
NT-proBNP	Body weight	-0.031	0.840
NT-proBNP	Change in body weight	0.427	0.004

Explanations for abbreviations are given below Table 2.

Table 5

The degree of correlation of serum NT-proBNP values with other parameters after hemodialysis

Variable 1	Variable 2	R	*p*
NT-proBNP	VCId	0.107	0.501
NT-proBNP	VDIi	-0.061	0.707
NT-proBNP	VCIinsp	0.109	0.491
NT-proBNP	VCIexp	0.152	0.336
NT-proBNP	VCI collapsibility	-0.287	*0.060*
NT-proBNP	ICF	-0.137	0.370
NT-proBNP	ECF	0.242	0.109
NT-proBNP	OH	0.373	*0.012*
NT-proBNP	TBW	0.046	0.766
NT-proBNP	ECF/ICF	0.425	*0.004*
NT-proBNP	Ultrafiltration	0.175	0.255
NT-proBNP	Body weight	0.739	< 0.0005
NT-proBNP	Change in body weight	0.249	0.103

Explanations for abbreviations are given below Table 2.

Discussion

The results of many studies suggest that hyper- or hypovolemia in patients on hemodialysis can be determined by ultrasound measurement of the diameter of the IVC [27, 28]. It is usually stated in the literature that the IVCd indexed to the body surface (IVCi) greater than 11.5 mm/m^2 correlates with mean pressure in the right atrium greater than 7 mmHg or with significant hypervolemia, while this index smaller than 8 mm/m^2 correlates with significant circulatory hypovolemia. However, this index is not sufficiently accurate, as other factors such as heart rate, arterial pressure, and antihypertensive drug therapy have an effect on it.

The results of our study show that there was no statistically significant difference in the measurement of the IVCd during normal breathing, inspirium, and expirium, among the three groups of patients with different degrees of ultrafiltration. A statistically significant difference was observed by comparing the IVCd before and 30 min after hemodialysis. After hemodialysis, the IVCd significantly decreases.

In the available literature, it is stated that the values of NT-proBNP positively correlate with the risk of mortality in patients on dialysis [29]. However, one measurement of the NT-proBNP value cannot be a reliable parameter for the assessment of the condition of volemia because it depends on both the volemia and the degree of myocardial damage. However, serial measurement of this marker may be a good indicator of the condition of volemia measured by bioimpedance [29]. In our study, we measured the values of NT-proBNP before and after hemodialysis. Our results show that the measured values of NT-proBNP before hemodialysis positively correlate with the IVC diameter. Moreover, the higher NT-proBNP values before hemodialysis were positively correlated with ECF/ICF and body fluid changes. However, only a positive correlation between the value of this marker and the condition of volemia was recorded by measuring the value of NT-proBNP after hemodialysis. The results of our study are similar to the results of a study in which the cut-off for the value of NT-proBNP was determined (from 5,000 to 7,700 pg/mL) as an indicator of hypervolemia [30]. In their cross-section study, Velasco et al. [30] described an excellent correlation between the average volemia assessed by BCM before hemodialysis and the levels of NT-proBNP measured before hemodialysis in patients aged up to 72 years. In the study by Paunic et al. [31], normovolemic patients (also estimated by BIS measurement) have NT-proBNP up to 4,700 pg/mL, and hypervolemic have this value above 5,800 pg/mL.

A study by David et al. [29] showed a significant correlation between serum NT-proBNP and the ratio of extracellular water and body weight only in hemodialysis patients with systolic left ventricular dysfunction but not in those without systolic dysfunction. Although the level of NT-proBNP can be increased with the increase in volume load, the summary of currently available evidence gives the impression that this marker has a limited role in assessing the state of hydration in the dialysis population. The use of this cardiac biomarker in assessing the condition of volemia in patients on hemodialysis has not yet entered the standard procedure due to the high cost and poor specificity of the tests, as well as due to the lack of a clear criterion for the normal range of NT-pBNP values in hemodialysis patients [32]. Consistent with the above study results, the results of our study cannot provide a clear cut-off value of NT-proBNP (range 5,188 to 7,536 pg/mL).

Our results show that hemodialysis treatment has a statistically significant effect on the values of parameters for assessing the state of volemia measured by BIS. The values of the parameters measured by BIS after hemodialysis treatment are highly statistically significantly lower compared to the values before hemodialysis. Our results correlate with the results of the study conducted by Chamney et al. [33].

Furthermore, our results show that the parameters obtained by BIS provide objective, qualitative, and useful data on the state of volemia in patients treated with hemodialysis. The results obtained by this method correlate with the biohumoral cardiac marker NT-proBNP. Similar results were obtained in the study by Velasco et al. [30].

Conclusion

Neither IVC diameter, BIS nor NT/proBNP measurement can be used as a stand-alone test for monitoring the condition of hydration of patients on hemodialysis. The results obtained by these methods must be interpreted individually and adapted for each patient. Only in this way could these parameters add value to the clinical judgment of an individual patient's hemodialysis optimal body weight.

Conflict of interest

None declared.

R E F E R E N C E S

1. *Petrović D*. Chronic kidney disease in clinical practice. Kragujevac: InterPrint; 2014. (Serbian)
2. *Henderson LW*: Symptomatic hypotension during hemodialysis. Kidney Int 1980; 17(5): 571–6.
3. *Cheriex EC, Leunissen KM, Janssen JH, Mooy JM, van Hooff JP*. Echography of the inferior vena cava is a simple and reliable tool for estimation of "dry weight" in haemodialysis patients. Nephrol Dial Transplant 1989: 4(6): 563–8.
4. *Di Lullo L, Floccari F, Granata A, D'Amelio A, Rivera R, Fiorini F*, et al. Ultrasonography: Ariadne's Thread in the Diagnosis of the Cardiorenal Syndrome. Cardiorenal Med 2012; 2(1): 11–7.
5. *Gheorghiade M*, *Pang PS*. Acute heart failure syndromes. J Am Coll Cardiol 2009; 53(7): 557–3.
6. *Cristina Di Gioia M, Gascuena R, Gallar P, Cobo G, Camacho R, Acosta N*, et al. Echocardiographic findings in haemodialysis patients according to their state of hydration. Nefrología 2017; 37(1): 47–53.
7. *Sabaghian T, Hajibaratali B, Samavat S*. Which echocardiographic parameter is a better marker of volume status in hemodialysis patients? Ren Fail 2016; 38(10): 1659–64.
8. *Cohen-Solal A*. Left ventricular diastolic dysfunction: pathophysiology, diagnosis and treatment. Nephrol Dial Transplant 1998; 13(Suppl 4): 3–5.
9. *Hamlin SK, Villars PS, Kanusky JT, Shaw AD*. Role of diastole in left ventricular function II: diagnosis and treatment. Am J Crit Care 2004; 13(6): 453–66; quiz 467–8.
10. *Kaptein MJ, Kaptein JS, Oo Z, Kaptein EM*. Relationship of inferior vena cava collapsibility to ultrafiltration volume achieved in critically ill hemodialysis patients. Int J Nephrol Renovasc Dis 2018; 11: 195–209.
11. *Brennan JM, Ronan A, Goonewardena S, Blair JE, Hammes M, Shah D*, et al. Handcarried ultrasound measurement of the inferior vena cava for assessment of intravascular volume status in the outpatient hemodialysis clinic. Clin J Am Soc Nephrol 2006; 1(4): 749–53.
12. *Munizt Pazeli J, Fagundes Vidigal D, Cestari Grossi T, Silva Fernandes NM, Colugnati F, Baumgratz de Pula R*, et al. Can Nephrologists Use Ultrasound to Evaluate the Inferior Vena Cava? A Cross-Sectional Study of the Agreement between a Nephrologist and a Cardiologist. Nephron Extra 2014; 4(1): 82–8.
13. *Natori H, Tamaki S, Kira S*. Ultrasonographic evaluation of ventilatory effect on inferior vena cava configuration. Am Rev Resp Dis 1979; 120(2): 421–7.
14. *Lyon ML, Verma N*. Ultrasound Guided Volume Assessment Using Inferior Vena Cava Diameter. Open Access Emerg Med 2010; 3(1): 22–4.
15. *Gargani L*. Lung ultrasound a new tool for the cardiologist. Cardiovasc Ultrasound 2011; 9: 6.
16. *Picano E*, *Gargani L*, *Gheorghiade M*. Why, when and how to assess pulmonary congestion in heart failure: pathophysiological, clinical, and methodological implications. Heart Fail Rev 2010; 15(1): 63–72.
17. *Wang H*, *Liang S*, *Wang M*, *Gao J*, *Sun C*, *Wang J*, et al. Potential serum biomarkers from a metabolomics study of autism. J Psychiatry Neurosci 2016; 41(1): 27–37.
18. *Zoccali C, Mallamaci F, Benedetto FA, Tripepi G, Parlongo S, Cataliotti A*, et al. Cardiac natriuretic peptides are related to left ventricular mass and function and predict mortality in dialysis patients. J Am Soc Nephrol 2001; 12(7): 1508–15.
19. *Booth J, Pinney J, Davenport A*. N-terminal proBNP - Marker of cardiac dysfunction, fluid overload, or malnutrition in hemodialysis patients? Clin J Am Soc Nephrol 2010; 5(6): 1036–40.
20. *Madsen LH, Ladefoged S, Corell P, Schou M, Hildebrandt PR, Atar D*. N terminal pro-brain natriuretic peptide predicts mortality in patients with end-stage renal disease in hemodialysis. Kidney Int 2007; 71(6): 548–54.
21. *Mark PB, Stewart GA, Gansevoort RT, Petrie CJ, McDonagh TA, Dargie HJ*, et al. Diagnostic potential of circulating natriuretic peptides in chronic kidney disease. Nephrol Dial Transplant 2006; 21(2): 402–10.
22. *Matthie JR*. Bioimpedance measurements of human body composition: critical analysis and outlook. Expert Rev Med Devices 2018; 5(2): 239–61.
23. *Davies SJ, Davenport A*. The role of bioimpedance and biomarkers in helping to aid clinical decision-making of volume assessments in dialysis patients. Kidney Int 2014; 86(3): 489–96.
24. *Wabel P, Moissl U, Chamney P, Jirka T, Machek P, Ponce P*, et al. Towards improved cardiovascular management: The necessity of combining blood pressure and fluid overload. Nephrol Dial Transplant 2008; 23(9): 2965–71.
25. *Machek P, Jirka T, Moissl U, Chamney P, Wabel P*. Guided optimization of fluid status in haemodialysis patients. Nephrol Dial Transplant 2010; 25(2): 538–44.
26. NKF-K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy: update 2000. Am J Kidney Dis 2001; 37(1 Suppl 1): S7–S64.
27. *Krause I, Birk E, Davidovits M, Cleper R., Blieden L, Pinhas L*, et al. Inferior vena cava diameter: a useful method for estimation of fluid status in children on haemodialysis. Nephro Dial Transplant 2001; 16(6): 1203-6.
28. *London GM*. Ultrafiltration intensification for achievement of dry weight and hypertension control is not always the therapeutic gold standard. J Nephrol 2011; 24(4): 395–7.
29. *David S, Kumpers P, Seidler V, Biertz F, Haller H, Fliser D*. Diagnostic value of N-terminal pro-B-type natriuretic peptide (NT-proBNP) for left ventricular dysfunction in patients with chronic kidney disease stage 5 on haemodialysis. Nephrol Dial Transplant 2008; 23(4): 1370–7.
30. *Velasco N, Chamney P, Wabel P, Moissl U, Imtiaz T, Spalding E*, et al. Optimal fluid control can normalize cardiovascular risk markers and limit left ventricular hypertrophy in thrice weekly dialysis patients. Hemodial Int 2012; 16(4): 465–72.
31. *Paunic Z, Dekleva-Manojlovic M, Markovic-Nikolic N, Rancic N, Dimkovic N*. Impact of active fluid management on cardiac

hemodynamic and mechanics in patients on maintenance hemodialysis. Vojnosanit Pregl 2020; 77(1): 60–9.

32. *Tabinor M, Elphick E, Dudson M, Kwok CS, Lambie M, Davies SJ.* Bioimpedance-defined overhydration predicts survival in end-stage kidney failure (ESKF): systematic review and subgroup meta-analysis. Sci Rep 2018; 8(1): 4441.

33. *Chamney PW, Krämer M, Rode C, Kleinekofort W, Wizemann V.* A new technique for establishing dry weight in hemodialysis patients via whole body bioimpedance. Kidney Int 2002; 61(6): 2250–8.

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