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Original Paper

Total Body Water and Failure to Control Blood Pressure by Medication in Hemodialysis Patients

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Key Words

Extracellular volume · Bioimpedance analysis · Blood pressure · Hemodialysis

Abstract

Background: Volume overload is the main factor responsible for the pathogenesis of hypertension in dialysis patients. Few studies have evaluated the interpretation of the parameters obtained by bioelectrical impedance (BIA) to manage these patients. The aim of this study was to assess the best cutoff level of volume overload obtained by BIA able to predict the absence of hypertension control in hemodialysis patients. **Methods:** Volume overload was calculated as the difference between total body water (TBW) measured by bioimpedance and TBW estimated by the Watson formula in chronic stable hemodialysis patients. Inadequate control of blood pressure (BP) was defined as the mean of measurements obtained before five hemodialysis sessions $\geq 140 \times 90$ mm Hg. The best cutoff level of volume overload assessed by BIA able to predict the absence of BP control in patients on chronic hemodialysis was determined by the receiver operating characteristic (ROC) curve using the Youden method. **Results:** We included 205 patients, 53% male, aged 56 ± 14.5 years. The largest area under the ROC curve was found for predialysis volume overload (0.660, 95% CI 0.556–0.765, $p = 0.004$). The ROC curve of postdialysis volume overload also reaches statistical significance. The best cutoff point was found for predialysis volume overload ≥ 1.4 liters with a sensitivity of 69% and a specificity of 67%. **Conclusion:** The association of TBW and inadequate BP control highlights the importance of volume management in hemodialysis patients. Predialysis volume overload of 1.4 liters was the parameter that best discriminated the presence of inadequate BP control.

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Introduction

Arterial hypertension has a high prevalence in dialysis patients ranging from 60 to 80% [1]. A study carried out in our clinic showed that 66% of patients on regular hemodialysis (HD) had inadequate blood pressure (BP) control [2], and this value reached approximately 86% when added to those who had BP controlled by antihypertensives (the prevalence being similar in the literature [3]). The available literature considers volume overload as the main factor responsible for the pathogenesis of arterial hypertension in dialysis patients [4]; however, some studies have reported a nonlinear relation between the BP levels and interdialytic weight gain (IDWG). Savage et al. [5] reported no correlation between interdialytic BP change, evaluated by 48-hour ambulatory BP monitoring, and weight gain in HD patients and a Brazilian study did not find a significant correlation between the average 44-hour BP and IDWG [6]. Thus, IDWG cannot be considered as a single parameter for volume overload quantification in these patients, and it is fundamental for the clinical practice to seek other methods for this evaluation.

Bioelectrical impedance (BIA) is a simple and low-cost method that can be useful in clinical practice to estimate the volume overload in HD patients [7–9]. However, until the present time, few studies showed parameters for the interpretation of the data provided by BIA associating them with total body water (TBW) or BP control.

Katzarski et al. [10], using multifrequency BIA, have validated a parameter for the evaluation of the hydration state in HD; however, studies using monofrequency BIA with this objective have not been published. This study aimed to evaluate the best cutoff point of the TBW assessed by monofrequency BIA, which is able to predict the lack of BP control in HD patients.

Patients and Methods

This retrospective cross-sectional study was performed at the Dialysis Unit of the University Hospital of the Botucatu Medical School, UNESP, Brazil. All patients having been treated for at least 3 months with regular HD were included (the information was obtained from the medical records). The study was approved by the institutional ethics committee. Exclusion criteria were patients with a heart failure, a liver failure, alcoholism, or an artificial pacemaker. Predialysis BP was defined as the average of the measurements obtained at the beginning of five consecutive dialysis sessions preceding the assessment by BIA. Body weight was evaluated during two periods, before and after dialysis, over the last five sessions that preceded the BIA. The mean IDWG was obtained by subtracting the average of the postdialysis weight of the last five sessions from the average of predialysis weights.

Demographic and clinical data as well as drug prescriptions were obtained from medical records. Inadequate BP control was defined as BP $\geq 140 \times 90$ mm Hg in the predialysis period.

To obtain the parameters of body water volume, a monofrequency BIA device (Biodynamics[®], model 450, 800 μ A, 50 kHz) was used which measures the whole body impedance. This assessment was performed 30 min after the end of the dialysis session. The measurements were performed with the patient in the supine position, on the side opposite the HD vascular access. An electrode was attached to the dorsal surface of the wrist and another on the dorsal surface of the third metacarpal bone. The second pair of electrodes was placed on the anterior surface of the ankle and the third metatarsal bone, respectively [11, 12]. The estimated parameters by BIA included extracellular water (ECW), intracellular water and TBW. The ratio between ECW and TBW (ECW/TBW ratio) was calculated. The TBW value obtained by BIA was compared to the value estimated by the Watson formula [13]; the difference

Table 1. Clinical and demographic characteristics of the sample studied

Characteristic	Value
Mean age ± SD, years	56 ± 14.5
Female gender, %	47
Race, %	
White	69
Black	16
Mestizo	14
Asian	1
Diabetics, %	37
Antihypertensive drug classes, n (%)	2 (1–3)
Mean systolic BP ± SD, mm Hg	141 ± 16.8
Mean diastolic BP ± SD, mm Hg	86 ± 14.4
Mean body mass index ± SD	25.0 ± 5.19

between them was considered as postdialysis fluid overload. Predialysis fluid overload was defined as the sum of postdialysis fluid overload plus the mean IDWG.

Statistical Analysis

Data were expressed as means ± standard deviations or medians and first and third quartiles, according to the variable distribution. For the comparison of several groups, one-way analysis of variance followed by Tukey's test was used. Receiver operating characteristic (ROC) curves were plotted, considering as endpoint variable the presence of inadequate predialysis BP control and as independent variables the presence of pre- and postdialysis fluid overload and the ECW/TBW ratio. The best cutoff point was determined by the Youden index (higher sum of sensitivity plus specificity). A p value <0.05 was considered statistically significant.

Results

We enrolled 205 patients, 53% of whom were male. Their mean age was 56 ± 14.5 years. The median number of antihypertensive classes per patient was 2 (interquartile range 1–3). The remaining characteristics are shown in table 1.

Patients were divided into two groups according to BP control classification (adequate or inadequate). Table 2 shows the number of prescribed antihypertensive classes and the measurements of pre- and postdialysis fluid overload in these groups. There was no patient taking 4 or more classes of antihypertensive drugs among those with adequate BP control. Fluid overload was higher among patients with inadequate BP control taking 4 or more classes of antihypertensive drugs compared to those with adequate BP control and receiving 1 class of antihypertensive drugs (p = 0.02). Figure 1 shows the areas under the ROC curve of the measures of pre- and postdialysis fluid overload and the ECW/TBW ratio to predict the presence of inadequate BP control. The greatest area under the ROC curve corresponds to predialysis fluid overload (0.660, 95% CI 0.556–0.765, p = 0.004); the ROC curve of postdialysis fluid overload also reached statistical significance (0.617, 95% CI 0.509–0.724, p = 0.039). The best cutoff point was a predialysis fluid overload of 1.4 liters with a sensitivity of 69% and a specificity of 67%. The ECW/TBW ratio did not have a significant association with inadequate BP control.

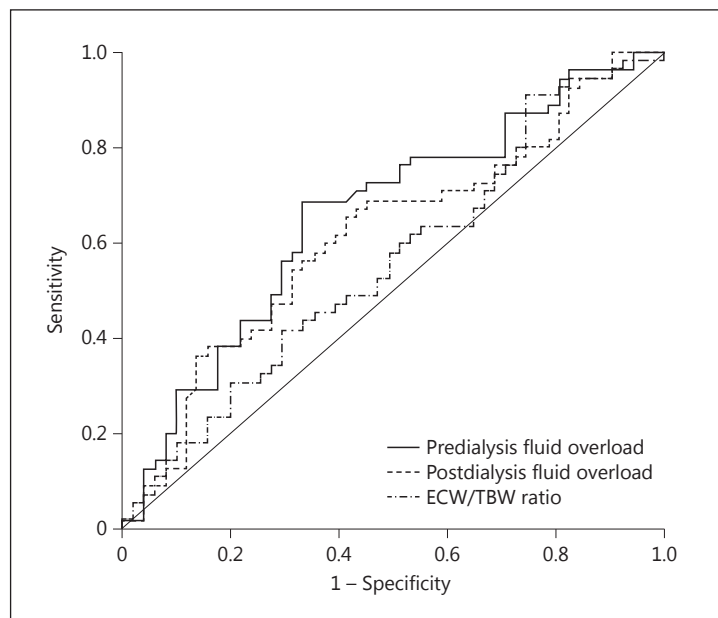


Fig. 1. ROC curves: pre- and post-dialysis fluid overload, ECW/TBW ratio and the presence of inadequate BP control.

Table 2. Pre- and postdialysis fluid overload, according to the number of antihypertensive drugs taken by patients, with adequate or inadequate BP control

Number of classes	Predialysis fluid overload, l	Postdialysis fluid overload, l
Adequate		
0	0.42 (–0.86; 2.91)	–1.89 (–3.24; 0.68)
1	–0.63 (–2.65; 1.26)	–1.96 (–5.71; –0.62)
2	0.08 (–3.03; 1.88)	–2.03 (–4.67; –0.89)
3	0.91 (–1.42; 5.49)	–0.49 (–2.74; 2.90)
Inadequate		
0	0.53 (–2.36; 1.81)	–1.70 (–4.14; 0.54)
1	0.81 (–1.10; 3.37)	–1.65 (–4.38; 1.07)
2	2.34 (–0.85; 3.94)	–0.49 (–3.36; 1.26)
3	1.96 (–0.61; 3.40)	–0.87 (–3.53; 1.00)
4	3.09 (1.49; 6.33) ^b	–0.32 (–1.29; 2.66) ^a

Figures in parentheses indicate interquartile interval.

^a p = 0.02 vs. adequate using 1 class of antihypertensive drugs; ^b p = 0.02 vs. adequate using 1 class of antihypertensive drugs.

Discussion

BIA is a noninvasive and nonexpensive method with a high sensitivity and reproducibility [14]. In this study, TBW measured by BIA was associated with BP control in HD patients. For instance, fluid overload estimated by the difference between TBW and body water volume calculated by an anthropometric formula was able to predict the lack of BP control in spite of medication taken by these patients, and predialysis fluid overload was a valid parameter to predict it.

We used the Watson formula [13] to estimate TBW, an equation validated by a tracer dilution technique in normal people to estimate adequate fluid volume and supply a reference value regarding volume overload in comparison with measured TBW.

Predialysis volume overload was utilized considering this moment as the volume overload peak; thus, predialysis volume overload was estimated adding IDWG to postdialysis volume overload, directly measured by BIA.

To estimate BP control, the average of five sessions was used, because in a previous study we verified that this number of measurements is best to estimate ambulatory BP, as well as left ventricular mass [15]. In addition to BP evaluation, we used the average of five sessions to estimate IDWG.

Another study using monofrequency BIA showed that hypertensive patients had a higher percentage of ECW; in contrast, the present study found no differences in TBW between normotensive and hypertensive patients. Some studies have suggested parameters of BIA as tools to evaluate the hydration status in patients with chronic kidney disease [17–19]; however, none of them showed a cutoff point applicable to clinical practice predicting the lack of BP control particularly using monofrequency BIA. We used monofrequency BIA which has advantages in terms of handling simplicity and low cost to facilitate the use in developing countries [16].

Other methods to evaluate fluid overload include biochemical markers, such as atrial natriuretic peptide and guanidine cyclic monophosphate; these are high-sensitivity methods but with specific limitations, for instance congestive heart failure, mitral and tricuspid valve diseases, and atrial hemodynamic changes. Furthermore, these markers require an advanced technology at high costs, available to only a few centers, which limits its use for clinical routine.

Some limitations of this study should be taken into account; in particular, multifrequency BIA is more accurate to measure ECW and intracellular water than monofrequency BIA [17, 20–22], which we used; this may explain the absence of a relationship between ECW/TBW ratio and BP control. In addition, BIA measurements were not performed before dialysis, the study design was cross-sectional, and its results need confirmation by a longitudinal study. The sensitivity of 69% and specificity of 67% was not perfect, but significant. So, the clinical use of this parameter is possible; however, we need to interpret the results cautiously and also consider other clinical parameters of dry weight.

On the other hand, strengths of this study should also be highlighted. This work is the first to establish a simple parameter for the interpretation of data from monofrequency BIA regarding the evaluation of fluid overload, which allows establishing a practical reference for clinical practice. Indeed its results are supported by an expressive sample size reinforcing their consistency.

Conclusion

TBW assessment by BIA is associated with BP control in HD patients, reinforcing the importance of volume fluid management in these patients. Predialysis fluid overload was the best parameter to predict lack of BP control; it was possible to establish a cutoff point for use in daily clinical routine.

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