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To cite this article: Tahereh Sabaghian, Bahareh Hajibaratali & Shiva Samavat (2016) Which echocardiographic parameter is a better marker of volume status in hemodialysis patients?, Renal Failure, 38:10, 1659-1664, DOI: 10.1080/0886022X.2016.1229968

To link to this article: https://doi.org/10.1080/0886022X.2016.1229968

Published online: 20 Oct 2016.

Article views: 688

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CLINICAL STUDY

Which echocardiographic parameter is a better marker of volume status in hemodialysis patients?

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\textbf{ABSTRACT}

\textbf{Aim:} Bio-impedance analysis (BIA) is a preferred method for estimating the volume status. However, it cannot be utilized in daily practice. Since the assessment of the volume status is important and challenging for hemodialysis (HD) patients, the aim of study was to determine the volume status in chronic HD patients using echocardiographic parameters and assess its correlation with BIA.

\textbf{Methods:} In this cross-sectional analysis, echocardiography and BIA were performed on 30 chronic HD patients 30 min before and 30 min after dialysis. All the cases of dialysis were performed in the middle of the week. This study also assessed the correlation between echocardiographic parameters and BIA parameters.

\textbf{Results:} There were significant differences between ECW, TBW, and TBW\% (TBW/W) before and after HD. Significant differences were observed between echocardiographic parameters of IVC, IVC\textsubscript{imin}, IVC\textsubscript{imax}, IVC\textsubscript{imax}, and IVRT, were improved after dialysis, too. There was a significant correlation between IVC\textsubscript{imin} as an index of volume status, ECW\% and TBW\% before HD and IVC\textsubscript{imin} change after dialysis had a significant correlation with %ECW change after dialysis. Comparison between hypertensive and non-hypertensive groups indicated IVC\textsubscript{imin} was significantly lower in non-hypertensive group after dialysis.

\textbf{Conclusion:} Our results showed a correlation between IVC\textsubscript{imin} and BIA parameters before HD. So, it seems that IVC\textsubscript{imin} can be a good parameter for determining the volume status of HD patients. However, further studies, with larger sample size and with a prospective study design, are required to confirm these results.

\textbf{Introduction}

Fluid balance in hemodialysis (HD) patients is considered as an important component of the treatment for these patients.\textsuperscript{1,2} However, the occurrence of chronic hypervolemia in these patients can lead to hypertension, increased arterial stiffness, chronic heart failure (CHF), left ventricular hypertrophy (LVH), increased morbidity and mortality, and other adverse outcomes.\textsuperscript{3–8}

On the other hand, dehydration can lead to hypotension, cramps, dizziness, etc.\textsuperscript{9} Chronic hypervolemia is the cause of 80\% of the cases of hypertension in HD patients,\textsuperscript{10,11} and cardiovascular complications in these patients is one of the major causes of death\textsuperscript{12}; hence, accurate control of the volume can lead to blood pressure reduction, regression of LVH, and increased survival.\textsuperscript{13,14} There is no simple and easy method to determine the dry weight.\textsuperscript{1} In most dialysis centers, dry weight is determined via a trial and error method that hampers the control of blood pressure control and leads to some complications during dialysis.\textsuperscript{15} From a clinical point of view, dry weight is the lowest weight a patient can tolerate after dialysis without having clear signs of hypotension or overload.\textsuperscript{9} Clinical methods are not able to estimate changes in lean body weight and nutritional status and they cannot avoid errors as well. Therefore, several methods have been proposed to determine the volume status of HD patients.\textsuperscript{16} The gold standard for the diagnosis of the volume status is radioimmunoassay which cannot be used in clinical settings.\textsuperscript{17} In some studies, bio-impedance analysis (BIA) has been proposed as the preferred technique for determining the hydration status.

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of the patients because this method is noninvasive and can be performed easily. Among different BIA measures, the percentage of extracellular water (ECW%) and the reduction in the index of ECW/total body water (TBW) are proposed for the assessment of hydration status. However, due to changes in extracellular fluid (ECF) and shifts of fluid from inside to outside of the cells (shift of intracellular water (ICW) to ECF) in dialysis patients during and after dialysis, it is important to choose the right time for BIA, because choosing a wrong time may result in inaccurate estimation of the fluids volume and inappropriate ultrafiltration. In addition, BIA may not be available in many centers.

Echocardiography is one of the other well-known methods for the assessment of the volume status in HD patients. It has been shown that inferior vena cava diameter (IVCD) and blood volume are reduced proportionally during dialysis and are increased two hours after dialysis through refilling intravascular space. As a result, IVCD changes are supposed to reflect the volume changes. As echocardiography is available in most centers and as BIA is proposed as the preferred technique for determining the volume, the aim of this study was to compare BIA parameters and echocardiographic parameters for estimating dry weight; it was also aimed to determine the best echocardiographic parameter associated with BIA.

Methods

This cross-sectional study was conducted on 90 chronic HD patients in the Labbafinejad Hospital in 2014. Inclusion criteria were: being older than 18 years, and having a history of dialysis for at least three months. Exclusion criteria were the followings: having a metal prosthesis, having a pacemaker, amputation of limbs, severe valvular heart diseases (mitral or tricuspid regurgitation higher than average), atrial fibrillation, ejection fraction less than 50%, pericardial disease, right ventricular failure, pulmonary disease, pulmonary artery hypertension, and daily urine volume of more than 400 cm³.

Of the total 90 dialysis patients who referred to the center, 51 patients did not met the inclusion criteria because of the following reasons: cardiac problems (29 persons); history of dialysis less than three months (six persons); 24-h daily urine volume of more than 400 cm³ (six persons); amputation and prosthesis (five persons); ascites (four persons); and being younger than 18 years (one person). In addition, nine patients were not willing to participate in the study. So in the end, 30 patients were enrolled in the study and written consent form was obtained from all the patients. Moreover, ethical approval was obtained from the ethics committee of the Labbafinejad Hospital.

Using bicarbonate, all cases of dialysis were performed as low flux and in the middle of the week. We collected data about the hemodynamic clinical parameters of the patients including weight, systolic and diastolic blood pressure, hematocrit (Hct), BIA, and echocardiography that were done half an hour before and half an hour after the dialysis. BIA was performed using Body stat 4000UK Quadscan Multi-frequency analyzer (Isle of Man, UK); to perform BIA, first the patient was set in a supine state for about 3–5 min and four electrodes were placed on one side of the body (two electrodes on foot and the two other electrodes on hand, opposite to the fistula or graft). The parameters of TBW, ECW, TBW% (TBW/Weight), and ECW% (ECW/Weight) were recorded to determine the hydration status of the patients. Echocardiography was performed by a cardiologist who was blinded to the results of the BIA; a EKO-7-Medison echocardiography device was used and tissue-Doppler 2D was done in all the standard views and the following parameters were recorded: left atrial diameter (LAD), LA area, left ventricular ejection fraction (LVEF), left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), mitral valve inflow (MVI), E', E/E', isovolumic relaxation time (IVRT), interventricular septum (IVS), IVCD, inferior vena cava collapse-ability index (IVCCI) (IVCDmax-IVCDmin+100), IVCD index maximum (IVCDmax) (IVCDmax/BSA), IVCD index minimum (IVCDmin) (IVCDmin/BSA), deceleration time (DT), pulmonary capillary wedge pressure (PCWP), and pulmonary artery pressure (PAP). Body surface area (BSA) was calculated using the Dubois formula before and after dialysis.

In addition, the patients were divided into two groups of hypertensive patients (systolic blood pressure (SBP) ≥140 or diastolic blood pressure (DBP) ≥90) and non-hypertensive patients (SBP <140 and DBP <90). The parameters measured before and after dialysis were compared within the two groups.

The collected data was analyzed using the SPSS software, version 18 (SPSS Inc., Chicago, IL). Quantitative variables were described using mean and standard deviation, and qualitative variables were described using frequencies and percentages. Paired t-test was used to evaluate the changes in the clinical, echocardiographic, and BIA parameters before and after dialysis; moreover, Pearson’s correlation coefficient was used to analyze the relationship between echocardiographic and BIA parameters. Finally, independent t-test was used to compare different parameters between the two groups of hypertensive and non-hypertensive patients. The receiver operating characteristics (ROC) curve was
used to determine the cutoff point for the IVCD\textsubscript{imin} in parameters with significant correlation with BIA. \( p \) Value <.05 was considered as the significance level.

**Results**

Of the 30 patients studied, 17 (57\%) were male and 13 (43\%) were female. The mean age of patients was 50 ± 16 years. Moreover, the mean duration of dialysis in patients was 7.2 ± 7.4 years. The access route was fistula in 22 patients (73\%), was permanent catheter in five patients (17\%), and was graft in three patients (10\%). The mean delivered KT/V and UF were 1.52 ± 0.97 and 2.27 ± 0.79 L, respectively. The major cause of end stage renal disease (ESRD) were the followings: diabetes in five patients, hypertension in three patients, glomerulonephritis in four patients, and autosomal dominant polycystic kidney disease (ADPKD) in two patients. In other cases, the cause of ESRD was unknown.

Table 1 presents the comparison of hemodynamic parameters of the patients before and after dialysis; the results indicate a significant reduction in weight and blood pressure and a significant increase in Hct after dialysis \((p < .05)\). Table 2 presents the comparison of the echocardiographic parameters and their changes before and after dialysis; according to the results, IVCD, LA area, LAD, LVEDD, LVESD, MVI, \(E/E'\), IVRT, IVCD\textsubscript{imin}, IVCD\textsubscript{imax}, PCWP, and PAP significantly decreased after the dialysis \((p < .05)\). Table 3 presents the comparison of the BIA parameters before and after dialysis; according to the results, ECW, TBW, and TBW% significantly decreased after the dialysis \((p < .05)\).

Table 4 shows the correlation between echocardiographic and BIA parameters before and after dialysis; as shown, there was only a significant correlation between the changes in IVCD\textsubscript{imin} and ECW% and TBW% before the dialysis \((p < .05)\).

There was no significant difference between the two groups of hypertensive and non-hypertensive patients by age, sex, cause of ESRD, weight, and Hct before and after dialysis. Table 5 presents the comparisons between echocardiographic and BIA parameters before and after dialysis in the two groups of hypertensive and non-hypertensive patients. According to the results, LAD, LVEF, and LVESD were significantly lower in non-hypertensive group before dialysis. After dialysis, \(E'\) in this group was significantly higher and IVCD\textsubscript{imin} was significantly lower \((p < .05)\).

IVCD\textsubscript{imin} 4.25 mm/m\textsuperscript{2} with sensitivity of 64\% and specificity of 79\% and area under the curve (AUC) of 65\% was able to distinct between overload and dehydrate patients (define based on BIA) before HD.

**Discussion**

Maintenance of fluid and electrolyte balance is an important issue in HD patients because hydration imbalance is associated with mortality. According to many studies, BIA is a preferred method for determining the dry weight.\textsuperscript{20,21} ECW changes are related to total exchangeable sodium.\textsuperscript{22} In this study, the evaluation of BIA parameters showed a significant reduction in ECW, TBW, and TBW% after a dialysis session. Therefore, these parameters can be used as the factors affecting the volume in HD patients. Other studies have also reported that ECW and ECW% are associated with the hydration balance.
of patients. However, in many dialysis centers, due to limited access to the BIA, time limits, and other limiting conditions, the volume status of patients are determined only via clinical methods. As echocardiography is noninvasive, repeatable, and is able to check heart performance, hence it can be used as a substitute for BIA.

IVCD has been proposed as a good indicator of the status of the right heart and jugular venous pressure (JVP). It has also been proposed as the reflector of changes in body fluid, especially circulatory blood volume during dialysis. Several studies have proposed its usefulness for the estimation of the volume status. We assessed correlation between echocardiographic indices such as IVCD diameter, IVC collapsibility index, IVCDimin, IVCDimax etc. and BIA index as the most accurate method. The major findings of the present study were:

1. The hydration status indices of BIA and most of the echocardiographic parameters such as LAD, LVEDD, MVI, IVRT, PCWP, IVCDimax and IVCDimin significantly decreased after dialysis.

2. There was a significant difference between the two groups of hypertensive and non-hypertensive patients in terms of LAD, LVEDD, and LVESD before dialysis. In addition, there was a significant difference between the two groups in terms of IVCDimin after dialysis.

3. There was relationship between IVCDimin with ECW% and TBW% before dialysis and the significant relationship between its changes with the changes in ECW% after HD. Then IVCDimin is a potentially useful marker for estimation hydration status in adult HD patients.

4. We calculated cutoff point for IVCDimin that is distinct between overload and dehydrate patients (define base on BIA).

Two techniques used in this study showed that there is a reduction in many indices after HD. This result agrees with other studies. In our study, we found IVCDimin significantly higher in hypertensive group after dialysis. Comparison of IVCDimin in two groups, hypertensive and non-hypertensive, has not been assessed in other studies. In El-Ahwal study, there was a significant
difference between the two groups of hypertensive and non-hypertensive patients in terms of IVCD and other indices such as peak pulmonary vein systolic velocity (S) and diastolic velocity (D) and its ratio and A/E ratio (peak early mitral inflow velocity (E)/peak late mitral inflow velocity (A))30 that we did not investigate.

Collapsibility indices of IVC and IV diameter have been shown in other studies to correlate with BIA in HD patients but we were unable to find statistical correlation between these indices with BIA. This could partly be explained the time required for transferring the fluid from interstitium to intravascular compartment.30 In reality, BIA devices assess ECW so this cannot measure intravascular volume directly but IVCD is a method that reflects the intravascular volume.31 If measurements were performed a few hours after HD, these techniques have further agreed.32 As a result, because of the relationship between IVCDimin with ECW% and TBW% before dialysis and the significant relationship between its changes with the changes in ECW%, we can introduce IVCDimin as an appropriate echocardiography factor associated with hydration status in adult HD patients. We suggest cutoff point 4.25 mm/m² after HD. Pre-HD IVCDimin in dehydrated and overhydrated patients were <4.25 mm/m² and ≥4.25 mm/m², respectively.

Although our study was a cross-sectional study with a small sample size, it showed that IVCDimin could be a good indicator of hydration status in HD patients. Therefore, it is recommended to determine the cutoff points of IVCDimin for determination of the status of the patients in future studies with large sample size. In addition, future studies can also evaluate the effects of different methods used for determination of the volume status in HD patients on the survival of these patients.

Conclusion

The findings of this study showed that because of the relationship between IVCDimin with ECW% and TBW% before dialysis and the relationship between its changes with the changes in ECW%, then in our opinion, IVCDimin index assessment may be a promising noninvasive tool and the best echocardiographic parameter associated with hydration status in HD patients.

Disclosure statement

No potential conflict of interest was reported by the authors.

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