Title
BIS and postdialysis hypotension

Journal
Hemodialysis International, 19(4)

ISSN
1492-7535

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Publication Date
2015-10-01

DOI
10.1111/hdi.12305

Peer reviewed

HHS Public Access

Author manuscript

Hemodial Int. Author manuscript; available in PMC 2016 October 01.

Published in final edited form as:

Hemodial Int. 2015 October ; 19(4): 536–542. doi:10.1111/hdi.12305.

Association of bioimpedance spectroscopy-based volume estimation with postdialysis hypotension in patients receiving hemodialysis

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Abstract

Clinical examination to determine the dry weight of patients on hemodialysis (HD) has been problematic, with studies showing discordance between physician assessment and objective measures of volume status. We studied the association between predialysis bioimpedance spectroscopy (BIS)-based estimates of fluid overload and postdialysis hypotension in 635 patients in the United States Renal Data System ACTIVE/ADIPOSE (A Cohort study To Investigate the Value of Exercise/Analyses Designed to Investigate the Paradox of Obesity and Survival in ESRD) study receiving HD in 2009–2011. We recorded predialysis and postdialysis weight and blood pressures over 3 consecutive HD sessions and performed BIS before a single session. Using a previously reported method of estimating normohydration weight, we estimated postdialysis fluid overload (FO_{post}) in liters. We used logistic regression with extracellular water/total body water (ECW/TBW) or estimated FO_{post} as the primary predictor and 1 or more postdialysis systolic blood pressures less than 110 mmHg as the dependent variable. Models were adjusted for

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DISCLOSURE

The interpretation and reporting of the data presented herein are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the US government.

No author reports a conflict of interest.

This study was presented, in part, as a poster at Kidney Week 2014 (Annual Meeting of the American Society of Nephrology); November 15, 2014; Philadelphia, PA.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

age, sex, race, ultrafiltration rate per kilogram of body weight, end-stage renal disease vintage, diabetes mellitus, heart failure, and albumin. Higher ECW/TBW was associated with lower odds of postdialysis hypotension (odds ratio [OR] 0.35, 95% confidence interval [CI] 0.15–0.84 per 0.1, P = 0.02). Every liter of FO_{post} was associated with lower adjusted odds of postdialysis hypotension (OR 0.86, 95% CI 0.79–0.95, P = 0.003). Prospective studies are needed to determine whether this application of BIS could improve current clinical efforts to minimize episodes of postdialysis hypotension without leading to volume overload.

Keywords

Bioimpedance spectroscopy; end-stage renal disease; hemodialysis; volume status

INTRODUCTION

Accurate assessment of volume status in patients receiving hemodialysis (HD) is essential because chronic volume overload can contribute to left ventricular hypertrophy, decompensated heart failure, arrhythmias, and higher mortality, whereas volume depletion can lead to hypotension, tachycardia, cramps, and poor tolerance of dialysis or shortened treatments.[1,2] Clinical examination to determine the dry weight in patients on dialysis has been problematic, with multiple studies showing discordance between physician assessment and objective measures of volume status.[3,4] Other novel methods of volume assessment have important limitations. For example, algorithmic dry weight probing improved blood pressure control in a randomized controlled trial, but probing of dry weight carries the risk of precipitating hypotension, dizziness, and cramps.[5–7] Although some studies reported benefits with relative plasma volume monitoring, its use resulted in an increase in hospitalization and mortality in a randomized trial, and attempts to establish relative plasma volume monitoring as a quantitative tool have not been successful.[8,9] Studies using bioelectrical vector analysis to titrate dry weight have shown promising results but lack norms that would allow for estimation of fluid overload in liters.[10–12]

Postdialysis blood pressure below 110 mmHg has been associated with higher cardiovascular and all-cause mortality in multiple observational studies, with some authors speculating that these adverse outcomes may be related to excessive quantity or rates of ultrafiltration.[13,14] In addition, peri-dialysis declines of ≥30 mmHg in systolic blood pressure are associated with lower patient survival, highlighting the importance of cautious volume removal and blood pressure monitoring.[15]

A recent randomized controlled trial found that use of bioimpedance spectroscopy (BIS), a method of measuring tissue conductivity to estimate volume status, led to improvements in the control of hypertension and hypervolemia, but the value of predialysis BIS in predicting episodes of postdialysis hypotension was not explored.[16] We used data from the United States Renal Data System (USRDS) ACTIVE/ADIPOSE (A Cohort study To Investigate the Value of Exercise/Analyses Designed to Investigate the Paradox of Obesity and Survival in ESRD) cohort to determine whether predialysis BIS-based volume assessment could predict episodes of postdialysis hypotension.

METHODS

ACTIVE/ADIPOSE is a cohort study of the USRDS Rehabilitation/Quality of Life and Nutrition Special Studies Centers that enrolled 778 prevalent patients receiving HD from the San Francisco Bay Area and the Atlanta metropolitan area between July 2009 and August 2011. We included the 635 (82%) patients with complete blood pressure and BIS data in the analytic sample. The study was approved by the Institutional Review Boards at Emory University and the University of California, San Francisco, and study participants provided informed consent. The methods and description of the ACTIVE/ADIPOSE study have been published elsewhere.[17] We included English-speaking or Spanish-speaking patients who had been on dialysis for at least 3 months. We recorded predialysis and postdialysis weight and blood pressures over 3 consecutive dialysis sessions, and performed BIS before a (fourth) single mid-week or end-of-week dialysis session immediately following (Supporting Information Figure S1). Because data on postdialysis weights were not available for the HD session immediately following the BIS testing, we estimated ultrafiltration volume as the postdialysis weight subtracted from the predialysis weight, averaged over the 3 previous sessions. We recorded HD session length from the patient's HD prescription.

Bioimpedance spectroscopy

Prior to a HD session, we performed whole-body BIS using a device that scans 256 frequencies between 4 and 1000 kHz (SFB7; ImpediMed, SanDiego, CA, USA). We placed electrodes on patients in a tetrapolar configuration on the hand and foot opposite to the side of dialysis access after patients were supine for at least 10 minutes. The proximal and distal electrodes were placed 5 cm apart, and 10 measurements were performed within 1 minute. We estimated total body water (TBW) by extrapolating resistance to infinite frequency and extracellular water (ECW) by extrapolating resistance to zero frequency.[18]

ECW/TBW ratio

Although we were primarily interested in assessing the potential utility of a clinically relevant estimate of fluid overload, we first performed a "proof of principle" examination of the association between untransformed BIS parameters and postdialysis hypotension. The ratio of extracellular water to total body water (ECW/TBW) is a basic indicator of fluid status in BIS studies.[19,20] We examined whether ECW/TBW based on BIS estimates was associated with postdialysis blood pressure lower than 110 mmHg.

Estimation of fluid overload

Ultrafiltration volume is generally prescribed as the difference between the patient's predialysis weight and the target postdialysis weight, often referred to as the "dry weight" or "estimated dry weight." In order to mimic this practice, we used a previously published formula to estimate fluid overload.[21] Briefly, investigators used deuterium and sodium bromide dilution to determine TBW and ECW, respectively, in a group of healthy individuals. Accounting for body fat estimated by multiple techniques, they generated a formula to estimate fluid overload across a range of body fat content. We selected this formula over a previous formula developed in patients on HD by the same research group[22] because it accounts for varying body composition. We applied this formula (Equation 1) to estimate volume overload. Average ultrafiltration volume (UF) was subtracted from volume overload (VO) to determine the residual fluid overload (FO_{post}):

$$\mathrm{VO}=1.136\times\mathrm{ECW_{WB}}-0.430\times\mathrm{ICW_{WB}}-0.114\times\mathrm{M_{WB}} \quad (1)$$

$$\mathrm{FO_{post}}=\mathrm{FO_{pre}}-\mathrm{UF} \quad (2)$$

VO is the volume overload (kg); ECW_{WB} is the extracellular body water (L); ICW_{WB} is the intracellular body water (L); M_{WB} is the body weight (kg); UF is the average ultrafiltration volume; FO_{pre} is the fluid overload, predialysis; and FO_{post} is the fluid overload, postdialysis.

Blood pressure

Postdialysis blood pressure was taken as part of routine care and was recorded for the previous 3 HD sessions before the study visit with BIS measurement. The dependent variable for this analysis was having at least 1 postdialysis systolic blood pressure below 110 mmHg.

Covariates

We selected covariates based on a clinical conceptual model and included demographic characteristics, patient comorbidities, and HD-related factors extracted from the dialysis medical record, including the most recent clinical laboratory results. Demographic covariates included age, sex, and race (African American vs. non-African American). We adjusted for patient characteristics that could be associated with volume status and postdialysis hypotension such as diabetes mellitus, serum albumin concentration, and heart failure. We obtained data on diabetes and heart failure from the Centers for Medicare and Medicaid Services (CMS) Medical Evidence Form 2728. We measured a contemporaneous serum albumin concentration with nephelometry.[17] To further account for HD factors that are likely to contribute to postdialysis hypotension, we adjusted for ultrafiltration volume per hour of prescribed dialysis time per kilogram of body weight and ESRD vintage (time since first end-stage renal disease [ESRD] treatment).

Statistical analysis

We compared patient characteristics by quartile of fluid overload using chi-square tests, ANOVA, and linear regression as appropriate. We examined residuals of continuous variables for normal distribution and log-transformed those with non-normal distribution (e.g., ESRD vintage). In our “proof of principle” analysis, we used multivariate logistic regression with ECW/TBW as the primary predictor. We repeated the analysis using postdialysis fluid overload as the primary predictor. A spline curve was generated displaying the association between postdialysis fluid overload and the log-odds of postdialysis systolic blood pressure less than 110 mmHg. Knots were placed by the statistical package symmetrically based on the predictor distribution at −2.86, 0.47, and 4.23 L of postdialysis fluid overload. As a sensitivity analysis, we examined the mean difference between predialysis weight from the day of the BIS testing and mean predialysis weight used in the analysis and repeated the analysis excluding patients with a difference of >0.5 kg. We conducted all analyses using Stata 13 (StataCorp LP: College Station, Texas, USA).

RESULTS

Of the 778 patients included in ACTIVE/ADIPOSE, 140 patients did not have BIS data available. BIS was not performed in patients with pacemakers, amputations, or metal hardware or implants within the path of the circuit. An additional 3 patients were missing data on postdialysis blood pressure or weight, and the remaining 635 patients made up the analytic cohort. The mean age of the cohort was 57 years (SD 15; Table 1). There were no significant differences in mean age, or the distribution by sex or race when comparing patients included in the analytic sample to those who were not included.

ECW/TBW ratio

When examining the univariate relationship between ECW/TBW and postdialysis hypotension, we found that higher ECW/TBW was associated with lower odds of postdialysis hypotension (odds ratio [OR] 0.47 per 0.1, 95% confidence interval [CI] 0.24–0.93). In a multivariable model, higher ECW/TBW was also associated with lower odds of a postdialysis blood pressure of less than 110 mmHg (OR 0.35 per 0.1, 95% CI 0.15–0.84; Table 2). Longer ESRD vintage was significantly associated with higher odds of having at least 1 episode of postdialysis hypotension, while age, sex, and diabetes mellitus were not.

Postdialysis fluid overload

Patients in the highest quartile of postdialysis fluid overload were older and more likely to have a lower ultrafiltration volume per kilogram of body weight when compared to patients in the lowest quartile. Longer vintage was again associated with higher odds of postdialysis hypotension, whereas African American race and diagnosis of heart failure were associated with lower odds of postdialysis hypotension. After adjusting for covariates, higher BIS-based postdialysis fluid overload was associated with lower adjusted odds of postdialysis hypotension (OR 0.86 per liter, 95% CI 0.79–0.95; Table 3). This association persisted when average predialysis systolic blood pressure was included as a covariate (OR 0.83; 95% CI 0.71–0.96). A multivariate spline showed that when ultrafiltration volume exceeded predialysis fluid overload, the odds of postdialysis hypotension were higher with greater postdialysis volume depletion (Figure 1).

Sensitivity analysis

Because BIS estimates were measured before a fourth HD treatment following the 3 treatments from which blood pressure and weight data were obtained, we examined the mean difference between the mean of the predialysis weights used in the analysis and the predialysis weight from the day of BIS testing. The mean difference between the weights was 0.36 kg (95% CI 0.23–0.48; SD 1.6). The associations between fluid overload or ECW/TBW and postdialysis hypotension did not substantively change when participants with a weight difference greater than 0.5 kg were excluded from the analysis (n = 268; per liter of fluid overload: OR 0.83, 95% CI 0.71–0.96; per 0.1 higher ECW/TBW: OR 0.88, 95% CI 0.77–0.996).

DISCUSSION

We demonstrated a statistically significant association between BIS-based measures of fluid overload and the odds of developing postdialysis hypotension in a cohort of prevalent HD patients. There was a graded association between postdialysis fluid overload and hypotension such that at higher levels of postdialysis fluid overload, the odds of postdialysis hypotension were lower.

The association of lower ECW/TBW and postdialysis hypotension is expected because ECW/TBW is a common surrogate for hydration status that has been used in multiple studies.[19,20] Because this ratio is conceptually difficult to apply in a clinical setting, we converted the BIS volume measurements into liters of extracellular fluid overload, which is more intuitive because ultrafiltration goals are generally prescribed in liters. The relation between postdialysis fluid overload and postdialysis hypotension persisted after adjustment for other variables expected to be related to postdialysis hypotension, including demographics, comorbidities, and ultrafiltration rate.

The association of the diagnosis of heart failure with lower odds of hypotension was surprising. We recorded heart failure simply as present or absent as a clinical diagnosis, and we did not have information on ejection fraction or cardiac function that could have placed certain participants at higher risk for postdialysis hypotension. Therefore, we speculate that the diagnosis of heart failure may have been based, in part, on the presence of symptomatic fluid overload rather than impaired systolic function. Contrary to systolic dysfunction, symptomatic fluid overload would be expected to be associated with lower risk of postdialysis hypotension, as we observed. Given the importance and clinical heterogeneity of heart failure in the dialysis population, this finding should be explored more carefully with echocardiographic data.

Since BIS measurements take minutes to perform, BIS volume assessments could be performed when routine predialysis vital signs are obtained, making it theoretically possible for this method of BIS-based volume assessment to be used by nursing staff and physicians to estimate a target ultrafiltration goal prior to a HD session. This approach may be particularly useful during unstable clinical periods or periods of probing dry weight, such as with the initiation of dialysis or after hospital discharge. The results of our study are encouraging and could be used in the design of a clinical trial of such a strategy.

Volume status is a known contributor to blood pressure in patients receiving HD and appropriate ultrafiltration is essential to avoid low postdialysis blood pressure (while also avoiding potentially detrimental fluid overload).[23,24] Postdialysis blood pressure less than 110 mmHg has been associated with higher mortality in patients on HD when compared with a blood pressure of 140–149 mmHg.[14] Subsequent studies have shown that the HD treatment has been linked to repetitive myocardial ischemia and that reversing the level of dialysis-induced hypotension was associated with a decrease in cardiac injury,[6,25] In our study, when ultrafiltration volume exceeded predialysis fluid overload, the odds of postdialysis hypotension were higher than if ultrafiltration volume was equal to or less than predialysis fluid overload. These findings raise the intriguing possibility that use of bioimpedance could minimize the detrimental effects of dialysis-associated hypotension.

The strengths of our study include the relatively large cohort from 2 regions of the United States that had direct predialysis bioimpedance measurements. In contrast to prior studies using single-frequency bioimpedance analysis, we used multifrequency BIS, which uses a range of frequencies to estimate ECW and TBW and provides more accurate extracellular fluid estimation.[26] We had access to carefully collected information about prescribed HD time and weights. Despite these strengths, some limitations must be addressed. First, we relied on a single BIS measurement for each patient and compared predialysis volume status and blood pressures over the prior 3 treatments. This strategy may have biased our results toward the null. Second, we analyzed blood pressures that were obtained as part of routine clinical care which was likely to have added variation to the outcome, but aligns with the data clinicians routinely have available for decision-making. Third, our outcome of postdialysis blood pressure does not address dyspnea or other adverse clinical symptoms that could be related to residual postdialysis volume overload. Fourth, we did not have information on antihypertensive administration prior to HD or delivery of intravenous fluids during dialysis that could have altered their blood pressure during the course of the treatment. However, both of these factors would have biased the results toward no association between BIS-estimated fluid overload and postdialysis hypotension. Finally, the equation used to estimate fluid overload was derived from healthy participants using deuterium oxide and sodium bromide, and we used BIS, which likely resulted in additional variation in fluid compartment estimation.[27]

Our findings demonstrate that BIS-based estimates of fluid overload were associated with postdialysis hypotension. This finding raises the possibility that bioimpedance could be used to determine an ultrafiltration goal that will minimize episodes of postdialysis hypotension. Prospective studies are needed to determine whether this application of BIS could be used to improve current clinical efforts to minimize episodes of postdialysis hypotension without leading to volume overload.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported through contracts N01-DK-7-0005 and N01-DK-7–5004 from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), a K24DK085153 grant, and a K23DK093584 (LSD) grant.

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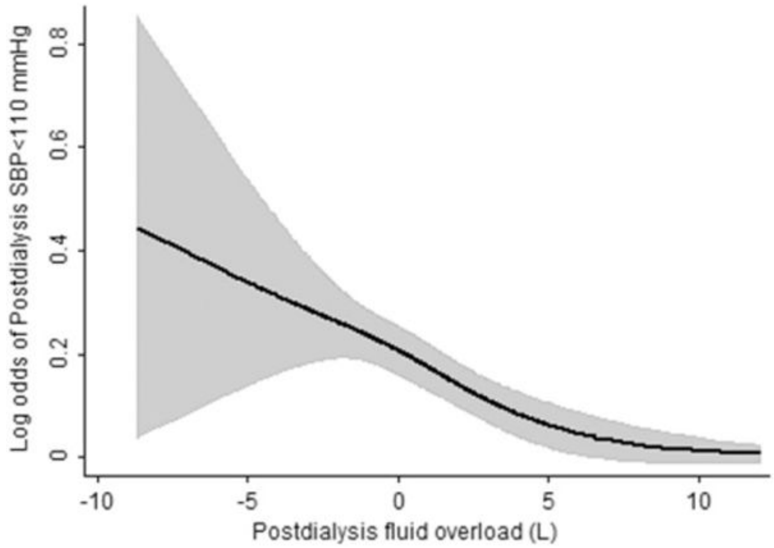

Figure 1.

Multivariable spline curve, adjusted for age, sex, African American race, diabetes, heart failure, serum albumin, ultrafiltration rate, body weight, and end-stage renal disease vintage, between bioimpedance spectroscopy-estimated postdialysis fluid overload (L) and 1 or more postdialysis blood pressures less than 110 mmHg.

Table 1

Patient characteristics based on quartile of postdialysis fluid overload

	All (N = 635)	Quartile 1 (N = 159)	Quartile 2 (N = 159)	Quartile 3 (N = 159)	Quartile 4 (N = 158)	P value
Mean (SD) postdialysis fluid overload (L)	0.6 (2.9)	−2.9 (1.4)	−0.4 (0.50)	1.4 (0.61)	4.4 (1.8)	—
Age (y)	57 (15)	52 (15)	57(14)	58(14)	60(14)	<0.001
Race[a]						
White	147 (23%)	39 (25%)	40 (25%)	41 (26%)	27 (17%)	0.49
African American	398 (63%)	97 (61%)	95 (60%)	96 (60%)	110 (70%)	—
Other	89 (14%)	23 (14%)	24 (15%)	22 (14%)	20 (13%)	—
Heart failure	105 (17%)	24 (15%)	29 (18%)	30 (19%)	22 (14%)	0.6
Diabetes mellitus	273 (43%)	58 (36%)	74 (47%)	73 (46%)	68 (43%)	0.2
Prescribed hemodialysis time (h)	3.49 (0.45)	3.51 (0.48)	3.41 (0.45)	3.51 (0.43)	3.51 (0.43)	0.13
ESRD vintage (y) [median, 25th, 75th percentile)]	3.1 (1.4, 6.7)	4.1 (1.7, 7.9)	2.8 (1.1, 6.5)	3.3 (1.2, 6.0)	3.0 (1.3, 6.4)	0.05
UF volume/weight (%)	3.2 (1.4)	3.6 (1.3)	3.4 (1.4)	3.1 (1.3)	2.8 (1.4)	<0.001
Albumin (g/dL)	4.0 (0.4)	4.0 (0.3)	4.0 (0.3)	4.0 (0.3)	3.9 (0.4)	0.05
ECW/TBW	0.47 (0.03)	0.44 (0.02)	0.46 (0.02)	0.47 (0.02)	0.50 (0.03)	<0.001
Mean predialysis systolic blood pressure (mmHg)	152.5 (22.8)	150.3 (23.6)	150.5 (21.9)	155.7 (22.3)	153.3 (23.2)	0.1
Mean postdialysis systolic blood pressure (mmHg)	138.4 (21.0)	133.4 (20.2)	135.1 (19.2)	141.8 (20.7)	143.4 (22.4)	<0.001

[a]Includes one missing value.

ECW = extracellular water; TBW = total body water; UF = ultrafiltration.

Table 2

Multivariable association between extracellular water/total body water (ECW/TBW) and odds of postdialysis systolic blood pressure <110 mmHg

	Odds ratio (95% CI)	P value
ECW/TBW (per 0.1)	0.35 (0.15–0.84)	0.02
Demographic factors		
Age (y)	1.00 (0.99–1.02)	0.57
African American race	0.60 (0.38–0.95)	0.03
Male sex	1.04 (0.65–1.68)	0.87
Patient factors		
Diabetes mellitus	1.50 (0.95–2.38)	0.08
Heart failure	0.47 (0.24–0.93)	0.03
Albumin (g/dL)	0.78 (0.42–1.44)	0.43
Hemodialysis factors		
UF rate (mL/h/kg)	0.99 (0.93–1.04)	0.60
ESRD vintage (log)	1.32 (1.07–1.62)	0.008

CI = confidence interval; ESRD = end-stage renal disease; UF = ultrafiltration.

Table 3

Multivariable association between postdialysis fluid overload (FO_{post}, L) and odds of postdialysis systolic blood pressure <110 mmHg

	Odds ratio (95% CI)	**P value**
Postdialysis fluid overload (L)	0.86 (0.79–0.95)	0.003
Demographic factors		
Age (y)	1.00 (0.98–1.02)	0.75
Male sex	1.26 (0.75–2.11)	0.38
African American race	0.60 (0.38–0.94)	0.03
Patient factors		
Diabetes mellitus	1.39 (0.89–2.18)	0.15
Heart failure	0.44 (0.22–0.87)	0.02
Albumin (g/dL)	0.80 (0.44–1.48)	0.48
Hemodialysis factors		
UF rate (mL/h/kg)	0.97 (0.91–1.02)	0.22
ESRD vintage (log)	1.28 (1.04–1.56)	0.02

CI = confidence interval; ESRD = end-stage renal disease; UF = ultrafiltration.