



Use of body composition measurements to guide the assessment of dry weight in anuric dialysis patients: improvements in blood pressure control



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ABSTRACT

Purpose: Fluid management using a body composition monitor (BCM) based on bioimpedance spectroscopy has been found to be beneficial for maintenance hemodialysis (MHD) patients. Our purpose was to provide a management procedure for the adjustment of post-dialysis overhydration (OH_{post}) and to evaluate whether this approach could improve blood pressure.

Methods: Post-dialysis fluid status was assessed weekly using the BCM. The reference value of OH_{post} and the flow procedure for post-dialysis target weight (PDTW) adjustment were established via measurements of OH_{post} in 60 normotensive MHD patients. In the interventional study, we adjusted the PDTW of hypertensive patients to the optimal OH_{post} range, with a 0.2–0.5 kg change in PDTW per week.

Results: This observational study included 130 anuric MHD patients, of whom 60 were in the pre-dialysis systolic blood pressure ($\text{sBP}_{\text{pre}} < 140$ mmHg) group. On multivariate logistic regression analysis, we found that only OH_{post} was significantly associated with $\text{sBP}_{\text{pre}} \geq 140$ mmHg (odds ratio = 2.293, $p = 0.000$). Patients in the $\text{OH}_{\text{post}} < -1.8$ L group were mainly male and younger, and had higher post-dialysis diastolic blood pressure, ultrafiltration volume, levels of nutrition markers (serum albumin and creatinine), body mass index, and lean tissue index (LTI). On multiple stepwise regression analysis, only the change in LTI was found to be an independent predictor of OH_{post} [R^2 0.208, $\beta = -0.196$, 95% CI (-0.296, -0.095), $p < 0.001$]. The reference value of OH_{post} was found to deviate by -2.5 – 0.5 L from that of normotensive patients. At the end of the study, the systolic blood pressure of 38 patients was less than 140 mmHg after PDTW adjustment. The changes in OH_{post} from the initial to last adjustment were significant ($t = 5.431$, $p < 0.001$), with a substantial decrease in the sBP_{pre} ($t = 11.208$, $p < 0.001$).

Conclusions: Assessment of OH_{post} and LTI using a BCM with a patient-specific optimal PDTW adjustment flow can lead to significantly better control of hypertension in anuric MHD patients.

1. Introduction

Overhydration and hypertension are the most common complications in end-stage renal disease (ESRD) patients and are linked to increased mortality [1,2]. Fluid status is regarded to be the most important factor predisposing dialysis patients to hypertension or hypotension [3]. Many studies have shown that healthy blood pressure levels can be achieved in a large majority of patients, without using anti-hypertensive medication, by avoiding excess extracellular water through accurate fluid status assessment [4,5].

Clinical evaluation of fluid overload can be difficult in maintenance hemodialysis (MHD) patients and is prone to underestimation or overestimation [6,7]. Various objective methods have been recommended for defining fluid overload, such as measuring the inferior

vena cava diameter, evaluation of N-terminal pro brain natriuretic peptide, lung ultrasonography, and use of a body composition monitor based on bioimpedance spectroscopy (BCM-BIS) [8–13]. The BCM[®] (Fresenius Medical Care, Bad Homburg, Germany) is perhaps the best validated device in defining fluid status, with good overall agreement with the gold-standard isotope dilution techniques [14,15].

Some randomized controlled studies and observational studies have shown that BCM-BIS can help to establish an optimal post-dialysis target weight (PDTW) and obtain better clinical outcomes [16–21]. However, the best reference range for OH has still not been agreed universally. There may be differences in OH levels among ethnic groups, and OH levels may be affected by the time of measurement (pre- or post-dialysis) and diet (especially sodium intake) [22].

The aim of this study was to establish the optimal target values for

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post-dialysis overhydration (OH_{post}) in anuric MHD normotensive patients, and to provide a management procedure for the adjustment of PDTW, to evaluate whether this approach could improve blood pressure.

2. Materials and methods

2.1. Subjects

This observational study was performed at the dialysis unit of the BaoTou Central Hospital, Inner Mongolia, China, between October 2017 and January 2018. All patients who were treated for at least 3 months using regular hemodialysis (HD) were included, after obtaining their written informed consent. The study was approved by the institutional ethics committee of the BaoTou Central Hospital. The participants were clinically stable. The following patients were excluded from the study: 1) those aged < 18 years; 2) those with mechanical valves, pacemakers, coronary artery stents or implanted metallic devices; 3) those with hypotension and cramping in the last six intradialysis sessions; 4) those with daily urine \geq 200 mL.

2.2. Body composition measurements

In all patients, the assessment of body composition was carried out weekly using the BCM. The measurements were performed approximately 20 min after the mid- or end-week HD session. Regarding the quality of measurements, a numerical indicator was displayed on the same screen as the Cole-Cole plot during measurements; a quality value close to 100% (usually \geq 90%) and a smooth dome shape for the Cole-Cole plot indicated a successful measurement. BCM measurements were performed at baseline for all subjects.

The parameters obtained using the BCM were over-hydration (OH), total body water, intracellular water (ICW), extracellular water (ECW), ECW to ICW ratio (E/I), fat tissue index (FTI), and lean tissue index (LTI).

2.3. Clinical information

A patient questionnaire documenting sociodemographic status, personal and family health history, dialysis prescription, and medication for hypertension was completed by each patient, with the aid of doctors or nurses. Blood samples for standard laboratory parameters were obtained before the HD session. To improve the reproducibility of the blood pressure measurements, pre-dialytic systolic blood pressure (sBP_{pre}) recordings of six previous dialysis sessions were averaged.

2.4. The observational study

OH_{post} was the main parameter used for PDTW adjustment in the current study. The study flow diagram is shown in Fig. 1. In the observational study, through retrospective analysis of the normotensive group of patients, we obtained a reference value for OH_{post} . OH_{post} was

combined with LTI to obtain the optimal PDTW adjustment protocol.

2.5. The intervention study

In the intervention study, 70 hypertensive MHD patients participated in the study, all of whom were anuric. In accordance with the flow procedure for PDTW adjustment, we adjusted PDTW to the optimal OH_{post} range, with a 0.2–0.5 kg change in PDTW per week. During the period of weight reduction, antihypertensive medication was continually reviewed and progressively reduced where possible.

2.6. Statistical methods

Patient characteristics were summarized using standard descriptive statistics. Categorical variables were presented as frequencies and percentages and continuous variables as mean \pm standard deviation or as median and interquartile ranges, as appropriate. Baseline differences between normotensive and hypertensive patients were evaluated using an independent samples *t*-test for continuous variables and chi-square tests for categorical variables. Multivariate analysis was performed when differences in variables were significant in the univariate analysis. Comparison between variables was performed through one-way ANOVA in different categorical groups (grouped by OH_{post} data), and *post hoc* analysis was performed using the Bonferroni test. Correlations were also established between the OH_{post} and the variables using the Spearman rho test. Intragroup comparisons were performed using a paired *t*-test.

All statistical tests were performed using the Statistical Package for the Social Sciences 20.0 software. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Basic demographic data

There were 75 males (57.692%) and 55 females (42.308%) enrolled in this study. The patient baseline characteristics are shown in Table 1.

3.2. Comparison between the groups

We compared the different clinical parameters and body composition parameters in patient groups with different systolic blood pressures before dialysis ($\text{sBP}_{\text{pre}} < 140$ mmHg and $\text{sBP}_{\text{pre}} \geq 140$ mmHg). The results are summarized in Table 2. Except for lower antihypertensive medication (AHT), lower OH_{post} , and lower E/I ratio in the $\text{sBP}_{\text{pre}} < 140$ mmHg group, no clinical and body composition parameters were different between the $\text{sBP}_{\text{pre}} < 140$ mmHg group and the $\text{sBP}_{\text{pre}} \geq 140$ mmHg group.

Multivariate logistic regression analysis based on OH_{post} , E/I ratio, and ECW parameters showed that only OH_{post} was significantly associated with $\text{sBP}_{\text{pre}} \geq 140$ mmHg (odds ratio (OR) = 2.293, $p = 0.000$).

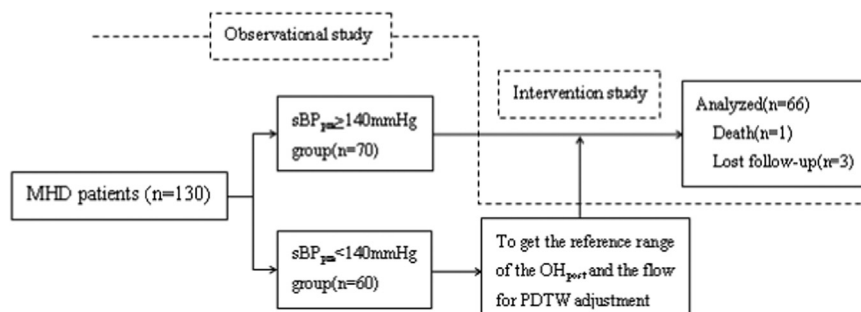


Fig. 1. Study flow diagram.

Table 1
Baseline characteristics of the patients.

Parameter	n = 130
Age (y)	56.100 ± 12.872
Gender [male/female, n (%)]	75 (57.692%)/55 (42.308%)
Etiology, n (%)	
Chronic glomerulonephritis	27 (20.769)
Diabetic nephropathy	34 (26.154)
Hypertensive nephropathy	34 (26.154)
Polycystic kidney disease	5 (3.846)
Lupus or vasculitis	6 (4.615)
Chronic interstitial nephritis	5 (3.846)
Other	3 (2.308)
Undetermined	16 (12.308)
Hemodialysis vintage (mo)	41.631 ± 29.372

3.3. Relationships between OH_{post} and clinical presentation in the $sBP_{pre} < 140$ mmHg group

The OH_{post} data in the $sBP_{pre} < 140$ mmHg group were normally distributed with a mean of -0.958 ± 1.160 L. The normal distribution of the OH_{post} in this cohort is summarized in Table 3. To detect possible relationships between patient OH_{post} and clinical presentation, we compared the different clinical parameters in $sBP_{pre} < 140$ mmHg group patients in different OH_{post} ranges. In accordance with the OH_{post} data quartiles, the patients were grouped into $OH_{post} < -1.8$ L, $OH_{post} -1.8$ to -0.25 L and $OH_{post} > -0.25$ L (Table 4). Patients in the $OH_{post} < -1.8$ L group were mainly male and younger, had higher post-dialysis diastolic blood pressure (dBp_{post}), higher ultrafiltration volume (UFV), increased levels of nutrition markers (serum albumin and creatinine), a higher body mass index (BMI), and higher LTI. We did not find a significant association between OH_{post} and dialysis vintage, diabetes mellitus, hemoglobin, AHT, or FTI (Table 4).

Multivariate regression analysis was performed to identify the independent predictors of OH_{post} in the $sBP_{pre} < 140$ mmHg group. Multiple stepwise regression analysis was performed using OH_{post} as the dependent variable, and clinical parameters including age, sex, BMI, dBp , UFV, creatinine, serum albumin, and LTI as independent variables. Only LTI was an independent predictor of OH_{post} [$R^2 = 0.208$, $\beta = -0.196$, 95% CI (-0.296, -0.095), $p < 0.001$]. A correlation was observed between OH_{post} and LTI ($\gamma = -0.456$, $p < 0.001$).

Table 2
Patient clinical parameters and body composition differences between groups.

	Grouped by systolic blood pressure before dialysis (n = 130)		t or χ^2	p	Beta Exp	p
	$sBP_{pre} < 140$ mmHg (n = 60)	$sBP_{pre} \geq 140$ mmHg (n = 70)				
Age (y)	55.233 ± 13.642	56.743 ± 12.277	-0.664	0.508		
Sex (f/m)	27/33	28/42	0.331	0.565		
Vintage (mo)	40.450 ± 31.272	42.257 ± 27.974	-0.348	0.729		
Diabetes mellitus (%)	17 (28.333%)	17 (24.286%)	0.274	0.601		
Ultrafiltration volume (mL)	2354.167 ± 781.963	2387.143 ± 820.555	-0.233	0.816		
AHT	0.783 ± 0.993	1.586 ± 1.222	-4.064	0.000		
Hemoglobin (g/L)	121.867 ± 15.546	119.029 ± 15.899	1.025	0.307		
Creatinine (mmol/L)	918.983 ± 263.320	878.300 ± 244.462	0.913	0.363		
Serum albumin (g/L)	40.885 ± 3.128	41.260 ± 3.287	-0.663	0.508		
Na^+ (mmol/L)	139.450 ± 3.321	138.571 ± 2.932	1.602	0.112		
Body mass index	23.303 ± 3.668	22.743 ± 4.649	0.754	0.452		
OH_{post} (L)	-0.958 ± 1.160	0.267 ± 1.672	-4.776	0.000	2.293	0.000
Total body water (L)	27.812 ± 5.672	28.120 ± 6.315	-0.291	0.772		
Extracellular water (L)	12.253 ± 2.195	13.024 ± 2.952	-1.666	0.098	1.069	0.458
Intracellular water (L)	15.558 ± 3.779	14.674 ± 4.454	1.209	0.229		
E/I	0.806 ± 0.118	0.876 ± 0.126	-3.238	0.002	0.278	0.596
Lean tissue index (kg/m^2)	11.392 ± 2.702	11.286 ± 2.694	0.223	0.824		
Fat tissue index (kg/m^2)	12.180 ± 4.385	11.534 ± 3.738	0.906	0.366		

sBP_{pre} , pre-dialysis systolic blood pressure; AHT, antihypertensive medication; OH_{post} , post-dialysis overhydration.

3.4. Flow procedure for PDTW adjustment protocol

In accordance with the above results, OH_{post} and LTI were the main parameters used for post-dialysis target weight (PDTW) adjustment. The reference value for OH_{post} was determined by excluding values lower than the 10th percentile and higher than the 90th percentile for data collected from normotensive patients, yielding -2.5 L and 0.5 L, respectively. LTI data in the $sBP_{pre} < 140$ mmHg group were normally distributed with a mean of 11.392 ± 2.702 kg/m^2 . The normal distribution of the LTI in this cohort is summarized in Table 3. We chose the 50th percentile ($LTI = 11.1$ kg/m^2 and $OH_{post} = -1.0$ L) as the cut-off value for the PDTW adjustment protocol. A flow diagram showing the PDTW adjustment procedure is provided in Fig. 2. When patients have symptomatic hypotension and severe cramps, the adjustment must be stopped whether or not the blood pressure is normal.

3.5. Interventional study in $sBP_{pre} \geq 140$ mmHg patients

The adjustment flow procedure of the interventional study is depicted in Fig. 2. Of the 70 hypertensive patients who underwent PDTW adjustments, four were excluded from further analysis because of a lack of follow-up ($n = 3$) or death ($n = 1$), leaving a total of 66 patients in the interventional study cohort. Of these, the systolic blood pressure of 38 patients (57%) was less than 140 mmHg after PDTW adjustment (Fig. 3). The changes in OH_{post} from the initial to last adjustment were significant ($t = 5.431$, $p < 0.001$), with a substantial decrease in the sBP_{pre} ($t = 11.208$, $p < 0.001$). Consequently, the systolic blood pressure of 28 patients (43%) did not reach the normotensive level after PDTW adjustment. The changes in OH_{post} and sBP_{pre} from the initial to last adjustment failed to reach statistical significance ($t = 1.820$, $p = 0.080$; $t = 1.162$, $p = 0.255$). Twelve patients had intradialytic symptoms in the last study week (eight patients suffered cramps, two suffered hypotensive episodes, one suffered cold sweating, and one suffered hoarseness). Of these, five patients (including two hypotensive patients and three patients who experienced cramps) were in the blood pressure target achievement group, and seven were in the blood pressure target non-achievement group.

4. Discussion

Among the factors causing hypertension in MHD patients, overhydration is thought to be the most important [23–25]. Dry weight is

Table 3
Summary statistics of OH_{post} and LTI in 60 normal systolic blood pressure patients.

Variable	Mean ± SD	Range	5th pctl	10th pctl	25th pctl	50th pctl	75th pctl	90th pctl	95th pctl
OH _{post} (L)	-0.958 ± 1.160	-3.100 – 2.900	-2.595	-2.490	-1.800	-0.950	-0.250	0.490	1.085
LTI (kg/m ²)	11.392 ± 2.702	5.900 – 17.200	16.980	15.530	13.000	11.100	9.725	7.900	6.835

OH_{post}, post-dialysis overhydration; LTI, lean tissue index.

more important in anuric MHD patients. Persistent hypervolemia causes hypertension and congestive heart failure, and leads to higher mortality. At present, there is no objective gold standard method to estimate target dry weight, and clinical assessment is unreliable. Recently, a meta-analysis reported that bioimpedance analysis-based interventions for the correction of overhydration improved systolic blood pressure control in end-stage kidney disease [26]. Moissl et al. reported that every 1 L change in fluid overload was accompanied by a 9.9 mmHg/L change in pre-dialysis systolic blood pressure [21]. In the current study, we found that only OH_{post} was significantly associated with sBP_{pre} ≥ 140 mmHg (OR = 2.293, *p* = 0.000). OH_{post} was one of most important and potentially adjustable causes of hypertension in MHD patients.

Although detailed BCM-based dry weight adjustment protocols have been previously published, there is still no uniform reference range for OH [16,18,21,27]. There are multiple reasons for the discrepancies in the target range, including different BCM measuring times, different ethnic groups and subjects, ages, sodium intake, variations in daily urine volume, and different body compositions. To minimize the effects of these factors, we selected subjects with daily urine < 200 mL and without hypotension or cramping during the last six intra-dialysis sessions. Chen et al. provided a simple and applicable algorithm for PDTW adjustment with BCM-BIS. The only shortcoming was that OH_{post} was the only parameter in the algorithm, and the range of reference values was derived from MHD patients generally [18]. Our clinical experience indicated that MHD patients with different nutritional statuses had different tolerances to ultrafiltration, suggesting that the optimal OH_{post} range for particular MHD patients may be associated with nutritional parameters. This was confirmed in the current study, in which patients in the OH_{post} < -1.8 L group were mainly male and younger, and had

higher dBp_{post}, UFV, levels of nutrition markers (serum albumin and creatinine), BMI, and LTI. In the multivariate regression analysis, only LTI was an independent predictor of OH_{post} [*R*² = 0.208, β = -0.196, 95% CI (-0.296, -0.095), *p* < 0.001]. Therefore, we chose OH_{post} and LTI as the main parameters for PDTW adjustment. In the current study, the reference value of the OH_{post} was determined by excluding values lower than the 10th percentile and higher than the 90th percentile for data collected from normotensive patients, yielding -2.5 L and 0.5 L, respectively. We also chose the 50th percentile (LTI = 11.1 kg/m² and OH_{post} = -1.0 L) as the cut-off value for the PDTW adjustment protocol (Fig. 2).

The novelty of this study includes its use of OH_{post} combined with LTI to adjust the PDTW. It considers differences in body composition, which makes the management strategy for OH_{post} safer and more patient-specific. Although we used the PDTW adjustment protocol to guide better blood pressure control, we still insisted that if adverse reactions happened during adjustment, we would not force patients to reach the target. Using our PDTW adjustment protocol, up to 57% of hypertensive patients showed a significant change in OH_{post} from the initial to last adjustment (*t* = 5.431, *p* < 0.001) with a substantial decrease in the sBP_{pre} (*t* = 11.208, *p* < 0.001) (Fig. 3). Lowering dry weight in dialysis patients can lead to intradialytic complications [28]. Previous studies have relied on the clinician's best judgment and clinical experience of volume assessment, and found that a strict dry-weight control may lead to vascular access problems and an increased number of hospitalizations [29]. In the current study, two of the 38 blood pressure target achievement patients could not be brought into the target range of the OH_{post} because of hypotension or for personal reasons. For patients whose OH_{post} was within the reference range, four patients had intradialytic symptoms in the last study week (three

Table 4
The relationship between clinical parameters and hydration status in the sBP_{pre} < 140 mmHg group.

	Grouped by OH _{post} (n = 60)		
	< -1.8 L	-1.8 to -0.25 L	> -0.25 L
Age (yr)	41.214 ± 9.023 * #	59.065 ± 10.930	60.400 ± 13.968
Sex (m/f)	12/2 [Ⓔ]	14/17 [Ⓔ]	7/8 [Ⓔ]
Vintage (mo)	30.500 ± 18.245	47.000 ± 20.987	45.600 ± 46.394
Diabetes mellitus (%)	1/14	10/31	6/15
sBP _{post} (mmHg)	130.500 ± 7.133	128.387 ± 9.711	128.333 ± 9.217
dBp _{post} (mmHg)	81.214 ± 5.899 ^{&}	74.581 ± 7.932	70.400 ± 12.894
Antihypertensive medication	1.071 ± 0.997	0.710 ± 1.071	0.667 ± 0.817
Ultrafiltration volume (L)	2864.286 ± 874.077 [§]	2295.161 ± 618.918	2000.000 ± 802.674
serum albumin (g/L)	42.686 ± 3.321 [§]	40.765 ± 2.368	39.453 ± 3.672
Creatinine (mmol/L)	1186.500 ± 177.341 ^{£V}	883.548 ± 230.276	742.533 ± 204.133
Hemoglobin (g/L)	117.929 ± 14.248	124.032 ± 13.870	121.067 ± 19.779
Body mass index (kg/m ²)	24.457 ± 3.499 [†]	23.884 ± 3.471 [‡]	21.027 ± 3.449
Lean tissue index(kg/m ²)	13.914 ± 2.089 ^{††}	11.084 ± 2.344	9.673 ± 2.281
Fat tissue index (kg/m ²)	11.400 ± 4.731	13.116 ± 4.367	10.973 ± 3.907

OH_{post}, post-dialysis overhydration; sBP_{post}, post-dialysis systolic blood pressure; dBp_{post}, post-dialysis diastolic blood pressure.*: < -1.8 L Vs -1.8~-0.25 L, *P* < 0.001; #, < -1.8 L Vs > -0.25 L, *P* = 0.000.&: < -1.8 L Vs > -0.25 L, *P* = 0.006.§: < -1.8 L Vs -1.8~-0.25 L, *P* = 0.001; II, < -1.8 L Vs > -0.25 L, *P* = 0.000.£: < -1.8 L Vs > -0.25 L, *P* = 0.014.£: < -1.8 L Vs -1.8~-0.25 L, *P* < 0.001; ¥, < -1.8 L Vs > -0.25 L, *P* = 0.000.§: < -1.8 L Vs > -0.25 L, *P* = 0.007.¶: < -1.8 L Vs > -0.25 L, *P* = 0.030; †, -1.8~-0.25 L Vs > -0.25 L, *P* = 0.034.Ⓔ: *p* = 0.031.

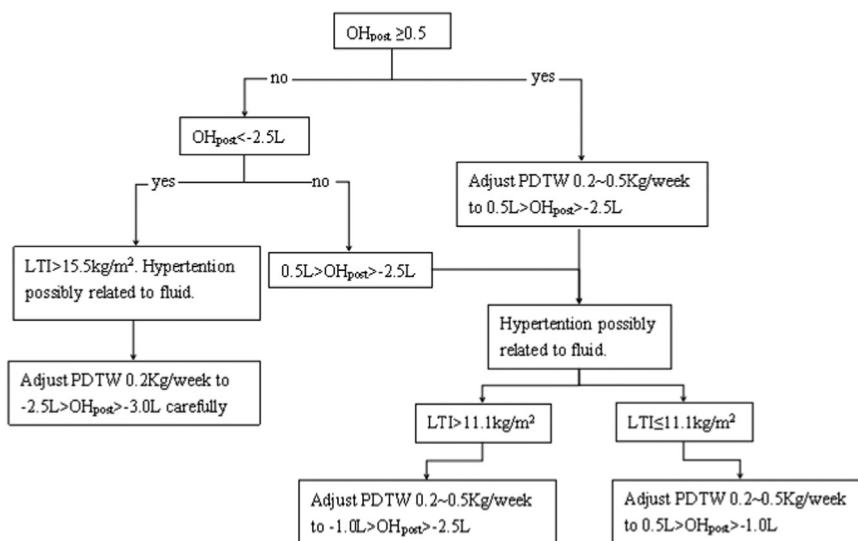


Fig. 2. Flow diagram showing the PDTW adjustment procedure with BCM results in hypertensive patients. The 50th percentile values for OH_{post} and LTI were $-1.0L$ and 11.1 kg/m^2 , respectively.

patients with cramps, one patient with hypotensive episodes). However, these complications did not result in hospitalization or other adverse outcomes. Although the systolic blood pressure of 28 patients (43%) did not reach the normotensive level after PDTW adjustment, more than 75% of patients showed a systolic blood pressure of under 160 mmHg. The changes in OH_{post} and sBP_{pre} from the initial to last adjustment failed to reach statistical significance ($t = 1.820, p = 0.080$; $t = 1.162, p = 0.255$). There are several factors to be considered in this context. First, nine patients were not willing to decrease their PDTW, although the BCM clearly indicated overhydration. Second, the OH_{post} of 19 patients was in the reference range, but their blood pressure was above normotensive level. Some studies have also reported that a small subgroup of dialysis patients demonstrate a state of normohydration but have an elevated mean systolic BP. It was not possible to control hypertension through fluid removal because of hypotension and ischemia [25]. In the current study, we also observed that adverse effects were more common in these patients (five patients suffered cramps, one suffered cold sweating, and one suffered hoarseness). It remains to be demonstrated whether improved control of blood pressure in these patients is possible by following different management strategies.

There were limitations to this study. First, the present study was

conducted in one medical center and included a relatively small number of patients. Patients were not randomized into control and intervention groups, and the accuracy of the management strategy for OH_{post} adjustment in hypertension patients requires further study. A second limitation is that the study had a short follow-up period. Charra et al. reported a lag phenomenon in blood pressure control in dialysis patients [30]. Our results showed that OH_{post} reduction was associated with an improvement in blood pressure in 57% of patients, and that it might be possible in the future to increase the percentage if a longer follow-up period was used. Third, there was no examination of sleep apnea, renal artery stenosis, primary aldosteronism or pheochromocytoma in our patient exclusion criteria, which may have an impact on the results.

In conclusion, this is one of the first prospective studies to detect the optimal OH_{post} target in anuric MHD patients. This study provided an effective and applicable management strategy for PDTW that can either normalize blood pressure or make hypertension easier to control in the great majority of anuric MHD patients. It considers differences in body composition (LTI), which makes this management strategy safer and more patient-specific than previous approaches.

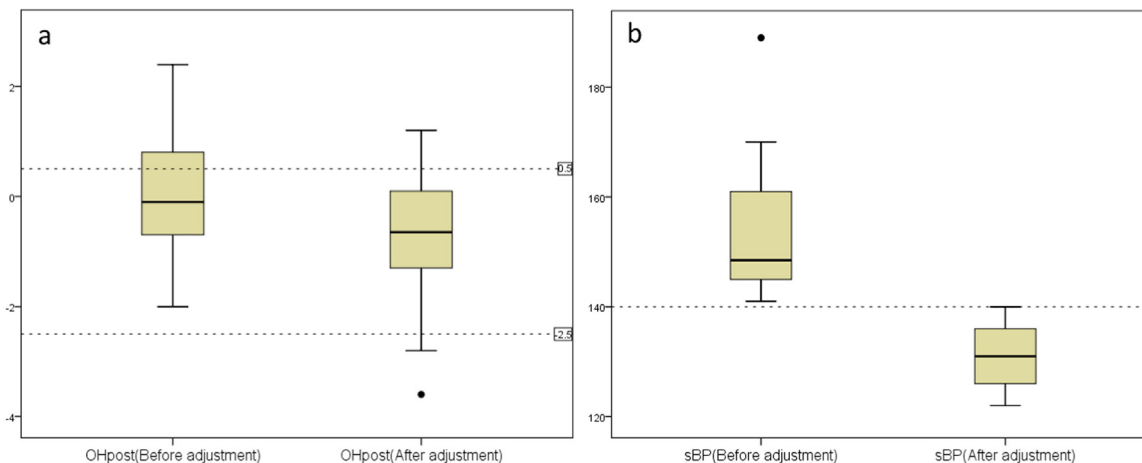


Fig. 3. Changes in OH_{post} (a) and sBP_{pre} (b) in blood pressure target achievement patients. Each box summarizes the results before and after PDTW adjustments. The target range for OH_{post} after dialysis treatment (0.5 to $-2.5L$) is indicated. The boundaries of the boxes are the 25th and the 75th percentiles.

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Appendix A. Transparency document

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bbrep.2019.01.005.

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