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ORIGINAL ARTICLE

Evaluation of factors affecting time to achieve dry weight among hemodialysis patients using bioimpedance spectroscopy

Amjad Khan[1,2,3] · Amer Hayat Khan[1,2] · Azreen Syazril Adnan[2] · Syed Azhar Syed Sulaiman[1] · Nafees Ahmad[4] · Siew Hua Gan[5]

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Abstract

Background Achieving and maintaining dry weight appears to be an effective strategy for controlling and maintaining normotension among hypertensive patients on hemodialysis (HD).

Objective The present study aimed to determine the time at which the majority of patients achieve postdialysis dry weight using bioimpedance spectroscopy (BIS).

Methods A total of 220 HD patients were prospectively assessed for fluid overload using the Fresenius body composition monitor (BCM). BCM readings were taken at 30 and 45 min postdialysis.

Results Among the 220 patients included in this study, 120 (54.5%) achieved a euvolemic state at 30 min, and 25 (11.4%) achieved it at 45 min according to the BCM. In the multivariate analysis, vascular access other than arteriovenous fistula (AVF) (OR = 0.286, p value = 0.049) and cardiovascular disease (OR = 0.384, p value = 0.026) had a statistically significant negative association and receiving HD at Hospital Universiti Sains Malaysia (HUSM) (OR = 2.705, p value = 0.008) had a statistically significant positive association with achieving a euvolemic state at 30 min.

Conclusion This suggests that assessing the hydration status at 45 min postdialysis in all patients or in those with identified risk factors for not achieving a euvolemic state at 30 min will provide a relatively accurate assessment for most patients.

Keywords Body composition monitor · Dry weight · Hemodialysis · Hypertension

Strengths and limitations of the study

- This study involved heterogeneous group of patients from tertiary-level teaching hospital of Malaysia.
- Use of Fresenius body composition monitor (BCM) for dry-weight analysis.
- To the best of the authors' knowledge, the current study is strengthened by its prospective nature, and it is the first study to evaluate and suggest the optimal time for dry weight assessments in a clinical setting.
- For determining the predictors of achieving a euvolemic state at 30 min, multivariate analysis was conducted.
- Nevertheless, a multicenter study with a large sample size and longer follow-up time is needed to confirm the findings of the current study.

✉ Amjad Khan
amjadkhan@qau.edu.pk

[1] Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia

[2] Chronic Kidney Disease Resource Centre, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerain 16150, Kelantan, Malaysia

[3] Department of Pharmacy, Quaid-i-Azam University, Islamabad 45320, Pakistan

[4] Faculty of Pharmacy and Health Sciences, University of Balochistan, Quetta 87300, Pakistan

[5] Human Genome Centre, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

Introduction

Consistent fluid overload is a leading cause of hypertension and left ventricular hypertrophy (LVH) [1]. However, there is little authentic information confirming the role of fluid overload in causing hypertension in HD patients. It is known from the literature that hypertension control without antihypertensive drugs is the best strategy for improving HD patient survival; such control can be achieved by reducing the fluid overload in 70–90% of patients [2]. A predialysis fluid overload level of 2.5 L has been reported to be a risk factor for mortality among HD patients [3, 4]. On the other hand, dehydration results in intradialytic symptoms and cardiac stunning [5]. Controlling fluid status within an ideal range and keeping patients euvolemic is thus essential for reducing cardiovascular risks and improving quality of life and survival among HD patients.

There is a plethora of techniques available to assess fluid status in HD patients, e.g., clinical examination; ultrasonic evaluation of inferior vena cava diameter; echocardiographic assessment; relative plasma volume monitoring; total body water measurement; analysis of biomarkers such as atrial natriuretic peptide, brain natriuretic peptide (BNP), and N-terminal pro brain natriuretic peptide (NT-pro BNP); and bioimpedance analysis [6], but body composition monitoring based on bioimpedance spectroscopy (BCM-BIS) appears to be the most promising technique to objectively and quantitatively assess fluid status [7].

Dry weight is defined as "the lowest tolerated postdialysis weight achieved via gradual change in postdialysis weight at which there are minimal signs or symptoms of hypovolemia or hypervolemia" [8]. One of the major aims of dialysis therapy is to obtain a normal volume state or dry weight to control BP and cardiovascular events in HD patients [9]. Hyperhydration is associated with arterial hypertension, dialysis-associated hypotension, pulmonary and peripheral edema, LVH, and heart failure, while dehydration leads to intradialytic adverse events [3]. Guiding the patient along the narrow path between the undesirable effects of hyperhydration and dehydration should be the clinical goal [10]. BIS is the most useful technique for dry weight evaluation in HD patients [11–15]. The findings of a recent study showed that BIS-guided fluid adjustment led to significant reductions in systolic BP and in the prescription of antihypertensive drugs in hypervolemic HD patients while preventing adverse reactions in hypovolemic HD patients [10]. The principle of current flow measurement through the body is based on the applied frequency. Current usually passes through extracellular space at low frequencies and through both intracellular and extracellular water at higher frequencies [16]. BCM has been intensively validated against different gold standards in general and HD populations [17–19]. Several previous studies reported bioimpedance-guided fluid management and dry weight adjustment in hypertensive hemodialysis patients [20–22]; however, data regarding the optimal time to achieve dry weight or euvolemia are lacking, and this issue is of utmost importance and therefore must be precisely addressed. Therefore, the current study aimed to determine the optimal time in which to achieve postdialysis dry weight using BIS.

Materials and methods

Study location and participants

The current multicenter, cross-sectional, observational study was conducted among HD patients who were receiving HD at Hospital Universiti Sains Malaysia (HUSM), a tertiary care hospital and group of private centers outside the hospital in Kelantan, Malaysia. As depicted in the flow diagram (Fig. 1), among 272 HD patients at the study centers, a total of 220 met the eligibility criteria and were included in the study. The remaining 52 patients were excluded due to various reasons (29 did not fulfill the prerequirements for BCM, five had liver cirrhosis, two were pregnant females, six were younger than 18 years, and 10 were not willing to undergo BCM). Diagnosis of cardiovascular disease and other comorbidities were based on documentation from patient's medical record. Patients with IHD, HF, and LVH were considered to have CVD.

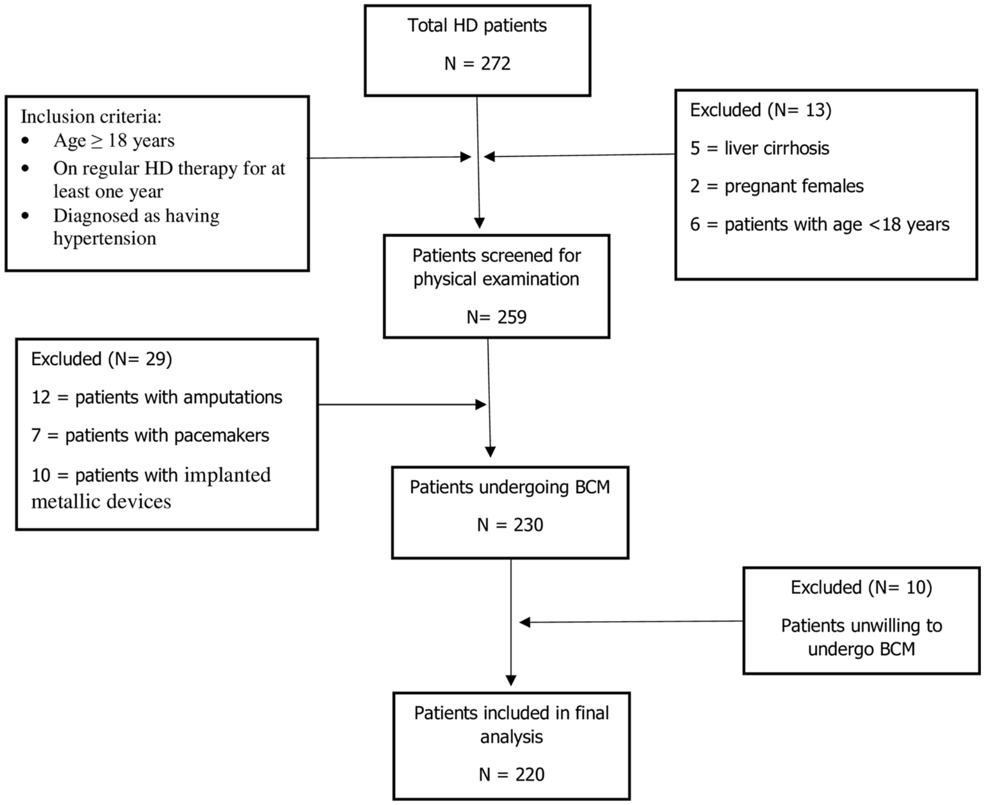
Data collection

Using a standardized data collection form, socio-demographic and clinical data were collected from the regularly updated Advanced Dialysis Nephrology Application Network (ADNAN) at study sites (URL http://www.dialisis.my). Height, weight, and blood pressure were measured during a physical examination. One single calibrated manual sphygmomanometer was used to measure blood pressure (BP). BP was taken as an average of three consecutive measurements with 10-min intervals. Patients with an average systolic/diastolic blood pressure of $\geq$ 140/90 mmHg were categorized as hypertensive. Variables were included on the basis of advisory committee suggestions, extensive literature review, hypothetical possible association, and nephrologist's suggestions.

Measurement of fluid status

A multi-frequency (5–1000 kHz) portable bioimpedance spectroscopy device (BCM; Fresenius Medical Care, Germany) was used to assess fluid status. This device is portable and easily operated, and it provides a direct reading of fluid volume on its display [23] and measures impedance spectroscopy at 50 frequencies. In the present study, the

Fig. 1 Legend: study design



measurements were performed 30 and 45 min after the dialysis procedure with the patient lying in the supine position. Electrodes were attached to one hand and one foot of the patient on the same side of the body. Electronic devices that potentially interact with transmission were removed before initiating the procedure. Moreover, the procedure was performed after confirming that the patient had not consumed any beverages that included alcohol or caffeine in the 24 h prior to the test. Absolute overhydration/fluid overload (OH), extracellular fluid volume (ECW), intracellular fluid volume (ICW), and total body water (TBW) were determined based on a bioelectrical impedance analysis model described by Moissl et al. [23]. The BCM-calculated overhydration (OH) value was used as a fluid overload indicator. In the general population, the 90th percentile of OH is + 1.1 L. Accordingly, OH > 1.1 L was categorized as fluid overload or hypervolemia. An OH value lower than the 10th percentile (− 1.1 L) was defined as hypovolemia. An OH value of ± 1.0 L was defined as euvolemia, i.e., normal volume status [14, 24, 25].

Statistical analysis

Statistical Package for Social Sciences (SPSS version 21) was used for data analysis. Means and standard deviations were calculated for continuous variables, whereas categorical variables are presented as frequencies and percentages. The chi-squared test was used to determine associations between categorical variables. Multivariate logistic regression analysis with the Wald statistical criteria was used to obtain a final model. A p value of < 0.05 was considered statistically significant. Relevant variables with a p value < 0.25 in the univariate analysis were included in the multivariate analysis. We confirmed the correlations among variables entered in the multivariate analysis.

Data sharing statement

All data generated or analyzed during this study are included in this current article. No additional data are available.

Results

The mean patient age was 56.58 ± 11.09 years. The majority of the patients were male (55.5%), 41–60 years old (59.1%), of a normal BMI (67.3%), on dialysis for more than 5 years (36.4%), and suffering from hypertension (91.8%; Table 1).

Table 2 describes association between postdialysis euvolemic state and goal BP. Upon cross-tabulation, statistically significant association was observed between euvolemic state at 45 min and goal BP. The patients who have achieved euvolemia at 45 min were significantly (p value < 0.001) more

Table 1 Sociodemographics and clinical characteristics

Variables	No. (%)
Gender	
Female	98 (45.5)
Male	122 (55.5)
Age mean (± SD)	56.58 (± 11.09)
Age group (years)	
< 40	17 (7.7)
41–60	130 (59.1)
> 60	73 (33.2)
BMI mean (± SD)	23.57 (± 4.31)
BMI classification	
Underweight	12 (5.5)
Normal	148 (67.3)
Overweight	46 (20.9)
Obese	14 (6.4)
Socioeconomic status	
Low	39 (17.7)
Middle	155 (70.5)
High	26 (11.8)
Education level	
Uneducated	74 (33.6)
Educated	146 (66.4)
Marital status	
Single	18 (8.2)
Married	202 (91.8)
Race	
Malay	212 (96.4)
Others	8 (3.6)
Smoking status	
Current smoker	73 (33.2)
Non-smoker	147 (66.8)
Alcohol	
Current drinker	18 (8.2)
Non-drinker	202 (91.8)
Drug addiction	
Current drug addiction	35 (15.9)
No drug addiction	185 (84.1)
Employment	
Unemployed	120 (54.5)
Employed	100 (45.5)
Dialysis years	
1 year	62 (28.2)
2–4 years	78 (35.5)
> 5 years	80 (36.4)
Hemodialysis centers	
Private	129 (58.6)
NGO	33 (15)
Governmental	58 (26.4)
Vascular access	
Fistula	204 (92.7)
Others	16 (7.3)
Hypertension	
No	18 (8.2)
Yes	202 (91.8)
Diabetes mellitus	
No	81 (36.8)
Yes	139 (63.2)
Cardiovascular diseases	
No	185 (84.1)
Yes	35 (15.9)
Cerebrovascular accident	
No	199 (90.5)
Yes	21 (9.5)
Hyperlipidemia	
No	196 (89.1)
Yes	24 (10.9)
Gouty arthritis	
No	191 (86.8)
Yes	29 (13.2)
Other comorbidities	
No	156 (70.9)
Yes	64 (29.1)

Other comorbidities include blood clots, depression, asthma, osteoarthritis, pregnancy losses/birth defects, and osteoporosis. Low socioeconomic status (≤ RM 2300 or 531 USD), middle socioeconomic status (RM 2301–5600 or 531–1294 USD), and high socioeconomic status (> RM 5600 or 1294 USD)

SD standard deviation, *BMI* body mass index

likely to be at goal BP (84%) than those who did not achieve it at this time point (29.7%).

Univariate analysis

Among the 220 patients included in the current study, 120 (54.5%) achieved a euvolemic state at 30 min, and 25 more (11.4%) achieved it at 45 min according to the BCM procedure. In the univariate analysis, receiving HD at HUSM (OR = 2.085, p value = 0.026) and the presence of cardiovascular disease (OR = 0.320, p value = 0.004) had a statistically significant association with achieving a euvolemic state at 30 min (Table 3).

Multivariate logistic regression analysis

In the multivariate logistic regression analysis, achieving a euvolemic state at 30 min according to the BCM procedure had a statistically significant positive association with receiving hemodialysis at HUSM (OR = 2.705, p value = 0.008) and

Table 2 Cross-tabulation between postdialysis euvolemic status at 30 and 45 min and goal BP

Variable	Postdialysis BP on goal (< 130/80 mmHg) (no. %)	Postdialysis BP not on goal (≥ 130/80 mmHg) (no. %)	*p* value
Euvolemic state at 30 min			
Achieved	33 (27.5)	87 (72.5)	0.375
Not achieved	33 (67)	67 (67)	
Euvolemic state at 45 min			
Achieved	21 (84)	4 (16)	< 0.001
Not achieved	58 (29.7)	137 (70.3)	

a statistically significant negative association with vascular access other than AVF (OR = 0.286, *p* value = 0.049) and the presence of cardiovascular disease (OR = 0.384, *p* value = 0.026). This model fit was based on a non-significant Hosmer-Lemeshow test (*p* value = 0.356) and an overall percentage of 69.5% from the classification table (Table 4).

Discussion

Establishing the ideal weight for HD patients to maintain remains an ongoing goal of clinical research. The current study, the first in a Malaysian setting, assessed the fluid status in a cohort of 220 HD patients by using BCM after dialysis sessions. A total of 145 (65.9%) patients achieved a euvolemic state in the present study. Among them, 120 (54.5%) achieved it early, i.e., at 30 min, and 25 (11.4%) achieved by 45 min after the HD session. In the current study, the proportion of patients who achieved a euvolemic state was high compared with that reported among peritoneal dialysis patients in the EuroBCM study (40%) [26]. The cumulative percentage of patients who achieve a euvolemic state notably increased from 54.5% at 30 min to 65.9% at 45 min postdialysis. This signifies that taking the first reading at 45 min postdialysis will maximize the proportion of euvolemic patients, thus providing better justification for the prescription of antihypertensive drugs. Several factors are potentially significantly associated with the euvolemic state of these patients, including type of dialysis center (hospital-based or stand-alone), CVD, acute decompensated heart state, gouty arthritis, and type of vascular access.

In a multivariate analysis, patients who received HD at HUSM, a tertiary referral hemodialysis center/inpatient hemodialysis setting, were significantly more likely to achieve a euvolemic state at 30 min postdialysis than those who received HD at private and non-governmental organization (NGO) dialysis centers. The possible reasons for this finding could be the comparatively more experienced and skilled nursing staff under the supervision of consultant nephrologists, calibrated instruments, regularly changed dialysate, dry weight assessment via BCM, and well-maintained dialysis records.

In the current study, an interesting and statistically significant negative association was found between CVD and normal volume status at 30 min. It has been well documented in the literature that chronic volume overload is closely associated with hypertension, LVH, increased arterial stiffness, heart failure, and higher morbidity and mortality rates [27]. CVD patients, especially those who are elderly and undergoing dialysis, have low plasma refilling capacity, even in the presence of an increased volume [28]. These patients commonly present with intradialytic hypotension; normal saline is commonly infused in such patients to restore the blood pressure. This may contribute to the delay in achieving a euvolemic state in CVD patients. However, further studies should be conducted to confirm this finding.

Acute decompensated heart failure (ADHF) can occur in patients without any preexisting cardiac disease, including conditions such as severe hypertension, fluid overload, severe renal disease, or renal artery stenosis [29]. In HD patients, 3.5 L of fluid is usually extracted through ultrafiltration (UF); however, in patients with ADHF, ultrafiltration of more than 3.5 L of fluid may lead to cardiovascular events. Ischemic heart disease (IHD) in patients with single-, double-, or triple-vessel disease is usually associated with impaired left ventricular (LV) function. The ultrafiltration process during hemodialysis activates sympathetic/adrenergic activity, leading to tachycardia that results in increased peripheral resistance. The renin-angiotensin-aldosterone system could contribute to the increased blood pressure upon removal of blood volume. During HD, the normal blood flow rate (Qb) is prescribed at 300–400 mL/min, but the Qb is reduced to 180–200 mL/min in IHD patients.

Vascular access is essential for hemodialysis treatment. Two types of vascular access designed for long-term use include the arteriovenous (AV) fistula and the AV graft. A third type of vascular access—the venous catheter—is for short-term use. In our study, vascular access other than AVF was an independent risk factor for fluid overload. The slow blood flow rate due to the comparatively smaller diameter of a venous catheter is a possible explanation for its negative association with achieving a euvolemic state at 30 min.

Table 3 Univariate analysis of predictors of achieving a euvolemic state at 30 min

Variables	Euvolemic state achieved at 30 min (no. %)		OR (95% CI)	*p* value
	No	Yes		
Gender				
Female	39 (39.8)	59 (60.2)	Referent	
Male	61 (50)	61 (50)	0.661 (0.386–1.132)	*0.132*
Age				
≤ 40	5 (29.4)	12 (70.6)	Referent	
41–60	65 (50)	65 (50)	0.417 (0.139–1.250)	*0.118*
> 60	30 (41.1)	43 (58.9)	0.597 (0.190–1.872)	0.597
BMI				
Underweight	6 (50)	6 (50)	Referent	
Normal	65 (43.9)	83 (56.1)	1.277 (0.393–4.144)	0.684
Overweight	19 (41.3)	27 (58.7)	1.421 (0.397–5.084)	0.589
Obese	10 (71.4)	4 (28.6)	0.400 (0.079–2.022)	0.268
Education level				
Uneducated	37 (50)	37 (50)	Referent	
Educated	63 (43.2)	83 (56.8)	1.317 (0.752–2.309)	0.336
Marital status				
Single	7 (38.9)	11 (61.1)	Referent	
Married	93 (46)	109 (54)	0.746 (0.278–2.002)	0.560
Race				
Malay	96 (45.3)	116 (54.7)	Referent	
Others	4 (50)	4 (50)	0.828 (0.202–3.397)	0.793
Smoking status				
Current smoker	38 (52.1)	35 (47.9)	Referent	
Non-smoker	62 (42.2)	85 (57.8)	1.488 (0.847–2.616)	*0.167*
Alcohol				
Current drinker	8 (44.4)	10 (55.6)	Referent	
Non-drinker	92 (45.5)	110 (54.5)	0.957 (0.363–2.523)	0.928
Drug addiction				
Current drug addiction	16 (45.7)	19 (54.3)	Referent	
No drug addiction	84 (45.4)	101 (54.6)	1.013 (0.490–2.091)	0.973
Employment				
Unemployed	54 (45)	66 (55)	Referent	
Employed	46 (46)	54 (54)	0.960 (0.564–1.637)	0.882
Dialysis years				
1 year	34 (54.8)	28 (45.2)	Referent	
2–4 years	31 (39.7)	47 (60.3)	1.841 (0.937–3.616)	*0.076*
> 5 years	35 (43.8)	45 (56.3)	1.561 (0.801–3.043)	*0.191*
Hemodialysis centers				
Private	65 (50.4)	64 (49.6)	Referent	
NGO	16 (48.5)	17 (51.5)	1.079 (0.502–2.319)	0.845
Governmental	19 (32.8)	39 (67.2)	2.085 (1.091–3.985)	*0.026*
Vascular access				
Fistula	89 (43.6)	115 (56.4)	Referent	
Others	11 (68.8)	5 (31.3)	0.352 (0.118–1.049)	*0.061*
Hypertension				
No	5 (27.8)	13 (72.2)	Referent	
Yes	95 (47)	107 (53)	0.433 (0.149–1.260)	*0.125*
Diabetes mellitus				
No	31 (38.3)	50 (61.7)	Referent	
Yes	69 (49.6)	70 (50.4)	0.629 (0.360–1.099)	*0.103*
Cardiovascular diseases				
No	76 (41.1)	109 (58.9)	Referent	
Yes	24 (68.6)	11 (31.4)	0.320 (0.148–0.691)	*0.004*
Cerebrovascular accident				
No	89 (44.7)	110 (55.3)	Referent	
Yes	11 (52.4)	10 (47.6)	0.736 (0.299–1.811)	0.504
Hyperlipidemia				
No	87 (44.4)	109 (55.6)	Referent	
Yes	13 (54.2)	11 (45.8)	0.675 (0.288–1.582)	0.366
Gouty arthritis				
No	80 (41.9)	111 (58.1)	Referent	
Yes	15 (51.7)	14 (48.3)	0.912 (0.783–1.809)	0.823
Other comorbidities				

Table 3 (continued)

Variables	Euvolemic state achieved at 30 min (no. %)		OR (95% CI)	*p* value
	No	Yes		
No	76 (48.7)	80 (51.3)	Referent	
Yes	24 (37.5)	40 (62.5)	1.583 (0.873–2.878)	*0.130*
Predialysis hypertension				
No	25 (46.3)	29 (53.7)	Referent	
Yes	75 (45.2)	91 (54.8)	1.046 (0.565–1.937)	0.886
Patient assessment				
Hypotensive	9 (60)	6 (40)	Referent	
Hypertensive	66 (44.6)	82 (55.4)	1.864 (0.631–5.502)	0.260
Normotensive	25 (43.9)	32 (56.1)	1.920 (0.603–6.112)	0.270

Other comorbidities include blood clots, depression, asthma, osteoarthritis, pregnancy losses/birth defects, and osteoporosis

The italic numbers representing only those variables with p-value cut off point of <0.25 in univariate analysis that were included in multivariate analysis

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *NGO* non-governmental organization, *ACE-I* angiotensin-converting enzyme inhibitors, *ARB* angiotensin receptor blocker, *CCB* calcium channel blocker

Study limitations

The present study has several limitations, including its cross-sectional observational design. Changes in fluid status over time were not considered and drugs were not analyzed. Moreover, BCM provides a value for overhydration solely based on excess extracellular fluid. In some pathological conditions (liver cirrhosis, congestive heart failure, excess use of diuretics, and nephrotic syndrome), excess extracellular water might be accompanied by intravascular hypovolemia. Therefore, in such conditions, signs of intravascular hypovolemia must be carefully monitored. Despite the above-mentioned limitations, the current study is strengthened by its prospective nature, and it is the first study to evaluate and suggest the optimal time for dry weight assessments in a clinical setting.

Conclusion

The current study revealed that almost half of the study participants (45.5%) had not achieved a euvolemic state at 30 min postdialysis. The cumulative percentage of euvolemic patients increased from 54.5 to 65.9% by 45 min postdialysis. This suggests that assessing volume status at 45 min postdialysis in all patients or in those with identified risk factors for not achieving euvolemia at 30 min will provide a relatively accurate assessment for the majority of patients, help prevent the

Table 4 Multivariate analysis of predictors of achieving a euvolemic state at 30 min

Variables	*B*	SE	OR (95% CI)	*p* value
Male	− 0.211	0.328	0.810 (0.426–1.541)	0.521
Age (40–60 years)	− 0.045	0.673	0.956 (0.256–3.574)	0.947
Age (> 60 years)	0.294	0.688	1.342 (0.348–5.169)	0.669
Smokers	0.340	0.350	1.405 (0.707–2.790)	0.332
Dialysis years (2–4 years)	0.308	0.394	1.361 (0.629–2.945)	0.435
Dialysis years (> 5 years)	0.103	0.400	1.109 (0.507–2.426)	0.796
Hemodialysis centers (NGO)	0.290	0.448	1.337 (0.556–3.217)	0.517
Hemodialysis centers (governmental)	0.995	0.375	2.705 (1.297–5.641)	*0.008*
Vascular access (other than AVF)	− 1.252	0.636	0.286 (0.082–0.996)	*0.049*
Hypertension	− 0.264	0.641	0.768 (0.219–2.694)	0.680
Diabetes mellitus	− 0.395	0.346	0.673 (0.342–1.326)	0.253
Cardiovascular diseases	− 0.958	0.431	0.384 (0.165–0.892)	*0.026*
Other comorbidities	0.230	0.355	1.258 (0.628–2.521)	0.517

Other comorbidities include blood clots, depression, asthma, osteoarthritis, pregnancy losses/birth defects, and osteoporosis

NGO non-governmental organization, *AVF* arteriovenous fistula

Italic numbers representing those variables which were considered statistically significant overestimation of hypertension, encourage the rational use of antihypertensive drugs, reduce adverse effects, and improve patient quality of life.

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Authors' contributions Conceived and designed the experiments: AK and AHK. Performed the experiments: AK, AHK, and ASA. Analyzed the data: AK and NA. Contributed reagents/materials/analysis tools: SASS, AK, and SHG. Wrote the paper: AK. Final approval of manuscript: AHK, ASA, and SASS.

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Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

Ethics approval Our study was approved by the Human Resource Ethics Committee of Hospital Universiti Sains Malaysia (USM/JEPeM/16020058). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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