

Evaluation of clinical dry weight assessment in haemodialysis patients using bioimpedance spectroscopy: a cross-sectional study

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Abstract

Background. Dry weight assessment (DWA) is essential to efficient therapy of haemodialysis (HD) patients. However, so far objective methods for DWA have not been applicable to daily routine. Thus, exact fluid management in HD remains difficult and is often based on clinical criteria. The aims of this study were (1) to objectively define pre- and post-dialytic ranges of extracellular volume in a large cohort of HD patients (in whom DWA had been defined according to clinical criteria), (2) to compare the hydration status between diabetic and non-diabetic patients, and (3) to assess a patient subgroup that might benefit from correction of target weight.

Methods. We measured fluid overload (FO) prior to a mid-week HD session in 370 randomly selected HD patients (50% with diabetes) from five dialysis centres. A new bioimpedance spectroscopy (BIS) device that implies a validated body composition model was applied. This tool allows correct quantification of extracellular FO or – deficiency in comparison to a healthy reference population (normal range –1.1 to 1.1 L according to the 10th and 90th percentile of measurements). In addition, weight and blood pressure were recorded before and after treatment.

Results. Pre-dialytic FO ranged from –0.5 to 4 L and post-dialytic FO from –2.5 to 2 L (10th and 90th percentile of measurements), indicating that on average the hydration status of healthy subjects is considered as the optimal target weight in HD patients. Comparison of FO between diabetic and non-diabetic patients revealed no difference. Based on the consideration that an FO < –1.1 L before and >1.1 L after HD indicates inadequate DWA, we identified 98 (26%) patients who might benefit from correction of target body weight.

Conclusion. BIS is an interesting, objective method to support clinical DWA. Further studies should be performed to investigate beneficial clinical effects of this approach.

Keywords: bioimpedance spectroscopy; extracellular volume; haemodialysis

Introduction

Adequate control of the extracellular fluid volume is a principal goal of renal replacement therapy in patients with end-stage renal disease (ESRD). Chronic fluid overload (FO) was shown to be present even in early stages of renal insufficiency [1] and may significantly contribute to hypertension, accelerated arteriosclerosis and the high prevalence of left ventricular hypertrophy observed in ESRD patients. Removal of excess fluid is therefore considered crucial for blood pressure control and, thus, for cardiovascular protection in dialysis therapies. However, correct quantification of FO by assessing the individual dry weight in patients still remains a challenge. The simplified concept ‘the dryer—the better’ has been questioned by recent studies on the protective role of residual diuresis in dialysis patients (reviewed in [2]) which is clearly compromised by excessive ultrafiltration. Moreover, the latter may predispose the patient to intra-dialytic hypotension, cramps, arrhythmias and reduced well-being after treatment. Therefore, state-of-the-art treatment aims to balance adequate blood pressure control and conservation of sufficient residual diuresis over longer periods of time.

Several objective methods have been proposed to support the correct estimation of dry weight in dialysis patients, including ultrasound of the inferior vena cava, radionuclide dilution techniques and echocardiography. However, these methods are either time-consuming or difficult to handle in everyday practice. In addition, they are often unable to quantify fluid excess or deficiency. In most dialysis centres, dry weight assessment is therefore solely based on subjective clinical criteria.

Very recently, a new bioimpedance spectroscopy (BIS) device (Body Composition Monitor (BCM), Fresenius Medical Care) has been introduced. For the first time, this tool allows quantification of excess extracellular volume by comparison with a healthy population. In this cross-sectional study, we were interested in the applicability and limitations of clinical dry weight assessment in a representative cohort of HD patients. More specifically, the aims of

this study were (1) to define pre- and post-dialytic ranges of extracellular hydration in a large cohort of HD patients in whom dry weight assessment was solely based on clinical criteria, (2) to reveal differences between diabetic and non-diabetic patients in this context, (3) to estimate the number of patients who could potentially benefit from correction of their prescribed target weight, and (4) to investigate the association between volume and blood pressure in the study cohort.

Methods

Subjects

A total of 370 randomly selected prevalent HD patients from five German dialysis centres gave informed consent to participate in this study which was approved by the local Ethics committee of the University Hospital Carl-Gustav-Carus, Dresden. Patients with pacemakers, major amputations of extremities, HIV infection, as well as pregnant patients, were excluded.

Measurement of excess extracellular volume by the BCM

FO was measured using a newly developed BIS device (BCM, Fresenius Medical Care). The BCM device determines whole body impedance at 50 frequencies. A body composition model is integrated into the BCM and calculates FO based on measurements of intra- and extra-cellular water (ECW) and the patient's body weight [3]. Briefly, the determination of FO comprises the following steps: Firstly, the body impedance from very low to very high frequencies (impedance spectroscopy with 50 frequencies 5 kHz to at least 1000 MHz) is measured with a very high precision. By using this method, the ECW and total body water (TBW) volume can be determined. In a second step, the FO is calculated using an advanced physiological body composition model that is based on tissue properties [3].

The BCM together with the model was validated in extensive studies, e.g. against gold-standard dilution methods, against dual X-ray absorptiometry and the detection of changes in the fluid status. A detailed overview on the validation studies performed so far is given in a recent review on this topic [4]. Reference values for FO in the normal population have been previously obtained [5]. Normal FO has been shown to range from -1.1 to 1.1 L (according to the 10th and 90th percentile of FO measurements in 1.242 healthy subjects).

Patients were studied prior to a dialysis session after a short dialysis-free interval. The BCM measurement was performed immediately before the dialysis session, after patients had rested in the supine position for at least 10 min. Electrodes were placed on the wrist of the arm without the arterio-venous fistula and on the ipsilateral ankle and were connected to the BCM device.

Parameters

In all patients age, height and body mass index were documented. Weight was determined before and after dialysis. In addition, the prescribed target weight and the effective ultrafiltration volume were recorded. Furthermore, systolic and diastolic blood pressures were measured before and 20 min after the end of extracorporeal circulation. The state of diabetes and the individual number of prescribed antihypertensive drugs (diuretics were excluded) were documented.

Calculations and statistics

While pre-dialysis FO (pre-FO) was measured directly, post-dialysis FO (post-FO) was calculated as follows:

$$\text{Post-FO} = \text{Pre-FO} - \text{UF Volume.}$$

In a recent study, this approach was shown to provide reliable results [6].

Comparisons of mean values were performed by two-sided Student's *t*-test for unpaired values. A *P*-value <0.05 was considered to be statistically significant. Calculations were performed by the computer program SPSS 15.0 (SPSS Inc.).

Table 1. Characteristics of the study population

Characteristic	Total	Non-diabetic (ND)	Diabetic (D)	<i>P</i> -value (ND versus D)
<i>N</i>	370	187	183	
Male/female	199/171	105/82	94/89	
Age (years)	63 ± 15	60 ± 16	66 ± 13	0.0001
Height (cm)	167 ± 10	167 ± 16	167 ± 13	n.s.
Body mass index	27 ± 6	26 ± 6	28 ± 6	0.006
Time on HD (months)	53 ± 53	62 ± 62	44 ± 39	0.001
Pre-weight (kg)	75 ± 18	73 ± 17	77 ± 18	0.02
Post-weight (kg)	73 ± 17	71 ± 17	75 ± 18	0.02
Dry weight (kg)	73 ± 17	71 ± 17	75 ± 18	0.02
Ultrafiltration volume (L)	1.9 ± 1.3	1.8 ± 1.3	2.0 ± 1.3	n.s.
No. of antihypertensives	2.0 ± 1.5	1.9 ± 1.6	2.0 ± 1.3	n.s.
Pre-systolic BP (mmHg)	137 ± 27	137 ± 27	138 ± 26	n.s.
Pre-diastolic BP (mmHg)	75 ± 13	76 ± 13	74 ± 12	n.s.
Pre-pulse pressure (mmHg)	62 ± 21	61 ± 20	64 ± 22	n.s.
Post-systolic BP (mmHg)	126 ± 25	123 ± 25	130 ± 24	0.003
Post-diastolic BP (mmHg)	70 ± 14	71 ± 15	69 ± 14	n.s.
Post-pulse pressure (mmHg)	57 ± 19	52 ± 18	61 ± 19	0.0001

Table 2. Raw impedance data of the study population given as extracellular resistance (R_e) and intracellular resistance (R_i)

	Total	Non diabetic	Diabetic	<i>P</i> -value
R_e (Ω)	582 ± 121	596 ± 131	568 ± 109	n.s.
R_i (Ω)	1721 ± 497	1733 ± 514	1711 ± 481	n.s.

Results

The patient characteristics are shown in Table 1. Out of 370 patients, 183 were diabetics (49.5%). The diabetic patients were slightly older, had a higher body mass index and a shorter total time on haemodialysis. While there were no significant differences between diabetic and non-diabetic subjects in pre-dialytic blood pressure and ultrafiltration volume, we found diabetic patients to have higher post-dialytic systolic blood pressure and pulse pressure values. The raw impedance values measured using the BCM device before processing with the body composition model are given in Table 2.

Pre- and post-dialytic FO

The histograms showing the distribution of pre-dialytic FO within the total population and separated for non-diabetic and diabetic subjects are given in Figure 1. Of the total population, 234 patients (63%) had an FO >90 th percentile of the reference population (1.1 L). No significant differences were observed between non-diabetic [108 out of 187, (58%)] and diabetic patients [126 out of 183, (69%)]. 117 patients of the total population (32%) were within the

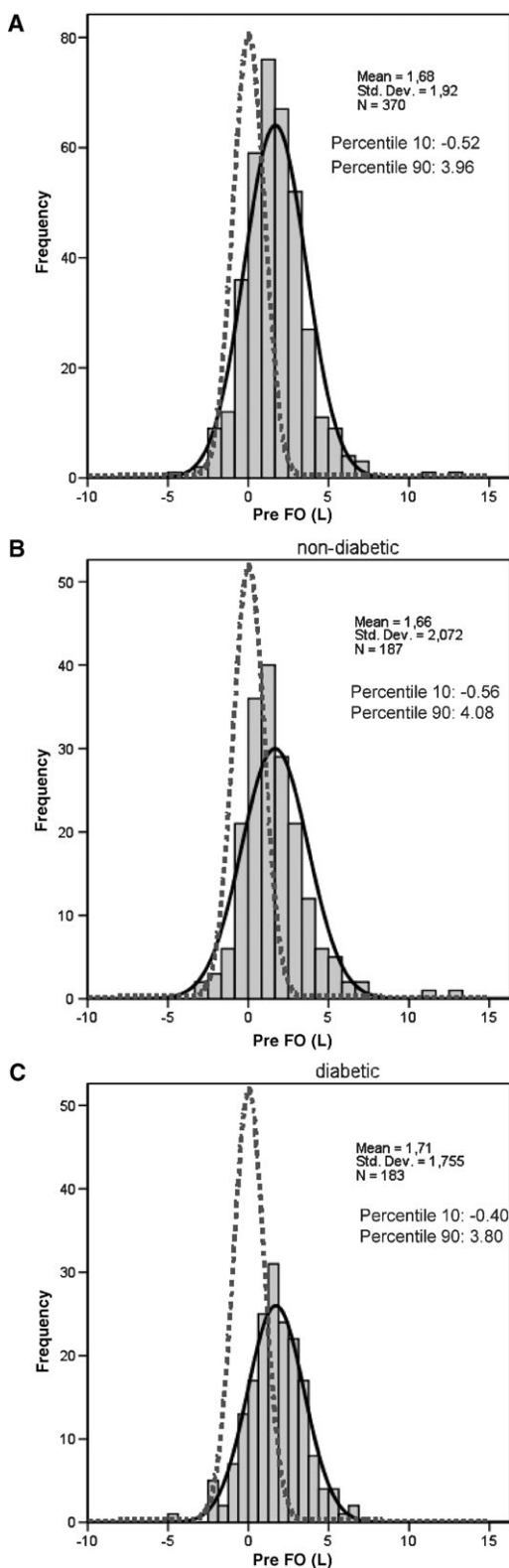


Fig. 1. Histograms showing the distribution of pre-dialytic fluid overload (Pre-FO) in the entire study population (A) and in the subgroups of non-diabetic, (B) as well as diabetic HD patients (C). The dotted bell-shaped curve marks the FO distribution within a representatively healthy population of 500 subjects randomly selected from previously recorded data [7].

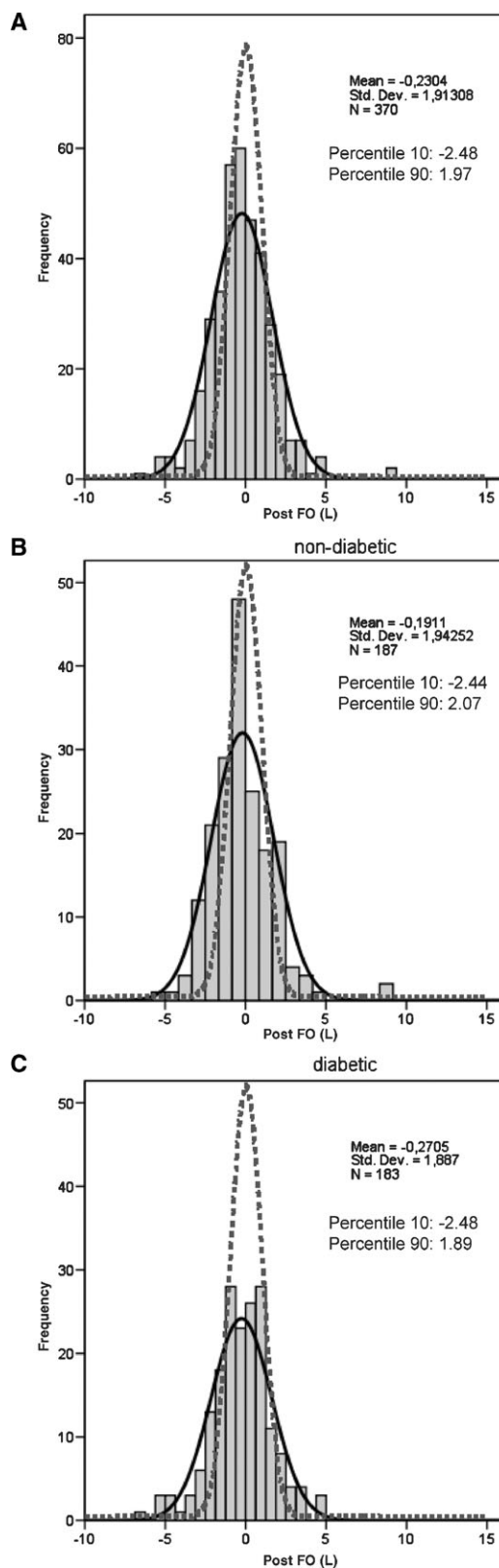


Fig. 2. Post-dialytic extracellular volume overload (Post-FO) in the entire study population (A), in the subset of non-diabetic (B), and diabetic patients (C). Again, the dotted bell-shaped curve marks the FO distribution within a representatively healthy population.

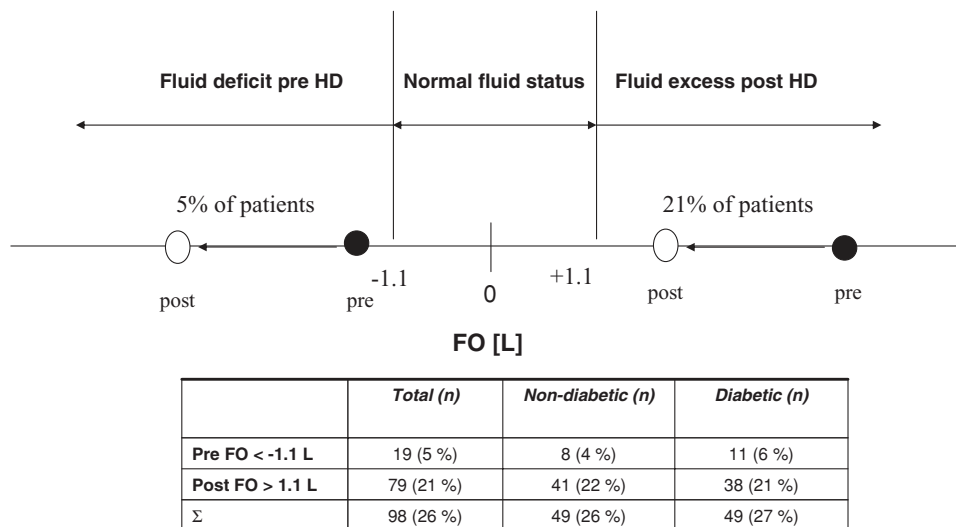


Fig. 3. Schematic diagram of patients that could benefit from an adjustment in dry weight. Those patients who never reach the normal range of FO between the 10th and 90th percentile of the reference population (patient group A: pre-HD FO < -1.1 L, patient group B: post-HD FO > +1.1 L) are considered to benefit from dry weight correction. Results are summarized in the table.

normal range of FO [non-diabetics: 71, (38%); diabetics: 46, (25%)]. Remarkably, 19 patients of the total population (5%) were below the normal range of FO pre-dialysis [non-diabetics: 8, (4%); diabetics: 11, (6%)].

The distribution of post-dialytic FO within the total population as well as diabetic and non-diabetic subjects is given in Figure 2. Post-dialytic FO of the majority of patients [182, (49%)] was within the normal range [non-diabetics: 92, (49%); diabetics: 90, (49%)]. A substantial portion of patients [109, (30%)] was volume-deficient post-dialysis [non-diabetics: 54, (29%); diabetics: 55, (30%)]. 79 patients (21%) still had significant volume excess post-dialysis [non-diabetics: 41, (22%); diabetics: 38, (21%)].

To estimate the number of patients who could likely benefit from correction of their target weight, we counted those subjects who never reached the normal range of extracellular volume (i.e. those patients who were volume depleted before or had excess volume post-dialysis, Figure 3). As indicated in Figure 3, 98 subjects of the total population (26%) fulfilled these criteria showing a comparable distribution within the non-diabetic and the diabetic population.

Association between FO and blood pressure

To assess the volume and blood pressure relationship in both groups, we generated scatter plots relating pre- and post-FO to pre- and post-systolic blood pressure (Figure 4). In non-diabetic subjects, there was a weak but significant correlation between pre-FO and pre-systolic blood pressure, while there was no such correlation in diabetics (Figure 4A). Likewise, pre-FO was positively correlated to pre-pulse pressure in non-diabetics ($r^2 = 0.044$, $P < 0.005$) but not in diabetic patients ($r^2 = 0.0001$, $P = \text{n.s.}$). Comparable associations could be demonstrated for post-FO and post-systolic blood pressures (Figure 4B) as well as for post-FO and post-pulse pressures (non-diabetics: $r^2 = 0.123$, $P < 0.001$; diabetics: $r^2 = 0.002$, $P = \text{n.s.}$).

Furthermore, in non-diabetic subjects, we observed a significant correlation between FO and the number of antihypertensive drugs prescribed (pre-FO: $r^2 = 0.044$, $P < 0.005$, post-FO: $r^2 = 0.029$, $P < 0.05$), while such association was not demonstrable in diabetic patients (pre-FO: $r^2 = 0.005$, $P = \text{n.s.}$, post-FO: $r^2 = 0.006$, $P = \text{n.s.}$, Figure 5).

Discussion

Due to the absence of adequate renal function, the extracellular volume of dialysis patients is determined intuitively by the responsible nephrologist. This study was conducted to evaluate the degree of extracellular volume overload in HD patients when dry weight assessment was based on clinical criteria. For this purpose, a large cohort of unselected HD patients from five German dialysis centres was studied. For determination of FO, we used a newly developed BIS device in combination with a thoroughly validated body composition model [3,7] which was also successfully tested in HD patients [5,8]. Furthermore, by comparing different approaches, a recent study identified BIS as the currently most promising technical system for both accurate and practicable fluid management in dialysis [9]. FO was exclusively measured prior to the individual dialysis session. However, after defining the effective ultrafiltration volume, we were also able to calculate post-FO at the individually prescribed target weight. The adequacy of this approach has been recently shown in a study by Wabel *et al.* [6]. Our results demonstrate that clinical dry weight assessment allows for the achievement of mean post-dialytic FO (i.e. target weight) close to a physiological hydration status but presents a much larger variability. We were further interested in differences between diabetic and non-diabetic subjects in this context. From a clinical point of view, correct assessment of dry weight in diabetic subjects appears to be more difficult. These patients frequently present

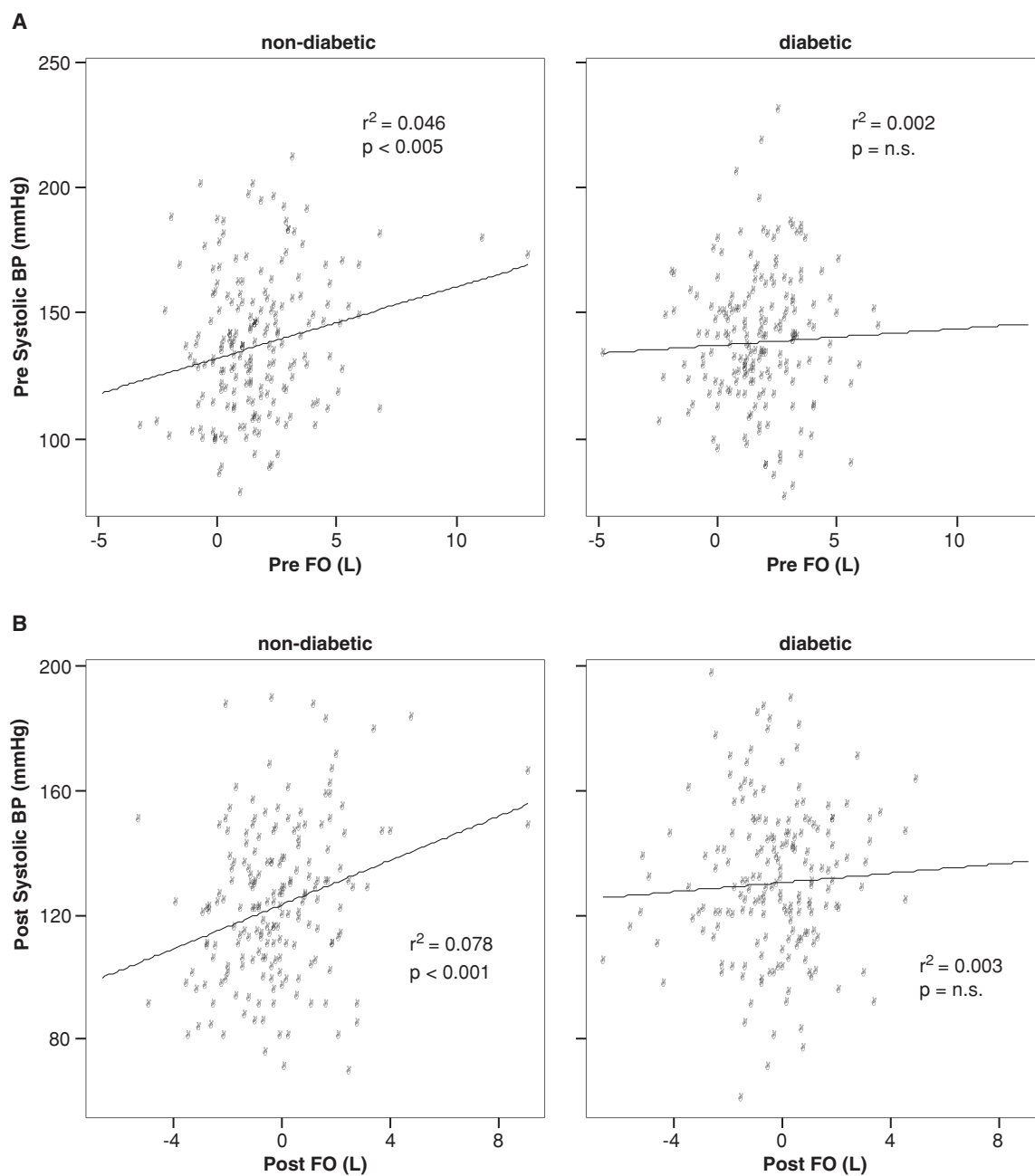


Fig. 4. Scatter plots showing individual values of pre-dialytic systolic blood pressure and pre-dialytic FO in non-diabetic and diabetic HD patients (**A**). A weak but significant correlation of both parameters can be demonstrated in non-diabetic, but not in diabetic patients. Comparable results were obtained for the association between post-dialytic FO and post-dialytic systolic blood pressure in both groups (**B**). All relationships shown here are best represented by linear correlation.

pre-dialytic systolic hypertension. Reducing target weight, however, is hampered by their reduced tolerance to ultrafiltration. Surprisingly, we found comparable post-dialytic FO values in diabetic and non-diabetic subjects indicating that clinical dry weight assessment estimates the volume status likewise in both groups. Based on the assumption that at least those patients who never reach the normal range of FO during their inter-dialytic variation of extracellular volume are in need for a correction of their target weight, we identified 98 (26%) subjects of the total population in whom a

more active dry weight management could prove beneficial. These results do not exclude the possibility that further patients may benefit from target weight correction. However, the question to which extent dry weight management using BIS would be able to improve both the clinical situation and outcome of HD patients clearly requires further studies.

In addition, we were interested in the FO and blood pressure relationship in the patients studied. For this purpose, we used pre- and post-dialytic blood pressure measurements. It has been demonstrated that this approach is less

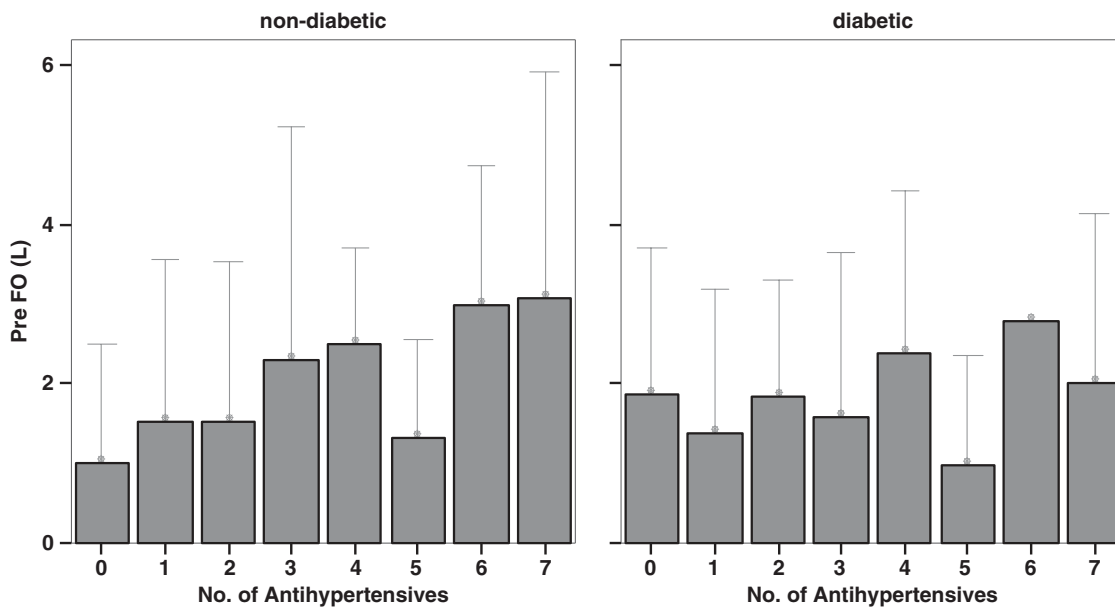


Fig. 5. Association between the number of prescribed antihypertensive drugs and pre-dialytic FO. In non-diabetic patients, there is a weak but significant positive correlation between both parameters ($r^2 = 0.044$, $P < 0.005$) while such an association could not be demonstrated in diabetic patients.

appropriate to characterize inter-dialytic ambulatory blood pressure [10] and is of a less prognostic value [11]. However, in this particular study, we were especially interested in blood pressure values obtained during maximum and minimum FOs. We observed a weak (but significant) positive correlation between pre- and post-dialytic systolic blood pressures and the FO measured in non-diabetic subjects. In addition, we found that in non-diabetic patients, pre- and post-dialytic FO correlates positively to the number of antihypertensive drugs prescribed. It is conceivable that active dry weight management by BIS may improve blood pressure management and save costs by reducing the amount of antihypertensive drugs at least in a subgroup of these patients. Interestingly, in diabetic subjects, an association between FO and blood pressure was not detectable. Very likely, the stronger presence of autonomic neuropathy and increased vascular stiffness in this subset of patients are responsible for our observation. Accordingly, we found no correlation between pre- and post-dialytic FO and the prescription of antihypertensive drugs in diabetic subjects. This particular finding corresponds to the clinical experience that an adequate blood pressure control appears to be more difficult in diabetic HD patients and that volume control in these subjects has to be accompanied by a carefully selected antihypertensive therapy with an adequate timing of drug intake. Collectively, our data support the view that a single pre-dialytic blood pressure value poorly reflects the volume status of patients and that this observation is especially relevant for diabetics.

Using a comparable methodology as in the present study, Wabel *et al.* analysed data from 500 HD patients with the primary focus on the relationship between pre-dialysis blood pressure and pre-dialysis FO [12]. These authors inaugurated a hydration reference plot where FO is plotted against blood pressure. Their approach is interesting; how-

ever, as long as the boundaries for reference values of the dialysis population are chosen rather arbitrarily (because of lack of reliable data in this context), this concept remains somewhat speculative. A small shift of those boundaries would likely be associated with a substantial change in the percentage of patients reported in the different regions of this plot. For this reason, we deliberately avoided this approach.

In summary, in a cohort of unselected HD patients, we found that clinical dry weight assessment on average allows for the achievement of hydration status comparable to that observed in healthy subjects but is associated with a far bigger range of variability. Based on our results, we assume that at least one-quarter of the total population investigated could potentially benefit from a more active dry weight management based on BIS. Furthermore, we found that the FO and blood pressure relationship was preserved in a minority of non-diabetic HD patients only. Such an association was not at all detectable in diabetic patients.

Further studies should be designed to test whether dry weight management based on BIS would be able to improve blood pressure control, well-being and outcome of patients on chronic haemodialysis.

Conflict of interest statement. None declared.

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Received for publication: 14.8.08; Accepted in revised form: 4.9.09

Nephrol Dial Transplant (2010) 25: 551–557

doi: 10.1093/ndt/gfp395

Advance Access publication 12 August 2009

NT-proBNP, fluid volume overload and dialysis modality are independent predictors of mortality in ESRD patients

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Abstract

Background. N-terminal fragment of B-type natriuretic peptide (NT-proBNP) is a marker of both fluid volume overload and myocardial damage, and it has been useful as a predictor of mortality in patients with end-stage renal disease (ESRD). It has been suggested that continuous ambulatory peritoneal dialysis (CAPD), automated peritoneal dialysis (APD) and haemodialysis (HD) may have different effects on fluid volume and blood pressure control; however, whether the independent predictive value of NT-proBNP for mortality is preserved when analysed in conjunction with fluid overload and dialysis modality is not clear.

Methods. A prospective multicentre cohort of 753 prevalent adult patients on CAPD, APD and HD was followed up for 16 months. Plasmatic levels of NT-proBNP, extracellular fluid volume/total body water ratio (ECFv/TBW) and tradi-

tional clinical and biochemical markers for cardiovascular damage risk were measured, and their role as predictors of all-cause and cardiovascular mortality was analysed.

Results. NT-proBNP level, ECFv/TBW and other cardiovascular damage risk factors were not evenly distributed among the different dialysis modalities. NT-proBNP levels and ECFv/TBW were correlated with several inflammation, malnutrition and myocardial damage markers. Multivariate analysis showed that NT-proBNP levels and ECFv/TBW were predictors of both all-cause and cardiovascular mortality, independently of dialysis modality and the presence of other known clinical and biochemical risk factors.

Conclusions. NT-proBNP is a reliable predictor of death risk independently of the effect of dialysis modality on fluid volume control, and the presence of other clinical and biochemical markers recognized as risk factors for all-cause and cardiovascular mortality. NT-pro-BNP is a good