Baseline hydration status in incident peritoneal dialysis patients: the initiative of patient outcomes in dialysis (IPOD-PD study)†

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†The study has been registered in January 2011 at www.clinicaltrials.gov as NCT 01285726.

ABSTRACT

Background. Non-euvolaemia in peritoneal dialysis (PD) patients is associated with elevated mortality risk. There is an urgent need to collect data to help us understand the association between clinical practices and hydration and nutritional status, and their effects on patient outcome.

Methods. The aim of this prospective international, longitudinal observational cohort study is to follow up the hydration and nutritional status, as measured by bioimpedance spectroscopy using the body composition monitor (BCM) of incident PD patients for up to 5 years. Measures of hydration and nutritional status and of clinical, biochemical and therapy-related data are collected directly before start of PD treatment, at 1 and 3 months, and then every 3 months. This paper presents the protocol and a pre-specified analysis of baseline data of the cohort.

Results. A total of 1092 patients (58.1% male, 58.0 ± 15.3 years) from 135 centres in 32 countries were included. Median fluid overload (FO) was 2.0 L (males) and 0.9 L (females). Less than half of the patients were normohydrated (38.7%), whereas FO > 1.1 L was seen in 56.5%. Systolic and diastolic blood pressure were 139.5 ± 21.8 and 80.0 ± 12.8 mmHg, respectively, and 25.1% of patients had congestive heart failure [New York Heart Association (NYHA) 1 or higher]. A substantial number of patients judged to be not overhydrated on clinical judgement appeared to be overhydrated by BCM measurement. Overhydration at baseline was independently associated with male gender and diabetic status.

Conclusions. The majority of patients starting on PD are overhydrated already at start of PD. This may have important consequences on clinical outcomes and preservation of residual renal function. Substantial reclassification of hydration status by BCM versus on a clinical basis was necessary, especially in patients who were not overtly overhydrated. Both clinical appreciation and bioimpedance should be combined in clinical decision-making on hydration status.

Keywords: bioimpedance, end-stage renal disease, hydration status, peritoneal dialysis, prospective cohort study, volaemia

INTRODUCTION

Maintenance of normohydration is an important objective in the management of patients with advanced chronic kidney disease (CKD). Overhydration is a frequent complication in this patient group [1–4], and is associated with enhanced cardiovascular risk [5]. Transient dehydration might have negative consequences on residual renal function (RRF), which is also associated with outcome [6]. This positive impact of RRF on survival is, however, mainly driven by the fact that it enables patients to maintain a correct fluid balance [7, 8]. Both overhydration [9] and dehydration [10] can result in faster deterioration of RRF.

In a recent study (EuroBCM Study) [4], more than 50% of patients were overhydrated as assessed by bioimpedance...
spectrum dialysis patients [3]. In the EuroBCM Study [4], overhydration was associated with unmodifiable patient characteristics, such as age, gender and diabetes, but also with factors that probably can be accounted for with appropriate peritoneal dialysis (PD) prescription, such as avoidance of hypertonic glucose solutions or a regimen adapted to membrane transport status [4, 11]. It can be hypothesized that awareness of the correct hydration status can trigger a more precise diagnosis of the underlying causes of non-euvolaemia, a more appropriate PD prescription, and ultimately a better long-term technique and patient survival by preserving RRF and peritoneal membrane integrity, while avoiding complications associated with fluid overload (FO) [6, 12].

The present prospective, international, observational cohort study was set up to provide more in-depth insights into hydration and nutritional status of incident PD patients. We also want to observe the factors influencing the evolution of hydration and nutritional status, RRF and outcomes, and how all these are associated with treatment practices.

**Materials and Methods**

**Proposal for terminology**

We use the terms dehydration, normohydration and overhydration to describe hydration status in a qualitative way. We use FO (in litres) only to express hydration status in a quantitative manner, irrespective of the direction. A dehydrated patient can thus be described in this study as having a (negative) FO of minus 1.2 L, an overhydrated patient as having a (positive) FO of 1.2 L. Relative FO (in percentage) expresses FO relative to the extracellular water (FO/ECW).

*Total fluid removal* (in litres) refers to the composite of residual diuresis and (peritoneal) ultrafiltration. *Fluid balance* (in litres) refers to the difference between total (dietary) *fluid intake* and total fluid removal.

**Study objectives**

The study aims at assessing hydration and nutritional status of incident PD patients and their evolution over time using BIS measurement.

We assess hydration status, FO, total body water (TBW), ECW, intracellular water (ICW) based on BIS as primary outcomes.

Patient characteristics such as residual renal function [estimated glomerular filtration rate (eGFR), urinary output, measured creatinine and urea clearance], peritoneal membrane transport status, nutritional status [lean tissue index (LTI), fat tissue index (FTI), body mass index (BMI)] based on BIS, technique survival and mortality will be associated with treatment practices such as PD prescription [use of hypertonic exchanges, biocompatible versus non-biocompatible solutions, use of polyglucose, use of automated PD versus continuous ambulatory PD (CAPD)] and relevant medication (secondary outcomes).

**Study design and present analysis**

This is an international, prospective, observational, cohort study of incident PD patients in centres using BIS in their clinical practice, with a maximal follow-up time of 5 years. This paper presents the protocol and the results of a pre-specified interim analysis with baseline cross-sectional data of the study population on hydration status.

**Study subjects**

During a regular visit before the actual start of PD, patients were screened for eligibility and inclusion and exclusion criteria were checked (Supplementary Table S1). Maximal effort was made to have this screening performed in all consecutive patients starting PD in the participating centres. Patients had to be naive to any renal replacement therapy.

**Study procedures**

According to the observational nature of the study, data were collected from routine procedures of patient evaluation in the participating centres. No additional specific interventions or obligatory investigations, except the three-monthly body composition monitor (BCM) measurement, were performed.

As baseline value, we considered the most recently documented BCM measurement and laboratory parameters before start of PD therapy. Furthermore, data were collected 1 and 3 months after the actual start of PD, and then every 3 months until the patient changes renal replacement modality (technique failure, transfer to HD or kidney transplantation), terminates the study prematurely for other reasons or end of the study.

The variables to be documented are listed in Supplementary Table S2. Hydration status, FO, TBW, ECW, ICW and nutritional status, including lean tissue mass (LTM) and adipose tissue mass (ATM) are derived from the BCM-measurement as described below.

Routine laboratory parameters are based on data provided by the laboratories of the respective centres. eGFR was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [7]. As measuring these parameters was considered to be part of practice variation between the different centres, potentially influencing the primary outcome parameters, they were not obligatory, and their measurement versus no measurement are handled as an instrumental variable. Date and reason for terminating the study are documented.

Data collection was performed through secured electronic data capture (EDC).

**Bioimpedance spectroscopy with the body composition monitor**

Bioimpedance spectroscopy is a non-invasive method to obtain information about body composition, including FO, fat mass and lean body mass.

All body composition analyses were performed with the BCM device (Body Composition Monitor, Fresenius Medical Care, Bad Homburg, Germany), which provides precise and reproducible results when compared with the gold standard isotopic dilution technique [13, 14]. The BCM measures impedance at 50 different frequencies between 5 kHz and 1 MHz. For the measurement, electrodes are attached to one hand and one foot at the ipsilateral side with the patient in a recumbent position. Due to biophysical reasons and conceptually intended, BIS does not measure sequestered fluid in the trunk. Therefore,
presence or absence of PD fluid in the abdomen does not influence the readings of hydration status [15], which is a big advantage for comparison between patients or if the patients present in different filling states of the peritoneal cavity. For weight, we used the weight adjusted for empty abdomen. Reproducibility of BCM-derived parameters is high, with a coefficient of variation for the inter-observer variability for ECW and TBW around 1.2% [16] in studies performed in HD patients. Therefore, only one BCM measurement was performed in each individual patient at each time point.

FO, lean tissue (LT) and fat tissue (FT) were derived from the impedance data based on a physiologic tissue model that separates the body into three compartments [13]: surplus water, normohydrated LT and normohydrated FT. (Absolute) FO represents the difference between the measured amount of ECW and the amount of water expected in normohydrated tissue conditions. The use of absolute FO has some advantages, especially in the communication between clinical staff and the patient—therefore, the absolute measures were preferred over relative. In line with the definition of BMI, LT and FT are defined as LT/(height)^2 and FT/(height)^2, respectively. The BCM results have been shown to be valid in different ethnicities [14].

Patients are considered ‘dehydrated’ or ‘overhydrated’ when their absolute FO is below the 10th or above the 90th percentile of the normal, presumed healthy, reference population, respectively (corresponding to 1.1 L of negative or positive FO, respectively) [17, 18].

Ethical considerations
The study was carried out in accordance with the current version of the Declaration of Helsinki, and the respective national laws and regulations. Where required according to national regulations, the study was submitted to ethics committees and/or national authorities. Before enrolling a patient, the subject was informed verbally and in writing about the study. Written informed consent was obtained according to applicable law.

Statistical analysis
All analyses were done with SAS V9.2 (SAS Institute Inc., Cary, NC, USA). According to protocol, an interim analysis on baseline data and month 1 and 3 was performed. Baseline data were analysed descriptively and are given as mean ± standard deviation, unless stated otherwise. According to the observational nature of the study, only available data were considered; no substitution procedure for missing data was applied. Pre-specified subgroups were compared. Multivariate multinomial logistic regression (nominal dependent variables with more than two categories) were used to assess independence of associations. Degree of inter-rater agreement was assessed with the kappa coefficient.

RESULTS

Hydration status in incident PD patients

Recruitment. Between January 2011 and December 2012, 135 centres recruited 1092 incident PD patients into the study. Study centres were located in Asia, Europe and Latin America (2, 27 and 3 countries, respectively). Out of 1092 patients enrolled into the study, data were complete for 1031 patients to comprise the baseline analysis population employed for this interim analysis.

Patient characteristics. Baseline patient data and biochemical parameters according to hydration status are reported in Tables 1 and 2.

PD therapy. About 50% of the patients started PD within 30 days after catheter implantation. CAPD and automated PD regimen (APD) was planned as a first modality in 77.6 and 22.4% of patients. Transporter status of the peritoneal membrane was assessed within the first 3 months of PD treatment in only 62.1% of the patients. Of the patients in whom such assessment was performed, 11.6% were fast, 39.5% fast-average, 25.9% slow average and 23.0% slow transporter (Table 3).

Parameters of hydration status
Hydration status is given in Figure 1. In the total cohort, 4.9, 38.7 and 56.4% of patients were dehydrated, normohydrated and overhydrated, respectively, following the defined criteria.

A mean of 17.3 ± 4.0 L of ECW and 18.6 ± 4.7 L of ICW was measured, with ECW/ICW equal to 0.9 ± 0.2.

FO was higher in fast transporters versus other categories, and in males versus females, diabetics versus non-diabetics in all peritoneal transport categories (Figure 2).

Only 24.5% of total patients are both in the normal range of systolic blood pressure and normohydrated, whereas 28.2% of the patients are overhydrated and have a systolic blood pressure higher than 140 mmHg. Normal or low systolic blood pressure despite overhydration is present in 28.2%, and 1.5% of patients have a high systolic blood pressure despite dehydration (Figure 3 and Supplementary Table S3).

For patients who were deemed by clinical judgement to be dehydrated, BCM measurement confirmed this in only in 36% of cases, whereas 40 and 24% were labelled as normohydrated and overhydrated. Of those called ‘normohydrated’ by clinical appreciation, 58.2% were also labelled as euvoalamic by BCM, whereas 5.6 and 36.2% were labelled as dehydrated and overhydrated by BCM. On the other hand, of those clinically assessed as overhydrated, 81.4% were also overhydrated according to BCM (Figure 4). The kappa coefficient was 0.412 (95% CI: 0.362–0.461) [19]. When BCM was considered the gold standard, a clinical judgement ‘not overhydrated’ (so either normohydrated or dehydrated) was only correct in two-thirds of cases, whereas a clinical judgment ‘overhydrated’ was only false in a minority of cases (positive and negative predictive value of clinical appreciation 64.3 and 18.6%, respectively).

In multinomial logistic regression analysis, overhydration was independently associated with gender and diabetic status (Table 4).

Residual renal function (eGFR) was 10.8 ± 13.3 mL/min/1.73 m² in the complete cohort, and 8.7 ± 4.7 mL/min/1.73 m², 11.7 ± 15.2 mL/min/1.73 m² and 10.4 ± 12.4 mL/min/1.73 m²

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in dehydrated, normohydrated and overhydrated patients, respectively.

**DISCUSSION**

This paper presents baseline data on hydration in a large cohort of incident PD patients.

The BIS analysis reveals that the majority (56.4%) of patients is overhydrated already before the start of PD therapy, with a mean absolute FO of 1.9 ± 2.4 L. Overhydration is more severe in males and diabetics in terms of mean FO values, and 66.8% of the male and 71.3% of the diabetic patients were overhydrated. For the first time, we documented a discrepancy between clinically appraised and effectively measured hydration status of PD patients: of patients who were deemed to be ‘normohydrated’ or even ‘dehydrated’ on a clinical basis, more than one out of three appeared to be overhydrated when volume status was actually measured. ‘Overhydration’, however, was accurately assessed by the clinicians.

The presence of overhydration in a substantial part of incident PD patients is in line with previous reports in end-stage renal disease (ESRD) patients [4]. The fact that the observed absolute FO values are comparable to those reported previously in prevalent PD patients (1.9 ± 2.4 versus 1.7 ± 2.3 L) is remarkable. Several hypotheses can be proposed to explain this. First, it could be that conservative practices in the pre-dialysis period are inappropriate to successfully correct overhydration. Therefore, the further prospective follow up of this international cohort will provide valuable insights on how far PD practices are associated with successful correction of overhydration. At least for some of the factors associated with overhydration, such as diabetes, or transport status, a more appropriately adapted PD prescription can potentially positively influence hydration status. The hypothesis of the IPOD-PD study is that a patient-tailored PD prescription, with a prescription adapted...
to the transport status of the patient [20], dietary restriction of salt intake [21, 22], avoidance of hypertonic exchanges [19], use of highly biocompatible solutions [21, 22] and regular assessment of hydration status by BCM will result in better preservation of peritoneal membrane integrity, RRF and in better control of hydration status.

Second, it might be that factors leading to overhydration are inherent to the patient, and that therefore, correction of overhydration is cumbersome, e.g. in the presence of very low serum albumin levels. Additionally, it must be noted that the definition of overhydration in this study should not be misinterpreted as target ranges for PD patients—potentially these target ranges could be set up with the outcome data of this study.

Third, it might be that clinicians incorrectly judge patients to be normohydrated, and accordingly do not make enough effort to correct overhydration. In our cohort, a substantial part of patients who are deemed to be normohydrated or dehydrated on a clinical basis appear to be overhydrated when volume status is actually measured. The relatively low positive predictive value of a clinical appraisal of normohydration can be attributed to different factors. Many physicians still associate normo- or hypotension with absence of overhydration. As in previous studies [3, 4, 17], our current study, however, demonstrates that approximately 15% of patients are overhydrated despite normal or low blood pressure, mostly a sign of cardiac dysfunction, or of autonomic dysfunction. Furthermore, clinical signs such as oedema only become apparent when substantial amounts of fluid have accumulated [23]. Last, patients with congestive heart failure based on diastolic dysfunction or right heart failure need high venous filling pressures to assure adequate filling of the left ventricle. It is important to note that the BCM cannot separate between intravascular and extravascular volume—it

<table>
<thead>
<tr>
<th>Baseline hydration category</th>
<th>N</th>
<th>Mean ± SD</th>
<th>Median [Min,Max]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin [g/dL]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>50</td>
<td>11.4 ± 1.4</td>
<td>11.6 [6.8,14.5]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>387</td>
<td>11.2 ± 1.5</td>
<td>11.2 [7.0, 16.9]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>564</td>
<td>10.7 ± 1.8</td>
<td>10.6 [6.7, 20.6]</td>
</tr>
<tr>
<td>total</td>
<td>1001</td>
<td>10.9 ± 1.7</td>
<td>11.0 [6.7, 20.6]</td>
</tr>
<tr>
<td>Haematocrit [%]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>43</td>
<td>34.0 ± 4.2</td>
<td>34.1 [20, 41]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>342</td>
<td>34.3 ± 4.3</td>
<td>34.0 [22, 47]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>499</td>
<td>32.6 ± 5.0</td>
<td>32.4 [20, 67]</td>
</tr>
<tr>
<td>total</td>
<td>884</td>
<td>33.3 ± 4.8</td>
<td>33.0 [20, 67]</td>
</tr>
<tr>
<td>Urea [mg/dL]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>49</td>
<td>173.8 ± 52.5</td>
<td>173.3 [64,291]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>386</td>
<td>155.7 ± 51.4</td>
<td>153.8 [30,426]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>567</td>
<td>149.8 ± 52.2</td>
<td>146.0 [11,423]</td>
</tr>
<tr>
<td>total</td>
<td>1002</td>
<td>153.3 ± 52.2</td>
<td>150.7 [11,426]</td>
</tr>
<tr>
<td>Creatinine [mg/dL]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>50</td>
<td>6.9 ± 2.8</td>
<td>6.0 [2.5,14.8]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>387</td>
<td>6.3 ± 2.3</td>
<td>6.0 [1.7, 18.0]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>570</td>
<td>6.8 ± 2.7</td>
<td>6.3 [1.8, 25.3]</td>
</tr>
<tr>
<td>total</td>
<td>1007</td>
<td>6.6 ± 2.5</td>
<td>6.2 [1.7, 25.3]</td>
</tr>
<tr>
<td>Albumin [g/L]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>48</td>
<td>39.7 ± 4.4</td>
<td>40.0 [26.7, 51.0]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>367</td>
<td>39.2 ± 5.0</td>
<td>39.3 [24.0, 51.9]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>534</td>
<td>35.9 ± 5.8</td>
<td>36.9 [16.0, 49.0]</td>
</tr>
<tr>
<td>total</td>
<td>949</td>
<td>37.4 ± 5.7</td>
<td>38.0 [16.0, 51.9]</td>
</tr>
<tr>
<td>CRP [mg/L]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>44</td>
<td>10.4 ± 19.5</td>
<td>3.0 [0.0,80.0]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>307</td>
<td>9.3 ± 18.7</td>
<td>4.0 [0.0, 165.6]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>469</td>
<td>10.3 ± 20.2</td>
<td>4.6 [0.0, 216.0]</td>
</tr>
<tr>
<td>total</td>
<td>820</td>
<td>9.9 ± 19.6</td>
<td>4.1 [0.0, 216.0]</td>
</tr>
<tr>
<td>Glucose [mg/dL]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>45</td>
<td>116.6 ± 50.6</td>
<td>97.0 [67,266]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>342</td>
<td>109.9 ± 44.2</td>
<td>97.7 [13,445]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>512</td>
<td>123.8 ± 59.7</td>
<td>104.8 [12,499]</td>
</tr>
<tr>
<td>total</td>
<td>899</td>
<td>118.2 ± 54.2</td>
<td>101.0 [12,499]</td>
</tr>
<tr>
<td>HbA1c [%]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dehydrated</td>
<td>25</td>
<td>6.8 ± 2.1</td>
<td>6.7 [4.2, 13.8]</td>
</tr>
<tr>
<td>euvaloeamic</td>
<td>190</td>
<td>6.0 ± 1.3</td>
<td>5.6 [3.4, 10.9]</td>
</tr>
<tr>
<td>overhydrated</td>
<td>262</td>
<td>6.3 ± 1.6</td>
<td>5.9 [3.0, 14.0]</td>
</tr>
<tr>
<td>total</td>
<td>496</td>
<td>6.2 ± 1.5</td>
<td>5.8 [3.0, 14.0]</td>
</tr>
</tbody>
</table>

### Table 3. Transport status separated by gender, overhydration or diabetic status

<table>
<thead>
<tr>
<th>Transporter status</th>
<th>Low (slow)</th>
<th>Low (average)</th>
<th>High (average)</th>
<th>High (fast)</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>n %</td>
<td>n %</td>
<td>N %</td>
<td>n %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>79 21.1</td>
<td>90 24.0</td>
<td>157 41.9</td>
<td>49 13.1</td>
<td>P = 0.1239</td>
</tr>
<tr>
<td>Female</td>
<td>68 25.7</td>
<td>76 28.7</td>
<td>96 36.2</td>
<td>25 9.4</td>
<td></td>
</tr>
<tr>
<td>Overhydration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>77 27.7</td>
<td>79 28.4</td>
<td>100 36.0</td>
<td>22 7.9</td>
<td>P = 0.0043</td>
</tr>
<tr>
<td>Yes</td>
<td>70 19.3</td>
<td>87 24.0</td>
<td>153 42.3</td>
<td>52 14.4</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>93 23.0</td>
<td>105 25.9</td>
<td>163 40.2</td>
<td>44 10.9</td>
<td>P = 0.8946</td>
</tr>
<tr>
<td>Yes</td>
<td>54 23.0</td>
<td>61 26.0</td>
<td>90 38.3</td>
<td>30 12.8</td>
<td></td>
</tr>
</tbody>
</table>
has no insight into the circulating volume. Thus, it might be that a patient can be dehydrated on BCM (overall fluid status) but still have congestive heart failure which causes him/her to have an expanded circulating volume.

On the other hand, a high positive predictive value of clinical appreciation of ‘overhydration’ was found. Taken together with the rather low positive predictive value for absence of overhydration, a two-staged approach to assessment of hydration status can be proposed: if the patient is clinically judged to be overhydrated, treatment should be adapted accordingly; when the patient has no overt clinical signs of overhydration, assessment of hydration status by bioimpedance to confirm true absence of overhydration should be performed.

Overhydration is prevalent in incident PD patients, despite substantial remaining residual urinary output. Probably, there is a mismatch between the output and dietary intake of water, which might be due to a too permissive salt intake. Similar observations have been done in prevalent patients [4, 11]. Even more remarkable is the association between overhydration and RRF. The ongoing longitudinal

\[\text{FIGURE 1: Hydration status in different subcategories (univariate). (A) Gender, (B) diabetes and (C) Transport status. Dotted lines reflect range of euvolaemia (±1.1 L).}\]
observation should bring more clarity to the relation between hydration status and decline of RRF.

The size of the study cohort is a strength of the study, with the multicentre, multinational nature and the geographical expansion over three continents of the study guaranteeing a dilution of any possible local effect. We acknowledge that further associations of patient and treatment parameters with hydration status will have to be interpreted with some caution in view of the observational nature of the data. On the other hand, the inclusion of a large number of patients from a substantial number of centres allows treating practice variation as an instrumental variable which might or might not be associated with certain outcomes. This type of non-interventional cohort study reflecting clinical practice are valuable as hypothesis generating experiments, as prospective randomized studies assessing multiple interventions are expensive and difficult to perform.

In conclusion, in this large incident PD population, a significant amount of patients are overhydrated already at start of PD treatment. Substantial discrepancy between clinical appraisal and actual measurement of hydration status was observed, which might be one of the factors explaining this
high prevalence of overhydration. The routine use of BIS can help to refine evaluation of the hydration status of ESRD and PD patients.

![Figure 3: Scatter plot on fluid overload (L) versus systolic blood pressure (mmHg).](image)

**SUPPLEMENTARY DATA**

Supplementary data are available online at http://ndt.oxfordjournals.org.

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CONFLICT OF INTEREST

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