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Extracellular volume expansion, measured by multifrequency bioimpedance, does not help preserve residual renal function in peritoneal dialysis patients

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Residual renal function is a major survival determinant for peritoneal dialysis patients. Hypovolemia can cause acute kidney injury and loss of residual renal function, and it has been suggested that patients receiving peritoneal dialysis should preferably be maintained hypervolemic to preserve residual renal function. Here we determined whether hydration status predicted long-term changes in residual renal function. Changes in residual renal function and extracellular water (ECW) to total body water (TBW) measured by multifrequency bioimpedance in 237 adult patients who had paired baseline and serial 12 monthly measurements were examined. Baseline hydration status (ECW/TBW) was not significantly associated with preservation of residual renal function, unlike baseline and follow-up mean arterial blood pressure. When the cohort was split into tertiles according to baseline hydration status, there was no significant correlation seen between change in hydration status and subsequent loss in residual renal function. Increased ECW/TBW in peritoneal dialysis patients was not associated with preservation of residual renal function. Similarly, increments and decrements in ECW/TBW were not associated with preservation or reduction in residual renal function. Thus, our study does not support the view that overhydration preserves residual renal function and such a policy risks the consequences of persistent hypervolemia.

Kidney International (2013) **85,** 151–157; doi:10.1038/ki.2013.273; published online 24 July 2013

KEYWORDS: bioimpedance; extracellular water; peritoneal dialysis; residual renal function

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Received 23 September 2012; revised 13 May 2013; accepted 16 May 2013; published online 24 July 2013

In the light of studies that reported that for every 1 ml/min increase in residual renal function (RRF) in a peritoneal dialysis (PD) cohort there was a 50% reduction in the risk of death[1] and that a 250-ml increase in daily urine output was associated with a 36% reduction in mortality (reanalysis of the CANUSA study[2]), preservation of RRF has become one of the most important goals in the long-term management of the patients on PD. Loss of RRF has subsequently been shown to be associated with many complications of chronic uremia: protein–energy wasting,[3–6] hyperphosphatemia,[6,7] left ventricular hypertrophy,[3,6,8] arterial stiffness,[9] anemia,[3,5,6] inflammation,[8] a poorer quality of life,[10,11] technique failure,[12] and ultimately patient death.[1,6,13,14]

One of the strengths of PD is that this modality is associated with greater preservation of RRF when compared with hemodialysis (HD).[15] A possible explanation for this observation is that intravascular dehydration leads to a loss in RRF,[16] and because of the nature of fluid removal in PD, there are fewer episodes of hypovolemia.[15,16] Careful intravascular volume control to prevent dehydration has been used to minimize loss of RRF. Although multifrequency bioimpedance[17] has the potential of being superior to clinical assessment and has become a routine part of patient management in the United Kingdom, we do not know whether attaining bioimpedance-defined euvolemia will accelerate RRF loss. Contrasting paradigms of volume control strategies have been put forward to maintain RRF: running patients 'wet' and running patients 'dry.'

In favor of running patients 'wet'

Intravascular volume depletion and hypotension are known to lead to a loss in RRF;[16,18] this fear of volume depletion has led some clinicians to run their patients 'wet.' Evidence in favor of this comes from a study by Gunal *et al.*[19] who reported that strict volume control with salt and water restriction and/or increased ultrafiltration led to a 2.8-kg weight loss and a fall in systolic blood pressure; however, the cost was a 28% reduction in urine output and a 10% reduction in weekly Kt/V urea. Their group found a similar effect of improving blood pressure control at the cost of loss

in RRF in a HD cohort.[20] Similarly, the Maastricht group reported that intravascular volume depletion in PD patients due to icodextrin could lead to a loss of RRF.[21]

On the other hand, patients treated by PD who had a slower decline of RRF were reported to have spent more time being volume overloaded as compared with HD patients.[22]

In favor of running patients 'dry'

Overhydration is associated with hypertension, left ventricular hypertrophy,[21,23] and excess mortality,[24] and hypertension has been reported to lead to the loss of RRF.[16] In addition, high levels of prohormone of brain natriuretic peptide driven by volume overload[25] have been shown to be an important predictor of survival in the ADEMEX study.[26] The Tassin experience in France with a HD cohort demonstrates that intensive blood pressure control and normalization of extracellular volume can improve patient outcomes.[27] Rodriguez-Carmona *et al.*[28] reported that PD patients treated with automated peritoneal dialysis cyclers had lower levels of salt and water removal and were more hypertensive; however, despite this volume overload, these patients lost RRF more quickly than in a continuous ambulatory peritoneal dialysis cohort.

We undertook a study to examine whether hydration status assessed using longitudinal bioimpedance measurements predicted long-term changes in RRF.

RESULTS

We identified 237 adult uric PD patients (median age 61 years, 54% male, 30% diabetic, and 46% Caucasoid) for analysis (Table 1).

Factors correlated with a loss in RRF

Simple correlation analysis showed that the following factors were associated with faster loss of RRF: greater initial RRF, higher baseline and follow-up mean arterial pressure, and lower baseline serum phosphate, urea, and cholesterol. At follow-up, faster loss in RRF was associated with a higher creatinine, phosphate, and potassium concentrations, and lower serum albumin concentrations (Table 2).

Many characteristics of the cohort were not significantly correlated with loss in RRF, as measured by the change in weekly urine Kt/V at follow-up compared with baseline. Baseline variables that were not significantly correlated with a loss in weekly urine Kt/V included age, sex, ethnicity, PD vintage, body mass index, presence of diabetes, PD modality (continuous ambulatory peritoneal dialysis vs. cycler automated peritoneal dialysis), 24-h PD ultrafiltration volume, serum sodium, parathyroid hormone, glucose, hemoglobin, albumin, creatinine, calcium, bicarbonate, potassium, and C-reactive protein. At follow-up, factors that were not correlated with loss in RRF included peritoneal adequacy (weekly Kt/V peritoneal), 24-h PD ultrafiltration volume, body mass index, serum sodium, parathyroid hormone, glucose, hemoglobin urea, calcium, bicarbonate, cholesterol, and C-reactive protein. Overall use of antihypertensive agents was not associated with a loss in RRF; furthermore, when each antihypertensive was considered individually (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, furosemide, spironolactone), the use of the individual drug was not associated with a significant loss in RRF. Furthermore, the choice of PD fluid (Icodextrin, physiological (Physioneal), or high strength (dextrose $\geqslant$2.27%)) solutions at baseline or follow-up was not associated with an alteration in loss in RRF.

Importantly, neither baseline ($r = 0.06$, $P = 0.36$) nor follow-up ($r = 0.07$, $P = 0.24$) hydration status was correlated with loss in RRF. In addition, an absolute change in extracellular water/total body water (ECW/TBW) ratio from

Table 1 | Baseline characteristics of the study cohort

Age (years)	61 (50–72)
Sex (% male)	128 (54%)
Body mass index (kg/m^2)	25.6 (22.7–29.5)
Ethnicity: White	109 (46%)
Ethnicity: Black	33 (14%)
Ethnicity: Asian	85 (36%)
Ethnicity: Other	10 (4%)
Diabetes	70 (30%)
PD vintage (months)	5.5 (2–20)
Dialysis modality (CAPD)	86 (36%)
Baseline ECW/TBW	0.39 (0.38-0.4)
Baseline urine output (ml/24 h)	793 (408–1335)
Weekly urine Kt/V	0.8 (0.42–1.31)
Weekly PD Kt/V	1.41 (1.1–1.74)
Daily PD ultrafiltration volume (ml)	492 (200–885)
Mean arterial pressure (mm Hg)	99 (88–110)
Sodium (mmol/l)	140 (137–142)
Potassium (mmol/l)	4.2 (3.6–4.6)
Hemoglobin (g/dl)	11.8 (10.9–12.7)
Urea (mmol/l)	17.8 (14.3–21.9)
Creatinine (μmol/l)	667 (559–854)
Calcium (mmol/l)	2.32 (2.22–2.44)
Phosphate (mmol/l)	1.45 (1.22–1.72)
Parathyroid hormone (ρmol/l)	22.8 (12.1–42.6)
Total cholesterol (mmol/l)	4.5 (3.9–5.3)
Albumin (g/l)	38 (36–41)
C-reactive protein (mg/l)	5 (4–10)
Bicarbonate (mmol/l)	25 (24–27)
Hemoglobin A1c (%)	5.4 (6–5.2)
Glucose (mmol/l)	5.4 (4.7–7.25)
Antihypertensive use	
Number of antihypertensive medications	2 (1–3)
Angiotensin receptor blocker	57 (24%)
Calcium channel blocker	64 (27%)
β-Blocker	68 (28%)
Furosemide	123 (52%)
Spironolactone	19 (8%)
'Other' antihypertensive	45 (20%)
PD fluid use	
Icodextrin	141 (59%)
'High-dextrose' fluid[a]	98 (41%)
'Physiological' fluid[b]	43 (18%)

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; ECW, extracellular water; PD, peritoneal dialysis; TBW, total body water.
Data are displayed as median (interquartile range (IQR)), with the exception of categorical data that are displayed as *n* (%).
[a]High-dextrose fluid was defined as any patient receiving PD solutions with a dextrose concentration of $\geqslant$2.27%.
[b]Physiological PD fluid was defined as any patient using Physioneal solution.