Longitudinal bioimpedance vector plots add little value to fluid management of peritoneal dialysis patients

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Bioimpedance (BI) has the potential to enable better management of fluid balance, which can worsen over time on peritoneal dialysis (PD) due to loss of residual kidney function and progressive muscle wasting. We undertook a prospective, randomized, open-label, blinded end-point controlled trial to determine whether availability of longitudinal BI measures as vector plots helped clinicians maintain stable fluid status over 12 months in 308 peritoneal dialysis patients from the United Kingdom and Shanghai, China. Patients were recruited into 4 groups nested within a single trial design according to country and residual kidney function. Nonanuric subjects from both countries demonstrated stable fluid volumes irrespective of randomization. Hydration worsened in control anuric patients in Shanghai with increased extracellular/total body water (ECW/TBW) ratio (0.04; 95% CI: 0.01, 0.06) and reduced TBW (−1.76 L 95% CI: −2.70, −0.82), but was stable in the BI intervention group whose dialysate glucose prescription was increased. However, multilevel analysis incorporating data from both countries showed worsening ECW/TBW in active and control anuric patients. Clinicians in the United Kingdom reduced target weight in the nonanuric BI intervention group causing a reduction in TBW without beneficial effects on ECW or blood pressure. Thus, routine use of longitudinal BI vector plots to improve clinical management of fluid status is not supported.

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Optimal fluid management is one of the primary objectives of dialysis treatment, and there is significant concern that peritoneal dialysis (PD) patients can become progressively fluid-loaded with time on treatment, especially as residual kidney function declines.[1,2] There is a growing body of evidence that bioimpedance (BI) analysis has a role to play in assisting the clinician in managing fluid status;[3] this is primarily based on observational studies showing that overhydration, as determined from BI, predicts worse survival[4,5] and the demonstration that BI can detect changes following interventions designed to improve fluid status.[6,7] BI data comprise the following two components: resistance to an electrical current, typically passed through the body from the wrist to the ankle, which is inversely proportional to total body water (TBW), and reactance, which is the impedance to this alternating current, also measured in Ohms, as it passes through tissues with cell membranes and thus it is proportional to cell mass. These two components can be plotted as a two-dimensional vector and used to track changes in fluid status that could support clinical decisions (Figure 1). However, few clinical trials have been conducted that clearly demonstrate a benefit of BI over and above good-quality standard clinical management.

Longitudinal studies of body composition indicate that progressive overhydration is usually associated with a decline in muscle mass and a potential failure to adjust the dialysis prescription so as to reduce the extracellular water (ECW) volume down in parallel with this.[8–11] We hypothesized that the longitudinal application of BI alongside clinical evaluation would help the clinician identify this problem and thus make appropriate adjustments to the prescription. To test this hypothesis, we undertook a randomized controlled trial to determine whether the additional information available from longitudinal BI over 12 months could assist in maintaining stable or improved fluid status. Using the same basic design, we included four independent randomization groups comprising nonanuric and anuric patients from three UK dialysis centers (Stoke-on-Trent, Leeds, and Sheffield) and one Chinese center (Shanghai), respectively. Our aim was to determine whether routine clinical management supported by the longitudinal plot of the BI vector, which shows the direction in which fluid status is changing, resulted in more

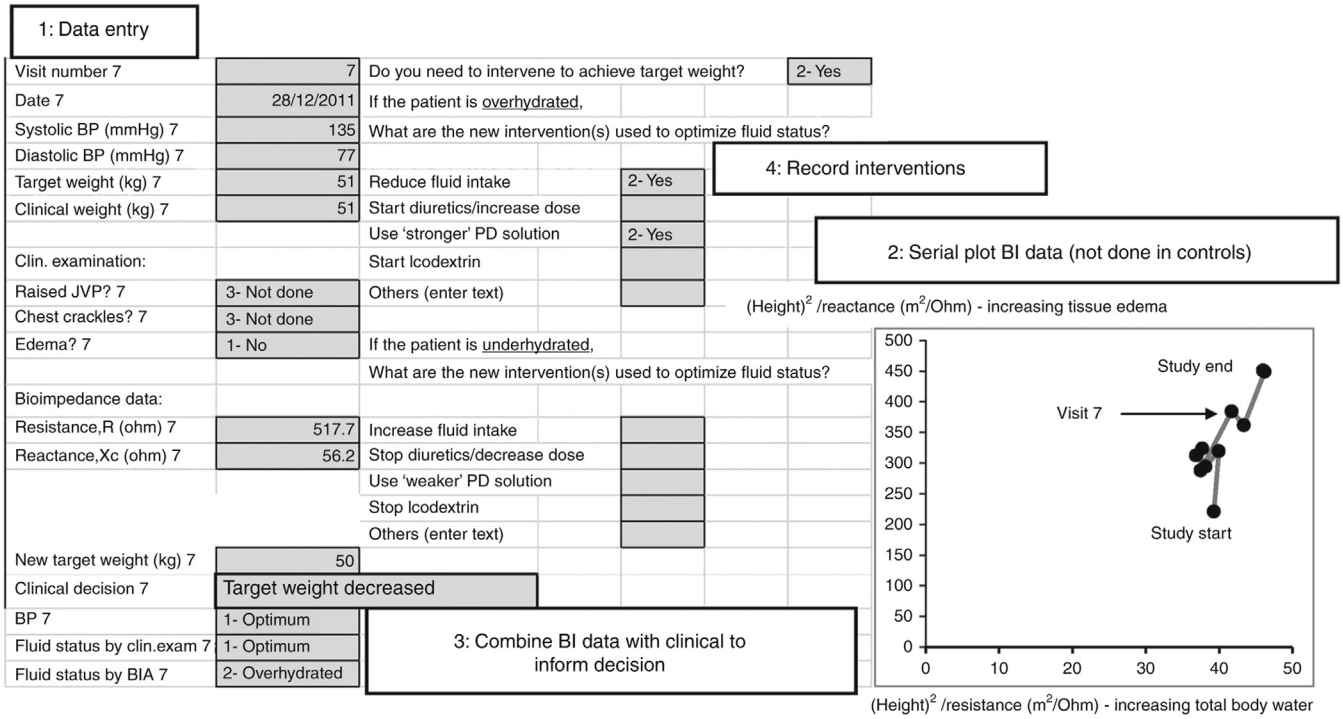

Figure 1 | The procedure for documenting clinical interventions is summarized. (Step 1) The clinical and bioimpedance (BI) data were entered onto an electronic clinical research record. For the intervention group, only BI data were automatically plotted (step 2) as the serial reciprocal height^2 (H^2) normalized data. In this format, increasing H^2/resistance implies increasing total body water and H^2/reactance reflects increasing extracellular fluid. (Step 3) This was then combined with clinical observations to inform the decision. In this example shown at assessment number 7, although the patient was clinically euvolemic, the BI indicated a progressive overhydration with lengthening and widening of the BI vector, and hence the target weight was reduced. Step 4 records the methods used to achieve this, in this case both advising reduced fluid intake and increased glucose prescription. This resulted in a temporary reduction in the phase angle, but this patient went on to become progressively overhydrated despite further reductions in target weight. This example shows that patients with unstable fluid status could have additional assessments (i.e., more than the five standard study visits; see also Supplementary Material online for further examples).

stable fluid status than control subjects. The outcome, to which the clinicians were blinded, was fluid volumes, ECW, TBW, and their ratio (ECW/TBW), as determined from the BI measurements after the trial was completed.

RESULTS

Patient characteristics

Recruitment, randomization, and dropout to and from the four study groups are summarized in the consort diagram (Figure 2). With the exception of the UK anuric group, recruitment was sufficient to test our primary outcome with 80% power to detect a 1-kg change (in ECW) in the Shanghai (nonanuric and anuric) patients and a 0.8-kg change in the UK nonanuric (UK nonanuric) patients. Failure to achieve power in the UK anuric group was because of a combination of lack of recruitment indicative of the low proportion of anuric patients in the three UK centers and a high dropout (66%). There was a nonsignificant increase in deaths in this patient group randomized to the BI intervention; careful analysis of these 4 deaths (cancer or sepsis) and adverse outcomes did not indicate any common factor or plausible relationship to the intervention, but this group was excluded from further analysis apart from the multivariate models. Dropout in the remaining groups was well balanced over the course of the study, as shown by Kaplan–Meier plots and log-rank tests (Supplementary Data, Supplementary Figure S1 online).

There were no significant differences between patients randomized to the BI intervention or control arm in any of the groups in terms of their baseline demography, dialysis prescription, residual kidney function, peritoneal membrane function, blood pressure, or body composition (Table 1). Shanghai patients tended to be younger (mean age 54.0 vs. 58.6 years), have less comorbidity (20 vs. 60% with at least one other diagnosis), and weigh significantly less than UK patients (58.9 vs. 76.8 kg), which was reflected in a lower dialysis prescription volume. The average blood pressure and peritoneal solute transport rates (PSTR) were lower in the Shanghai patients. On comparing the nonanuric patients, normalized residual renal clearances were higher in UK patients, as was the absolute residual urine volume, unless this was corrected for body weight when the difference was nonsignificant (16.7 vs. 17.4 ml/kg). As expected, anuric patients had been on PD for longer periods: Shanghai-anuric versus Shanghai-nonanuric, 58 (26–90) versus 19 (7–41) months; and UK anuric versus UK nonanuric, 57 (36–72) versus 22 (7–33) months.