Changes in body composition following haemodialysis as assessed by bioimpedance spectroscopy

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Abstract

Background

Patients with chronic kidney disease treated by haemodialysis (HD) are at increased risk of sarcopenia. Bioelectrical impedance spectroscopy (BIS) can be used to determine body composition, and is one of several potential screening tools for sarcopenia. The newer generation of portable hand held devices can be readily used in dialysis centres. The results from BIS devices using a two compartmental model of body composition can be affected by hydration status

and so ideally measurements should be made when patients are not overhydrated. More recently BIS devices using a three compartmental body model, which separate normally hydrated lean tissues from extracellular water (ECW) excess. We wished to determine whether body composition measured using such a BIS device was affected by hydration status.

Methods

We performed BISs pre and post-haemodialysis using a three body compartmental model .

Results

BISs were recorded in 48 patients; 68.8% male; mean age 67.70±14.21 years, weight pre dialysis 70.54±18.07, which fell post to 68.58±17.78 kg, Extracellular water fell (16.92±4.76 vs 15.66±4.43 L, $p<0.001$), whereas there was no change for intracellular water (14.84±4.27 vs 14.90±4.68 L).Fat free mass index (FFMI) fell (7.87±3.98 vs 16.78±3.97 kg/$m^{2,}$ $p<0.001$), whereas fat mass index(FMI) increased from (7.87±3.98 vs 8.12±3.81 kg/m^2, $p=0.002$). A fall in FFMI was associated with an increase in FMI ($r=0.804$, $p<0.001$).

Conclusion

FMI and FFMI measured by BIA are both confounded by hydration status. Although pre-dialysis measurements are more convenient, we suggest BIS should preferably be performed post-dialysis when patients are less over-hydrated and have less electrolyte imbalances.

The authors have no conflict of interest
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Introduction

Patients with chronic kidney disease (CKD) at increased risk of sarcopenia, and once sarcopenia has developed then patients are at increased risk for mortality. Muscle mass can be determined from anthropomorphic measurements and muscle wasting assessed as part of the subjective global assessment (SGA) [1]. However these methods are relatively insensitive in detecting early changes, observer dependent, and potentially time consuming. As such other screening tests including dual energy X ray absorptiometry (DXA)

and bioelectrical impedance assessment (BIA) have been recommended as alternatives [2,3].

DXA scanning and most bioimpedance devices divide the body into 2 compartments; fat mass and fat free mass [4]. Previous reports have demonstrated a strong correlation between body composition as assessed by multi-frequency BIA and DXA scanning in dialysis patients [5,6]. However BIA assessments of body hydration status and body composition can be affected by localised fluid, such as ascites and intra-peritoneal fluid [7,8], and also by over hydration [9]. Haemodialysis patients gain fluid between dialysis sessions, and then this excess fluid is removed during the haemodialysis session. This relatively rapid change in body fluid following dialysis has been demonstrated to lead to a change in body composition as determined by BIA [10]. As such BIA should preferably be made when the haemodialysis patient is closest to their dry or target weight and not pre-dialysis when they are volume overloaded.

In clinical practice it is much more convenient to make BIAs prior to the haemodialysis session, rather than asking patients to remain behind for BIAs. More recently BIS devices using 3 compartmental body composition models have been developed [11]. These devices determine the normally hydrated lean body mass, and as such should not be affected by the changes in hydration that occur with haemodialysis. We therefore decided to review body composition data from patients who had corresponding pre and post haemodialysis BIS to determine whether there were no changes in body composition with dialysis, so that pre-dialysis measurements of body composition alone would suffice.

Methods

We audited the results of body composition estimations taken pre and post haemodialysis using bioimpedance spectroscopy (BodyStat multiscan 5000 ,BodyStat, Douglas, Isle of Man). Four electrodes were placed according to the manufacturer's instructions on the dorsal surface of the contra-lateral hand and foot and ankle to the arterio-venous fistula or arterio-venous graft. Patients were weighed and height recorded prior to dialysis (Marsden Weighing Group, Rotherham, UK). Pre dialysis measurements were made with patients lying supine on a bed. Patients dialysed using Fresenius 4008H (Fresenius Bad Homberg, Germany) or Dialogue R+ (BBraun, Melsungen, Germany) with high flux polysulfone dialyzers (Elisio, Nipro Corporation, Osaka, Japan) [12] and anticoagulated with bolus low molecular weight heparin (Tinzaparin, Leo Laboratories, Hurley, Berkshire, UK) [13]. Dialysis machines were regularly serviced and dialysate conductivity checked against flame photometry [14]. We audited 48 consecutive patients attending for haemodialysis with corresponding pre and post dialysis measurements. Patients were not allowed to eat during dialysis and were restricted to one small drink (180 ml). After the haemodialysis session had been completed and the fistula needle sites had stopped bleeding, then patients were reweighed using the same scales, returned to lying supine on their bed, rested and then post dialysis measurements were repeated. There was no change in the position of the electrodes between measurements.

Ethics

Standard of care for haemodialysis patients at the Royal Free Hospital has been to measure bioimpedance pre and post dialysis sessions. We audited the results of pre and post haemodialysis BIS measurements to determine whether bioimpedance derived body composition should be measured pre or post dialysis to be the standard of care for routine clinical practice. Ethical approval fulfilled UK NHS clinical service development and audit (UK NHS guidelines for clinical audit and service development (http://www.hra.nhs.uk/documents /2013/09/ defining-research.pdf)) with all patient data being anonymised.

Statistical methods

Statistical analysis was by parametric or non-parametric pair testing by Student's t test or Mann Whitney U test, and Anova. Univariate correlation was by Pearson or Spearman correlation (Prism 6.0, Graph Pad, San Diego, USA), and Bland Altman analysis (version 3.0, Analyse It, Leeds, UK), with significance at the $p<0.05$ level. Data is reported as mean ± standard deviation, median and interquartile range or percentage.

Results

BIS was measured pre and post-dialysis in 48 patients; 68.8% male; mean age 67.70±14.21 years (mean ± standard deviation), attending for in-centre haemodialysis treatments. Median urine output was <50 (<50-58) ml/day, Stoke-

153 Davies co-morbidity grade 1 (0-1), and Canadian Society of Geriatrics frailty
154 score 4 (4-5.8). Fourteen patients had diabetic nephropathy, 13 undetermined
155 cause, 5 interstitial renal diseases, 4 hypertensive nephropathy, 4 primary
156 glomerular disease, 3 myeloma kidney, 2 systemic lupus erythematosus, one each
157 of haemolytic uraemic syndrome, pre-eclampsia, and amyloid. All patients were
158 prescribed folic acid and B vitamin supplements, and 50% of patients were
159 additionally prescribed anti-hypertensive medications and 22% diuretics.

160 Mean weight pre dialysis was 70.54±18.07 kg, height 165.80 ±11.34 cm,
161 and body mass index (BMI) was 25.52 ±6.11 kg/m^2.

162 The median dialysis session time was 4.0 (3.5-4) hours, dialysate
163 temperature 35 (35-35.5)^{0}C, sodium 137 (136-138) mmol/l, potassium 2.0 (1.0-
164 2.0) mmol/l, calcium 1.35 (1.25-1.35) mmol/l, magnesium 0.5 mmol/l, bicarbonate
165 32 mmol/l, acetate 3.0 mmol/l.

166 Weight fell post dialysis, as did extracellular water (ECW), but there was
167 no overall significant change in intracellular water (ICW) (Table 1). Assessments
168 of body composition showed an increase in measurements for body fat and a fall
169 in fat free tissues (table 1). As changes in ECW and ICW lead to corresponding
170 changes in BIS derived body composition, we then looked for differences at the
171 individual patient level, by Bland Altman analysis comparing the differences
172 between corresponding pre and post-dialysis values

173 There was an overall negative mean bias for ICW (Figure 1), suggesting a
174 small increase in ICW following dialysis and a positive bias for ECW (Figure 2)
175 showing a loss of ECW. As such there was a mean negative bias for fat mass

index (FMI) of -0.23 (95% limits of agreement -1.16 to 0.71 kg) corresponding to an increase in FMI post-dialysis, and a mean positive bias for fat free mass index (FFMI) of 0.83 (-0.4 to 1.79), with a loss of FFMI post-dialysis. The corresponding coefficient of variation for FMI and FFMI were 0.49 and 0.24 respectively.

There were positive correlations between the change in pre and post dialysis ICW and the change in fat free mass ($r= 0.29$, $p=0.042$) and muscle mass ($r=0.31$, $p=0.031$), and a negative correlation with the change in fat mass ($r=-0.30$, $p=0.037$)). There were positive correlations between the change in pre and post dialysis ECW and change in fat free mass ($r=0.95$, $p<0.001$), muscle mass (Figure 3) lean dry mass ($r=0.37$, $p=0.01$) and a negative correlation with fat weight ($r= 0.78$,$p<0.001$). There was a strong correlation between the change in muscle mass and fat mass ($r=0.82$, $p<0.001$) (Figure 4).

To ensure that patients had re-equilibrated post-dialysis, and that measurements did not change following dialysis, two additional BIS measurements were made post-dialysis . There were no significant differences between 1st, 2nd or 3rd post-dialysis measurements (table 2).

Discussion

BIA devices have advanced from single frequency to multiple frequency and bio-impedance spectroscopy (BIS) devices [15] with measurements comparable to isotopic methods [16]. Standard BIA devices use a 2 compartmental model of body composition, dividing the body into fat and fat

free mass. However this approach is affected by hydration status, and as muscle contains more water than fat, when over hydrated then muscle mass is over estimated [9,10,17]. As such we made measurements with a BIS device using a 3 compartmental model approach which aims to distinguish normally hydrated muscle mass from pathologic fluid overload when assessing body composition [11]. This is based on comparing measured ECW and that estimated using the slope of ECW volume and body weight at normovolaemia, where the slope is 0.239 L/kg for men and 0.214 L/kg for women [11]. As such these bioimpedance devices potentially have the advantage of being able to assess body composition using a single pre-dialysis measurement, as there should be no change in fat free index or fat index with dialysis, whereas standard bioimpedance devices using a 2 compartment model require post-dialysis measurements to prevent errors due to hydration status [10].

We observed that whereas both weight and ECW fell post dialysis there was no significant change in ICW. Associated with weight loss there were changes in body composition following haemodialysis, with a fall in fat free mass, muscle and dry lean tissue, and an increase in fat mass. The changes in muscle mass we observed are in keeping with an earlier version of the BodyStat [18], but differ from studies using other manufacturers 3 compartmental BIS devices [18]. When we looked at the individual patient basis, then the greater the fall in ECW, there was a corresponding greater fall in fat free mass and muscle mass, but with a negative correlation with fat mass. We observed that a fall in ICW following haemodialysis was associated with a reduction in muscle

mass, whereas a gain in ICW was associated with an increase in muscle mass, which is in keeping with studies using 3 compartmental BIS devices from different manufacturers [18].

So in keeping with other 2 and 3 compartmental BIA and BIS models this device over estimated muscle mass and under estimated fat mass pre dialysis compared to post dialysis values. As such despite a model designed to separate ECW excess from normo-hydrated fat free tissues this model was affected by over hydration. This may not be surprising as these models use predictive models based on ECW relative to ICW, and the relative increase in ECW and ICW between dialysis sessions varies between patients due to differences in sodium and water gains. In addition, previous reports have suggested that BIA measurements can also be affected by body temperature, electrolyte imbalances, and haematocrit [19].

Previous studies of patient pre dialysis, when patients were over hydrated, showed that the BIS over estimated total body skeletal muscle mass compared to magnetic resonance in patients with lower muscle mass and conversely under estimated total body skeletal muscle mass in those patients with greater muscle mass [20]. These differences may be due to errors in estimating normo-hydrated fat free tissue [11], as muscle in dialysis patients may not simply just contain more water pre dialysis, but also urea and other azotaemic toxins, and more recently studies have additionally reported higher sodium content, and that sodium can be removed from tissue stores during a haemodialysis session [21].

Following a haemodialysis session there is redistribution of urea and other electrolytes, and fluid, which tends to be greater with faster blood flows [22]. To overcome this rebound phenomenon, dialysis adequacy studies based on changes in serum urea concentrations advocate taking a delayed post dialysis serum urea sample to overcome this effect [23]. It is therefore important that BIS is performed after re-equilibration [24,25]. We waited for fistula needle sites to have stopped bleeding, and then re-weighed patients, waited for patients to return to their beds, resume the supine posture, allowed additional time for the postural change and then performed BISs [26]. We then repeated BISs to ensure that there were no discernible changes to establish that patients were in a stable state post dialysis.

Patients with chronic kidney disease are at increased risk of sarcopenia, and portable hand held BIS devices could be used to screen patients for sarcopenia [2]. Although there are different classifications for defining sarcopenia, many simply use a cut-off point of more than 2 standard deviations from the normal healthy adult lean body mass index. As such, there could potentially be a difference in the number of patients being classified with sarcopenia depending upon whether BIS is measured pre or post haemodialysis, with fewer patients being recorded as having sarcopenia when using pre-dialysis compared to post dialysis estimations.

Bioimpedance measurements are dependent upon the length of the circuit and the cross sectional area. As such, moving the electrode placements changes the results, so one advantage of the Multiscan 5000 was that the larger

electrodes remained in position during dialysis, and no electrodes had to be replaced. However this device measures whole body fluid volumes and body composition using paired ipsi-lateral hand and foot electrodes, with the assumption that patients are symmetrical. However dialysis patients may be asymmetrical due to amputations, previous deep venous thrombosis, or central venous occlusion, stroke, polio etc.

Most haemodialysis patients are over hydrated and following a haemodialysis session there are changes in ICW and ECW [27,28]. Despite using a BIS device based on a 3 compartmental body model, there were still changes in body composition associated with over hydration. So although pre dialysis BIA measurements are more convenient to both patients and dialysis centre staff, for greater reliability BIS measurements should preferably be made when a are closest to their normo-hydrated state to reduce errors in estimation of body composition when patients are over hydrated.

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Figure 1. Bland Altman analysis comparing pre haemodialysis intracellular water (ICW) and post haemodialysis ICW in litres. Mean bias -0.23, 95% limits of agreement -1.16 to 0.71 L.

Figure 2. Bland Altman analysis comparing pre haemodialysis extracellular water (ECW) and post haemodialysis ECW in litres. Mean bias 0.83, 95% limits of agreement -0.39 to 2.83 L.

Figure 3. Change in intracellular water (ECW) pre and post-dialysis, comparing with the change muscle mass. Pearson correlation.

Figure 4. Change in fat free mass and fat mass following a haemodialysis session. Pearson correlation.