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Original Articles

The effect of vascular access modality on changes in fluid content in the arms as determined by multifrequency bioimpedance

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Abstract

Introduction. Intradialytic hypotension remains the commonest complication of routine outpatient haemodialysis treatments. Multifrequency bioimpedance allows assessment of body fluid volumes. Multifrequency bioimpedance can potentially monitor changes in extracellular volume during dialysis and may therefore help to reduce intradialytic hypotension. Hypotension-prone patients have been reported to start dialysis with relatively more fluid distributed in the trunk than the arms. However, as arterio-venous fistulae are the preferred form of vascular access and fistulae could potentially affect fluid retention in the arm, we investigated whether multifrequency bioimpedance could detect differences in fluid distribution in the arms with haemodialysis in patients with different vascular access modalities.

Methods. We audited the change in extracellular water (ECW) and total body water (TBW) in the arms following haemodialysis in 100 patients attending for routine outpatient haemodialysis at a university centre by multifrequency bioimpedance using an eight-electrode contact technique.

Results. Patients with fistulae had greater ECW/TBW % in the fistula arm both prior to and post dialysis compared with central venous catheter (CVC) (pre 38.9 ± 0.1 vs 38.3 ± 0.1 and post 38.4 ± 0.1 vs 37.8 ± 0.1, $P < 0.01$), with a greater absolute difference between arms (0.53 ± 0.01 vs 0.05 ± 0.01, $P < 0.01$) and greater arm ECW/TBW % compared with total body ECW/TBW % predialysis (forearm fistula 99.4 ± 0.4 vs CVC 97.2 ± 0.3, $P < 0.01$).

Conclusion. Absolute and also relative extracellular fluid volumes are increased in the fistula arm of haemodialysis patients. Thus, if algorithms are to be developed to monitor relative segmental changes in extracellular volumes to help prevent intradialytic hypotension using bioimpedance, then the dialysis vascular access and site will have to be considered, particularly if using relative changes in the upper limbs. Thus, alterative sites which are not so affected by vascular access, such as the calf, may prove advantageous.

Keywords: arterio-venous fistula; extracellular fluid; haemodialysis; multifrequency bioimpedance

Introduction

Although haemodialysis has progressed rapidly over the last 60 years from an experimental treatment for a limited number of patients with acute kidney injury to a routine outpatient therapy for hundreds of thousands of patients with chronic kidney disease worldwide, intradialytic hypotension [1] remains the commonest complication, with a prevalence of around one in six routine outpatient treatments [2]. Advances in haemodialysis machine technology, including volumetric ultrafiltration control and relative blood volume monitoring, have been introduced to help reduce intradialytic hypotension [3]. Despite these technological developments, intradialytic hypotension persists [4].

More recently, bioimpedance has been introduced as a method of assessing body fluid status. Bioimpedance refers to the resistance offered by tissue to the passage of an electrical current. The conductance of human tissues is directly proportional to the volume of ionic content that is accessible to the passage of electrical current, and resistance to conduction occurs at non-conducting surfaces, such as bones and lungs. Using multiple alternating current frequencies, a stepwise recruitment of conduction may be induced through different body compartments allowing calculation of different compartment volumes. Studies with multifrequency bioimpedance in haemodialysis patients have shown that the majority of extracellular fluid removed during a haemodialysis session comes from the truncal area, followed by the legs and arms [5]. Although bioimpedance may be helpful in assessing fluid volume status in dialysis patients and directing reappraisal of target or dry weights [6], it has not been shown to predict intradialytic hypotension.

During dialysis, as ultrafiltration takes place, there is initially compensatory movement of extracellular fluid to refill the vascular compartment. As patients approach their target or dry weight, this compensatory response becomes compromised [7], with increased risk of intradialytic hypotension. By measuring changes in extracellular fluid volume, bioimpedence can potentially be used to monitor the effect of ultrafiltration during dialysis. As different compartments contain different amounts of extracellular fluid, it has been suggested that the relative change of extracellular fluid between compartments could be used to predict an increased risk of intradialytic hypotension [5]. Some multifrequency bioimpedance machines only have two pairs of electrodes and, although they can track total fluid volume changes during dialysis, cannot directly compare changes in fluid volumes between the two arms or the two legs. As we are now dialysing more patients with arterio-venous fistulae in the UK, following a Department of Health initiative to reduce the number of haemodialysis patients using central venous access catheters and increase the number of patients dialysing with arterio-venous fistulae [8], we decided to assess whether access modality affected changes in fluid volume in the arms using multifrequency bioimpedance measurements derived from eight tactile electrodes.

Materials and methods

To determine whether the type of vascular access used for haemodialysis affected the change in fluid volumes in the arms during a haemodialysis session, we analysed multifrequency bioimpedance data from 100 healthy haemodialysis outpatients who attended for thrice weekly outpatient haemodialysis in a university dialysis centre based in a tertiary referral hospital. The study group comprised 51 males, mean age 55.4 ± 1.7 years, 31% diabetics with 18% of patients prescribed insulin, median dialysis vintage 26 months (9.5–75).

Patients were dialysed using a 4008 dialysis machine (Fresenius FMC, Bad Homberg, Germany), and access recirculation was measured using the incorporated thermodilution method 30 min into the dialysis session. Formal Doppler assessment of forearm and upper arm fistulae blood flow were measured in a minority of patients in the University College London Medical School, department of vascular studies, at the Royal Free Hospital.

Bioelectrical impedance measurements were performed prior to and then 20–30 min post the mid-week haemodialysis session, designed to allow for re-equilibration in a standardized manner using the InBody 720 Body Composition Analysis (Biospace, Seoul, South Korea). Direct segmental multifrequency bioelectrical impedance analysis (MF-BIA) method was employed using the tetrapolar eight-point tactile electrode system, with 30 impedance measurements taken by using six frequencies (1, 5, 50, 250, 500 and 1000 kHz) at each of five segments (right arm, left arm, trunk, right leg and left leg) and reactance by 15 impedance measurements using three frequencies (5, 50 and 250 kHz) at each of the five segments. Measurements were made with the patient standing on the bioimpedance machine, with the arms dependent. To assess reliability of the bioimpedance measurements, bioimpedance was compared in four patients on six different days. The coefficient of variation for the ratio of fluid volumes within the right arm was 0.0159 and 0.017 for the left arm.

All patients attending for routine regular outpatient dialysis treatments at our university dialysis centre were studied as part of their routine clinical care, apart from those with cardiac pacemakers, implantable defibrillators, amputees and those unable to stand on the bioimpedance machine, who were excluded.

Serum biochemistry samples were analysed with a standard multi-channel biochemical analyzer (Roche Integra, Roche diagnostics, Lewes, UK), N-terminal probrain natriuretic peptide (NTproBNP) was measured by immunoassay (ECLIA Roche Diagnostics, GMBH, Mannhein, Germany), and inter-dialysis 24-h urine collections were analyzed to determine urine volume and sodium content.

Ethical approval was granted by the local ethical committee as part of audit and clinical service development.

Statistical analysis

Results are expressed as mean ± standard deviation, median and interquartile range or percentage. Statistical analysis was by Students' paired *t*-test for parametric and the Wilcoxon rank sum pair test for nonparametric data, with Bonferroni correction for multiple analyses where appropriate, and Pearson correlation analysis (Graph Pad Prism version 3.0, Graph Pad, San Diego, CA, USA). Chi-square analyses were corrected for small numbers by Yates' correction. Statistical significance was taken at or below the 5% level.

Results

Forty patients underwent dialysis using central venous access catheters (Ash split catheter, Medcomp, IL, USA), 40 patients forearm arterio-venous fistulae and 20 upper arm fistulae (Table 1). More male patients had forearm fistulae, and those in the fistula group were heavier. Patients who underwent dialysis with upper arm fistulae were marginally older than those using central venous catheters (P = 0.035), who had a shorter dialysis vintage. There was also a difference in vascular access between racial groups; for those who underwent dialysis with central venous catheters: 57.5% Caucasoid, 17.5% African-Afro-Caribbean, 20% South Asian subcontinent; forearm fistulae: 60% Caucasoid, 10% African-Afro-Caribbean, 27.5% South Asian subcontinent; and upper arm fistulae: 30% Caucasoid, 40% African-Afro-Caribbean, 20% South Asian subcontinent. Although more patients from the ethnic minorities had upper arm fistulae, this was not significantly different from those who underwent dialysis with forearm fistulae (X^2 = 3.67, P = 0.055) or central venous catheters (X^2 = 3.012, P = 0.083). The mean on-line recirculation, assessed by thermodilution, was 7.5 ± 0.3%. Thirty-two patients with fistulae had formal Doppler assessment with a mean flow of 978 ± 122 mL/min. There was a negative correlation between access flow and recirculation, P = −0.48, P = 0.01. Doppler flows tended to be greater with upper arm fistulae, 1133 ± 215 mL/min, than forearm fistulae, 847 ± 168 mL/min, but were not statistically different, and there was no difference in recirculation rates 7.55 ± 0.6% vs 7.29 ± 0.3%. There was no correlation between the ratio of fluid volumes within the fistula arm and Doppler blood flow (*r* = 0.134, P = 0.49) and access recirculation (*r* = 02.5, P = 0.107).

There were no differences between the groups in terms of residual renal function, predialysis C reative protein or post dialysis NTproBNP concentrations. During dialysis, no patients suffered symptomatic intradialytic hypotension or required intravenous fluid administration.

Multifrequency bioimpedance data showed that, as the fistula group were predominantly male and heavier, this group had greater mid-arm circumference and both whole-body intracellular and extracellular volumes (Table 2). To overcome differences in bioimpedance according to sex, age and body size, we took the ratio of extracellular water (ECW) to total body water (TBW), which did not differ between the groups.

Table 1. Demographics of the patient groups

	Venous catheter	Forearm fistula	Upper arm fistula
Number	40	40	20
Age year	52.2 ± 2.7	56 ± 2.6	62.2 ± 3.9
Male %	45*	67.5	30*
Diabetics %	22.5	37.5	35
Caucasoid %	57.5	60	30
Vintage months	17 (4–38.5)*	32.5 (16–84.5)	37 (24–74.5)
Predialysis weight (kg)	63.7 ± 2.3**	73.8 ± 2.9	67.2 ± 3.3
Postdialysis weight (kg)	62.7 ± 2.3*	71.6 ± 2.9	64.5 ± 3.3
Urine volume mL/day	57.5 (0–851)	0 (0–525)	0 (0–586)
% prescribed BP meds	32.5	25	15
No of BP meds/pt	1.33 ± 0.1	1.43 ± 0.2	0.85 ± 0.3
CRP mg/L	4.5 (2.5–22)	7 (2.5–18)	4 (2–7.5)
NTproBNP	236 (78–888)	276 (94–652)	172 (57–426)

Vintage, dialysis vintage; % prescribed BP meds, percentage of patients prescribed antihypertensive medications: No of BP meds/pt, number of different types of antihypertensive medications prescribed; CRP, C reactive protein; NTproBNP, N terminal probrain natriuretic peptide. Values expressed as mean ± SEM or median (inter quartile range) or percentage.

*P <0.05.

**<0.01 vs forearm fistula group.

In terms of segmental bioimpedance, 35 patients underwent dialysis with a left forearm fistula and five patients a right forearm fistula, and similarly, 14 patients underwent dialysis with a left upper arm fistula and six patients a right upper arm fistula. We therefore elected to compare arm bioimpedance measurements between the fistula arm in the fistula groups and the right arm in the catheter group (this being the dominant arm as patients were right handed) and between the non-fistula arm and left arm in the catheter group. As expected, the ratio of ECW/TBW in the arms decreased following dialysis, indicating excess fluid loss from the extracellular compartment with ultrafiltration (Figure 1). Prior to dialysis, the ratio of ECW/TBW was greater in the fistula arms compared with the non-fistula arms, whereas although there was no difference between the arms in the catheter group, the ECW/TBW ratio for the left arm was marginally greater than the right arm. The difference in ECW/TBW ratio between the two arms prior to dialysis was least in the CVC group, 0.083 ± 0.09, compared with the forearm fistula group, 0.465 ± 0.09, P = 0.0052, and the upper arm group, 0.366 ± 0.1, P = 0.022. Following dialysis, the ECW/TBW ratio fell in both arms in each of the groups. However, post dialysis, the ratio was greater in the fistula arms in the two fistula groups compared with the catheter group, whereas the non-fistula arms were similar to the arms in the central venous catheter group. Post dialysis difference in ECW/TBW between the two arms was least in the CVC group, 0.056 ± 0.1, compared with both the forearm fistula group, 0.533 ± 0.01, P = 0.0051, and the upper arm group, 0.532 ± 0.1, P = 0.007.

The ratio of ECW/TBW in the arm was also compared with total body ECW/TBW. The ratio was less than 100% in all groups but greater in the fistula arms compared with the non-fistula arms (Figure 2), predialysis forearm fistula 99.4 ± 0.4% vs CVC 97.2 ± 0.3%, P < 0.01. The ratio increased significantly post dialysis in both arms in the catheter group, although the increase was not statistically significant with the fistula arms.

Table 2. Multifrequency bioimopedance measurements in patients according to vascular access

	Venous catheter	Forearm fistula	Upper arm fistula
MAC pre HD cm	29.6 ± 0.6*	29.5 ± 0.7*	31.8 ± 0.6
MAC post HD cm	29.4 ± 0.7*	29.2 ± 0.8*	31.7 ± 0.6
ICW pre HD l	21.3 ± 0.9	23.7 ± 0.9*	19.9 ± 0.9
ICW post HD l	20.5 ± 0.9	22.4 ± 0.9*	19.3 ± 0.9
ECW pre HD l	13.8 ± 0.5	15.2 ± 0.5*	12.9 ± 0.6
ECW post HD l	12.8 ± 0.5	14.0 ± 0.5*	12.3 ± 0.6
ECW/TBW pre HD	0.395 ± 0.002	0.391 ± 0.002	0.392 ± 0.004
ECW/TBW post HD	0.385 ± 0.002	0.386 ± 0.003	0.388 ± 0.003

MAC, Mid arm circumference; ICW, total intracellular water; ECW, extracellular water; TBW, total body water.

*P <0.05 vs upper arm fistula group.

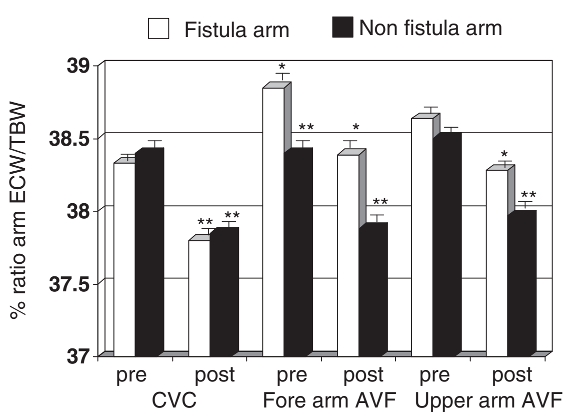

Fig. 1. Multifrequency bioimpedance estimate of extracellular water (ECW) and total body water (TBW) in patients' arms pre and post haemodialysis session. Fistula arm or dominant right arm in central venous catheter (CVC) group compared with non-fistula arm or non-dominant left arm in CVC group. *P <0.05 vs CVC group, **P <0.001 pre vs post dialysis values.

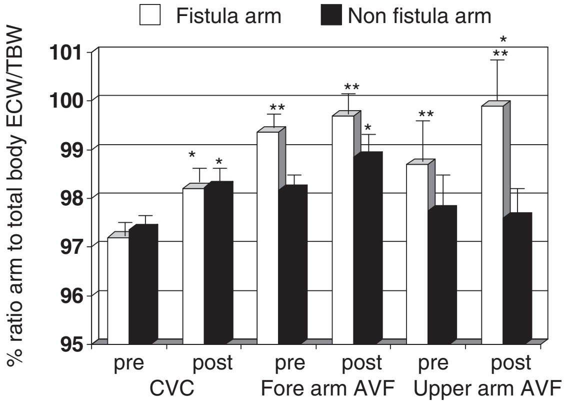

Fig. 2. Multifrequency bioimpedance estimate of extracellular water (ECW) and total body water (TBW) in patients' arms pre and post haemodialysis session compared with total body ECW/TBW. Fistula arm or dominant right arm in central venous catheter (CVC) group compared with non-fistula arm or non-dominant left arm in CVC group. **P <0.01 fistula arm vs non-fistula arm, and *P <0.05 pre vs post dialysis values.

Discussion

In this audit, some 60% of patients underwent dialysis using arterio-venous fistulae. Patients who underwent dialysis with central venous access catheters had been established on dialysis for a shorter period compared with those using fistulae. Patients with forearm fistulae were more likely to be male and heavier than those using central venous catheters. As there is a current UK clinical practice guideline to increase the number of patients undergoing dialysis with fistulae [9], some 20% of patients underwent dialysis with an upper arm fistula. Patients with upper arm fistulae were more likely to be female and from the ethnic minorities.

As bioimpedance depends upon height and volume, those patients who underwent dialysis with forearm arterio-venous fistulae had greater measured extracellular volume and total body water [10], while patients with upper arm fistulae had greater upper arm circumference [11]. This is in agreement with animal experiments performed by Guyton in the 1960s, when he observed that animals with fistulae compensated by increasing heart rate and contractility in combination with fluid retention, particularly intravascular volume expansion [12]. The local haemodyamics of the fistula would be expected to increase fluid retention in the surrounding tissues. This could be affected by blood flow, both arterial in-flow stenoses and also obstruction to venous return. In our series of outpatient haemodialysis patients, we could not demonstrate a relationship between fistula flows or access recirculation measurements and fluid retention within the fistula arm. However, we measured access recirculation using the Fresenius blood temperature module, which detects changes in temperature and so differs from other devices used for monitoring access based on ultrasound or conductivity, in terms of response times, and so does not discriminate between access recirculation and cardiopulmonary recirculation [13]. As such, we were unable to correct our recirculation measurements for cardiopulmonary recirculation. Although there was a relationship between recirculation rates and Doppler flows, only a minority of our patients had formal Doppler studies, as this is not part of our routine clinical care and is typically only requested for cases with suspected fistula malfunction. The number of patients with very poor fistula flows was too small to be able to comment on the effect of severe arterial in-flow stenosis or venous obstruction. However, it would be expected that severe in-flow stenosis would limit fluid retention within the fistula arm and, conversely, venous obstruction would increase fluid retention.

To adjust for the differences in case mix between the three groups [14], we compared ECW/TBW between arms. Prior to dialysis, the ECW/TBW ratio was greatest in the arm of those who underwent dialysis with forearm fistulae and least in those who underwent dialysis through central venous catheters. Following dialysis with weight loss, the ratio of ECW/TBW as expected fell significantly in both arms in the catheter group, but although ECW/TBW fell in both the fistulae groups, only the fall in the non-fistula arm was statistically significant. After dialysis, the ECW/TBW ratio was greater in the fistula arms compared with the central venous catheter group, suggesting that extracellular fluid was increased in the fistula arm. This effect was greater in those with forearm fistulae. Multifrequency bioimpedance detected a greater difference between the arms of those patients dialysing with fistulae compared with the catheter group, and this difference remained significant post dialysis. Thus, the presence of a fistula leads to an increase in extracellular water not only prior to dialysis but also after dialysis. The degree of fluid retention would be expected to be increased by both fistula venous outflow stenosis and central venous obstruction or occlusion. On the contrary, arterial in-flow stenosis would be expected to reduce fluid accumulation.

Previous studies have reported that relatively less extracellular water is removed from the arms during a dialysis session than from the truncal region or legs [5]. In keeping with this observation, the relative ratio of ECW/TBW was less than that for the total body multifrequency bioimpedance measurements for all arms, suggesting that interdialytic extracellular fluid gain is greater in other body segments compared with the arms. However, predialysis, relatively more extracellular fluid was retained in the fistula arms compared with the non-fistula arm and the arms of those patients who underwent dialysis through central access catheters. Following fluid removal with dialysis, relatively more extracellular water was removed from the arms than from other body compartments as the ratio increased, particularly with the fistula arms, but also those who underwent dialysis with central venous catheters.

As ultrafiltration proceeds during dialysis, compensatory changes occur to sustain plasma volume [15]. However, if the ultrafiltration rate exceeds the plasma refilling rate, then compensatory mechanisms may be exceeded and the patient may be more prone to intradialytic hypotension [7]. Although the response to ultrafiltration is not predicted by change in total volumes as assessed by multifrequency bioimpedance [16], previous work has suggested that hypotensive prone haemodialysis patients may have relatively less extracellular volume in the limbs than the trunk compared with those patients who are cardiovascularly stable during treatment [5]. Our data would suggest that the extracellular volume of the arms is affected by vascular access, being greatest in those with arteriovenous fistulae, and this additional volume persists post dialysis.

Thus, if algorithms are to be developed to try and prevent intradialytic hypotension by monitoring segmental changes in extracellular fluid volumes by multifrequency bioimpedance, then studies need to consider body segments which are not affected by vascular access. Zhu and colleagues have recently studied changes in calf bioimpedance during haemodialysis [5], which would be expected to be more reliable than changes in upper limbs. However, further studies are required to assess the effect of previous deep venous thrombosis and whether increased iliac or femoral vein pressures from thigh grafts or fistulae and previous renal transplantation impact on the reliability of changes in calf bioimpedance.

Conflict of interest statement. None declared.

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