The diagnostic accuracy of multi-frequency bioelectrical impedance analysis in diagnosing dehydration after stroke

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The diagnostic accuracy of multi-frequency bioelectrical impedance analysis in diagnosing dehydration after stroke

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Non-invasive methods for detecting water-loss dehydration following acute stroke would be clinically useful. We evaluated the diagnostic accuracy of multi-frequency bioelectrical impedance analysis (MF-BIA) against reference standards serum osmolality and osmolarity.

Material/Methods: Patients admitted to an acute stroke unit were recruited. Blood samples for electrolytes and osmolality were taken within 20 minutes of MF-BIA. Total body water (TBW%), intracellular (ICW%) and extracellular water (ECW%), as percentages of total body weight, were calculated by MF-BIA equipment and from impedance measures using published equations for older people. These were compared to hydration status (based on serum osmolality and calculated osmolarity). The most promising Receiver Operating Characteristics curves were plotted.

Results: 27 stroke patients were recruited (mean age 71.3, SD10.7). Only a TBW% cut-off at 46% was consistent with current dehydration (serum osmolality >300 mOsm/kg) and TBW% at 47% impending dehydration (calculated osmolarity ≥295–300 mOsm/L) with sensitivity and specificity both >60%. Even here diagnostic accuracy of MF-BIA was poor, a third of those with dehydration were wrongly classified as hydrated and a third classified as dehydrated were well hydrated. Secondary analyses assessing diagnostic accuracy of TBW% for men and women separately, and using TBW as a percentage of lean body mass showed some promise, but did not provide diagnostically accurate measures across the population.

Conclusions: MF-BIA appears ineffective at diagnosing water-loss dehydration after stroke and cannot be recommended as a test for dehydration, but separating assessment by sex, and using TBW as a percentage of lean body weight may warrant further investigation.

Key words: **dehydration • electric impedance • osmolar concentration • body water • sensitivity and specificity • serum osmolality**

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Background

Multi-frequency BIA is described as a tool able to assess total, extracellular and intracellular fluid in humans [1–4], but its ability to diagnose water-loss dehydration has not been previously assessed.

Water-loss dehydration, signified by raised serum osmolality and due to insufficient fluid intake and sometimes increased output is common after stroke [5,6] and associated with increased mortality and morbidity [5–8]. Dysphagia, depression and concern over continence all increase the risk of dehydration, and stroke is more common in those who are already dehydrated [9,10]. Hydration status can alter rapidly in people not drinking adequately [11,12], so monitoring hydration status in this particularly vulnerable group is important especially in non-hospital settings such as residential and nursing homes.

Serum osmolality, the best reference standard for water-loss (or hypertonic) dehydration [8] is the osmolar concentration or osmotic pressure of serum, reflecting the concentration of dissolved particles per kilogram of serum [8,13,14]. Serum osmolality reflects the osmolality of intracellular fluid, and thus cell volume, as most cell walls are permeable to water allowing osmolality to equalise between the intra- and extra-cellular fluid. As osmolality is carefully controlled by the body, any change suggests important alterations in cellular hydration. Serum osmolality has advantages as a reference standard for dehydration as it can be used alone, and without prior measurement [13]. Weight change has been used as a marker for dehydration but requires at least 2 measurements (so cannot be used on an unknown patient), and can be masked by changes in other body components (fat and muscle) as well as mimicked or masked by constipation and oedema [15]. Thus serum osmolality has the best easily measurable characteristics of a reference standard for water-loss dehydration and is the diagnostic standard against which the accuracy of other measures should be judged [8,14,16].

The Dehydration Council's cut-off points for serum osmolality are specific to water-loss dehydration in older people. Serum osmolality of 295–300 mOsm/kg equates to impending dehydration, and >300 mOsm/kg to current dehydration [8], definitions used in this study.

In clinical practice serum osmolality is often not directly measured, but calculated from the combined concentrations of serum sodium, potassium, glucose and urea, referred to as serum osmolarity ($[2\times Na^+]+[2\times K^+]$+Urea+Glucose, all in mmol/L) [15]. There is a small difference between measured serum osmolality and calculated osmolarity, known as the osmolar gap (as some components of osmolality are not included in the formula to calculate osmolarity) [17].

Methods to assess hydration status which do not require blood samples would be helpful for use in those who have had a stroke once they leave hospital, especially in situations where there is no quick and easy access to laboratory facilities such as rehabilitation services, care homes and the community. There is some evidence that signs used to indicate water-loss dehydration in older people such as urinary and physical assessments [15] are unreliable and inaccurate [18].

While single frequency bioelectrical impedance assumes full hydration and so is unable to assess hydration status, multi frequency bioelectrical impedance analysis (MF-BIA) unlike single frequency BIA, can provide estimates of total body water (TBW), intracellular water (ICW), and extracellular water (ECW) volumes and as percentages of body weight. This is because the 5 kHz frequency can estimate ECW, while frequencies over 50kHz predict TBW (and ICW=TBW-ECW) [19]. The Maltron website states "The BioScan 920-2S Multi-frequency Analyser with its unique features is a rapid, non-invasive, inexpensive method for evaluating hydration and nutrition status... The advance (sic) circuitry and processing power of the BioScan 920-2S allows it to measure Extracellular (ECF) and Intracellular Fluid (ICF) volume" (see *www.maltronint.com/products/bioscan920-2S.php*, accessed 6/11/2012). Despite this claim of evaluating hydration status, the diagnostic accuracy of MF-BIA in diagnosis of dehydration has not previously been published to our knowledge.

This study aimed to assess the diagnostic accuracy of MF-BIA, to help understand whether MF-BIA can be used to monitor hydration status in place of serum osmolality after stroke.

Material and Methods

This prospective study was carried out in the Norfolk and Norwich University Hospital in the East of England. Twenty seven stroke patients admitted within 48 hours of symptom onset were recruited from 1st April to 15th Oct 2011. Patients were included if older than 17 years, with newly diagnosed stroke (first or recurrent). Exclusions included those with severe stroke (National Institute of Health Stroke Scale, NIHSS, score >30), co-existing terminal illness, expected survival <48 hours as judged by a stroke physician, or inability or unwillingness to give informed consent. Co-morbidities including diabetes and renal impairment were noted. Routine medical, nursing and therapist care was unaffected by entry into the study. All eligible patients who provided informed consent during the study period were recruited.

Upon consent a venous blood sample was taken for serum osmolality, sodium, potassium, random glucose, urea and creatinine and analysed by the hospital pathology laboratory immediately. Serum osmolality was analysed using freezing point depression on an Advanced Instruments model 2020

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osmometer (Advanced Instruments Inc, Massachusetts 02062 USA), and all other measures were made on an Abbott c8000 analyser (Abbott Laboratories, Abbott Park, Illinois 60064, USA) standardised and automated. Glucose was measured using a hexokinase based enzymatic method (reagent serial number 3L82-20), sodium and potassium using an indirect ion sensitive electrode (reagents were ICT Sample Diluent 2P32, and ICT reference solution 1E49), creatinine was measured using an alkaline picrate reagent system. All reagents were supplied by Abbot, the reagents kit serial number was 3L81-31.

Participants removed any jewellery, and were asked if they would like to micturate before the MF-BIA measurement was carried out. Two consecutive MF-BIA measurements (BioScan 920-2, Maltron International Ltd, Essex; using brand new equipment) were taken within 20 minutes of the blood sampling with the subject supine, before serum osmolality results were available (the assessor was blinded to hydration status). MF-BIA measurements were undertaken using the manufacturers recommended method with two electrodes attached to the skin between the talus and the 3rd and 5th digits of the foot and two more attached to the same side between the 3rd and 5th knuckles of the hand and the wrist.

Patients were weighed using a chair scale (SECA 955 electronic scale, SECA scales and measuring systems, Birmingham, UK), and those unable to stand were weighed using a hoist (Locomotor multi-lift hoist, Select Healthcare, Northants, UK). Height was estimated from ulna length (measured using the distance between the olecranon and styloid processes of the left hand) [20]. Weight, height, age, gender, and race were entered into the device and the MF-BIA measurements made over a couple of seconds. The recording was repeated a few minutes later. After measurements were recorded and saved, data were downloaded onto a laptop using Maltron MF-BIA software (MiStat 920). Impedances at 5, 50 and 100 kHz, and MF-BIA calculations of total body water as a percentage of body weight (TBW%), intracellular water as a percentage of TBW (ICW%) and extracellular water as a percentage of TBW (ECW%) were noted for each recording. Modified Rankin Scores (MRS, a measure of disability) were recorded by an occupational therapist.

Ethical Approval for this study was gained from Cambridgeshire I Research Ethics Committee; REC reference number 10/H0304/18 in April 2011.

Statistical analysis

All statistical analyses were carried out using PASW 18 for Windows (Polar Engineering and Consulting, formerly known as SPSS). Mean, standard deviation (SD) and range were presented for continuous and numbers (percentages) were presented for categorical data. Percentages of patients diagnosed with impending (serum osmolality 295–300 mOsm/kg; serum osmolarity 295–300 mOsm/L) and current dehydration (serum osmolality >300 mOsm/kg; serum osmolarity >300 mOsm/L) were calculated. A paired sample Student's t-test was carried out to compare the difference in serum osmolality and calculated osmolarity values overall and stratified by hydration status; hydrated, impending, and current dehydration. An average was calculated for each two consecutive measurements taken by MF-BIA of same variable for use in subsequent calculations. For the one participant where the two consecutive estimates of TBW% varied by >3% the first data set was used.

The internal consistency of MF-BIA was assessed by carrying out a reliability analysis of the 2 separate measurements of impedance at 5 kHz for each individual. This was repeated for impedance measures at 50 and 100 kHz, and the MF-BIA equipment calculation of TBW (L).

Impedance outputs (mean from the two readings) were used to calculate TBW (L) and ECW (L) using equations developed for use in older people (mean age 67, similar to our participants) by Vaché [19] and Visser [21] (as quoted in Ritz (22)), and TBW%, ECW% and ICW% were calculated as percentages of body weight[1]. Total body water (BW) was calculated using Vaché equations (19) and used in estimating TBW:

$$TBW = (2.896)+(0.366*height^2/R100)+(0.137*weight)+(2.485*G)$$

where R100 is impedance at 100Hz, G is gender (0 for women and 1 for men) and height and weight are measured in meters and kilograms.

Extracellular water was estimated using equations by Visser [21] (as quoted in Ritz [22]):

$$ECW\ (men) = (4.8) + (0.225*height^2)/(R5)$$
$$ECW\ (Women) = (1.7) + (0.2*height^2)/(R5)+(0.057*weight)$$

where R5 is impedance at 5Hz.

TBW%, ECW%, ICW% and ECW: ICW ratio from the internal calculations of the MF-BIA equipment, and those calculated from equations derived specifically for older people were each plotted in 2×2 tables against impending and current serum osmolality and calculated serum osmolarity. These tables were used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), pre- and post-test probability

1. Please note that ECW% and ICW% were calculated by the internal Maltron equations as a percentage of TBW, but when we used the Ritz equations they were calculated as a percentage of body weight.

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Table 1. Baseline characteristics of the 27 included participants stratified by serum osmolality (directly measured) and serum osmolarity (calculated) as being hydrated or having impending or current dehydration.

	Serum osmolality (mOsm/kg)			Serum osmolarity (mOsm/L)		
	Hydrated	Impending dehydration	Current dehydration	Hydrated	Impending dehydration	Current dehydration
Number of participants	12 (44.4%)	9 (33.3%)	6 (22.2%)	8 (29.6%)	7 (25.9%)	12 (44.4%)
Mean Age (SD), yrs	72.3 (12.5)	68.7 (8.0)	73.5 (11.4)	71.0 (14.5)	71.1 (9.9)	71.7 (9.1)
Age Range, yrs	46–92	59–81	59–88	46–92	59–82	59–88
Weight (SD), kg	80.5 (17.1)	74.3 (9.0)	90.0 (13.6)	78.2 (19.6)	81.2 (9.9)	81.7 (14.5)
Height (SD), m	1.7 (0.1)	1.6 (0.1)	1.7 (0.1)	1.7 (0.1)	1.7 (0.1)	1.8 (0.1)
Body Mass Index (SD), kg/m^2	29.1 (5.4)	27.7 (2.4)	31.1 (4.2)	28.6 (5.4)	29.0 (4.2)	29.5 (4.1)
Pre-morbid Rankin Score*						
0 (no symptoms)	6	3	1	3	3	4
1–2 (no significant to slight) disability	5	2	2	5	2	2
3–4 (moderate to moderately severe disability)	0	1	2	0	0	3
5 (Severe disability)	1	0	0	0	1	0
Type of feeding						
Normal Food	9	6	3	6	5	7
Pureed or soft mashed	1	3	2	1	1	4
Nil-by-Mouth	2	0	1	1	1	1
NIHSS score (stroke severity)**						
1–9	9	7	3	6	5	8
10–20	1	1	2	1	0	3
>21	1	0	0	0	1	0

* N=23 as not all participants were assessed; ** N=24 as not all participants were assessed.

of each for impending and current dehydration [23]. Where any of these values were not calculable due to the presence of zeros in the 2×2 table, 0.1 was added to each cell of the table. As published cut-off points of TBW, ECW and ICW for dehydration are not readily available, three arbitrary cut-off points were selected for each measure (TBW%, ECW%, ICW% and the ratio).

Receiver operating characteristic (ROC) curves were created for both impending and current dehydration, then additional promising cut-off points (where cut-offs may possibly have both sensitivity and specificity >60%) were added to fill in the ROC curves. At the ends of the ROC curve, once either sensitivity or specificity was below 50%, no further outlying points were added. An acceptable cut-off point was considered to be one with both sensitivity and specificity greater than 60% and represented by the point closest to the top left corner of the ROC plot. There is no definition of "good enough" sensitivity and specificity but we chose a minimum of 60% for both as suggesting that the measure was at least promising [24]. For all cut-off points we also calculated positive predictive value (PPV), negative predictive value (NPV), and positive and negative post-test probabilities.

No sample size calculation was performed as there were no data available previously reporting diagnostic accuracy of MF-BIA against serum osmolality. Twenty seven participants were a realistic sample given the time frame we were able to use for this study. The results have been reported in line with the STARD reporting guidelines [25].

Results

Participant characteristics

Of the 27 included participants 12 (44%) were well hydrated (serum osmolality 275 to <295 mOsm/kg), 9 (33%) had impending

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Table 2. Body fluid compartments and serum components stratified by hydration status (serum osmolality (measured) and osmolarity (calculated)) for the 27 participants with valid MF-BIA data.

Average (SD)	Serum osmolality (mOsm/kg)			Serum osmolarity (mOsm/L)		
	Hydrated	Impending dehydration	Current dehydration	Hydrated	Impending dehydration	Current dehydration
Total population (%)	12.0 (44.4%)	9.0 (33.3%)	6.0 (22.2%)	8.0 (29.6%)	7.0 (25.9%)	12.0 (44.4%)
Total body water%*	51.9 (4.0)	52.5 (5.8)	50.7 (4.2)	52.3 (3.7)	51.5 (3.6)	51.7 (5.9)
Extracellular water%*	45.4 (2.8)	46.1 (2.3)	45.3 (1.0)	45.9 (3.1)	44.8 (2.5)	45.9 (1.5)
Intracellular water%*	54.6 (2.8)	53.9 (2.3)	54.7 (1.0)	54.1 (3.1)	55.2 (2.5)	54.1 (1.5)
ECW: ICW	0.83 (0.1)	0.86 (0.1)	0.83 (0.03)	0.85 (0.1)	0.82 (0.08)	0.85 (0.05)
Serum osmolality mOsmol/kg	288.6 (4.3)	298.4 (1.7)	305.0 (2.6)	287.6 (4.8)	296.7 (6.5)	300.1 (5.1)
Serum osmolarity mOsm/L	293.2 (5.8)	301.3 (4.3)	303.6 (5.2)	290.2 (3.6)	297.1 (1.1)	304.3 (3.9)
Serum sodium mmol/l	135.8 (2.0)	140.4 (2.0)	138.7 (3.4)	134.9 (1.7)	137.9 (1.1)	140.1 (2.9)
Serum potassium mmol/l	4.1 (0.3)	4.4 (0.3)	4.6 (0.5)	4.2 (0.43)	4.3 (0.6)	4.4 (0.3)
Serum creatinine µmol/L	74.3 (15.1)	72.7 (6.6)	90.3 (20.6)	75.4 (10.8)	75.3 (16.9)	79.8 (18.2)
Serum urea mmol/L	5.1 (1.1)	5.5 (1.4)	8.4 (6.6)	5.1 (1.2)	5.7 (1.0)	6.7 (4.9)
Serum glucose mmol/L**	8.4 (4.3)	6.3 (1.8)	8.8 (3.9)	7.0 (2.6)	7.3 (1.7)	8.7 (4.8)

* Expressed as a percentage of body weight; ** N=26.

dehydration (serum osmolality 295–300 mOsm/kg) and 6 (22%) were dehydrated (serum osmolality >300 mOsm/kg). Stratified by calculated serum osmolarity 8 (30%) were well hydrated (275 to <295 mOsm/L), 7 (26%) had impending dehydration, and 12 (44%) had current dehydration (>300mOsm/L) (Table 1). 11% (n=3) were receiving a nil-by-mouth feeding regimen because of dysphagia (as they were being fed nasogastrically). One patient was on pureed diet and 19% (n=5) on soft-mashed diets due to slight swallowing difficulties. Sixty seven percent (n=18) were on normal oral diets without manipulation of food texture. No adverse events occurred as a result of any of the tests used.

Serum osmolality, osmolarity, age, height and weight were normally distributed (both Kolmogorov-Smirnov and Wilk-shapiro p-values were >0.05 suggesting that the data came from a normal distribution).

Internal consistency and reliability of MF-BIA measurements

Cronbach's alpha (α) was 0.960 for the reproducibility of the two impedance measures at 5 kHz (n=27), suggesting excellent internal consistency. Cronbach's alpha also suggested excellent internal consistency for impedance at 50 kHz, and 100 kHz, and TBW (l) (0.974, 0.978 and 0.995 respectively).

Dehydration status by osmolality and osmolarity

Current dehydration (>300 mOsm/L) diagnosed on serum osmolarity criteria was twice as common as when based on serum osmolality (>300 mOsm/kg), the reference standard (Table 2). As calculated osmolarity (in mOsm/L) is often used in clinical practice in place of measured osmolality (in mOsm/kg) we directly compared the two for individuals. Mean calculated serum osmolarity was 298.2 (6.9) mOsm/L while mean measured serum osmolality was 295.5 (7.5) mOsm/kg. Direct comparison showed that there was a significant difference of 2.72 (95% CI 0.6 to 4.8; p=0.014). When stratified by hydration status serum osmolarity was greater than osmolality for hydrated participants (mean difference 4.7, 95% CI 1.1 to 8.2, p=0.02) and those with impending dehydration (mean difference 2.9, 95% CI 0.2 to 5.6, p=0.04) but not for those with current dehydration (mean difference –1.4, 95% CI –7.4 to 4.5, p=0.57).

Mean serum sodium, potassium, creatinine, urea and glucose values were always higher in those with current dehydration than those who were well hydrated (Table 2), but the mean values for impending dehydration were not always between those of hydrated and currently dehydrated groups. There were few clear patterns in TBW%, ECW%, ICW% or ECW: ICW ratio by serum osmolality or calculated serum osmolarity (Table 2).

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Supplementary Table 1. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by measured osmolality. Based on internal Maltron equations for TBW, ICW and ECW as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.13	0.92	0.67	0.46	0.56	0.54	0.67
50%	0.33	0.75	0.63	0.47	0.56	0.53	0.63
52%	0.40	0.67	0.6	0.47	0.56	0.53	0.60
54%	0.80	0.25	0.57	0.50	0.56	0.50	0.57
55%	0.87	0.08	0.54	0.33	0.56	0.67	0.54
57%	0.93	0.08	0.56	0.50	0.56	0.50	0.56
				ICW%			
53%	0.20	0.75	0.50	0.43	0.56	0.57	0.50
54%	0.40	0.50	0.50	0.40	0.56	0.60	0.50
55%	0.67	0.50	0.63	0.55	0.56	0.46	0.63
56%	0.93	0.42	0.67	0.83	0.56	0.17	0.67
57%	0.93	0.33	0.64	0.80	0.56	0.20	0.64
				ECW%			
42%	0.00	0.92	0.00	0.42	0.56	0.58	0.00
45%	0.33	0.50	0.46	0.38	0.56	0.63	0.46
46%	0.60	0.50	0.60	0.50	0.56	0.50	0.60
47%	0.80	0.33	0.60	0.57	0.56	0.43	0.60
50%	1.00	0.08	0.58	1.00	0.56	0.00	0.58
				ECW: ICW			
0.60*	0.01	0.99	0.50	0.45	0.56	0.56	0.50
0.75	0.07	0.58	0.17	0.33	0.56	0.67	0.17
0.80	0.13	0.58	0.29	0.35	0.56	0.65	0.29
0.85	0.60	0.50	0.60	0.50	0.56	0.50	0.60
0.90	0.80	0.25	0.57	0.50	0.56	0.50	0.57
1.10*	0.99	0.01	0.56	0.50	0.56	0.50	0.56

* 0.1 fraction added to all 4 cells of the 2x2 table due to the presence of a zero in one of the cells that prevents at least one of the properties being calculated. PPV – positive predictive value; NPV – negative predictive value. TBW was expressed as a percentage of body weight (TBW%), and ICW and ECW were expressed as a percentage of total body water (ICW%, ECW%).

Diagnostic accuracy of MF-BIA *vs.* dehydration by serum osmolality

No cut-off point for TBW%, ICW%, ECW% or ECW: ICW ratio (calculated by the MF-BIA equipment) had both a sensitivity and specificity above 60% for impending (Supplementary Table 1) or current (Supplementary Table 2) dehydration as assessed against (measured) serum osmolality. None of the impending dehydration ROC curves neared the upper left hand corner. Figure 1 shows the ROC plot for ICW% for impending

Supplementary Table 2. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing current dehydration (>300 mOsm/kg) by measured osmolality. Based on internal Maltron equations for TBW, ICW and ECW as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-of point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.17	0.91	0.33	0.79	0.22	0.21	0.33
50%	0.33	0.71	0.25	0.79	0.22	0.21	0.25
52%	0.33	0.62	0.20	0.77	0.22	0.24	0.20
53%	0.67	0.48	0.27	0.83	0.22	0.17	0.27
54%	1.00	0.29	0.29	1.00	0.22	0.00	0.29
55%	1.00	0.14	0.25	1.00	0.22	0.00	0.25
				ICW%			
53%	0.00	0.71	0.00	0.71	0.22	0.29	0.00
55%	0.50	0.38	0.19	0.73	0.22	0.27	0.19
56%	1.00	0.29	0.28	1.00	0.22	0.00	0.29
57%	1.00	0.23	0.27	1.00	0.22	0.00	0.27
				ECW%			
42%	0.00	0.95	0.00	0.77	0.22	0.23	0.00
45%	0.50	0.62	0.27	0.81	0.22	0.19	0.27
46%	0.67	0.48	0.27	0.83	0.22	0.17	0.27
47%	1.00	0.33	0.30	1.00	0.22	0.00	0.30
49%	1.00	0.10	0.24	1.00	0.22	0.00	0.24
50%	1.00	0.05	0.23	1.00	0.22	0.00	0.23
				ECW: ICW			
0.60*	0.02	1.00	0.50	0.78	0.23	0.22	0.50
0.75	0.00	0.71	0.00	0.71	0.22	0.29	0.00
0.85	0.67	0.48	0.27	0.83	0.22	0.17	0.27
0.90	1.00	0.29	0.29	1.00	0.22	0.00	0.29
0.95	1.00	0.14	0.25	1.00	0.22	0.00	0.25

Notes as for Supplementary Table 1.

dehydration by serum osmolality and Figure 2 shows the ROC plot for ECW% for current dehydration by serum osmolality). Diagnostic accuracy for TBW%, ICW%, ECW% and ECW: ICW calculated using the equations specifically developed for older people [19,21,22] (rather than those programmed into the MF-BIA equipment) compared to serum osmolality resulted in no cut-off points with both sensitivity and specificity >60% for impending dehydration (Supplementary Table 3), and one cut-off point for current dehydration (Supplementary Table 4). TBW% with a cut-off at 46% of body weight, was diagnostic of current dehydration by osmolality with sensitivity of 67% (95% CI 49% to 85%), specificity 62% (95% CI 44% to 80%) (Supplementary Table 4, Figure 3). The positive likelihood ratio (LR^+) for this cut-off was 1.75 and negative likelihood ratio (LR^-) was 0.54.

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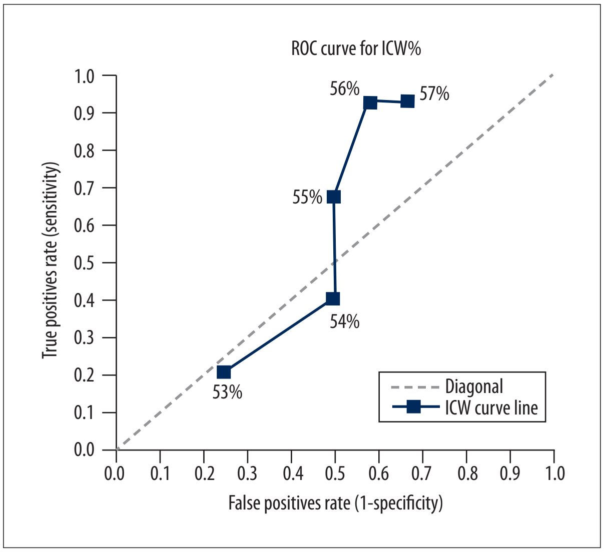

Figure 1. ROC curve assessing the diagnostic accuracy of MF-BIA assessment of intracellular water as a percentage of total body water (ICW% by the Maltron equations) in estimating impending dehydration (≥295 mOsm/kg).

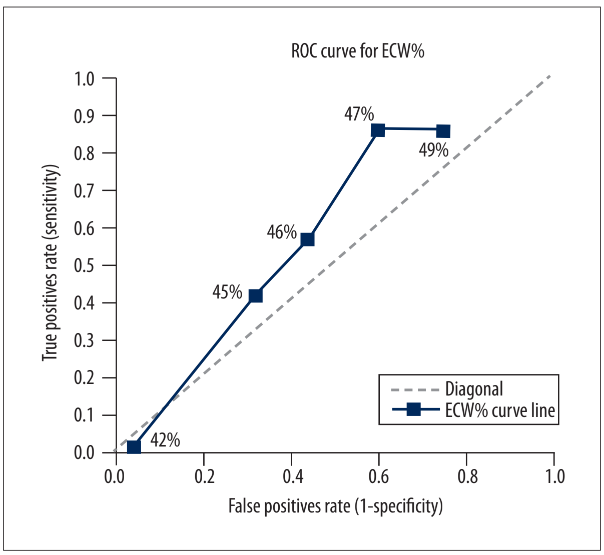

Figure 2. ROC curve assessing diagnostic accuracy of MF-BIA assessment of extracellular water as a percentage of total body water (ECW%) in estimating current dehydration (>300 mOsm/kg).

Diagnostic accuracy of MF-BIA *vs.* dehydration assessed by calculated serum osmolarity

No cut-off points for TBW%, ICW%, ECW% or ECW: ICW as calculated by the MF-BIA equipment against calculated serum osmolarity had a sensitivity and specificity above 60% for impending (≥295 mOsm/L serum osmolarity, Supplementary Table 5) or current dehydration (≥295 mOsm/L, Supplementary Table 6, Suplementary Figures 1–5).

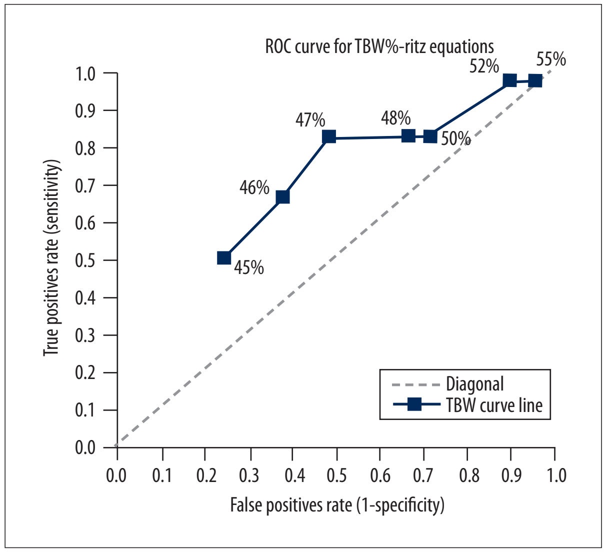

Figure 3. ROC curve assessing diagnostic accuracy of TBW% calculated from equations for older people (22) against current dehydration by serum osmolality (>300 mOsm/kg). The 46% cut-off point had a sensitivity of 67% (95% CI 49%-85%), and specificity of 62% (95% CI 44%-80%).

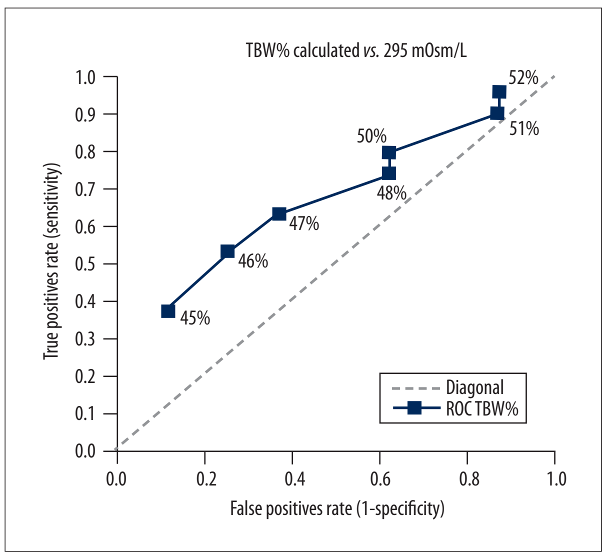

Figure 4. ROC curve assessing diagnostic accuracy of TBW% calculated from Ritz 2001 [22] equations for older people against impending dehydration as calculated by serum osmolarity (≥295 mOsm/L). The 47% cut off point had a sensitivity and specificity of 63% (95%CI 45% to 81%) each.

Diagnostic accuracy for water fractions calculated using the equations for older people against calculated serum osmolarity resulted in one cut-off point with both sensitivity and specificity of at least 60%. TBW% at 47% of body weight was diagnostic of impending dehydration by calculated osmolarity with sensitivity and specificity of 63% (95% CI 45% to 81%)

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Supplementary Table 3. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by measured osmolality. Based on alternate equations for TBW, ICW and ECW in older people (Ritz 2001) as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.40	0.83	0.75	0.53	0.56	0.47	0.75
46%	0.53	0.67	0.67	0.53	0.56	0.47	0.67
47%	0.67	0.58	0.67	0.58	0.56	0.42	0.67
48%	0.80	0.42	0.63	0.63	0.56	0.38	0.63
49%	0.87	0.42	0.65	0.71	0.56	0.29	0.65
50%	0.87	0.42	0.65	0.71	0.56	0.29	0.65
51%	0.93	0.17	0.58	0.67	0.56	0.33	0.58
52%	0.93	0.08	0.56	0.50	0.56	0.50	0.56
				ICW%			
25%	0.33	0.83	0.71	0.5	0.56	0.50	0.71
27%	0.60	0.58	0.64	0.54	0.56	0.46	0.64
28%	0.73	0.42	0.61	0.56	0.56	0.44	0.61
29%	0.80	0.33	0.60	0.57	0.56	0.43	0.60
30%	0.93	0.17	0.58	0.67	0.56	0.33	0.58
32%*	0.99	0.01	0.56	0.50	0.56	0.50	0.56
				ECW%			
20%	0.60	0.50	0.60	0.50	0.56	0.50	0.60
21%	0.87	0.25	0.59	0.60	0.56	0.40	0.59
22%	0.93	0.17	0.58	0.67	0.56	0.33	0.58
23%	0.93	0.08	0.56	0.50	0.56	0.50	0.56
25%*	0.93	0.01	0.54	0.08	0.56	0.92	0.54
				ECW: ICW			
0.60	0.01	0.99	0.50	0.45	0.56	0.56	0.50
0.75	0.53	0.50	0.57	0.46	0.56	0.54	0.57
0.80	0.60	0.33	0.53	0.40	0.56	0.60	0.53
0.85	0.80	0.08	0.52	0.25	0.56	0.75	0.52
0.90*	0.99	0.01	0.56	0.50	0.56	0.50	0.56

Notes as for Supplementary Table 1.

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Supplementary Table 4. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing current dehydration (>300 mOsm/kg) by measured osmolality. Based on alternate equations for TBW, ICW and ECW in older people (Ritz 2001) as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.50	0.76	0.38	0.84	0.22	0.16	0.38
46%	0.67	0.62	0.33	0.87	0.22	0.13	0.33
47%	0.83	0.52	0.33	0.92	0.22	0.08	0.33
48%	0.83	0.33	0.26	0.88	0.22	0.13	0.26
50%	0.83	0.29	0.25	0.86	0.22	0.14	0.25
52%	1.00	0.10	0.24	1.00	0.22	0.00	0.24
55%	1.00	0.05	0.23	1.00	0.22	0.00	0.23
				ICW%			
25%	0.33	0.76	0.29	0.8	0.22	0.20	0.29
26%	0.50	0.71	0.33	0.83	0.22	0.17	0.33
27%	0.67	0.52	0.29	0.85	0.22	0.15	0.29
28%	0.67	0.33	0.22	0.78	0.22	0.22	0.22
29%	0.83	0.29	0.25	0.86	0.22	0.14	0.25
30%	1.00	0.14	0.25	1.00	0.22	0.00	0.25
				ECW%			
18%	0.33	0.76	0.29	0.80	0.22	0.20	0.29
19%	0.50	0.67	0.30	0.82	0.22	0.18	0.30
20%	0.67	0.48	0.27	0.83	0.22	0.17	0.27
21%	0.83	0.19	0.23	0.80	0.22	0.20	0.23
22%	1.00	0.14	0.25	1.00	0.22	0.00	0.25
				ECW: ICW			
0.60	0.02	1.00	0.50	0.78	0.22	0.22	0.50
0.70	0.33	0.67	0.22	0.78	0.22	0.22	0.22
0.75	0.67	0.52	0.29	0.85	0.22	0.15	0.29
0.80	0.67	0.38	0.24	0.80	0.22	0.20	0.24
0.85	1.00	0.19	0.26	1.00	0.22	0.00	0.26

Notes as for Supplementary Table 1.

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Supplementary Table 5. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by calculated osmolarity. Based on Maltron MF-BIA internal equations for TBW, ICW and ECW as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.16	0.99	0.97	0.34	0.70	0.67	0.97
50%	0.32	0.75	0.75	0.32	0.70	0.68	0.75
52%	0.37	0.63	0.70	0.29	0.70	0.71	0.70
53%	0.53	0.38	0.67	0.25	0.70	0.75	0.67
54%	0.79	0.25	0.71	0.33	0.70	0.67	0.71
55%	0.90	0.13	0.71	0.33	0.70	0.67	0.71
				ICW%			
53%	0.16	0.63	0.50	0.24	0.70	0.76	0.50
55%	0.58	0.38	0.69	0.27	0.70	0.73	0.69
57%	0.84	0.25	0.73	0.40	0.70	0.60	0.73
59%	0.99	0.01	0.70	0.50	0.70	0.50	0.70
				ECW%			
50%	1.00	0.13	0.73	1.00	0.70	0.00	0.73
47%	0.84	0.38	0.76	0.50	0.70	0.50	0.76
46%	0.21	0.99	0.98	0.35	0.70	0.65	0.98
45%	0.42	0.63	0.73	0.31	0.70	0.69	0.73
42%	0.00	0.88	0.00	0.27	0.70	0.73	0.00
				ECW: ICW			
0.6	0.01	0.99	0.50	0.30	0.70	0.70	0.50
0.75	0.16	0.63	0.50	0.24	0.70	0.76	0.50
0.80	0.21	0.63	0.57	0.25	0.70	0.75	0.57
0.9	0.84	0.38	0.76	0.50	0.70	0.50	0.76
1.1	0.99	0.01	0.70	0.50	0.70	0.50	0.70

Notes as for Supplementary Table 1.

(Supplementary Table 7; Figure 4). The LR^+ and LR^- were 1.7 and 0.6 respectively for this cut-off. No cut-offs were accurate for current dehydration (Supplementary Table 8).

Diagnostic accuracy of MF-BIA using TBW as a percentage of fat free mass *vs.* dehydration by serum osmolality

Due to the very limited diagnostic accuracy of TBW%, ICW%, ECW% or ECW: ICW secondary analyses were considered. As the fluid content of fatty tissue is minimal we hypothesised that diagnostic accuracy might be improved if we separated men and women (as men and women have different proportions of fatty tissue), or analysed total body water as a percentage of fat free mass (lean body weight). Analyses were run using total body water data as TBW% was the measure with most diagnostic accuracy in previous analyses.

Separating out men and women (using TBW as a percentage of total body weight) improved diagnostic accuracy for men for current dehydration (using the Ritz equations), and provided

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Supplementary Table 6. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing current dehydration (>300 mOsm/kg) by calculated osmolarity. Based on Maltron MF-BIA internal equations for TBW, ICW and ECW as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test probability (–ve)	Post-test probability (+ve)
TBW%							
45%	0.25	0.99	0.97	0.62	0.45*	0..38	0.97
50%	0.33	0.73	0.50	0.58	0.44	0.42	0.5
52%	0.42	0.67	0.50	0.59	0.44	0.42	0.5
53%	0.42	0.67	0.47	0.58	0.44	0.42	0.47
54%	0.75	0.20	0.43	0.50	0.44	0.5	0.43
55%	0.83	0.07	0.42	0.33	0.44	0.67	0.42
ICW%							
53%	0.17	0.73	0.33	0.52	0.44	0.48	0.33
55%	0.67	0.47	0.50	0.64	0.44	0.36	0.5
57%	1.00	0.33	0.55	1.00	0.44	0.00	0.55
ECW%							
49%	0.92	0.13	0.46	0.67	0.44	0.33	0.46
47%	0.83	0.26	0.48	0.67	0.44	0.33	0.48
46%	0.58	0.47	0.47	0.58	0.44	0.42	0.47
45%	0.33	0.53	0.36	0.50	0.44	0.50	0.36
42%	0.00	0.93	0.0	0.54	0.44	0.46	0.00
ECW: ICW							
0.6	0.01*	0.99	0.50	0.56	0.45*	0.44	0.50
0.75	0.00	0.60	0.00	0.43	0.44	0.57	0.00
0.85	0.58	0.47	0.47	0.58	0.44	0.42	0.47
0.9	0.83	0.27	0.48	0.67	0.44	0.33	0.48
0.95	0.92	0.13	0.46	0.67	0.44	0.33	0.46

Notes as for Supplementary Table 1.

a cut-off for impending dehydration (Table 3, Supplementary Tables 9 and 10). The cut-off of 46% for TBW% showed sensitivity of 67% and specificity of 85% for current dehydration while 47% diagnosed impending dehydration (sensitivity 63%, specificity 75%) (Supplementary Figures 6 and 7). However, there were no useful cut-offs for women.

Analysing TBW as a percentage of lean body weight provided a potentially useful cut-off for women for impending dehydration at 84% (sensitivity 71%, specificity 75%), but none for current dehydration or for men alone, or men and women combined (Supplementary Tables 11 and 12, Supplementary Figures 8–10).

Discussion

Although we tried different ways of calculating TBW, ICW and ECW, assessed TBW as a percentage of total body weight or lean body weight, separated participants by gender and defined dehydration using both serum osmolality and serum osmolarity only 8 cut-off points had both sensitivity and specificity of

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Supplementary Table 7. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by calculated osmolarity. Based on alternate equations for TBW, ICW and ECW in older people (Ritz 2001) as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.37	0.88	0.88	0.37	0.70	0.63	0.88
46%	0.53	0.75	0.83	0.40	0.70	0.60	0.83
47%	0.63	0.63	0.80	0.42	0.70	0.58	0.80
48%	0.74	0.38	0.74	0.38	0.70	0.63	0.74
49%	0.79	0.38	0.75	0.43	0.70	0.57	0.75
50%	0.79	0.38	0.75	0.43	0.70	0.57	0.75
51%	0.90	0.13	0.71	0.33	0.70	0.67	0.71
52%	0.95	0.13	0.72	0.50	0.70	0.50	0.72
				ICW%			
25%	0.32	0.88	0.86	0.35	0.70	0.65	0.86
27%	0.53	0.50	0.71	0.31	0.70	0.69	0.71
28%	0.68	0.38	0.72	0.33	0.70	0.67	0.72
29%	0.74	0.25	0.70	0.29	0.70	0.71	0.70
30%	0.95	0.25	0.75	0.67	0.70	0.33	0.75
				ECW%			
20%	0.58	0.50	0.73	0.33	0.70	0.67	0.73
21%	0.84	0.25	0.73	0.40	0.70	0.60	0.73
22%	0.90	0.13	0.71	0.33	0.70	0.67	0.71
23%	0.95	0.13	0.72	0.50	0.70	0.50	0.72
				ECW: ICW			
0.6	0.01	0.99	0.50	0.30	0.70	0.70	0.50
0.75	0.53	0.50	0.71	0.31	0.70	0.70	0.71
0.8	0.63	0.38	0.71	0.30	0.70	0.70	0.71
0.85	0.84	0.13	0.70	0.25	0.70	0.75	0.70
0.9*	0.99	0.01	0.70	0.50	0.70	0.50	0.70

Notes as for Supplementary Table 1.

at least 60%. The only cut-off with limited diagnostic accuracy for both men and women was observed for TBW% at 46% when calculated using equations developed for older people (sensitivity 67%, specificity 62%) for current dehydration by measured osmolality (>300 mOsmol/kg), but positive and negative likelihood ratios were poor (1.75 and 0.54 respectively). Similarly TBW at 47%, only with equations developed for older people, also showed limited diagnostic accuracy (sensitivity 63% and specificity 63%, LR^+ 1.7 and LR^- 0.6) for impending dehydration as assessed by calculated serum osmolarity (≥295 mOsmol/L). When internal equipment equations for estimating TBW were used no cut-offs were even minimally diagnostic. In secondary analyses cut-offs of TBW as a percentage of total body weight were partially useful in diagnosing

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Supplementary Table 8. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing current dehydration (>300 mOsm/kg) by calculated osmolarity. Based on alternate equations for TBW, ICW and ECW in older people (Ritz 2001) as percentages of total body weight, in the 27 men and women with reliable MF-BIA data.

Cut-off point	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
				TBW%			
45%	0.42	0.80	0.63	0.63	0.44	0.37	0.63
46%	0.50	0.60	0.50	0.60	0.44	0.40	0.50
47%	0.67	0.53	0.53	0.67	0.44	0.33	0.53
48%	0.83	0.40	0.53	0.75	0.44	0.25	0.53
50%	0.91	0.01	0.42	0.08	0.44	0.37	0.63
				ICW%			
25%	0.33	0.80	0.57	0.60	0.44	0.40	0.57
26%	0.42	0.73	0.56	0.61	0.44	0.39	0.56
27%	0.58	0.53	0.50	0.62	0.44	0.38	0.50
28%	0.75	0.40	0.50	0.67	0.44	0.33	0.50
29%	0.83	0.33	0.50	0.71	0.44	0.29	0.50
30% a	0.92	0.13	0.46	0.67	0.44	0.33	0.46
				ECW%			
18%	0.25	0.73	0.43	0.55	0.44	0.45	0.43
19%	0.42	0.67	0.50	0.59	0.44	0.41	0.50
20%	0.58	0.47	0.47	0.58	0.44	0.42	0.47
21%	0.83	0.20	0.46	0.60	0.44	0.40	0.46
22% a	0.92	0.13	0.46	0.67	0.44	0.33	0.46
				ECW: ICW			
0.6 a	0.01	0.99	0.50	0.56	0.45*	0.45	0.50
0.75	0.50	0.47	0.43	0.54	0.44	0.46	0.43
0.8	0.58	0.33	0.41	0.50	0.44	0.50	0.41
0.85	0.83	0.13	0.44	0.50	0.44	0.50	0.44
0.9*	0.99	0.01	0.45	0.50	0.44	0.50	0.45

Notes as for Supplementary Table 1.

impending and water-loss dehydration (by serum osmolality) in men, but none were useful in women. One cut-off for TBW as a percentage of lean body mass was useful in women in diagnosing impending dehydration, but none for current dehydration or in men. In this small population of 27 people with recent strokes, MF-BIA did not fulfil its promise as a diagnostic tool for water-loss dehydration.

Calculated serum osmolarity was not good at predicting those with current dehydration by the reference standard, measured serum osmolality, and using calculated osmolarity resulted in 44% of our population being labelled as having current dehydration, compared to 22% by serum osmolality. Research is needed to assess the health impacts of dehydration as measured by changes in serum osmolality, serum osmolarity and

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Table 3. Table of potentially useful cut-offs (where both sensitivity and specificity are at least 60%) of MF- BIA measures of total body water (TBW) for diagnostic accuracy of impending and current water-loss dehydration defined by serum osmolality.

Men or women	Method	Serum osmolality ≥295 (impending)			Serum osmolality >300 (current)		
		Cut off	Sensitivity	Specificity	Cut off	Sensitivity	Specificity
Total body water as a % age of total body weight							
Men & women combined	Maltron	NA			NA		
	Ritz	NA			46%	0.67	0.62
Men alone	Maltron	NA			53%	0.67	0.62
	Ritz	47%	0.63	0.75	46% 47%	0.67 1.00	0.85 0.69
Women alone	Maltron	NA			NA		
	Ritz	NA			NA		
Total body water as a % age of lean body weight							
Men and women combined	Maltron	NA			NA		
Men alone	Maltron	NA			NA		
Women alone	Maltron	84% 85%	0.71 0.71	0.75 0.75	NA		

NA – not applicable – no cut offs suggested both sensitivity and specificity were at least 60%.

weight change, so that we can be sure which is the most useful measure of dehydration to use in future.

Diagnostic accuracy

The limited diagnostic accuracy for current dehydration by osmolality at TBW% of 46% (sensitivity 67%, specificity 62%) using the impedance output from MF-BIA to calculate TBW% suggests that only 67 of every 100 people with current dehydration by serum osmolality will be "positive" using TBW% as the test, meaning that 33 of every 100 with current dehydration will be missed. Similarly the specificity of 62% suggests that for every 100 people without current dehydration 62 will have a negative test but 38 will have a positive test[2]. This is a very high level of false positives and negatives, suggesting that MF-BIA is not useful in diagnosing water-loss dehydration independently of other clinical or biochemical data.

The test's positive (PPV) and negative (NPV) predictive values[3] as well as pre and post-test probabilities provide more information on the utility of TBW% at the 46% cut off point. The PPV of 33% (equivalent to the positive post-test probability of 33%) suggests that only 33% of those who are diagnosed as having current dehydration by MF-BIA truly have current dehydration by serum osmolality. The NPV of 87% is clearly better, meaning that 87% of those diagnosed as not having current dehydration are truly without current dehydration (and this is another way of stating the negative post-test probability of 13%). The positive likelihood ratio (LR^+) was 1.75 and negative likelihood ratio (LR^-) 0.54[4] suggesting that for a person "positive" for dehydration by this test the odds are 1.75 that dehydration is present compared to 1.00 for a person "negative" for dehydration.

Studies evaluating the utility of MF-BIA in diagnosing dehydration in clinical settings are scarce. Systematic reviews have suggested that MF-BIA estimation of TBW is valid. Meta-analysis of studies in which TBW was estimated using BIA and validated against the reference standard method, deuterium isotope dilution, found that MF-BIA estimated TBW more closely to the reference standard (WMD 0.18L, 95% CI –1.62 to 1.98) than either single frequency (SF) BIA (WMD 3.00L, 95% CI 1.43 to

2. Sensitivity is the proportion of people who have the disorder who test positive. Specificity is the proportion of people who do not have the disorder who test negative.
3. The positive predictive value is the ratio of true positives to all positives, and represents the proportion of those with a positive result that are correctly diagnosed (according to the reference standard). The negative predictive value is the proportion of those with a negative result that are correctly diagnosed (so test negative on the reference standard).
4. The likelihood ratio for a positive result (LR^+) tells you how much the odds of dehydration increase when a test is positive. The likelihood ratio for a negative result (LR^-) tells you how much the odds of dehydration decrease when a test is negative.

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Supplementary Table 9. Secondary analyses. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by measured osmolality, split by sex. Based on Maltron MF-BIA internal equations for TBW, or equations for older people (Ritz 2001), expressed as a percentage of total body weight, in the 16 men and 11 women with reliable MF-BIA data.

Cut-off point, TBW%	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (–ve)	Post-test probability (+ve)
Men only, Maltron equations							
45%	0.13	0.99	0.92	0.53	0.50	0.47	0.92
50%	0.13	0.88	0.50	0.50	0.50	0.50	0.50
52%	0.25	0.75	0.50	0.50	0.50	0.50	0.50
53%	0.38	0.50	0.43	0.44	0.50	0.56	0.43
54%	0.75	0.38	0.55	0.6	0.50	0.40	0.55
55%	0.88	0.13	0.50	0.50	0.50	0.50	0.50
Women only, Maltron equations							
45%	0.14	0.75	0.50	0.33	0.64	0.67	0.50
50%	0.57	0.50	0.67	0.40	0.64	0.60	0.67
52%	0.57	0.50	0.67	0.40	0.64	0.60	0.67
54%	0.57	0.50	0.67	0.0.40	0.64	0.60	0.67
55%	0.86	0.02	0.60	0.09	0.63*	0.92	0.60
Men only, equations for older people							
45%	0.13	0.99	0.92	0.53	0.50	0.47	0.92
46%	0.38	0.88	0.75	0.58	0.50	0.42	0.75
47%	0.63	0.75	0.71	0.67	0.50	0.33	0.71
48%	0.75	0.50	0.60	0.67	0.50	0.33	0.60
49%	0.88	0.50	0.64	0.80	0.50	0.20	0.64
50%	0.88	0.50	0.64	0.80	0.50	0.20	0.64
51%	0.88	0.25	0.54	0.67	0.50	0.33	0.54
52%	0.88	0.13	0.50	0.50	0.50	0.50	0.50
Women only, equations for older people							
45%	0.71	0.50	0.71	0.50	0.64	0.50	0.71
46%	0.71	0.25	0.63	0.33	0.64	0.67	0.63
47%	0.71	0.25	0.63	0.33	0.64	0.67	0.63
48%	0.86	0.25	0.67	0.50	0.64	0.50	0.67
50%	0.86	0.25	0.67	0.50	0.64	0.50	0.67
52%	0.99	0.02	0.63	0.50	0.63*	0.50	0.63

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Supplementary Table 10. Secondary analyses. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration (≥295 mOsm/kg) by measured osmolality, split by sex. Based on Maltron MF-BIA internal equations for TBW, or equations for older people (Ritz 2001), expressed as a percentage of total body weight, in the 16 men and 11 women with reliable MF-BIA data.

Cut-off point, TBW%	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test probability (–ve)	Post-test probability (+ve)
Men only, Maltron equations							
45%	0.34	0.99	0.92	0.86	0.20*	0.14	0.92
50%	0.33	0.92	0.50	0.86	0.19	0.14	0.5
52%	0.33	0.77	0.25	0.83	0.19	0.17	0.25
53%	0.67	0.62	0.29	0.89	0.19	0.11	0.29
54%	1.00	0.38	0.27	1.00	0.19	0.00	0.27
55%	1.00	0.15	0.21	1.00	0.19	0.00	0.21
Women only, Maltron equations							
45%	0.00	0.75	0.00	0.67	0.27	0.33	0.00
50%	0.33	0.38	0.17	0.60	0.27	0.40	0.17
52%	0.33	0.38	0.17	0.60	0.27	0.40	0.17
53%	0.67	0.25	0.25	0.67	0.27	0.33	0.25
54%	1.00	0.13	0.30	1.00	0.27	0.00	0.30
55%	1.00	0.13	0.30	1.00	0.27	0.00	0.30
Men only, equations for older people							
45%	0.34	0.99	0.92	0.86	0.20*	0.14	0.92
46%	0.67	0.85	0.50	0.92	0.19	0.08	0.50
47%	1.00	0.69	0.43	1.00	0.19	0.00	0.43
48%	1.00	0.46	0.30	1.00	0.19	0.00	0.30
50%	1.00	0.39	0.27	1.00	0.19	0.00	0.27
52%	1.00	0.15	0.21	1.00	0.19	0.00	0.21
55%	1.00	0.08	0.20	1.00	0.19	0.00	0.20
Women only, equations for older people							
43%	0.33	0.63	0.25	0.71	0.27	0.29	0.25
44%	0.33	0.50	0.20	0.67	0.27	0.33	0.20
45%	0.67	0.38	0.29	0.75	0.27	0.25	0.29
46%	0.67	0.25	0.25	0.67	0.27	0.33	0.25
47%	0.67	0.25	0.25	0.67	0.27	0.33	0.25
48%	0.67	0.13	0.22	0.50	0.27	0.50	0.22
50%	0.67	0.13	0.22	0.50	0.27	0.50	0.22
51%	0.97	0.01	0.28	0.50	0.28	0.50	0.22
52%	0.97	0.01	0.28	0.50	0.28*	0.50	0.28
55%	0.97	0.01	0.28	0.50	0.28*	0.50	0.28

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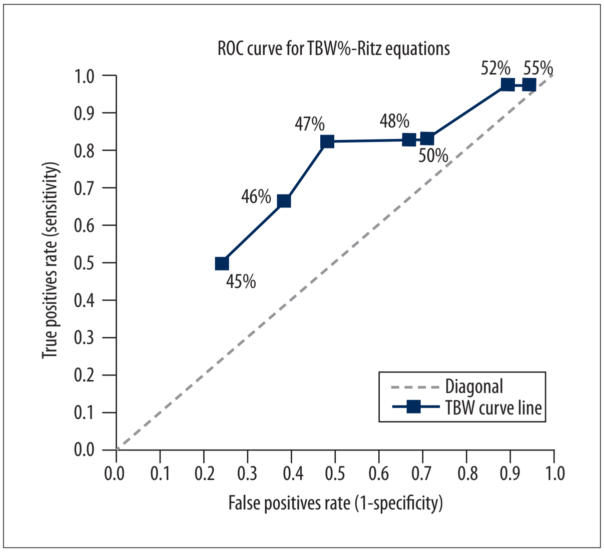
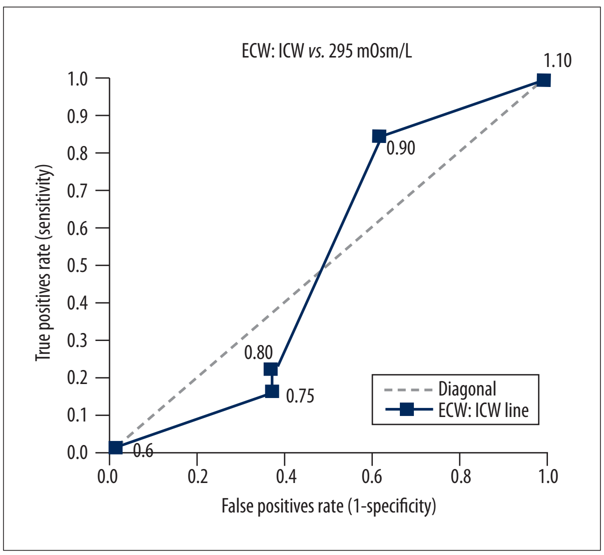
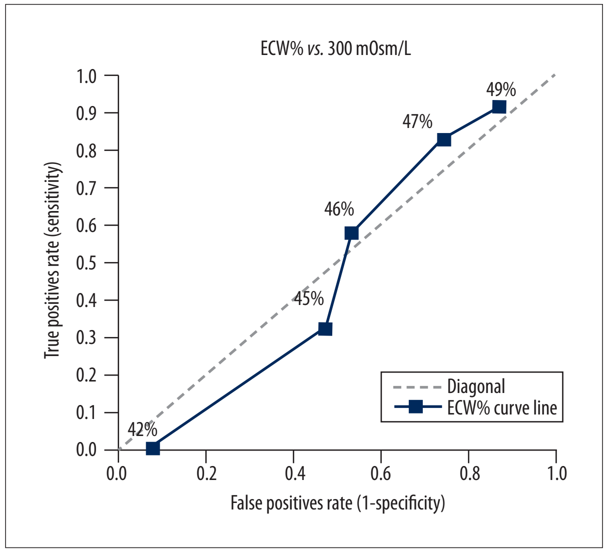


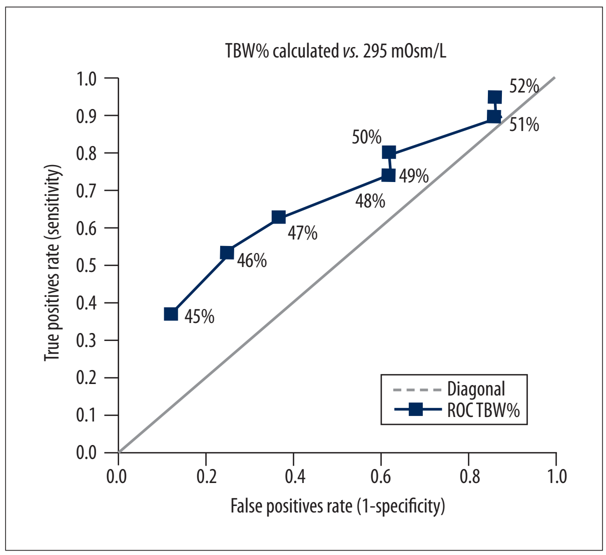
Supplementary Figure 1. ROC curve assessing diagnostic accuracy of MF-BIA assessment of total body water as a percentage of body weight (TBW%) in estimating current dehydration (>300 mOsm/kg), for men and women, using the specific equations for older people from Vaché 1998 as suggested by Ritz 2001.



Supplementary Figure 2. ROC curve assessing diagnostic accuracy of MF-BIA assessment of ECW: ICW against impending dehydration as calculated by serum osmolarity (≥295 mOsm/L), for men and women.



Supplementary Figure 3. ROC curve assessing diagnostic accuracy of MF-BIA assessment of ECW% against current dehydration as calculated by serum osmolarity (>300 mOsm/L), for men and women.



Supplementary Figure 4. ROC curve assessing diagnostic accuracy of calculated TBW% from Ritz 2001 equation against impending dehydration as calculated by serum osmolarity (≥295 mOsm/L), for men and women.

4.57) or bioelectric impedance spectroscopy (WMD 2.80L, 95% CI 1.03 to 4.58) [2]. However, there are other indications in the literature that assessment of TBW may not be sufficiently accurate in conditions of change in hydration status and when body compartments are undergoing acute changes [26]. This may be because changes in the ratio of intra- to extra-cellular water, and of acute changes in these compartments, also influence resistivity [26–29]. This may mean that there are fundamental problems with MF-BIA in assessing TBW and so in using MF-BIA in predicting hydration status. Our results suggesting that MF-BIA is not a useful diagnostic tool are in broad

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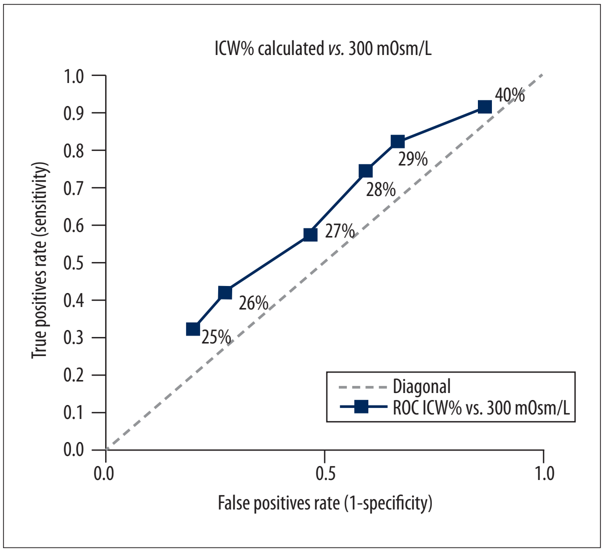
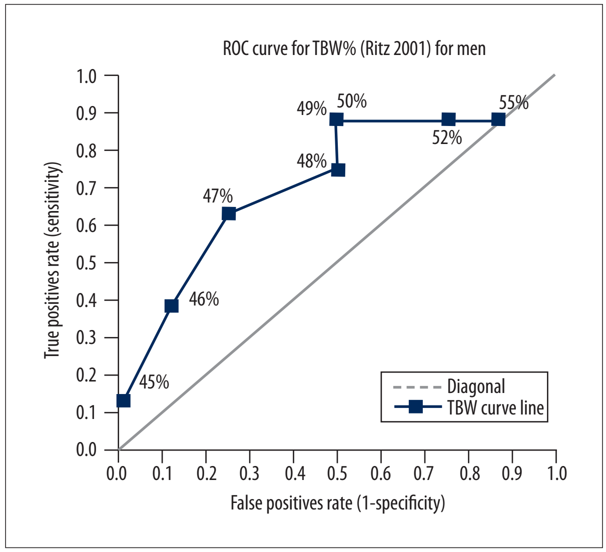
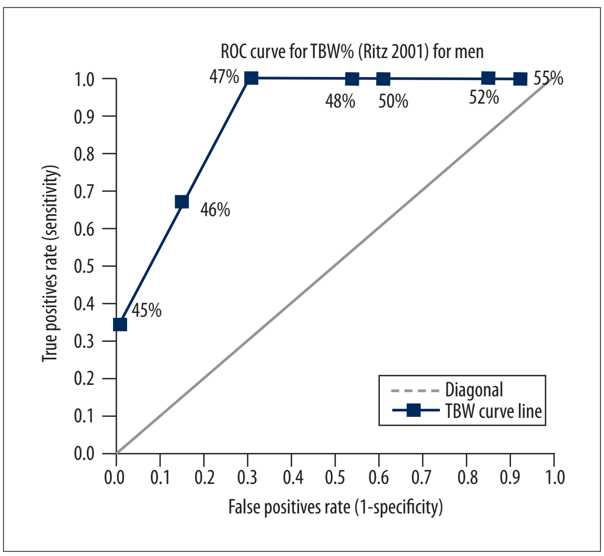


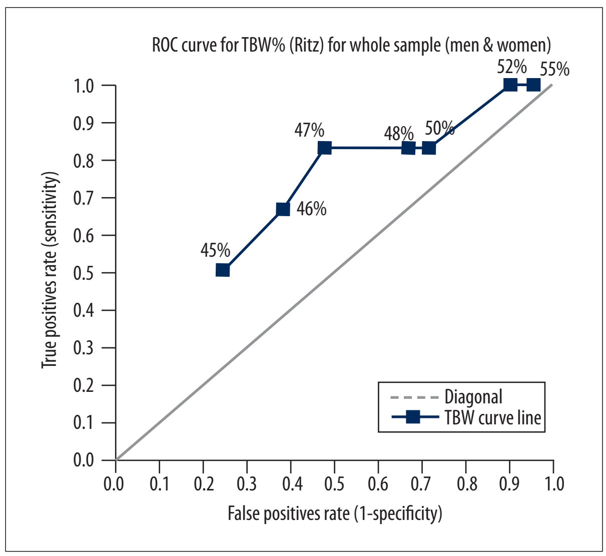
Supplementary Figure 5. ROC curve assessing diagnostic accuracy of calculated ICW% from Ritz 2001 equation against current dehydration as calculated by serum osmolarity (>300 mOsm/L), for men and women.



Supplementary Figure 7. Secondary analysis. ROC curve assessing diagnostic accuracy of TBW% for men calculated from equations for older people (Ritz 2001) against impending dehydration by serum osmolality (≥295mOsm/kg). The 47% cut off had a sensitivity of 0.63 (95% CI 0.39 to 0.87) and specificity of 0.75 (95% CI 0.54 to 0.96).



Supplementary Figure 6. Secondary analysis. ROC curve assessing diagnostic accuracy of TBW% for men calculated from equations for older people (Ritz 2001) against current dehydration by serum osmolality (>300 mOsm/kg). The 46% cut-off had sensitivity of 0.67 (95% CI 0.44 to 0.90) and specificity of 0.85 (95% CI 0.68 to 1.00), the 47% cut off had a sensitivity of 1.00 (95% CI 0.99 to 1.00) and specificity of 0.69 (95% CI 0.46 to 0.92).



Supplementary Figure 8. Secondary analysis. ROC curve assessing diagnostic accuracy of TBW% for both men and women calculated from equations for older people (Ritz 2001) against current dehydration by serum osmolality (>300 mOsm/kg). The 46% cut-off had sensitivity of 0.67 (95% CI 49 to 0.85) and specificity 0.62 (95% CI 0.44 to 0.80).

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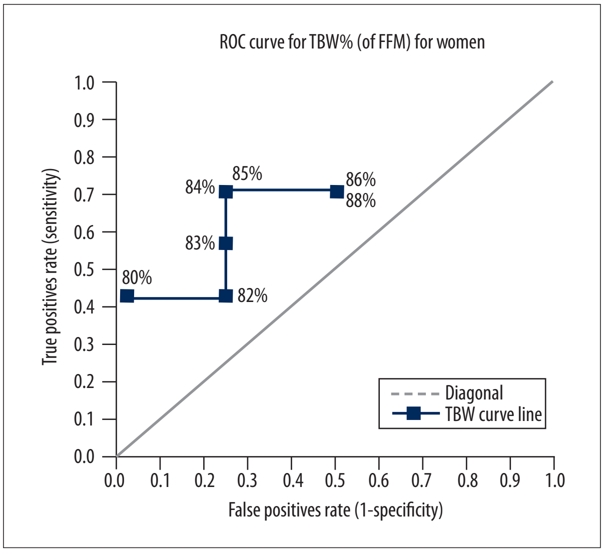
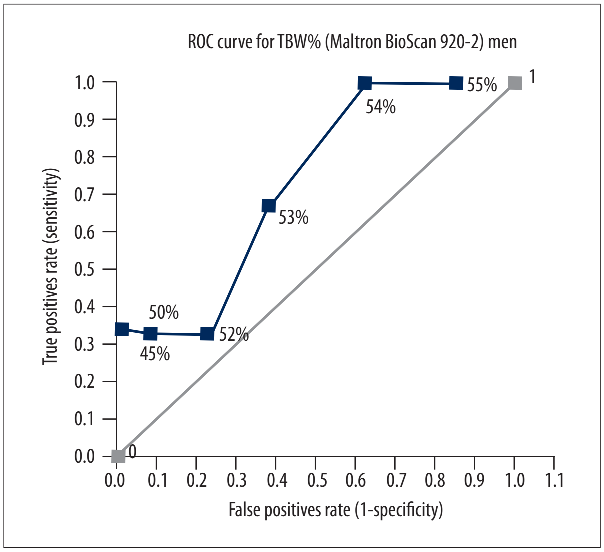


Supplementary Figure 9. Secondary analysis. ROC curve assessing the diagnostic accuracy of TBW% calculated as a percentage of fat free mass of women against impending dehydration by serum osmolality (≥295 mOsm/kg). The 84% & 85% both had similar cut-offs with a sensitivity of 0.71 (95% CI 0.44 to 0.98) and a specificity of 0.75 (95% CI 0.49 to 1.00).



Supplementary Figure 10. Secondary analysis. ROC curve assessing the diagnostic accuracy of TBW% for men calculated by internal Maltron equations against current dehydration by serum osmolality (>300 mOsm/kg). The 53% cut off had a sensitivity of 0.67 (95% CI 0.44 to 0.90) and a specificity of 0.62 (0.38 to 0.86).

agreement with those of Olde Rikkert 1997. They found that in dehydrated geriatric patients (N=53) the sensitivity of diagnosing dehydration using 100 kHz MF-BIA measurements was only 14% – very poor sensitivity, and sensitivity was not improved when other frequencies were tested [30]. The sensitivity and specificity of MF-BIA were similar to that of the much simpler measure, tongue dryness, found in a recent Australian study [31]. Tongue dryness is easier and quicker to assess, and does not need additional investment or electrical supplies, so would be a more appropriate measure to use in most situations than MF-BIA if its diagnostic accuracy is similar.

The importance of MF-BIA results

Leaving the mathematics of diagnostic accuracy of MF-BIA aside and observing data generated by MF-BIA also suggested that MF-BIA generated outcomes are not coherent with the diagnosis of dehydration. Table 2 suggested no significant difference in MF-BIA measures between hydrated, impending, and currently dehydrated groups. The intracellular water content reflects information on the state of hydration at the cellular level. Cellular hydration status can change within minutes under the effects of stress, nutrients, hormones, and other factors [32]. MF-BIA does not appear to usefully reflect changes observed in serum osmolality or osmolarity or to sensitively identify the dehydrated state at the cellular level.

The state of hydration at a cellular level is important. Haussinger [32] suggested that while a well hydrated cell increases anabolic processes, a dehydrated cell shifts metabolism to catabolism, especially in muscle tissue. If recovery is to occur in a highly stressed patient after stroke, we want to ensure they are in an anabolic rather than a catabolic state. Catabolism could inhibit liver function and weaken muscles, delaying functional recovery and rehabilitation. Dehydration correlates with poor outcomes after stroke. Bhalla [6] found that the 30% of their 167 stroke patients who had raised serum osmolality (>296 mOsm/kg) had increased odds of mortality at 3 months (OR 2.4, 95%CI 1.0 t 5.9). Kelly [7] found that in their 102 acute ischaemic stroke patients raised serum osmolality (>297 mOsm/kg, in 24% of their patients) on day 9 following admission was associated with increased odds of venous thromboembolism (OR 4.7, 95% CI 1.4 to 16.3).

The convenience of the Maltron BioScan 920-2

The Maltron website states that “The BioScan 920-2 Multi-frequency Analyser with its unique features is a rapid, non-invasive, inexpensive method for evaluating hydration and nutrition status” (see *www.maltronint.com/popup_pages/BioScan9202.htm*, accessed 23/2/2012). Among other things it suggests applications in “fluid retention” and “effects of hydration and dehydration”. We were unable to verify this.

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Supplementary Table 11. Secondary analyses. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing impending dehydration ((≥295 mOsm/kg) by measured osmolality. Based on Maltron MF-BIA internal equations for TBW, expressed as a percentage of lean body mass, in the 16 men and 11 women with reliable MF-BIA data.

Cut-off point, TBW as % lean body mass	Sensitivity	Specificity	PPV	NPV	Pre-test probability	Post-test probability (–ve)	Post-test probability (+ve)
Men & women							
80%	0.40	0.58	0.55	0.44	0.56	0.56	0.55
82%	0.47	0.42	0.50	0.39	0.56	0.62	0.50
83%	0.67	0.42	0.59	0.50	0.56	0.50	0.59
84%	0.87	0.33	0.62	0.67	0.56	0.33	0.62
85%	0.87	0.33	0.62	0.67	0.56	0.33	0.62
87%	0.87	0.17	0.57	0.50	0.56	0.50	0.57
Men only							
80%	0.38	0.38	0.38	0.38	0.50	0.63	0.38
82%	0.50	0.25	0.40	0.33	0.50	0.67	0.40
83%	0.75	0.25	0.50	0.50	0.50	0.50	0.50
84%	1.00	0.13	0.53	1.00	0.50	0.00	0.53
85%	1.00	0.13	0.53	1.00	0.50	0.00	0.53
Women only							
80%	0.43	0.98	0.97	0.50	0.63	0.50	0.97
82%	0.43	0.75	0.75	0.43	0.64	0.57	0.75
83%	0.57	0.75	0.80	0.50	0.64	0.50	0.80
84%	0.71	0.75	0.83	0.60	0.64	0.40	0.83
85%	0.71	0.75	0.83	0.60	0.64	0.40	0.83
86%	0.71	0.50	0.71	0.50	0.64	0.50	0.71
88%	0.71	0.50	0.71	0.50	0.64	0.50	0.71

Despite the Maltron website reporting that it is "quick, safe and easy" and "no assistance or technical knowledge is required" (see *www.maltronint.com/popup_pages/BioScan9202.htm*, accessed 23/2/2012) we found the machine is not user friendly. Without a keyboard, data entry and saving of data are slow and may result in errors and data loss. Re-running a second measurement for the same participant requires re-entering all the same information again or the new test overwrites existing data. Analysed data are not easily accessible to visual check without downloading the full data set, and there is no warning when unrealistic readings are registered. On-site readout of each variable for each participant was time consuming and unrealistic in an acute stroke unit.

Strengths and weaknesses

In assessing MF-BIA we followed the guidelines of the European Society of Clinical Nutrition and Metabolism [34]. The battery was charged between measurements, cables were of appropriate length, and the equipment calibrated for all participants reported in this paper. Weight and height were measured by the investigator or by a health professional (not self-reported), MF-BIA measurements were carried out at ambient temperature and manufacturer guidelines on positioning of electrodes were followed. Before measurements our participants were in a supine position for least 10 min and during measurement they had no contact with any metal object (such as a bed frame). Electrodes were attached to the non affected side to record measurements

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Supplementary Table 12. Secondary analyses. Diagnostic accuracy of MF-BIA measures (at several cut-off points) in diagnosing current dehydration (>300 mOsm/kg) by measured osmolality. Based on Maltron MF-BIA internal equations for TBW, expressed as a percentage of lean body mass, in the 16 men and 11 women with reliable MF-BIA data.

Cut-off point, TBW as% lean body mass	Sensitivity	Specificity	PPV	NPV	Pre-test Probability	Post-test Probability (-ve)	Post-test probability (+ve)
Men & women							
80%	0.17	0.52	0.10	0.69	0.22	0.31	0.10
82%	0.17	0.38	0.07	0.62	0.22	0.38	0.07
83%	0.67	0.38	0.24	0.80	0.22	0.20	0.24
84%	0.83	0.24	0.24	0.83	0.22	0.17	0.24
85%	0.83	0.24	0.24	0.83	0.22	0.17	0.24
87%	0.83	0.14	0.22	0.75	0.22	0.25	0.22
Men only							
80%	0.33	0.46	0.13	0.75	0.19	0.25	0.13
82%	0.33	0.31	0.10	0.67	0.19	0.33	0.10
83%	1.00	0.31	0.25	1.00	0.19	0.00	0.25
84%	1.00	0.08	0.20	1.00	0.19	0.00	0.20
Women only							
80%	0.00	0.63	0.00	0.63	0.27	0.38	0.00
82%	0.00	0.50	0.00	0.57	0.27	0.43	0.00
84%	0.67	0.50	0.33	0.80	0.27	0.20	0.33
85%	0.67	0.50	0.33	0.80	0.27	0.20	0.33
86%	0.67	0.38	0.29	0.75	0.27	0.25	0.29
88%	0.67	0.38	0.29	0.75	0.27	0.25	0.29

and to skin with no abrasions or deformation that may affect current conductance. None of our participants suffered from edema due to excessive hydration by IV/electrolyte infusion or very low albumin levels. One of the main limitations in a ward setting is the inability of researchers to completely control participants fasting or bladder voidance, but the investigator did ensure that participants had fasted for at least 2 hours before MF-BIA measurements were taken and all participants were asked if they would like to void their bladder before measurements commenced [33]. Small sample size was also a weakness.

Study strengths included the use of serum osmolality and calculated osmolarity as reference standards, a population with high levels of dehydration, and recording serum osmolality and other serum measures (sodium, potassium, glucose, urea) within 20 minutes of MF-BIA measurements (enabling us to capture cellular hydration status as evaluated by MF-BIA and its coherence with reference serum values).

Conclusions

MF-BIA does not appear appropriate for the diagnosis of water-loss dehydration after stroke. Diagnostic accuracy is far too low to usefully diagnose current or impending dehydration at any selected cut-off point. However, separating assessment by sex, and using TBW as a percentage of lean body weight may warrant further investigation.

Abbreviations

MF-BIA – Multi-frequency Bioelectrical Impedance Analysis; **TBW** – Total Body Water; **TBW%** – Total Body Water as a percentage of body weight; **ECW** – Extracellular Water; **ECW%** – Extracellular Water as a percentage of body weight; **ICW** – Intracellular Water; **ICW%** – Intracellular Water as a percentage of body weight; **ECW: ICW** – Extracellular to Intracellular Water Ratio; **ROC curve** – Receiver Operating Characteristics Curve;

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PPV – Positive Predictive Value; **NPV** – Negative Predictive Value; **LR⁺** – Likelihood Ratio Positive; **LR⁻** – Likelihood Ratio Negative.

Acknowledgments

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Statement of authorship

MWK and LH devised the study and MWK applied for funding. MWK gained ethical approval. MWK, DD and AHW recruited participants and collected data. MWK carried out the analyses with advice from LH, PKM and JP. MWK wrote the first version of the paper, and all authors read, commented on and agreed the final version of the paper.

Conflict(s) of interest/Disclosure(s)

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