

Evaluation of Nutritional Status and Hydration in Patients on Chronic Hemodialysis by Bioelectrical Impedance Analysis

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Abbreviated title: Nutrition and hydration in hemodialysis

Abstract

Background: Nutrition and hydration of the dialysis patients have major influences on the outcomes of chronic hemodialysis.

Purpose: To characterize the states of nutrition and hydration in patients on chronic hemodialysis at Jos University Teaching Hospital (JUTH) and to evaluate the usefulness of measurements by bioelectrical impedance analysis (BIA) for these characterizations.

Methods: Investigation pre-and post-hemodialysis of (A) the state of nutrition by body mass index (BMI), serum albumin and pre-albumin, and BIA-derived estimates of the fraction body fat over body weight (BF/W) and phase angle, and (B) the state of hydration by clinical examination for volume excess and BIA-derived estimates of body water (V), extracellular volume (ECFV), and the fractions ECFV/V and V over fat-free mass (V/FFM) in 10 patients on chronic hemodialysis at JUTH.

Results: (A) Nutritional estimates post-dialysis: BMI 22.3 ± 2.9 kg/m², with 5 values in the normal range (20-25 kg/m²), 4 values < 20

kg/m² and 1 value > 27.5 kg/m²; serum albumin 29.8 ± 6.8 g/L, with 1 value in the normal range (35-50 g/L) and 9 values < 35 g/L; serum pre-albumin 0.26 ± 0.12 g/L, with 6 values in the normal range (0.18-0.45 g/L) and 4 values < 0.18 g/L; BF/W 0.19 ± 0.08 , with 5 values in the normal range, 4 values indicating fat deficit and 1 value indicating fat excess; phase angle 4.4 ± 0.8 degrees, with 5 values in the normal range (5-8 degrees) and 5 values indicating malnutrition (< 4 degrees). There was strong concordance between hypoalbuminemia, low serum pre-albumin and low values of BF/W and phase angle. Pre- and post-dialysis values agreed closely. (B) Post-dialysis estimates of hydration by BIA: V 38.6 ± 9.8 L; ECFV 18.8 ± 6.6 L; ECFV/V 0.48 ± 0.06 ; V/FFM 0.73 ± 0.04 . The change in V during dialysis (-0.7 ± 3.3 L) correlated highly ($r = 0.99$) with the corresponding change in body weight (-0.8 ± 3.3 kg). The fractions V/FFM and ECFV/V were higher in patients with clinical evidence of volume overload than those with post-dialysis euvolemia. BIA appeared to underestimate the excess body water in a patient with ascites and pleural effusions.

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Conclusions: With the exception of patients with large fluid collections in body cavities, BIA provides reliable estimates of nutrition and hydration in Nigerian patients on chronic hemodialysis. Both malnutrition and overhydration are common in JUTH patients on chronic hemodialysis. These findings may assist in designing preventive and therapeutic interventions for these patients.

Key Words: Hemodialysis, nutrition, hydration, bioimpedance, Nigeria

Introduction

The number of patients reaching end-stage renal disease (ESRD) is increasing globally. In tertiary care centers in Nigeria, renal failure accounts for 8% of the total hospital admissions^{1,2}. In the medical wards of the Jos University Teaching Hospital (JUTH), renal failure was found to be the sixth leading cause of death after AIDS-related disease, chronic liver disease, neoplasms, cardiovascular disease, and the non-ESRD complications of diabetes mellitus³.

Chronic dialysis prevents death from uremia, but is associated with high rates of mortality from other causes. Proper nutrition^{4,5} and prevention of overhydration⁶ are critical for the survival of patients on chronic dialysis. In this study, we evaluated the nutritional and hydration status of patients on chronic dialysis at JUTH by bioelectrical impedance analysis (BIA), a simple bedside procedure which has been used to evaluate the state of nutrition⁷⁻¹⁴ and hydration¹⁵⁻¹⁹ in patients on chronic dialysis. We compared the findings of BIA to clinical estimates and pertinent laboratory values. The purposes of the study were to characterize the usefulness and limitations of BIA in assessing nutrition and hydration of patients on chronic dialysis, and to identify potentially correctable deficits in the procedures used in the dialysis of ESRD patients in Nigeria.

Materials and methods

Subjects and procedures

We recruited into the study 10 patients who received chronic hemodialysis at the dialysis unit in JUTH between June 15, 2003 and August 15, 2003. Six patients were studied once while four patients were studied twice with an interval of 10 to 30 days between the two studies. The protocol of the studies and the informed consent forms had been approved by the Institutional Review Boards of the Faculty of Medical Sciences at Jos University and the University of New Mexico School of Medicine. During interviews conducted prior to a dialysis session, the patients were informed about the purpose and methods of the study. All interviewed patients indicated that they understood the study and provided signed informed consent.

After signing the informed consent form, the patients had their height and weight measured by an experienced dialysis nurse and a member of the research team. They then had their body composition evaluated by single-frequency BIA using a BIA-Quantum impedance analyzer (RJL Inc, Clinton Township, Mich.). The instrument delivers an alternating 800 μ A current at a frequency of 50 kHz. Impedance measurements were made as the patients lay in the supine position on a nonconducting surface with limbs abducted approximately 30° from the body. Signal introducing electrodes were placed on the first joint of the middle finger and just below the middle toe. The detecting electrodes were placed with the upper edge of the electrode bisecting the ulnar head of the wrist and the median malleolus of the foot. Care was taken that the signal and detecting electrodes were not closer than 5 cm. Duplicate measurements of impedance were made in each subject²⁰⁻²⁶. The BIA procedure is brief and without discomfort or danger. The electrical current is not perceived by the subjects studied.

After the BIA procedure, a 20 mL sample of blood was obtained pre-dialysis and the dialysis session was started. A 10 mL blood sample was obtained immediately post-dialysis. Both blood samples were obtained from the arterial dialysis blood line. Post-dialysis body weight was measured by the

same personnel measuring the pre-dialysis weight and on the same scale. The patients did not consume food during dialysis. Consequently, the weight change during a dialysis session reflected body fluid changes. Approximately 10 minutes after the end of the dialysis session, the patients had a repeated evaluation of body composition by BIA.

Estimates of nutrition

Body mass index (BMI), and serum albumin and pre-albumin were the nutritional parameters that were compared to the parameters derived from BIA. The normal range for BMI is 20-25 kg/m². BMI values > 27.5 kg/m² indicate obesity. BMI values < 20 kg/m² indicate weight deficit. Low BMI, an index of poor nutrition, predicts high mortality in ESRD patients (27). Weight deficit is found in 40% of the JUTH patients approaching ESRD (28).

Serum albumin was measured by the bromocresol green method. The normal range for serum albumin values by this method is 35-50 g/L. Serum albumin values < 30 g/L indicate severe hypoalbuminemia. Serum pre-albumin was determined by turbidimetric measurement of antigen-antibody complexes using an antibody to pre-albumin. The normal range for pre-albumin is 0.18-0.45 g/L.

In BIA studies, impedance (Z) is the vector sum of resistance (R) and reactance (Xc), which are the two measurements directly reported by the BIA instrument. Resistance is the opposition to an electrical current. In cylindrical wires conducting electrical current, resistance is determined by the material of the wire plus the length and diameter of the cylinder. BIA measurements are based on the assumption that the human body is made up of a series of serially connected cylinders (arms, legs, trunk) with known length and diameter. In this case, the only unknown determinant of resistance is the composition of the fluids in these cylinders. Reactance reflects the portion of impedance due to the presence of capacitive elements, such as cell membranes⁹.

R and Xc from each BIA measurement are entered in a computer software program along with demographic information (gender) and anthropometric measurement (weight and

height) of the subject. The software programs contain equations that derive from the variables entered as parameters of body composition, nutrition and hydration. Body weight (W) consists of body fat (BF) and fat-free mass (FFM). The BIA parameters that are related to nutrition include BF_{BIA} , FFM_{BIA} and phase angle, which is the tangent of the ratio Xc/R . The normal range for body fat content (BF/W) is 0.12-0.20 in males and 0.20-0.30 in females. BF/W values > 0.20 in males and > 0.30 in females indicate excess body fat. BF/W values < 0.12 in males and < 0.20 in females indicate fat deficit²⁹. Fat deficit detected by BF_{BIA} is an important indicator of poor nutrition in patients on chronic dialysis⁷. Phase angle has emerged as another nutrition index for patients on chronic dialysis with important prognostic value³⁰. The normal range for phase angle is 5-8 degrees. Phase angle values < 4 degrees predict high mortality in patients on chronic dialysis³⁰.

A second set of estimates of BF/W was obtained using the Gallagher formula ($BF_{Gallagher}/W$) for Caucasians and African Americans³¹:

$$(BF_{Gallagher}/W)100 = 64.5 \\ 848/BMI + 0.079Age \\ 16.4Gender + 0.05GenderAge \\ + 39Gender/BMI \\ \{1\}$$

where BMI is the post-dialysis BMI in kg/m^2 , age is in years, male gender is assigned the value one and female gender is assigned the value zero. $FFM_{Gallagher}$ was calculated as $W - BF_{Gallagher}$.

Estimates of hydration

BIA measurements permit one to estimate total body water (V), extracellular volume (ECFV) and intracellular volume (ICFV). Patients with renal failure usually have ECFV excess and may also have ICFV abnormalities. A hemodialysis session could potentially affect both ICFV and ECFV. Fluid shifts between the intracellular and extracellular compartments (internal shifts) are manifested by changes in serum sodium concentration. If the initial (pre-dialysis) ICFV ($ICFV_1$) is known, and $[Na]_1$ and $[Na]_2$ are respectively the initial (pre-dialysis) and final (post-

dialysis) serum sodium concentrations, the amount of fluid shifted internally (V_{int}) is calculated as:

$$V_{int} = ICFV_1([Na]_1/[Na]_2 - 1) \\ \{2\}$$

In equation 2, a decrease in $[Na]$ ($[Na]_1 > [Na]_2$) signals ICFV gain through transfer of fluid into the intracellular compartment, while an increase in $[Na]$ ($[Na]_1 < [Na]_2$) indicates loss of ICFV through fluid transfer outside the intracellular compartment. Since they provide estimates of the ICFV, BIA measurements allow one to calculate the amount of fluid transferred between the ICFV and the ECFV. The change in ECFV secondary to the loss or gain of ICFV is equal to the change in ICFV, but with an opposite sign.

In healthy individuals, extracellular volume varies with body size, gender, age, body fat, ethnicity, chronic illness and probably other factors including diet. To detect differences between genders, ethnic groups, or other groups of subjects, it is customary to normalize ECFV to parameters of body size, such as weight or height. To detect abnormalities in ECFV in this study, we normalized ECFV to total body water, which is affected by the same factors as ECFV. One BIA study reported a correlation of 0.8 between ECFV and V in normal subjects³². Despite this high degree of correlation, the relationship ECFV/V varies considerably between different groups of subjects without hydration abnormalities. For example, the development of obesity causes disproportionately larger increases in ECFV than in V³³. Largely because of its variation in subjects without hydration abnormalities, the normal range of the ratio ECFV/V has not been clearly defined. From BIA measurements, the mean ECFV/V values vary between 0.40 and 0.45, while the range of the normal ECFV/V values could be between 0.35 and 0.50^{32,34,36}.

Another way to characterize the state of hydration is by the use of the V/FFM ratio. This approach is based on the following facts: (a) in the body, water is distributed only in FFM (not in BF); and (b) in both animals and

humans with normal body water, the V/FFM ratio is constant at approximately 0.72 with a very narrow range of the normal values^{37,38}. FFM at normal hydration is called the edema-free, fat-free body mass.

In this study, we considered the range V/FFM as the “gold standard” of hydration assessment precisely because of the narrow range of the normal values. We considered V/FFM values > 0.74 as indicating water excess. We used the intradialytic changes in serum sodium concentration and the ratios ECFV/V and V/FFM to characterize the status of V, ICFV and ECFV. Purely isotonic changes in ECFV (isotonic external fluid shifts) affect the ratios V/FFM and ECFV/V, but not [Na], while internal fluid shifts between the two major body fluid compartments affect [Na] and the ratio ECFV/V, but not the ratio V/FFM. Measurement before and after a dialysis session of the serum sodium concentration and BIA hydration parameters (V, FFM, ICFV, ECFV) allow quantitative assessment of body fluid changes during dialysis.

In addition to V_{BIA}, a second estimate of body water was obtained from the Gallagher formula assuming normal body water content,

as follows:

$$V_{\text{Gallagher}} = 0.72\text{FFM}_{\text{Gallagher}}$$

{3}

Statistics and other comparisons

Continuous variables are presented as mean ± standard deviation. Statistical methods of comparison used included the two-tailed paired t test, the two-tailed Student's t test, correlation, and the Bland-Altman statistic of limits of agreement (d ± 2ds) where d is the mean difference between estimates of the same variable by two different methods and ds is the standard deviation of this mean difference³⁹.

Qualitatively, we tested whether the BIA measurements of body water recorded accurately the direction of the change in body water content (the ratio V/W) during a dialysis session. When there is net fluid loss the ratio V/W mathematically decreases from the pre-dialysis to the post-dialysis state, whereas when there is net fluid gain during a dialysis session the ratio V/W increases⁴⁰.

In one unique patient who had progressive weight gain due to fluid retention from a known “dry” weight status, we compared the BIA estimates of nutrition and hydration to estimates obtained from a method of

Table 1. Patient characteristics

Patient	Gender (M, F)	Age years	Height m	Weight* kg	Dialysis duration months
1	M	44	1.74	64.2	4
2	F	58	1.74	85.3	5
3	M	36	1.74	71.0 [#]	9
4	M	53	1.73	59.6	108
5	F	22	1.64	55.7	38
6	F	47	1.57	49.1	3
7	M	42	1.88	81.5	1
8	M	53	1.57	60.2	1
9	F	20	1.56	58.7	3
10	M	60	1.60	46.0	13
Mean		43.6	1.68	63.1	18.5
SD		6.6	0.11	7.9	33.3

* Post-dialysis after the first study. [#] Stable post-dialysis weight for at least one month obtained four months prior to the BIA study. In the ensuing three months, patient 3 had progressive weight gain secondary to the development of massive ascites, bilateral pleural effusions and anasarca. On the day of the BIA study, his post-dialysis weight was 104 kg. SD = standard deviation.

Table 2. Nutrition indices, first study post dialysis

	Mean SD	Normal values N (Percent)	Low values N (Percent)	High values N (Percent)
Body mass index (kg/m ²)	22.3 2.9	5 (50)	4 (40)	1 (10)
Serum albumin (g/L)	29.8 6.8	1 (10)	9 (90)	0
Serum pre-albumin (g/L)	0.26 0.12	6 (60)	4 (40)	0
BF _{BIA} /W (kg/kg)	0.19 0.11	5 (50)	4 (40)	1 (10)
BF _{Gallagher} /W (kg/kg)	0.22 0.08	7 (70)	1 (10)	2 (20)
Phase angle (degrees)	4.4 0.8	5 (50)	5 (50)	0

SD = standard deviation; BF = body fat; W = weight; BIA = bioelectrical impedance; Gallagher = Gallagher formula. Pre- and post-dialysis values agreed closely

Table 3. Hydration indices, first study

Variable	Pre-dialysis	Post-dialysis	p-Value
V _{BIA} (L)	39.4 10.4	38.6 9.8	<0.05
V _{Gallagher} (L)	34.7 6.8	34.4 6.7	<0.05
ICFV _{BIA} (L)	19.1 5.7	20.6 5.9	<0.05
ECFV _{BIA} (L)	20.3 6.2	18.8 6.6	<0.05
ECFV/V _{BIA} (L/L)	0.50 0.09	0.48 0.06	<0.05
V/FFM _{BIA} (L/kg)	0.73 0.04	0.73 0.04	NS

V = body water; BIA = by bioimpedance; Gallagher = from the Gallagher formula; ECFV = extracellular volume; ICFV = intracellular volume; FFM = fat free mass. The values are presented as mean standard deviation.

Table 4. Estimates by the Gallagher formula and by BIA in a patient with fluid gain

Parameter	Gallagher formula ¹	Gallagher formula ²	BIA
BF, kg	13.0	13.0	17.1
FFM, kg	58.0 ³	58.0 ³	86.8
V, L	41.8	74.8	67.1
V/FFM, L/kg	0.72 ⁴	1.29 ⁴	0.77
ICFV, L	25.1 ⁵	25.1 ⁵	31.0
ECFV, L	16.7 ⁶	49.7 ⁷	36.1
ECFV/V, L/L	0.40	0.66	0.54
V/W, L/L	0.59	0.72	0.65

BF = body fat; FFM = fat-free mass; V = body water; ICFV = intracellular volume; ECFV = extracellular volume; W = body weight

¹ Calculation of body composition at a "dry" body weight of 71 kg; ² V and ECFV estimates obtained by adding the difference between actual and dry weight (104 - 71 = 33 L) to dry weight (71 kg) Gallagher estimates of V and ECFV, respectively;

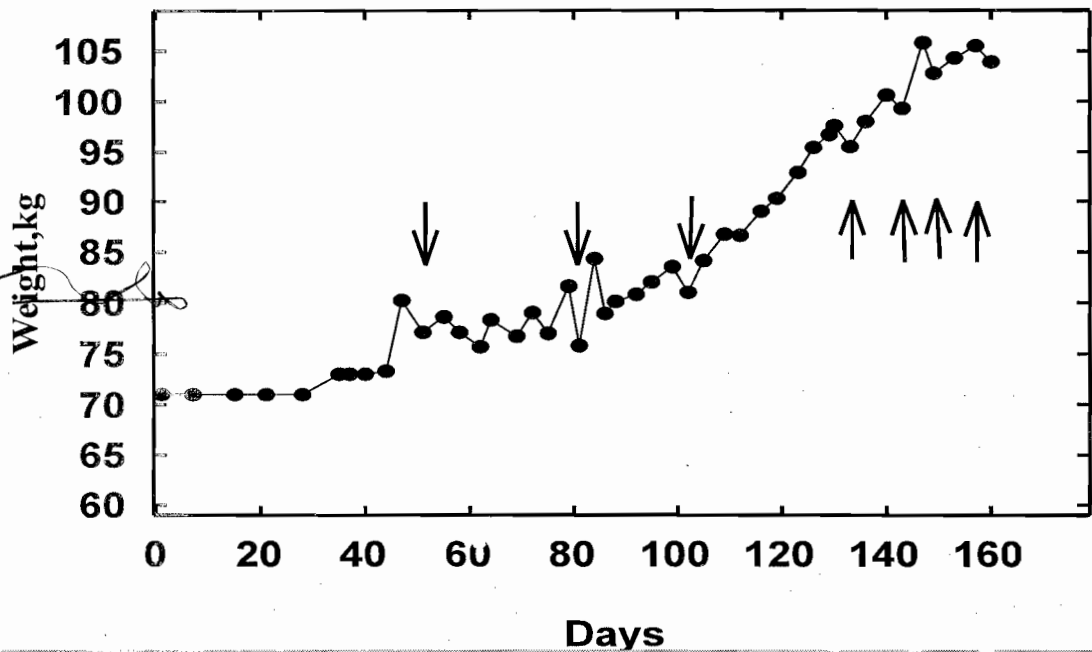
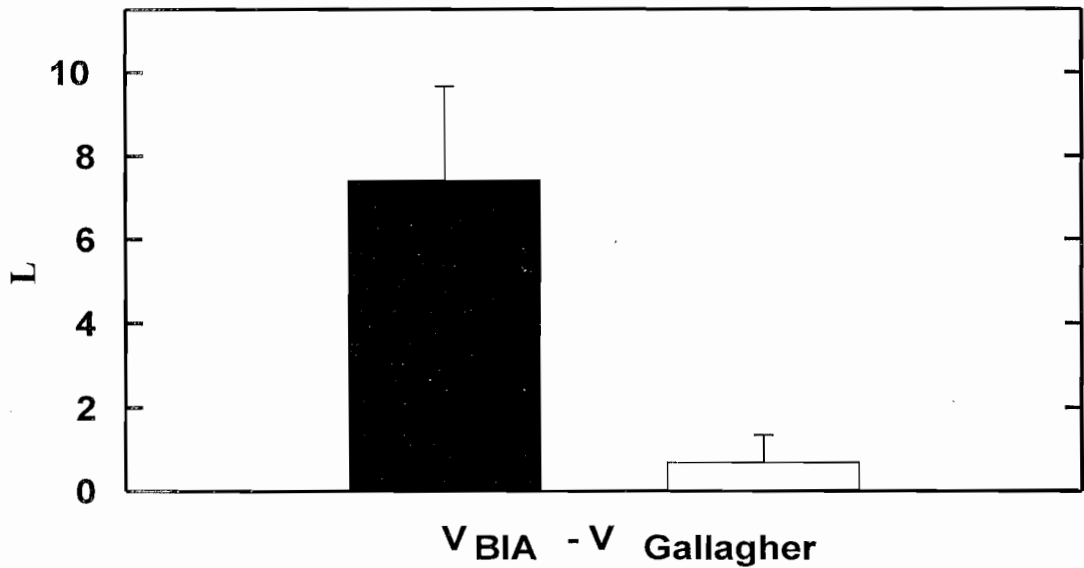
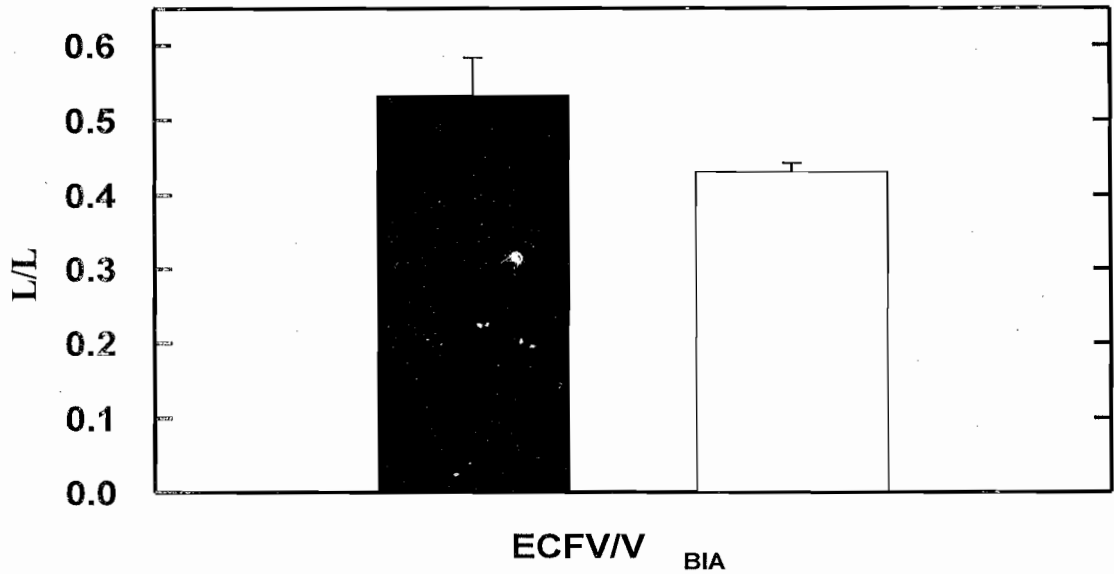
³ The so-called edema-free, fat-free mass; ⁴ The ratio of body water over edema-free, fat-free mass;

⁵ 0.6(body water obtained from the Gallagher formula at 71 kg of weight); ⁶ 0.4(body water obtained by the Gallagher formula at 71 kg of weight) ⁷ (Dry weight value obtained from the Gallagher formula) + 33 L.

LEGENDS

Figure 1. Comparison of the post-dialysis values ECFV/V_{BIA} (upper panel) and V_{BIA} V_{Gallagher} (lower panel) between five patients with excess body water by BIA (V/FFM_{BIA} > 0.74, dark bars) and five patients without excess body water (V/FFM_{BIA} 0.74, open bars) in the first study. Differences were significant at p < 0.001.

Figure 2. Evolution of post-dialysis weight in a JUTH patient on chronic hemodialysis with progressive development of massive ascites, bilateral pleural effusions and anasarca. Arrows: progress height gain post dialysis.



Discussion

This study documented the frequency and magnitude of nutrition and hydration abnormalities in patients on chronic hemodialysis at JUTH and illustrated some of the limitations of BIA as a method for analyzing hydration. Malnutrition is common in dialysis populations and has dire consequences⁴²⁻⁴⁴. This potentially preventable condition has a higher prevalence in JUTH patients with pre-ESRD stages of chronic kidney disease (CKD) than in normal controls from the same population²⁸. Consequently, early diagnosis of CKD with timely intervention (nutritional assistance, management of associated catabolic conditions, timely initiation of dialysis and adequate dialysis) is the best way to combat malnutrition in these patients.

Two of the indices estimated from BIA, body-fat content and phase angle, are considered as indices of nutrition in patients on dialysis⁷. These BIA indices correlated closely with the serum indices of nutrition. This finding raises the question whether BIA evaluation of nutritional status is redundant in patients on chronic dialysis. However, BIA has certain advantages including the detection of body-fat deficit, which may not be detected by formulas based on BMI because of excess body water (see below), and the calculation of the phase angle, which is a strong predictor of outcomes in patients on chronic dialysis³⁰. In addition, low serum albumin may reflect not nutritional status, but inflammatory state in a large percent of patients on chronic dialysis⁴⁵, while serum pre-albumin is not measured routinely.

The role of BIA in assessing hydration of dialysis patients appears to be even more important than its role in assessing their nutritional status. Clinical estimates of hydration, although indispensable, can be misleading, especially when subtle abnormalities are present, which nevertheless have clinical implications in dialysis patients⁶. In this study, BIA estimates of hydration were compared to estimates obtained using the Gallagher formula.

The Gallagher formula was derived by comparing BMI to estimates of body composition obtained in healthy subjects by a

reference method²⁸. A comparable formula for assessing body composition in Nigerians is not available and should be developed. The two most important sources of systematic error associated with any formula predicting body composition from BMI are hydration abnormalities and deviations of body fat from the fat content expected for a given BMI⁴⁶. Patients on chronic dialysis frequently develop both fat deficits and fluid excesses. BIA can detect hydration abnormalities not detectable by anthropometric formulas including formulas based on BMI⁴⁷⁻⁴⁹. We showed that the differences between the estimates of body water by BIA and by the Gallagher formula were related to the hydration status of the patients (Fig. 1). BIA estimates of hydration agreed with the clinical presence or absence of edema and with the known intradialytic change in body water. Thus BIA estimates of hydration have a clear advantage over estimates obtained from anthropometry in patients on dialysis.

Our study also illustrated certain limitations of BIA in estimating hydration. The direction of the intradialytic change in body water content estimated by BIA was erroneous in three of the ten patients. This finding may be due to the relatively small changes in body water during dialysis in two patients. The last patient in this group was the patient who had the massive fluid gain. BIA clearly underestimated body water and extracellular volume in this patient. The differences in these volumes shown in Table 4 likely represent underestimates of the actual differences because we assumed that body composition (body fat, edema-free fat-free mass) did not change over the months of fluid gain. However, the patient reported continuous anorexia and frequent vomiting during this period and may well have lost body fat. BIA appears to underestimate fluid excesses when there are large collections of fluid in central body cavities.

In conclusion, BIA is very useful in documenting hydration abnormalities in patients on chronic dialysis, while its use in documenting nutritional deficits is tempered by the fact that certain biochemical parameters, particularly serum albumin, which is routinely measured, have a sensitivity

in detecting poor nutrition similar to or greater than that of BIA. Both poor nutrition and overhydration are prevalent in JUTH patients on chronic dialysis. Prevention of malnutrition in these patients should start in the early stages of CKD. An effort to prevent overhydration by aggressive ultrafiltration during dialysis is warranted. Use of repeated BIA measurements to achieve normal hydration would be desirable. In its absence, continuous evaluation for correction of edema and hypertension is the indicated clinical practice.

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