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TECHNICAL NOTE

Nutritional and prognostic correlates of bioimpedance indexes in hemodialysis patients

QUIRINO MAGGIORE, SANTI NIGRELLI, CARLA CICCARELLI, CRISTINA GRIMALDI, GIUSEPPE A. ROSSI, and CLAUDIO MICHELASSI

Dialysis and Nephrology Unit, S.M. Annunziata Hospital and Torregalli Hospital, Florence; Dialysis Unit, S.M. Maddalena Hospital, Volterra; and Institute of Clinical Physiology, Department of Statistics, National Council of Research, Pisa, Italy

Nutritional and prognostic correlates of bioimpedance indexes in hemodialysis patients. We carried out a cross sectional and longitudinal study to assess whether bioimpedance indexes (resistance, Rz; reactance, Xc; phase angle, PA) reflect the nutritional status of hemodialysis (HD) patients, and bear a significant association with their long-term survival. The bioimpedance data of 131 patients on chronic HD treatment were compared with those of 272 healthy controls matched for age and sex. Nutritional status was assessed by anthropometric variables, serum albumin (SA), normalized protein catabolic rate (nPCR), and subjective global assessment (SGA). All three bioimpedance indexes varied significantly with HD treatment, however, with the exception of Xc in post-HD, they were on average significantly ($P < 0.016$) different from controls either pre- and post-HD. Post-HD PA appeared to be the best index of nutritional status, being significantly correlated with SA, age, mid arm muscle circumference (MAMC), SGA, and nPCR ($R^2 = 0.44$; $P < 0.01$). However, depending on the cut-off levels, PA failed to detect clinically overt malnutrition in one to two thirds of the 12 patients with the worst SGA score. During the follow-up the changes in bioimpedance indexes reflected poorly the changes in dry body weight, only the ΔRz bore a significant correlation ($r = -0.29$; $P < 0.01$) with Δbody wt. Patients having baseline phase angle values within the lower quartile had a significantly lower two-year survival rate than patients having higher values (59.3% vs. 91.3%; $P < 0.01$). Cox's analysis (proportional hazard model) showed that phase angle as a predictor of death outweighed all other parameters included in the model (age, SA, nPCR, MAMC, SGA), with a relative risk of 2.6 (95% CI = 1.6 to 4.2). Bioimpedance indexes do not appear to be reliable in detecting clinically overt depletion of lean body mass. However, the strong association of PA with patient survival suggests that this bioimpedance index reflects some dimension of the illness, which is not fully identifiable with the deranged nutritional status.

Bioimpedance analysis (BIA) is increasingly used for assessing the nutritional status in sick patients, including those on chronic hemodialysis (HD) treatment [1–5]. BIA relies on the measurement of the voltage drop occurring when a constant, alternating electrical current is applied to the living organism. The impedance (Z) signal obtained from BIA is separated into two components, resistance (Rz) and reactance (Xc), both measured in ohms. Rz and Xc are used to estimate body composition by means of empirical equations based on their correlations with validated reference methods. In these equations Rz is used to predict total body water, and lean body mass (LBM) [6, 7]; the ratio Xc/Rz or its geometrical derivative, phase angle (PA) is used to predict the total body cell mass (BCM) [8]. There are, however, some pitfalls with the use of BIA equations. First, the equations contain other variables beside the bioimpedance indexes, such as body weight, height, and age, which by themselves can quite accurately predict TBW in both healthy subjects and HD patients [9–11]. Second, the elaboration of bioimpedance indexes into volume estimates stems from the theory equating the human body to a homogeneous cylindrical conductor of the electrical current. In its application to human beings BIA is, however, far removed from this model, because the contribution of one arm and one leg to total body Rz is disproportionately higher (90%) than that of the trunk (10%), which represents nearly 50% of the body wt [12]. In applying the standard BIA equations to sick patients, one has to rely on the unproven assumptions that the disease states do not alter neither the relative contributions of the various body segments to total Rz, nor the specific tissue resistance [13]. Due to these drawbacks, studies in HD patients based on standard BIA equations deserve reappraisal.

In this investigation we explored the clinical meaning of bioimpedance parameters without expanding them into volume estimates. To this purpose we looked for their nutritional and prognostic correlates in a fairly large population of patients on chronic HD treatment. As nutritional correlates we chose the parameters most commonly assessed in dialysis patients. As prognostic correlate we chose the mortality rate recorded during the follow-up.

Methods

Study populations

All hemodialysis outpatients receiving treatment for longer than six months in three Hospital Dialysis Units were enrolled into the study. One hundred thirty-one patients entered into the study over the period of April 1991 to October 1992. All patients were Caucasian, 65 were women, 36 had severe comorbid conditions such as cancer [4], symptomatic peripheral vascular disease [7], symptomatic cardiac disfunction [17], and chronic obstructive pulmonary disease [8]. On study entry, the mean age was 62.5± (SD) 13.6 years, and mean duration on dialysis treatment was 75 ±

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58.6 months. The underlying renal diseases sustaining the terminal uremic state were chronic glomerulonephritis in 29, chronic interstitial nephritis in 21, hypertension in 18, polycystic kidney disease in 20, diabetic nephropathy in 8, and other disorders in 35. To get the normal values of bioimpedance indexes, we studied 272 healthy subjects matched for age and sex with the entire patient population. They were recruited among hospital personnel and healthy volunteers in the general population.

Dialysis prescription

All patients were on a thrice weekly HD regimen: 44 with cellulosic membrane, 87 with noncellulosic membrane (63 high flux, 24 low flux). High efficiency treatment with shortened dialysis time (150 to 180 min) and large surface dialyzers (1.8 to 2 m^2) were used in 44 patients, while the duration of dialysis time was 210 to 240 minutes in the remaining patients, whatever the membrane used.

Study design

Upon enrollment, each patient underwent nutritional assessment and bioimpedance measurements. Patients were then monitored for up to 41 months. To assess whether the bioimpedance indexes reflect the intra-individual changes in nutritional indexes occurring over time, we repeated all the determinations after 6 to 12 months in all patients still available to follow-up. Clinical outcomes monitored were death, transplantation, transferral to other dialysis technics or to other Dialysis Centers.

Nutritional assessment

Clinical indexes of nutritional status were assessed concurrently with BIA on the same midweek dialysis day. Assessment of nutritional status was based on measurements of serum albumin (SA) levels, anthropometric indexes, normalized protein catabolic rate (nPCR), and subjective global assessment (SGA). To minimize the variability among the Dialysis Units involved in this investigation, chemical measurements were all made in the same laboratory and the clinical assessments by a single physician. Serum albumin was determined by laser immunonephelometry on blood samples collected at the start of the hemodialysis session. Anthropometric indexes were obtained at the end of the dialysis treatment: upper arm circumference was measured on the non-access limb with a tape with the arm hanging relaxed; triceps skinfold was measured with a Lange skin-caliper. Mid arm muscle circumference (MAMC) was derived from mid arm cicumference (MAC) and triceps skinfold (TS), where MAMC = MAC − 3.14 * TS. Body mass index (BMI) was calculated as the ratio between end-dialysis body weight in kg, and the square of height in nPCR was calculated by the equation of Gotch and Sargent based on the urea appearance rate [14]. To determine the urea appearance rate, we measured the increment of serum urea over the midweek dialytic interval starting 30′ after the end of the dialysis session, to make an allowance of urea rebound, which in high efficiency treatments may be higher than 20% [15]. Total body water was estimated by the equations of Watson et al [16]. SGA was based on the method described by Detsky et al [17] with slight modifications. The subjective assessment was carried out by an investigator (SN) who was blinded to the results of the other nutritional tests. According to his judgment nutritional status was scored either one (normal), two (moderately impaired), or three (severely impaired), based on the presence or absence of an history of recent weight loss, anorexia and vomiting, and an estimate of muscle wasting and loss of subcutaneous fat.

Bioimpedance indexes

Bioimpedance indexes were measured with a bioimpedance instrument (BIA 101; Akern RJL Systems, Florence, Italy). Measurements were made with the subjects lying in bed with the arms and limbs abducted. Injection electrodes were placed over the dorsum of the hand (contralateral to the access limb in dialysis patients) in the midline, just proximal to the phalangeal-metacarpal joint, and over the dorsum of the homolateral foot just proximal to the metatarso-phalangeal joint. The detection electrodes were placed on the dorsum side of the hand midway between the radial and ulnar styloids, and midway between the malleoli of the leg. Adherence of electrodes to the skin was insured through self adhesive tape. An excitation current of 800 micro Amp at fixed 50 kHz was introduced into the subjects at the distal electrodes of the hand and foot, and the voltage drop was detected by the proximal electodes. All measurements were taken in triplicate, in HD patients they were obtained both before and after the HD session. In preliminary crossover studies, we found that post-HD bioimpedance indexes are not significantly affected by the variations in serum electrolytes usually met with the various treatment modalities used in this study, provided that the amount of body fluid removed during each session was held unvaried. Bioimpedance indexes are affected by body fluid removal [1, 4], and it is known that immediately after the dialysis session equilibration among body water compartments has not yet reached the steady state. Therefore, to assess how stable are the bioimpedance indexes shortly after the dialysis treatment, we repeated the measurements after 90 minutes in 7 patients crossed over through the various dialysis modalities used in the population study. Xc and PA did not vary significantly during this interval, while Rz decreased by 10 ohms only, from 614 ± 33 to 604 ± 36 ($P < 0.01$ by paired t-test). To minimize the cyclical variations in bioimpedance indexes due to changes in hydration state of the patients, we based our analysis on values obtained at the end of HD treatment. The coefficient of variation between paired post-HD measurements performed two weeks apart on 18 patients were 5.3% for Rz, 7.5% for Xc, 7% for PA.

Statistical methods

We used the paired and unpaired two-tailed Student's t-tests (P values significant if less than 0.05) with the Bonferroni correction for multiple comparisons. To assess the strength of associations between variables, we used Pearson's correlation r, or Spearman rank correlation coefficient for selected analyses. Stepwise multiple regression analyses were carried out with the help of a statistical software (Statgraphics, version 4). Survival was computed by the Kaplan-Meier method and the difference between survival curves by the Mantel-Haenszel (log-rank) statistics. We examined the independent relationship to mortality risk of bioimpedance indexes and nutritional variables using a proportional hazard regression model (BMDP program P2L, Dept. of Biomathematics, University of California, Los Angeles, 1990) based on the data recorded on initial enrollment. By a stepwise selection process, variables were entered or removed from the regression equation on the basis of the maximized partial likehood ratio. Nutritional and bioimpedance indexes were treated as categorical variables with breakpoints corresponding to the quartile cut-offs

Table 1. Bioelectric indexes in controls and HD patients

	Controls	HD patients	
M/F	136/136	65/66	
Age *years*	61.6 (14.5)	62.5 (13.6)	
Height *cm*	162 (10.3)	161 (9.7)	
		pre-HD	post-HD
Body wt *kg*	66.8 (11.8)	63.7 (12.4)[a]	61.4 (12.2)[ab]
R_z *ohms*	535 (73)	565 (98)[a]	656 (115)[ab]
X_c *ohms*	56.3 (10.1)	41.5 (10.2)[a]	58.6 (14.8)[b]
PA *rad*	6.0 (.9)	4.2 (1.0)[a]	5.1 (1.3)[ab]

Data are mean (± 1 SD).
[a] $P \leq 0.016$, no superscript denotes $P > 0.016$ in the comparisons between patients (pre-HD and post-HD values) and controls by the Bonferroni *t*-test
[b] $P < 0.01$ in comparison between pre-HD and post-HD values (paired *t*-test)

in the HD population. The relative risk for each independent variable was expressed as the exponential of the coefficient of the variable in the hazard equation.

Results

Bioimpedance indexes in controls and HD patients

The bioimpedance data obtained in controls and HD patients at the baseline examination are shown in Table 1. Before starting the HD treatment the patients had higher Rz ($P < 0.016$), and lower Xc and PA ($P < 0.016$ for both indexes) than normal controls. HD treatment caused an increase in all three bioimpedance indexes, but brought to normal only Xc, while Rz increased further above the normal values, and PA remained still significantly below them. The changes in bioimpedance indexes (difference between pre-HD and post-HD values) were inversely related to the amounts of body fluid removed during the HD session, with Pearson's r values of -0.39 ($P < 0.01$) for Rz, -0.48 ($P < 0.01$) for Xc, and -0.36 ($P < 0.01$) for PA.

Relationships between bioimpedance and nutritional indexes

The r values of the simple correlations between the post-HD bioimpedance parameters and nutritional indexes, including age, are shown in Table 2. Rz appeared to reflect the anthropometric characteristics of the patients better than the two other bioelectric indexes, especially MAMC. PA correlated significantly with all nutritional indexes except BMI. Stepwise regression analysis was performed to determine which of the variables listed in Table 2 were independent predictors of bioimpedance indexes. Significant ($P < 0.01$) predictors were MAMC and SGA for Rz ($R^2 = 0.41$); age, SA, and nPCR for Xc ($R^2 = 0.28$); SA, age, MAMC, SGA, and nPCR for PA ($R^2 = 0.44$). Table 3 shows the relationships between PA and nutritional indexes in patients subdivided according to the lower quartile, interquartile and upper quartile of PA values adjusted for sex. The lower quartile patients were on average older and had most nutritional indexes significantly more deranged than those belonging to the upper quartile, while they differed from those in the interquartile range for BMI, SA, and nPCR. Table 4 shows the relationship between SGA and PA quartiles. Limiting the analysis to the lower PA quartile, this included 8 of the 12 patients scored SGA three (sensitivity = 67%), and 26 of the 119 patients scored SGA one or two (specificity = 78%). If the cutoff limits of PA are lowered to the tenth percentile, the specificity increases to 91%, but the sensitivity drops to 33%. The diagnostic yields of Rz or Xc were even lower than that of PA (data not shown).

Changes in bioimpedance and nutritional indexes during follow-up

A repeat examination was carried out after 7.4 ± 1.9 months on 118 patients. On this occasion, the correlation levels between bioimpedance and nutritional indexes were very close to those recorded at baseline (data not shown). Noteworthy is the fact that nearly 80% of patients having PA values within the lower quartile at the baseline evaluation were still in this category at the repeat examination, which now included a further 12 patients previously belonging mostly to the interquartile range (Table 5). The intra-individual variations in nutritional indexes recorded at the repeat examination were on average of modest degree, but their ranges were considerably wide (Table 6). The changes in nutritional indexes that were significantly correlated with the changes in bioimpedance indexes were the following: Δbody wt with ΔRz only ($r = -0.29$; $P < 0.01$), ΔMAC with ΔXc ($r = 0.26$; $P = 0.01$) and ΔPA ($r = 0.31$; $P < 0.01$), ΔnPCR with ΔXc ($r = 0.19$; $P < 0.05$) and ΔPA ($r = 0.20$; $P < 0.05$).

Prognostic value of bioimpedance indexes

During the follow-up lasting 26.6 ± 8.9 months, 23 patients died, 6 had renal transplants and 3 were transferred to other dialysis Centers or began peritoneal dialysis treatment. Causes of death were cachexia in 4, infectious complications in 6, cerebrovascular accidents in 3, cardiovascular complications in 3, gastrointestinal hemorrage in 2, and other accidents in 5. Most deaths (15 out of 23) occurred in patients having phase angle values within the lower quartile at baseline. The actuarial survival curves for patients having baseline PA values above and below the 25th percentile are shown in Figure 1. The difference between the two survival curves is highly significant ($P < 0.01$), the probability of surviving longer than 24 months being 91.3% and 51.3%, respectively. A Cox proportional hazard analysis was done to determine how PA compared with other nutritional variables in the predictive power of long-term survival of patients. The covariates examined were age, PA, MAMC, nPCR, SA, scored 1 to 4 according to the quartile cutoffs (score 4 for lower quartile, score 1 for upper quartile of all variables, except age, which was scored in the opposite way), and SGA scores (Table 7). Significant risk predictors of death were PA, SGA, age, and SA (Table 8). However, the stepwise procedure selected PA as the only significant predictor (chi square = 17.8; $P = 0.000$), having a beta coefficient of 0.94 ± SE 0.26 (relative risk of death 2.6; 95% CI, range 1.6 to 4.2).

Discussion

In this investigation we found that HD patients had on average significantly different bioimpedance data from those of control population. As previously found by others [1, 4], bioimpedance indexes varied with dialysis treatment in relation to the body fluid removal, but their changes did not reflect accurately the changes in body wt, as shown by r^2 values of 0.23 or less. The removal of fluid excess notwithstanding, two bioelectrical indexes, namely Rz and PA, remained significantly different from normal at the end of diaysis treatment. These abnormalities could be partially accounted for by the deranged nutritional status of HD patients. In

Table 2. *r* values for simple correlations between bioelectrical indexes and other variables in HD patients

	Age	Body wt	BMI	MAC	MAMC	nPCR	SA	SGA
R_z	0.05	−0.48[a]	−0.33[a]	−0.38[a]	−0.62[a]	−0.19	−0.18	0.29[a]
X_c	−0.45[a]	−0.12	−0.14	0.003	−0.09	0.35[a]	0.34[a]	0.21
PA	−0.42[a]	0.25[a]	0.10	0.29[a]	0.36[a]	0.22[a]	0.46[a]	−0.43[a]

All *r* values are Pearson's correlation coefficients except those reported in the SGA column, which are Spearman's rank correlation coefficients.
[a] $P \leq 0.01$; no superscript denotes $P > 0.05$

Table 3. Relationships between nutritional indexes and phase angle quartiles in HD patients

	A Lower quartile $N = 34$	B Interquartile $N = 68$	C Upper quartile $N = 29$
Age *years*	67.1 (12.3)	64.8 (11.0)	51.6 (15.1)[bc]
Body wt *kg*	57.7 (10.6)	61.5 (12.5)	66.4 (12.1)[b]
BMI *kg/m²*	22.1 (3.3)	23.9 (3.8)[a]	24.4 (3.8)[b]
MAC *cm*	26.5 (3.5)	28.1 (2.1)	29.7 (3.5)[b]
MAMC *cm*	20.0 (2.7)	21.2 (2.3)	22.3 (2.5)[b]
nPCR	.90 (.26)	1.04 (.26)[a]	1.01 (.22)
SA *g/dl*	3.25 (.63)	3.58 (.38)[a]	3.84 (.42)[bc]

Values are expressed as means (± 1 SD).
Superscripts denote significant differences by the Bonferroni *t*-test ($P \leq 0.016$).
[a] Group B vs. Group A
[b] Group C vs. Group A
[c] Group C vs. Group B
No superscript denotes $P > 0.016$

Table 4. Relationship between SGA scores and PA quartiles

	PA quartiles		
SGA score	Lower quartile	Interquartile	Upper quartile
One	12	53	25
Two	14	11	4
Three	8	4	0

Data represent the number of patients.

Table 5. Changes in patient distribution among PA quartiles during follow-up

	Follow-up		
Baseline	Lower quartile	Interquartile	Upper quartile
Lower quartile	23	6	0
Interquartile	11	41	9
Upper quartile	1	8	19

Table 6. Changes in nutritional and bioelectrical indexes during follow-up

Variables	$\overline{X}$	SD	Range	
Δ Body wt *kg*	−0.9	2.8	−10.6	6.9
Δ R_z *ohms*	6.0	56.3	−189	179
Δ X_c *ohms*	−2.7	11.8	−37	32
Δ PA *rad*	−0.26	0.86	−2.9	1.9
Δ MAC *cm*	−0.2	1.4	−5.0	4.0
Δ MAMC *cm*	−0.17	1.7	−5.5	4.3
Δ nPCR *g/kg/day*	−0.02	0.23	−0.71	0.79
Δ SA *g/dl*	−0.01	0.53	−2.0	1.0

Values express the mean difference, with SD and range, between baseline and follow-up determinations

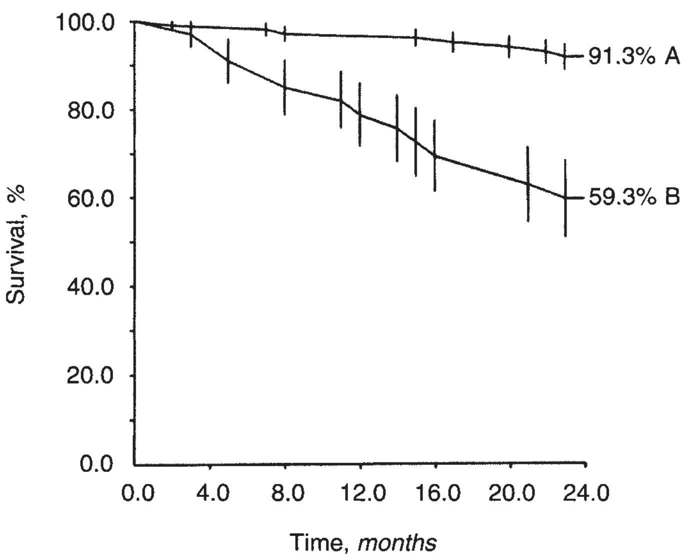

Fig. 1. *Survival curves (Kaplan-Meier estimate) in patients having PA values above (curve A) and below (curve B) the 25th percentile at the baseline.* Vertical bars represent the 95% confidence intervals. The difference between the two survival curves is highly significant. $P < 0.01$ by the log-rank test.

fact, we found significant correlations between post-HD bioimpedance indexes and the clinical-laboratory indexes of nutritional status, especially between PA and indexes of body protein depletion. PA appeared to more comprehensively epitomize the patients' nutritional status than Rz or Xc, being correlated with SA, age, MAMC, SGA, and nPCR, which together accounted for 44% of its variance. Overall, our results denote a trend for bioimpedance parameters to reflect the nutritional status of HD patients, and agree with previous studies [18–21] showing that these indexes, especially PA, tend to be altered in severe malnutrition due to various disease states.

We noted, however, important limitations regarding the reliability of bioimpedance parameters as nutritional indexes. First, depending on the cut-off value chosen, PA failed to reflect the overt malnourished state in one third to two thirds of the 12 patients who scored 3 SGA. Results with the other two bioimpedance indexes were even worse. In our opinion, the failure to reflect a clinically obvious muscle wasting, even if only in a small patient sample, speaks against the validity of bioimpedance parameters for nutritional assessment. Second, the changes in the bioimpedance indexes that were detected several months after the baseline examination correlated poorly (the Rz) or not at all (Xc and PA) with the changes in dry body wt, which in several patients

Table 7. Quartile cutoffs of variables entered into the Cox model

Percentiles		25	50	75
Age *years*		55	66	73
SA *g/dl*		3.3	3.6	3.9
nPCR *g/kg/day*		0.82	0.96	1.15
MAMC *cm*	M	20.7	22.7	24.0
	F	18.4	19.7	21.6
PA *rad*	M	4.5	5.2	6.2
	F	4.2	4.8	5.4

Table 8. Independent predictors of death in 131 HD patients in the multivariate regression model

	χ^2	*P* value
Age	5.67	0.017
PA	17.77	0.0000
MAMC	1.37	0.24
SA	3.95	0.047
SGA	11.14	0.0008
nPCR	3.2	0.074

were so large as to bring about a clinically evident reduction in muscular mass. This observation agrees with previous studies in nonuremic individuals [22, 23]. Forbes, Simon and Amatruda [22] reviewed seven studies of adults undergoing changes in body weight due to diet plus exercise. Only two of these studies showed significant correlations between the changes in LBM, assessed by independent methods, and the changes in Rz. By contrast, five of the seven studies showed a significant relationship between the changes in LBM and changes in body weight. The authors concluded that "body wt change appears to be more reliable predictor of LBM change than is change in body resistance."

On the other hand, our findings seem to disagree with the results of a recent study on HD patients [3], but a close scrutiny of the data show that the discrepancies are more apparent than real. In this study, Chertow et al found in HD patients a high correlation (r = 0.92) between BCM derived from BIA and that estimated by the reference method (dual-energy X-ray absorptiometry and NaBr space). However, the differences between the results of the two methods had such wide a range, from 0 to nearly −15 kg, as to make uncertain the validity of the BIA estimates. Moreover, they failed to find significant correlations between the BIA estimates and most nutritional indexes in their population sample, which was considerably smaller than ours.

The limitations outlined above might be overcome with the use of the multi-frequency BIA (MFBIA), which is becoming increasingly popular. Because at low frequency the electrical current passes predominantly through extracellular fluids, while at higher frequency it can penetrate the cell membrane and thus pass through both intracellular and extracellular fluid, MFBIA could provide more accurate estimates than the single-frequency BIA of the extracellular water and total body water [24], and hence a more reliable index of the nutritional status [6]. However, a recent study on surgical patients failed to show any significant improvement of MFBIA over BIA when both methods were matched with the reference radioisotopic methods used to assess total body water and extracellular water [25]. The authors attributed the failure of MFBIA to reduce the error of the estimates to the difficulties inherent in the theory assuming the human body as homogeneous conductor of the electrical current. Should this be the case, one might overcome these problems by performing segmental body measurements. Pending such studies, the data at hand suggest that bioimpedance measurements can provide, at most, a generic index of health derangement in HD patients, and as such are only indirectly related to the nutritional status. In this regard, the clinical implications of the PA resemble that of the SA. Even though neither index can be considered a specific marker of lean body mass depletion [26], each tends to reflect the severity of the patient's "sickness." Therefore, it is usual to find that both are deranged in the more compromised patients, as we did in the cross sectional assessment. However, since they express quite different aspects of the disease process, it comes as no surprise that they follow independent courses over the follow-up period, as we observed in the longitudinal assessment.

The growing importance of nutritional assessment in the management of dialysis patients stems from observations showing that several nutritional indexes are significantly associated with patient survival [27–29]. Therefore, the appraisal of a new nutritional index should include the assessment of its prognostic bearings. We did so, and found that, notwithstanding its limited value as a nutritional index, PA was significantly associated with survival. In fact, patients having PA values within the lower quartile at baseline showed a much lower two-year survival rate (51.3%) than those having higher values (91.3%). It appears unlikely that this is a fortuitous association due to fleeting abnormalities of PA detected at the moment of baseline determinations, because most patients categorized in the lower PA quartile at baseline were still within this category several months later. Moreover, the shorter survival of these patients is not an unexpected result, because at baseline they showed worse prognostic markers than those in the upper quartiles. Indeed, the Cox analysis showed that PA was associated with survival more strongly than age or nutritional indexes previously shown to be endowed with prognostic power [27–29]. The prognostic importance of PA is supported also by a recent study in AIDS patients [30] where this index was found to be a more powerful predictor of their long-term survival than the usual nutritional indexes. It is difficult to provide a plausible explanation for these empirical observations, because the biological meaning of PA is not yet fully understood. Some authors believe that PA might reflect derangements in the electrical charges of cell membranes, which are often associated to an altered water partitioning between the intracellular and extracellular compartment [30–31], but direct evidence supporting this interpretation is lacking. Whatever the mechanism, these observations suggest that PA reflects some dimension of the illness that is not fully identifiable with the deranged nutritional status, which must be important for the prognosis. Obviously, these results need to be confirmed on larger patient populations before being accepted as conclusive. Moreover, further studies are required to clarify the biological meaning of the bioelectrical indexes in order to better understand their abnormalities in disease states.

In conclusion, compared with normal population a substantial proportion of HD patients showed marked changes in bioimpedance indexes. These indexes appeared to be little reliable in detecting the gross changes in lean body mass. However, compared with the usual nutritional parameters, PA appeared to be a better prognostic index of patient mortality. Our and analogous observations reported by others suggest that PA reflects some as yet unknown biologic properties, of which the nutritional status is but one expression.

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Reprint requests to Quirino Maggiore, M.D., Dialysis and Nephrology Unit, S. Maria Annunnziata Hospital, USL 10, 50011 Florence, Italy.

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