A low bioimpedance phase angle predicts a higher mortality and lower nutritional status in chronic dialysis patients

2010 J. Phys.: Conf. Ser. 224 012104

(http://iopscience.iop.org/1742-6596/224/1/012104)

A low bioimpedance phase angle predicts a higher mortality and lower nutritional status in chronic dialysis patients

Francis Dumler MD

Division of Nephrology, William Beaumont Hospital, Royal Oak, MI 48073, USA

fdumler@beaumont.edu

Abstract. Bioelectrical impedance analysis is an established technique for body composition analysis. The phase angle parameter, an index of body cell mass, tissue hydration, and membrane integrity, makes it suitable for assessing nutritional status and survivability. We evaluated the significance of a low phase angle value on nutritional status and mortality in 285 chronic dialysis patients during a longitudinal prospective observational study. Patients in the lower phase angle tertile had decreased body weight, body mass index, fat free mass, body cell mass, and lower serum albumin concentrations than those in the higher tertile (P<001). In addition, mortality rates were significantly lower (P=0.05) in the highest tertile patients. In conclusion, the phase angle is a useful method for identifying dialysis patients at high risk for malnutrition and increased mortality.

1. Introduction

The evaluation of nutritional status is of significance importance in the care of dialysis patients. Even though improvements in management of cardiovascular diseases, infections, and dialysis therapies have been significant, mortality in the chronic kidney disease population continues unabated. Malnutrition, whether alone or in association with a micro inflammatory state, affects 30-70% of patients and is clearly identified as a significant risk factor for survival [1-4]. Anthropometric and biochemical parameters have been traditionally used for nutritional assessment in clinical practice. More recently, bioelectrical impedance analysis (BIA) has established itself as a technique for evaluating body composition and nutritional status [5]. In addition, the phase angle parameter (arctangence of the reactance to resistance ratio) provides an index of tissue hydration, cell membrane integrity, and cell mass [6]. The objective of this study was to determine if a low phase angle is associated with a decreased nutritional status and/or higher mortality in chronic dialysis patients.

2. Patients and methods

This is a prospective longitudinal observational study of 285 chronic maintenance dialysis patients. Bioelectrical impedance analysis was done with a single 50 kHz frequency analyzer using tetrapolar electrodes attached to the ipsilateral wrist and ankle 15 minutes post hemodialysis or before a fill in peritoneal dialysis patients. Even at this low frequency the influence of stray capacitance cannot be neglected. For this reason, a parallel model (Cyprus™ 1.2 RJL Systems, MI, USA) was used for body composition calculations [7]. Briefly, this model assumes a parallel circuit composed of a resistor Rp positioned in parallel with a capacitor Cp, where both electrical processes occur independently, thus allowing evaluation of the bulk electrical properties of tissues.

Parameters: body weight, body mass index and serum chemistries (blood urea nitrogen, creatinine, and albumin) were evaluated monthly. Bioimpedance parameters (phase angle, and derived body cell mass, fat free mass and fat mass) were measured biannually. Fat free mass was calculated as:

Males: $-10.68 + 0.65 \times (\text{Height}^2/\text{Resistance}) + 0.26 \times \text{Weight} + 0.02 \times \text{Resistance}$

Females: $-9.35 + 0.69 \times (\text{Height}^2/\text{Resistance}) + 0.17 \times \text{Weight} + 0.02 \times \text{Resistance}$

Statistical analysis: mean values for the entire observation period were obtained. Patients were divided into tertiles according to phase angle values. Comparisons between tertile groups were made by analysis of variance and post hoc testing.

3. Results

Demographic characteristics were as follow: age: 62 ± 14 years; weight: 75 ± 18; body mass index: 26.3 ± 5.2 kg/m2, 59% male, and 37% black. The prevalence of diabetes was 43%. Dialysis modality was 72% hemodialysis and 28% peritoneal dialysis. The median observation time was 18 months.

Body weight and body mass index values were significantly different in the phase angle tertile groups ($P < 0.001$); with the lesser values corresponding to the lower tertile in both hemodialysis and peritoneal dialysis patients (table 1, table 2). No differences were noted in mean phase angle values between hemodialysis and peritoneal dialysis patients. As expected, peritoneal dialysis patients had a higher body weight than their hemodialysis counterparts. Biochemical profiles were also significantly different in the tertile groups ($P < 0.001$) with the smallest values in the low tertile group in both hemodialysis and peritoneal dialysis patients (table 1, table 2). No differences were noted in mean phase angle values between hemodialysis and peritoneal dialysis patients. As expected, peritoneal dialysis patients had lower serum albumin concentrations than their hemodialysis counterparts.

In hemodialysis and peritoneal dialysis patients significant differences between all tertile groups were noted for body cell and fat free mass ($P < 0.01$). Fat mass was decreased only in the lowest tertile hemodialysis group (table 1). Further analyses were done combining hemodialysis and peritoneal dialysis patients. All nutritional parameters were significantly lower ($P < 0.05$) in the low tertile group when compared to the other groups (table 3). Mortality rates, calculated per 1000 patient months, was significantly decreased ($P< 0.05$) in the upper tertile group (table 3).

4. Discussion

The use of bioelectrical impedance analysis is becoming more widespread in the renal community due to ease of use and a low coefficient of variation for the direct measurements (±1%). In addition, several population reference values have been reported recently [6-10]. This facilitates comparisons between patients and a more specific general (healthy) population. Its reliability and sensitivity also makes it very useful for longitudinal monitoring of chronic kidney disease patients.

This study demonstrates that bioelectrical impedance analysis, in particular the phase angle, is a useful clinical tool for detecting malnutrition in dialysis patients. The phase angle reflects the relative contribution of body fluid (resistance) and cellular membrane integrity (capacitance). Malnutrition reduces cellular membrane mass and integrity and promotes shifts in fluid balance. As a consequence of these changes the phase angle decreases. Conversely, a higher phase angle implies larger body cell mass and preserved membrane integrity.

Patients with smaller phase angle values, defined by < 4.10 (lowest tertile group), had lower body weight and body mass index than their counterparts. In addition, serum creatinine concentration was concomitantly decreased, implying less dietary protein intake and lower muscle mass. Finally, body cell mass and fat free mass were also decreased in patients with a low phase angle.

The finding of a lower mortality rate among patients in the higher phase angle tertile is expected, as this group had a better nutritional status. One large multicenter study has shown a direct relationship between phase angle and survival in hemodialysis patients [1]. Another study in forty eight peritoneal dialysis patients found a close relationship between phase angle and mortality [11]. Our study has the advantage of including a relatively large patient population treated at a single facility by the same health care team.

Uremic malnutrition and chronic inflammation are highly prevalent in maintenance dialysis patients [12]. A low phase angle may be a consequence of both processes. Of interest in this regard is the observation that phase angle is a predictor of all-cause mortality after adjusting for serum C-reactive protein concentrations [13]. The use of ultrapure dialysis fluid and polyamide dialyzers for on-line predilution hemodiafiltration over a six month period has also been linked to a significant decrease in inflammatory markers and improved nutritional parameters [14]. In that particular study a dramatic fall in C-reactive protein was time related to a significant increase in phase angle. Of interest, several studies have shown an inverse relationship between phase angle and survival rates in a variety of disease processes including HIV, post-operative complications, cancer, and cirrhosis [6, 15].

In conclusion, these results suggest that bioelectrical impedance analysis and phase angle measurements are a useful tool for identifying dialysis patients at high risk for malnutrition and/or increased mortality.

References

[1] Chertow GM, Johansen KL, Lew N, Lazarus JM and Lowrie EG 2000 Vintage, nutritional status, and survival in hemodialysis patients *Kidney Int.* **57** 1176-81

[2] Pifer TB, McCullough KP, Port FK, Goodkin DA, Maroni BJ, Held PJ and Young EW 2002 Mortality risk in hemodialysis patients and changes in nutritional indicators: DOPPS Kidney Int. **62** 2238-45

[3] Dwyer JT, Larive B, Leung J, Rocco MV, Greene T, Burrowes J, Chertow GM, Cockram DB, Chumlea WC, Daugirdas J, Frydrych A and Kusek JW for the HEMO Study Group 2005 Are nutritional status indicators associated with mortality in the hemodialysis (HEMO) study? *Kidney Int.* **68** 1766-76

[4] Araújo CI, Kamimura MA, Draibe SA, Canziani MEF, Manfredi SR, Avesani CM, Sesso R and Cuppari L 2006 Nutritional parameters and mortality in incident hemodialysis patients *J. Renal Nutr.* **16** 27-35

[5] Dumler F and Kilates C 2000 Use of bioelectrical impedance techniques for monitoring nutritional status in chronic dialysis patients *J. Renal Nutr.* **10** 116-24

[6] Selberg O and Selberg D 2002 Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis *Eur. J. Appl. Physiol.* **86** 509-16

[7] Dumler F and Kilates C 2003 Body composition analysis by bioelectrical impedance in chronic maintenance dialysis patients: comparisons to the National Health and Nutrition Examination Survey III *J. Renal Nutr.* **13** 166-72

[8] Piccoli A, Pillon L and Dumler F 2002 Impedance vector distribution by sex, race, body mass index, and age in the United Status: standard reference intervals as bivariate Z-scores *Nutrition* **18** 153-67

[9] Barbosa-Sila MC, Barros AJ, Wang J, Heymsfield SB and Pierson RN Jr 2005 Bioelectrical impedance analysis: population reference values for phase angle by age and sex *Am. J. Clin. Nutr.* **82** 49-52

[10] Jha V, Jairam A, Sharma MC, Sakhuja V, Piccoli A and Parthasarathy S 2006 Body composition analysis with bioelectric impedance in adult Indians with ESRD: comparison with healthy population *Kidney Int.* **69** 1649-53

[11] Mushnick R, Fein PA, Mittman N, Goel N, Chattopadhyay J and Avram MM 2003 Relationship of bioelectrical impedance parameters to nutrition and survival in peritoneal dialysis patients *Kidney Int.* 64: S53-6

[12] Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM and Kopple JD 2003 Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences *Am. J. Kidney Dis.* **42** 864-81

[13] Pupim LB, Caglar K, Hakim RM, Shyr Y and Ikizler TA 2004 Uremic malnutrition is a predictor of death independent of inflammatory status *Kidney Int.* **66** 2054-60

[14] Savica V, Ciolino F, Monardo P, Mallamace A, Savica R, Santoro D and Bellinghieri G 2006 Nutritional status in hemodialysis patients: option for on-line convective treatment *J. Renal Nutr.* **16** 237-40
[15] Gupta D, Lammersfeld CA, Vashi P, King J, Dahlk SL, Grutsch JF and Lis CG 2009 Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer *BMC Cancer* **9** 37

Table 1. Nutritional and biochemical parameters in chronic hemodialysis patients.

	Lower Tertile (n=64)	Middle Tertile n=97)	Upper Tertile (n=46)
Phase Angle(º):*	3.64 ± 0.44	5.04 ± 0.53	6.83 ± 0.48
Weight (kg):*	66.1 ± 13.8	76.3 ± 18.5	82.5 ± 16.7
Resistance (ohms):	582 ± 126	540 ± 91	522 ± 111
BMI (kg/m^2):*	23.1± 3.8	26.7 ± 6.0	28.2 ± 6.0
S. Creatinine: (mg/dL)*	7.3 ± 2.2	8.9 ± 2.6	11.9 ± 2.7
S. Albumin (g/L):*	37.1 ± 3.3	39.5 ± 3.2	40.4 ± 2.3
Body Cell Mass (kg)*	19.9 ± 4.8	23.0 ± 5.6	28.5 ± 6.8
Fat Free Mass (kg)*	51.6 ± 11.6	53.2 ± 12.8	59.9 ± 14.4
Fat Mass (kg)	15.1 ± 8.6†	22.8 ± 12.1	22.6 ± 8.3

*P < 0.001 (difference between all groups) †P<0.01(difference between lower and upper tertile groups)

Table 2. Nutritional and biochemical parameters in chronic peritoneal dialysis patients.

	Lower Tertile(n=64)	Middle Tertile (n=97)	Upper Tertile (n=46)
Phase Angle (º):*	3.68 ± 0.38	5.11 ± 0.54	6.60 ± 0.45
Weight (kg):*	76.8 ± 16.4	78.2 ± 14.9	87.9 ± 11.6
Resistance (ohms)	503 ± 126	497 ± 124	465 ± 85
BMI (kg/m^2):	27.2 ± 3.8	26.9 ± 4.7	28.9 ± 4.5
S. Creatinine: (mg/dL)*	7.6 ± 2.7	11.0 ± 4.5	11.7 ± 4.5
S. Albumin (g/L):*	32.5 ± 5.4	35.5 ± 5.4	38.9 ± 3.6
Body Cell Mass (kg)*	21.3 ± 6.4	25.4 ± 6.1	30.2 ± 6.5
Fat Free Mass (kg)*	54.7 ± 16.0	58.0 ± 14.1	63.0 ± 13.0
Fat Mass (kg)	20.9 ± 6.5	25.4 ± 6.1	30.2 ± 6.5

*P < 0.001 (difference between all groups)

Table 3. Bioimpedance, nutritional and mortality parameters in the combined dialysis population.

	Lower Tertile (n=90)†	Middle Tertile (n=132)	Upper Tertile (n=36)
Phase angle (º):	3.65 ± 0.42	5.06 ± 0.53	6.78 ± 0.48
Weight (kg):*	69.2 ± 15.3	76.8 ± 17.6	84.0 ± 15.6
Resistance (ohms):	555 ± 123	528 ± 102	503 ± 105
BMI (kg/m^2):	24.3 ± 4.5	26.9 ± 5.7	28.4 ± 5.6
Fat Free Mass (kg):*	52.3 ± 12.7	55.0 ± 13.4	60.0 ± 14.1
Body Cell Mass (kg):*	20.3 ± 5.2	23.7 ± 5.8	28.6 ± 6.7
Expired:	41	50	13
Patient months:	1,518	2,673	982
Mortality (%):	45	38	18
x1000 pt. months:*	27	19	12

*P<0.05 (difference between all groups) †P<0.01(difference between lower and upper tertile groups)