Bioelectrical impedance phase angle as a predictor of survival in patients with advanced cancer.

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Abstract— **Bioelectrical impedance phase angle is a potentially sensible indicator of alterations in body composition due to malnutrition, frequent in advanced cancer patients. Malnutrition is characterized by changes in cellular membrane integrity and alterations in fluid balance leading to alterations in body composition. Aim of this study was to investigate the role of phase angle as a predictor of survival in patients with advanced cancer. Twenty patients (12 males, 8 females: age 50.2 ± 3.2 years, weight 51.9 ± 7.1 kg; BMI 19.8 ± 1.8 kg/m²), with advanced cancer were evaluated. Single-frequency BIA was carried out and the BIA variables, resistance (*R*), reactance (Xc) and phase angle (PhA), were measured. Some anthropometric and biochemical parameters were performed in all patients. Phase angle resulted strictly related (*p* <0.001) with survival time, slightly (p = 0.055) related with lymphocyte count, but not related with the other anthropometric and biochemical parameters evaluated. Identification of a predictor of survival in advanced cancer patients is important to improve the therapeutic programme for the disease. Phase angle seems to have a role as a marker of morbidity and mortality in a wide range of disease conditions. Similar studies on larger sample sizes are needed to further validate the prognostic significance of phase angle in advanced cancer patients.**

Keywords— **BIA, phase angle, cancer, time survival, malnutrition**

I. Introduction

Malnutrition is a frequent manifestation of advanced cancer and is a major contributor to morbidity and mortality [1]. Malnutrition is characterized among others by changes in cellular membrane integrity and alterations in fluid balance [2]. As a result, measurement of body composition is an important component of overall nutritional evaluation in cancer patients [3-5]. Nutritional status has been evaluated by different measures, including anthropometric (weight change, arm muscle circumference, and triceps skinfold thickness) and laboratory (serum albumin, transferrin assays) measurements. Bioelectrical Impedance Analysis (BIA) is an easy-to-use, non invasive, and reproducible technique for evaluating changes in body composition. BIA has been validated for the assessment of body composition and nutritional status in several chronic diseases, including cancer patients [1, 4, 6-16]. BIA measures body component resistance (*R*) and capacitance (*X*c) by recording a voltage drop in applied current [17]. Capacitance causes the current to lag behind the voltage, which creates a phase shift. This shift is quantified geometrically as the angular transformation of the ratio of capacitance to resistance, or the phase angle [18]. Phase angle, calculated as capacitance (Xc)/resistance (R) and expressed in degrees, reflects the relative contributions of fluid (resistance) and cellular membranes (reactance) of the human body. Lower phase angle suggests cell death or decreased cell integrity, while higher phase angle suggests large quantities of intact cell membranes. Phase angle has been found to be a prognostic marker in several clinical conditions, such as HIV infection, liver cirrhosis, chronic obstructive pulmonary disease, hemodialysis, sepsis, and lung cancer [19-25].

Aim of the present study was to evaluate the association of BIA-derived phase angle with survival in patients with different type of cancer.

II. Writing the paper

A. Patients and Methods

Twenty patients (12 males, 8 females: age 50.2 ± 3.2 years, weight 51.9 ± 7.1 kg; BMI 19.8 ± 1.8 kg/m²), with advanced cancer consecutively referred to the Clinical Nutrition Unit of Federico II University, in Naples for artificial nutrition procedure were evaluated. Primary cancer localization was colorectal in 5, gastric in 7, esophageal in 3, pancreatic in 3 and pulmonary in 2. All measurements were performed by the same operator following standard procedures. Weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. Body mass index (BMI) was then calculated as weight (kg)/height²(m²).Single-frequency BIA was carried out by the same operator using a BIA 101(injection of an alternating current, at 800 μA and 50 kHz) (RJL⁄Akern System, Florence, Italy). Measurements were performed on the non-dominant side of the body, at room temperature of 22–24 ◦C, after voiding and after being in the supine position for 20 min. The BIA variables considered were resistance (*R*), reactance (Xc), and phase angle (PhA). Laboratory measurements (serum albumin, prealbu-

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min and transferrin, cholesterol, lymphocytes, haemoglobin, cholinesterase) were also performed.

All patients were free of visible edema or ascites so there was control for obvious overhydration.

The survival time was calculated from the day of first patient visit to the hospital to the date of death from any cause. The Kaplan-Meyer method was used to calculate survival and Cox model to evaluate the prognostic effect of phase angle independently of other clinical and nutritional variables. A difference was considered to be statistically significant if the *p* value was less than or equal to 0.05.

B. Results

In the sample as a whole, the following parameters were registered: age 50.2±3.2 (range 42-61) years, weight 51.9 ± 7.1 (34-64) kg; BMI 19.8 ± 1.8 (13.7-22.6) kg/m²); weight loss 14.3 ± 6.5 kg in the last 6 months. Serum albumin levels were 3.35 ± 0.33 g/dl, cholesterol 136 ± 21.3, cholinesterase 5419 ± 1421, lymphocytes 1219 ± 390 mm^3, thus indicating that the study sample as a whole was at high nutritional risk.

Phase angle (mean 4.25 ± 1.2; range 2.86 to 5.91) resulted strictly related ($r = 0.420$, $p < 0.001$) with survival time, slightly ($p = 0.055$) related with lymphocyte count, but not related with the other anthropometric and biochemical parameters evaluated.

C. Discussion

A similar study carried out in patients with advanced lung cancer stratified the patient cohort by the mean phase angle score of 4.5 [25]. Patients with phase angle scores less than or equal to 4.5 had a significantly shorter survival than those with phase angle scores greater than 4.5. Similarly, in advanced colorectal cancer patients, phase angle above the median cut-off of 5.6 was associated with better survival [26]. In stage IV pancreatic cancer, phase angle above the median cut-off of 5 was associated with longer survival [27]. Similar studies on larger sample sizes are needed to further validate the prognostic significance of phase angle in advanced cancer patients.

III. CONCLUSIONS

It is of great relevance from a clinical point of view to identify possible survival predictors in advanced cancer patients. Phase angle reflects not only body cell mass, but it is also one of the best indicators of cell membrane function, related to the ratio extracellular/intracellular water and has been indicated to be an indicator of the nutritional status. This preliminary study confirms phase angle as a prognostic indicator in patients with advanced cancer, independently from the site of primary tumor and it seems to have a role as a marker of morbidity and mortality in a wide range of disease conditions.

REFERENCES

1. Sarhill N, Mahmoud FA, Christie R et al. (2003) Assessment of nutritional status and fluid deficits in advanced cancer. Am J Hosp Palliat Care 20:465–73
2. Barbosa-Silva MC, Barros AJ, Post CL et al. (2003) Can bioelectrical impedance analysis identify malnutrition in preoperative nutrition assessment? Nutrition 19:422–6
3. Cox-Reijven PL, van Kreel B, Soeters PB (2003) Bioelectrical impedance measurements in patients with gastrointestinal disease: validation of the spectrum approach and a comparison of different methods for screening for nutritional depletion. Am J Clin Nutr 78:1111–9
4. Fredrix EW, Saris WH, Soeters PB et al. (1990) Estimation of body composition by bioelectrical impedance in cancer patients. Eur J Clin Nutr 44:749–52
5. Kushner RF (1992) Bioelectrical impedance analysis: a review of principles and applications. J Am Coll Nutr 11:199–209
6. Nagano M, Suita S, Yamanouchi T (2000) The validity of bioelectrical impedance phase angle for nutritional assessment in children. J Pediatr Surg 35:1035–9
7. Marken Lichtenbelt WD, Westerterp KR, Wouters L et al. (1994) Validation of bioelectrical-impedance measurements as a method to estimate body-water compartments. Am J Clin Nutr 60:159–66
8. Desport JC, Preux PM, Bouteloup-Demange C et al. (2003) Validation of bioelectrical impedance analysis in patients with amyotrophic lateral sclerosis. Am J Clin Nutr 77:1179–85
9. Adami GF, Marinari G, Gandolfo P et al. (1993) The use of bioelectrical impedance analysis for monitoring body composition changes during nutritional support. Surg Today 23:867–70
10. Azcue M, Fried M, Pencharz PB et al. (1993) Use of bioelectrical impedance analysis to measure total body water in patients with cystic fibrosis. J Pediatr Gastroenterol Nutr 16:440–5
11. Chertow GM, Lowrie EG, Wilmore DW et al. (1995) Nutritional assessment with bioelectrical impedance analysis in maintenance hemodialysis patients. J Am Soc Nephrol 6:75–81
12. Fein PA, Gundumalla G, Jorden A et al. (2002) Usefulness of bioelectrical impedance analysis in monitoring nutrition status and survival of peritoneal dialysis patients. Adv Perit Dial 18:195–9
13. Lukaski HC, Johnson PE, Bolonchuk WW et al. (1985) Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 41:810–7
14. Pencharz PB, Azcue M (1996) Use of bioelectrical impedance analysis measurements in the clinical management of malnutrition. Am J Clin Nutr 64(suppl):485S–8S
15. Pupim LB, Kent P, Ikizler TA (1999) Bioelectrical impedance analysis in dialysis patients. Miner Electrolyte Metab 25:400–6
16. Simons JP, Schols AM, Westerterp KR et al. (1995) The use of bioelectrical impedance analysis to predict total body water in patients with cancer cachexia. Am J Clin Nutr 61:741–5
17. Zarowitz BJ, Pilla AM (1989) Bioelectrical impedance in clinical practice. DICP 23:548–55.
18. Baumgartner RN, Chumlea WC, Roche AF (1988) Bioelectric impedance phase angle and body composition. Am J Clin Nutr 48:16–23
19. Selberg O, 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

20. Faisy C, Rabbat A, Kouchakji B et al. (2000) Bioelectrical impedance analysis in estimating nutritional status and outcome of patients with chronic obstructive pulmonary disease and acute respiratory failure. Intensive Care Med 26:518–25
21. Maggiore Q, Nigrelli S, Ciccarelli C et al. (1996) Nutritional and prognostic correlates of bioimpedance indexes in hemodialysis patients. Kidney Int 50:2103–8
22. Ott M, Fischer H, Polat H et al. (1995) Bioelectrical impedance analysis as a predictor of survival in patients with human immunodeficiency virus infection. J Acquir Immune Defic Syndr Hum Retrovirol 9:20–5
23. Schwenk A, Ward LC, Elia M et al. (1998) Bioelectrical impedance analysis predicts outcome in patients with suspected bacteremia. Infection:277–82
24. Schwenk A, Beisenherz A, Romer K et al. (2000) Phase angle from bioelectrical impedance analysis remains an independent predictive marker in HIV-infected patients in the era of highly active antiretroviral treatment. Am J Clin Nutr 72:496–501
25. Toso S, Piccoli A, Gusella M et al. (2000) Altered tissue electric properties in lung cancer patients as detected by bioelectric impedance vector analysis. Nutrition 16:120–4
26. Gupta D, Lis CG, Dahlk SL et al. (2008) The relationship between bioelectrical impedance phase angle and subjective global assessment in advanced colorectal cancer. Nutr J 30:7–19
27. Gupta D, Lis CG, Dahlk SL et al. (2004) Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. Br J Nutr 92(6):957–62

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