Bioelectrical phase angle on hospital admission as predictor of short- and middle-term mortality in elderly medical patients

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Malnutrition in elderly hospitalized patients is a significant public health problem affecting 60-70% of this subpopulation. In fact, it is recognized as an important independent risk factor for morbidity and mortality. To date there are no well-defined clinical, instrumental and blood markers to diagnose malnutrition in this specific group of patients and to allow adequate follow-up of nutritional treatment as well as to predict events. The bioelectrical impedance analysis (BIA) is now a widely used method for the evaluation of body composition. In particular, the phase angle (PA), a BIA derived indicator based on body resistance and reactance and resistance, is assumed as an indicator of cellular membrane integrity and water distribution between the intra- and extra-cellular spaces and for these reasons it has also been used as an indicator of general and nutritional wellness. Moreover, even the Mini Nutritional Assessment (MNA) is a test that has been used for the assessment of nutritional status in the elderly.

This study was carried out to evaluate longitudinally the ability of BIA and MNA tests to predict mortality in the short and medium term beyond the traditional anthropometric and laboratory measurements in a group of hospitalized elderly patients.

One-hundred-fifty patients aged 73.5±7.9 years (mean ± sd) admitted to the internal medicine ward were included in the study regardless of the admitting diagnosis. After discharge clinical informations were obtained via telephone contact every 4 months with a maximum follow-up duration of 16 months (4 months: n = 130, 8 months: n = 94, 12 months n = 24, 16 months: n = 7 patients). At the end of the observation period 12 deaths were recorded. The definition of malnutrition according to the MNA was not able to predict mortality (P= 0.73). According to the median values of PA (4.0°), MNA (22) and serum albumin concentration (2.7 g/dl), the values of these variables were dichotomized as "low" or "high" respectively when below or above the median value. A low PA value was able to predict mortality (figure 1A) and even more when a cluster that aggregates low PA, low MNA and low albumin concentrations was considered (figure 1B).

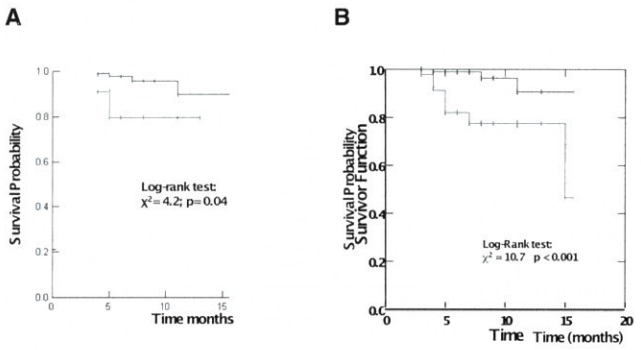

Figure 1. Kaplan-Meyer curves describing the probability of surviving of resident elderly medical patients according to (A) the value of PA (≤ 4.0°, red –lower- line; >4.0°, blue –upper- line) or (B) a combination of PA ≤ 4.0° + albuminemia ≤ 2.7 mg/dl + score of MNA test < 22 (red –lower- line) or, respectively, > 4° + > 2.7 mg/dl + ≥ 22 (blue –upper- line).

Although the preliminary results of this study need to be confirmed in a larger sample of patients and for a longer follow-up period, it seems that BIA is a good candidate for the diagnosis of malnutrition and to predict mortality.

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Indirect calorimetry demonstrates that resting energy expenditure is increased in patients with poorly controlled diabetes and is normalized by insulin bolus

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It has been suggested that an increase in energy expenditure may promote the body weight reduction which is usually observed in diabetic patients with poor metabolic control.

Therefore, the resting energy expenditure (REE) was measured using a ventilated hood system of indirect calorimetry (Quark RMR; Cosmed, Roma, Italy) in 20 patients (8 males, 12 females) with poorly controlled type 2 diabetes (body mass index -BMI-: 34.3±2.1 kg/m^2; fasting plasma glucose -FPG-: 11.1±0.5 mmol/l), treated with oral hypoglycemic agents (n= 14) or nutritional treatment alone (n= 6). A group of non-diabetics (n= 14, 8 males and 6 females) with similar age and body size to that of the diabetic group (BMI: 35.2±1.9 kg/m^2, P= 0.76; FPG: 4.8±0.2 mmol/l, P< 0.001) was included as control group.

The diabetic group exhibited a REE normalized for the fat-free mass size (FFM, bioelectrical impedance; BIA-103, RJL, Detroit, MI, USA/Akern, Florence, Italy) higher by 6.8% (+123 kcal/24h, P = 0.04) than that of non diabetics.

Furthermore, the value of normalized REE for FFM was significantly correlated to the value of FPG (r= 0:58, P= 0.04) in diabetic patients, suggesting that the higher REE is dependent on glycemic control. As known, the value of FPG is strongly influenced by the gluconeogenesis, an energetically wasteful metabolic process. Therefore, the high REE observed in diabetic patients might be in consequence of the increased gluconeogenetic metabolism. In order to verify this hypothesis, it was administered an IV bolus of regular insulin (0.2 IU kg body weight; Actrapid®, NovoNordisk, Denmark) in 5 diabetic participants. Following the insulin bolus a progressive reduction of REE was observed as follows (REE change): 10 min: -11.6%; 20 min: -17.4%; 30 min: -19.9%; 45 min: -22.0%; 60 min: -20.1%, P= 0.04), similar reductions of blood glucose and lactate concentrations were observed. In conclusion, diabetic patients with poor metabolic control have a higher energy expenditure probably in consequence of a significantly higher activity of gluconeogenesis. This study may contribute, at least in part, to recognize the nature of body weight reduction that occurs in concomitance with poorly controlled diabetes and of body

weight gain as that commonly observed when the hypoglycemic treatment with, in particular, sulphonylureas and insulin is started.

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The BIA vector in obesity and diabetes

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Although the assessment of body water compartments is of great diagnostic value, appropriate methods are not readily available for routinely clinical application. Bioelectrical impedance analysis (BIA) is a safe, non-invasive, rapid and highly reproducible procedure that is strongly influenced by body water and intra-/extra-cellular distribution. Four-hundred-fifty-six adults (224 males and 232 females) were enrolled and divided in subgroups on the basis of the presence of obesity and diabetes (type 1 and type 2). The aim of the study was to investigate if different BIA measurements in terms of resistance (R), reactance (Xc) and phase angle (PA) were associated to these conditions. Plotting the average values of R and Xc normalized for height (h), a mean vector was obtained for each group. The vector displacement could be easily recognized on the basis of its length and of the angle described with the abscises axis (PA). When compared to the control groups, the vector resulted to be shorter in presence of obesity. The PA was slightly lower in the diabetic groups when compared to their body size matched non-diabetic groups. Fasting plasma glucose (FPG) was independently correlated to height normalized R (R/h) as in diabetic males ($r = 0.40$; $P < 0.001$) and in diabetic females ($r = 0.50$; $P < 0.001$). On the basis of BIA principles, these results are in agreement with the possibility that non diabetic obese patients have an increased body-water content but in average they maintain a distribution between intra- (ICW) and extra-cellular (ECW) water compartments similar to that of control subjects. Furthermore, diabetics have an increased ECW size and, as expected, with increasing FPG their body water content proportionally decreases. As a partial confirmation, the BIA vector of 9 diabetics with poor glycemic control was monitored during the course of rehydrating treatment. The BIA vector became progressively shorter but the PA remained unchanged. Therefore, the evolution of the BIA vector was in the sense of a progressive increase of total

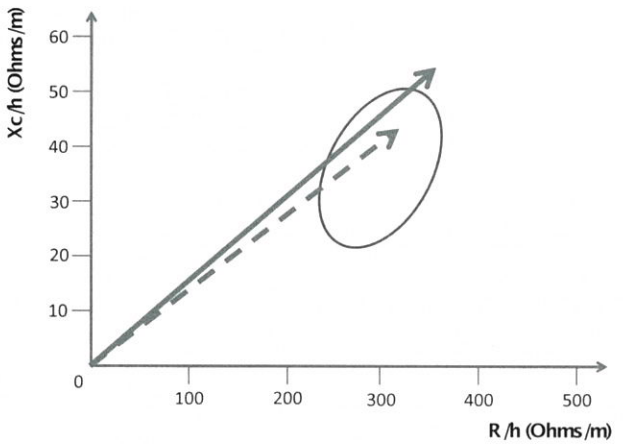

Figure 1. The average BIA vector of 9 male patients during poor diabetes control (FPG: 389±56 mg/dl; glycated hemoglobin: 11.2±1.1%; mean ± sd; solid arrow) and after hypoglycemic and rehydrating treatment (FPG: 164±28 mg/dl; dotted arrow).

body water content, equally distributed between ICW and ECW compartments. In conclusion, BIA measurements could be considered as specific body characteristics that expressed in terms of BIA vector may be useful to diagnose and monitoring imbalances of body water compartments.

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Identifying predictors of response to liraglutide in type 2 diabetes using recursive partitioning analysis

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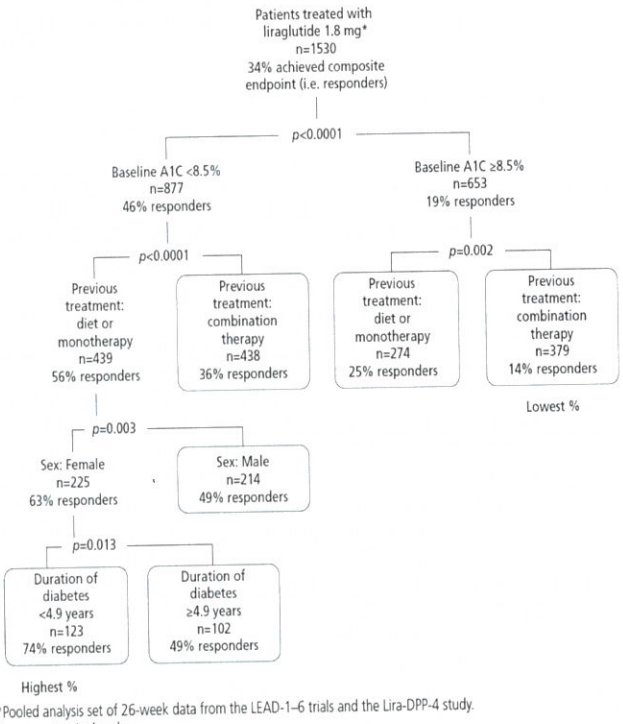
Randomized clinical trials provide unbiased databases for comparative effectiveness analyses to see which patients respond best to available interventions. We evaluated patient-level data pooled from 7 phase 3 clinical trials with liraglutide to examine responder subgroups, as defined by those achieving a composite endpoint of A1C <7%, no weight gain and no hypoglycemia (episodes requiring assistance or self-treated with PG <56 mg/dL) over 26 weeks. Overall 34% of individuals on liraglutide 1.8 mg achieved the prespecified composite endpoint: the highest response rate among compared therapies. Candidate predictor variables included baseline age, sex, ethnicity, BMI, A1C, beta-cell function, FPG, insulin resistance, previous treatments, and diabetes duration. Using recursive partitioning to create classification trees, baseline A1C was the most significant predictor, with a probability of achieving the composite outcome of 46% with baseline A1C <8.5% as opposed to 19% if baseline A1C ≥8.5% ($p<0.0001$). Subsequent splits (with p-values <0.05) produced a subgroup within pa-



*Pooled analysis set of 26-week data from the LEAD-1–6 trials and the Lira-DPP-4 study.
Boxes are terminal nodes.
A1C, glycated hemoglobin.

Figure 1.

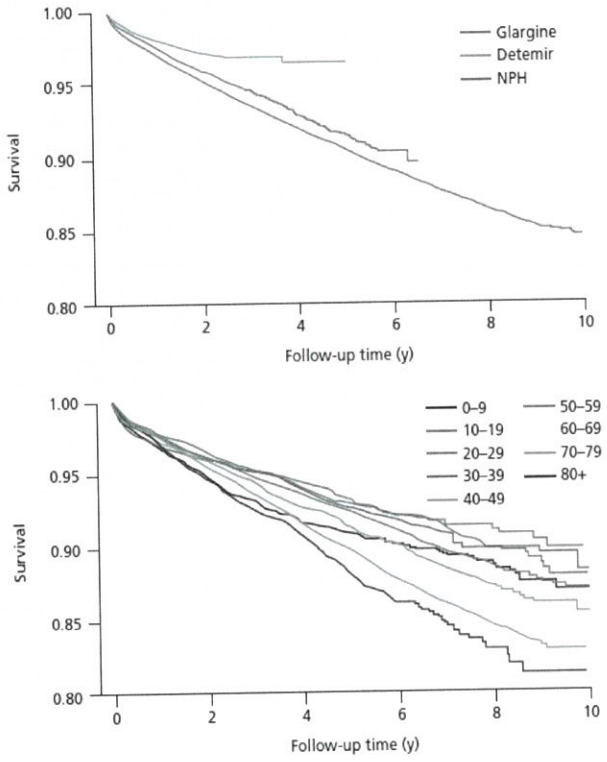


Figure.

tients with a baseline A1C <8.5% that was identified by previous treatment with diet or monotherapy, female sex, and diabetes duration <4.9 years increasing probability of success to 74%. Six homogeneous subgroups were identified with different probabilities of achieving the composite outcome (Fig). In summary, recursive partitioning identified individual characteristics and subgroups of patients predicting the response to therapy. Such analyses may guide clinicians in individualizing treatment approaches.

Type of insulin and age are predictors of hospitalization due to severe hypoglicemia: the epihypo study

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Incidence and recurrence of severe hypoglycemic (SH) events among patients with diabetes mellitus (DM) was evaluated in a retrospective nationwide register-based linkage study in Finland. SH was defined as a hospitalization or a secondary health care visit due to DM with severe hypoglycemia (ICD E10.00 or E11.00). Total population (n=140,035) comprised patients who purchased insulin during 2000–2009 and were followed-up for SH events until end of year 2009 or death. The present analysis comprised those 77,046 patients who had not used insulin glargine (IGla), insulin detemir (IDet) or NPH insulin (NPH) before year 2000. Stratified incidence rates with 95% CIs were calculated. Hazard ratios (HR) were estimated by Cox's proportional hazards model. 9716 SH events were identified. Type of DM (type 1 or 2) was not associated with risk of SH. Compared to IGla, risk of SH was lower during use of IDet (HR 0.76, CI 0.67–0.87), and higher during use of NPH (HR 1.19, CI 1.11–1.28) (Figure: upper panel). Female gender predicted lower risk (HR 0.93, CI 0.88–0.98), and increasing age predicted higher risk of SH (Figure: lower panel). Risk of SH recurrence was lower during IDet (HR 0.60, CI 0.52–0.69), and higher during NPH (HR 1.58, CI 1.46–1.71) compared to IGla.

In conclusion, our data show that increasing age and type of longacting insulin are predictors of hospitalization due to SH. Risk of hospitalization due to SH could potentially be modified by selection of long-acting insulin.

Different glucose tolerance status and endothelial function in newly diagnosed hypertensives

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Introduction: Endothelial dysfunction is an early marker of atherosclerotic disease and may predict cardiovascular events. Reactive hyperemia index (RHI) device is a non-invasive useful tool for assessment of endothelial function, providing information about the nitric oxide bioavailability. A plasma glucose value ≥155mg/dl for the 1-hour post-load plasma glucose (PLPG) during an oral glucose tolerance test (OGTT) identifies subjects with normal glucose tolerance (NGT) at high-risk for type-2 diabetes (T2D) and with subclinical organ damage.

Aim: We addressed the question if RHI varies according to different types of glucose tolerance status.