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Short communication

Association of mortality and phase angle measured by different bioelectrical impedance analysis (BIA) devices

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SUMMARY

Purpose: A high phase angle measured by the Nutriguard® bioelectrical impedance analysis device is associated with a reduced mortality risk in older people. This retrospective study aims to analyze whether this association persists with the other devices that have been used in our hospital.

Methods: This study encompasses all people 65 yrs and older who underwent a phase angle measurement between 1990 and 2011 at the Geneva University Hospitals, with the RJL-101® (RJL Systems), Xitron 4000B® (Xitron Technologies), Eugedia® (Eugédia-Spengler) and Bio-Z® (Spengler). Diseases at the time of phase angle measurement were reported in the form of the Cumulative Illness Rating Scale. Date of death was retrieved until December 2012. Phase angle values were categorized into sex- and device-specific quartiles, where quartile 1 represents the lowest quartile and reference value. Cox regressions were performed to evaluate the association between phase angle quartiles and mortality.

Results: We considered 1878 people (969 women), of whom 1151 had died. In univariate sex-specific Cox regressions, the death risk decreased progressively as the phase angle quartile measured by the Bio-Z® or RJL-101® increased. The HR (95% CI) in quartile 4 was 0.36 (0.26, 0.50) and 0.38 (0.29, 052) in women and men measured with the Bio-Z® (both $p < 0.001$), and 0.23 (0.14, 0.39) and 0.19 (0.10, 0.36) in women and men measured with the RJL-101® (both $p < 0.001$). The association between phase angle and mortality persisted when adjusted for age, body mass index or co-morbidities. The small number of deaths in people who underwent a measurement by Eugedia® ($n = 93$) or Xitron 4000B® ($n = 56$) did not allow performing multivariate Cox regressions.

Conclusions: Phase angle quartiles are associated with mortality in people aged ≥65 years when using the RJL-101® or Bio-Z device®.

1. Introduction

An increasing interest arises in the potential of phase angle to predict adverse outcomes like mortality [1–3]. Phase angle is a raw bioelectrical impedance analysis (BIA)-derived parameter which may reflect cell size, cell membrane integrity and/or the distribution of water in the extra- and intracellular compartments [4,5]. Mathematically, it can be obtained from the arctangent of the reactance to resistance ratio measured by BIA. Thus, phase angle values do not depend on equations and their inherent assumptions, in contrast to BIA-derived body composition, i.e. fat mass and fat-free mass.

In a recently published cohort study, we have included all people ≥65 yrs who had undergone a BIA measurement at the Geneva University Hospitals between 1990 and 2011 ($n = 3181$) [6]. Mortality was reported until December 2012. We have shown that the lower the phase angle quartile at the last BIA measurement performed with the Nutriguard® device ($n = 1307$) (Data Input GmbH, Darmstadt, Germany), the higher was the death risk, independently of the co-morbidities [7]. We had focused on the measurements performed with the Nutriguard® device because 1) this

Abbreviations: BIA, bioelectrical impedance analysis; BMI, body mass index; CIRS, Cumulative Illness Rating Scale.

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device is still used in our hospital, and 2) phase angle reference values using the same brand of BIA device have been published [8] and allowed us to standardize the values for age and body mass index (BMI).

However, we have not reported the association of mortality and the phase angle measured by the other BIA devices that we have used over the time span of 21 years. The rationale of performing additionally these analyses is that, in the absence of a gold standard, phase angle values likely differ between devices. This retrospective study aims to analyze whether phase angle values measured by the other BIA devices than the Nutriguard® are also associated with mortality.

2. Material and methods

We included the remaining 1878 people of our previously described cohort study [6], which encompassed all people ≥65 yrs who underwent a BIA measurement at the Geneva University Hospitals between 1990 and 2011. This study population included hospitalized and ambulatory patients followed in clinical routine by the nutrition unit, and healthy people recruited for research purpose in leisure clubs, the hospital staff, at fun runs and through advertisement in local newspapers. The proportion of hospitalized patients was about 50% ($n = 967$). BIA measurements were performed at 50 kHz and 0.8 mA, while the subject was lying in the supine position with electrodes placed on the right hand, wrist, angle and foot. The following devices were used: RJL-101® (1990–1995) (RJL Systems, Inc., Clinton Township, MI, USA), Xitron 4000B® (1990–2011) (Xitron Technologies, San Diego, CA, USA), Eugedia® (1994–2000) (Eugédia-Spengler, Cachan, France) and Bio-Z® (1996–2002) (Spengler, Paris, France). All devices were calibrated for phase angle with a calibration jig (CJ 4000, Xitron Technologies, San Diego, CA, USA), before their use in our institution. A limit of ±2° for phase angle and ±5Ω for impedance was tolerated at 50 kHz. To test method agreement, we had measured the phase angle values of 8 healthy people with the RJL-101®, the Xitron®, and the Bio-Z®, without changing the position of the people nor the placement of the electrodes. Method agreement, calculated as the mean phase angle difference (2SD) obtained from the Bio-Z® minus the RJL-101® or the Xitron®, was −1.49° (0.45) and −1.50 (0.24), respectively. We also calculated fat-free mass with the Geneva formula [9], which was validated against DXA specifically in older persons [10]. Fat mass was obtained by subtracting fat-free mass from body weight. Fat-free mass index and fat mass index were calculated as follows: fat-free mass or fat mass (kg)/body height $(m)^2$.

Date of death was considered until December 2012, and retrieved from the hospital computer database, the death registry of the state of Geneva and the Swiss National Cohort [11]. We reported co-morbidities at the time of the BIA measurement in the form of the Cumulative Illness Rating Scale (CIRS) [12]. It rates 14 systems and organs from 0 (healthy) to 4 (severe disease needing immediate intervention or hospitalization), and takes into account lifestyle modes as smoking and alcohol consumption. Its final score ranges from 0 (healthy) to 56 points.

2.1. Statistics

Results are shown as median (interquartile range) for continuous variables as they were not normally distributed according to Shapiro–Wilk tests. Comparisons between devices were performed with Kruskall–Wallis test.

Age, body mass index and CIRS were categorized like in our former study, because their distribution, tested by Shapiro–Wilks test, was not normal: age as 65–74 yrs, 75–84 yrs and ≥85 yrs, BMI as <18.5, 18.5–24.9, 25–29.9 and ≥30 kg/m^2 [13], and CIRS as quartiles of the population measured by the considered device. The association between mortality and device- and gender-specific phase angle quartiles was evaluated by univariate Cox regressions. We performed multivariate Cox regressions with adjustments for age (model 1), BMI (model 2) or CIRS categories (model 3) because we did not observe enough events to follow the rule of Harrell et al. [14]. This rule supposes a maximum of 1 variable for 10 events.

3. Results

The characteristics of the study subjects measured by the different BIA devices are shown in Table 1. They were significantly different regarding age, body mass index, co-morbidities and phase angle.

The small number of deaths in women ($n = 16$) and men ($n = 39$) who underwent a BIA measurement by Xitron 4000B precluded the use of sex-specific phase angle quartiles in the Cox regressions. We thus focused on the three other devices ($n = 1683$). In sex-specific univariate Cox regressions, the association between phase angle quartiles measured with the Bio-Z® and RJL-101® devices and mortality could be highlighted, although the cut-off quartiles differed between the BIA devices (Table 2). No association between phase angle and mortality was observed when using the Eugedia® device. Sex-specific multivariate Cox regressions could be performed with the Bio-Z® and the RJL-101® device (Table 3). They confirmed the findings of univariate Cox regressions even when adjusting for age, BMI or CIRS categories, i.e. the higher the phase angle quartile, the lower the death risk.

4. Discussion

This study shows that the mean phase angle values differed significantly between the subjects measured with the Bio-Z®, RJL-101®, Eugedia® and Xitron® devices. A low phase angle quartile was associated with a high death risk in people aged ≥65 years, when using a Bio-Z® or a RJL-101® device. When adjusting for age, body mass index or disease, a low phase angle remained a risk factor of mortality.

The characteristics of the study population (age, BMI, diseases), or the technology itself may explain the differences in phase angle values between the devices. Reference values for phase angle are 7.7 and 10.5% lower in the Swiss women and men (using several BIA brands cross-calibrated for resistance) [15], and 12.5 and 16% lower in the German women and men (using Data Input devices) [8] compared to the American population (using an RJL device) [16]. Bosy-Westphal et al. reported that a discrepancy of 0.3° for phase angle may be related to differences between the Xitron® and Data Input devices, and that, although age and BMI influence phase angle values, they do not explain the differences between populations [8]. This suggests that differences of phase angle values between our study groups may be related to different anthropometric characteristics, BIA devices or other unidentified factors. Thus, when evaluating the potential of a phase angle value on outcome at a population level, and in the absence of a gold standard for phase angle measurement, it is essential to use a single brand of BIA to avoid at least the confounding impact of different BIA devices.

Whether using an RJL-101® or a Bio-Z® device, a phase angle in the low quartile is associated with a high risk of mortality. This result confirms our previous findings using a Nutriguard® device but also other studies performed in older persons. A phase angle <3.5°, measured by a Nutriguard® device at admission to a German hospital, increased the in-hospital mortality by four times [17].

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