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Bioelectric impedance phase angle is associated with hospital mortality of geriatric patients

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ABSTRACT

Malnutrition is regularly associated with weight loss and changes in body composition, which lead to an increase in disability, complications and mortality. Bioelectric impedance analysis (BIA) is a simple and non-invasive bedside body composition analysis technique. In particular, bioelectric impedance phase angle (PA) has been shown to predict prognosis and mortality in several clinical conditions. The purpose of this study was to determine the relationship of BIA measurements and hospital mortality in multimorbid geriatric patients. The data obtained from the routine clinical admissions of 1071 consecutive patients (783 women and 288 men, age 81.4 ± 8.5 years) to a geriatric hospital unit was analyzed retrospectively. A significant difference of PA (50 kHz) between survivors ($4.2 \pm 1.1^\circ$) and non-survivors ($3.6 \pm 1.2^\circ$; $p < 0.001$) of the hospital stay could be detected. Subjects with a PA below 3.5° showed a significant fourfold increased hospital mortality of 20% (95% CI = 15–24%) compared to all other subjects (5%; 95% CI = 4–7%). No calculated parameters of BIA reflecting body composition were associated with hospital mortality. Although the extent to which the PA may be regarded as a marker of nutritional state is still controversial, it was associated with hospital mortality in geriatric patients.

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1. Introduction

Due to its high prevalence and serious consequences in the geriatric population, malnutrition is a growing health concern (Pirlich et al., 2006). Malnutrition is regularly associated with weight loss and changes in body composition (Newman et al., 2005) and leads to increased disability, complications and mortality (Broadwin et al., 2001; Newman et al., 2001; Sullivan et al., 2002). Its nutritional treatment ranges from dietary modification, food fortification and supplementation to tube feeding and parenteral nutrition. Bioelectric impedance analysis (BIA) is a simple, non-invasive and easily performed bedside technique of body composition analysis (Kyle et al., 2004a). While it provides reliable measurements for fat mass (FM) and fat-free mass (FFM) in healthy subjects, including the elderly (Kyle et al., 2001a), these measurements are not reliable in patients, especially those with chronic disease (Kyle et al., 2004b). BIA works mainly through the measurement of the body's resistance and reactance to an alternative electrical current. Resistance (R) depends primarily on the fluid and electrolyte content of the body. Cell membranes

produce capacitive reactance (X_c) by storing parts of the electric charge as a capacitor. This storage of current creates a phase shift, which can be regarded as the ratio of resistance and reactance and is expressed geometrically as phase angle (PA). By using predictive equations, whole body water can be calculated fairly precisely (Miller et al., 1999). FM and FFM are calculated with the working assumption that the hydration of FM is insignificantly low and the hydration of FFM is constantly near 73%; however, this is only true in healthy subjects. That is why BIA measurements of FM and FFM are not precise in chronically ill patients, who often suffer from disturbances of fluid distribution and content (Montagnani et al., 1998). To avoid these problems, several studies suggested the use of BIA raw measurements, such as resistance, reactance and PA, in clinical practice. Of all the direct measures of BIA, especially PA at 50 kHz has been shown to be predictive for prognosis and mortality in several clinical conditions, including cancer, hemodialysis, HIV and amyotrophic lateral sclerosis and postoperative complications (Ott et al., 1995; Maggiore et al., 1996; Nagano et al., 2000; Schwenk et al., 2000; Gupta et al., 2004a,b, 2008a,b, 2009; Barbosa-Silva and Barros, 2005a; Muller et al., 2006; Desport et al., 2008; Davis et al., 2009).

Malnutrition and alterations in body composition are very common in elderly patients, and their influence on mortality has been shown in several studies (Newman et al., 2001; Pirlich et al.,

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2006). So far no study has investigated whether BIA measurements are predictive for the outcome of multimorbid geriatric patients. This retrospective study examines whether any BIA measurements or calculated parameters are associated with hospital mortality of geriatric patients.

2. Subjects and methods

2.1. Patients and study design

This study is a retrospective cross-sectional study of 1071 consecutive multimorbid patients in an acute geriatric hospital unit. The patients were admitted in the year 2000, and there were no exclusion criteria except an age of less than 60 years.

2.2. Data collection

We analyzed each individual patient's body weight, body height, body mass index (BMI), age, sex, hospital mortality and the data of multifrequent BIA to obtain information about body composition in relation to hospital mortality. All of the data were obtained from routine clinical assessments in an 80-bed geriatric hospital department with a 6-bed intensive care unit incorporated. The measurements were performed within the first three days of each patient's hospital stay. Data about length of stay, survival and main treatment diagnosis was obtained from the hospital information system.

2.3. Bioelectric impedance measurement

Bioelectric impedance was measured with a BIA-2000-M of Data-Input GmbH device (Darmstadt, Germany) in a multi-frequency, tetrapolar technique on the right side of the body in supine position. Red Dot 2271 electrodes by 3 M (Neuss, Germany) were used. The time of measurement was not standardized. All measurements were performed with the examination at admission. FFM was calculated with the formula provided by Kyle et al. (2001a): $FFM = -4.104 + (0.518 \times \text{height}^2/\text{resistance} (50 \text{ kHz})) + (0.231 \times \text{weight}) + (0.130 \times \text{reactance} (50 \text{ kHz})) + (4.229 \times \text{sex} (\text{women} = 0; \text{men} = 1))$. FM was calculated by simple subtraction from body weight ($FM = \text{body weight} - FFM$)

(Kyle et al., 2001a). To relate FM and FFM to body weight, both are given as a percentage of body weight. In addition, the fat mass index (FMI) and fat-free mass index (FFMI) were calculated as analogs to BMI ($FMI + FFMI = BMI$) (Pichard et al., 2004; Kyle et al., 2005; Wirth et al., 2007).

2.4. Statistics

The data analysis was performed using SPSS Version 16 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to calculate item frequency, mean, standard deviation, range and 95%-confident intervals (95% CI). Correlation analysis was done with Spearman's rank correlation coefficient. Age correction was performed by regression. For group comparisons of metric data, we used the Mann–Whitney–U-test, and for group comparisons of ordinal and nominal data, we used the chi-square test. A $p < 0.05$ was considered statistically significant.

3. Results

The main characteristics, BIA measures and calculations of all patients are shown in Table 1. All patients were multimorbid with multiple diagnoses. Ninety patients (8.4%) were admitted because of heart failure, 79 (7.4%) due to dementia, 75 (7.0%) suffered from acute stroke, 39 (3.6%) from pneumonia, 37 (3.5%) were admitted because of a fracture and 34 (3.2%) because of hypertension. All other patients were admitted because of various conditions like chronic obstructive pulmonary disease (2.9%), syncope (2.7%), myocardial infarction (2.1%), depression (1.3%), Parkinson's disease (0.8%), angina pectoris (0.8%), and various other diseases (53.6%). Body weight could be measured in 93% of the patients. In 7% this was not possible due to the severity of the disease. The body weight of these patients was estimated. Body height was measured for 91% of the patients. If this was not possible (9%), body height was approximately measured in bed.

Except for hospital mortality, reactance (100 kHz) and PA (100 kHz), nearly all measures were significantly different between males and females.

Group comparisons of survivors and patients who died during their hospital stay (non-survivors) are shown in Table 2. These

Table 1

Subject characteristics, BIA measurements and calculated values, n (%), or mean \pm SD (range).

Parameter	Females	Males	$p <$
N = 1071	783 (73.1)	288 (26.9)	
Age, years	82.8 \pm 7.7 (60–101)	77.4 \pm 9.1 (60–96)	0.001
Length of hospital stay, day	21.7 \pm 16.0 (1–197)	18.1 \pm 15.0 (1–97)	0.001
Hospital mortality	70 (8.9)	30 (10.4)	0.462
Body weight, kg	61.5 \pm 13.7 (30–120)	73.7 \pm 13.4 (42–111)	0.001
Body height, cm	161 \pm 7 (140–185)	173 \pm 8 (150–192)	0.001
BMI, kg/m ²	23.7 \pm 4.9 (11.6–47.2)	24.6 \pm 4.2 (13.9–40.4)	0.005
Resistance at 1 kHz, Ω	633 \pm 383 (0–6990)	568 \pm 313 (0–4038)	0.010
Resistance at 5 kHz, Ω	675 \pm 239 (263–6143)	589 \pm 113 (338–1003)	0.001
Resistance at 50 kHz, Ω	615 \pm 128 (235–1160)	537 \pm 105 (294–933)	0.001
Resistance at 100 kHz, Ω	590 \pm 128 (51–1130)	520 \pm 116 (283–1443)	0.001
Reactance at 5 kHz, Ω	27.0 \pm 18.1 (1–225)	21.3 \pm 15.0 (1–91)	0.001
Reactance at 50 kHz, Ω	43.8 \pm 13.7 (7–105)	40.5 \pm 12.0 (14–76)	0.001
Reactance at 100 kHz, Ω	39.1 \pm 20.1 (1–431)	36.9 \pm 27.4 (1–412)	0.137
Phase angle at 5 kHz, $^\circ$	2.3 \pm 1.5 (0.1–19.4)	2.1 \pm 1.6 (0.1–11.3)	0.032
Phase angle at 50 kHz, $^\circ$	4.1 \pm 1.1 (1.1–8.0)	4.4 \pm 1.2 (1.7–7.4)	0.001
Phase angle at 100 kHz, $^\circ$	3.9 \pm 2.6 (0.1–47.6)	4.1 \pm 2.6 (0–40.3)	0.326
FM, kg	26.8 \pm 9.2 (2.9–89.4)	27.1 \pm 8.7 (2.8–52.1)	0.742
FFM, kg	34.7 \pm 7.4 (17.7–68.7)	46.7 \pm 8.2 (25.4–75.3)	0.001
FMI, kg/m ²	10.3 \pm 3.4 (1.0–32.9)	9.1 \pm 2.9 (1.0–19.2)	0.001
FFMI, kg/m ²	13.4 \pm 2.6 (7.8–28.4)	15.6 \pm 2.4 (10.0–23.2)	0.001
FM, % of body weight	43.0 \pm 8.0 (4.9–74.5)	36.2 \pm 8.0 (5.1–57.7)	0.001
FFM, % of body weight	57.0 \pm 8.0 (25.5–95.1)	63.8 \pm 8.0 (42.3–95.0)	0.001
PA at 50 kHz, $^\circ$, age-corr.	4.2 \pm 1.0 (1.3–8.5)	4.2 \pm 1.1 (0.9–7.8)	0.559

Table 2
Group characteristics, BIA measurements and calculated parameters, n (%), or mean ± SD (range).

	Survived	Death in hospital	p<
Number	971 (90.7)	100 (9.3)	
Age, years	81.1 ± 8.5 (60–101)	83.3 ± 7.7 (60–98)	0.002
Gender			
Male	258 (26.6)	30 (30.0)	0.461
Female	713 (73.4)	70 (70.0)	0.461
LOS, days	20.9 ± 15.9 (1–197)	18.6 ± 14.9 (1–93)	0.083
Body weight, kg	65.0 ± 14.6 (30–120)	62.7 ± 14.3 (32–110)	0.139
Body height, cm	164 ± 9 (140–192)	164 ± 9 (145–190)	0.823
BMI, kg/m ²	24.0 ± 4.7 (11.6–47.2)	23.2 ± 5.0 (13.9–40.0)	0.095
Resistance at 1 kHz, Ω	619 ± 357 (0–6990)	586 ± 450 (0–4039)	0.039
Resistance at 5 kHz, Ω	653 ± 221 (289–6143)	638 ± 162 (263–1238)	0.405
Resistance at 50 kHz, Ω	594 ± 125 (279–1042)	595 ± 149 (235–1160)	0.980
Resistance at 100 kHz, Ω	571 ± 127 (51–1443)	578 ± 145 (241–1130)	0.709
Reactance at 5 kHz, Ω	25.4 ± 17.3 (1–225)	26.0 ± 21.4 (1–102)	0.404
Reactance at 50 kHz, Ω	43.5 ± 13.0 (7–105)	37.2 ± 15.5 (9–100)	0.001
Reactance at 100 kHz, Ω	39.0 ± 22.3 (1–431)	34.3 ± 21.6 (6–192)	0.001
Phase angle at 5 kHz, °	2.2 ± 1.5 (0.1–19.4)	2.4 ± 1.9 (0.1–9.6)	0.581
Phase angle at 50 kHz, °	4.2 ± 1.1 (1.1–8.0)	3.6 ± 1.2 (1.8–7.5)	0.001
Phase angle at 100 kHz, °	4.0 ± 2.7 (0–47.6)	3.4 ± 2.1 (1.2–21.0)	0.001
FM, kg	27.1 ± 9.0 (2.9–89.4)	25.4 ± 9.7 (2.8–63.8)	0.097
FFM, kg	38.0 ± 9.3 (17.7–75.3)	37.3 ± 8.9 (18.6–68.7)	0.590
FMI, kg/m ²	10.1 ± 3.3 (1.0–32.8)	9.4 ± 3.4 (1.0–22.1)	0.129
FFMI, kg/m ²	14.0 ± 2.7 (7.8–25.1)	13.8 ± 3.2 (7.8–28.4)	0.337
FM, % of body weight	41.3 ± 8.4 (4.9–74.5)	39.9 ± 10.0 (5.1–58.0)	0.428
FFM, % of body weight	58.7 ± 8.4 (25.5–95.1)	60.1 ± 10.0 (42.0–95.0)	0.438
PA 50 kHz, °, age-corr.	4.2 ± 1.0 (0.9–8.5)	3.7 ± 1.2 (1.2–7.8)	0.001

comparisons revealed significant differences in age, resistance at 1 kHz, reactance at 50 and 100 kHz and PA at 50 and 100 kHz. Because PA (50 kHz) showed the most pronounced difference between survivors and non-survivors (4.2 ± 1.1° vs. 3.6 ± 1.2°; *p* < 0.001) and most previous studies refer to PA at 50 kHz, a further analysis of PA at 50 kHz was performed. Since age and PA showed a significant correlation (*r* = 0.32; *p* < 0.001; Fig. 1), an age correction of PA data was performed. Although the mean PA was significantly lower in females (4.1°; 95% CI = 4.1–4.2°) than in males (4.4°; 95% CI = 4.2–4.5°), this difference was not evident after age correction (4.2°; 95% CI = 3.7–4.1° vs. 4.2°; 95% CI = 3.8–4.4°). We therefore performed no sex-specific analysis of PA. After adjusting for age, PA remained significantly lower in subjects who died during the hospital stay compared to survivors (3.7 vs. 4.2; *p* < 0.001; Fig. 2). In addition, a cluster analysis of groups with different PAs was conducted in steps of

0.5° and revealed a significant association of PA value and hospital mortality (Table 3a and Fig. 3). The group with a PA of 5.0–5.4° showed the lowest hospital mortality at 3% (95% CI = 0–6%) with a significant increase in hospital mortality below a PA of 4.0° (15%; 95% CI = 12–18%) and an insignificant increase in PA above 6.4° (12%; 95% CI = 0–23%). A polynomial regression formula for hospital mortality (*y*) in dependence to PA (*x*) could be calculated ($y = 0.9x^2 - 12.1x + 43.2$) and showed a high level of determination (*R*² = 0.97). Further, an additional group analysis showed that patients with a PA < 4.0° had a threefold increase in hospital mortality (15%; 95% CI = 12–18%) compared to all other subjects (5%; 95% CI = 3–7%). Patients with a PA < 3.5° had a fourfold

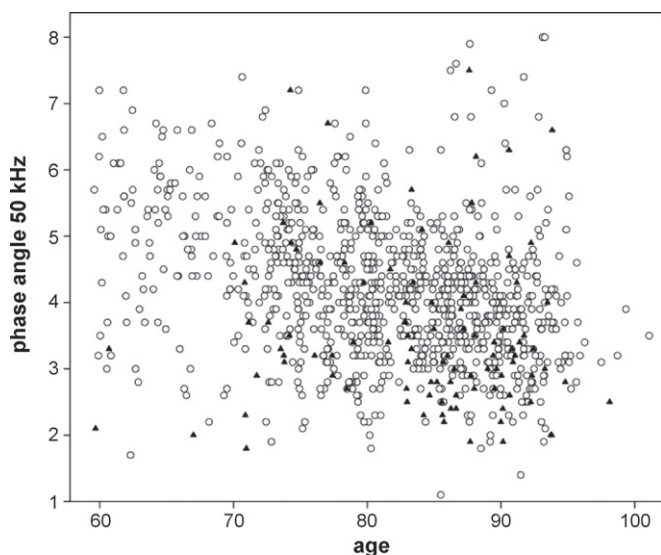


Fig. 1. Age (years) and BIA-phase angle (°), (○) survivors and (▲) non-survivors.

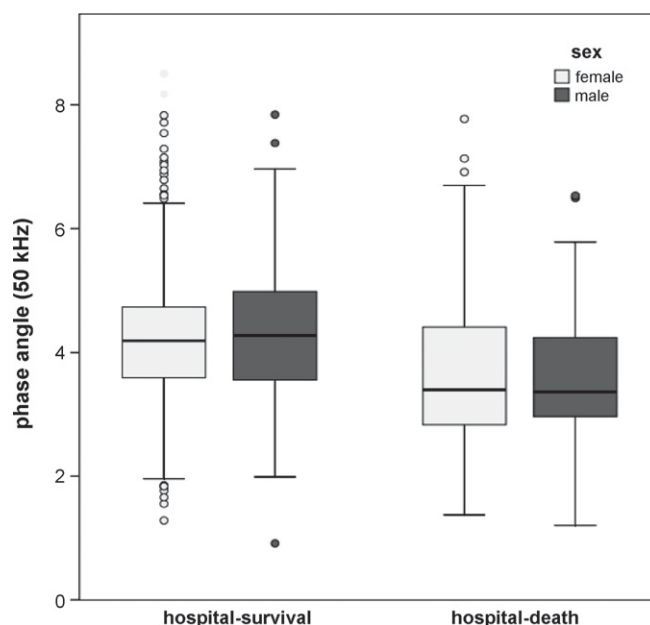


Fig. 2. Age corrected and sex-specific phase angle (°) in survivors and non-survivors (boxplots with median, interquartile range, minimum, maximum, outliers, °).

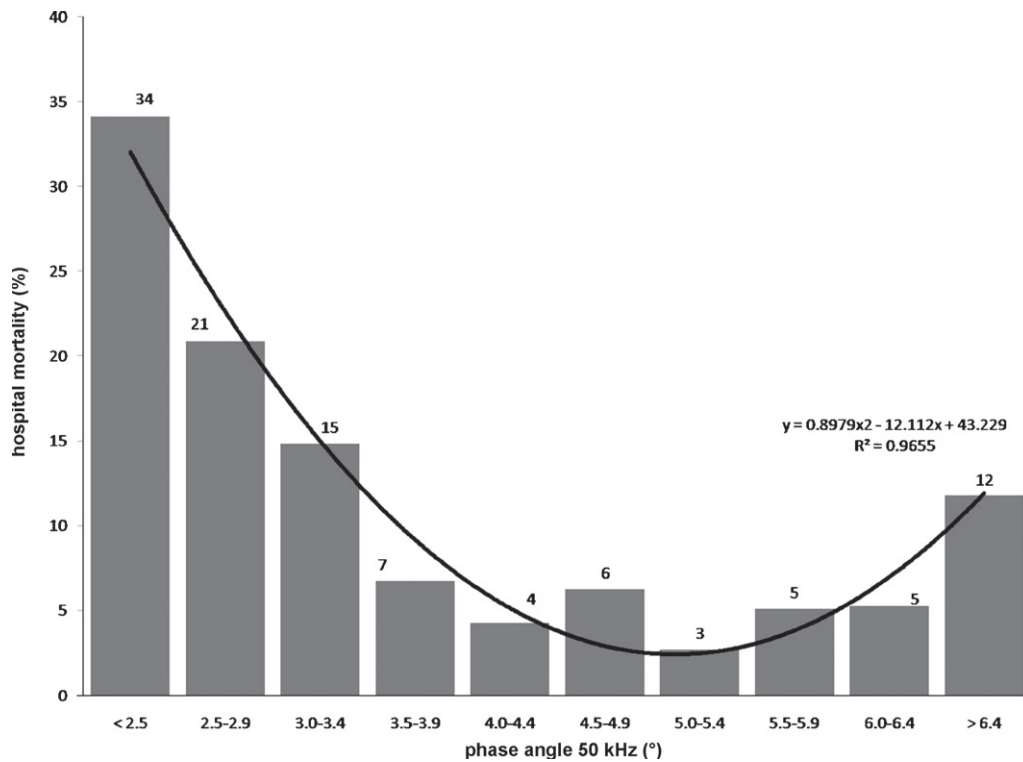


Fig. 3. Phase angle and hospital mortality (for confidence intervals see Tables 3a and 3b).

Table 3a
Cluster analysis of hospital mortality and phase angle.

Phase angle at 50 kHz (°)	n	Hospital deaths (n)	Hospital mortality % (95% CI)
<2.5	44	15	34 (20-49)
2.5-2.9	96	20	21 (13-29)
3.0-3.4	155	23	15 (9-20)
3.5-3.9	178	12	7 (3-10)
4.0-4.4	212	9	4 (2-7)
4.5-4.9	144	9	6 (2-10)
5.0-5.4	111	3	3 (0-6)
5.5-5.9	59	3	5 (0-11)
6.0-6.4	38	2	5 (0-13)
>6.4	34	4	12 (0-23)
Total	1071	100	9 (8-11)

Table 3b
Group analysis of hospital mortality and phase angle.

Phase angle at 50 kHz (°)	n	Hospital deaths (n)	Hospital mortality % (95% CI)
<3.5	295	58	20 (15-24)
≥3.5	776	42	5 (4-7)
Total	1071	100	9 (8-11)

increase in hospital mortality (20%; 95% CI = 15-24%) compared to all other subjects (5%; 95% CI = 4-7%, Table 3b).

4. Discussion

The average PA of all subjects in this study population ($4.2 \pm 1.1^\circ$) was substantially below the existing age-specific reference values (Kyle et al., 2001b; Dittmar, 2003; Barbosa-Silva et al., 2005), which reflects the fact that these patients were multimorbid and severely ill. Our results show that BIA PA

(50 kHz) is associated with hospital survival and mortality in these geriatric patients. Subjects with a PA below 3.5° had a fourfold increase of hospital mortality, and subjects with a PA between 5.0° and 5.5° had the lowest hospital mortality.

PA is a measure of electrical current storage. Although the biological meaning of PA is not completely understood, it seems to reflect body cell mass (BCM) and cell membrane function (Barbosa-Silva and Barros, 2005b). Recently it was also demonstrated that BIA vector, which is substantially determined by PA, correlated well with muscle function (Norman et al., 2009). All these data support the opinion that PA is a measure of cell mass, nutritional state and general health (Baumgartner et al., 1988). Therefore, it is not surprising that it is associated with prognosis and mortality in some clinical conditions, especially those related to chronic disease.

To our knowledge, this is the first study demonstrating this association in geriatric hospital patients. The trend analysis of this data suggests a U-shaped relation between PA and geriatric patients' hospital mortality with a high coefficient of determination. The trend toward a higher mortality with a high PA (above 6.4°) in this population might be explained by the clinical observation that some severely diseased geriatric patients show a high PA that can be attributed mainly to dehydration. A PA = 6.5° or higher is normal in healthy subjects and serves as a marker of good general health. Among elderly hospital patients who are multimorbid, a PA > 6.4° is very unusual and should be interpreted with caution. For most of those patients PA decreases after rehydration, reflecting hydration's influence on PA. The extent to which PA can be regarded as a nutritional marker is still controversial, however several studies have demonstrated its association with other markers of nutritional state (Nagano et al., 2000; Wirth and Miklis, 2005; Gupta et al., 2008b). Therefore, whether or not PA could be a useful measure of malnutrition is still uncertain, but it seems to predict patients at high risk for unfavorable outcome in different clinical situations including geriatric patients.

Further studies should reproduce these results and determine whether PA and outcome can be improved for example by nutritional therapy. One advantage of PA is that it is a direct measurement of BIA and can be directly obtained from the patient. This implies that body weight and height, which are often difficult to obtain for severely ill geriatric patients and lead to data inaccuracies, are not necessary measurements. Additionally, no calculation with the raw data has to be done to obtain relevant data like PA. This minimizes calculation bias and also provides a way to assess the nutritional status of immobile patients, whose height and weight measurements may be impossible to obtain. Furthermore, no sex-specific consideration of PA values seems to be necessary when analyzing multimorbid geriatric hospital patients.

There are some limitations in this study. First, was its retrospective design. Second, BIA measurements were not performed at a standardized time, as recommended, but directly at admission, which may have contributed to inaccuracy in the BIA data. By contrast, because this data was obtained during routine clinical admission, the real-life circumstances of the data's collection positively reflect its reliability. Another advantage of this study is the considerably high number of recorded patients. Further, BIA measurements influencing outcome have been investigated before, but this is the first study that analyzes the association of BIA measurements and clinical outcome in geriatric hospital patients.

In conclusion, the results of this study show that low BIA PA is associated with high hospital mortality in geriatric hospital patients, indicating that PA might be a predictor of poor outcome for this population.

Conflict of interest statement

None.

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