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Applied nutritional investigation

Phase angle is associated with length of hospital stay, readmissions, mortality, and falls in patients hospitalized in internal-medicine wards: A retrospective cohort study

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A R T I C L E I N F O

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A B S T R A C T

Objectives: The aim of this study was to investigate the predictive value of bioimpedance phase angle (PA) on selected clinical outcomes in patients hospitalized in internal-medicine wards.
Methods: This was a retrospective observational study of 168 patients admitted to the internalmedicine service (52.9% women, 47.1% men), with a mean (± SD) age of 73.9 ± 15.9 y. Anthropometric examination, laboratory tests, and bioelectrical impedance analysis were performed. Bioimpedance-derived PA was the study's parameter. Length of hospital stay, prospective all-cause hospital readmission, mortality, and falls were the clinical endpoints.
Results: Across the four PA quartile groups, age was incrementally higher ($P \leq 0.001$). Multivariate linear regression models showed that PA quartile 1 was significantly associated with length of hospital stay (β, SE) in both crude and adjusted models—respectively, β (SE) = 6.199 (1.625), $P \leq 0.001$, and β = 2.193 (1.355), $P = 0.033$. Over a 9-mo follow-up period, the hazard ratios for readmission, in-hospital falls, and mortality were associated with the lowest phase angle (PA quartile 1 versus quartiles 2–4)—respectively, 2.07 (95% confidence interval [CI], 1.28–3.35), 2.36 (95% CI, 1.05–5.33), and 2.85 (95% CI, 1.01–7.39). Associations between narrow PA and outcomes continued to be significant after adjustments for various confounders.
Conclusions: In internal-medicine wards, bioimpedance-derived PA emerged as a predictor of length of hospital stay, hospital readmission, falls, and mortality. The present findings suggest that in the hospital setting, PA assessment could be useful in identifying patients at higher risk who need specific nutritional support.

Introduction

Hospital malnutrition represents an important public health problem, leading to undesired patient outcomes and increasing health care costs worldwide [1–3]. In patients hospitalized in internal-medicine wards, the prevalence of malnutrition is very high, ranging from 20% to 50% depending on the method of assessment [4,5]. A recent large multicenter study in internal-medicine wards found an alarming prevalence of more than 70% [6]. Moreover, an increasing amount of evidence has highlighted the clinical benefits of early identification of malnourished patients at hospital admission, followed by individualized nutritional interventions [7,8]. Nevertheless, this condition still represents an underestimated challenge for hospital health care systems.

Previous studies have found an association between malnutrition and risk of mortality, higher hospitalization costs, increased length of stay, high readmission rates, and impaired recovery [9–11]. However, most previous studies have focused on exploring malnutrition risk factors and their prognostic role in selected samples of patients or in specific diseases [12,13]. In the hospital setting, studies have been conducted more frequently with patients hospitalized in surgical wards [12,13].

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In recent years, interest has grown in the daily bedside use in clinical practice of non-invasive, user-friendly, and inexpensive tools to assess malnutrition, such as bioelectrical impedance (bioimpedance) analysis (BIA) [14]. BIA is a useful method of nutritional assessment, indirectly able to estimate body composition through the passage of low-frequency electrical currents throughout the body, providing measurements of impedance, resistance, and reactance and a number of estimates [15].

Among BIA-derived parameters, phase angle (PA) is one of the most attractive and studied measurements. Different from other bioimpedance parameters, PA is independent of weight and height, and derives from parameters that are directly measured (ratio of reactance to resistance ratio) [16]. It could be considered a more objective nutritional parameter, representing an index of the integrity of cell membranes and a measure of cellular health [16].

Previous evidence has suggested the utility of PA assessment in predicting survival in several clinical conditions, as well as nutritional status and clinical disease progression [17,18]. Low PA values have been associated with impaired muscle function and survival, and, in critically ill patients, with prolonged hospitalization [19,20]. Interestingly, in a prospective cohort of community-dwelling older adults, lower PA values were associated with increased risk of falls compared with individuals with normal or high PA values [21]. Furthermore, a study conducted by Rinninella et al. [22] showed that in patients admitted to an internal-medicine department, PA was an independent prognostic factor of length of hospital stay (LOS).

To date, however, despite the consistent body of evidence on the clinical utility of PA assessment, only a few studies have investigated the predictive role of PA in outcomes for patients in internal-medicine wards. In the present study, the primary aim was to evaluate the prognostic value of PA assessment for LOS in patients hospitalized in an internal-medicine ward. Secondary endpoints were investigation of the predictive value of PA for hospital readmissions, mortality, and in-hospital falls.

Materials and methods

Study design and participants

This study was designed as a retrospective observational cohort study in adult patients ($\geq$18 y) admitted to the internal-medicine service of the Regional Teaching Hospital of Bellinzona and Valli (Switzerland) during July 2019. All clinical and nutritional assessments were obtained in the course of routine clinical procedures. Patients not suitable for BIA evaluation, exhibiting concomitant anasarca, or having body mass index less than 16 kg/m^2 or greater than 35 kg/m^2 (n = 18) were excluded from the analysis. Readmissions, length of hospital stay, deaths, and in-hospital falls were tallied. The final sample was 168 patients.

The study was conducted in accordance with the Declaration of Helsinki. It was exempt from institutional review board approval by the Swiss Ethics Committee because it involved anonymous secondary data only.

Outcome measures

The primary endpoint was to evaluate the prognostic value of PA assessment for LOS in patients hospitalized in an internal-medicine ward. The secondary endpoint was to determine the predictive value of PA for hospital readmissions, mortality, and in-hospital falls. LOS was calculated from admission to internal medicine to discharge from the same service, expressed in days. Readmission was defined as an unplanned admission to the same hospital and at the same internal-medicine service during the 9-mo follow-up period. Mortality was defined as in-hospital death occurring during the index admission or the 9-mo follow-up. Falls were defined as occurring during the index or in further admissions in the 9-mo follow-up.

Statistical analysis

The sample size was calculated considering the primary endpoint and assuming, according to the literature [8], an estimated mean LOS in well-nourished and malnourished individuals, with an estimate precision of 0.05 and a confidence level of 0.9. The required sample size calculated was 162. Descriptive statistics are presented as mean $\pm$ SD for continuous variables and as number (percentage) for categorical variables. Data were analyzed according to PA quartiles (quartile 1: PA $\leq$ 4.0°; quartile 2: PA = 4.0°–4.8°; quartile 3: PA = 4.8°–5.9°; quartile 4: PA $\geq$ 5.9°). Differences among PA quartiles were analyzed by analysis of variance and χ^2 tests for continuous and categorical variables, respectively.

To explore the association between LOS and PA, linear regression models were constructed with PA quartile 4 considered as the reference group. Crude (Model 1) and adjusted models (Model 2) were created. Model 2 was adjusted for selected covariates to examine potential confounding effects. Age, gender, case mix, hemoglobin, creatinine, sodium, potassium, body mass index, nutritional risk screening, and fat-free mass were included in the multivariate model as covariates. The β coefficients and confidence intervals relative to PA quartile categories were calculated.

Kaplan–Meier analysis with log-rank test was used to estimate the cumulative incidence of readmissions and deaths over time and to compare patients in the first PA quartile with those in higher quartiles (PA quartile 1 versus quartiles 2–4). To assess the associations between PA and risk of readmission, falls, and death, a Cox proportional-hazard ratio was applied. Hazard ratios (HRs) with 95% confidence intervals (CIs) and P values testing the null hypothesis that the HR is 1 were determined. Risk was assessed considering PA quartile 1 versus quartiles 2–4, and unadjusted and adjusted models were used. Model 2 was adjusted for sex, age, case mix, previous cardiovascular disease, hypertension, systolic blood pressure, diastolic blood pressure, heart rate, chronic obstructive pulmonary disease, cancer, and chronic kidney disease. The case mix index represents the relative value assigned to the Swiss diagnosis-related group at hospital discharge, corresponding to the cost weights of all hospitalized patients in a period divided by the number of admissions. The choice of this parameter was based on the administrative nature of the data of the present study. Moreover, the case mix index is routinely calculated in our hospital network, and it has previously been widely used in other research using care-centered hospital data. Data analysis was performed using R statistical software (www.r-project.org) and SPSS (version 18.0, Chicago, IL, USA). Statistical significance for all outcomes was set at $P \leq 0.05$.

Anthropometry and BIA

Demographic characteristics, comorbidities, dates of hospital admission and discharge, deaths, falls, clinical and anthropometric data, laboratory values, and other nutritional measures were collected. The case mix index was recorded for each patient. BIA was performed with patients supine, arms not touching the torso and legs positioned according to accepted standards. A multifrequency device (BIA 101, Akern Bioresearch, Florence, Italy) was used. Whole-body impedance values of resistance and reactance were measured to calculate PA, total body water, fat-free mass, and fat mass, as provided by the manufacturer and validated in different clinical settings [18,23,24]. Fat mass index and fat-free mass index were then calculated by dividing fat mass (kg) and fat-free mass (kg) by the square of the patient's height in meters .

Results

Data from 168 patients admitted to the internal-medicine ward were analyzed. Demographic and clinical characteristics are displayed in Table 1. Results are shown for the whole sample and by PA quartile. Differences among PA quartiles were also explored. Of the sample, 89 (53%) were female and 79 (47%) were male. The mean age was 73.9 $\pm$ 15.9 y. Patients in the lowest PA quartile were significantly older than those with higher PA—mean age per respective quartile: 81.2 $\pm$ 9.6 y, 75.1 $\pm$ 12.9 y, 72.5 $\pm$ 14.4 y, and 64.7 $\pm$ 21.3 y, $P \leq 0.001$—and had a higher proportion of women: 70.6% in quartile 1 versus 37.6% in quartile 4.

Regarding comorbidities, a significant difference ($P \leq 0.001$) in hypertension was found, with higher prevalence in those with lower PA (quartile 1: 80%) versus those with higher PA (quartile 4: 55%). Rates of diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and cancer did not differ by PA quartile. Significantly lower values of hemoglobin were also found in individuals with lower PA (117.7 $\pm$ 18.2 g/L) compared to those with higher PA (127.0 $\pm$ 17.2 g/L). Hospital disease severity was investigated with the standard hospital indicator of case mix, and no significant differences across PA quartiles were found.

Markers of body composition, frailty, and malnutrition by PA quartile are presented in Table 2. Patients with lower PA had lower fat-free mass and higher ratio of extracellular water to total body

Table 1
Baseline characteristics of the study population by PA quartile

Characteristic	Total (n = 168)	Quartile 1, PA ≤ 4.0° (n = 51)	Quartile 2, PA = 4.0°–4.8° (n = 38)	Quartile 3, PA = 4.8°–5.9° (n = 39)	Quartile 4, PA ≥ 5.9° (n = 40)	P
Age (y)	73.9 ± 15.95	81.2 ± 9.6	75.1 ± 12.9	72.5 ± 14.4	64.7 ± 21.3	≤0.001*
Sex females	89 (53)	36 (70.6)	18 (47.4)	20 (51.3)	15 (37.5)	0.013*
Body mass index (kg/m^2)	25.2 ± 4.1	24.6 ± 4.2	25.3 ± 4.6	25.7 ± 3.7	25.5 ± 3.9	0.6331
Case mix index	1.19 ± 1.27	1.47 ± 1.81	1.19 ± 1.07	0.96 ± 0.62	1.08 ± 1.01	0.2477
SBP (mm Hg)	134.8 ± 21.1	139.1 ± 21.3	135.2 ± 21.4	129.8 ± 20.5	133.4 ± 20.8	0.2421
DBP (mm Hg)	74.3 ± 10.5	72.6 ± 10.2	72.3 ± 12.4	74.8 ± 8.4	78.3 ± 9.9	0.0430*
Heart rate (beats/s)	75.0 ± 13.8	70.7 ± 11.7	76.2 ± 12.2	74.9 ± 12.6	79.9 ± 17.2	0.0193
Laboratory parameter						
Hemoglobin (g/L)	123.8 ± 20.5	117.7 ± 18.2	121.8 ± 24.2	130.2 ± 20.9	127.0 ± 17.2	0.022*
Creatinine (μmol/L)	130.6 ± 102.9	143.2 ± 105.9	149.2 ± 124.9	99.2 ± 49.9	126.6 ± 109.7	0.140
Sodium (mmol/L)	136.9 ± 5.9	136.0 ± 6.5	137.2 ± 4.7	137.8 ± 5.8	136.7 ± 6.3	0.5890
Potassium (mmol/L)	4.1 ± 0.6	4.2 ± 0.6	4.3 ± 0.7	4.1 ± 0.5	3.9 ± 0.6	0.065
Calcium (mmol/L)	2.28 ± 0.21	2.33 ± 0.12	2.25 ± 0.23	2.25 ± 0.32	2.31 ± 0.14	0.2145
Comorbidity						
CVD	4 (7.8)	4 (7.8)	4 (10.5)	4 (10.3)	2 (5.0)	0.795
Diabetes mellitus	44 (26.2)	16 (31.4)	13 (34.2)	10 (25.6)	5 (12.5)	0.119
Hypertension	109 (64.8)	41 (80.4)	27 (71.1)	19 (48.7)	22 (55.0)	≤0.001*
Hypercholesterolemia	80 (47.6)	25 (49.0)	19 (50.0)	19 (48.7)	17 (42.5)	0.904
COPD	14 (8.3)	5 (9.8)	2 (5.3)	4 (10.3)	3 (7.5)	0.840
CKD	33 (19.6)	13 (25.5)	8 (21.1)	4 (10.3)	8 (20.0)	0.343
Cancer	22 (13.1)	6 (11.8)	4 (10.5)	7 (17.9)	5 (12.5)	0.772
Discharge to home	116 (69.1)	33 (64.7)	28 (73.7)	29 (74.4)	26 (65.0)	0.647
Discharge to other facilities	40 (23.8)	13 (25.5)	5 (13.2)	9 (23.0)	13 (32.5)	0.247
Discharge to nursing home	12 (7.1)	5 (9.8)	5 (13.2)	1 (2.6)	1 (2.5)	0.161

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; SBP, systolic blood pressure.
All values are expressed as mean ± SD or number (percentage).
*$P \leq 0.05$.

water ($P < 0.001$). PA quartiles were associated with nutritional status, as assessed by Nutritional Risk Screening 2002 (NRS-2002): NRS ≥3 ($P \leq 0.001$) [25].

Mean LOS was 11.0 ± 7.8 d. It was significantly higher ($P \leq 0.001$) in PA quartile 1 (14.5 ± 9.8 d) than in quartile 2 (11.3 ± 6.3 d), quartile 3 (9.1 ± 6.7 d), and quartile 4 (8.3 ± 5.1 d). Considering a long LOS as one that is above the 75th percentile (ie, ≥15 d), a higher prevalence of long LOS was found in patients with low PA (39.2%) compared to those in higher quartiles ($P \leq 0.001$).

Over a follow-up period of 9 mo, a total of 75 (44.6%) patients were readmitted, 147 (10.1%) experienced an in-hospital fall, and 24 (14.3%) died. The distribution of primary and secondary endpoints according to PA quartile is presented in Table 3. Patients with lower PA had a significantly higher incidence of readmissions (P = 0.018) and falls (P = 0.015). The incidence of death in the lowest PA quartile was significantly higher compared with quartiles 2–4 (P = 0.033). The cumulative risk of readmission was significantly higher in quartile 1 than in quartiles 2 to 4 (Fig. 1A).

The association between LOS and PA was investigated using multivariate linear regression models. Table 4 shows the linear associations between PA quartiles (using quartile 4 as a reference) and LOS. A significant association was found in both the crude and adjusted models for quartile 1. More specifically, quartile 1 showed an increased LOS in both the crude model and the adjusted model—respectively, β = 6.11 (SE = 1.63), $P < 0.001$, and 2.91 (1.35) P = 0.033.

In Cox proportional-hazard model, quartile 1 was associated with a significantly increased risk of readmission relative to quartiles 2 to 4—HR = 2.07, 95% CI, 1.28–3.35; $P \leq 0.001$—which was confirmed in the adjusted model: HR = 1.79, 95% CI, 1.04–3.10, P = 0.036 (Table 5).

A significantly different cumulative incidence of death was also found in quartile 1 compared with quartiles 2 to 4 (Fig. 2). Cox proportional-hazard models showed a significantly increased risk of death in quartile 1 compared with quartiles 2 to 4—HR = 2.36, 95% CI, 1.05–5.33, P = 0.038—which was confirmed in adjusted models.

Table 2
Body composition and nutritional markers by PA quartile

Characteristics	Total	Quartile1 PA ≤4.0°	Quartile 2 PA 4.0°–4.8°	Quartile 3 PA 4.8°–5.9°	Quartile 4 PA ≥5.9°	p-value
PA (°)	5.6 ± 3.0	3.6 ± 0.34	4.5 ± 0.24	5.4 ± 0.29	9.4 ± 4.2	≤0.001*
ECW (L)	20.2 ± 5.6	23.0 ± 5.5	21.2 ± 5.3	19.1 ± 5.1	16.6 ± 4.0	≤0.001*
TBW (L)	40.9 ± 11.3	38.2 ± 9.1	39.5 ± 10.1	39.2 ± 10.4	47.5 ± 13.4	≤0.001*
ECW/TBW	0.50 ± 0.10	0.60 ± 0.05	0.54 ± 0.01	0.49 ± 0.01	0.36 ± 0.08	≤0.001*
Fat-free mass (kg)	52.0 ± 11.8	46.5 ± 8.5	50.8 ± 10.1	51.1 ± 10.9	61.0 ± 12.9	≤0.001*
Fat-free mass index	19.2±3.2	17.8 ± 2.2	18.8 ± 2.5	19.3± 3.4	21.1 ± 3.8	≤0.001*
Fat mass (kg)	16.1 ± 9.6	17.8 ± 8.2	16.9 ± 9.6	16.8 ± 9.6	12.4 ± 10.7	0.049*
Fat mass index	6.1 ± 3.7	6.8 ± 3.1	6.5 ± 3.9	6.4 ± 3.7	4.4 ± 3.8	0.007*
BCM (kg)	9.6 ± 3.5	6.9 ± 1.1	8.5 ± 1.2	9.7 ± 1.8	13.9 ± 4.2	≤0.001*
Risk of malnutrition (NRS 2002)	2.5 ± 1.1	2.7 ± 0.7	2.6 ± 1.2	2.4 ± 1.1	2.3 ± 1.4	0.165
Malnutrition based on NRS 2002	83 (49.4)	33 (64.7)	22 (57.9)	12 (30.7)	16 (40.0)	≤0.001*

BCM, body cell mass; ECW, extracellular water; NRS, Nutritional Risk Screening; PA, phase angle; TBW, total body water.
All values are expressed as mean ± SD or number (percentage).
*$P \leq 0.05$.

Table 3
Distribution of primary and secondary endpoints by PA quartile

Characteristic	Total (n = 168)	Quartile 1, PA ≤ 4.0° (n = 51)	Quartile 2, PA = 4.0°–4.8° (n = 38)	Quartile 3, PA = 4.8°–5.9° (n = 39)	Quartile 4, PA ≥ 5.9° (n = 40)	*P*
Length of hospital stay (d)	11.0 ± 7.8	14.5 ± 9.8	11.3 ± 6.3	9.1 ± 6.7	8.3 ± 5.1	≤0.001*
Prolonged hospital stay, ≥ 15 d	40 (23.8)	20 (39.2)	11 (28.9)	4 (10.3)	5 (12.5)	≤0.001*
Readmission within 30 d	75 (44.6)	31 (60.8)	18 (47.4)	12 (30.8)	14 (35.0)	0.018*
Falls	17 (10.1)	10 (19.6)	5 (13.2)	1 (2.6)	1 (2.5)	0.015*
Deaths	24 (14.3)	11 (21.6)†	4 (10.5)	4 (10.3)	5 (12.5)	0.352/0.033*,†

PA, phase angle.
All values are expressed as mean ± SD or number (percentage).
*$P \leq 0.05$.
†Quartile 1 vs. quartiles 2 to 4.

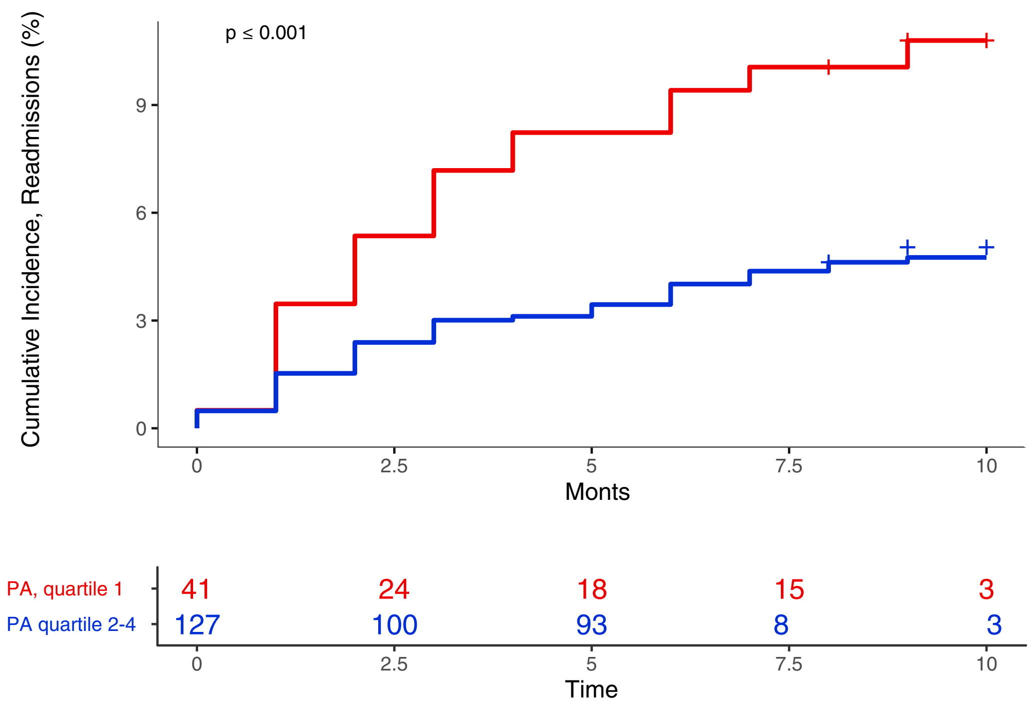

Fig. 1. Cumulative incidence of readmissions according to PA quartiles: quartile 1 (red line) compared with quartiles 2 to 4 (blue line). *P* value by log rank. PA, phase angle.

The risk of falls was also significantly higher in quartile 1, in both the crude and adjusted Cox models—respectively: HR = 2.85, 95% CI, 1.01–7.39; and HR = 3.11, 95% CI, 1.04–9.28 (Table 5). Receiver operating characteristic curve analyses were performed in order to investigate if the addition of NRS score to PA increased the predictive ability for outcomes. For PA and PA + NRS, area under the curve was 0.60 versus 0.62 for readmissions (P = 0.445); 0.60 versus 0.80 for death (P = 0.001); and 0.63 versus 0.67 for falls (P = 0.280).

Table 4
Association between length of hospital stay and phase angle quartile

Quartile	Length of hospital stay	*P*
	Model 1	
1	6.199 (1.623)	≤0.001*
2	2.630 (1.737)	0.132
3	0.676 (1.725)	0.696
4	Reference	
	Model 2	
1	2.193 (1.355)	0.033*
2	2.381 (1.333)	0.076
3	1.723 (1.344)	0.202
4	Reference	

All values are expressed as β (standard error). Model 1: unadjusted. Model 2: adjusted for age, gender, case mix index, hemoglobin, creatinine, serum sodium, serum potassium, body mass index, Nutritional Risk Screening, and fat-free mass.
*$P < 0.05$.

Discussion

The prognostic evaluation of hospitalized patients represents a challenge as well as a way to improve quality of care; however, in-hospital indicators are still lacking. The present study aimed to evaluate the performance of PA in predicting clinical outcomes in the hospital setting, in patients admitted to an internal-medicine ward. We found that a narrow phase angle was significantly associated with prolonged length of hospital stay and an increased risk of hospital readmission, mortality, and falls.

The role of phase angle as a nutritional and health status indicator is nowadays well established, and its intriguing role as a prognostic factor for clinical outcomes was previously investigated in many diseases and in different selected categories of patients [26,27]. However, to our knowledge, this is the first study evaluating the prognostic value of the phase angle for several clinical outcomes in patients hospitalized in an internal-medicine service.

Previous studies have highlighted [10,11] independent associations of malnutrition with LOS, while in critically ill patients a low

Table 5
Crude and adjusted risk of readmission, mortality, and falls for phase angle quartile 1 vs. quartiles 2 to 4

	Model 1		Model 2	
Risk	Hazard ratio (95% CI)	*P*	Hazard ratio (95% CI)	*P*
Readmission	2.07 (1.28–3.35)	≤0.001*	1.794 (1.038–3.100)	0.036*
Mortality	2.36 (1.05–5.33)	0.038*	2.79 (1.07–7.34)†	0.036*
Falls	2.85 (1.01–7.39)	0.024*	3.11 (1.04–9.28)‡	0.041*

CI, confidence interval.
Model 1: unadjusted. Model 2: adjusted for sex, age, previous cardiovascular disease, hypertension, systolic blood pressure, diastolic blood pressure, heart rate, chronic obstructive pulmonary disease, cancer, and chronic kidney disease.
*$P < 0.05$.
†Adjusted for age, sex, case mix index, hypertension, previous cardiovascular disease, chronic kidney disease, and cancer.
‡Adjusted for age, sex, systolic blood pressure, diastolic blood pressure, diuretics, benzodiazepines, vitamin D, antihypertensive medications, neurological diseases, and serum sodium.

PA has been found to be associated with an increased risk of prolonged LOS [28] . Our results corroborate the independent association between malnutrition and LOS, showing that patients with a low PA (≤4.0°) had increased LOS. These findings confirm the importance of investigating malnutrition at hospital admission in internal-medicine wards, and suggest PA as a good indicator of LOS and prolonged hospital stay.

Many efforts worldwide are aimed at reducing LOS, considering the high impact on inpatient and postdischarge outcomes and the burden of health care costs [28]. Identification of patients at risk of increased length of hospital stay therefore represents a challenge for hospitals [29].

In this study, values of phase angle lower than 4.0 obtained at hospital admission were, moreover, associated with a higher risk of hospital readmission, in-hospital falls, and mortality in a 9-mo follow-up. The fact that PA significantly predicts the risk of hospital readmissions in hospitalized patients has, to the best of our knowledge, been previously investigated only in a small cohort of patients with chronic intestinal failure [30]. Hospital readmissions represent an important public health problem that can negatively impact cost and patient outcomes [31]. Many efforts have thus been addressed to identifying predictors of readmissions, but it is nevertheless complex, and predictors are still scarcely defined. A previous study in older adults admitted in the general-medicine department of a tertiary-care hospital found that malnutrition, assessed using a nutritional assessment tool, was able to predict readmissions, suggesting the inclusion of nutritional state in risk-prediction models [32].

In the present study, we found that PA could be a useful predictor of hospital readmission risk. The mechanism underlying this association may be the negative impact of malnutrition on convalescence, rehabilitation, and resistance to infections, leading to degraded clinical outcomes and consequently to readmissions [33,34].

However, we have to emphasize that considering the wide heterogeneity of patients admitted to our internal-medicine ward, we cannot exclude the possibility that readmissions to other hospitals could have been happening during the observation period. Moreover, health care delivery in Switzerland is largely based on patients' choices; thus, we have to take into account the possibility that during the observation phase, patients could have decided to be treated at another hospital. However, considering the consistence of the associations found, despite the fact that the investigation was based on only one internal-medicine ward, it is conceivable that our results would not have been significantly different after correcting for further confounders.

We found that lower phase angles were independently associated with an increased risk of in-hospital falls in a 9-mo follow-up; this association persisted after adjustment for medications, the strongest risk factor for in-hospital falls. The association between low PA and falls has been previously investigated in community-

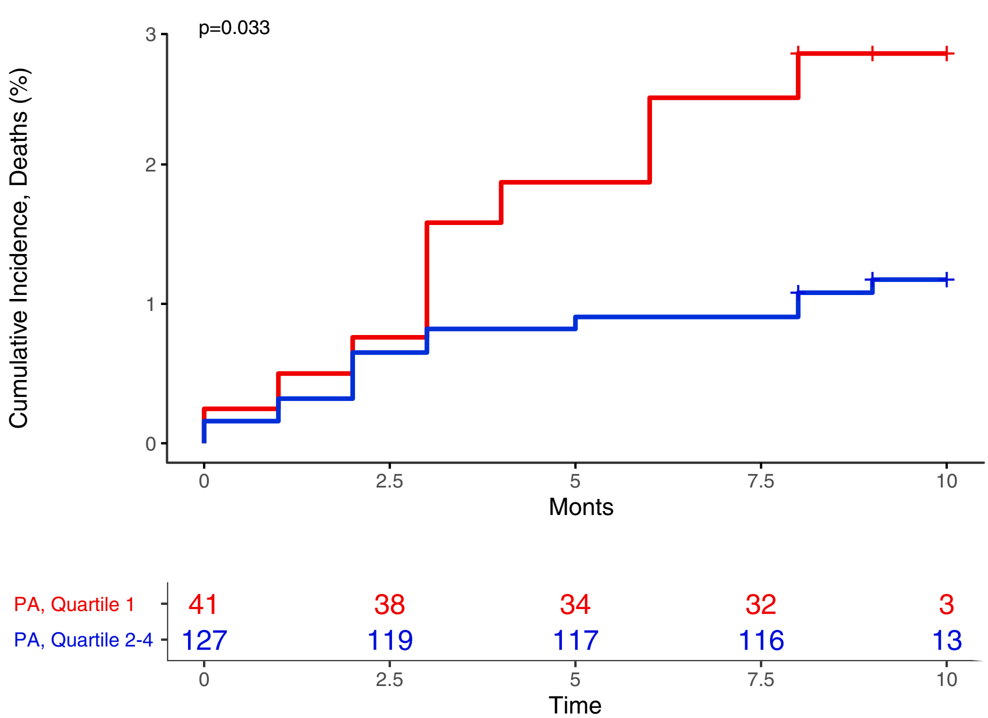

Fig. 2. Survival curves, stratified by PA quartile: cumulative incidence of deaths in quartile 1 (red line) compared with quartiles 2 to 4 (blue line). *P* value by log rank. PA, phase angle.

dwelling older adults, where those with lower phase angles were more likely to experience falls than those with typical or high phase angles [21]. No previous studies have investigated this association in patients hospitalized in internal-medicine wards. Even if we cannot elucidate the mechanisms underlying this association, we can speculate that the risk is multifactorial, with low PA also being a marker of cellular aging and conveying multiple risk factors for falls, ranging from malnutrition to sarcopenia and reduced physical activity.

Study participants with phase angles in the first quartile showed more than double the hazard of mortality compared to those with wider phase angles (above 4.1°). Furthermore, a narrow phase angle was significantly associated with mortality, even after accounting for several confounders and comorbidities. This suggests that measurement of phase angle could help to identify patients at high risk independent of their comorbidities. Previous studies have found an association between low PA and mortality, with variable cutoff values, in populations with different diseases and conditions. The predictive value of phase angle for mortality has in particular been demonstrated in individuals with lung, colorectal, and pancreatic cancers, and chronic diseases such as liver cirrhosis and HIV [35–38]. Even if the exact mechanisms underlying this association are not completely understood, a link with the peculiar characteristic of PA as a measure of cellular integrity has been postulated.

We have to acknowledge several limitations of our study. The first is the heterogeneity of the population under analysis, which was affected by several conditions at hospital admission; this corresponds, however, to the internal-medicine ward in real life, and associations persisted after correction for age and multiple comorbidities, including cancer. Second, the small sample size of patients analyzed does not allow us to draw definitive conclusions; further validation studies in a larger population of hospitalized patients in internal-medicine wards are needed to transfer the results to clinical practice. Third, no consensus exists regarding cutoff values for PA, limiting the possibility of a systematic comparison with previous results. However, our study highlights that PA is an important independent predictor for different clinical outcomes in patients hospitalized in internal medicine. Nevertheless, considering the observational nature of the study design, on the one hand, even if an association between PA and outcomes was found, this does not imply a causality relationship; and on the other, data were exposed to possible residual unmeasured confounders.

Moreover, it is important to highlight that prolonged or increased LOS is a hospital outcome parameter with a wide range of definitions, and several studies have found that it can be the consequence of several medical and non-medical factors [39]. On one hand, in some studies prolonged LOS has been strongly influenced by the definition of discharge (e.g., transfer from the hospital to nursing homes or other intermediate facilities instead of home), and on the other hand, some studies have found that about 25%–30% of excessive LOS is related to non-medical determinants, such as logistic or social factors (unwillingness to go home; lack of home assistance) [40–42]. Overall, considering all these factors and the fact that LOS is a hospital quality indicator in many health care systems, it has also been suggested that it be adjusted for clinical and non-clinical factors. In the present study, LOS was calculated from admission to discharge in the same hospital ward (internal medicine); nevertheless, we were not able to adjust our analysis for all possible confounders.

Last but not least, in 2016 several clinical nutrition societies founded the Global Leadership Initiative on Malnutrition (GLIM) [43], which was followed by the launch of the GLIM criteria. The primary objective was to reach a consensus for the diagnosis of malnutrition in the clinical setting. Moreover, diagnosis of malnutrition based on the GLIM criteria has been found to be associated with good predictive value on several patient outcomes [44]. However, few studies thus far have explored the agreement between BIA-derived parameters and GLIM in predicting patient outcomes [45]. Even if it had been of interest, a comparison in the present study between PA and GLIM was not performed, because it was far from the aims of the investigation.

It is important to note that recently, the results of a large trial (the Effect of Early Nutritional Therapy on Frailty, Functional Outcomes and Recovery of Undernourished Medical Inpatients Trial (EFFORT)) have demonstrated the benefits on clinical outcomes of a systematic screening of nutritional risk, followed by nutritional assessment and introduction of nutritional support at hospital admission, independent of the medical condition [7]. We believe that the results of our study underline an important critical question: Could evaluation of the phase angle represent an additional useful marker to ameliorate clinical outcomes of patients admitted in internal-medicine wards in order to start an early nutritional intervention support? On the basis of the present observational findings, we obviously cannot provide a definitive answer; we can only affirm that in-hospital assessment of bioimpedance-derived PA could help clinicians identify patients at high risk of the worst outcomes. Moreover, results of previous studies have highlighted the possibility of obtaining an improvement in hospital management, in terms of postoperative complications, LOS, and hospital costs, after starting a hospital nutritional intervention in surgical colon-cancer patients [46].

Finally the present study underlines once again the clinical need for nutritional screening in hospitalized patients. Even if screening tools to identify patients at nutritional risk are available, also using a simple device to measure the phase angle could help clinicians identify patients at high risk and in need of nutritional intervention. Considering the high prevalence of malnutrition in patients admitted in internal-medicine wards worldwide, prompt and easy recognition of this condition is imperative. Phase angle could be a non-invasive and operator-independent candidate marker, being quickly and easily assessable.

Further randomized clinical trials are advocated to explore the clinical benefits on clinical outcomes and hospital costs obtained from PA assessment in patients admitted in internal-medicine wards.

Conclusions

In conclusion, PA seems a promising, useful indicator of clinical outcomes in patients hospitalized in internal-medicine wards. In the present study, it emerged as an independent predictor of length of hospital stay and upcoming rehospitalizations, as well as a good marker of death and in-hospital falls.

The present findings support the use in hospital settings of bioimpedance PA assessment to help clinicians identify patients at high risk for the worst out comes in order to provide more nutritional attention.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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