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Evaluation of Bioelectrical Impedance Analysis in Critically Ill Patients: Results of a Multicenter Prospective Study

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Abstract

Background: In critically ill patients, muscle loss is associated with adverse outcomes. Raw bioelectrical impedance analysis (BIA) parameters (eg, phase angle [PA] and impedance ratio [IR]) have received attention as potential markers of muscularity, nutrition status, and clinical outcomes. Our objective was to test whether PA and IR could be used to assess low muscularity and predict clinical outcomes. *Methods:* Patients (≥18 years) having an abdominal computed tomography (CT) scan and admitted to intensive care underwent multifrequency BIA within 72 hours of scan. CT scans were landmarked at the third lumbar vertebra and analyzed for skeletal muscle cross-sectional area (CSA). CSA ≤170 cm^2 for males and ≤110 cm^2 for females defined low muscularity. The relationship between PA (and IR) and CT muscle CSA was evaluated using multivariate regression and included adjustments for age, sex, body mass index, Charlson Comorbidity Index, and admission type. PA and IR were also evaluated for predicting discharge status using dual-energy X-ray absorptiometry–derived cut-points for low fat-free mass index. *Results:* Of 171 potentially eligible patients, 71 had BIA and CT scans within 72 hours. Area under the receiver operating characteristic (c-index) curve to predict CT-defined low muscularity was 0.67 ($P \leq .05$) for both PA and IR. With covariates added to logistic regression models, PA and IR c-indexes were 0.78 and 0.76 ($P < .05$), respectively. Low PA and high IR predicted time to live ICU discharge. *Conclusion:* Our study highlights the potential utility of PA and IR as markers to identify patients with low muscularity who may benefit from early and rigorous intervention. (*JPEN J Parenter Enteral Nutr*. XXXX;xx:xx-xx)

Keywords

body composition; research and diseases; critical care; adult; life cycle; bioimpedance; phase angle; impedance ratio

Clinical Relevancy Statement

This research is clinically relevant in that it addresses a critically important issue faced by clinicians caring for critically ill patients: the lack of validated bedside tools for assessing muscle mass. This work may help identify a surrogate marker for muscle mass and help identify the adequacy of nutrition intervention through monitoring changes in muscle mass throughout hospital admission.

Introduction

Lean tissue, primarily consisting of skeletal muscle, is central to the body's healthy response to injury and illness.[1,2] Muscle wasting often occurs in the setting of illness and inflammation due to increased metabolic demands on the body. Critically ill patients often experience major losses of lean tissue due to severity of illness and organ dysfunction, prolonged immobility, and malnutrition.[3] Loss of this highly metabolic tissue is associated with increased morbidity and mortality,[4,5] infections,[6] and length of stay.[7] For intensive care unit (ICU) survivors, muscle atrophy may lead to decreased functional capabilities.[8]

Despite the prognostic significance of lean tissue loss in acute and chronic disease, its estimation is not commonly performed in hospital settings in part due to the limited availability of valid objective bedside methods.[1,9] Instead, clinicians often rely on subjective physical examination techniques,[10,11] alone or as part of the Subjective Global Assessment (SGA).[12] Subjective evaluation of muscle mass, however, is potentially error prone, particularly in obese and edematous states.[1,13]

Clearly, there is a significant and growing need for easily accessible and accurate methods for assessing lean tissue in the clinical setting. Very few available techniques are appropriate for use at the bedside or for repeated measures. Bioimpedance spectroscopy and the more commonly available multifrequency bioelectrical impedance analysis (MF-BIA) technique offer the potential for easy, rapid, and portable assessment of lean tissue and fluid status in the clinical setting. The MF-BIA approach has been evaluated for its

validity in healthy populations[14,15] and multiple clinical populations.[16,17] The MF-BIA approach for whole-body estimates of lean tissue requires the use of population-specific prediction equations and is predicated on meeting various underlying assumptions (eg, normal body geometry, hydration of lean tissue, and fluid distribution), which are often violated in critical illness, typically due to fluid shifts and edema present during illness and trauma.[18]

Inaccuracies in whole-body lean tissue estimates have led to recent interest in the use of raw BIA parameters (eg, 50-kHz phase angle [PA] and 200/5-kHz impedance ratio [IR]) as potential markers of nutrition status, disease severity, and outcomes in various clinical populations.[17,19–23] It has been hypothesized that PA may be related to cell membrane integrity,[24] and IR may be related to hydration status.[1] To obtain PA, reactance (Xc) and resistance (R) at 50 kHz must be obtained from the BIA device. Xc is the resistive force that cell membranes and tissue interfaces have on an electric current; R is the inability of an electric current to flow through the body, inversely related to the volume of fluid within tissues.[24] Subsequently, PA is calculated from the arctangent of the ratio of Xc to R at 50 kHz.

$$\mathrm{PA} = \mathrm{arctangent}\left(\mathrm{Xc} / \mathrm{R}\right) \times 180^\circ / \pi.$$

There is growing interest in the use of IR at 200 kHz/5 kHz as a potential marker of nutrition and clinical status.[1]

$$\mathrm{IR} = \frac{\sqrt{\mathrm{Xc}^2 + \mathrm{R}^2 \mathrm{at}\,200\,\mathrm{kHz}}}{\sqrt{\mathrm{Xc}^2 + \mathrm{R}^2 \mathrm{at}\,5\,\mathrm{kHz}}}.$$

Grounding of these raw bioimpedance parameters by comparison to a reference technique such as dual-energy X-ray absorptiometry (DXA) or computed tomography (CT), particularly for the ability to identify low muscle mass and monitor response to targeted nutrition interventions, is necessary before they can be accepted as useful tools in any clinical population. CT imaging has been shown to be reliable and precise in quantifying skeletal muscle mass.[25] Moreover, the cross-sectional area (CSA) of skeletal muscle in a single transverse CT image at the third lumbar (L3) region has excellent correlation with whole-body skeletal muscle mass.[26,27] However, CT is limited in its bedside applicability. MF-BIA–generated PA and IR offer the advantages of noninvasiveness, portability, and repeatability.

We are interested to know if PA and IR can be used as surrogate markers of muscle mass as measured by abdominal CT scans. Ultimately, as low muscularity is one of the key defining criteria to determine malnutrition, we are interested in whether these parameters can give insight into the nutrition status and adequacy of nutrition intervention throughout hospitalization. Furthermore, we investigated whether PA and IR had any prognostic capabilities to predict low CT-derived muscle CSA or clinical outcomes, such as ICU and hospital length of stay. Finally, we determined whether the creation of reference values (defined by mean PA and IR for healthy individuals falling at or below the fifth percentile for fat-free mass index [FFMI; FFM/height] measured by DXA in the most recent National Health and Nutrition Examination Survey [NHANES]) could improve their prediction capabilities of clinical outcomes. We hypothesized that PA and IR would have a strong linear association with abdominal CT muscle CSA and subsequent strong capabilities in predicting low muscularity and live hospital and ICU discharge.

Methods

Study Design

This was a prospective, multicenter observational study that was conducted across 3 ICUs, including the University of Minnesota Health, Minneapolis–St Paul, St Paul, Minnesota; VU University Medical Center Amsterdam, Amsterdam, the Netherlands; and Rush University Medical Center, Chicago, Illinois. This study was approved by the local and institutional research ethics committees. Patients ≥18 years of age were included if they were admitted to the ICU and had a CT scan of the L3 vertebra performed for clinical reasons <24 hours prior to or <72 hours after admission to the ICU. Moribund patients not expected to survive and other vulnerable populations, including pregnant women, prisoners, and mentally disabled individuals, were excluded.

Once enrolled, patients underwent BIA within 72 hours of the initial CT scan. Physical data, including age, sex, height, and weight, were obtained for all patients. Since all patients

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were bedridden, height was taken by a registered nurse with the patient lying flat, and weight was calculated using a bed scale, with bed items zeroed prior to measurement. Clinical data obtained or calculated upon ICU admittance included admission type (surgical vs medical), Acute Physiology and Chronic Evaluation II (APACHE II) score (a score to assess the severity of disease in the ICU),[28] Sequential Organ Failure Assessment (SOFA) score (a score to assess the degree of organ dysfunction in the ICU),[28] Charlson Comorbidity Index (designed to predict mortality by categorizing severity of comorbidities),[29] Functional Comorbidity Index (designed to predict physical function, not mortality, by categorizing severity of comorbidities),[30] number of mechanical ventilation days, ICU length of stay, hospital length of stay, ICU mortality, and hospital mortality. Height and weight were used to calculate body mass index (BMI; kg/m^2) for each patient, which was further classified into the following categories: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI >30 kg/m^2).

Bioimpedance Analysis

Bioimpedance analysis, in order to acquire PA and IR, was done using a MF-BIA QuadScan 4000 (Bodystat LTD, Isle of Man, UK) and was conducted as close as possible to a CT scan done for clinical reasons. PA and IR were directly measured by the Quadscan 4000. Electrodes were placed in a standard tetrapolar position (on the hands and feet), and patients were placed in a recumbent position with arms abducted from the body and legs separated, using rolled blankets as needed to ensure physical separation, as described previously.[1] MF-BIA was not performed on individuals with pacemakers or electronic implantable devices. For improved interpretation of the PA and IR data, we used bioimpedance and DXA data from NHANES (1999–2000, 2001–2002, and 2003–2004) to generate reference cut-points. Data generated from a spectroscopy device (Hydra Model 4200; Xitron Technologies, San Diego, CA) and a whole-body DXA scanner (Hologic QDR 4500 A; Hologic, Bedford, MA) were available in a healthy ethnically diverse sample of men (n = 149) and women (n = 137) between the ages of 18 and 49 years. Cut-points were defined by mean PA and IR for individuals falling at or below the fifth percentile for DXA-derived FFMI.

CT Scan Analysis

PA and IR were compared separately with CT-derived muscle CSA of the L3 region. CT images were sent to the University of Waterloo (Waterloo, Ontario, Canada) for analysis of muscle volume. Scans were analyzed using SliceOmatic image analysis software (version 4.3; TomoVision, Montreal, Quebec, Canada). All scans were analyzed by trained analysts, and reliability measures were performed. The mean coefficient of variation for intrarater and interrater reliability for muscle CSA was 1.0% and 1.9%, respectively. Intrarater and interrater reliability measures completed were similar to the coefficients of variation described in the literature.[26] Patients were categorized as having low muscularity if their skeletal muscle CSA was <110 cm^2 for females and <170 cm^2 for males. These cut-points have been previously established and associated with mortality in an ICU population.[5]

Statistics

Descriptive statistics were reported as mean ± standard deviation (SD) or median and interquartile range (Q1–Q3). PA and IR were further stratified by age (<65 years and >65 years) and sex to compare differences between groups using the Student *t* test. Linear regression, with and without consideration of covariates (BMI, age, sex, Charlson Comorbidity Index, and admission type), was performed to assess the ability of PA and IR to predict the variability in abdomen CT-derived muscle area. BMI, age, and sex are known to affect BIA parameters.[31] These and the other 2 covariates were retained in the regression model regardless of their statistical significance in predicting the dependent variable. Once patients were classified as having low muscularity (<110 cm^2 for females and <170 cm^2 for males), logistic regression, with and without consideration of the same covariates, was performed to assess the capabilities of PA and IR to predict CT-derived muscle area. Similarly, area under the receiver operating characteristic (ROC) curve was performed to assess prognostic capabilities, again taking into account covariates as described previously. Finally, Cox regression was performed to determine the predictive capabilities of PA and IR, with respect to live ICU and live hospital discharge. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), and all *P* values were 2-sided without correction for multiplicity.

Results

Descriptive Characteristics

Seventy-one of a total of 171 enrolled had both BIA and readable CT scans for comparison and were included for analysis, of whom 62% were male, and all fell at or below class I obesity. Overall, patients had a mean age of 57 ± 16 years and had a mean BMI of 29 ± 8 kg/m^2. Mean APACHE II score was 16 ± 7 (Table 1). According to BMI, 39% were classified as normal weight, 31% were overweight, and 30% were class I obese. Median ICU and hospital length of stay were 3 (2–7) and 10 (6–20) days, respectively, while ICU and hospital mortality were 4% and 6%, respectively (Table 1). There was no difference in PA or IR between males and females ($P = .09$ and $P = .07$, respectively). There was a trend toward differences between PA in young vs elderly ($P = .05$), but no significant differences were seen between IR when stratified by age ($P = .09$) (Table 2). CT scans revealed that 57% of patients had lower than normal muscularity, defined as CSA <110 cm^2 for females and <170 cm^2 for males. BIA occurred within 1.3 days to the CT scan.

Table 1. Patient Clinical and Physical Characteristics.[a]

Characteristic	All Patients (N = 71)
Age, y	57 ± 16 (21–87)
Sex	
Male	44 (62.0)
Female	27 (38.0)
Height, cm	172 ± 10 (152–196)
Usual weight, kg	85 ± 24 (51–186)
BMI, kg/m^2	29 ± 8 (19–57)
Normal	28 (39.4)
Overweight	22 (31.0)
Obesity class I	21 (29.6)
APACHE II score	16 ± 7 (3–31)
SOFA score	5 ± 4 (0–15)
Charlson Comorbidity Index	1 ± 1 (0– 5)
Functional Comorbidity Index	1 ± 1 (0– 4)
Admission type	
Medical	54 (76.1)
Surgical	17 (23.9)
Primary ICU admission	
Cardiovascular/vascular	17 (23.9)
Respiratory	12 (16.9)
Gastrointestinal	16 (22.5)
Neurologic	2 (2.8)
Sepsis	9 (12.7)
Trauma	10 (14.1)
Metabolic	1 (1.4)
Other	4 (5.6)
Mechanical ventilation duration, d	3 [1–6] (0–39)
Intensive care unit length of stay, d	3 [2–7] (1–22)
Hospital length of stay, d	10 [6–20] (2–72)
ICU mortality	4 (5.6)
Hospital mortality	6 (8.5)

APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment.
[a]Numbers are reported as mean ± SD (range), median [Q1–Q3] (range), or number (%).

PA and IR

Mean PA and IR were 4.34 ± 1.40 and 0.85 ± 0.04, respectively, for all patients. Using linear regression, PA alone was able to predict 20% of the variance in CT muscle CSA and 61% of the variance when covariates (age, sex, BMI, Charlson Comorbidity Index, and admission type) were added to the model (Tables 3 and 4). Similarly, IR alone was also able to predict 20% of the variance in CT muscle CSA and 60% of the variance when covariates were added. The area under the ROC (c-index) curve to predict CT-defined low muscle area was 0.67 for both PA and IR. With covariates added to logistic regression models including PA and IR, the c-indexes were 0.78 and 0.76, respectively (Figures 1A and 1B). PA and IR were both able to predict live ICU discharge (c-index = 0.611 and c-index = 0.608, $P = .008$ and $P = .009$, respectively) but not live hospital discharge (Table 5). When low FFMI cut-points for PA and IR derived from NHANES data were used, they were able to predict live ICU discharge with greater certainty (c-index = 0.77 and c-index = 0.79, $P = .04$ and $P = .01$, respectively) than that found without using low FFMI cut-points (Table 5).

Discussion

We conducted a critical comparison between BIA parameters and CT CSA analysis for muscle quantification in ICU patients. In a heterogeneous sample of 71 critically ill patients, we found that PA and IR accounted for 61% and 60% of the variance in CT muscle CSA ($P = .008$ and $P = .02$), respectively. Prediction of abdominal CT muscle CSA was improved when age, sex, BMI, Charlson Comorbidity Index, and admission type were added to the multivariate regression model. Based on ICU-derived sex-specific cut-points from CT analysis,[5] 57% of patients had low muscularity at admission to the ICU, which is similar to that seen in the literature for other ICU-specific studies.[4,5] ROC curve analysis showed that PA and IR had moderate capabilities in predicting low CT muscle CSA when controlling for covariates, appropriately diagnosing low muscularity 78% and 76% of the time, respectively. Furthermore, when DXA-derived low FFMI cut-points for PA and IR from an NHANES data set were applied in a logistic model, both were able to significantly predict live ICU discharge 77% and 79% of the time. Prediction of live ICU discharge was improved when applying reference cut-points from a large data set.

Loss of muscle and functional status are 2 of the defining criteria to determine the presence and severity of malnutrition in the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition Consensus definition.[10] PA and IR pose intriguing potential as markers to determine nutrition status and monitor nutrition intervention adequacy throughout treatment course. In the context of this study, PA performed well and is in agreement with previously published literature.[17,23,24] When patients with heart failure were classified by severity of disease, a lower PA was significantly associated with the severity of disease. Moreover, handgrip strength was lower and correlated with PA and severity of disease; similar results were seen with IR.[23] This points to the potential usefulness of PA and IR in predicting not only disease status but also functional status in this population. In individuals undergoing cardiac surgery, lower preoperative PA was associated with undernutrition (as specified by low BMI) and prolonged ICU and hospital length of stay.[17] This is consistent with the findings of our study. Furthermore, a lower PA has been shown to predict postoperative complications, nutrition risk, length of stay, and prognosis in various other clinical populations, including surgery,[32] human immunodeficiency virus,[33] and various cancers.[19,34] Although fewer studies have been conducted looking at IR, some researchers suggest it may be a

Table 2. Descriptive Data of Phase Angle and Impedance Ratio Stratified by Sex and Age.[a]

Measurement	All Patients (N = 71)	Males (n = 44)	Females (n = 27)	*P* Value	Young (<65 y) (n = 45)	Elderly (≥65 y) (n = 26)	*P* Value
Impedance ratio	0.85 ± 0.04 (69)	0.85 ± 0.04 (42)	0.86 ± 0.05 (27)	.07	0.85 ± 0.04 (43)	0.87 ± 0.04 (26)	.09
Phase angle	4.34 ± 1.40 (71)	4.54 ± 1.36 (44)	4.01 ± 1.42 (27)	.09	4.63 ± 1.42 (45)	3.85 ± 1.24 (26)	.05

[a]Numbers are reported as mean ± SD (n).

Table 3. Linear Regression of PA to Predict CT-Derived Muscle Area.[a]

Outcome	Predictors	R^2	Adjusted R^2	RMSE	*P* Value Model	*P* Value PA
CT muscle area (cm^2)	PA	0.21	0.20	37.7	<.0001	<.0001
CT muscle area (cm^2)	Covariates	0.60	0.57	27.5	<.0001	NA
CT muscle area (cm^2)	Covariates + PA	0.65	0.61	26.2	<.0001	.008

CT, computed tomography; NA, not applicable; PA, phase angle; RMSE, root mean square error.
[a]Covariates are age (linear), sex (binary), body mass index (linear), Charlson Comorbidity Index (linear), and admission type (binary). R^2 = % of variance in outcome explained by model.

Table 4. Linear Regression of IR to Predict CT-Derived Muscle Area.[a]

Outcome	Predictors	R^2	Adjusted R^2	RMSE	*P* Value Model	*P* Value IR
CT muscle area (cm^2)	IR	0.21	0.20	36.9	<.0001	<.0001
CT muscle area (cm^2)	Covariates	0.60	0.57	27.1	<.0001	NA
CT muscle area (cm^2)	Covariates + IR	0.63	0.60	26.1	<.0001	.02

CT, computed tomography; IR, impedance ratio; NA, not applicable; RMSE, root mean square error.
[a]Covariates are age (linear), sex (binary), body mass index (linear), Charlson Comorbidity Index (linear), and admission type (binary). R^2 = % of variance in outcome explained by model.

more robust marker of nutrition status and disease severity.[22] It has also been reported to identify malnutrition as defined by low total body nitrogen with greater sensitivity (79%) than PA (23%).[20] Our findings in light of published literature underscore the potential of PA and IR as clinical tools, and additional clinical evaluation is warranted.

Implementation of PA and IR Reference Cut-Points Derived From NHANES Data

The practical application of PA and IR measurements as biomarkers to define nutrition status requires that reference cut-points from healthy population data be established. Several researchers have published reference cut-points for PA in select populations, including German,[35,36] Swiss,[37] and American[31]; very little has been done with IR. To further establish the use of healthy population cut-points, the Continuous NHANES data set was used to produce reference cut-points for PA and IR to be applied in this study;[38] Grounding BIA parameters in a physiologically relevant end point, all individuals falling at or below the fifth percentile for FFMI as determined by DXA were grouped together. Mean PA and IR values were then found for this group of individuals with low muscularity, which subsequently became the reference cut-points applied to our critically ill population. Upon inspecting the ability of PA and IR to predict live ICU and hospital discharge, we found that when we applied our healthy reference cut-points, PA and IR predictive capabilities improved. However, more work is needed to establish appropriate cut-points based on age, BMI, sex, and ethnicity from larger, more robust data sets composed of DXA or other reference methods, if raw bioimpedance parameters are going to be used in a meaningful way at the clinical level, particularly with regard to the identification of malnutrition.

Strengths and Limitations

The strengths of this study include the use of expert analysis of abdominal muscle CSA using CT images to evaluate our BIA parameters. In addition, the multisite nature of this collaboration that recruited a heterogeneous ICU population with multiple operators enhances the generalizability of the findings. Admitting diagnoses included patients with a plethora of medical and surgical conditions. We believe the heterogeneous nature of our population adds strength to the results, as we would expect to see even stronger associations and predictive capabilities of PA and IR with a more homogeneous sample. Another strength to our study was that we attempted to

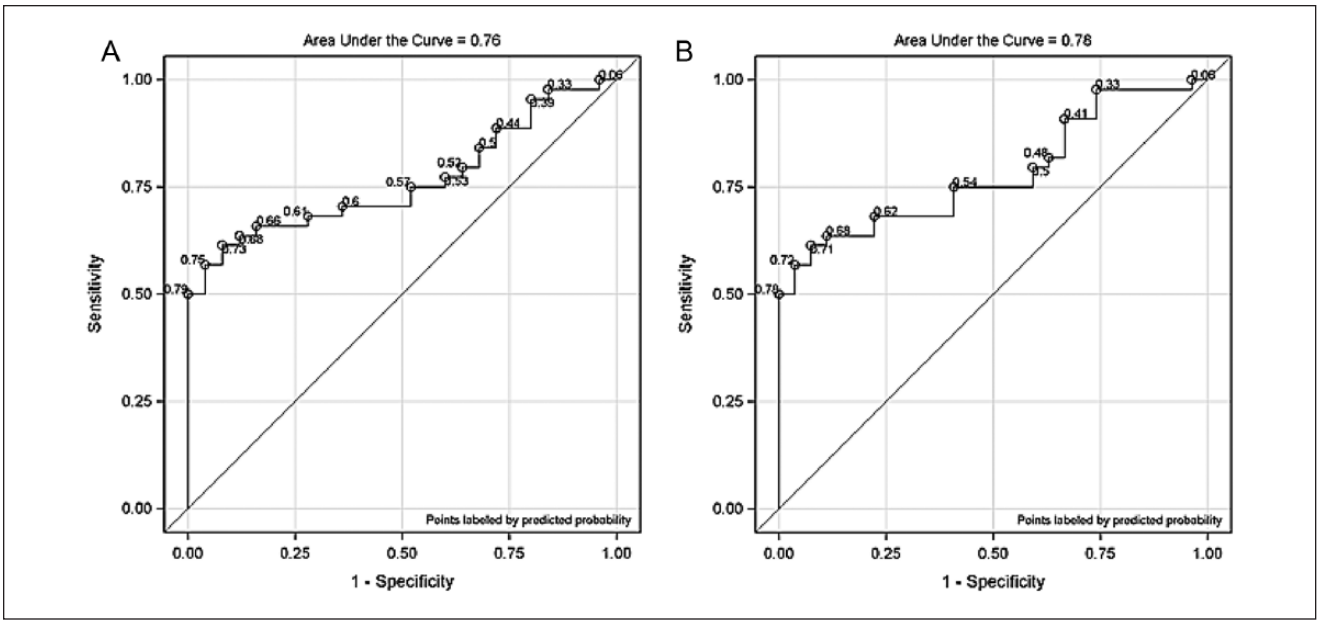

Figure 1. (A) Receiver operating characteristic curve for impedance ratio with covariates to predict low muscle area. (B) Receiver operating characteristic curve for phase angle with covariates to predict low muscle area. Receiver operating characteristic curve analysis is used to quantify how accurately medical diagnostic tests can discriminate between 2 patient states—in this case, low muscle mass or normal muscle mass. Area under the curve or c-index of 0.5 indicates no ability of the model to discriminate between low and normal muscle mass, while a c-index of 1 implies the ability to perfectly discriminate lower and normal muscle mass.[39]

Table 5. Cox Regression for the Ability of PA and IR to Predict Relative Time to Live Discharge.[a]

Predictor	Outcome	c-Index of Model	*P* Value of PA or IR
PA (continuous)	Time to live ICU discharge	0.599	**.028**
PA (continuous)	Time to live hospital discharge	0.528	.49
PA (continuous) + covariates	Time to live ICU discharge	0.611	**.008**
PA (continuous) + covariates	Time to live hospital discharge	0.599	.43
PA <5% cut-point	Time to live ICU discharge	0.774	**.04**
PA <5% cut-point	Time to live hospital discharge	0.613	.70
IR (continuous)	Time to live ICU discharge	0.584	**.032**
IR (continuous)	Time to live hospital discharge	0.513	.46
IR (continuous) + covariates	Time to live ICU discharge	0.608	**.0095**
IR (continuous) + covariates	Time to live hospital discharge	0.587	.39
IR <5% cut-point	Time to live ICU discharge	0.786	**.01**
IR <5% cut-point	Time to live hospital discharge	0.563	.75

Boldface numbers represent significant values at $P < .05$. ICU, intensive care unit; IR, impedance ratio; PA, phase angle.
[a]Covariates in model include sex, age (as linear), and body mass index (as linear). PA cut-point is 6.75 for men and 5.85 for women. IR cut-point is 0.78 for men and 0.81 for women.

generate physiologically relevant cut-points based on a large U.S. population sample to better interpret our data. However, it must be noted that the reference data were generated by a different bioimpedance device than the device used in our study; interdevice differences are potential sources of error but are not well documented. The study was limited by its relatively small sample size and the small number of confounding variables that were collected at the start of the study for inclusion into statistical modeling. Given that a pragmatic approach was taken with the implementation of the BIA protocol, logistical challenges in patient positioning and measurement procedures in light of the ICU setting likely contributed to the variability in measurements. Furthermore, our final sample did not include individuals with class II and III obesity due to the inability to obtain both BIA and CT scans for comparison in these individuals.

Conclusions

PA and IR were moderately associated with CT-derived muscle CSA at the L3 level with covariates added to the model. That is, lower PA and higher IR values were associated with lower muscle CSA. Furthermore, PA and IR appeared to predict low CT-derived muscle CSA. Using a healthy population data set, DXA-derived cut-points of low FFMI for PA and IR seemed to predict ICU discharge with greater certainty than did PA and IR (with covariates) alone. From a clinical standpoint, the simplicity, noninvasiveness, and easy repeatability of BIA have substantial appeal as a bedside assessment tool, and the idea that a PA below a certain value or an IR above a certain value could indicate low muscle mass, show poor nutrition status, and/or predict clinical outcomes is compelling. However, it remains to be established if these parameters can be effectively used to assess and monitor muscle mass and nutrition status with greater sensitivity than other clinically accessible techniques. Successful implementation of PA and IR as assessment tools in the ICU will require adherence to standardized measurement protocol and utilization of appropriate reference cut-points for these parameters. In summary, PA and IR show promise in being able to aid in the identification of low muscularity and poor nutrition status in the ICU setting; additional research is warranted.

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Statement of Authorship

A. Kuchnia contributed to the acquisition and analysis of the data, wrote the paper, and had primary responsibility for final content; L. Teigen, A. Cole, M. Paris, P. Weijs, W. Looijaard, G. Beilman, R. Leung, R. Dhaliwal, and C. Compher equally contributed to the revision of the manuscript; M. Mourtzakis and A. Day contributed to the design of the research, interpretation, and revision of the manuscript; H. Oudemans-van Straaten, S. Peterson, and H. Roosevelt contributed to the acquisition and analysis of the data and revision of the manuscript; C. Earthman contributed to study design and implementation, acquisition and analysis of the data, and critical revisions to the manuscript; D. K. Heyland contributed to the overall research plan and study oversight, and the revision of the manuscript and primary responsibility for final content; L. Teigen contributed to acquisition, analysis, and interpretation of data, critically revised the manuscript, gave approval of manuscript, and agrees to be accountable for all aspects of work; M. Paris and W. Looijaard contributed to study design, acquisition, analysis, and interpretation of data, critically revised the manuscript, gave approval of manuscript, and agree to be accountable for all aspects of work; P. Weijs, G. Beilman, R. Leung, C. Compher, and R. Dhaliwal contributed to study conception and design, critically revised the manuscript, gave approval of the manuscript, and agree to be accountable for all aspects of the work. All authors helped draft the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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