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Original Study

The Bioimpedance Phase Angle Predicts Low Muscle Strength, Impaired Quality of Life, and Increased Mortality in Old Patients With Cancer

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A B S T R A C T

Objectives: We investigated the impact of low phase angle (PhA) values on muscle strength, quality of life, symptom severity, and 1-year mortality in older cancer patients.
Design: Prospective study with 1-year follow-up.
Participants: Cancer patients aged >60 years.
Methods: PhA was derived from whole body impedance analysis. The fifth percentile of age-, sex-, and body mass index-stratified reference values were used as cut-off. Quality of life was determined with the European Organization of Research and Treatment in Cancer questionnaire, reflecting both several function scales and symptom severity. Muscle strength was assessed by hand grip strength, knee extension strength, and peak expiratory flow.
Results: 433 cancer patients, aged 60–95 years, were recruited. Patients with low PhA (n = 197) exhibited decreased muscle strength compared with patients with normal PhA (hand grip strength: 22 ± 8.6 vs 28.9 ± 8.9 kg, knee extension strength: 20.8 ± 11.8 vs 28.1 ± 14.9 kg, and peak expiratory flow: 301.1 ± 118 vs 401.7 ± 142.6 L/min, $P < .001$). Physical function, global health status, and role function from the European Organization of Research and Treatment in Cancer questionnaire were reduced, and most symptoms (fatigue, anorexia, pain, and dyspnea) increased in patients with low PhA ($P < .001$). In a risk-factor adjusted regression analysis, PhA emerged as independent predictor of physical function (ß: −0.538, $P = .023$), hand grip strength (ß:−4.684, $P < .0001$), knee extension strength (ß:−4.548, $P = .035$), and peak expiratory flow (ß:−66.836, $P < .0001$). Low PhA moreover predicted 1-year mortality in the Cox proportional hazards regression model, whereas grip strength was no longer significant.
Conclusions: PhA below the fifth reference percentile is highly predictive of decreased muscle strength, impaired quality of life, and increased mortality in old patients with cancer and should be evaluated in routine assessment.

Body composition assessment is an important tool for the identification of low muscle mass and sarcopenia, as well as the monitoring of nutritional status during, for example, nutritional therapy. Cancer patients, in particular, are at risk of impaired clinical outcome when their body composition is negatively affected. Bioelectrical impedance analysis (BIA) is a safe, noninvasive, and inexpensive bedside method to assess body composition, and BIA has gained considerable popularity in the clinical setting over the last decades. It measures whole body impedance, which is the opposition to an applied low amplitude alternating current consisting of 2 components: resistance (R) and reactance (Xc).

Using the measured impedance parameters and further variables such as sex, weight, and height, total body water and lean body mass can reliably be estimated in healthy subjects provided that adequate equations are applied.[1] The calculation of body compartments is,

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however, not considered valid in patients with altered hydration, such as edema, fluid shifts, and ascites, or with extreme body mass index (BMI) (<16 and >35 kg/m^2).[1] The use of direct impedance parameters that are not prone to equation inherent errors has, therefore, increased in recent years.[1–7] The phase angle (PhA) is a raw parameter derived from whole body impedance analysis, reflecting the contribution of R, the pure resistance of the body to the flow of the alternating electric current, and Xc, the resistive effect produced by the double layer of the cell membranes.[8,9] Thus, the PhA has been interpreted as a superior prognostic index of cell membrane integrity. Disease, inflammation, malnutrition, or prolonged physical inactivity can result in disturbed electric tissue properties, which directly affect the PhA. In sepsis, for instance, fluid shifts from intracellular to extracellular space occur at an early stage[10] and are accompanied by a decrease of PhA. Not surprisingly, a low PhA has, therefore, been associated with impaired outcome in cancer or severe disease[2,3,10–18] and in multimorbid geriatric patients.[19] Using established reference values, we have previously shown that patients with cancer whose PhA is below the fifth reference percentile have a significantly higher 6-month mortality even if adjusted for other potential risk factors such as disease severity and weight loss.

Older patients with cancer are at particularly high risk of malnutrition[20,21] and sarcopenia, which both have detrimental effects on physical function and mobility, and which are associated with increased morbidity and mortality. Rapid identification of patients at risk for impaired clinical outcome is necessary to allow an early or more targeted intervention. Assessing body composition in hospital is, however, frequently hampered because of costs, time, and limited availability of established methods.

The aim of this study was, therefore, to investigate the impact of the fifth percentile of age-, sex-, and BMI-stratified PhA reference values in older patients with cancer on muscle strength of upper and lower extremities, health-related quality of life, and cancer-related symptoms in a cross-sectional analysis. In a second step, we also evaluated the prognostic value of the fifth reference percentile on 1-year mortality in a risk factor adjusted Cox regression analysis.

Methods

Participants

We included 433 consecutive patients aged >60 years, admitted to the Department of Gastroenterology, the Department of Oncology and Hematology, or the Department of Radiotherapy at the Charite University Medicine. All cancer types and stages were considered. Patients were eligible for the study if they were older than 60 years and were suffering from solid or hematologic tumor disease and gave written informed consent. Patients with implanted pacemakers or defibrillators were excluded, and patients with neuromuscular degenerative disease, hemiplegia, or severe arthritis in the hands/limbs were excluded to avoid potential confounders on muscle strength. The Ethics Committee of the Charite Universitätsmedizin Berlin approved the study.

All measurements were made within 48 hours of admission to hospital. Demographic characteristics, age and sex, as well as clinical variables such as duration of disease (defined as length of time in years since diagnosis), tumor location, and the Union Contre le Cancre (UICC) stage classification were documented. Moreover, type of treatment was recorded. Karnofsky performance scale, which rates patients' wellbeing, physical ability, and activities of daily life on a scale from 0 (none) to 100 (normal, no complaints) was determined. In order to evaluate mortality rate, patients were contacted by telephone 1 year after the first assessment; if patients could not be reached, the local death register was consulted.

BIA

BIA was performed using a Nutriguard M (Data Input GmbH, Darmstadt, Germany) applying alternating electric current of 800 μA at 50 kHz and the R and Xc were measured. The PhA was calculated as follows: PhA (degrees) = arctan (Xc/R) × (180/П) and categorized as low if falling below the fifth reference percentile of age-, sex-, and BMI-stratified reference values generated in a large healthy cohort (n = 214,732).[22] The percentage of patients with low PhA values was determined and compared with patients with normal PhA values (ie, above the fifth reference percentile). Values for the single fifth reference percentiles can be found in the article by Bosy-Westphal et al.[22] Measurements were done according to a standardized protocol as described in detail elsewhere.[22] In brief, patients were measured in the morning after an overnight fast, in the supine position with arms and legs abducted from the body. Source and sensor electrodes (Ag/AgCl, Bianostic Classic Electrodes; Data Input GmbH) were placed on the dorsum of both hand and foot of the dominant side of the body.

Anthropometric Measurements and Weight Loss

Body weight was measured in light clothes with a portable electronic scale (Seca 910; Seca, Hamburg, Germany) to the nearest 0.1 kg, and height was measured with a portable stadiometer (Seca 220 telescopic measuring rod; Seca) to the nearest 0.1 cm. Weight and height were used to calculate BMI [weight (kg)/height (m)^2].

Weight loss in the 6 months prior to hospital admission was determined and patients with a weight loss >5% were considered malnourished, and patients with a weight loss >10% were deemed severely malnourished.

Muscle Strength

Hand grip strength

Hand grip strength was measured in the nondominant hand with a Jamar dynamometer (Sammons Preston Rolyan, Chicago, IL). The patients performed the test while sitting comfortably with shoulder adducted and neutrally rotated forearm, elbow flexed to 90 degrees, and forearm and wrist in neutral position. The patients were instructed to perform a maximal isometric contraction. The test was repeated within 30 seconds, and the highest value of the 3 tests was used for the analysis.

Knee extension strength

Knee extension strength was measured while the patients were seated, legs not touching the floor. The right leg was then fixed with a sling, which was connected to the wall behind the patients and connected with a force sensor. Patients were then encouraged to perform maximum knee extension. The test was performed 3 times, and the highest value was documented.

Peak expiratory flow

Peak expiratory flow was assessed with the ASSESS Peak Flow Meter (Respironics HealthScan Inc, Cedar Grove, NJ). Patients were told to exhale as fast and forcefully as possible. The test was carried out 3 times, and the highest reading was recorded.

Health-Related Quality of Life and Symptom Severity

Quality of life was determined with the validated core questionnaire QLQ-C30 of the European Organization for Research and Treatment of Cancer (EORTC). The questionnaire assesses quality of life in 9 domains. It includes 30 questions exploring 5 functional