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REPETITIVE BIOELECTRICAL IMPEDANCE ANALYSIS TO PREDICT OUTCOME IN EARLY GERIATRIC REHABILITATION

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Abstract: *Objectives:* To evaluate prognostic value of bioelectrical impedance analysis in a geriatric acute care setting providing early rehabilitation. *Design:* Observational study. *Setting:* Geriatric acute care ward. *Participants:* A case series of 33 elderly patients admitted to early geriatric rehabilitation course after severe deconditioning in the context of acute disease. *Measurements:* Comprehensive geriatric assessment, Mini-Nutritional-Assessment (MNA), bioelectrical impedance analysis (BIA). Telephone based assessment 6 months after discharge. *Results:* 11 patients showed a favorable rehabilitation course (gain of at least 10 ADL points) and 22 patients did not. A positive increment of reactance in the repetitive analysis was significantly associated with an unfavorable outcome, whereas baseline values of functionality markers and BIA were not. 11 patients died within a 6-month interval after discharge. Lower ADL-score, reactance and phase angle were found to be significantly associated with 6-month-mortality. A phase angle below 4° comprised a 3.7 fold mortality-risk. *Conclusion:* Assessment of phase angle that could be easily obtained even in bedridden subjects may represent a comprehensive additional marker to estimate 6-month prognosis of an individual patient undergoing early geriatric rehabilitation treatment in an acute care setting. For short-term improvement of functionality during rehabilitation course the assessment of increments in BIA-markers reveals more promising.

Key words: Deconditioning, bioimpedance, rehabilitation, sarcopenia.

Introduction

Early geriatric rehabilitation is performed in elderly patients with severe functional loss (deconditioning) during acute care course pointing to an increased risk of a remaining severe disability (1) and leaving them unable to be referred to a secondary rehabilitation unit. Among a huge variety of geriatric conditions, premorbid loss of muscle mass by sarcopenia and poor nutritional status are discussed to be significant factors influencing rehabilitation prognosis (2). However in an acute care setting, measurement of nutritional status and body-composition is impeded by bed-rest, delirium or other patient related aspects. In this circumstance bioelectrical impedance analysis (BIA) provides an easy to perform assessment of body composition and hereby may allow to indirectly estimate nutritional status and muscle mass.This method is widely accepted as a reliable method in nutritional care and medicine (3). However, its diagnostic value has been less well analyzed in acute care patients. A main limitation in this setting may be instable fluid balance and efficacy of BIA therefore has been found to be lower than in ambulatory populations.

BIA allows not only the initial detection of a critical premorbid reduction of muscle mass or increased body fluid but also may give some impression of cell membrane stability in general as parameters of a biological conductor may be altered by several factors related to this aspect e.g. cell size, membrane permeability and intracellular fluid composition (4). All these aspects have been found associated with a negative outcome in different patient groups and settings (5-7). Furthermore, BIA alleviates the monitoring of changes in body tissue composition aspects as repetitive measurements can easily be performed.

Raw parameters derived directly from BIA are:
- reactance (related to cellular membranes)
- resistance (related to the amount of water in body tissue)

BIA measures the shift of applied current behind the voltage. This shift reflects the relative contribution of reactance (cell membranes) and resistance (fluid) and is quantified as the phase angle (8, 9).

- phase angle = arctan $\frac{reactance}{resistance} * \frac{180°}{\pi}$

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As mentioned above, phase angle is positively associated with intact cell membranes of the human body (8). Respectively a lower phase angle may suggest a decrease in intact cell membranes (cell death or poor integrity) (10). The assessment of these parameters does not require body weight or height, which is particularly advantageous in the examination of bedridden patients.

Recently a consensus conference has proposed criteria to classify the sarcopenia-syndrome (11). Although this consensus defines sarcopenia as acomposite of muscle mass and muscle strength, BIA-derived parameters offer the opportunity to estimate muscles mass in a bed-side manner and hereby resemble an estimation of the sarcopenia-syndrome (12). Janssen et al determined cutpoints for identifying elevated risk for disability in older adults (13) and this may be used also as a diagnostic measure for sarcopenia. These BIA-derived criteria mainly rely on resistance, actual body weight and height. However, these measurements are recommended in a stable situation as fluid imbalance or active disorder may strongly influence BIA-measurement. Therefore the true prognostic value of these measurements in a dynamic clinical situation remains a topic of discussion, and data concerning this issue in the elderly are sparse. BIA-derived markers have not yet been analyzed in elderly patients with significant deconditioning undergoing early rehabilitation.

Material and Methods

Inpatients attending a geriatric ward for early geriatric rehabilitation after stroke or fracture after fall with severe deconditioning were eligible. Inclusion period was 12 month. An additional inclusion criterion was age 65 and over. Exclusion criteria were previously present immobilization, previously living in a nursing home and implanted cardiac pacemaker or defibrillator. In the latter case, BIA-analysis is discouraged. Early geriatric rehabilitation was initiated following a distinct clinical algorithm described in detail elsewhere (14). In summary initiating the early rehabilitation course was depending on functional capacity expressed as score of activities of daily living - ADL (usually less than 30 out of a maximum of 100), preserved rehabilitative prognosis and active comorbidities requiring an ongoing acute care such as delirium, heart failure or pneumonia. ADL-score following the Barthel Index was applied. It consists of 10 items and covers a range from 0 to 100 (15). Early rehabilitation course was scheduled for a median duration of 14 days but discharge from the program was determined on an individual and clinical base. Positive or favorable outcome of the early rehabilitation course was defined as a gain in ADL-score of at least 10 points (difference between ADL at beginning of early geriatric rehabilitation course and ADL at discharge). A difference less then 10 points or in hospital death were defined as unfavorable outcome. Informed consent was obtained according to the Declaration of Helsinki.

BIA was applied repeatedly (at least two times) during the rehabilitation course (BIACORPUS RX4000, MediCal HealthCare, Karlsruhe, Germany). Measurements were obtained at the dominant body-site using single-way electrodes (CE certified electrodes provided by MediCal Health Care – Biaphaser tabs) except if there was an existent disability on this side to minimize measurement-failure due to local fluid shift Measurement parameters were 50kHz and 800μA. Actual body weight was measured using a bed scale. Current measurement guidelines as given by the ESPEN conference(16) were followed.

BIA-derived parameters allow an estimation of skeletal muscle mass and skeletal muscle index (SMI). Formulas given by Janssen et al. (12, 17) were applied:

$$SM\ (kg) = \frac{\text{height (cm)}^2}{\text{Rx0}}.401 + (\text{sex} * \text{x}\ 3.2825) + (\text{age} * \text{x}(-0.071)) + 5.102$$

(SM: skeletal muscle mass, R: resistance, sex: men=1 women=0)

$$SMI(\%) = \frac{\text{SM}}{\text{weight (kg)}} * 100$$

For comparison a second formula from the literature to calculate fat free mass (FFM) from BIA-data was applied (18):

$$FFM\ (kg) = 7.4238 + 0.4414 * \frac{height\ (cm)^2}{R} + 0.1249 * weight\ (kg) + 0.0552 * Xc$$

$$+ 2.1270 * sex + 0.0586 * (sex * weight\ (kg))$$

(R: resistance, Xc: reactance, sex: men=1 women=0)

Proportion of fat free mass (PFFM) was calculated as follows:

$$PFFM = \frac{FFM}{weight}$$

Both SMI and PFFM were derived from the initial BIA-measurement.

For further analysis of repetitive BIA-analysis increments were calculated between the first and last BIA-measurement. These increments were calculated for resistance, reactance and phase angle:

$$\Delta phase\ angle\ = phase\ angle\ t2 - phase\ angle\ t1$$

Clinical data were obtained from patients charts. This covered data from the initial comprehensive geriatric assessment at beginning of the rehabilitation course: ADL-score (15), MNA (Mini Nutritional Assessment (19)), GDS (Geriatric depression scale20) and MMSE (Mini-Mental-State-Examination 21). Six months after discharge a telephone based assessment took place to evaluate outcome focusing on mortality and self-management capacity (ADL-score). The interview was performed applying predefined questions, assessing ADL-status from the patient or proxy, place of living, self-rated quality of life, information about intermittent hospital stays and mortality if the patient has deceased. However, details concerning the cause of death could not be acquired. From these interviews only information about mortality was taken as a second outcome-variable (6month-mortality after discharge calculated from the date of death).

For statistical analysis BIA-derived factors and other clinical variables are compared with regard to the two predefined outcome-variables. As the majority of clinical variables is expected either not truly continuous or not normally distributed (e.g. ADL, GDS, MMSE) non-parametric tests are applied for comparison between distinct groups (Wilcoxon-test for continuous and Fisher´s exact test for discrete variables). Variables disclosing an association with the outcome variables were included in subsequent ROC-analysis. Statistics were performedapplying SAS and Sigmaplot software packages.

Results

33 (age 65-96) out of a total of 138 elderly inpatients undergoing early geriatric rehabilitation during the inclusion period met all inclusion criteria and agreed with the additional BIA. 11 patients showed a positive outcome of the rehabilitative course whereas 22 did not. Univariate analysis of possible predictors revealed no association with initial markers derived from BIA(phase angle, resistance, reactance, skeletal muscle index, PFFM), nor with markers of functionality (ADL, premorbid mobility impairment) or malnutrition (table 1). In the repetitive analysis (median time increment 13 days (6-28)) a negative increment of phase angle, reactance or resistance was related to an unfavorable outcome as derived from ROC- and Sensitivity-analysis (figure 1). Nevertheless AUC in ROC-curves remained low for all parameters (below 0.8).

Six months after discharge, data could be assessed by telephone-based interview in 31 subjects, 2 were missing. Out of the remaining 20 patients had survived and 11 had died. Univariate group comparison between survivors and non-survivors revealed significant differences in age, initial ADL-score, initial reactance and initial phase angle. Median age in survivors was 78 years vs. 87 years in non-survivors (p=0.011), median baseline-ADL-score in survivors was 15 vs. 0 in non-survivors (p=0.013), median reactance was 48 Ω vs. 27 Ω in non-survivors (p=0.004) and median phase angle in survivors was 4.7° vs. 3.3° in non-survivors (p=0.002).Univariate analysis disclosed no significant differences between survivors and non-survivors with regard to other BIA-derived parameters (resistance, increments of reactance, resistance and phase angle). Moreover, there weren´t any significant differences found between those groups concerning SMI, PFFM or pre-hospital functionality. ROC-analyis therefore was restricted to parameters identified by univariate testing to be associated with the outcome-variable. This ROC-analysis resulted in an AUC of 0.839 for phase angle, 0.816 for reactance and 0.764 for the initial ADL-score (figure 2). All ROC-curves were found significantly different from 0.5. Sensitivity-analysis of different phase angle cut-off-limits revealed 4° as a comprehensive prognostic marker (sensitivity of 6-month-mortality 0.73, specificity 0.75). An initial phase angle below 4° was associated with a 3.7 fold increase in 6-month mortality.

Table 1
Univariate analysis of possible predictors of rehabilitation outcome

	Improvement[a] N=11	Stagnation N=22	p[b]
age (years)	78 (65-90)	80.5 (71-96)	0.276
ADL[c]	15 (0-70)	0 (0-85)	0.189
IADL[d]	3 (0-8)	6 (0-8)	0.311
GDS[c]	5 (1-10) missings=4	4 (1-8)missings=15	0.575
hemoglobin g/dl [c]	11.5 (8.4-15.0)	11.6 (9.0-16.7)	0.731
CRP mg/l [c]	33.4 (4.8-136.4)	23.9 (2.6-120.7)	0.147
Albumin g/l [c]	27.4 (15.7-35.1)	27.8 (20.1-38.4)	0.647
creatinine mg/dl [c]	0.8 (0.4-2.4)	0.9 (0.5-3.3)	0.894
SMI (kg/m²) [e]	7.48 (5.62-10.40)	7.36 (5.08-10.69	0.380
PFFM [e]	0.60 (0.50-0.70)	0.59 (0.44-0.82)	0.775
MNA[c]	24.3 (15-27.5)	23 (19-27)	0.651
resistance (Ω) [c]	528 (433-661)	577 (422-780)	0.456
phase angle (°) [c]	4.3 (2.5-7.1)	4.0 (2.5-6.8)	0.633
reactance (Ω) [c]	43 (23-66)	39 (20-81)	0.985
Δphase angle (°) [f]	0.1 (-0.5-0.9)	-0.3 (-1.5-0.9)	0.064
Δ reactance (Ω) [f]	5 (-4-19)	-3 (-17-9)	0.014
Δresistance (Ω) [f]	44 (-41-241)	5 (-154-106)	0.056
no need for care[g]	2 (18.2%)	4 (18.2%)	1
mobility impairment[g]	2 (18.2%)	1 (4.5%)	0.252
nursing home[g]	4 (36.4%)	3 (13.6%)	0.187

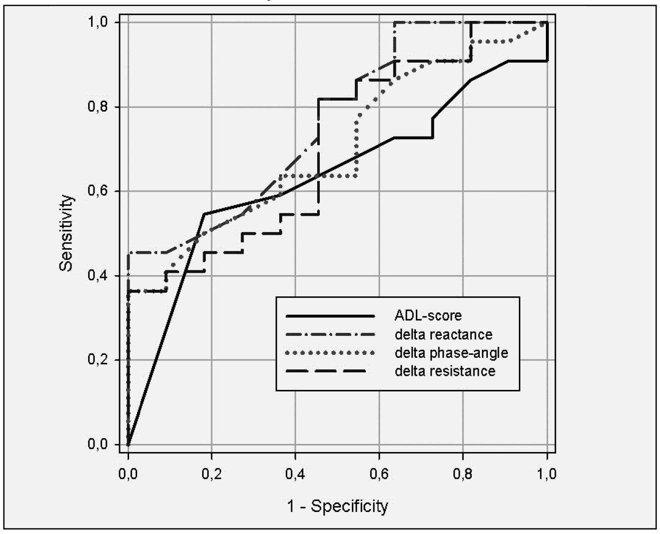
Data is given as median (min-max) for discrete or frequency for categorical data; MNA: Mini-Nutritional-Assessment; a. defined as gain in ADL-score of at least 10 points; b. Wilcoxon (discrete variables) or Fishers´ Z (categorical variables); c. at beginning of the rehabilitation-course; d. according to Lawton and Brody before hospital admission; e. derived from BIA at beginning of the rehabilitation-course; f. measurement 2 – measurement 1; f. anamnestic information concerning situation before hospital admission; g; before hospital admission.

Discussion

This preliminary data from early geriatric rehabilitation of severely impaired inpatients due to acute diseases provide results concerning bioimpedance markers. The raw data from the analysis all showed increased variability compared with data from healthy cohorts of elderly (22, 23). Regarding median values, resistance was increased whereas reactance and phase angle were decreased. The most predominant difference to the above mentioned healthy cohorts of elderly was a reduced phase angle in some patients down to 2.5°, pointing to membrane instability and membrane damage in these subjects. Instable body composition and membrane performance are more predictive for short time result of the rehabilitative course than initial patient characteristics such as reduced muscle mass, present malnutrition or general functionality.Especially SMI derived by BIA disclosed no difference between the two different groups. Lower limit of normal 95%-confidence interval of phase angle in elderly aged 70 years and over has been reported 4.2° in women and 4.8° in men (2). Decreased phase angle has been found in a variety of cohorts of different diseases associated to higher mortality rates and pronounced morbidity (25). This also could be confirmed in a cohort of patients after surgical interventions where reduced phase angle was strongly associated with the occurrence of postoperative complications (26). Finally in a cohort of geriatric inpatients, a decreased phase angle below 3.5° was associated with a significant increase of in-hospital mortality (27). However this cohort represents an unselected geriatric population of acute-care in-patients. In contrary to these data neither raw parameter of initial bioimpedance analysis nor functionality-scores disclosed any prognostic value in univariate analysis to determine an unfavorable outcome in early rehabilitation course. This may be due to the rather low number of observations in this preliminary study but also may be explained by the more highly selected patients in our study excluding severely impaired patients without rehabilitative perspective on the one hand and rather robust elderly with no need for structured rehabilitation program on the other.

Figure 1

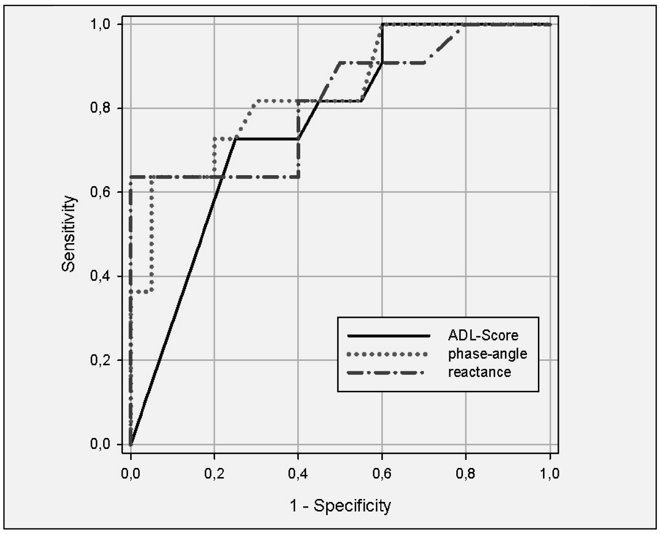
ROC-analysis - predictors of an unfavorable outcome of early rehabilitation



As rehabilitation course and outcome depends on a dynamic interplay between different factors, short-term variation in bioimpedance reflecting metabolic and total body response to rehabilitative treatment may predict outcome more effectively than initial nutritional and bioelectrical state alone. Data analyzing short and median time increments in bioimpedance analysis are sparse, particularly in geriatric settings. A multivariate analysis of repetitive nutritional assessment in patients with amyotrophic lateral sclerosis failed to show an independent prognostic effect of phase angle or another single aspect of BIA to predict mortality in contrast to a change in BMI (28). In contrary to these data we found median negative increments for reactance phase angle and stagnation for resitance associated with negative outcome, where statistical significance was reached only for reactance. The subsequent ROC-analysis however revealed still low diagnostic efficacy as AUC-values remain below 0.8. Furthermore no significant difference in this respect was found compared to initial ADL-values. Due to the rather limited number of participants in this study and consecutively low power as light difference in diagnostic efficacy may be left undetected. Compared with initial ADL-score repetitive measurement of BIA showed rather high variability in the rehabilitation course both presenting negative and positive increments for all raw parameters. This underlines the highly dynamic character and pattern of BIA-data in the setting of acute care resp. early rehabilitation.

Figure 2

ROC-analysis - predictors of 6month-mortality



Considering 6-month mortality, both initial ADL-values and markers derived from body-impedance-analysis disclosed significant prognostic value. In ROC-analysis phase angle proved the best AUC-values. This result is in good accordance to previous studies in different populations (6) including the elderly (17). This outlines the predictive value for an unfavorable outcome not only with regard to hospital mortality as previous studies already have shown but also associated to medium-time outcome. Phase angle may more precisely reflect an underlying critical vulnerability of elderly recovering from severe acute disease than baseline functionality or markers of sarcopenia such as skeletal muscle index do. Furthermore estimation of muscle mass or fat free mass by formula - although from a theoretical point of view significan tfor rehabilitation course in this cohort - was clearly inferior to raw BIA-parameters or general functionality. However, as number of observations was limited in this pilot study, this does not necessarily mean that there is no influence at all and our results have to be confirmed in larger studies. Nevertheless, this also may be a result of inheritant limitations with formula estimation of body composition that indeed requires stable conditions not present in acute care patients. Therefore assessment of phase angle remains as the most valuable and easily obtainable marker in bedridden subjects undergoing acute hospital care and may represent a comprehensive additional marker to estimate 6-month prognosis of an individual patient undergoing early geriatric rehabilitation treatment in an acute care setting.

Some limitations of the study have to be mentioned. The number of subjects was rather limited and in those subjects several factors may have influenced accuracy of BIA: instable fluid homeostasis in general, paresis of limbs due to stroke or recently undergone limb surgery which both may have resulted in local fluid shifts. Second, this is a monocentric study and although geriatric treatment in an early rehabilitation setting on acute care wards in Germany is following a consented general frame-work with regard to level of functionality and index diagnosis, local conditions may influence the pattern and amount of clinical factors determining the patients and hereby our results may not be valid for geriatric inpatients in general or geriatric rehabilitation in other settings. However, study setting was very close to every-day practice on geriatric wards and hereby our results may encourage physicians to implement BIA in daily routine for an early identification of geriatric patients at highest risk. The value of phase angle should be confirmed in larger scale and multicentric studies.

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