Assessment of adult malnutrition with bioelectrical impedance analysis: phase angle as a measure of malnutrition and detailed body composition in two different age groups of healthy Caucasians – A MaNuEL study

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Main findings

- In a healthy population 12.5% had a low PA representing an impaired quality of lean mass (=malnutrition).
- A low PA was observed in normal weight as well as overweight subjects.
- A low Pa showed no correlation with BMI and FFM/FM ratio

1. Introduction

Malnutrition has been associated with famines in developing countries, but malnutrition (and especially malnutrition in hospitals) are also challenging in developed countries. Malnutrition results from shortage in dietary (e.g. energy and/or nutrient) intake e.g. as protein-energy malnutrition. Causes of poor nutritional status in older people are complex and include age-related physiological, psychological and social determinants which affect food intake and body weight. In addition, acute and chronic diseases add to malnutrition in the elderly [1]. Protein-energy malnutrition results in weight loss, reduced body weight, fat free mass (FFM) and fat mass (FM), which are associated with disturbances in physical and metabolic functions. From the 1970s onwards malnutrition in hospital patients has been described with prevalence's between 20 to 62% [2-4]. Malnutrition adds to complications leading to longer hospital stay [5, 6], a higher rate of re-submission after hospital discharge, nosocomial infections and a higher mortality of patients [3, 7-10]. Prevalence of malnutrition varies depending on screening tools to evaluate a person's malnutrition risk. During the last years a number of screening tools has been developed to assess malnutrition in different setting e.g. hospital (NRS-2002, SGA) or home care [11, 12]. Most of these screening tools are based on a low BMI and weight loss history. BMI resembles a low weight but failed to give precise information's about body composition [13]. Based on body composition assessments in elderly patients, Winter et al. [14] proposed that a BMI below 23 kg/m² instead of 18.5 kg/m² reflect the risk of malnutrition in this group. Vice versa a high BMI reflects a considerable variance in the relationship between FM and FFM which impacts the health status of a subject [15]. It is obvious that besides BMI body composition analysis is necessary to discover the risk and characteristics of malnutrition.

Bioelectrical impedance analysis (BIA) is easy to use as a measure of total body water, FFM, skeletal muscle mass and FM [16, 17]. In addition, the phase angle (PA) as a geometrically ratio of resistance and reactance can be calculated from the raw data determined by BIA [18, 19]. PA became popular during the last years since it has been shown that a low PA is associated with poor outcomes in different disease states [20] or elderly people [21, 22]. A low PA is associated with low body cell mass and poor cell integrity [23, 24] However up to now neither the prevalence of a low PA nor its association with quantitative measures of skeletal muscle mass have been evaluated.

The two aims of this study were to evaluate (i) the prevalence of malnutrition based on age, sex and BMI specific PA and (ii) to determinate what specific body composition characteristics (skeletal muscle mass and adipose tissue) are related to a low PA.

2. Experimental Section

2.1. Participants and Setting

The study population used for body composition analysis consisted of 664 healthy Caucasians (56.5 % females, median age 48 years (IQR 39 – 65 years, median BMI 26.9 kg/m² (IQR 24.0 – 31.1). Body composition analysis has been performed at the "*German Reference Center for Body Composition*" (Institute of Human Nutrition and Food Science) with specific competence in comprehensive methods of body composition analysis. The study was conducted according to the guidelines laid down in the "Declaration of Helsinki" and were approved by the local ethical committee of the Christian-Albrechts-University zu Kiel. Written informed consent was obtained from all subjects before participation.

2.2. Body composition analysis

Anthropometric measurements

Body height was measured to the nearest 0.5 cm with subjects wearing no shoes (Seca Stadiometer; Vogel & Halke, Hamburg, Germany). Weight was assessed to the nearest 0.01 kg with an electronic scale (Tanita, Tokyo, Japan).

Magnetic resonance imaging (MRI)

Skeletal muscle mass (SM), total, subcutaneous and visceral adipose tissue (AT, SAT and VAT) were measured using whole body multislice MRI in a subgroup of 227 subjects (56.8 % females). Scans were obtained with a 1.5T scanner (Magnetom Vision Siemens, Erlangen, Germany) as previously described [25]. Subjects were placed on the platform with their arms extended above their heads. Images were obtained using a T1 weighted gradient-echo sequence and manual analyzed from wrist to ankle using the SliceOmatic software (version 4.3; Tomovision, Montreal, Canada). MRI estimated SM volumes were converted to mass using a density of 1.04 kg/L. VAT, SAT and AT were converted using a density of 0.92 kg/L [26]. Intra-observer coefficient of variation was 1.8 % for total SM. SM-Index (SMI) and AT-Index (ATI) were created by dividing SM respectively AT by squared height (m²) and were used in the SMI/ATI ratio.

Bioelectrical Impedance Analysis (BIA)

A single tetra polar BIA measurement of resistance (R) and reactance (Xc) was taken at a frequency of 50 kHz at the right side of the subject between the right wrist and ankle while in a supine position with a body impedance analyzer (BIA 2000-S, Data Input, Frankfurt, Germany). Gel electrodes (Bianostic MG, Data Input) were placed at defined anatomical sites (dorsal surfaces of the hand, wrist, ankle, and foot). Phase angle (PA) was calculated by using the following equation: *Phase angle (°) = arctan*

*(Xc/R) * (180/π)*. Fat mass (FM) was calculated by the equations of Sun et al. [27] and the FFM/FM ratio calculated. Skeletal muscle mass (SM) was calculated according to study group specific regression [28]. Malnutrition groups were differentiated by corresponding age, sex and BMI specific PA percentiles: no malnutrition (≥50th percentile), risk of malnutrition (10th to 50th percentile) and malnutrition (≤ 10th percentile) [18].

Air Displacement Plethysmography (ADP)

ADP was performed by the BOD POD® device (Cosmed s.r.l., Rome, Italy). Participants wore tight-fitting underwear and a swim cap. Two repeated measurements of body volume were performed, averaged and corrected for predicted body surface area and thoracic gas volume using BOD POD® software (version 4.5.0). Percentage fat mass (FM_{ADP}) was calculated from body density using the equation by Siri et al. [29]. Fat free mass (FFM_{ADP}) was calculated as body weight minus FM_{ADP}.

Definition of sarcopenia

Sarcopenia was defined based on the method of Newman et al. [31] using residuals of linear regression on skeletal muscle mass (from BIA) instead of appendicular lean mass adjusted for fat mass as well as height. Subjects in the lowest quartile were marked as sarcopenic according to their sex specific residuals (men -2.21 and women -1.54). This method is also mentioned by the "The European Working Group on Sarcopenia in Older People (EWGSOP)" [32].

Statistical analysis

Statistical analysis was performed using SPSS statistical software (SPSS 24.0, Inc., Chicago; IL, USA). All data are given as median and corresponding interquartile range (IQR). Differences between malnutrition groups were tested using Kruskal-Wallis test. Spearmen and partial correlations were used to determine the relationship between phase angle and different body composition parameters. Mediation and moderation analysis were performed using PROCESS Procedure for SPSS Release 2.16.3 (Written by Andrew F. Hayes, Ph.D.) Figures were performed using Excel 2010. A *p*-value <0.05 was accepted as the limit of significance.

3. Results and Discussion

3.1. Results

From 664 subjects who participate in different body composition studies 239 subjects were older than 60 years (35.9 %). Median age of the whole study population was 48 years (range 18 to 84 years) and median BMI was 26.9 kg/m² (range 17.6 to 52.4 kg/m²). The study population was 56.5% female. The detailed characteristics of subjects younger and older than 60 years are presented in **Table 1**.

Younger subjects were taller and heavier than older subjects. Detailed body composition showed that that younger subjects had higher ATI_{MRI}, subcutaneous adipose tissue (SAT_{MRI}), SMI_{MRI}, than older subjects. Phase angle, Xc50 and calculated SM_{BIA} were higher in younger subjects when compared to older subjects. FFM as assessed by ADP was higher in younger than elderly subjects. There were no differences in inflammation (**Table 1**).

There were no significant differences in the prevalence of overweight/obesity and malnutrition between younger and older subjects (**Table 1, Figure 1**).

According to BMI groups in younger and older subject's typical differences in anthropometric (higher weight) and detailed body composition data (higher SMI_{MRI}, SAT_{MRI}, VAT_{MRI}, ATI_{MRI}, FFM_{ADP}, FM_{ADP} and FFM_{ADP}/FM_{ADP}) were observed (**Table 2**). Specific phase angle groups were not different between normal weight and overweight/obese subjects in both age groups.

There were no significant differences in the prevalence of sarcopenia between age groups (**Table 1**). In younger and older subjects, the prevalence of sarcopenia was higher in normal weight subjects (**Table 2**). Comparing non and malnutrition groups in both age showed that in the malnutrition group more subjects were sarcopenic (<60 years: 9.6% vs. 17.6%; >60 years: 10.2% vs. 25.8%; $p< 0.05$). In the older group subjects with sarcopenia and malnutrition had a significant lower median PA than not malnourished sarcopenic subjects (median PA 4.00° vs. 4.40°; $p< 0.05$).

MRI assessed muscle mass and MRI derived BIA muscle mass showed very high correlations in the whole study group ($r= 0.95$; $p< 0.05$), in both age groups (<60 years: $r= 0.95$; >60 years: $r=0.93$; $p< 0.05$) and in BMI groups (NG: $r= 0.94$; OW/OB: $r= 0.94$; $p< 0.05$), this was also true in both age groups. Therefore, MRI derived BIA muscle mass (SM_{BIA}) are displayed in further results.

Correlations between phase angle and body composition

There were significant but low correlations between PA and BMI ($r= 0.08$) or age ($r= -0.42$). More significant correlations were shown between PA, FFM_{ADP}/FM_{ADP} ($r= 0.22$) SM_{BIA} ($r= 0.50$), SM_{BIA}/FFM_{ADP} ($r=0.52$) and SM_{BIA}/FM_{ADP} ($r= 0.29$) for the whole study population.

Age adjusted correlations were performed on all other body composition measurements and PA. PA correlated with FFM_{ADP}/FM_{ADP} ($r= 0.17$) SM_{BIA} ($r= 0.42$), SM_{BIA}/FFM_{ADP} ($r=0.44$) and SM_{BIA}/FM_{ADP} ($r= 0.23$) in the group as a whole.

In a second step age and BMI adjusted correlations were performed between PA and body composition components, the correlations between FFM_{ADP}/FM_{ADP} ($r= 0.22$) SM_{BIA} ($r= 0.42$), SM_{BIA}/FFM_{ADP} ($r=0.44$) and SM_{BIA}/FM_{ADP} ($r= 0.28$) still remained.

In a third step sex was included additionally to age and BMI. PA was significantly correlated to SM_{BIA} (r= 0.32), SM_{BIA}/FFM_{ADP} (r=0.33) and SM_{BIA}/FM_{ADP} (r= 0.12).

Figure 2 showed the relationship between the ratio of FFM_{ADP}/FM_{ADP} and FMI_{ADP} for the total study population (**A**) and healthy elderly subjects (**B**) based on the Forbes curve. A low PA is represented over a wide range of corresponding Forbes curve (orange dots).

3.2 Discussion

Today both, malnutrition and overnutrition are common characteristics of patients in clinical practice in industrial countries. Beside nutritional screening tools like MNA, MUST or NRS-2000 bioelectrical impedance (BIA) can be used as a nutritional assessment tool (phase angle or BIVA). Phase angle (PA) depends on cell membrane integrity and on body cell mass. There exists a correlation between PA values and body cell mass, which in consequence could give information's about quality and quantity of the lean mass. PA correlated for example with the Barthel Index in institutionalized elderly (r=0.35) or with the SGA (r=0.53) [33, 34]. BIVA allows a more detailed understanding of cell mass and hydration in comparison to PA. A differentiation between a malnourished (low PA and long vector) and a healthy lean subjects (normal PA and long vector) is possible with BIVA. BIVA could be a reliably tool to assess and monitor longitudinal changes in cell mass and hydration of a person. The assessment of nutrition status may help to detect healthy subjects and patients at risk of malnutrition.

Phase angle is the arc tangent of reactance to resistance and is related to body cell mass of a subject. Clinically PA could be used as a prognostic factor. For the comparison of PA in different groups e.g. age groups R should be comparable between these groups. In our data we could observe that R was not significant different in age groups (Table 1). The decrease in PA is due to the reduction of cell mass and could be seen as an indicator of nutritional status changes. Many authors mentioned PA as an useful indicator of nutritional status [34, 35]. PA could add more information to the used malnutrition screening tools. As our data showed older subjects as well as younger subjects of a healthy population were malnourished at the level of the 10^{th} age, BMI and sex specific PA. In our healthy population 12.5% were at risk of malnutrition according to the 10^{th} percentile over all ages. Norman et al. [34] showed in 112 nursing home residents that nearly 9% of them were malnourished (MNA based). Malnourished persons had a lower PA than non-malnourished persons. Whereas Buffa et al. [35] showed that in free living elderly subjects 1.2% were malnourished and 35.9% were at risk of malnutrition. Both groups had lower PA than the non-malnourished group. The PAs were between 5.0° (females) and 5.2° (males) which was in line with the PAs in our group of subjects $<10^{th}$ percentile (Interquartile range 4.30° – 5.26°).

In addition, cut-off values were calculated with ROC analyses and compared to results of malnutrition screening tools. Using NRS-2000 and Subjective Global Assessment (SGA) in patients at hospital admission/hospital stay cut-off values were calculated for PA (females 4.6° and males 5.0°) by Kyle et al. [36, 37]. Sensitivity and specificity between PA and screening tools showed a good validity. Ringaitiene et al. [38] used the 15th percentile of a specific age and sex group to determine malnutrition and showed that fewer patients were classified malnourished by the new ESPEN criteria than by PA. The authors recommended the implementation of PA into the ESPEN criteria.

In our data a low PA percentile was independent of subjects BMI (Table 1). PA could therefore discriminate between different terms of malnutrition independent from BMI. Guida et al. [39] showed in overweight and obese hemodialysis patients that they had lower PA when compared to normal weight patients or BMI matched controls. The other way round comparing nearly normal to underweight subjects e.g. anorexia nervosa and ballet dancers showed that athletes (dancers) had higher PA than anorexia nervosa patients. PA reflected the higher amount of muscle mass in dancers.

Thus, in consequence the addition of PA to malnutrition screening tools could give us further information about a person's nutrition status and adequacy of nutrition interventions independent of its BMI. PA as a surrogate marker of muscle mass could give us an information on "muscularity" and quality of lean mass. Muscle mass is the main component of lean mass and loss of muscle mass is one of the main keys to define malnutrition. A challenge of using PA as an assessment tool is the gap of cut-off points. This is due to the fact that device, sex, age, health and ethic specific cut-offs are needed. As we know that different devices are in use in different populations and that PA could differ for example within Caucasians [18, 40, 41].

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