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Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis

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Abstract This study investigates whether bioimpedance indexes rather than derived body compartments would be adequate for nutritional assessment. Evidence is provided that the phase angle as determined by conventional tetrapolar whole body bioelectrical impedance analysis at 50 kHz (1) was largely determined by the arms and legs and not the trunk, (2) was higher in control subjects than in hospitalized patients [mean (SD) 6.6° (0.6°) vs 4.9° (1.2°), $P < 0.001$], (3) discriminated poorly between cirrhotic patients of different Child-Pugh class, and (4) was positively correlated with muscle mass ($r = 0.53$) and muscle strength ($r = 0.53$) in these patients (each $P < 0.01$). In a prospective study of patients with liver cirrhosis Kaplan-Meier and log rank analyses of survival curves demonstrated that patients with phase angles equal to or less than 5.4° had shorter survival times than patients with higher phase angles [6.6° (1.4°)] and that phase angles less than 4.4° were associated with even shorter survival times ($P < 0.01$). The prognostic roles of the phase angle and standard nutritional parameters such as total body potassium, anthropometric measurements, and impedance derived fat free mass, body cell mass and fat mass were evaluated separately by Cox regression which eliminated all variables except the phase angle as predictors of patient survival time ($P < 0.01$). We concluded that for the clinical assessment of patients the phase angle may be superior to commonly used body composition information.

Keywords Body composition analysis · Impedance analysis · Impedance data

Introduction

Indirect in vivo methods of analysing body composition have widely proliferated, because the only true direct methods of assessment are by tissue dissection and analysis. Bioelectrical impedance analysis (BIA) has proved to be a safe, non-invasive and portable method of estimating body composition and has attracted much attention within the last 20 years. However, despite extensive use of BIA there is general uncertainty regarding its validity and value in clinical practice (Elia 1993; Foster and Lukaski 1996; Mueller 2000). One of the difficulties in the development of BIA as a technique has been determining what the measurements mean in biological terms, because it is not clear exactly what – at the physiological level – BIA at 50 kHz is measuring (Holt et al. 1994). Another uncertainty stems from the fact that BIA-derived body composition data rely mostly on empirical equations based on correlations of resistance (R) and reactance (X_c) with the results of reference methods of certain patient populations.

The phase angle was originally used as a tool for diagnosing metabolic disorders and investigations focused on the associations of phase angles with physiological variables such as basal metabolic rate (Baumgartner et al. 1988). The phase angle is the angle the impedance vector forms relative to the R vector and calculated as the arc tangent of the ratio of the X_c to the R transformed to degrees. The geometrical relationships among impedance, R , X_c , phase angle, and frequency of an electrical current are illustrated in Fig. 1.

This study correlated primary impedance data with physical, nutritional and prognostic parameters in healthy control subjects, hospitalized patients and patients suffering from liver cirrhosis requiring either medical or non-transplantation surgical therapy. We have discussed and provided evidence for the clinical

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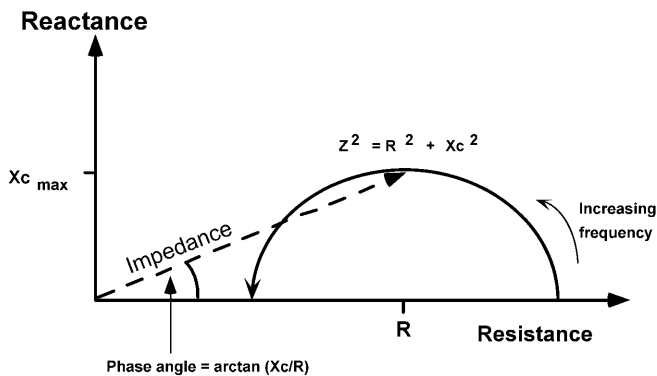


Fig. 1 Diagram of the graphical derivation of the phase angle; its relationship with resistance (R), reactance (X_c), impedance (Z), and the frequency of the applied current

relevance of the phase angle and suggested reference values.

Methods

Procedure and patients

The BIA was measured using a BIA-101 impedance analyser (RJL Systems, Clinton Twp., Mich.) using the standard four-electrode arrangement at 800 μ A and 50 kHz, at which current flow is through both the intra- and extracellular fluids (Chumlea and Baumgartner 1990). The use of a 50 kHz current in single-frequency bioelectrical impedance analysers to estimate body composition was derived from the original work of Nyboer (1970), who determined that this was the critical frequency of muscle tissue at which its maximal X_c occurred. Although the critical frequency is highly variable among individuals and is possibly slightly lower than 50 kHz, single frequency BIA has been extensively validated and provides estimates of body cell mass (BCM) and total body water in different patient populations (Chertow et al. 1995, 1997; Houtkooper et al. 1996; Thomas et al. 1998). Moreover, multiple frequency bioelectrical impedance analysis may not provide any clinically significant improvement over measurements at only 50 kHz for the estimation of body compartments (Hannan et al. 1994; Patel et al. 1996).

During the BIA-measurements the subjects lay supine with arms and legs angled outwards so that the medial surface of the limbs did not touch the rest of the body. For conventional whole body measurements the electrodes were placed between the hand and foot of the dominant side as described for study group 2. Phase angles for the whole body and segments were calculated in radians using the equation $\alpha = \arctan (X_c/R)$, and converted to degrees by multiplying by 57.296 ($180^\circ/3.14$). The rationale for measuring the impedance of body segments was to identify the determinants of the phase angle as measured by standard whole body BIA.

Approval of the studies was given by the Ethics Committee of the Medical School of Hanover before commencement of the studies, and informed consent was obtained from each patient after a full explanation of the purpose, nature and risks of the procedures had been given. All clinical research has been conducted in accordance with the principles for human experimentation as defined in the declaration of Helsinki of the World Medical Association.

Five study groups were investigated to assess:

1. Reference intervals of the phase angle
2. Anatomical determinants of the phase angle
3. Alterations of the phase angle in hospitalized patients
4. Physiological correlates of the phase angle in these patients, and

5. The prognostic significance of the phase angle in comparison with standard nutritional parameters in patients suffering from cirrhosis of the liver.

Study group 1

A group of 50 healthy control subjects [30 women and 20 men, mean (SD) age 36 (11) years, height 172 (11) cm, body mass 70 (14) kg] were assessed using standard whole body BIA as well as total body potassium (TBP) counting of 40-K in a whole body-counter with a precision equal to 3% (Lautz et al. 1992; Mariss et al. 1978).

Study group 2

A group of 5 hospitalized patients who required nutritional counselling by the dietitian [3 men and 2 women, age 43 (11) years, height 173 (7) cm, body mass 59 (10) kg] were assessed for whole body and segmental bioelectrical impedance indexes. For electrode placement the following sites were chosen: hands, shoulder, upper thigh, and feet. At the hand the voltage-sensing electrode was placed anteriorly at the midpoint between ulnar and radial processes, and the source electrode 8 cm distal to this on the back of the hand. The receiving electrode at the shoulder was positioned at the midpoint between the anterior axillary fold and the acromion, and the source electrode 8 cm medial to the receiving electrode. On the upper thigh the receiving electrode was placed at the midpoint of the anterior thigh in the same plane as the gluteal crease and the source electrode was placed 8 cm proximal to this. The source and receiving electrodes were reversed at the shoulder and upper thigh when measuring the trunk. The electrodes were positioned on the foot in the standard position with the receiving electrode at the midpoint anteriorly between the malleoli of the ankle and the source electrode 8 cm distal to this.

Study group 3

A heterogeneous group of patients of the Medical School Hannover who required nutritional counselling or nutritional intervention by the nutrition team was also investigated by standard whole body BIA. A total number of 1,035 different patients (589 men, 446 women) were studied at initial presentation: age men 49 (16) years (range 15–89 years), age women 44 (19) years (range 15–88 years), body height 175 (7) cm (men), body height 164 (6) cm (women), body mass 64.7 (13.6) kg (men), and body mass 54.9 (11.9) kg (women).

Study group 4

A group of 55 patients with biopsy-proven cirrhosis of the liver [20 post-hepatic, 10 alcohol-related, 9 biliary, 5 autoimmune, 6 cryptogenic, 7 others; age range 18–70 years, 17 women and 38 men, height 173 (8) cm, body mass 72.5 (14.8) kg] were investigated in respect of (1) shoulder abduction strength, (2) hip adduction strength, (3) arm muscle area, (4) 24 h urinary creatinine excretion, and (5) standard whole body BIA. Muscle strength testing was performed using a Nicholas Manual Muscle Tester model 01160 (Lafayette Instruments, Ind., USA). Repeated measurements of shoulder abduction strength (coefficient of variation 11.1%) and hip adduction strength (coefficient of variation 8.4%) according to standardized instructions were made on the dominant side by the same skilled investigator. Average values of two measurements were calculated and used for statistical analysis. Urinary creatinine was measured using a modified kinetic Jaffe procedure (Merckotest Creatinin, Merck, Darmstadt, Germany) and used as a nutritional estimate of muscle mass (Pirlich et al. 1996).

Study group 5

Several nutritional parameters were obtained in a heterogeneous group of 305 patients with biopsy-proven cirrhosis of the liver who

were assessed prospectively for survival time (162 men and 143 women; diagnoses: 107 posthepatic, 61 alcohol-related, 61 biliary, 29 cryptogenic, 8 autoimmune, 8 metabolic, 4 Budd-Chiari, 27 other causes). Blood samples were collected through a needle introduced into an antecubital vein. Aliquots were transferred into different tubes placed on ice for the determination of concentrations of albumin, gamma-globulins, and bilirubin, and prothrombin time, and cholinesterase activity which were all determined using standard in-house methods. The clinical classification was based on the plasma concentrations of bilirubin and albumin, the prothrombin time, and the occurrence of ascites, and clinical signs of encephalopathy (i.e. Child-Pugh score; Pugh et al. 1973). The degree of ascites was determined in each patient using ultrasound and divided into five grades: grade 0=no ascites; grade 1=little ascites, namely perihepatic or in the pouch of Douglas; grade 2=ascites of less than 2–2.5 l; grade 3=moderate ascites of more than 2–2.5 l treatable by diuretic therapy; grade 4=massive, therapy-resistant ascites. Peripheral oedema (grade 0=not present; grade 1=present) was classified by clinical judgement.

Nutritional status was assessed using standard anthropometric procedures (skinfold thickness of triceps, biceps, abdomen, subscapula, and mid-arm circumference) as described by Lohmann et al. (1988). Whole-body muscle mass was calculated as described by Heymsfield et al. (1982a). The BIA-derived body compartments (fat mass, fat free mass, BCM) were estimated using the software program Body version 4.1/32B/SF (Data Input, Frankfurt, Germany). Body mass index was calculated as: body mass (kg) body height⁻² (m⁻²). The TBP was determined in a subgroup of 166 patients as described for study group 1.

Statistical analysis

All data were recorded in a database system using a personal computer using SPSS for Windows V. 6.13. Data are given as mean (SD) if not indicated otherwise. The Mann-Whitney *U*-test was used for comparisons between groups, and $P < 0.05$ was considered significant. Correlation lines were derived from least squares linear regression analysis. Multiple comparisons between groups of patients and phase angles of different body segments were performed using one factor analysis of variance (ANOVA) and subsequent Student Newman Keuls tests. For assessment of survival times, the homogeneity of survival curves over strata of prognostic variables was tested by the log rank test. A forward stepwise Cox regression analysis for survival was performed to identify variables that add to the prediction of patient survival-time of study group 5. Further, to describe covariations of the parameters investigated, correlation coefficients between the respective values were calculated and processed by factor analysis with subsequent varimax rotation.

Results

Study group 1

A scatterplot of X_c and phase angle values from 50 healthy control subjects is shown on Fig. 2 A. Mean R , X_c and phase angle were as follows: 555 (87) Ω , 65 (10) Ω , and 6.6° (0.6)°, respectively. The mean phase angle of men (range 6.1°–8.5°) was not significantly different from that of women (range 5.3°–7.3°) subjects [6.8° (0.6)° compared to 6.5° (0.5)°, $P = 0.1$]. A uniform reference range was calculated for both sexes, based on the mean and 2 SD, as being 5.4°–7.8°. The BCM calculated from BIA data and TBP showed good correlation ($r = 0.95$). Age (range 20–60 years) was not

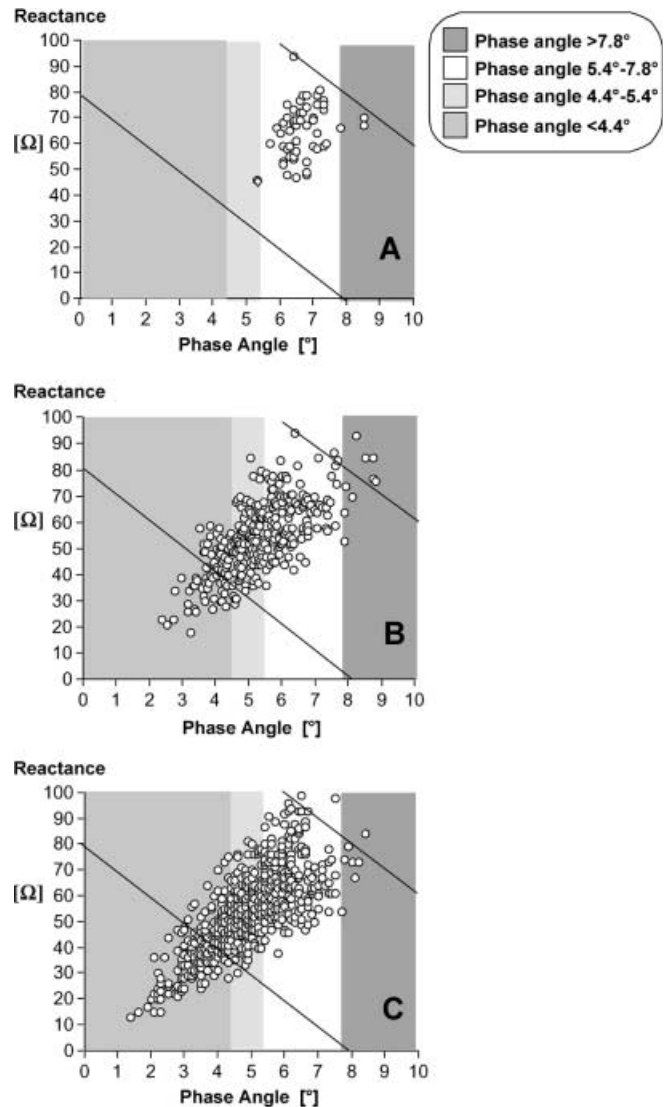


Fig. 2 Scatterplot of reactance and phase angle of **A** healthy control subjects ($n = 53$, group 1), **B** patients with liver cirrhosis ($n = 305$, group 5), and **C** a heterogeneous group of hospitalized patients at the Medical School of Hannover ($n = 1035$, group 3). Patients having phase angles greater than 10° were observed in study group 5 ($n = 3$) and study group 3 ($n = 3$) and are not shown. The area between the straight lines includes patients that would be classified “normal” according to the graphical Biagram method of Talluri and Magia (1995); patients outside the two lines would be classified “abnormal”. The shaded areas indicate from left to right our suggested classification system of low ($< 4.4^\circ$), borderline ($4.4\text{--}5.4^\circ$), normal ($5.4\text{--}7.8^\circ$), and supra-normal ($> 7.8^\circ$) phase angles

significantly correlated with the phase angle ($r = 0.2$, n.s.).

Study group 2

Results of whole body, trunk and segmental phase angles of 5 patients are shown in Table 1. The average phase angle of the trunk was significantly higher than the mean phase angle of the whole body and of the

Table 1 Segmental, trunk and whole body phase angles

Patient	Arm (°)	Both arms (°)	Leg (°)	Both legs (°)	Extremities ^a (°)	Body ^b (°)	Trunk (°)
1	5.51	5.49	8.09	6.77	6.47	6.50	10.01
2	5.37	4.98	6.02	4.87	5.31	5.14	10.15
3	3.90	4.46	6.02	5.89	5.07	4.88	6.17
4	3.66	3.82	4.24	4.14	3.97	4.28	3.69
5	4.33	4.43	4.42	4.35	4.38	4.43	8.58
Mean	4.55	4.64	5.76	5.20	5.04	5.05	7.72 ^c
SD	0.85	0.63	1.55	1.11	0.96	0.88	2.7

^aMean of all four appendicular measurements^bStandard electrode placement^c $P < 0.05$ vs body phase angle

extremities, i.e. the average of all four appendicular measurements.

Study group 3

Mean R , Xc and phase angle of the whole group were as follows: 638 (121) Ω , 54 (16) Ω , and 4.9° (1.2)°, respectively. The mean phase angle was significantly lower than in healthy control subjects of group 1 [4.9° (1.2)° compared to 6.6° (0.6)°, $P < 0.001$]. The mean phase angles of men and women patients were similar [4.9° (1.3)° compared to 4.8° (1.2)°, n.s.].

The histogram of whole body phase angle (study group 3) divided into intervals of 0.5° showed a symmetrical, bell-shaped pattern as found in Gaussian distributions. The suggested reference range 5.4°–7.8° (see results of study group 1) was compared to published data of the phase angle in healthy subjects (Table 2) and to the results of the survival time analysis (see results study group 5). Whereas values below 4.4° are abnormal in all instances (Table 2), values between 5.4° and 4.4° vary in their significance and are therefore classified as *borderline*. There were 14 patients (1.1%) who showed increased phase angle values above 7.8°. The body mass index of patients showing low, borderline, normal and high phase angles was 20.0 (3.8), 20.5 (4.7), 21.8 (4.1) and 22.7 (2.9) $\text{kg}\cdot\text{m}^{-2}$, respectively (ANOVA $P < 0.05$).

Study group 4

Mean shoulder abduction and hip adduction strength was 13.2 (7.0) kg and 27.1 (10.9) kg, respectively. Average hip adduction strength values were –12 (30) % or –4.3 (8.3) kg below expected values as supplied by the manufacturer. Hip adduction as well as shoulder abduction strength values were both significantly correlated with several estimates of body composition: R , BCM, phase angle, urinary creatinine excretion, and anthropometric muscle mass (each $P < 0.01$).

Study group 5

A scatterplot of Xc and phase angle values of all patients is given in Fig. 2 B. The mean phase angle of all 305 patients was 5.4 (1.5)°, TBP was 81 (32) g. The phase angle was weakly related to several nutritional variables: 24 h urinary creatinine excretion ($r = 0.21$, $P < 0.05$), TBP ($r = 0.19$, $P < 0.05$), anthropometric muscle mass ($r = 0.16$, $P < 0.05$), mid-arm circumference ($r = 0.17$, $P < 0.05$), arm muscle area ($r = 0.16$, $P < 0.05$) and serum albumin concentration ($r = 0.23$; $P < 0.05$); but was independent of body mass ($r = 0.09$) and stature ($r = 0.06$, each n.s.). The phase angle was also weakly related to the hydration status (ascites $r = 0.20$, oedema $r = 0.12$; each $P < 0.05$). The associations between phase angle and nutritional variables were hardly changed if

Table 2 Published data for norms of whole body bioimpedance phase angle at 50 kHz in healthy subjects

Author and year	Number	Sex	Mean	Range ^a
This study (2002)	50	20 men, 30 women	6.6°	5.4°–7.8°
Baumgartner et al. (1988)	73	29 men 44 women	7.0° 6.3°	5.3°–8.8° 4.9°–7.7°
Mattar (1996)	265	87 men, 178 women	6.8°	4.4°–9.6° ^c
Pilla et al. (1990) ^b	15	15 men	7.5°	6.2°–8.8°
Zarowitz and Pilla (1989)	114	47 men 67 women	8.2° 6.7°	6.0°–10.4° 4.9°–8.5°
Talluri and Magia (1995)	888	^d	6.4°	4.6°–8.1° ^e

^aRange given as 2 standard deviations either side of the mean^bAge range 24–35 years^cHighest and lowest limit of several ranges of different sex and age groups^dUniversity freshmen of both sexes^eData estimated from published scatterplot

the degree of ascites and the presence of clinical oedema were allowed for by partial correlation (data not shown).

There were 113 patients (37%) who died within the observation period, mean survival time was 24 (18) months. The average phase angle of patients who died within the observation period was significantly lower than the average phase angle of patients who survived (median 5.0° compared to 5.5°, $P < 0.01$). The association between phase angle and Child-Pugh score is shown in Fig. 3 and the survival time of patients grouped by their phase angles is shown on Fig. 4. Patients showing a phase angle of less than 5.4° had reduced survival times ($P < 0.01$).

Using a multivariate approach (stepwise Cox regression model) several nutritional variables were subjected as covariates to an analysis of survival time. This regression approach was significant only for the phase angle ($P < 0.05$), none of the remaining variables making a significant contribution to the prediction of survival time over that of the phase angle. A factorial analysis of

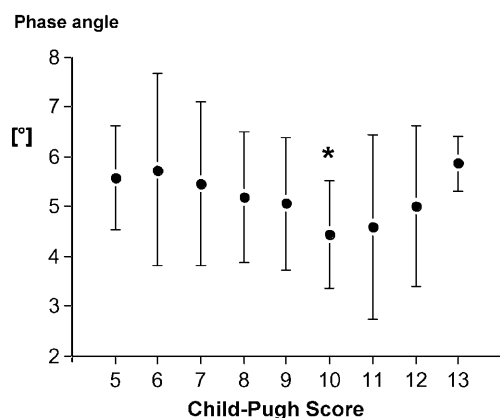


Fig. 3 Mean phase angles of patients suffering from cirrhosis of the liver grouped by their Child-Pugh score (Pugh et al. 1973; $n = 305$). The phase angle of patients having a Child-Pugh score of 10 was significantly lower than the phase angle of patients having a score of 6 ($P < 0.05$)

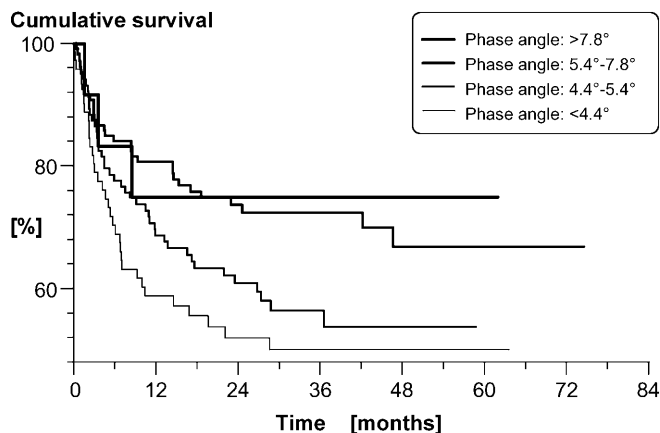


Fig. 4 Survival times of patients suffering from cirrhosis of the liver (study group 5; $n = 305$) grouped by their phase angle. Patients having phase angles less than 5.4° had significantly lower cumulative survival times than other patients ($P < 0.01$)

possible determinants of phase angle was made using orthogonal transformation and subsequent varimax rotation (Table 3). The phase angle appeared in a separate factor and was associated with length of survival.

Analysis by Biagram and R/Xc graph

Two alternative approaches to applying primary BIA data in the clinical assessment of patients have been proposed. Talluri and Maggia (1995) developed the Biagram, which allows a graphical classification of patients according to their phase angles and Xc values into normal and abnormal populations. It is shown in Fig. 2 that virtually all patients classified as abnormal by Talluri and Maggia (1995) are also classified as abnormal according to our suggested cut-off value of 4.4° for the phase angle. But several patients, who have clearly reduced phase angle values (Fig. 2B, C; Table 2) are missed by the Biagram.

Piccoli et al. (1994) developed the R/Xc graph which allows monitoring of fluid overload and removal during haemodialysis. According to the R/Xc graph which plots $Xc/height$ against $R/height$ a progressive shortening and down-sloping of the impedance vector indicates progressive fluid overloading, a progressive lengthening and steepening of the vector indicates fluid removal (Piccoli 1998).

We have analysed our data of study groups 1, 3 and 5 by the R/Xc graphical method (Fig. 5). The normalized impedance vector was calculated as the square root of $[(R/height)^2 + (Xc/height)^2]$ and was 328 (66) $\Omega \cdot m^{-1}$ for study group 1, 378 (79) $\Omega \cdot m^{-1}$ for study group 3, and 352 (77) $\Omega \cdot m^{-1}$ for study group 5. Cirrhotic patients with oedema had shorter impedance vectors than cirrhotic patients without oedema [336 (77) $\Omega \cdot m^{-1}$ compared to 360 (75) $\Omega \cdot m^{-1}$; $P < 0.01$]; cirrhotic patients with and without significant amounts of ascites had almost identical impedance vectors [352 (76) $\Omega \cdot m^{-1}$ compared to 352 (77) $\Omega \cdot m^{-1}$]. Normal values of bioelectrical impedance vector length published by Piccoli et al. (1995) (mean of both sexes estimated from published confidence ellipses: 335 $\Omega \cdot m^{-1}$) compare well the results of our control group (see above).

Discussion

Our study demonstrated that the phase angle of the whole body is similar to the mean phase angle of arms and legs, whereas the trunk has a larger phase angle (Table 1). Moreover, the phase angle is positively correlated with TBP and muscle mass as well as with muscle strength in patients suffering from cirrhosis of the liver (Results section). Thus, the phase angle represents a simple muscle index, which has so far been unavailable in the clinical setting (Heymsfield et al. 1982b). Appendicular skeletal muscle tissue appears to be the main determinant of the phase angle as measured by conventional

Table 3 Factorial analysis of possible determinants of phase angle in patients suffering from cirrhosis of the liver. *TBP* Total body potassium, *FFM* fat free mass, *BCM* body cell mass, *CHE* cholinesterase, *PT* prothrombin time, *BMI* body mass index, *PA* phase

Factor I		Factor II		Factor III		Factor IV	
TBP	0.73	Albumin	0.71	Fat mass	0.89	PA	0.78
Muscle	0.76	CHE	0.79	BMI	0.73	Survival	0.62
FFM	0.90	γ -globulins	0.81	Skinfolds ^a	0.73		
BCM	0.86	PT	0.71				

^aSum of four skinfold thicknesses (triceps, biceps, abdomen, subscapula)

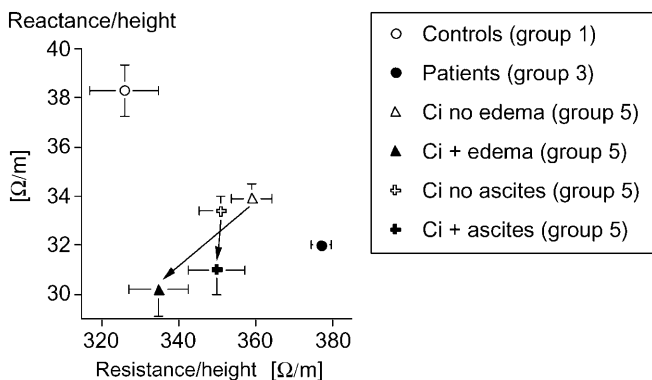


Fig. 5 Resistance/reactance (R/X_c graph) according to Piccoli et al. (1994). Hospitalized patients ($n=1035$) are characterized by lower phase angles (down-sloping of the impedance vector) and increased length of the impedance vectors (distance to 0/0 intercept), which can be calculated as the square root of $[(R/\text{height})^2 + (X_c/\text{height})^2]$. The arrows serve to emphasize the different spatial changes of the impedance vectors in cirrhotic (*Ci*) patients with oedema ($n=103$) or ascites ($n=158$). Peripheral oedema is associated with shortening of the impedance vector whereas the presence of significant amounts of ascites is mainly associated with a down-sloping of the impedance vector, i.e. lower phase angles

BIA. It is known that the contribution of one arm and one leg to total R is disproportionately higher than the contribution of the trunk, which represents nearly 50% of body mass (Chumlea and Baumgartner 1990). Similarly, Organ et al. (1994) showed that the trunk contributes no more than 8% to total body impedance.

Higher phase angles as seen in healthy people (Fig. 1A) appear to be consistent with large quantities of intact cell membranes of skeletal muscle and BCM. For this reason the phase angle is used by BIA equations to predict total BCM as follows: $\text{BCM} = \text{fat free mass} \times \text{constant} \times \log(\text{phase angle})$ (Lautz et al. 1992). This equation implies that there is a fixed relationship between phase angle and the extracellular to BCM ratio (ECM:BCM ratio), i.e. the distribution between intra- and extracellular spaces. This relationship reflects the main assumption inherent in BIA-derived predictions of BCM and ECM (Fig. 6). It demonstrates that changes of the ECM:BCM-ratio are probably associated with changes of the phase angle. The ECM:BCM-ratio is a known sensitive marker of malnutrition (Cohn 1987; Shizgal 1981) and the phase angle appears to reflect its prognostic significance. In addition, the ratio of

exchangeable sodium to exchangeable potassium ($\text{Na}_e:\text{K}_e$), which itself can be computed from BIA-data (Shizgal 1988), is closely associated with the phase angle. Since the $\text{Na}_e:\text{K}_e$ ratio has been originally described by Tellado et al. (1989) as a prognostic marker, the association of the phase angle with survival is not unexpected.

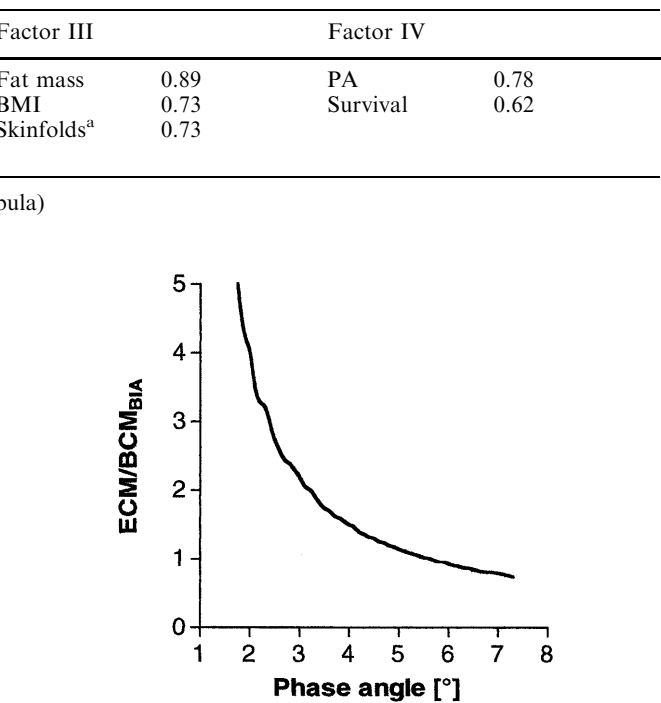


Fig. 6 Relationship between the extracellular (*ECM*) to body cell mass (*BCM*) ratio and the phase angle used by the software program Body 4 (Data Input, Frankfurt, Germany) as calculated from data of patient group 3 ($n=1,035$). Note the shallow course of the curve in the range of 0.5–1.2 of the ECM:BCM ratio. BIA Bioelectrical impedance analysis

exchangeable sodium to exchangeable potassium ($\text{Na}_e:\text{K}_e$), which itself can be computed from BIA-data (Shizgal 1988), is closely associated with the phase angle. Since the $\text{Na}_e:\text{K}_e$ ratio has been originally described by Tellado et al. (1989) as a prognostic marker, the association of the phase angle with survival is not unexpected.

The phase angle of our patients suffering from cirrhosis of the liver is also related to survival (Table 3). We have demonstrated that low phase angles are associated with reduced survival times in these patients. Patients with abnormally low and borderline phase angles have clearly reduced survival times (Fig. 4). At the same time the phase angle is not simply associated with the stage of the disease as assessed using the Child-Pugh score (Fig. 3).

Maggiore et al. (1996) point out that BIA does not detect muscle loss in certain patients with clinically obvious muscle wasting. The association of ECM:BCM ratio with the phase angle may explain why muscle wasting in these patients is not always associated with reduced phase angles. We speculate that the phase angle is a marker of clinically relevant malnutrition which is characterized by both increased ECM and decreased BCM (i.e. largely muscle mass), and probably by a loss

of function. In cases of severe tissue loss without alterations in the ECM:BCM ratio a normal phase angle would be accompanied by obvious malnutrition. Thus, although the phase angle may not be reliable in certain patients in detecting depletion of lean body mass, it may be superior in identifying patients with clinically relevant malnutrition and poor prognosis (Heymsfield et al. 1982b). In this respect it is noteworthy that Kreyman et al. (1995) observed that the Xc/R quotient correlates highly with mortality in septic patients and that Schwenk et al. (1998) showed that BIA-derived raw data as well as the calculated ECW:TBW ratio predict the outcome in patients with suspected bacteraemia.

Published whole body phase angle data of healthy control subjects presenting mean values as well as ranges covering each approximately 95.5% of the observations, i.e. means and 2 SD (for Gaussian distributions) are summarized in Table 2. The effect of age on the phase angle is small and was not significant in our controls of study group 1 (see Results) (Wu 1992). The lower limit of the normal range of the phase angle is fairly reproducible with values observed between 4.4° and 6.2° , the latter in a group of young male subjects. According to our own data from healthy subjects (study group 1) and hospitalized patients, and in consideration of the survival time analysis in patients suffering from cirrhosis of the liver, we suggest classifying phase angles greater than 5.4° as normal, in the range 4.4° – 5.4° as borderline, and less than 4.4° as abnormal. High phase angles are known to occur in athletes and body-builders (Lukaski et al. 1990). We observed phase angles of more than 7.8 in only a small number of subjects of our study groups (1.1%–3.9%). High phase angles were related to increased BMI (study group 3) or higher TBP status and lengthened survival times (study group 5). Taken together, supra-normal phase angle values do not indicate a state of disease but can be considered a positive prognostic sign.

The phase angle is only determined by tissue cellularity, tissue hydration and membrane potential. Although it remains unclear what bioelectrical impedance measures in a strict biological sense, its reliability and clinical relevance is obvious. The phase angle of healthy control subjects was higher than of hospitalized patients. We demonstrated that the phase angle as measured by standard technique was largely determined by arms and legs, and associated with TBP, muscle mass, and muscle strength. At the same time it is not a simple correlate of disease stage in patients suffering from cirrhosis of the liver and is superior to standard information on body composition in predicting survival times. Taken together the phase angle represents a simple muscle index with significant prognostic power.

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of the Medical School of Hannover, the nursing staff of the gastroenterology wards, and the staff of the whole body counter. The experiments of this study comply with the current laws of Germany.

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