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Original Article

Bioimpedance vector analysis as a measure of muscle function

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SUMMARY

Introduction: The impedance vector produced by an alternating current in the bioimpedance analysis can be seen as a standardised test of cellular mass and function since reactance is believed to reflect the mass and integrity of cell membranes. This study investigated the association between resistance and reactance normalised for height (*R*/*H* and Xc/*H*), and muscle function as assessed by hand grip strength.

Methods: 363 patients (172 male, 191 female) from Berlin and Copenhagen were included in the analysis. Whole body impedance was determined by BIA 2000M (Berlin) or EFG2.0 (Copenhagen). Hand grip strength was measured with Digimax electronic hand dynamometer (Berlin) or Jamar dynamometer (Copenhagen). The general linear model was used to assess the association between *R*/*H*, Xc/*H* and hand grip strength.

Results: We observed a significant association between the impedance parameters *R*/*H* and Xc/*H* and hand grip strength after adjusting for confounding variables (hand grip strength = −36.9−0.063 × R/H + 0.573 × Xc/H + 40.7 × Height + 0.115 × Weight − 0.09 × Age + 3.41 (gender = male) + 1.87 (Centre Berlin); Weight: $P = 0.04$, all other coefficients: $P < 0.0005$. $r^2 = 0.708$).

Conclusions: The impedance parameters *R*/*H* and Xc/*H* are related to hand grip strength and might therefore be used as a cooperation-independent method to reproducibly assess muscle function.

1. Introduction

Loss of function and muscle strength occurs with both disease and malnutrition and is of major clinical significance.[1] Patients who have lost more than 20% of their body weight inevitably suffer from physiological impairment.[2] Muscle function, as assessed by hand grip strength, has been reported to be closely related to total body protein and even more to protein loss.[2] However, muscle function is also frequently reduced in disease before any weight loss can be determined.

Hand grip strength, a commonly used method to assess muscle function, has been shown to be predictive of postoperative complications[3,4] and predicts surgical risk better than weight loss alone.[5] It is, moreover, a superior prognostic parameter compared to biochemical and anthropometric markers of nutritional status.[6] Hand grip strength on admission to hospital has also been reported to be a predictor of loss of functional status in hospitalised patients,[7] of one year outcome in patients with liver cirrhosis,[8] and of onset of ADL (activities of daily living) dependence in the elderly.[9] Reduced midlife grip strength has also been associated with long-term mortality,[10] which suggests that higher strength might provide a greater physiologic and functional reserve that protects against mortality and morbidity.

However, although hand grip strength measurement is an easy method to estimate muscle function, it still requires the patient's cooperation in terms of compliance and ability. Alternative methods that reflect functionality would therefore be helpful in the clinical setting.

Bioimpedance analysis is an easy-to-use, portable, inexpensive and non-invasive method, which has gained a lot of popularity in the last decades. It is independent of patient cooperation and can be repeated frequently. It measures whole body impedance, which is the opposition to an alternating current consisting of two components: resistance (*R*) and reactance (Xc). Resistance is the decrease in voltage reflecting conductivity through ionic solutions. Reactance is the delay in the flow of current measured as a phase-shift, reflecting dielectric properties, i.e., capacitance, of cell membranes and tissue interfaces.[11]

In the Bioelectrical Impedance Vector Analysis (BIVA) approach, introduced by Piccoli et al., resistance and reactance normalised for

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height, *R*/*H* and Xc/*H*, respectively, are plotted as a bivariate vector (*R*Xc graph).[12,13] The normalisation for height allows for the length of the conductor and thus provides an intensive property of body tissues that does not depend on body size, i.e., a qualitative measure. The length of the vector indicates hydration status and a migration sideways of the vector indicates tissue structure and mass. The BIVA approach has gained attention as a valuable tool to assess and monitor patients' hydration status[14–16] and nutritional status[12,17–21] since it is independent of disputable regression equations for calculation of lean body mass and fat mass as well as independent of measurement of body weight.[22]

The dielectric properties of cell membranes are related to the area and integrity of cell membranes. Integrity of cell membranes is a determinant of membrane potential and, together with area, thereby probably a determinant of cell function.[23] Resistance and reactance may therefore also reflect function in terms of, e.g., muscle strength.

Therefore, we investigated the association between the BIVA parameters, *R*/*H* and Xc/*H*, and hand grip strength and we tested the hypothesis of whether a vector migration in the BIVA RXc graph is related to muscle function as assessed by hand grip strength. Furthermore, data from two different centres were combined to elucidate the generalisability of this approach.

2. Patients and methods

We merged data obtained separately in two centres, a secondary hospital in Berlin, Germany, and a tertiary hospital in Copenhagen, Denmark.

281 patients (123 male and 158 female) consecutively admitted to the Dept. of Internal Medicine and Dept. of Surgery, HELIOS Klinikum Emil von Behring in Berlin, and 82 patients (49 male and 33 female) admitted to Rigshospitalet, the university hospital in Copenhagen, were entered into the study. Patients were considered eligible if they were over the age of 18 years and not admitted to intensive care units. Exclusion criteria were implanted defibrillators or severe hyperhydration for the bioelectrical impedance analysis and patients with neuromuscular disease, hemiplegia or rheumatoid arthritis were excluded from the hand grip strength measurements due to the possible bias.

All patients gave written informed consent and the study was approved by the ethics committees in both centres.

2.1. Muscle function

Hand grip strength was measured in the nondominant hand with a Digimax electronic dynamometer (Mechatronic GmbH, Darmstadt, Germany) in Berlin and in the dominant hand with a Jamar dynamometer (Sammons Preston Rolyan, Chicago, USA) in Copenhagen. 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 s and the highest value of three tests was used for the analysis.

In order to compare the hand grip strength values, the values obtained by the Digimax were converted from *N* to kg (conversion factor = 9.80665).

The study population was then divided into gender stratified hand grip strength value quintile groups in order to form groups (group I–V) that could be displayed in the *R*Xc graph.

2.2. Bioimpedance

Bioelectrical impedance analysis was performed using a BIA 2000M (Data Input GmbH, Darmstadt, Germany) applying 800 μA in Berlin and an EFG2.0 (Akern, Florence, Italy) applying 330 μA in Copenhagen. Both devices applied alternating electric currents at 50 kHz and Ag/AgCl source and sensor electrodes were used. The BIA devices were checked at regular intervals against the calibration circuit standard with known resistance and reactance values supplied by the manufacturers to ascertain the accuracy of measurement of resistance and the intactness of the electrodes in both Berlin and Copenhagen. Due to the retrospective nature of this analysis, the devices were however not calibrated against each other.

Patients were measured in the morning after an overnight fast and in supine position with arms and legs abducted from the body. Source and sensor electrodes were placed on the dorsum of both hand and foot of the right side of the body.

Table 1
Demographic and nutritional characteristics of the study population.

	All	Berlin	Copenhagen	*P* value
N (male/female)	363 (172/191)	281 (123/158)	82 (49/33)	<0.0001
Age [years]	63.1 ± 16.0	63.9 ± 16.2	60.2 ± 14.9	0.035
Height [m]	1.69 ± 0.10	1.69 ± 0.09	1.70 ± 0.10	n.s.
Weight [kg]	71.1 ± 15.1	72.3 ± 15.5	66.7 ± 13.4	
BMI [kg/m^2]	24.7 ± 4.5	25.2 ± 4.4	23.0 ± 3.4	0.0001
R/H [ohm/m]	346.4 ± 71.0	352.2 ± 70.7	326.6 ± 68.5	<0.001
(min–max)	(154.0–618.4)	(154.0–618.4)	(209.6–496.2)	
Xc/H [ohm/m]	29.8 ± 8.5	30.6 ± 8.5	27.1 ± 7.6	0.003
(min–max)	(9.2–60.1)	(9.2–60.1)	(12.3–45.4)	
Hand grip strength	30.3 ± 12.9	30.9 ± 13.2	28.2 ± 11.7	n.s.
[kg] (min–max)	(2.0–67.7)	(5.6–67.7)	(2.0–52.0)	

Data given as mean ± standard deviation.
R/H resistance standardised for height, Xc/*H* resistance standardized for height.

2.3. Bioelectrical impedance vector analysis

Measurements of resistance (*R*) and reactance (Xc) obtained at 50 kHz were normalised for the height of the patients (expressed in ohm per metre) and the mean *R*/*H* and Xc/*H* of the hand grip strength quintiles were plotted as bivariate vectors on the RXc graph. The 95% confidence intervals, which describe the mean vector distribution, were then calculated for the grip strength quintile groups.

Mean vectors of groups can easily be compared in regard to their *R* and Xc values (group vector analysis), but the individual vector can also be compared to reference 50, 75, 95% tolerance ellipses calculated in a healthy population of the same gender and ethnic origin (individual vector analysis) for monitoring of the patients.

2.4. Statistical analysis

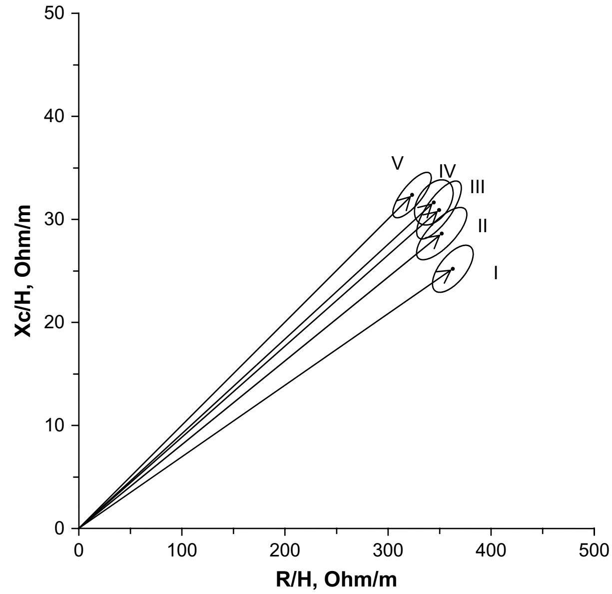
Statistical analysis was carried out using the software package Systat 11, SPSS Inc., Chicago, USA.

All data are given as mean and standard deviation. Pearson's correlation was calculated to assess the relationship between variables.

Table 2
Results from the GLM regression analysis showing similar associations between resistance and reactance standardised for height and hand grip strength in the two individual centres and in the combined population.

	Constants	Coefficients		R^2	*P* (model)
		Xc/H	R/H		
Berlin (281)	64.17	0.752*	−0.160*	0.477	<0.0001
Copenhagen (82)	40.20	1.167*	−0.134*	0.577	<0.0001
All (363)[a]	58.09	0.820*	−0.154*	0.479	<0.0001

*$P < 0.0001$ for coefficient.
All distributions of residuals were compatible with a normal distribution.
[a] Not shown: coefficient for centre Berlin = 1.922, $P = 0.0014$.



Groups	T²	D	P value
I vs II	19.6	0.74	<0.0001
II vs III	6.3	0.42	0.047
III vs IV	1.2	0.18	n.s.
IV vs V	8.8	0.49	0.0146

Groups	N (m/f)	HGS [kg]
I	71 (34/37)	17.3 ± 6.5
II	72 (35/37)	24.7 ± 6.7
III	73 (34/39)	29.5 ± 8.8
IV	75 (35/40)	35.1 ± 10.3
V	72 (34/38)	44.6 ±12.0
One-way between groups analysis of variance (ANOVA) p<0.0001		

Fig. 1. Significant average vector displacement of the hand grip strength quintile groups except between groups III and IV. (Inserted table: HGS: hand grip strength presented as mean ± STD, *N* (male/female) in the hand grip strength quintile groups: I (lowest quintile), II, III, IV, V (highest quintile)) D = Mahalanobis distance between two groups defined by the two correlated variables, T^2 = Hotelling's statistic.

Statistically significant differences between the mean vectors of the hand grip strength quintile groups were assessed with the Hotelling's T^2 test for unpaired data. Mahalanobis distance *D*, a generalised measure of distance between the groups defined by two correlated variables, was also calculated. Vector analysis was performed with the BIVA software.[24]

Multiple comparisons between the hand grip quintiles were conducted using one-way between groups analysis of variance (ANOVA).

Regression analysis was performed with the General Linear Model (GLM) allowing adjustment for continuous and categorical variables in order to assess the relationship between the impedance parameters *R*/*H* and Xc/*H* and muscle strength while adjusting for variables known to be predictors of hand grip strength, such as age, gender, height, and weight.[25,26]

The centre was introduced as a categorical variable in order to control for the differences in procedures carried out in the two centres. An acceptable level of statistical significance was established a priori at $p < 0.05$.

3. Results

The demographic and nutritional data of the 363 patients included in the analysis are given in Table 1. Ethnic origin of all patients was Caucasian.

Thirty-five percent of the patients were suffering from cardiac disease, 28 percent were gastroenterology patients, 30 percent underwent general surgery and 7 percent suffered from other diseases.

About five percent were underweight according to the WHO (BMI below 18.5 kg/m^2), 50 percent had a BMI within 18.5 and 24.9 kg/m^2, 31.7 percent a BMI between 25 and 29.9 kg/m^2 and 12.7 had a BMI over 30 kg/m^2. Eleven percent of all patients had lost more than 5 percent of their weight in the previous three to six months.

As Table 2 shows, significant associations between the impedance parameters, R/H and Xc/H, and hand grip strength of the study patients were obtained individually in both centres as well as in the combined study population with adjustment for effect of centre by GLM.

Fig. 1 displays the mean impedance vectors of the hand grip strength quintile groups I–V with mean hand grip strength. A significant displacement of the vector due to both increased Xc/H and reduced R/H values with increasing grip strength was observed (except between group III and IV).

To elucidate whether the impedance parameters *R*/*H* and Xc/*H* provide independent information about grip strength, Table 3 shows a GLM regression analysis of hand grip strength and its relation to the known major determinants of muscle function: age, gender, height and weight.[25,26] It is also shown that hand grip strength, in addition, is related to both *R*/*H* and Xc/*H* even after adjustment for the other variables. Further stepwise forward regression analysis by GLM showed that the variables were included in the following order: Height, Age, Sex, Weight, Xc/*H*, *R*/*H* and Centre = Berlin.

4. Discussion

Resistance and reactance normalised for height were both associated with hand grip strength independent of the known predictors of hand grip strength, such as age and gender.[27] Xc/H was correlated positively with increases of 0.573 kg hand grip

Table 3
Association of hand grip strength with age, gender, height, weight and centre and with resistance and reactance standardised for height as analysed by GLM regression analysis.

	Coefficients	P (coefficient)
Constant	−36.9	*0.003*
Height	40.7	<0.0001
Male gender	3.41	<0.0001
Centre = Berlin	1.87	<0.0001
Weight	0.115	0.002
Age	−0.09	0.005
R/H	−0.063	<0.0001
Xc/H	0.573	<0.0001
R^2 (model)	0.69	
P (model)	<0.0001	

The distributions of residuals were compatible with a normal distribution.
R^2 when excluding *R*/*H* and Xc/*H* was 0.62, *P*(model): <0.0001.
R/*H* resistance standardised for height, Xc/*H* resistance standardised for height.

strength per additional Ohm/metre and R/H was correlated negatively to muscle function with a decrease of −0.063 kg strength each Ohm/metre. Also, there was a distinctive vector migration due to both increasing Xc/H and decreasing R/H in the *R*Xc graph with increasing hand grip strength. We interpret this as independent information about increased cell membrane surface and membrane integrity (Xc component) per unit of fluid volume (*R* component) i.e., qualitative measures, which reflect improved cell function and improved muscle function.

Our findings thus strongly indicate that the vector position and migration is associated with function as assessed by hand grip strength.

Impedance parameters have been shown to be of prognostic value in many disease settings. Reactance has proven to be predictive of hospitalisations[28] in chronic haemodialysis patients and of mortality in patients with lung cancer.[29] Relative changes in postoperative bioelectrical impedance itself provide a quantitative estimation of poor outcome in paediatric surgery.[30] Furthermore, phase angle, which is the angle of the impedance vector, has proven to be a reliable prognostic marker for outcome in numerous studies.[31–36] However, it cannot be determined from impedance magnitude alone or phase angle alone whether it is resistance (hydration) or reactance (membrane area and integrity) that is related to outcome.

In our study, we have shown that both impedance parameters Xc/H and R/H and thus vector migration are associated with changes of functional status as assessed by muscle function. This finding might partly explain the prognostic value of the impedance parameters. BIVA might be considered an interesting tool to reflect physiological function in hospitalised patients.

A limitation of our study is the use of different BIA analysers and muscle function dynamometers as well as the different procedures. Since we, however, observed similar associations between the R/H, Xc/H and hand grip strength in the two individual centres and also adjusting for the differences in methodology also obtained positive results in the combined population, we believe that our findings are not affected by this potential bias.

To our knowledge, our study is the first to investigate the association between BIVA and function assessed by hand grip strength. Our findings might be seen as a validation of the *R*Xc graph as a quantitative method indicating function rather than simply tissue structure or hydration status. This approach may be useful in monitoring the effects of nutritional support in patients who cannot cooperate for grip strength measurements. The *R*Xc graph approach in itself is useful in patients who cannot be weighed or in whom weight changes are dominated by changes in hydration.

5. Conclusion

The impedance parameters R/H and Xc/H are related to hand grip strength and the vector migration in the RXc graph is associated with an increase in hand grip strength. The possibility to assess a clinically relevant parameter, such as muscle function, even without patient cooperation is of great interest.

Conflict of interest

The authors declare that they have no conflict of interest.

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KN, MP, JK: concept and writing of the manuscript; KN, JK: statistical analysis; MK, JS, PC: recruitment and assessment of patients; HL, TS, JS: critical input and revision of the manuscript.

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