Altered tissue electrical properties in patients with cancers. Preliminary examinations

Zmiany właściwości elektrycznych tkanki neoplazmatycznej u pacjentów z chorobą nowotworową. Badania wstępne

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Abstract

Background. Malnutrition is a common condition in patients with advanced cancer. Nutritional deficits have a significant impact on mortality, morbidity and quality of life among those patients. Direct parameters (resistance, reactance, phase angle (PA)) determined by bioelectrical impedance analysis (BIA) may be used for monitoring of tissue electrical properties. These values may be used as prognostic markers in various disease conditions.

Objective. The aim of the study was to examine tissue electrical properties in patients with cancers.

Design. BIA was performed in a group of 13 patients with cancer before chemotherapy and 13 healthy volunteers (control group), whereas the ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia), was applied. The Shapiro-Wilk (S-W) test was used to assess the distribution conformity of examined parameters with a normal distribution; the Fisher (F) test was used to assess variance homogeneity. To compare the two groups (independent samples) according to the type of distribution and variance homogeneity a Student's T-Test was used. A p value < 0,005 was considered statistically significant.

Results. In cancer patients PA was significantly (p=0.002) lower than in the control group (4.62º ± 0,87 vs. 5.69º ± 0.71, respectively). Resistance was significantly (p = 0.048) larger in patients with cancer than in the control group (573.06 ± 63.78 ohm vs. 514.48 ± 78.78 ohm, respectively). No significant differences of reactance were found between cancer patients and the control group (46.3 ± 7.9 ohm vs. 50.62 ± 5.43 ohm; p = 0.12).

Conclusion. Patients with cancers have altered tissue electrical properties (resistance and phase angle).

Keywords: cancer, bioelectrical impedance analysis, phase angle, reactance, resistance

Streszczenie

Cel pracy. Niedożywienie wśród pacjentów z chorobą nowotworową stanowi istotny klinicznie problem, wpływając na zwiększoną śmiertelność, umieralność oraz jakość życia. Bezpośrednie pomiary bioimpedancji elektrycznej (opór indukcyjny, opór pojemnościowy, kąt fazowy) stanowić mogą prognostyczny marker stanu zdrowia. Celem badania było wykazanie różnic w wartościach oporu indukcyjnego, pojemnościowego i kąta fazowego pomiędzy pacjentami z chorobą nowotworową a zdrowymi ochotnikami.

Materiał. Pomiar bioimpedancji elektrycznej wykonano w grupie 13 pacjentów z potwierdzoną chorobą nowotworową przed chemioterapią i w grupie kontrolnej złożonej z 13 zdrowych ochotników (ImpediMed bioimpedance analysis SFB7 BioImp v1.55; Pinkenba Qld 4008, Australia).

Zastosowane metody. Wartości analizowanych parametrów scharakteryzowano za pomocą wartości średniej i odchylenia standardowego. Do oceny istnienia różnic parametrów mierzalnych między badanymi grupami zastosowano testy parametryczne, po uprzednim sprawdzeniu normalności rozkładu na podstawie testu W Shapiro-Wilka i jednorodności wariancji na podstawie testu F-Fischera. Do porównania dwóch grup niezależnych użyto testu t-Studenta. Przyjęto 5 proc. błąd wnioskowania i związany z nim poziom istotności p < 0,05, wskazujący na istnienie istotnych statystycznie różnic. Analizy statystyczne przeprowadzono w oparciu o oprogramowanie komputerowe STATISTICA v. 8.0 (StatSoft, Polska).

Wyniki. Wykazano istotną statystycznie różnicę wartości kątów fazowych pomiędzy pacjentami z chorobą nowotworową a grupą zdrowych ochotników (4,62º ± 0,87 vs. 5,69º ± 0,71; p = 0,002) oraz w oporze indukcyjnym pomiędzy pacjentami z chorobą nowotworową a grupą zdrowych ochotników (573,06 ± 63,78 ohm vs. 514,48 ± 78,78 ohm; p = 0,048). Nie wykazano istotnej statystycznie różnicy w oporze pojemnościowym pomiędzy pacjentami z chorobą nowotworową a grupą zdrowych ochotników (46,3 ± 7,9 ohm vs. 50,62 ± 5,43 ohm; p = 0,12).

Wnioski: Wykazano zmiany właściwości elektrycznych tkanki (opór indukcyjny i kąt fazowy) u pacjentów z chorobą nowotworową.

Słowa kluczowe: nowotwory, bioimpedancja elektryczna, kąt fazowy, opór indukcyjny, opór pojemnościowy

Introduction

Malnutrition is a common condition in patients with advanced cancer [1]. Nutritional deficits have a significant impact on mortality, morbidity and quality of life among those patients [1]. Bioelectrical impedance analysis – BIA has been established as a valuable tool for the evaluation of body composition and nutritional status, also in cancer patients [2, 3]. BIA evaluates tissue characteristics such as resistance (R) and reactance (Xc) by recording a voltage drop in applied current [4]. Resistance is the restriction to the flow of an electric current, primarily related to the amount of water present in the tissue. Reactance is the resistive effect produced by tissues interfaces and cell

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membranes [5]. Reactance causes the current to lag behind the voltage creating a phase shift, which is quantified geometrically as the angular transformation of the ratio of reactance to resistance, or PA [6].

PA reflects the relative contributions of fluid (resistance) and cellular membranes (reactance) of the human body. By definition, PA is positively associated with reactance and negatively associated with resistance [6]. Decreased cell integrity or cell death suggest lower PA, while intact cell membranes suggest higher PA [7]. Because PA detects changes in tissue electrical properties, it has been found as a prognostic marker in various disease conditions, e.g. liver cirrhosis, acute respiratory failure, end-stage renal disease, human immunodeficiency virus infection, suspected bacteremia, advanced pancreatic cancer, colorectal cancer, breast cancer and non-small cell lung cancer [7-18]. The primary objective of this study was to examine the nutritional role of BIA derived PA in patients with cancer.

Subjects and methods

13 prechemotherapy cancer patients (3 women, 10 men) with confirmed diagnosis of cancer (biopsy analysis), were included in this study (7 patients with lung carcinoma, 2 with pharynx tumors, 1 with testis tumor, 2 with rectal tumors, 1 with stomach tumor). This group was treated at the Oncology Department, Subcarpatia Cancer Center in Rzeszow, Poland between October 2009 and May 2010. As a control group, 13 healthy volunteers (3 women, 10 men) from the same region, were examined.

All patients underwent a baseline nutritional assessment, which included laboratory measurements of serum albumin, total protein; subjective global assessment (SGA) and BIA, whereas the control group underwent a baseline nutritional assessment, which included subjective global assessment (SGA) and BIA. BIA was performed by a medical doctor using a model ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia). BIA was conducted in a supine position, with legs apart and arms not touching the torso. All examinations were performed on the patients' right sides by using the 4 surface standard electrodes (tetra polar) on the hand and foot. R and Xc were measured directly in Ω at 5, 50, 100, 200 kHz. R and Xc values were measured three times in each patient, and the mean values were calculated. PA was obtained from the arc-tangent ratio Xc : R. To transform the results from radians to degrees, they were multiplied by 180º/π. For further considerations, values of R, Xc and PA measured at 50 kHz were taken. The baseline characteristics of the patients cohort and the control group are shown in Table 1. Biopsy analysis of cancer patients is shown is Table 2.

Statistical analysis: The Shapiro-Wilk (S-W) test was used to assess the distribution conformity of examined parameters with a normal distribution; the Fisher (F) test was used to assess variance homogeneity. To compare the two groups (independent samples) according to the type of distribution and variance homogeneity, the Student's T-Test was used for dependent samples. An accepted error was 5 % and the statistical significance associated with it was $p < 0.05$, which would reveal the existence of statistically significant differences of correlations. The statistical analysis of this study was performed using computer software STATISTICA v.8.0 (StatSoft, Poland).

The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving patients were approved by the Research Ethics Committee of the Medical University of Lublin, Poland (KE- 0254/170/2009).

Results

In cancer patients PA was significantly ($p = 0.002$) lower than in the control group (4.62º ± 0,87 vs. 5.69º ± 0.71, respectively) (Figure 1). Resistance was significantly ($p = 0.048$) larger in patients with cancer than in the control group (573.06 ± 63.78 ohm vs. 514.48 ± 78.78 ohm, respectively) (Figure 2). No significant differences of reactance ($p = 0,12$) were found between cancer patients and the control group (46.3 ± 7.9 ohm vs. 50.62 ± 5.43 ohm, respectively).

Discussion

Malnutrition is known to be associated with adverse outcomes in cancer patients. There are many methods for nutritional status assessment. One of them is BIA and the assessment of direct bioimpedance measures (resistance, reactance and PA). PA is considered to be a general marker of health. The biological meaning of PA is not well understood. It reflects body cell mass and is one of the best markers of cell membrane function. Selberg O. et al. stated that decreased cell integrity or cell death is marked by lower PA, while large quantities of intact cell membranes are marked by higher PA [10]. Anja Bosy-Westphal et al. pointed out that age, sex and body mass index (BMI) are the key determinants of phase angle values [19]. In healthy populations there are considerable differences between phase angle reference values that vary by population. Kyle UG. et al. found that in the Swiss population, PA values were lower (10.5% in men and 7.7% in women) than in the Americans (Barbosa-Silva MCG. et al.), and the lowest values have been found in

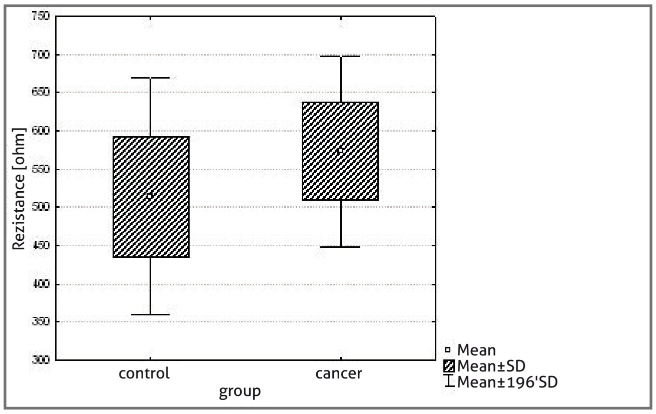

Fig. 1 Resistance in the cancer and control group

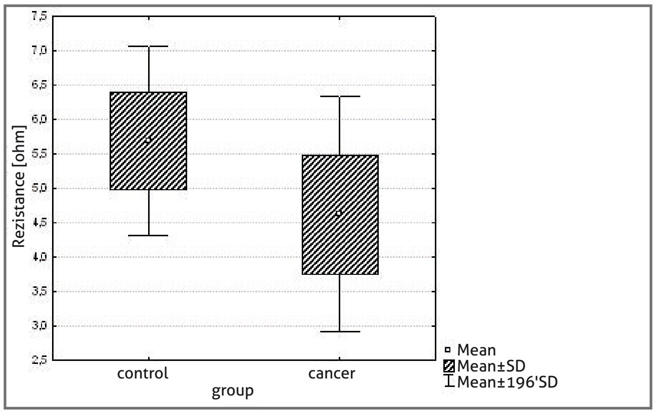

Fig. 2 Phase angle in the cancer and control group

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Table 1 Baseline characteristics of patients with cancer and control group[1]

PATIENT	Team QRS	Team QRS
Sex [n(%)] Male Female	 10 (76.9) 3 (23.1)	 10 (76.9) 3 (23.1)
Prior treatment history [n(%)] Progressive disease Newly diagnosed	 1 (7.7) 12 (92.3)	n/a
Age at diagnosis (women and men) (y) Age (women) Age (men)	63.85 ± 14.49 (26-85)[2] 72 ± 2.65 61.4 ± 15.8	55.46 ± 12.04 (39-82)[2] 64 ± 15.87 52.9 ± 10.28
Height (cm)	167.77 ± 10.88	167.08 ± 8.8
Weight (kg)	70.23 ± 9.63	77.88 ± 13.81
BMI (women and men) kg/m2 BMI (women) BMI (men)	25.1 ± 3.05 28.33 ± 3.45 24.13 ± 2.29	27.9 ± 4.2 25.3 ± 3.3 28.72 ± 4.26
Fat mass (kg)	24.17 ± 7.15	23.94 ± 6.63
Body cell mass (kg)	46.1 ± 8.28	53.94 ± 10.75
Subjective global assessment	Well-nourished 9 (69) Moderately malnourished 4 (31) Severely malnourished 0 (0) Unknown 0 (0)	Well-nourished 13 (100) Moderately malnourished 0 (0) Severely malnourished 0 (0) Unknown 0 (0)
Serum albumin (g/dL)	3.92 ± 0.52	n/a
Total protein (g/dL)	7.18 ± 0.7	n/a
Resistance (ohm)	573.06 ± 63.78	514.48 ± 78.78
Reactance (ohm)	46.3 ± 7.9	50.62 ± 5.43
Phase angle (women and men) (°) Phase angle (women) Phase angle (men)	4.62 ± 0.87 3.95 ± 0.29 4.82 ±0.9	5.69 ± 0.71 4.83 ± 0.7 5.95 ± 0.49

[1] *n = 13.*
[2] *x̄ SD; range in parentheses (all such values)*

Table 1 Baseline characteristics of patients with cancer and control group[1]

Type of cancer	n[1]	Biopsy analysis
Lung cancer	7	Carcinoma nonmicrocellulare probabiliter adenocarcinoma (1); Adenocarcinoma (3); Carcinoma planoepitheliale (1); Carcinoma microcellulare (1); Carcinoma mixtus (1)
Pharynx tumors	2	Carcinoma planoepitheliale partim keratodes; Lymphoma malignum
Rectal tumors	2	Adenocarcinoma tubular (2)
Testis tumor	1	Tumor germinalis mixtus testis
Stomach tumor	1	Adenocarcinoma tubular

[1] *n = 13.*

the German population in the study of Dittmar M. [20-22]. So far there are no such phase angle reference values available for a healthy Polish population. The German population reference values are probably most closely related to our population. Based on that information, the PA values reported by Dittmar M. on healthy subjects are clearly higher than the age and BMI matched values in the control group, observed in this study (women 5.59º ± 0.72 vs. 4.83º ± 0.7, respectively; men 6.41º ± 0.72 vs. 5.95º ± 0.49, respectively) [22]. The lack of established PA reference values for the Polish population, and the observed variability of national PA values may be one of limitations of this study.

During the past decade, several studies have characterized the role of PA as a prognostic tool and an indicator of nutritional status and cell membrane function in various disease conditions, including cancer. The prognostic role of PA in patients with cancer is most underscored in calculation of survival in relation to the value of PA.

In patients with advanced lung cancer the mean PA less than or equal to 4.5 degrees correlates significantly with a shorter survival than in those with PA greater than 4.5 degrees [23]. In the study in stage IV colorectal cancer patients it was found that PA above the median cut-off of 5.6º was associated with better survival [1]. Similarly, in stage IV pancreatic cancer, PA above the median cut-off of 5º was associated with improved survival [16].

PA seems to be the best indicator of cell membrane function as related to the ratio between extracellular water and intracellular water [8]. Schwenk et al. underlines that PA could be a good marker of malnutrition in HIV-infected patients [15]. A PA value less than 5.3º was considered to be the most important single predictor of survival [13]. In patients with liver cirrhosis PA equal to or less than 5.4º was associated with shorter survival as in the case of PA greater than 5.4 [10].

In our study the altered tissue properties were documented. The phase angle PA in cancer patients was 4.62º and significantly ($p = 0.002$) lower than in the control group (4.62º ± 0,87 vs. 5.69º ± 0.71, respectively). Comparing these values with German healthy population references values with matched age and BMI values, this difference would be even more visible [22]. In the literature, low PA values have only been observed in patients with advanced lung cancer, as described by Toso et al. [23]. PA by definition, is positively associated with reactance and negatively associated with resistance [9]. However, the relation between PA and reactance in our study was not shown. Most probably, it is a result that the cancer patients were not homogenous by cancer type.

Conclusion

Patients with cancers have altered tissue electrical properties. Further observations of the Polish population are required to implement direct bioimpedance measures (resistance, reactance, PA) determined by bioelectrical impedance analysis as a prognostic and nutritional marker in a clinical practice.

Competing interests

The authors declare that they have no competing interests.

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