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Body composition and lung function in adults with Cystic Fibrosis

Aleksandra John[1], Joanna Goździk-Spychalska[2], Magdalena Durda-Masny[1], Wojciech Czaiński[2], Marta Gębala[1], Jolanta Wlizło[2], Halina Batura-Gabryel[2], Anita Szwed[1]

[1]Institute of Human Biology and Evolution, Faculty of Biology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 6, 61-614 Poznań, Poland
[2]Department of Pulmonology, Allergology and Respiratory Oncology, Poznan University of Medical Sciences, Szamarzewskiego 82/84, 60-569 Poznań, Poland

ABSTRACT: The study aimed to assess: (1) differences in nutritional status and lung function between CF patients and the control group; (2) differences in body composition and lung function between groups of patients with CF designated by type of mutation; (3) the relationship between lung function and body composition in CF patients.
We studied 37 CF patients aged 19 to 51 years, and 41 healthy non-CF volunteers. Nutritional status was evaluated based on the BMI and the bioelectrical impedance analysis. The lung function was described by FEV1%. CF patients were classified according to the CFTR genotype based on five classes of mutations.
BMI were lower in CF patients compared to reference group (women: $Z = 3.76$, $p < 0.001$, men: $Z = 3.06$, $p = 0.002$). CF patients had a lower mean content of particular body components, as well as FEV1% values. BMI differed significantly depending on the type of mutation in females ($H = 10.33$, $p = 0.006$) and males ($H = 8.26$, $p = 0.016$). The lowest values of BMI were observed in the group of patients with severe types of mutations. Also, variables describing body composition were statistically significantly lower in patients with a severe type of mutations. The CFTR gene mutation type statistically significantly differentiated FEV1% ($H = 23.22$, $p < 0.000$). The results of the logistic regression analysis showed that the likelihood of dropping FEV1% below the norm was twice as high in undernourished females and males.
To assess the nutritional status of CF patients, more informative methods describing the proportions of body components are required.

KEY WORDS: cystic fibrosis, FEV1%, fat free mass, fat mass, nutritional status

Introduction

The nutritional status of Cystic Fibrosis (CF) patients plays an essential role in the course of the disease. Multiple studies have shown that nutritional status in patients with CF is associated with lung function, significantly determines

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their quality of life, and can be an important predictor of life expectancy (e.g Steinkamp and Wiedemann 2002; Sinaasappel et al. 2002; Kosińska et al. 2008; Szwed et al. 2018). Maintaining both the BMI (Body Mass Index) values at the right level and the proper proportions between the percentage of fat mass, (FM) fat free mass (FFM), muscle mass (MM) and total body water (TBW) are essential for the proper functioning of the body. Incorrect nutritional status not only affects the course and severity of CF but is also the very consequence of the disease (Pencharz and Durie 2000). Longitudinal studies on a large cohort of patients with CF confirmed that the nutritional status and lung function are strongly intertwined (Steinkamp and Wiedemann 2002). Both the nutritional status and lung function in CF can be modified by genetic factors such as the type of mutation. Patients with a severe type of mutation are more likely to be malnourished, experience worse respiratory disease, and have a lower probability of survival (Szwed et al. 2018; Dray et al. 2005; de Gracia et al. 2005; Shteinberg et al. 2017).

In studies, the BMI is widely used as a useful tool for assessing adult nutritional status, but this index simply describes the body size (kg/m2) and serves only as an approximate rather than a precise assessment of fat content. BMI does not distinguish between the major metabolically active components of body composition (FM and FFM) (Alvarez et al. 2016). There is still little data on the actual body composition of CF patients, in particular adults, which may give much more valuable information about the subject's health and help to monitor the progression of the disease.

The aim of this study was threefold: (1) estimation of differences in nutritional status and lung function between CF patients and the control group; (2) assessment of differences in body composition and lung function between groups of patients with CF designated by type of mutation; (3) assessment of the relationship between lung function and body composition in CF patients.

Materials and methods

The data used in this study were collected in 2015–2017 among patients with CF treated in the Department of Pulmonology, Allergology, and Respiratory Oncology of the University of Medical Sciences in Poznan. The studied group consisted of 37 adults aged 19 to 51 years, including 21 women and 16 men. For CF patients, the following inclusion criteria were used: age ≥18 years, confirmed CF diagnosis and recognized mutation on at least one chromosome, and no pulmonary exacerbation during the last four weeks preceding the study. In turn, the exclusion criteria were: pregnancy, smoking, use of systemic glucocorticosteroids, a chronic non-CF disease requiring long-term drug use, and long-term oxygen therapy or lung transplantation. The non-CF reference group was also selected, which consisted of 41 healthy non-CF volunteer students and employees at the Department of Pulmonology, Allergology and Respiratory Oncology of the University of Medical Sciences in Poznan aged from 20 to 46. The reference group included 15 men and 26 non-pregnant women – non-smoking, without chronic illness requiring prescription medications, and no acute illness in the prior four weeks of the study, and obesity.

The study was performed with the approval of the local research ethics com-

mittee (Bioethics Committee at the Karol Marcinkowski Poznan University of Medical Sciences, resolution No. 51/17). All participants had provided their written informed consent of participation in this study.

Nutritional assessment

The body height was measured, without shoes, with a GMP anthropometer with a measurement accuracy of 1 mm. Body weight was measured using a medical scale with a measurement accuracy of 100 g. In order to examine the nutritional status both the BMI index and analysis of body composition were used. BMI was calculated by dividing body weight by height squared (kg/m2). Based on the BMI index, the following groups were distinguished: undernourished (BMI<18.5), within the norm (18.5–24.9), and overweight (BMI≥25).

Body composition was assessed using bioelectrical impedance analysis (BIA). Body composition was measured using the AKERN BIA 101 ASE, a 4-point body composition analyzer at an operating frequency of 50 kHz. The development of the results of the body composition was done using the Bodygram Plus 1.2.0.2 software. All measurements were taken by the same investigator. The measurement was performed after an overnight fast, except for water and medication. The subjects were tested in a horizontal position. BIA method is widely used for estimating body composition in a non-invasive manner and allows us to calculate, among others, the percentage of fat mass, fat-free mass, muscle mass, total body water, and extracellular water (ECW). In the analysis of body composition following variables were examined: FFM, FM, TBW, ECW, MM, and body cell mass (BCM). Considering these variables both groups were divided into three subgroups: 1 – below the norm, 2 – within the norm, and 3 – above the norm.

Lung function testing

A spirometry test using a MicroLab ML 3500 (Micro Medical) spirometer was performed to assess lung function. Using spirometric measurements forced expiratory volume in one second (FEV1%) was obtained. Due to the FEV1% values, all subjects were divided into three subgroups: 1 – within the norm (FEV1%>70), 2 – with moderate pulmonary impairment (FEV1% 70-40), and 3 – severe pulmonary impairment (FEV1% < 40).

Other variables

Data on the type of mutation were obtained from the archives of medical records of the Department of Pulmonology, Allergology and Respiratory Oncology of the University of Medical Sciences in Poznan. The CF patients were classified according to the CFTR genotype based on five classes of mutations. Three groups of patients were distinguished: 1 – patients with severe types of mutation (I, II, III mutation class) on both alleles (I–III/I–III), 2 – heterozygous patients with a severe type of mutation on one allele and mild (I–III/IV–V) or unclassified mutation (other mutations, including those unknown) on another allele (I–III/n), 3 – patients with mild types of mutation (IV and V mutation class) on both alleles (IV–V/IV–V). The distribution of the CFTR mutations in our sample is provided in Table 2.

Statistical analysis

Statistical analysis was performed with Statistica 13.0 commercial package (StatSoft; Tulsa, OK). The nonparametric Mann–Whitney U test was used for the comparison of the body composition as well as lung function of non-CF people and patients with CF. The Kruskal–Wallis test by ranks was used for assessing the effect of the type of mutation in the CFTR gene on the variables describing the body composition of patients with CF, and the lung function. The logistic regression analyses were used to assess the association between lung function (FEV1%) and the variables describing the body composition of CF patients. The dependent variable was dichotomous. The odds ratio was used as a measure of association. A value of $p < 0.05$ was considered statistically significant.

Results

BMI values were significantly different between CF patients and reference group (women: Z=3.76, $p<0.001$; men: Z=3.06, $p=0.002$). Non-CF subjects had higher mean values of BMI (women: mean=22.65, SD=4.61; men: mean=24.15, SD=3.48) compared to CF patients (women: mean=18.78, SD=2.09; men: mean=20.97, SD=2.62). A total of 18 subjects with CF had BMI below the norm when in the reference group 3 people were underweight. Body composition also differed between the group of CF patients and non-CF reference group, both among women and men. The comparison of variables describing the body composition of non-CF subjects and CF patients is presented in Table 1. The amount of FFM in CF patients, measured in kg and kg/m2, were statistically significantly lower than in the reference group (respectively women: Z=3.67, $p<0.001$; Z=2.41, $p=0.012$; men: Z=2.39, $p=0.016$; Z=2.07, $p=0.032$). In terms of FFM, 12 CF patients were below the norm, and 25 were within the norm. In the reference group, 3 people were below the norm, 29 within the norm, and 9 above the norm in terms of FFM. Significant differences were also observed between the group of non-CF and CF

Table 1. The comparison of the body composition and lung function of non- CF people and patients with cystic fibrosis

	CF women	Non-CF women	Z	p	CF men	Non-CF men	Z	p
	Mean±SD	Mean±SD			Mean±SD	Mean±SD		
FFM kg	38.32±4.20	43.35±3.66	3.67	<0.000	53.11±5.71	61.24±6.95	2.39	0.016
FFM kg/m^2	14.53±1.39	15.55±1.61	2.41	0.012	17.31±1.40	19.08±2.47	2.07	0.032
FM kg	12.47±4.56	19.42±6.49	3.18	0.001	13.66±7.54	26.67±8.34	2.96	0.003
FM kg/m^2	4.70±1.63	6.98±3.25	2.85	0.004	4.35±2.09	8.31±4.68	3.02	0.002
TBW l	27.85±3.32	31.73±2.69	3.24	0.001	38.27±4.28	44.82±6.67	2.57	0.010
TBW l/m^2	10.56±1.05	11.38±1.19	2.32	0.020	12.48±1.66	13.96±1.82	2.19	0.020
ECW	14.42±2.40	16.49±1.89	3.02	0.003	17.48±3.04	21.92±6.19	2.55	0.011
MM	22.76±2.88	24.38±3.47	2.71	0.007	35.08±4.99	38.30±4.85	1.76	0.079
BCM	18.13±2.47	20.42±3.0	2.50	0.012	28.58±4.43	30.82±4.00	1.54	0.123

FFM – fat-free mass; FM – body fat mass; TBW – total body water; ECW – extracellular water; MM – muscle mass; BCM – body cell mass.

subjects in the amount of FM in kg and kg/m2 (respectively women: Z=3.18, p=0.001; Z=2.85, p=0.004, men: Z=2.96, p=0.003; Z=4.35, p=0.002). In turn, non-CF men, the mean FM was almost twice as much as in CF men (Table 1). Considering the amount of FM, 12 CF patients were below the norm, 20 within the norm, and 5 above the norm. It is noteworthy that in the group of 5 CF patients with FM above the norm, 4 had BMI at the lower limit of the norm (BMI<20.5), and 1 even below the norm (BMI=17.73). Interestingly, all of these patients were men. Those 4 CF patients with normal BMI had I–III/n type of mutation and were over 35 years of age. A man with a BMI below the norm and excessive FM had I–III/n type of mutation and was at the age of 21 (Table 2). In turn, in the group without CF, 4 were below the norm in terms of FM, 19 were within the norm and 18 exceeded the norm. In terms of TBW and ECW, both CF men and CF women were characterized by statistically significantly lower values than healthy subjects (respectively: TBW l women: Z=-3.24, p=0.001; men: Z=2.57, p=0.01; TBW l/m2 women: Z=2.22, p=0.02; men: Z=2.19, p=0.02; women ECW: Z=3.02, p=0.003; men: Z=2.55, p=0.011). The mean TBW and ECW values of the studied groups are presented in Table 1. Significant differences between women of CF and the non-CF reference group was also observed comparing MM. The amount of MM was statistically significantly lower in CF women than in non-CF group (Z=2.71, p=0.007) but not statistically significant in men (Z=1.76, p=0.079). In addition, BCM values of female CF patients were significantly lower (Z=2.50, p=0.012) than in healthy women.

As might be expected, there were significant differences in lung function between the group of patients with CF and the reference group. FEV1% was significantly lower in CF patients (Z=7.12, p<0.001) compared to the reference group. The mean FEV1% in the non-CF subjects was 102.56±12.52, while in CF patients 51.55±24.86.

Next, we have shown that nutritional status expressed by BMI differed significantly depending on the type of mutation in females and males (respectively: H=10.33, p=0.006; H=8.26, p=0.016). The lowest values of BMI were observed in the group of patients with severe types of mutation, while higher values in the group with I–III/IV–V mutations in females and I–III/n in males. The highest BMI was observed in females and males with mild types of mutations (Table 2).

Also, variables describing body composition, such as: FFM, FM, and TBW, were statistically significantly lower in patients with severe type of mutations (for females FFM kg: H=9.44, p=0.008; FFM kg/m^2: H=14.81, p=0.006; FM kg: H=7.98, p=0.03; FM kg/m^2 H=7.21, p=0.02; TBW l: H=8.98, p=0.01; TBW l/m^2 H=14.35, p<0.001 and males FFM kg: H=7.14, p=0.028; FFM kg/m^2: H=10.13, p=0.006; FM kg: H=6.97, p=0.04; FM kg/m^2: H=6.61, p=0.04; TBW l: H=6.96, p=0.04; TBW l/m^2: H=6.41, p=0.04). Although patients with severe type of mutations had lower ECW, MM, and BCM, the differences turned out to be statistically insignificant (Table 2).

When assessing the variation in lung function of adults with CF, we showed that the CFTR gene mutation type significantly differentiated FEV1% (H = 23.22, p <0.000). The lowest values of FEV1% were observed in the group of

Table 2. The effect of the type of mutation in the CFTR gene on the variables describing the body composition of patients with cystic fibrosis

	Females mutation category					Males mutation category				
	I–III/I–III; N=9	I–III/IV–V; N=6	IV–V/IV–V; N=6	H	p	I–III/I–III; N=7	I–III/n; N=5	IV–V/IV–V; N=4	H	p
	Mean±SD	Mean±SD	Mean±SD			Mean±SD	Mean±SD	Mean±SD		
BMI	17.34±1.48	19.39±1.67	20.34±2.01	10.33	0.006	19.15±1.41	23.80±1.45	21.80±2.69	8.26	0.016
FFM kg	35.28±2.52	39.65±3.94	41.56±3.68	9.44	0.008	50.37±3.87	54.90±1.63	56.82±2.58	7.14	0.028
FFM kg/m^2	13.21±0.82	15.37±0.88	15.74±0.42	14.81	0.006	16.38±0.97	17.36±0.55	19.09±9.10	10.13	0.006
FM kg	11.62±2.40	12.85±3.38	14.36±2.99	7.98	0.02	9.27±2.57	19.59±3.96	12.12±3.67	6.97	0.04
FM kg/m^2	4.33±1.21	4.46±1.38	4.49±1.91	7.21	0.03	3.12±1.51	6.61±1.49	4.82±3.67	6.61	0.04
TBW l	25.58±1.85	28.63±2.32	30.50±2.77	8.98	0.01	36.34±2.95	39.57±1.97	40.65±2.02	6.96	0.04
TBW l/m^2	9.57±0.61	11.08±0.69	11.84±0.63	14.35	<0.000	11.86±0.92	12.52±0.79	13.66±1.12	6.41	0.04
ECW	13.18±1.05	15.13±2.96	15.58±1.71	5.16	0.07	16.99±3.07	18.37±1.91	17.57±4.33	1.05	0.58
MM	21.03±2.08	23.10±1.96	25.02±2.27	5.24	0.07	32.51±4.81	35.85±2.76	39.43±4.38	5.53	0.06
BCM	16.79±1.79	18.33±1.98	19.93±2.84	5.31	0.07	26.40±4.11	29.13±2.63	32.40±4.38	5.21	0.07

BMI – body mass index; FFM – fat-free mass; FM – body fat mass; TBW – total body water; ECW – extracellular water; MM – muscle mass; BCM – body cell mass.

patients with severe types of mutation (FEV1%=37.15±15.31), while higher values in the group with I–III/IV–V or I–III/n in (FEV1%=56.44±14.30). The highest FEV1% was observed in females and males with mild types of mutation (FEV1%=74.65±15.39).

In order to estimate the association between lung function (FEV1%) and the variables describing the body composition of CF patients, the logistic regression analysis was applied. The results showed that the likelihood of dropping FEV1% below the norm was almost twice as high in undernourished females and twice as high in undernourished males. With a decrease in FFM and FM, the risk of lung malfunction was respectively: OR=2.6 and OR=1.83. In men, only a decrease in FFM increased by 1.93 times the probability of a drop in FEV1% below normal, while FM of men with CF did not show a

Table 3. Multiple/multinomial logistic regression analysis of body composition factors affecting FEV1

	Females OR (95% CI) p value for trend	Males OR (95% CI) p value for trend
BMI	1.85 (1.19; 2.88) 0.01	2.02 (1.34; 4.15) 0.03
FFM	2.60 (1.04; 6.52) 0.02	1.93 (1.18; 3.94) 0.03
FM	1.83 (1.23; 2.36) 0.01	1.08 (0.84; 1.46) 0.56
TBW	3.34 (1.13; 4.83) 0.01	1.88 (1.21; 2.93) 0.01
ECW	1.41 (0.89; 2.25) 0.12	0.93 (0.72; 1.19) 0.54
MM	1.61 (0.93; 2.77) 0.06	1.49 (0.90; 2.48) 0.06
BCM	1.66 (0.90; 2.97) 0.08	0.89 (0.66; 1.1) 0.44

BMI – body mass index; FFM – fat-free mass; FM – body fat mass; TBW – total body water; ECW – extracellular water; MM – muscle mass; BCM – body cell mass.

statistically significant relationship with lung function. In turn, the TBW decrease in men with CF almost doubled the risk of lung dysfunction, while in women the risk of FEV1% below normal was more than three times higher. Other variables: ECW, MM, and BCM did not increase statistically significantly the probability of abnormal lung function. The results of the logistic regression analysis are presented in Table 3.

Discussion

Due to the complicated clinical picture of CF, it is difficult to accurately describe a cause-and-effect scheme that would explain the reasons for the worsening of the patient's health and, consequently, his or her death. The studies carried out so far indicate a significant effect of a severe type of mutation and lung function, including numerous and advanced respiratory infections, on the decrease in survival of people with CF (Kerem et al. 19992). Nevertheless, it should be emphasized that CF is a multiorgan disease, and therefore the reasons for the decrease in survival are not a simple reflection of the impairment of lung function or dysfunction of the digestive system. Patients' life expectancy is modified by many factors closely related to each other, creating a so-called vicious circle. Pencharz and Durie (2000) have already written about this kind of phenomenon, describing in detail the pathogenesis of malnutrition in CF, including energy losses, energy intake, energy expenditure, and metabolism. The present study confirms the occurrence of undernutrition in a large number of CF people, as evidenced by BMI below the norm in as many as 49% of patients, as well as significantly lower values of almost all body components in CF patients compared to the non-CF control group. Undernutrition in CF subjects has been highlighted earlier by many researchers (Steinkamp and Wiedemann 2002; Sinaasappel et al. 2002; Kosińska et al. 2008; Szwed et al. 2018; Milla 2007; Umławska and Rams 2009). However, their research was based mainly on BMI, without considering a detailed body composition analysis.

The analysis of the body composition of children with CF and its comparison with the healthy group did not show any significant differences (Marín et al. 2004). In turn, the results of cross-sectional studies conducted by Steinkamp and Wiedemann (2002) showed that 19% of children with CF aged 2–6 years were undernourished, and the percentage of undernutrition increased with age to reach 38% in adulthood. The results of our work confirm that body composition significantly worsens as the disease progresses. Fat mass and fat free mass are important as the body's energy reservoir (fat mass) and reflect body mass not related to adipose tissue, including visceral protein, intracellular water, extracellular water, and bone mineral (fat free mass) (Kyle et al. 2004). The studies carried out so far underline the role of FM and FFM as effective indicators in the assessment of nutritional status [15]. In our study, the total amount of FM in adult CF patients was statistically significantly lower than in non-CF control group. According to Grey et al. (1993) total body fat mass for CF is 30% lower than in healthy people. The results of our research have shown that the average FM is almost 50% lower in men and about 34% lower in women compared to healthy people. Almost half of the CF patients had an FFM below the norm, and the mean FFM of the patients with CF

was statistically significantly lower, in women and men. Similar results were obtained by Ionescu et al. (2000), wherein the group of 22 CF patients, 12 people were below the norm in terms of FFM, and the average FFM between healthy and CF patients differed by around 10 kg. Low FM and FFM values in CF patients in relation to healthy people confirm undernutrition determined by the BMI. Particular attention should be paid to the fact that in our group of patients, in five men with BMI values at the lower limit of the norm, and even below, too high FM was demonstrated. Considering the key role of undernutrition in the progress of lung disease in CF patients, as well as maintaining adequate nutritional status, the use of BMI seems to be unreliable. Although only 5 patients showed excess FM, it is worth remembering that a high-protein and high-fat diet in CF should be monitored, because the use of high-calorie diets may be beneficial for the patient only to a certain critical moment, after which an adverse increase in body fat percentage occurs. Excessive body fat accumulation, although invisible in the study using BMI, negatively affects the functioning of the patient's body, may causing intra-abdominal adiposity, and thus improper functioning and deterioration of the patient's health. Similar results were obtained by Alvarez et al. (2016) who showed that about one-third of CF patients with normal BMI had an increased FM index, which was associated with decreased lung function and a lower FFM index. What's more, they emphasize that these results would not be identified using BMI as the only indicator of nutritional status, suggesting the need for direct measurement of body composition in patients with CF. Considering that proper diet is currently one of the main goals in developing a CF treatment strategy, the results of our research and research carried out by Alvarez et al. (2016) emphasize the need to focus on improving the percentage of FM and FFM, not on body weight or BMI, and for this purpose – constant monitoring of the supply of the right amount of nutrients, vitamins, and minerals to CF patients. Proper and controlled diet results are strengthening the body's immune system, which in turn may positively affect relieving the disease symptoms.

There are a number of reasons for undernutrition in CF people. They are associated not only with exocrine pancreatic insufficiency, malabsorption, CF related diabetes, but also chronic infection and recurrent exacerbations in the course of the disease (Matel and Milla 2009). Lung function and nutritional status thus form a system of mutual relations, affecting each other both indirectly and directly. Abnormal nutritional status is conducive to the development of numerous infections and aggravation of changes in the respiratory system due to the reduced immunity of the body and low potential to fight the disease. In turn, the deterioration of the function of the respiratory system is associated with an increased body energy requirement, which in combination with the devastating nature of numerous lung infections, contributes to the worsening of the nutritional status of CF patients. The overriding goal in the study of the biological status of the patient's body is therefore an attempt to identify specific cause-and-effect relationships in the course of the disease and the so-called critical moments. Critical moments will in turn be such values of indicators describing, among others. nutritional status and lung function, which will be associated with an increased

probability of a decline in the survival curve as a warning signal for clinicians.

Assessment of the lung function clearly confirmed that CF people have significantly lower values of FEV1% compared to non-CF, which is also reflected in the available literature (Dray et al. 2005; de Gracia et al. 2005; Shteinberg et al. 2017).

An additional factor complicating the picture of the disease is the effect of the type of mutation in the CFTR gene. Our results confirmed that the nutritional status and lung function of CF people depend on the type of mutation in the CFTR gene. Researchers confirm that the majority of malnourished patients fall into the group of people with a severe mutation of the CFTR gene, but these studies are based mainly on BMI values (Dray et al. 2005). This was confirmed by our research with the use of body composition analysis. Part of the body components of CF patients (FFM, TBW, ECW) was significantly lower in patients with severe types of mutation. However, it should be emphasized that in our sample, subjects with normal BMI and excessive FM had a mild type of mutation. Perhaps it is the presence of a mild mutation that is the factor that predisposes to hidden obesity and the deposition of excess body fat. However, this requires confirmation in further studies.

Our results and conducted by other researchers (de Gracia et al. 2005; Shteinberg et al. 2017; Pedreira et al. 2005) showed that there is a relationship between genotype and pulmonary function. The FEV 1% values were significantly higher in patients with genotype I–III/IV–V or I–III/n and IV–V/IV–V than those observed in patients with genotype I–III/I–III. These findings suggest that genotype as a prognostic factor of lung function in CF is very important. Considering the fact that patients with a severe type of mutation are diagnosed in early childhood (most of them up to 1 year old), the type of mutation takes on special significance, since from the moment CF is diagnosed, all patients receive specialist treatment. In contrast, patients with milder types of mutations often start treatment much later, often in adulthood. In such a situation, it would be expected that spirometric values in people with a late diagnosis of CF will be worse, however, the results of the research show clearly better lung function in patients with these types of mutations. On this basis, it can be concluded that the differences between CF patients may be related to the effect of mutations in the CFTR gene on the production and functioning of the CFTR protein. It is known that mutations that are associated with maintaining even a partial CFTR function are usually associated with a milder course of the disease, and thus better spirometric results (Shteinberg et al. 2017). On the other hand, as demonstrated by Garcia et al. (2005) having mutations from class I and II on both chromosomes is related to a higher risk of developing moderate to severe pulmonary disease.

Considering that both body composition and lung function are associated with the clinical severity of CF and each of these factors is determined by the class of the CFTR mutation, we have shown a link between nutritional status and lung function. Poor nutritional status, resulting from a decrease in BMI, FFM, FM, and TBW was associated with an increased risk of abnormal lung function. A statistically significant relationship between lung function and the amount of fat free mass and total body water in the body was previously underlined by re-

searchers. Pedreira et al. (2005) showed that in children with CF BMI and FFM significantly correlated with FEV1%. The lower the values of variables determining the nutritional status, the worse FEV1% were obtained by subjects. According to Ionescu et al. (2000) chronic catabolic state and inflammation in the body of the patient contribute to low bone mineral density, which is related to the low values of fat free mass. In turn, Zemel et al. (2000), Milla (2007) argue that improving nutritional status is associated with improved lung function. The negative impact of underweight on the long-term outcome of CF treatment has been repeatedly highlighted (Steinkamp and Wiedemann 2002; Kosińska et al. 2008; Szwed et al. 2018; Pencharz and Durie 2000; Dray et al. 2005; de Gracia et al. 2005). The results of longitudinal studies carried out by Steinkamp and Wiedemann (2002) in a large cohort of CF patients confirm that in CF the nutritional status and lung function are interdependent variables. Researchers showed that patients with normal body weight had a significantly smaller decrease in lung function over 2 years than those with undernutrition. This relationship was demonstrated by researchers in all analyzed age groups. Decreased body cellular mass values are observed in the case of weakening of the body, and its decrease is associated with catabolic states (Kyle 2004). Based on the conducted research, it can be concluded that the deterioration of the nutritional status expressed by the impaired body composition components have a negative effect on the lung condition. The relationship between lung function and nutritional status was also demonstrated by Schoni and Casaulta-Aebischer (2000), who proved the existence of a correlation between FEV1% and fat free mass. Researchers have found a complex interaction between nutrition, the functioning of skeletal and respiratory muscles, and energy expenditure in patients with CF. They showed that undernutrition, which is not only a consequence of pancreatic insufficiency, significantly contributes to muscle weakness in CF patients and leads to deterioration of lung function. However, it should be emphasized that researchers often focus on the adverse relationship of undernutrition with lung function, without paying attention to the possibility of adverse excess of fat mass. The top-down assumption that all CF people are experiencing worsening undernutrition puts the researchers' vigilance down. As we showed – there are patients who, in spite of normal BMI, have excess fat mass, which also adversely affects lung function.

In conclusion, we showed that body composition in adults with CF is associated with lung function and CFTR mutation. When analyzing only body weight and BMI, it is not possible to estimate the exact proportion of the body components of the patients. That is why it is worth expanding the range of methods used in assessing the nutritional status by using studies describing the proportions of particular body components. This is all the more important because we have demonstrated the existence of patients with normal BMI and excess of FM. Although this requires confirmation and further research, especially with the use of longitudinal methods, it is worth emphasizing that the presence of elevated FM in patients with CF may have significant long-term health consequences. Further studies on the body composition of CF adults are necessary to compare the results of body composition tests at

various medical centers and find out how big is the CF people group with elevated FM. Perhaps for this group of patients it would be necessary to modify the standards of care in the field of nutrition.

Limitations of the study

One limitation of the study was the small sample size. As the study was designed as a single-center study, only adult CF patients treated at the Department of Pulmonology, Allergology and Respiratory Oncology of the University of Medical Sciences in Poznan were recruited.

The Authors' contributions

AJ – conceptualization, investigation, formal analysis, writing – original draft; JG-S – conceptualization, investigation, supervision, writing – review & editing; MD-M – data curation, formal analysis, validation, writing – review & editing; WC – investigation, writing – review & editing; MG – investigation, writing – review & editing; JW – investigation, writing – review & editing; HB-G – supervision, writing – review & editing; AS – conceptualization, project administration, formal analysis, supervision, writing – original draft.

Conflict of interest

The authors declare that there is no conflict of interest.

Corresponding author

Anita Szwed, Institute of Human Biology and Evolution, Faculty of Biology, Adam Mickiewicz University, Uniwersytetu Poznańskiego 6, 61-614 Poznań, Poland
e-mail: aniszwed@amu.edu.pl

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