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Original Article

Evaluation of nutritional status and related factors in children with cystic fibrosis

Aylin Yücel[1], Sevgi Pekcan[2], Beray Selver Eklioğlu[3], Hasan Ali Yüksekkaya[1], Gökçen Ünal[2], Aslı İmran Yılmaz[2]

Departments of [1]Pediatric Gastroenterology, Hepatology and Nutrition, [2]Pediatric Chest Diseases and [3]Pediatric Endocrinology, Necmettin Erbakan University, Meram Medical Faculty, Konya, Turkey.

ABSTRACT

Background. This study aimed to evaluate the nutritional status and body composition in children with cystic fibrosis (CF), in accordance with the new nutritional targets defined by European Society for Clinical Nutrition and Metabolism (ESPEN), the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Cystic Fibrosis Society (ECFS) 2016.

Methods. In this cross-sectional study, data were collected prospectively in a single centre. A record was made for a total of 95 patients with CF of clinical data. Anthropometric data were evaluated using the World Health Organization growth standards. The bone mineral density (BMD) z-score was adjusted for height by measuring dual-energy X-ray absorptiometry (DXA). The speed of sound z-score values were measured with quantitative ultrasound (QUS).

Results. The nutritional status was normal in 37.9% of patients aged <2 years and 33.3% of patients aged 2-18 years. When the DXA BMD z-score values were corrected for height, it was determined that the BMD deficit was less. The calcaneus QUS SOS z-score mean value was lower than the mean height for age z-score adjusted BMD (BMD_{HAZ}).

Conclusions. The malnutrition rates of CF patients were higher than the rates previously reported in literature. As there are insufficient nutritional data in Turkey, there is a need for multi-centre studies to determine the frequency of malnutrition according to the new classifications. It is clear that QUS measurements cannot replace DXA in the diagnosis of osteopenic bone disease. However, when low values are determined with QUS as the first recommended measurement in the screening of bone status, it can be considered appropriate to confirm the status with DXA.

Key words: bone densitometry, cystic fibrosis, malnutrition, nutritional status, quantitative ultrasound, height for age z-score adjusted BMD.

Cystic fibrosis (CF) is an autosomal recessive, multi-systemic disorder which forms as a result of mutation in the protein encoding gene known as cystic fibrosis transmembrane conductance regulator (CFTR). The two most significant problems determining survival are malnutrition and pulmonary disease.[1] The nutritional status in CF is related to insufficient macro/micronutrient intake, maldigestion/malabsorption, increased energy requirement, and genotype.[2] Maldigestion and malabsorption associated with exocrine pancreatic failure cause loss of energy. This loss may be increased in conditions such as accompanying intestinal inflammation, small intestinal bacterial overgrowth, insulin resistance and impaired liver functions. In addition, total and resting energy expenditure (TEE, REE) are increased

✉ Aylin Yücel
ayucel82@hotmail.com

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in CF patients, and CF-related infections and persistent pulmonary inflammation cause a further increase in energy requirement. In addition to all these problems, loss of appetite because of infections, gastrointestinal problems or side-effects of medications and inability to obtain sufficient calorie intake have been found to contribute to malnutrition.[3]

Under-nutrition leads to retarded growth development, impaired respiratory muscle function, reduced exercise tolerance, immunological disorders and increased sensitivity to infections.[4] Severe nutritional deficiency in infancy and childhood can result in a significant deterioration in respiratory functions, short life expectancy and impairments in cognitive functions.[3] Correction of the nutritional status improves quality of life.[4]

In 2002, the European and US nutrition consensus reports for CF patients were published. Subsequently, it was reported that the ideal body weight percentage (IBW%) could ignore malnutrition in children of short height and could exaggerate the severity of malnutrition in tall children.[5] The nutritional classifications for CF patients were updated in 2016 by the European Society for Clinical Nutrition and Metabolism (ESPEN), the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Cystic Fibrosis Society (ECFS). The parameters recommended for use in nutritional status evaluation and the target values defined for use in the determination of a sufficient nutritional status has changed with these reports. According to this consensus, IBW% is no longer used. Malnutrition classification is made according to length and weight percentile in infants aged < 2years and according to body mass index percentile (BMIp) in children and adolescents aged 2-18 years. Normal nutritional status is defined as ≥50th percentile of these parameters, impaired nutritional status as 10th-50th percentile, and persistent under-nutrition as <10th percentile.

Another factor related to nutritional status is bone mineralisation, and the incidence of osteopenic bone disease in adolescents and adults with CF is extremely high.[6] In the 2016 ESPEN- ESPGHAN-ECSF nutrition consensus report in accordance with the 2011 European Cystic Fibrosis Bone Mineralisation guidelines, it is recommended for CF patients that bone mineral density (BMD) measurements are taken with dual-energy X-ray absorptiometry (DXA) at specific intervals starting with the first measurements at age 8-10 years. In the presence of risk factors for osteopenia, it has been stated that first measurements can be taken earlier. In the presence of short stature, the BMD z-score should be corrected for height, since the deficit in BMD will seem overestimated. Even though a sufficient nutritional status can currently be obtained at increasing rates in CF patients, under-nutrition remains an important problem and is a risk factor for osteopenic bone disease.[3,7]

BMD measurements made with quantitative ultrasound (QUS) is a rapid, easy to apply method and has the advantage of no radiation exposure.[8] Studies of adults on this subject and the few studies conducted on children with CF have reported that it can be used for screening purposes in CF patients with a sufficient nutritional status, but no consensus has been reached on this subject as yet.

There are insufficient data related to the nutritional status of CF patients in Turkey. The aim of this study was to determine the incidence of malnutrition in a cystic fibrosis centre in Turkey with anthropometric measurements made in accordance with the new nutritional classifications defined in 2016 by ESPEN, ESPGHAN and ECSF, and to evaluate the relationship of the nutritional status with clinical, laboratory and genetic characteristics and bone mineralisation values.

Material and Methods

Ethical statement

Ethical approval for the study has been obtained from the Ethics Committee of Necmettin Erbakan University Meram Medical Faculty (code number: 2017/990). In addition, written informed consent was obtained from parents or legal guardians of all children prior to any study-related procedure in the study.

Study Design

This single-centre, cross-sectional study included patients diagnosed with CF according to the 2016 consensus criteria who attended regular follow-up examinations in the period between 2017-2018, and for whom measurements were taken and recorded.[9] Patients were excluded from the study if they were aged >18 years, or if <18 years were determined with mutations not defined in the Cystic Fibrosis Mutation database following all gene DNA analysis, or were receiving systemic steroid treatment. For patients with hospitalisation within the previous month, pulmonary exacerbation, or antibiotic use, measurements were taken at the follow-up visit after clinical stabilisation was obtained. A total of 95 patients who met the study criteria and consented to participate, were included in the study.

Clinical parameters

A record was made for each patient of age, gender, gestational age, birthweight, number of hospitalisations, whether or not enteral nutrition support was administered, medical treatments and mutations. The mutations were separated into 3 groups according to the ECSF Patient Registry Annual Data Report 2015. Group 1 was classified as F508del homozygote, Group 2 as F508del heterozygote, and Group 3 as other mutations. For patients aged >5 years, the highest values from 2 consecutive spirometry measurements were selected. If there was a difference of >5% between the FEV1 and FVC values of the two spirometric measurements, it was applied for a third time. Patients without an acceptable spirometry value were not included in the study. In the evaluation of the nutritional status, the serum markers recommended in the 2015 consensus were used (blood count, iron status, plasma fat-soluble vitamin levels, serum liver function tests, and electrolytes). For the evaluation of body composition, total body DXA was applied and the BMD z-scores were recorded. Since the children included in our study were shorter in height for age, BMD measurements were also ajusted according to the height for age z-score (HAZ). The BMD z-scores below -2 are considered to be CF-related low BMD. Calcaneus QUS was applied using a Hologic Sahara bone sonometer device (35 Crosby Drive, Bedford, MA 01730). The z-score values of the QUS speed of sound (SOS) measurements were recorded.

Anthropometric measurements

Body weight, height, mid-upper arm circumference (MUAC), triceps skin fold (TSF) and subscapular skin fold (TSF, SSF) measurements were taken and recorded for each patient. Height measurements were taken with a stadiometer, standing for patients aged >2 years and lying down for patients <2 years. Body weight measurements were recorded using a 10-gram-sensitive infant scale for infants, who were weighed naked, and a 100-gram-sensitive digital adult scale for children aged >2 years. The MUAC was measured from the middle of the acromion notch and the olecranon notch of the left arm with the elbow joint in mild flexion. The TSF and SSF were measured by a single person using a Holtain Skinfold Caliper, and the average of 3 measurements was recorded for the analyses. Using the measured parameters, the body mass index (g/m^2) (BMI), weight-for-age (WA), height-for-age (HA), weight-for- height (WH) percentile and z-score values were calculated using the World Health Organisation (WHO) growth standards and Anthro/AnthroPlus (version 3.2.2, January 2011) software. In accordance with the recommendations of the new nutritional consensus, we used WA, HA

and WH percentile (WAp, HApandWHp) for nutritional classification in children younger than 2 years old, and BMI (g / m^2) percentile (BMIp) for children older than 2 years old. The non-adjusted real weight and height values were used in the analysis. Calculations not in Anthro/AnthroPlus program (TSF, SSF percentile, z-score calculations for children >5 years) were made using the Center for Disease Control and Prevention (CDC) growth standards. The z-scores of the anthropometric measurements were compared. Normal nutritional status was accepted as ≥50th percentile of the WAp and HAp in patients up to the age of 2 years and of the BMIp in those aged >2 years, impaired nutritional status was accepted as 10th-50th percentile and persistent under-nutrition as <10th percentile.[3]

Statistical analysis

Data obtained in the study were analysed statistically using SPSS 20.0 software (IBM Inc, Chicago, IL, USA). By calculating descriptive measurements, categorical variables were stated as frequency and percentage and numerical variables as mean ± standard deviation (SD) or median (interquartile range, IQR), as appropriate. Conformity of continuous variables to normal distribution was assessed with the Kolmogorov-Smirnov test. The variables were seen not to have normal distribution so the Mann-Whitney U-test and the Kruskal Wallis test were used in the comparisons. To determine correlations between categorical variables, Chi-square analysis with Monte Carlo correction was used and for correlations between numerical variables, Spearman's Rho correlation analysis was applied. Significant results were demonstrated with graphs. Taking the type-1 error value as 5% for the whole study, a value of $p<0.05$ was accepted as statistically significant.

Results

The 95 patients with CF included in the study comprised 51 (53.7%) girls and 44 (46.3%) boys with a mean age of 79 months (79.26 ± 61.18) and 66 (69.5%) patients were aged >2 years. According to gestational age, 13.7% were preterm. In almost half (45.3%) of the patients, there was parental consanguinity, and in 40% there was a familial history of CF. The median (IQR) number of hospitalisations was 2 (35). Other clinical characteristics are shown in Table I.

All anthropometric measurements of patients were evaluated according to the z-scores. The mean z-score values of the anthropometric measurements are shown as a box-plot graph in Figure 1.

When the nutritional classifications were examined in the 29 infants aged ≤2 years, normal nutritional status was determined in 27.6% (n=8) according to W-Ap, in 41.4% (n=12) according to H-Ap, and in 37.9% (n=11) according to W-Hp. In the 66 patients aged 2-18 years, normal nutritional status was determined in 33.3% (n=22) (Table II).

The nutritional classifications were compared with FEV1, FVC, BMD z-score, BMD_{HAZ}, SOS z-score and mutation classifications. Patients aged <2 years were only compared with mutation groups as BMD and spirometry values were not measured. A statistically significant correlation was determined between the presence of Delta F508 heterozygote mutation and normal and impaired nutritional status according to W-Ap (p=0.017). None of the patients with F508 homozygote mutation had normal nutritional status. Of the patients in the normal nutritional status group, 75% had other mutations, 54.5% of patients in the impaired nutritional status group had F508 del heterozygote mutation and 50% of the patients in the persistent under-nutrition group had F508del homozygote mutation. No statistically significant correlation was determined between the mutation groups and the H-Ap and W-Hp nutritional classifications (Table III).

In patients aged >2 years, the nutritional classifications made according to BMIp were compared with the clinical and laboratory parameters. In the 56 patients aged >5 years,

Table I. Clinical characteristics of 95 patients with cystic fibrosis.

Patients characteristics	Results
Age (month)	79.26 ± 61.18
Age at diagnosis (month)	19.12 ± 36.87
Height (cm)	108.95 ± 34.10
Weight (kg)	21.18 ± 14.30
Mutation, n (%)	
F508del homozygous	22 (23.2)
F508del heterozygous	17 (17.9)
Other mutations	56 (58.9)
Comorbidities, n (%)	
No	91 (95.8)
Hypothyroid	2 (2.1)
Phenylketonuria	1 (1.1)
Down's syndrome	1 (1.1)
Clinical presentation, n (%)	
Neonatal screening	24 (25.3)
Malnutrition	9 (9.5)
Cough	12 (12.6)
Recurrent pulmonary infections	7 (7.4)
Malnourishment/nausea	5 (5.3)
Chronic diarrhea	2 (2.1)
Pseudo-Bartter Syndrome	10 (10.5)
Nasal polyps	2 (2.1)
Elevated liver enzymes /cholestasis	4 (4.2)
Chronic/Recurrent pancreatitis	3 (3.2)
Meconium ileus	4 (4.2)
Respiratory distress/cyanosis	13 (13.7)
Medical treatments, n (%)	
PERT	85 (89.5)
Enteral nutrition supplementation	
Polymeric	34 (35.8)
Oligomeric	15 (15.8)
Fat-soluble vitamin	78 (82.1)
Proton pump inhibitor	23 (24.2)
Dornase alpha	89 (93.7)
Inhaler beta-2 agonist	41 (43.2)
Inhaler corticosteroids	26 (27.4)
Laboratory findings, mean ± SD	
Hemoglobin (g/dl)	12.81 ± 1.6
Serum iron (μg/dl)	64.72 ± 33.98
Iron-binding capacity(μg/dl)	262.3 ± 74.89
Ferritin (ng/ml)	57.29 ± 78.49
Vitamin A (μg/dl)	247.2 ± 180.45
Vitamin D (ng/ml)	27.28 ± 26.19

PERT: pancreatic enzyme replacement treatment

Table I. Continued.

Patients characteristics	Results
Laboratory findings, mean ± SD	
Vitamin E (µg/ml)	13.02 ± 7.44
Vitamin B12 (pg/ml)	520.96 ± 254.74
Folic acid (ng/ml)	17.19 ± 6.11
Zinc (µmol/l)	19.38 ± 34.7
Albumin (g/dl)	4.27 ± 0.46
Sodium (meq/L)	138.16 ± 3.91
Calcium (mg/dl)	9.68 ± 0.62
FEV1 (%)	86.36 ± 21.6
FVC (%)	81.33 ± 19.01
DXA/BMD z-score	0.32 ± 0.83
QUS/SOS z-score	-0.129 ± 1.21
BMD_{HAZ}	0.548 ± 0.698

BMD: bone mineral density, BMDHAZ: height for age z-score adjusted BMD, DXA: dual-energy X-ray absorptiometry, FEV1: forced expiratory volume in 1 second, FVC: forced vital capacity, PERT: pancreatic enzyme replacement treatment, QUS: quantitative ultrasound, SOS: speed of sound.

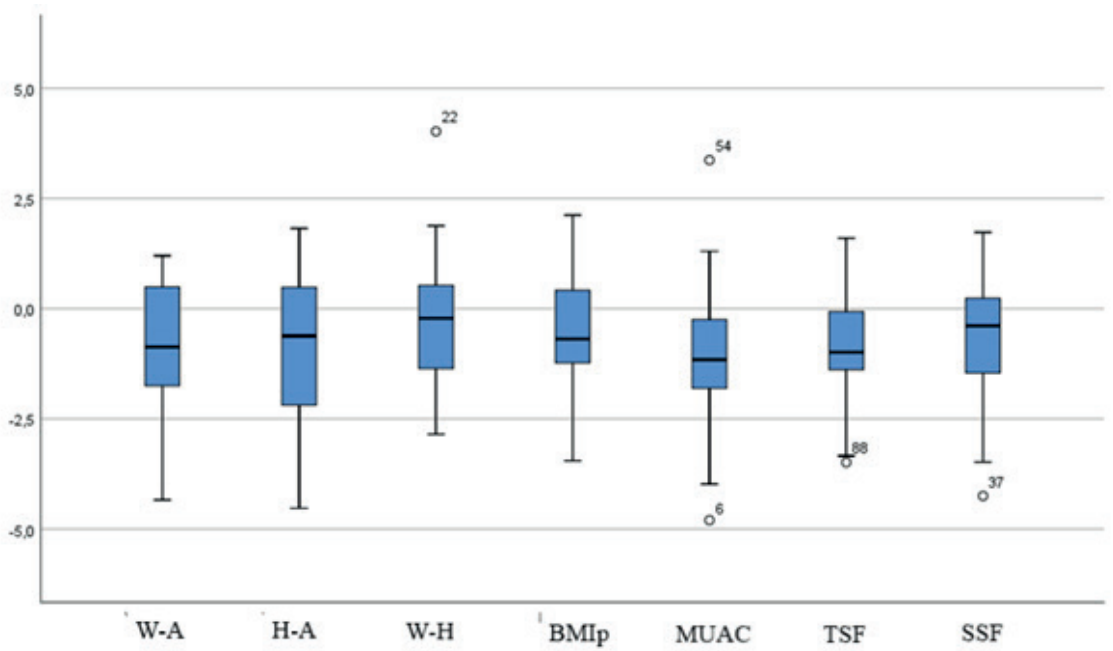

Fig. 1. Box-plots of z-scores of anthropometric measurements. BMI: body mass index, H-A: height-for-age, MUAC: mid-upper arm circumference, TSF: triceps skin fold, SSF: subscapular skin fold, W-A: weight-for-age, W-H: weight-for-height.

when the respiratory function tests, DXA and calcaneus QUS results were compared, the QUS SOS z-score value (p=0.041) and FVC (p=0.040) were found to be lower in the impaired nutritional status and persistent under-nutrition groups according to BMIp. When nutritional classifications according to BMIp were compared with BMD z-score and height for age z-score adjusted BMD (BMD_{HAZ}), although both parameters were measured quite

Table II. Nutritional classification based on age-specific anthropometric measurements.

Anthropometric parameters		n (%)
W-A percentile	Normal nutritional status (≥ 50th percentile)	8 (27.6)
(Infants ≤ 2 years)	Impaired nutritional status (10-50th percentile)	11 (37.9)
	Persistent under-nutrition (<10th percentile)	10 (34.5)
H-A percentile	Normal nutritional status (≥ 50th percentile)	12 (41.4)
(Infants ≤ 2 years)	Impaired nutritional status (10th-50th percentile)	9 (31)
	Persistent under-nutrition (<10th percentile)	8 (27.6)
W-H percentile	Normal nutritional status (≥ 50th percentile)	11 (37.9)
(Infants ≤ 2 years)	Impaired nutritional status (10-50th percentile)	9 (31)
	Persistent under-nutrition (<10th percentile)	9 (31)
BMI percentile	Normal nutritional status (≥ 50th percentile)	22 (33.3)
(Children 2-18 years)	Impaired nutritional status (10-50th percentile)	27 (40.9)
	Persistent under-nutrition (<10th percentile)	17 (25.8)

W-A: weight-for-age, H-A: height-for-age, W-H: weight-for-height, BMI: body mass index.

Table III. The mutation results of patients (< 2 years) according to nutritional classification system.

Mutation groups according to nutritional classification system		Nutritional status, n (%)			P value
		Normal	Impaired	Persistent undernutrition	
W-A percentile		(n=8)	(n=11)	(n=10)	
Mutation	F508del homozygous	0	3 (27.3)	5 (50)	0.017*
	F508del heterozygous	2 (25)[a]	6 (54.5)[b]	2 (20)	
	Other mutations	6 (75)	2 (18.2)	3 (30)	
H-A percentile		(n=12)	(n=9)	(n=8)	
Mutation	F508del homozygous	4 (33.3)	1 (11.1)	3 (37.5)	0.871
	F508del heterozygous	3 (25)	5 (55.6)	2 (25)	
	Other mutations	5 (41.7)	3 (33.3)	3 (37.5)	
W-H percentile		(n=11)	(n=9)	(n=9)	
Mutation	F508del homozygous	2 (18.2)	3 (33.3)	3 (33.3)	0.443
	F508del heterozygous	3 (27.3)	5 (55.6)	2 (22.2)	
	Other mutations	6 (54.5)	1 (11.1)	4 (44.4)	

* $p < 0.05$
a, b: percentages denoted by a different letter indicate significant differences between groups.
W-A: weight-for-age, H-A: height-for-age, W-H: weight-for-height.

low in the persistent undernutrition group, there was no significant difference between the groups (p=0.086, p=0.730) (Table IV).

The z-scores of the anthropometric measurements were compared with the BMD measurements and the spirometry results. A moderate positive correlation was determined between the W-A z-score and the BMD z-score (DXA), FEV1 and FVC. A significant correlation was determined between the H-A z-score and the BMD z-score (DXA) and FEV1. There was a negative correlation between BMD_{HAZ} and H-A z-scores, however it was not statistically significant. A low-level positive correlation was determined between the BMI z-score and FEV1 and FVC. Significant correlations were determined between the MUAC z-score and FEV1, between the TSF z-score and the BMD z-score (DXA) and FEV1, and between the SSF z-score and all the variables (Table V).

Table IV. The bone mineral density, spirometry and mutation results of patients (>2 years) according to the nutritional classifications.

Variables	BMIp Nutritional Classification			P value
	Normal (n=17)	Impaired (n=22)	Persistent undernutrition (n=17)	
DXA BMD z- score	0.54 ± 0.52	0.44 ± 0.50	-0.09 ± 1.23	0.086
BMDHAZ	0.67 ± 0.36	0.66 ± 054	0.27 ± 1.02	0.730
QUS SOS z- score	0.27 ± 1.18	0.001 ± 0.99	-0.74 ± 1.34[a]	0.041*
FEV1 (%)	95.12 ± 17.17	87.45 ± 18.20	76.70 ± 26.18	0.063
FVC (%)	87.02 ± 15.22	84.68 ± 16.24	71.58 ± 22.52[a]	0.040*
Mutation, n (%)				
F508del homozygous	5 (22.7)	7 (25.9)	2 (11.8)	0.298
F508del heterozygous	3 (13.6)	3 (11.1)	1 (5.9)	
Other mutations	14 (63.6)	17 (63)	14 (82.4)	

Data are parented as mean ± standard deviation unless otherwise specified.
BMDHAZ: height for age z-score adjusted BMD, BMIp: body mass index percentile, DXA BMD: dual-energy x-ray absorptiometry bone mineral density, FVC: forced vital capacity, FEV1: forced expiratory volume in 1 second, QUS SOS: quantitative ultrasound speed of sound.
* p<0.05

Table V. Relationships between the z-scores of the anthropometric measurements and the spirometry and bone mineral density values.

Measurements		BMD (DXA) z-score	BMD_{HAZ}	SOS (QUS) z-score	FEV1 (%)	FVC (%)
W-A z-score	R	0.340	-0.109	0.223	0.355	0.310
	p	0.010*	0.424	0.095	0.008*	0.021*
H-A z-score	R	0.284	-0.217	0.060	0.317	0.218
	p	0.033*	0.109	0.659	0.019*	0.111
W-H z-score	R	0.900	0.200	-0.200	0.500	0.500
	p	0.037*	0.800	0.747	0.667	0.667
BMI z-score	R	0.253	-0.003	0.307	0.306	0.289
	p	0.057	0.981	0.020	0.023*	0.033*
MUAC z-score	R	0.199	-0.041	0.204	0.326	0.253
	p	0.139	0.765	0.127	0.015*	0.062
TSF z-score	R	0.288	0.068	0.175	0.295	0.257
	p	0.030*	0.621	0.192	0.029*	0.058
SSF z-score	R	0.352	0.091	0.331	0.398	0.325
	p	0.007*	0.507	0.012*	0.003*	0.016*

BMI: body mass index, H-A: height-for-age, MUAC: mid-upper arm circumference, TSF: triceps skin fold, SSF: subscapular skin fold, W-A: weight-for-age, W-H: weight-for-height.
* p<0.05

Discussion

The recommended parameters and target values for use in the evaluation of nutritional status in patients with CF were changed with the most recent guidelines published in 2016 by the ECSF and the Cystic Fibrosis Foundation. In the 2002 consensus reports, height for age <5%, ideal body weight < 90% and BMIp<10% were defined as nutritional deficiency. "At-risk nutritional status" was defined as 10-25% of weight-for-length percentile in infants <2 years

and as 10-25% of BMIp for children >2 years. According to the most recent consensus, the 50th percentile was defined as the nutritional target, in other words, it was stated that to be able to be said to have a sufficient nutritional status, children with CF should have similar growth as their healthy peers. For acceptance of a population as mostly healthy, the mean z-score should be close to zero.[3,10]

According to the ECSF 2015 Patient Registry Annual Data Report, which included the data of 42,054 CF patients from 29 countries, including Turkey, in 20,196 patients aged ≤18 years, the mean W-A z-score ranged from -0.3 to -0.7, and the mean H-A score from -0.2 to -0.4. However, in the 2015 data, only 95 patients were reported from Turkey, and of those, height and weight measurements were available in only 35.[11] In the current study, the z-score values of all the anthropometric measurements of all 95 patients were negative (W-A z-score -1.016±1.36; H-A z-score -0.862±1.38; W-H z-score -0.313±1.41; BMI z-score -0.706±1.35; MUAC z-score -1.116±1.44; TSF z-score -0.752±1.13; SSF z-score -0.458±1.18).

In the evaluation of the current study according to nutritional classifications, 31% of the patients aged <2 years, and 25.8% of those aged >2 years were determined with persistent under-nutrition. In a 2016 study by Bahreyn et al.[12] which evaluated 109 CF patients, 72% were determined as malnourished. In a small study conducted in Brazil by Silva Pinta et al.[13] malnutrition was determined at the rate of 33.3%, and in a multi-centre study in Italy in 2009, Lucidi et al.[14] determined malnutrition in 12.9% of patients aged <2 years and in 20.9% of those aged >2 years.

Although the malnutrition rates in the current study were lower than those reported from other Asian countries, they were higher than the rates reported from European countries. In the current study population, a sufficient nutritional status was determined in only 37.9% (W-Hp>50%) of patients aged <2 years, and in 33.3% (BMIp>50%) of older children and adolescents. Lucidi et al.[14] reported a sufficient nutritional status in 64.4% (W-Hp>25%) of patients aged <2 years and in 69.5% (BMIp>25%) of children >2 years, although when BMIp >50% was used as the nutritional target, a sufficient nutritional status was reported in only 45.6%. Thus it can be seen that some patients who were accepted as having a normal nutritional status according to the old classifications should now be accepted as impaired nutritional status.

In the current study, it was observed that there was a proportional deterioration of the BMD (DXA, QUS) values with the spirometric parameters with progression from normal nutritional status towards persistent under-nutrition. There was a positive correlation between nutritional status and BMD in CF patients. Although there was no statistically significant relationship between BMD_{HAZ} and nutritional parameters, we found that BMD_{HAZ} values were better than BMD z-score values corrected for age and gender. BMD measurements are affected by height. In particular, conditions such as inflammation, immobilization, and malabsorption negatively affect both bone mineralization and linear growth.[15] In cases where linear growth is impaired, BMD z-score values adjusted for only age and sex may not reflect the truth and may overestimate the BMD deficit. In our study, we found that BMD deficit was less when BMD z-score values were corrected for height, however the difference was not statistically significant. Andrea Kelly et al.[16] compared BMD z-scores measured by DXA with height-adjusted BMD z-scores in 82 patients with cystic fibrosis and 322 healthy children and they found that BMD deficits were less when BMD values were adjusted for height. They stated that BMD deficits in children with cystic fibrosis can be attributed to the change in linear growth.[16] According to the 2011 European Cystic Fibrosis Bone Mineralisation Guidelines, DXA is the gold standard method for BMD evaluation in CF patients. In children z-score values corrected for height should be used. Those with a BMD z-score of <-2 can be accepted as CF-related low BMD. The guideline recommends that the first

measurement is taken at the age of 8-10 years, then repeated once every 5 years if the z-score is >-1, once every 2 years if between -1 and -2, and once a year if <-2, and if there is a risk factor for low BMD, the first measurement should be taken at a younger age.[7] In a study that compared the DXA and QUS methods in the BMD evaluations of adult CF patients, it was concluded that even if QUS was used instead of DXA, screening of these patients could be useful.[8] In the first study (2009) that evaluated the efficacy of QUS in BMD evaluations of children with CF, the QUS results of 29 relatively healthy CF patients with a sufficient nutritional status were found to be similar to those of a healthy control group. Similar results were reported in another study of 35 CF patients in Spain.[17,18]

In the current study group, which had higher rates of malnutrition compared to reports in literature, QUS and DXA were applied to the 56 patients aged >5 years and the QUS values were lower than the mean BMD_{HAZ} (BMD_{HAZ} 0,548±0,698; QUS/BMD z-score -0.129±1.21). Thus, the BMD was shown to be lower with QUS measurements than with DXA measurements. Considering that QUS has lower sensitivity and specificity than DXA, we suggest that screening QUS in CF patients and when a low BMD is detected confirming it by DXA may be an option to reduce the radiation exposure of patients.

Increasing awareness and determining the current nutritional status are the first steps to be taken in reaching nutritional targets in CF patients. When the new nutritional classifications are used, it is clear that fewer patients can be accepted as having a normal nutritional status. As there are insufficient nutritional data of CF patients in Turkey, there is a need for multi-centre studies using the new classifications.

QUS measurements cannot replace DXA in the diagnosis of osteopenic bone disease in CF patients. However, if low BMD is determined following QUS as the first recommended measurement in the screening of bone health, confirmation with DXA can be considered a better choice to be able to reduce radiation exposure.

Ethical approval

Ethical approval for the study has been obtained from the the Ethics Committee of Necmettin Erbakan University Meram Medical Faculty (code number: 2017/990).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: AY, SP, BSE, HAY; data collection: AY, GU, AIY; analysis and interpretation of results: AY; draft manuscript preparation: AY. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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