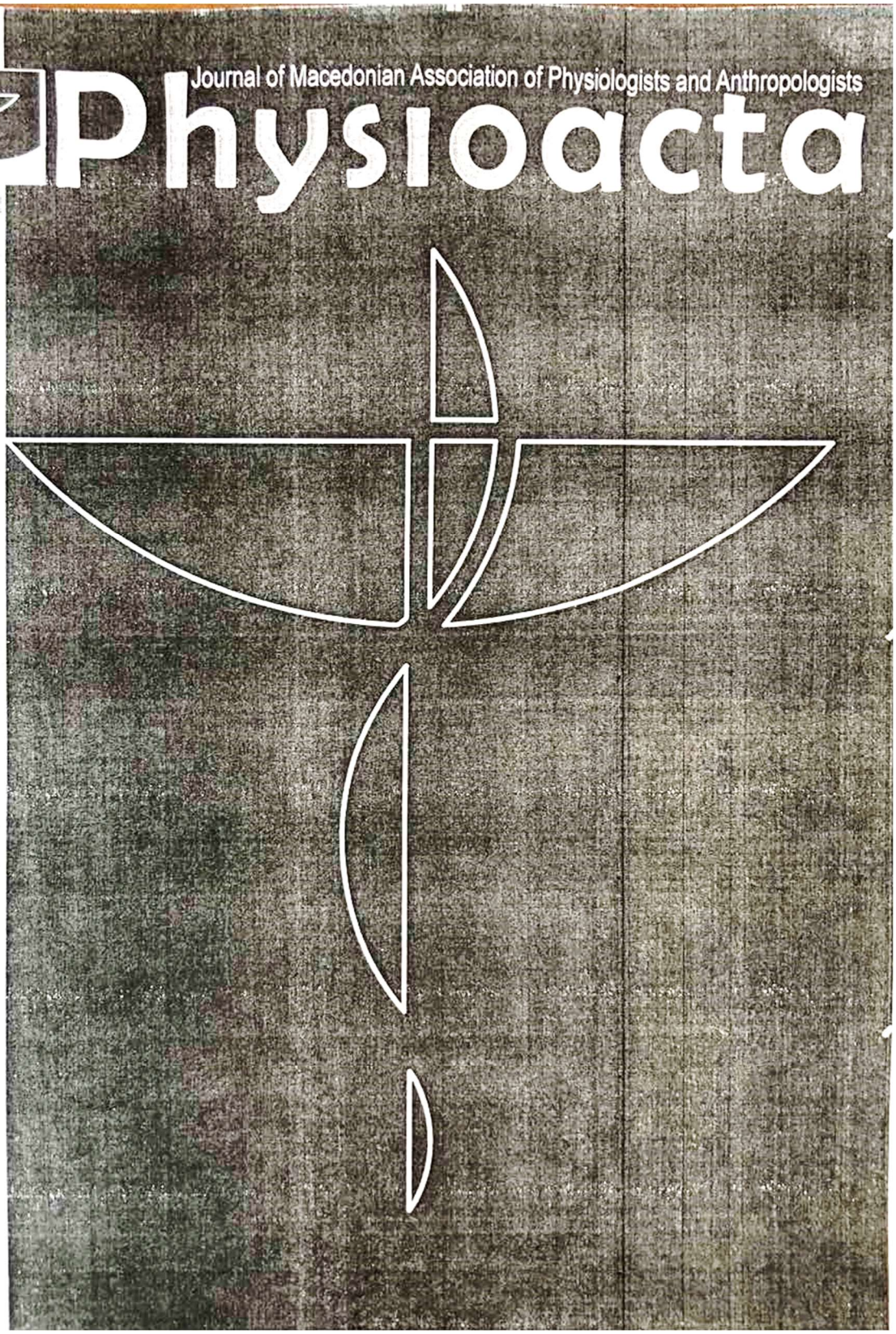
Journal of Macedonian Association of Physiologists and Anthropologists

Physioacta

Vol. 12 - No. 2
2018



UDK :61 ISSN 1857-5587

PHYSIOACTA

Journal of Macedonian Association of Physiologists and Anthropologists

Vol 12 No 2
2018

Physioacta

Journal of Macedonian Association of Physiologists and Anthropologists

Publisher

Medical faculty, Ss Cyril and Methodius University Skopje, R. Macedonia

Book cover designer
Milkica Stefanovska

UDK: 616-056.7:612.751.1.015.3(497.7)

BONE MINERALIZATION DISORDERS IN PATIENTS WITH CYSTIC FIBROSIS IN REPUBLIC OF MACEDONIA

Spirevska L, Jakovska T, Fustik S, Zorcec T.

University Clinic of Pediatric Diseases Skopje

Abstract

Deterioration of mineral bone density (BMD) is common in patients with cystic fibrosis (CF). It is a result of several reasons, such as poor nutritional status, chronic inflammation, use of glucocorticoid therapy and others. The aim of the study was to determinate the prevalence of deterioration of mineral bone density in patients with CF by the method of absorption of X-ray dual-wavelength (dual-energy X-ray absorptiometry - DXA) and the impact of clinical factors age, nutritional status and severity of lung disease on its appearance. The study included 80 patients with CF aged 5 to 36 years who are treated at the University Clinic for Children's Diseases in Skopje. Patients with CF were divided into 3 age groups:pre-puberty, from 5-11 years, puberty and adolescence, 12-18 years, and adults 19-36 years. All patients underwent examination of bone mineral density by DXA of the lumbar spine and some clinical parameters (body weight and height) and functional lung tests (forced expiratory volume in the first second -FEV1 and forced vital capacity-FVC). Most CF patients (68.75%) had normal mineral density (BMD); 21.25% were with osteopenia and 10% had osteoporosis. Patients with CF, who have osteoporosis and osteopenia,had statistically significantly worse clinical parameters compared to those with normal BMD. Early detection of bone disease and prompt treatment is important in order to prevent fractures and other complications.

Keywords: cystic fibrosis, mineral bone density, osteoporosis

НАРУШУВАЊА В ОКОСКЕНАТА МИНЕРАЛИЗАЦИЈА КАЈ ПАЦИЕНТИТЕ СО ЦИСТИЧНА ФИБРОЗА ВО РЕПУБЛИКА МАКЕДОНИЈА

Апстракт

Нарушувањето на минералната коскена густина (bone mineral density - BMD) често се среќава кај пациентите со цистичнафиброза (ЦФ). Тоа е резултат на повеќе причини, како што се: лош нутритивен статус, хроничен воспалителен процес, употреба на гликокортикоидна терапија и др. Целта на истражувањето беше евалуација на преваленцијата на нарушувањата во коскената минерализација кај пациентите со ЦФ преку методата на апсорпција на X зраци со двојна бранова должина (dual-energy X-rayabsorptiometry - DXA) и влијанието на клиничките фактори возраст, нутритивенстатус и тежина на белодробната болест врз нејзиното појавување. Во студијата беа вклучени 80 пациенти со ЦФ од двата пола на возраст од 5 до 36 години кои се лекуваат на Универзитетската клиника за детски болести во Скопје. Пациентите со ЦФ беа поделени во 3 возрасни групи, и тоа: претпубертетски, од 5 до 11 години, пубертет и адолесценција, од 12 до 18 години, и возрасни, од 19 до 36 години. Кај сите пациенти беше испитувана минералната коскена густина со DXA на лумбалниот дел на 'рбетниот столб и клиничките параметри (телесна тежина и висина) и функционалните белодробни тестови (форсиран експираторен волумен во прва секунда- FEV1 и форсиран витален капацитет- FVC).

Најголем број од ЦФ пациентите (68,75%) имаа нормален минерален дензитет (BMD); 21,25% беа со остеопенија и 10% имаа остеопороза. Пациентите со ЦФ,кои имаат остеопороза и остеопенија, имаа статистички сигнификантно полоши клинички параметри во однос на испитаниците со нормален BMD. Важно е навремено откривање на коскената болест и навремена терапија со цел превенција на фрактури и други компликации.

Клучни зборови: цистична фиброза, минерална коскена густина, остеопороза

Introduction

Cystic fibrosis is the most common autosomal recessive hereditary disease in the white population (1). The disease is multisystem. Major manifestations are pancreatic insufficiency and severe pulmonary dysfunction with chronic inflammatory processes and bacterial superinfections (4).

Osteoporosis is a systemic disease of the skeletal system characterized by low bone mass and/or microarchitectural disorders of the bone tissue that increase bone fragility and risk of bone fractures (3). Osteoporosis is very common in patients with CF and can further exacerbate their health (1,6).

The bone loss in CF population begins at a young age and continues with aging. The prevalence of osteoporosis and osteopenia is higher in patients with severe lung disease, malnutrition patients, and in patients who are receiving glucocorticoid therapy (5). The most characteristic manifestations are kyphosis, as well as decreased bone mineral density of the thoracic and lumbar vertebrae of the spinal column resulting in an increased percentage of fractures and the impaired pulmonary and general condition of patients (2).

The World Health Organization (WHO) recommends measurement of the bone mineral density (BMD) by using Dual-energy X-ray absorptiometry (DXA) absorption technique (3). Mineral bone density is expressed in SD, and one SD denotes approximately 10% of bone mass.

Material and methods

The study included 80 patients with CF, 48 females and 32 males, aged 5-36, who are regularly controlled at the University Clinic of Pediatric Diseases in Skopje. All patients were with a previously confirmed diagnosis of CF with a positive potency test (chloride values in sweat above 60 mmol / l) and a genetic diagnosis for CF.

Patients with CF were divided into 3 age groups: pre-pubertal, 5 to 11 years old, puberty and adolescence, 12 to 18 years and adults, from 19 to 36 years old.

In all patients the mineral bone density was studied with DXA scanning with the Lunar DPX-NT + 130191 apparatus on the lumbar spinal column (L2-L4). The results were compared with the corresponding values in given software packages by gender and age. The results were expressed as Z score ($\triangle Z$), i.e. how many standard deviations deviate from normal BMD values determined by age and gender tables, and T score ($\triangle T$), i.e. how many standard deviations deviate from the maximum of the bone mass. According to WHO:

- Normal result - when BMD is not lower than -1 SD of the average for the younger adult population
- Osteopenia - when BMD is between -2 and -1 SD from the average for the younger adult population
- Osteoporosis - when BMD is lower than -2 SD from the average for the younger adult population.

Body weight and height were measured from the clinical parameters and body mass index (BMI) and functional lung tests (forced expiratory volume in the first second - FEV1 and forced vital capacity - FVC) were calculated.

Statistical analysis

In the statistical processing of the results, the methods of descriptive statistics were used: arithmetic mean, standard deviation, and percentages.

Student's t-test was used to test statistical differences between the two groups of patients and analysis of variance (ANOVA) for differences between multiple groups. The values of p <0.05 were statistically significant.

Results

The study included 80 patients, aged 5 to 36 years. In the group of patients with CF there were 48 male patients (60%) and 32 (40%) female patients. CF group was divided into the following groups by age: 35 (44%) were aged 5-11, 24 (30%) aged 12-18 years and 21 (26%) were over the age of 18 years.

Table 1 presents the mean values of bone mineralization in patients with CF by age groups. In all age groups, CF patients had a decreased bone mineral density. We did not find a statistically significant difference between different age groups.

Table 1 Average values of mineral bone density in different age groups

	CF patients			p between the groups		
	5-11 age	12-18 age	Above18 age	5-11/ 12-18	5-11/ above 18	12-18/ above18
BMD Z/T score	-0.2 ±1.06	-0.7 ±0.9	-0.6 ± 1	NS	NS	NS

Osteopenia (Z / T <-1SD) was found in 22.25% of CF patients, and osteoporosis (Z / T <-2SD) was found in 10% of CF patients.

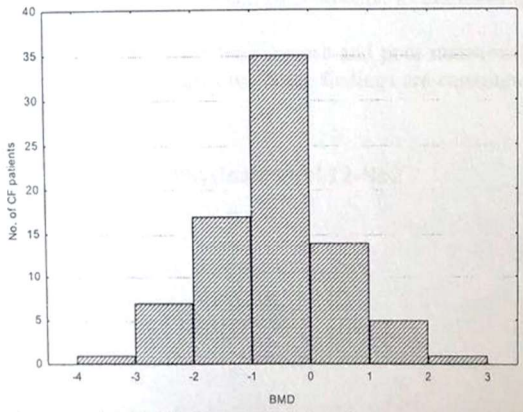


Figure 1 Distribution of DXA Z / T score in CF patients

Table 2 Distribution of DXA Z / T score in CF patients

Table 2. Distribution, mean and frequency of CF patients in relation to bone mineral metabolism

	Normal BMD	Osteopenia	Osteoporosis
Total	55	17	8
Average value	13.4±6.54	16.29±7.6	15.62±7.44
BMD Z/T score	0.05±0.73	-1.21±0.23	-2.48±0.35

Most CF patients (68.75%) had normal mineral density (BMD), 21.25% were with osteopenia, and 10% had osteoporosis (Table 2). A total of 31.25% of CF patients in this study were with reduced BMD.

Table 3 presents the mean values of some clinical parameters in CF patients depending on bone densities.

Table 3 Mean values of several clinical parameters depending on BMD

	Normal BMD	Osteopenia	Osteoporosis
BMI	20.48±24.32	19.27±2.65	17.97±2.92
FEV1	89.78±24.32	78.61±21.22	69.62±24.92
FVC	97.59±17.16	86.28±18.21	73.45±23.22

Patients with CF in the osteoporosis group had significantly lower BMI compared to subjects in the other groups ($p < 0.05$). The clinical parameters represented by pulmonary functional tests were significantly lower than those in the normal bone density group ($p < 0.01$) and significantly lower than those in the osteopenia group ($p < 0.05$).

Discussion

The introduction of modern therapy and medical management prolong the mean survival rate of people with CF from childhood to middle adulthood. The occurrence of osteoporosis is one of the complications of prolonged survival. Osteoporosis is a metabolic bone disease characterized by a decreased bone mass and a disorder of the microarchitecture of the bone, with a subsequent increase in bone fragility and an increased risk of fractures. The incidence of osteoporosis in CF patients in the world is about 30% (7).

In our study, the prevalence of bone disease among CP patients was 31.25%. Etiology is multifactorial, including poor nutritional status, repetitive respiratory infections, chronic lung inflammation, frequent use of glucocorticoids, hormonal imbalance, insufficient vitamin D intake, decreased physical activity, etc.

The purpose of this prospective study was to determine the incidence of osteopenia and osteoporosis in patients with CF who visit the Center for CF at the University Clinic for Pediatric Diseases in Skopje.

The mean BMD Z / T score of all CF patients was -0.5 SD, which showed that patients with CF had reduced mineral density. Osteopenia (Z / T score <-1SD) was found in 21.25% of CF patients, and 10% of CF patients had osteoporosis (Z / T score <-2SD). The prevalence of decreased bone density (osteopenia and osteoporosis) in the investigated CF group was 31.25%.

We showed that patients with severe lung disease and poor nutritional status had a worse BMD status, or a decreased bone density. These findings are consistent with more than 50

studies that have seen decreased bone mass and fractures in patients with CF. The prevalence of osteopenia may be up to 85% in the advanced phase of the CF (169). Several studies have shown that prevalence of bone disease increases with increasing severity of pulmonary disease and malnutrition (8,9,10,11,12,13,14,15).

DXA scans showed a reduced bone density in all age groups. The incidence of bone disease in the CF population was 31.25%. Ten percent of them had osteoporosis.

Conclusion

Preventive measures have a great importance in reducing the complications of bone disease. Maintaining good nutritional status, adequate pulmonary function control, maintenance of serum vitamin D levels above 30 ng/ml, regular physical activity is part of the measures that can help prevent bone disease in patients with CF. Early screening for bone disease with DXA can detect bone mineralization disorders and treatment with calcium and vitamin D in the recommended doses, and use of bisphosphonates in adults.

References

1. Aris RM, Merkel PA, Bachrach LK, et al. Guide to bone health and disease in cystic fibrosis. J ClinEndocrinolMetab. 2005;90:1888–96.European cystic fibrosis bone mineralization guidelines. Sermet-Gaudelusa I,
2. Bianchib ML, Garabedianc M, Arisd RM. JCystic Fibrosis. 2011;10(Suppl 2): S16–S23.
3. WHO. Scientific group on the prevention and management of osteoporosis. Prevention and management of osteoporosis: report of a WHO scientific group; 2008.
4. Riordan JR. CFTR function and prospects for therapy. Ann Rev Biochem. 2008;77:701–26.
5. Paccou J, Zeboulon N, Combescure C, et al. The prevalence of osteoporosis, osteopenia and fractures among adults with cystic fibrosis: a systematic literature review with meta-analysis. Calcif Tissue Int. 2010;86:1–7.
6. Sood M, Hambleton G, Super M, et al. Bone status in cystic fibrosis. Arch Dis Child. 2001;84:516-20.
7. Sood M, Hambleton G, Super M, et al. Bone status in cystic fibrosis. Arch Dis Child. 2001;84:516-20.
8. Aris RM, Ontjes DA, Buell HE, et al. Abnormal bone turnover in cystic fibrosis adults. Osteoporos Int. 2002;13:151–7.
9. Henderson RC, Madsen CD. Bone density in children and adolescents with cystic fibrosis. JPediatr. 1996;128:28–34.
10. Haworth CS, Webb AK, Egan JJ, et al. Bone histomorphometry in adult patients with cystic fibrosis. Chest. 2000;118:434–9.
11. Elkin SL, Vedi S, Bord S, et al. Histomorphometric analysis of bone biopsies from the iliac crest of adults with cystic fibrosis. Am J RespirCrit Care Med.2002;166:1470–4.
12. Papaioannou A, KennedyCC, Freitag A, et al. Alendronate once weekly for the prevention and treatment of bone loss in Canadian adult cystic fibrosis patients (CFOS Trial). Chest. 2008;134:794–800.
13. Bianchi ML, Romano G, Saraifoger S, et al. BMD and body composition in children and young patients affected by cystic fibrosis. J Bone Miner Res. 2006;21:388–96.
14. Gronowitz E, Garemo M, Lindblad A, Mellstrom D,Strandvik B. Decreased bone mineral density in normal growing patients with cystic fibrosis. ActaPaediatr. 2003;92:688–693.

15. Smith N, Lim A, Yap M, King L, James S, Jones A, Ranganathan S, Simm P. Bone mineral density is related to lung function outcomes in young people with cystic fibrosis-A retrospective study.PediatrPulmonol. 2017;52(12):1558-1564.
16. Sharma S, Jaksic M, Fenwick S, Byrnes C, Cundy T. Accrual of Bone Mass in Children and Adolescents with Cystic Fibrosis.J ClinEndocrinolMetab. 2017;102(5):1734-1739.