PECULIARITIES OF OSTEOPOROSIS IN COPD PATIENTS

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ABSTRACT — The high incidence of osteoporosis in patients with chronic obstructive pulmonary disease (COPD) explains relevance of our study. 79 women (overage age 66,9 ± 1,7 years) with postmenopausal osteoporosis without steroid treatment have been examined in order to identify peculiarities of osteoporosis in female population with COPD. Our Results showed that COPD patients demonstrate significantly lower values of FEV1, forearm BMD, forearm T-score and significantly more frequent forearm fractures to be compared with patients without obstructive lung disease and with bronchial asthma. Conclusions: Patients with COPD demonstrate more severe course of postmenopausal osteoporosis.

KEYWORDS — COPD, Osteoporosis, FRAX, fractures, T-score.

INTRODUCTION

The Chronic Obstructive Pulmonary Disease (COPD) is socially significant pathology and according to WHO data takes the 4th place in structure of mortality [1]. According to the BOLD study prevalence of GOLD II and more severe stages (GOLD III, IV) of COPD among persons senior than 40 years is approximately 10,1±4,8% in whole groop; 11,8±7,9% — for men and 8,5±5,8% — for women [3]. According to the GARD study [4, 5] conducted in Russia high prevalence of chronic respiratory diseases was revealed. The spirometric research data showed that 21,8% of respondents corresponded to COPD criteria. The extrapolation of these data on the general population showed that expected amount of patients with spirometric criteria of COPD must be approximately 15,3% of the Russian population, or 21 986 100 people, more than 9,3 times higher than official statistical data (2 355 275,6 people) [6]. The definition of COPD in the GOLD 2015 document tells that "COPD is a common preventable and treatable disease, which is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients"[2]. In addition to respiratory tract pathology, systemic effects of COPD due to systemic inflammation [9] with great

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role of cytokines (such as FNO-α, IL-1β and IL-6) [10, 11, 12] are described. Cachexia with loss of fat mass, hypotrophy and atrophy of skeletal muscles, depression, anemia, the increased risk of development of cardiovascular diseases, and osteoporosis are among the large number of comorbidities due to systemic inflamation [7, 8]. The World Health Organization in 1994 recognized osteoporosis (OP) "as general metabolic disease for which decrease in density of bone, the disturbance of its microarchitecture leading to increase of risk of fractures" [1]. The Russian epidemiological researches have shown that in age of 50 years and more osteoporosis is observed in 30–33% women and 22–24% men that makes more than 10 million people [14]. Frequency of osteoporosis (OP) in COPD patients in 2014 is 28–34%, according to official data of the Russian Respiratory Society [13]. Spontaneous, and also low-traumatic fractures define the medical social importance of OP. The femoral neck fractures have the greatest medical and social importance due to high invalidisation and mortality of patients. Frequency of femoral neck fractures in Russia in persons over 50 years and more has averaged 105,9 on 100 000 population, and is more often in women — 122,5, then in men — 78,8. The frequency of forearm fractures is observed more often in women population (563 on 100 000 people), than at men (426 on 100 000 population) too. Average values of mortality in Russia is 30–35%. 78% of the survived patients in year after fracture and 65,5% patients in two years after fracture needs permanent third-party assistance [15, 16]. There is increase of new cases of OP and osteopenia in process of pulmonary diseases progression [19, 20]. OP frequency was especially high at patients with end-stage of different chronic pulmonary diseases, including COPD, to be the candidates for lung transplantation [21]. Some authors speak about natural to "age comorbidity" of COPD and OP [17, 18].

THE MAIN AIM

of our work was to determine the osteoporosis peculiarities in elder women with obstructive lung diseases.

MATERIALS AND METHODS

We have examined 79 women with post-menopausal osteoporosis with middle age of 66,9±1,7 years. All women did not use oral glucocorticoid therapy. All patients under examination have been divided into 3 groups. 31 non-smoking women with the bronchial asthma (BA) with middle age of 65,9 ±2 years formed the first group. The second group included 23 smoking patients with COPD with middle age of 67,7±2,3 years. The average experience of smoking was approximately 14±2,2 packs/years. All patients of the first and second groups received inhaled glucocorticoids in daily dose of 1000 mkg (beclomethasone). The third group included 25 women without lung disease and smoking experience. The complex lung function examination including spirometry (MasterScreen spirograph) with the reversibility test, osteodensitometry(DXA) on the densitometer Lunar Prodigy General Electric (GE Healthcare) with assessment of bone mineral density(BMD) and T-score in femoral neck, lumbar spine and forearm, risks of law-traumatic fractures during 10 years with use of FRAX®, the tool to assessment risk of fractures developed by WHO (https://www.shef.ac.uk/FRAX/index.aspx), has been defined to all patients.

STATISTICAL ANALYSES

was carried out with IBM SPSS V.19.0 program (USA). Comparison of groups was done by means of the nonparametric Mann-Whitney test for quantitative variables and the Chi-square — for categorial signs. Pearson coefficient was used for carrying out the correlation analysis. Statistically significant we considered distinctions at $p < 0,05$.

RESULTS

The main characteristics of the studied parameters are provided in Table 1. Patients with COPD had a significantly lower value of FEV1, forearm BMI, T-score in forearm ($p \leq 0,05$) then patients with bronchial asthma and without lung disease. Fractures have been met more often in COPD patient to be compared with patients with BA. No significant distinctions in bone density indicators were found between patients with BA and subjects without lung diseases. However tendency for more frequent cases of fractures in BA patients was found due to values of BMD.

Table 1 and figure 1 show that FEV1, forearm BMD, T-score of forearm were significant lower in COPD patients to be compared with bronchial asthma patients and women without lung disease ($p \leq 0,05$). The greatest frequency of forearm and vertebral fractures were also observed in COPD patients.

The major osteoporotic and hip fractures risk assessment during 10 years in investigate group of patients are provided in table 2 and diagram 2.

As can be seen from table 2 and diagram 2 hip the major osteoporotic and hip fractures risk assessment during 10 years were higher in patients with obstructive lung diseases. The 10 years hip fractures risk was statistically significantly higher in COPD patients.

Results of the correlation analysis using Pearson's criteria between spirometry (pre-FEV1 and post-FEV1) and densitometry indexes in patients with obstructive lung diseases and in control group are provided in table 3.

Table 1. *The main indicators of BMD, T-score and obstruction level in patients of the different groups. (n± standard deviation)*

Group/ title	n	the average age	FEV1 %	Forearm BMD	Forearm T-score	Forearm fractures frequency (%)	Vertebral fractures frequency (%)
1 (Bronchial Asthma)	31	65,9±2,0	76,8±3,9	0,63±0,02	-2,80±0,17	51,6	19,3
2 (COPD)	23	67,7±2,3	57,1±3,6[1]	0,57±0,02[1]	-3,37±0,18[1]	65,2	34,8
3 (Without lung disease)	25	67,5±2,0	92,9±1,5[2,3]	0,63±0,02[2]	-2,67±0,2[2]	44,0	16,0

1 — p<0,05 in comparison of group 1 and 2
2 — p<0,05 in comparison of group 2 and 3
3 — p<0,05 in comparison of group 1 and 3

Table 2. *FRAX indicators in groups, n± standard deviation*

Group/title	n	10-year probability of a major osteoporotic fracture (FRAX)®	10-year probability of hip fracture(FRAX)®
1 (Bronchial Asthma)	31	20,47± 1,102	5, 216± 0,7271
2 (COPD)	23	21,74± 1,1582	7,909± 0,73134
3 (Without lung disease)	25	16, 47± 1,0763	4, 264± 0,7159

1 — p≤0,05 in comparison of group 1 and 2
2 — p≤0,05 in comparison of group 2 and 3
3 — p≤0,05 in comparison of group 1 and 3
4 — p≤0,05 in comparison of group 2 and 3

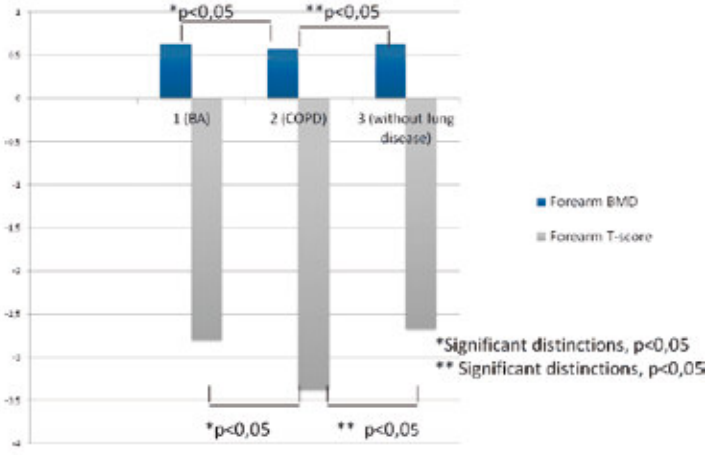

Figure 1. The mean value of BMD, T-score in patients with COPD and BA compared with control group without obstructive pathology.

Fig. 1. *The mean value of BMD, T-score in patients with COPD and BA compared with control group without obstructive pathology.*

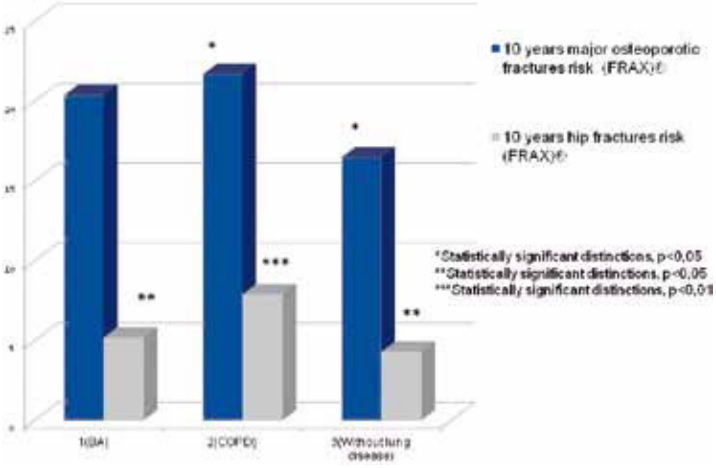

Figure 2. *10 years fractures risk in different groups (n± standard deviation)*

As can be seen from table 3, statistically reliable positive correlation between FEV1 values and densitometry data in patients with obstructive lung diseases (both BA and COPD) were revealed. Patients with COPD has greater number of this correlations. Statistically reliable correlations between FEV1 values and densitometry data in patients without lung diseases has not been revealed.

DISCUSSION AND CONCLUSIONS

The course of OP in COPD patients has certain peculiarities. OP proceeds with higher loss of bone mass compared to patients without COPD, often complicated with bones fractures. Our data demonstrate more severe duration of osteoporosis

Table 3. *The results of correlation analyses of spirometry and of densitometry indexes in different groups of patients.*

	Group/Title	1(Bronchial Asthma)	2(COPD)	3(Without lung disease)
Pre-FEV1 %	Femoral neck BMD	p>0,05	p<0,01 R= 0,611**	p>0,05
	Femoral neck T-score	p>0,05	p<0,01 R= 0,643**	p>0,05
	Forearm T-score	p<0,05 R= 0,413*	p<0,01 R= 0,546**	p>0,05
	Forearm BMD	p<0,01 R=0,457**	p<0,05 R= 0,418*	p>0,05
Post-FEV1 %	Femoral neck BMD	p>0,05	p<0,05 R= 0,452*	p>0,05
	Femoral neck T-score	p>0,05	p<0,05 R=0,489*	p>0,05
	Forearm T-score	p>0,05	p<0,05 R=0,389*	p>0,05
	Forearm BMD	p<0,01 R= 0,427**	p>0,05	p>0,05

** statistically reliable with p <0,05*
*** statistically reliable with p <0,01*

in COPD patients in comparison to BA patients and patients without lung diseases. It is confirmed by authentically significant decrease in values of BMI and T-score of forearm, statistically reliable increase in 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) and hip fractures (FRAX) at these patients. The main role of disturbances in bone metabolism in COPD patients is most probably related with smoking status and systemic inflammation. No differences in course of OP between BA and control group suggests minimal impact of allergic inflammation and inhaled glucocorticosteroid therapy on bone metabolism.

The conflicts of interests are absent.

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