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PREVALENCE AND CORRELATES OF LOW BONE MINERAL DENSITY AND OSTEOPOROSIS DURING CHRONIC OBSTRUCTIVE PULMONARY DISEASE DEVELOPMENT IN MALE PATIENTS

Summary
The article presents the results of study of the prevalence of osteoporosis (OPS) in male chronic obstructive pulmonary disease (COPD) patients as well as the relationship between OPS and the markers of bone metabolism, body composition and systemic inflammation in relation to COPD severity.
Decreased total bone mineral density (BMD) was detected in 67% of cases in general COPD group, while OPS was observed in 22% of cases with the prevalence of decreased BMD in lumbar spine. We found a significant increase in the proportion of patients with OPS during COPD development: none of $COPD_1$ patients had OPS, while in $COPD_{2,3}$ it was identified in 13% and 64% of patients respectively. Also it was shown that the low body mass index (BMI), lean mass index (LMI), bone mineral component index (BMCI) and the forced expiratory volume in 1 second levels were the significant contributors to BMD decrease in advanced COPD.
Thereby screen for OPS in $COPD_{2,3}$ male patients over 50 years, especially in those having a low BMI, LMI and BMCI is required.

Keywords
Chronic obstructive pulmonary disease, osteoporosis, inflammation, osteocalcin, β-crossLaps.

Osteoporosis (OPS) is a serious health problem for men with advanced chronic obstructive pulmonary disease (COPD). Among the extra-pulmonary effects of COPD secondary OPS development as a consequence of a loss of bone mineral density (BMD) have been widely recognized as the major comorbidity [21]. It was shown that COPD patients had significantly lower BMD than in normal population. The prevalence of OPS varies from 40 to 60% in COPD and it is 2-5 fold higher than that detectable in age-matched healthy subjects [4, 20, 26].

The pathophysiological link between COPD in male patients and low BMD and OPS has not been well understood in contrast to woman, although there is a definite association between COPD severity and low BMD [12]. Thus, a high Jaccard coefficient between OPS and COPD was detected [19]. The etiology of bone loss in COPD includes a multiple key determinants: older age, severe stage of disease, hypoxia, long-term therapy with systemic corticosteroids (sCS), chronic systemic inflammation, smoking, physical inactivity, vitamin D deficiency, hypogonadism, low body mass index (BMI) and lean mass index (LMI) [16, 22, 25]. The combination of these risk factors in the same patient may significantly increase the risk of OPS and these factors may deteriorate with COPD exacerbation [1, 2].

sCS and inhaled corticosteroids CS (ICS) are used as an evidence-base treatment of COPD acute exacerbations despite their negative effects on BMD. sSC action is similar to systemic inflammatory reaction in COPD and plays a significant role in bone resorption [16]. However, CS use does not full account for the low BMD and high prevalence of OPS in COPD. Thus, the significant loss of BMD may occur even in mild airway obstruction [3]. The majority of researches no found evidences of ICS effect at moderate dose on BMD loss, significant changes in osteocalcin level and a high prevalence of OPS in COPD patients [10, 27]. Probably, underlying COPD severity is more important in the etiology of reduced BMD in COPD patients, than chronic use ICS.

Advanced COPD patients had usually a lowered BMI, LMI, muscle strength and physical activity in addition to low BMD that favor OPS development [14, 23]. Hypodynamia also stipulates lower exposure to sunlight, which is one of the reasons for frequent vitamin D deficiency in severe COPD patients [8, 9, 24]. Additionally, smoking may directly or indirectly in-

duce a significant disorders the metabolism of bone tissue. BMD status is also substantially determined by the blood concentration of the phosphorus, parathyroid hormone (PTH), total and ionized calcium. These markers are used only for evaluation of bone turnover rate and the disorders of bone formation, but not for the diagnosis of OSP. The **main purpose** of this study was to evaluate the prevalence of OPS in male COPD patients as well as the relationship between OPS and the markers of bone metabolism, body composition and systemic inflammation in relation to COPD severity.

Material and methods

The study was undertaken at the Pulmonology Department of the 10th Minsk City Clinical Hospital. All participants gave their written informed consent. The study protocol was approved by the Human Studies Committee on Research Ethics at the Belarusian State Medical University. The inclusion criteria were the following: males aged 40-68 years with different COPD grades and FEV_1 increase <15% after bronchodilator tests were qualified for the study. We excluded the patients with a secondary causes of OPS such as: significant uncontrolled co-morbidities (cardiovascular or oncologic diseases; diabetes mellitus; untreated thyroid dysfunction; severe chronic hepatic or renal failure); history of fracture within the past year; alcoholic abuse (>400 g/week); maintenance treatment with sCS more than 4 consecutive weeks in dose >5 mg/day of prednisolone and the use of other drugs that may significantly affect bone and calcium metabolism.

The study group consisted of 92 patients (aged 40-67 years) with acute exacerbation of COPD who were divided on the GOLD guidelines (2011) into three groups according to severity of disease (mild — $COPD_1$; moderate — $COPD_2$ and severe — $COPD_3$) using FEV_1 post-bronchodilator test and clinical symptoms. The clinical investigation of these patients included: number of acute exacerbations for last year, self-reported co-morbidities and previous treatment, one-time respiratory spirometry on the 1st day at admission with the evaluation post-bronchodilator parameters (computerized portable spirometer «Spirovit SP-10» of «Shiller»), physical activities of daily living, physical examination, day-time pulseoximetry (psO_2), chest radiography and blood laboratory analyses. These patients did not complain of a pain syndrome in the spine and other bones nor did they inform us about their previous peripheral fractures or the ones in their next of kin.

$COPD_1$ patients had never used ICS or sCS. Only 34% and 46% of $COPD_{2,3}$ patients respectively had the past history of chronic ICS use in moderate doses of (usually 200-400 mcg/day in terms of bydesonide), mostly with never prescribed sCS. There were only two patients from $COPD_3$ group who had a two-four short ambulatory courses (<1 week in duration) of oral prednisolone (<20 mg/day) during period of acute exacerbation for the last year. The patients (mostly $COPD_{2-3}$) were treated in hospital with a combination of inhaled long-acting anticholinergic (rare β_2-agonists) plus ICS and sCS (5 days of dexametasone intravenously, 4 mg a day) according to an indications as well as broad spectrum antibiotics if there was clinical evidence of bacterial exacerbation. The control group consisted of 27 healthy male persons of comparable age, smoking status and BMI.

These patients and healthy males were one-time examined by dual-energy X-ray absorptiometry (DXA) («Prodigy Lunar» of General Electric Medical Systems, USA) with using the extensive reference base. Bone mineral density (BMD) was assessed by T- and Z-scores (criteria) according to the recommendation of International Society of Clinical Densitometry, while diagnosis of OPS was defined according to WHO criteria (1994) that was based on the quantitative evaluation of BMD as defining factor of bone strength. T-score was calculated in males by measuring the number of standard deviations higher and below the mean parameter of BMD in adults according to the NHANES III regulatory reference base. The Z-criterion in males under 50 years was used because in this group the diagnosis of osteoporosis could not have been made only by BMD data. Z-score was determined within expected parameters for the age group. Z-score <-2,0 was assessed as below the expected data for the age and testified the presence of a secondary cause of bone loss. We detected BMD, T- and Z-scores in lumbar spine (at the level of L_{1-4}) and femoral neck (FN). OPS was considered in males over 50 years by T-score <-2,5 whereas osteopenia was defined by T-score between -1,0 and -2,5, while the norm was accepted at the T-score >-1,0. Additionally, we calculated LMI and bone mineral component index (BMCI).

The level of total calcium and nonorganic phosphorus was detected by the biochemical analyzer «Hitachi 911» of Hoffman-La-Roch, while the concentration of ionizing calcium was assessed by ion-selective method on the analyzer of electrolytes «AVL-9880» of Hoffman-La-Roch. The levels of β-crossLaps (as a marker of bone resorption), osteocalcin (as a marker of bone formation) and PTH were detected by the analyzer «Modular E-170» with using the diagnostic kits of Roche Diagnostics. The following reference parameters for male were accepted: β-crossLaps from 0,16 to 0,44 ng/ml for patients under 50 years and from 0,10 to 0,50 ng/ml for those aged 50-70 years; osteocalcin from 14 to 42 ng/ml for 30-50 year-old patients and from 14 to 46 ng/ml for 50-70 year-old ones. TNF-α and free testosterone levels were detected by immynoenzyme methods.

The statistical analysis was performed using Statistica 8.0 software (2007, Statsoft Inc., USA). The

preliminary analysis of the variables under consideration was a Shapiro-Wilk test of correspondence to normal distribution. The results of the analysis were shown as median and interquartile range (25-75%) because all the parameters differed from normal distribution. The comparison of non-parametric parameters in two independent groups was carried out using a Mann-Whitney test. While in three or more independent groups it was performed using the Kruskal-Wallis rank sum test. Fisher's exact test was used to detect statistically significant differences between independent groups according to the frequency characteristic of the investigated parameter. Spearman's rank correlation coefficient (r_s) was used to describe the relationship between the two quantitative variables that differed from normal distribution. The level of statistical significance was set at p<0,05.

Table 1. Baseline characteristics of the control group and COPD groups according to different degrees of airflow limitation severity (GOLD spirometry level, 2011) on admission (Me; 25%, 75%)

Parameters	Control (n=27)	$COPD_1$ (n=23)	$COPD_2$ (n=47)	$COPD_3$ (n=22)
Age (years) <60/>60 years (%)	52 (47; 55) 72/28	54 (48; 58) 78/22	56 (52; 60)* 64/36	62 (56; 67)*,^,# 52/48
Body composition: BMI (kg/m^2)	28,3 (27,5; 29,1)	29,2 (26,8; 32,5)	29,5 (26,4; 32,2)	23,9 (20,7; 32,1)*,^,#
FFMI (kg/m^2)	20,6 (19,9; 22,0)	20,2 (20,0; 21,4)	19,9 (18,6; 21,2)	17,6 (16,4; 18,8)*,^,#
BMCI (kg/m^2)	1,1 (0,9; 1,2)	1,0 (0,9; 1,1)	1,0 (0,9; 1,1)	0,9 (0,8; 0,9)*,^,#
Smoking history: present smokers (%)	60	62	77	96*,^
packs/years index	18 (10; 30)	26 (12; 40)	24 (12; 36)	30 (25; 40)*,#
Median duration of COPD (years)	-	4 (2; 6)	9 (4; 12)	13 (10; 17)^,#
Number of exacerbations in the last year	-	1 (0,2; 2)	2 (1; 3)	3 (2; 5)^,#
FVC (% pred.)	100 (98; 111)	85 (75; 90)*	55 (48; 66)*,^	38 (28; 46)*,^,#
FEV_1 (% pred.)	86 (77; 94)	81 (75; 87)*	55 (50; 64)*,^	33 (22; 44)*,^,#
FEV_1/FVC (%)	95 (89; 105)	70 (66; 71)*	64 (57; 68)*,^	51 (39; 57)*,^,#
psO_2 (%)	97 (96; 97)	97 (96; 97)	96 (95; 98)	93 (90; 95)*,^,#
MRC index dyspnea (score)	-	0 (0; 1)	2 (1; 3)	3 (2; 3)^,#
C-reactive protein (mg/dL)	0,4 (0,1; 2,0)	0,5 (0,1; 1,3)	4,3 (1,9; 6,3)*,^	4,2 (1,3; 5,7)*,^
TNF-α (ng/ml)	8,6 (6,3; 12,0)	10,2 (4,9; 21,0)	13,8 (10,1; 23,2)*,^	14,7 (10,0; 71,4)*,^
Home treatment (%): ICS; intermittently sCS; with inhaled long acting anticholinergic; with inhaled long acting β_2-agonists	 - - - -	 - - - -	 34 - 22 2	 46 9# 8 18#

** — p<0,05 vs. the control group; ^ — p<0,05 vs. $COPD_1$; # — p<0,05 vs. $COPD_2$ group.*

Table 2. Dynamics of BMD, T- and Z-scores during COPD development (Me; 25%, 75%)

Parameter	Control group (n=27)	$COPD_I$ (n=23)	$COPD_2$ (n=47)	$COPD_3$ (n=22)
Total BMD (g/cm^2)	1,27 (1,21; 1,37)	1,24 (1,19; 1,30)	1,23 (1,15; 1,25)*	1,09 (1,04; 1,19)*,^,#
BMD in L_{1-4} (g/cm^2)	1,24 (1,18; 1,35)	1,17 (1,05; 1,22)*	1,11 (1,00; 1,21)*	0,98 (0,88; 1,10)*,^,#
BMD in FN (g/cm^2)	0,99 (0,95; 1,05)	0,96 (0,93; 1,05)	0,91 (0,84; 1,00)*,^	0,79 (0,75; 0,88)*,^,#
T-score in L_{1-4}	0,10 (-0,40; 1,00)	-0,5 (-1,5; -0,1)*	-1,0 (-1,9; -0,2)*	-2,1 (-2,9; -1,1)*,^,#
Z-score in L_1-L_4	0,10 (-0,60; 1,00)	-0,7 (-1,2; -0,2)*	-1,1 (-1,9; -0,4)*	-1,7 (-2,2; -0,7)*,^,#
T-score in FN	-0,60 (-0,90; -0,20)	-0,80 (-1,1; -0,1)	-1,2 (-1,8; -0,5)*,^	-2,1 (-2,5; -1,4)*,^,#
Z-score in FN	0,10 (-0,30; 0,30)	-0,20 (-0,8; 0,3)	-0,6 (-0,9; -0,2)*,^	-1,1 (-1,4; -0,5)*,^,#

** — p<0,05 vs. the control group; ^ — p<0,05 vs. $COPD_1$; # — p<0,05 vs. $COPD_2$ group.*

Results

The patients' characteristics are presented in Table 1. The control group did not differ from $COPD_1$ patients in terms of median age, body composition, intensity of smoking and the level of physical activity. Compared with the controls, $COPD_1$ patients had only decreased ventilation parameters, while $COPD_3$ patients had a significantly higher median age, disease duration, number of current smokers than in the control group and $COPD_{1,2}$ patients. Whereas median BMI, LMI, BMCI and parameters of spirometry in $COPD_3$ group was significantly lower than in $COPD_{1-2}$ groups. The index of dyspnea was progressively increased during COPD development that indicated a decrease in patient's physical activity. A significant increase in the number of exacerbations for the past year was found in $COPD_3$ compared with $COPD_{1,2}$. A higher CRP level and TNF-α in $COPD_{2,3}$ patients (p<0,05 vs. the control and $COPD_1$) reflected intensification of existing a low-grade systemic inflammation.

The levels of total BMD in the general COPD group (n=92) as well as BMD at L_{1-4} and FN were significantly decreased by 5%, 11% and 7% respectively vs. the control. T-Z-scores at L_{1-4} and FN were similarly changed. Thus, T-score was significantly decreased at L_{1-4} and FN by 10 and 2 times respectively vs. the control group.

As seen in Table 2, the level of total BMD was significantly decreased in $COPD_{2,3}$ compared with the control (by 4% and 14% respectively). A similar picture was observed concerning the changes of BMD at L_{1-4} and FN as well as T- and Z-scores. The prevalence of a low BMD was more detected in $COPD_3$ with concomitant low BMI, LMI and BMCI. There were no significant differences of BMD and Z-score at L_{1-4} and FN between the mixed subgroup of COPD male patients (aged from 40 to 50 years) and the comparable control group despite the presence of the patients with $COPD_{2,3}$ (6 and 1 patients respectively).

OPS was identified in 22% of cases in the general COPD group. We found a significant increase in the proportion of patients with OPS during COPD development (Fig.). Thus, none of $COPD_1$ patients

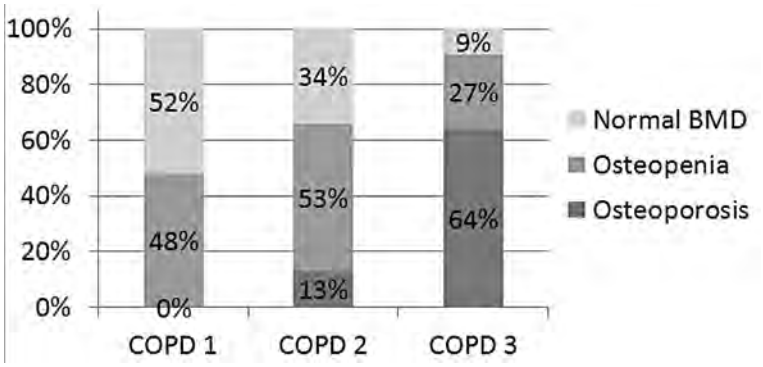

Figure. Dynamics the share of osteopenia and osteoporosis during COPD development

had OPS, while in $COPD_{2,3}$ it was identified in 13 and 64% of patients respectively (χ_2=18,8; p<0,05). Additionally, the number of patients with normal BMD value was significantly decreased during COPD progression (from 52% in $COPD_1$ to 9% in $COPD_3$). OPS was revealed at L_{1-4} and FN in 16% and 8% of cases respectively in the general COPD group, while OPS was more frequently detected at L_{1-4} than at FN (χ_2= 4,51; p<0,05).

The share of patients with the prevalence of OPS at L_{1-4} was progressively increased in $COPD_{1,2,3}$ groups and made up 0%, 11% and 50% respectively (p<0,05 between $COPD_2$ and $COPD_3$). The share of patients with the normal BMD at FN was decreased during COPD development from 65% in $COPD_1$ to 18% in $COPD_3$ (p<0,05). So, the number of COPD patients with OPS at FN was significantly increased in $COPD_{1,2,3}$ groups and made up 0%, 4%, 27% respectively (p<0,05 vs. $COPD_{1,2}$).

Median BMI level made up 29,9 kg/m^2 in osteopenic patients (n=42) from the general group, among whom $COPD_2$ patients dominated. Only 19% of these patients had a normal BMI level, whereas it exceeded the normal value in most of them (81%; χ_2=32, p<0,05). Median BMI level was decreased (to 22,7 kg/m^2) in patients with OPS (n=20), among whom $COPD_3$ patients dominated. Thus, BMI was significantly lower in osteoporotic COPD patients compared with osteopenic ones.

As seen from Table 3, the levels of total calcium and phosphorus did not differ in the study COPD groups from the control, while the level of ionizing calcium was significantly lower than in the control value, particularly in $COPD_{2-3}$ groups (p<0,05 vs. $COPD_1$). TNF-α level was increased by 18%, 60% and 70% in $COPD_{1,2,3}$ groups respectively compared with the control (p<0,05 for $COPD_{2,3}$). Free testosterone level was significantly decreased during COPD development. Concentration of osteocalcin and PTH was decreased in these groups compared with the control (p<0,05), while the level of β-crossLaps was significantly increased in $COPD_{2,3}$ groups vs. the control and $COPD_1$. A qualitative analysis showed that the level of β-crossLaps was within the normal range in most of the cases, while it was increased only in 6% of cases in $COPD_1$ and several frequently in $COPD_{2,3}$. The level of osteocalcin was decreased in 33, 45 and 47% of cases in $COPD_{1,2,3}$ groups respectively (p>0,05 between these groups).

Discussion

Two facts clearly emerge from our study: the high prevalence of OPS (both in terms of BMD total and T-score) in male $COPD_{2,3}$ patients and the strong relation between the presence of COPD-related systemic inflammation and low BMD. Our results are in agreement with other scientists [17] who concluded that a higher COPD stage and impaired pulmonary function (lower FEV_1 level with decreased exercise capacity) were correlated with low BMI, LMI and BMD. This suggests that in $COPD_3$ there is the relationship between loss both bone and muscle mass.

It is well known, that age and BMD are inversely correlated with bone formation. Indeed, the observed $COPD_3$ patients (who were older than $COPD_{1,2}$ patients) had a lower BMD, FEV_1 as well as the negative association between FEV_1 and OPS. Thus, as the abnormalities of BMD reached severer levels, COPD patients had gradually decreased values of FEV_1 because impaired pulmonary function may affect bone status [15].

We suggest that in $COPD_{2,3}$ the balance between bone resorption and formation was disturbed and bone resorption was increased while bone formation was depressed which led to BMD reduction and OPS development. This fact was confirmed by the prevalence of patients with a low level of osteocalcin (43%) from general COPD group and fewer patients (12%) with increased β-crossLaps level. The analysis of

Table 3. Dynamics of the bone metabolism markers during COPD development (Me; 25%, 75%)

Parameter	Control group (n=16)	$COPD_1$ (n=22)	$COPD_2$ (n=29)	$COPD_3$ (n=19)
Total calcium, mmol/l	2,21 (2,14; 2,27)	2,23 (2,15; 2,33)	2,28 (2,16;2,44)	2,17 (1,96; 2,37)
Ionizing calcium, mmol/l	1,20 (1,13; 1,25)	1,01 (0,94; 1,09)*	0,93 (0,83; 1,03)*,^	0,92 (0,88; 0,94)*,^
Inorganic phosphorus, mmol/l	1,30 (1,10; 1,40)	1,26 (1,10; 1,30)	1,34 (1,20; 1,50)	1,30 (1,00; 1,40)
Osteocalcin, ng/ml	19,43 (19,10; 23,67)	17,22 (13,3; 19,6)	15,4 (8,78; 20,3)*	15,3 (11,2; 18,4)*
β-crossLaps, ng/ml	0,28 (0,27; 0,36)	0,30 (0,24; 0,37)	0,40 (0,28; 0,50)*,^	0,39 (0,26; 0,44)*,^
Parathyroid hormone, pg/ml	38,5 (35,6; 46,7)	32,5 (24,6; 41,3)	26,6 (22,3; 33,6)*	24,9 (19,0; 35,4)*
Free testosterone, pg/ml	10,5 (6,7; 14,2)	7,5 (3,8; 11,0)*	7,3 (3,4; 11,2)*	5,6 (2,8; 8,7)*,^

** — p<0,05 vs. the control group; ^ — p<0,05 vs. $COPD_1$.*

the different variants of the interrelation between these markers showed the prevalence of the two following combinations: normal levels of β-cross-Laps and osteocalcin (in 52% of cases) as well as normal levels of β-crossLaps and decreased osteocalcin level (in 40% of cases). The latter indicated an increased rate of bone remodeling process in these patients that may stimulate enhanced bone mass loss.

As COPD and OPS are characteristic of the second period of life, they are strongly interrelated due to common risk factors and persisting low grade systemic inflammation which may be a key factor in reduced lung function and OPS development in advanced COPD [16, 20]. This inflammation is linked to the activation of osteoclastogenesis and may inhibit bone metabolism in different aspects promoting weight and bone loss [7]. Thus, the significant BMD reduction in $COPD_3$ suggests that mechanical defragment of lung structure might be may be associated in some pathways with the destruction of bone structure [5].

Our results may be to a certain extent explained by a increased level of inflammatory markers (CRP level was significantly higher in $COPD_{2,3}$) that could favor bone loss. We suggest that the more frequency of acute exacerbation in $COPD_3$ group within the past year can reflect a higher degree of systemic inflammation and negatively impact on bone metabolism and BMD. Thus, almost half of severe COPD patients who had suffered >3 acute exacerbation in the past year had OPS [11, 16]. The role of pro-inflammatory cytokines may be a central to the OPS associated with COPD. These cytokines (including IL-1, 6 and TNF-α) are responsible for characteristic loss of BMD through their effect on osteoclast activity and related bone resorption [18]. $COPD_{2,3}$ patients with OPS had a significantly higher levels of systemic inflammation than those with normal BMD. Thus, TNF-α was increased in $COPD_{2,3}$ (by 60% and 70% vs. the control and COPD1) suggesting that systemic inflammation response and increased production of TNF-α causes both weight and bone loss in advanced COPD patients [18]. Probably, the severity of airflow obstruction and the chronic use of ICS are less strongly associated with the loss BMD in $COPD_{2,3}$, than increased plasma level of pro-inflammatory cytokines.

A physical inactivity in severe COPD caused subsequent decrease of bone formation due to lower mechanical loading [13, 28]. Thus, $COPD_{2,3}$ patients had dyspnea during exertion that may lead to such physical inactivity and decreased muscle strength that can accelerate respiratory decline and negatively affect on BMD in weight-bearing bones. The significantly higher MRC score in $COPD_3$ ($p<0,05$ vs. $COPD_{1,2}$) indicated that a disease specific component was involved in the loss of BMD in severe COPD.

We revealed that $COPD_1$ patients did not have a low BMD and OPS. The significant loss of BMD in $COPD_2$ group (without sCS use) may indicate that the other mechanism might contribute to the increased prevalence of low BMD in these patients. We did not able to demonstrate the effect of ICS in moderate dose on BMD and bone metabolism markers as in other studies. However, COPD3 patients (who prescribed ICS plus sometimes short courses of sCS) had more often the changes in BMD and T-score at L_{1-4} and FN. BMD in two severe COPD patients (who had intermittent short courses of sCS and the cumulative dose of CS near by 400 mg) did not significant differ from BMD of similar patients who never used sCS. We do not think that rare ambulatory using sCS only in two patients (from 22 patients) significantly influenced the BMD level in this $COPD_3$ group.

In the present study there was the association between intensive smoking and low BMD in concordance with other studies [6, 12]. Thus, the number of current smokers and index of packs/year were significantly higher in $COPD_3$ as well as their serum levels of CRP and TNF-α compared with the control group and $COPD_1$.

The differences between the median level of the circulating biomarkers of bone metabolism in $COPD_1$ and the control were not detected. Probably, more expressed bone tissue changes in $COPD_{2,3}$ were associated with presence of low level of free testosterone and PTH that may play a certain role in the development of OPS.

All the above mentioned has illustrated a complex interactive relationship COPD severity with BMD level and OPS prevalence. Thus, the longer COPD duration and higher prevalence of OPS not always correlated with COPD severity. Our findings may indicate that OPS and COPD are likely to be related at the molecular level and some pathways may contribute to explain their co-occurrence.

Conclusions

1. BMD was lower in men patients from COPD general group than in healthy subjects. Thus, a low level of BMD was detected in 67% of cases in general COPD group, while OPS was observed in 22% of cases with the prevalence of decreased BMD in lumbar spine. There was no significant decrease in BMD in the patients aged 40 to 50 years vs. the comparable control group.
2. Progressing of GOLD stage was associated with high prevalence of low BMD and OPS in $COPD_{2,3}$ (13 and 64% respectively).
3. The low BMI, LMI and BMCI as well as FEV_1 levels are the significant contributors to BMD decrease in advanced COPD.
4. Screen for OPS in $COPD_{2,3}$ patients over 50 years, especially in those having a low BMI, BMCI and LMI is required.

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РАСПРОСТРАНЕННОСТЬ И КОРРЕЛЯТЫ НИЗКОЙ МИНЕРАЛЬНОЙ ПЛОТНОСТИ КОСТИ И ОСТЕОПОРОЗА ПРИ ПРОГРЕССИРОВАНИИ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ У ПАЦИЕНТОВ МУЖСКОГО ПОЛА

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Резюме

В статье представлены результаты исследования распространенности остеопороза (ОПС) у пациентов мужского пола с хронической обструктивной болезнью легких (ХОБЛ), а также изучения взаимосвязи между ОПС и маркерами костного метаболизма, компонентного состава тела и системного воспаления в зависимости от степени тяжести ХОБЛ.

Низкая минеральная плотность кости (МПК) выявлена у 67% в общей группе больных ХОБЛ, причем ОПС наблюдался у 22% (с преимущественным снижением МПК в области поясничного отдела позвоночника). По мере утяжеления ХОБЛ отмечалось значимое увеличение доли пациентов с ОПС: на I стадии ХОБЛ пациентов с ОПС не было, на II и III стадии он был выявлен у 13 и 64% больных соответственно. Показано, что снижение индексов массы тела, безжировой массы тела, костного минерального компонента тела и объема форсированного выдоха за первую секунду вносит существенный вклад в снижение МПК при тяжелой ХОБЛ.

Таким образом, необходимым является проведение скрининга на наличие ОПС у больных ХОБЛ II и III стадии мужчин старше 50 лет, особенно с низкими индексами массы тела, безжировой массы тела и костного минерального компонента тела.

Ключевые слова: хроническая обструктивная болезнь легких, остеопороз, воспаление, остеокальцин, β-кросслапс.