Chronic obstructive pulmonary disease (COPD) remains one of the greatest pressing medical and social problems of today both in Ukraine and worldwide. It is due to the high level of incidence, invalidization and lethality resulting both from the main disease as well as from pathologies related to COPD [1, 2].

Studies conducted in different countries reveal that COPD occurs in 4-10 % of adult population. In a state of exacerbation the rate of COPD mortality reaches 10 %. Mortality risk is related to sever course of the disease, development of respiratory failure, presence of sever related pathologies, it is also connected with possible mistakes at the time of the basic pharmacotherapy prescription which may not always adequately correspond to the severity of the disease [8, 9].

In 2000 there were 8 million doctor visits registered in the USA, 1.5 million emergency calls, 673 thousand hospitalizations due to COPD [9].

Ukraine is only beginning to collect COPD statistical data viewing it as a separate pathology. Up until 2009 COPD had not been rendered as a separate heading in Ukraine’s statistics as an independent nosologic unit, and all the official statistics data were handled via chronic bronchitis. Mortality and hospital lethality was several times greater than similar readings in pneumonia, bronchial asthma and asthmatic conditions.

In 2009 a Decree of the Ministry of Healthcare of Ukraine rendered chronic obstructive pulmonary disease in to a separate heading (out of the general heading of «chronic bronchitis») of statistical data reports (as it had been done in other countries a long time ago), which is targeted at ensuring early diagnosing.

The problem of COPD hypo diagnosing is particular not only to Ukraine but to all of the courtiers of the world, especial at the early stage when no clinical manifestations of COPD have yet been revealed, when it can only be recognized during screening studies (with the help of spirometry) [8].

There is a firm correlation that can be seen worldwide between the severity of COPD and expenses. The bulk of total expenses goes to hospitalizations and emergency medical assistance (73 % of total expenses). The cost of basic COPD drug therapy amounts to 12 % of the total expenses [9].

European countries analysis shows that, given the considerable expenses related to the issue of COPD, the money is utilized highly irrationally. Up to 74 % of economic harm pertains to the unemployment days, 12 % go for the ambulatory stage of treatment, and over 7 % - for the in-hospital stage. The rate of the expenses that go for COPD drugs is only 7 % which means that COPD patients are considerably undersupplied on the part of their drug therapy. This is given the fact that the total COPD expenditures exceed those for bronchial asthma several times over; those for pneumonia treatment almost 4 times and over 18 times the expenses for tuberculosis. It would be possible to decrease these expenses by early COPD diagnosing, early drug treatment, and prevention of possible complications.

According to the WHO guidelines in the international agreement paper GOLD, domestic Decrees of the Ministry of Healthcare of Ukraine (Decree of the Ministry of Healthcare of Ukraine No 311 dated December 30, 1999, No 499 dated October 28, 2003, and No 128 dated March 19, 2007) on the chronic obstructive pulmonary disease, the following strategies should be made optimal: early recognition of the disease at its beginning stages, smoking cessation, early prescription of continuous basic drug therapy, timely
and balanced exacerbation treatment, recognition and treatment of related diseases which slows down and prevents the development of life-threatening complications, prevents a steep decline of quality of life of the patients [4, 8, 9].

Besides lung damage, COPD leads to serous extra-pulmonary systemic effects, related diseases that exacerbate the course of the disease in some patients. COPD develops in people of predominantly middle and senior age with a considerable smoking experience, by which time the patients already have other diseases where smoking and age are also a factor. However COPD itself also leads to serious extra-pulmonary (systemic) effects which leads to development of related pathology. According to data presented by international experts, up to 25 % of population over 65 years of age has two, and 17 % have three chronic diseases simultaneously. The recognized extra-pulmonary effects of COPD are weight loss, eating disorders, spinal muscles dysfunction. COPD patients are at greater risk of a heart attack, stenocardia, osteoporosis, respiratory infections, bone fractures, depression, diabetes, sleep disorder, anemia, glaucoma, there are also data on lung cancer [4, 5, 6, 10].

At the present stage of medical assistance rendered to COPD patients there is no sufficient attention devoted to diagnosing and treatment of related osteoporosis, which in COPD patients is a secondary development that appears as a result of a systemic inflammatory process, metabolic disorders, long-term hypoxia arising on the background of respiratory failure, receiving inhaled and systemic glucocorticosteroids (GCS) and decreased physical activity, and it is systemic in its nature [3, 7, 12, 15, 17].

The most frequent sites of pathologic fracture preconditioned by osteoporosis are vertebræ, ribs, wrists, hip (femoral neck), proximal part of humerus, pelvic bones. Such fractures often lead to patient disability or fatality [11, 14, 19].

Development of secondary systemic osteoporosis in COPD patients leads to pathologic bone fractures and has a negative influence on periodontal tissues, the digestive system and the patients’ quality of life [13, 15].

As reported by some epidemiologic researches, the incidence of osteopenia and osteoporosis in COPD patients is up to 60 %. In case of long-term development and progression of COPD, osteoporosis has a more frequent occurrence [5, 6]. However, no research has been done as to study of osteoporosis. However COPD itself also leads to serious extra-pulmonary (systemic) effects which leads to development of related pathology. According to data presented by international experts, up to 25 % of population over 65 years of age has two, and 17 % have three chronic diseases simultaneously. The recognized extra-pulmonary effects of COPD are weight loss, eating disorders, spinal muscles dysfunction. COPD patients are at greater risk of a heart attack, stenocardia, osteoporosis, respiratory infections, bone fractures, depression, diabetes, sleep disorder, anemia, glaucoma, there are also data on lung cancer [4, 5, 6, 10].

Objective of the Research: To study incidence of osteoporosis in different clinical groups of patients with chronic obstructive pulmonary disease.

The work was funded by the state budget.

Materials and Methods of Research:

The study participants were 63 patients with COPD who have made up the I group (41 men and 22 women aged 40 to 80 years, mean age – (63,8 ± 1,1) years). In the group the forced expiratory volume within the first second (FEV1) before the sample with a bronchodilator was (46,2 ± 2,0) %; FEV1 / forced vital pulmonary capacity (FVC) - (50,6 ± 1,6). FEV1 after the sample with a bronchodilator – (48,8 ± 2,1) %; FEV1/FVC – (51,6 ± 1,6).

The patients selection was carried out in accordance with the disease severity and conducted under the Decree of the Ministry of Healthcare of Ukraine № 128 date March 19, 2007 «On Approval of Clinical Protocols of Medical Care in Pulmonology» [5].

The control group (II group) consisted of 30 practically healthy individuals (18 men and 12 women aged 40 to 80 years, mean age – (59,6 ± 1,3) years). FEV1 – (111,0 ± 3,3) %; FEV1/FVC – (78,0 ± 0,6), who volunteered to participate in the study. The practically healthy individuals were men and women aged 40 to 80 years who had no history of chronic somatic diseases that would require medical supervision and treatment, and whose general clinical and functional laboratory tests were within their age norm. Patients of the main and the control groups did not differ in age and gender. (Table 1).

All patients filled in a questionnaire, received clinical and functional examinations as well as quantitative computed densitometry (3D QCT).

Four clinical groups (A, B, C, D on the recommendations of GOLD (Global Initiative for Chronic Obstructive Lung Disease, 2011)), where the patients were attributed, were determined based on the evaluation of clinical symptoms, functional parameters and the risk of possible complications [6].

For a comprehensive evaluation of clinical symptoms in accordance with the GOLD 2011 Guidelines the COPD Assessment Test - CAT (COPD Assessment Test) was used [20].

The study of pulmonary ventilation function of all patients was carried out according to the analysis of the «flow-volume» spirogram curve of forced expiratory volume and considering the total body plethysmography performed on «Master Screen PFT» equipment manufactured by «Cardinal Health» company (Germany). When the diagnosing COPD and determining the clinical groups of patients (A, B, C, D) the following parameters were evaluated before and after tests with bronchodilators: FEV1, the FEV1 / FVC ratio. The tests were taken in the morning, after a 12-14-hour break in administration.
of medications. In order to determine the presence and reversibility of bronchial obstruction, the evaluation of external respiratory function was performed 15–30 minutes before and after 2 inhalation sessions (200 mcg) of β₂-short-acting agonist (salbutamol).

Examination for osteoporosis was performed on a multislice computer tomograph Aquilion TSX-101A «Tochiba» (Japan) using QST Pro licensed program based on a study of mineral density of the lumbar (L1-L3) vertebra.

Data aggregation and mathematical processing was performed with the use of the licensed software products included in the Microsoft Office Professional 2007 package, license of Russian Academic OPEN No Level № 17016297. Statistical analysis was performed with the use of mathematical and statistical features of MS Excel which employed methods of descriptive statistics. For the assessment of statistical significance of the differences, parametric (Student’s t-criterion) and nonparametric (Wilcoxon’s T-criterion) criteria were used.

Results and Discussion thereof

During the examination the 63 COPD patients were divided into four clinical groups (A, B, C, D in accordance with recommendations of GOLD (Global Initiative for Chronic Obstructive Lung Disease, 2011)), depending on the severity of clinical symptoms, functional parameters and the risk of possible complications [6]. It should be mentioned that patients participating in the study were the ones observed in the institute’s clinics, all of whom had medium or severe stage of the disease, thus at the time of questioning and clinical and functional examination there were no patients belonging to the clinical group A. Among the tested 22 (34,9 %) patients were allocated to the clinical group B, 12 patients (19,1 %) - to the clinical group C, and 29 (46,0 %) of the patients - to the clinical group D. Such distribution among the clinical groups reveals that most of the COPD patients referred from other medical institutions to the institute’s clinics for diagnosis verification, aggravations treatment and correction of their basic therapy were clinical group D patients.

During examination of COPD patients and the practically healthy individuals of the same age and gender employing the method of quantitative computer densitometry the Z and T criteria were determined. The T-test evaluated the presence of osteopenia or osteoporosis. In this case, we note that the term osteopenia means the preclinical state of osteoporosis. The T-criterion value was interpreted as follows: from 3,0 to -1,0 – norm; from -1,0 to -2,5 – osteopenia; from -2,5 to -5,0 – osteoporosis.

As a result of the examination, systemic pathological changes in bone tissue were detected in all patients with COPD. Osteopenia was detected in 18 (28,6 ± 5,7) % patients out of 63, and osteoporosis – in 44 (63,8 ± 5,8) %, which exceeded the diagnosis frequency in the control group 6 times over. Only one patient had no detected pathological change of the bone system (Table 2).

In the control group, when compared to the I Group, there were significantly more individuals without bone system pathology and significantly less individuals with osteoporosis. However, in the control group 14 (46,7 ± 9,1) % of individuals had manifestations of osteopenia that were mainly preconditioned by the patients’ senior age and the presence of involutional processes, which complies with the general statistical research in the population according to the literature data [3].

It deserves to mention that determination of osteopenia or osteoporosis in COPD patients varied among the clinical groups.

Table 3 shows results of the study - the incidence of osteopenia or osteoporosis in patients with COPD based on the clinical groups.

<table>
<thead>
<tr>
<th>Related Pathology</th>
<th>I Group (n = 63)</th>
<th>II Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related Pathology</td>
<td>Absolute %</td>
<td>Absolute %</td>
</tr>
<tr>
<td>No related pathology</td>
<td>1 ± 1,6</td>
<td>13 ± 4,3</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>18 ± 5,7*</td>
<td>14 ± 4,9</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>44 ± 6,3*</td>
<td>3 ± 2,7</td>
</tr>
</tbody>
</table>

Table 2

Table 3

<table>
<thead>
<tr>
<th>Related Pathology</th>
<th>B (n = 22)</th>
<th>C (n = 12)</th>
<th>D (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related Pathology</td>
<td>Absolute</td>
<td>%</td>
<td>Absolute</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>9 ± 4,4</td>
<td>14,3 ± 4,4</td>
<td>3 ± 2,7</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>12 ± 4,9</td>
<td>19,0 ± 4,9</td>
<td>9 ± 4,4</td>
</tr>
</tbody>
</table>

Note: * – The difference compared to the «No related pathology» patients within the groups is statistically significant (diff. < 0,01); # – The difference between osteopenia and osteoporosis within the groups is statistically significant (diff. < 0,01); & – The difference between the groups is statistically significant (diff. < 0,01).
COPD patients.

Clinical groups C and D. Picture 1 shows incidence of related pathology within the clinical groups of the same value in clinical groups В – (19,0 ± 4,9) %, diff. < 0,05 and С (14,3 ± 4,4) %, diff. < 0,05.

When analyzing the incidence of osteopenia and osteoporosis within the clinical groups, it was determined that osteoporosis was diagnosed significantly more often than osteopenia in the clinical groups C and D. Picture 1 shows incidence of related pathology within the clinical groups of COPD patients.

The results obtained testify to the fact that the patients of the clinical group B were diagnosed with osteopenia and osteoporosis with the same frequency. In the clinical groups С and D significantly predominant number of patients had osteoporosis.

Patients of the control group were diagnosed with osteoporosis only in 3 cases (10,0 ± 5,5) %, which was significantly different from the group of patients with COPD, where osteoporosis was observed in 44 (63,8 ± 5,8) % of patients, (diff. < 0,01), Table 2. It should be noted that osteoporosis in II Group was detected only in 3 women in menopause. Osteopenia in the control group was identified in 14 (46,7 ± 11,1) % of patients and in 13 (43,3 ± 9,0) % — no changes of mineral density of the bone system were found.

When analyzing osteoporosis diagnosing criteria the following peculiarities were observed. The main and the control groups differed significantly in Z and T criteria. Thus, the Z-test in the first group was (-1,03 ± 0,13), while in the second group – (-0,59 ± 0,23), diff. <0,001. The T-test in the first group was (-3,19 ± 0,14), while in the second group – (-1,29 ± 0,17), diff. <0,001. (Table 4).

When analyzing Z and T criteria in the clinical groups of COPD patients a statistically significant difference was also detected when comparing these with the similar values of the practically healthy individuals.

During a correlational analysis there was a weak negative reverse correlation determined between the T-criterion and the duration of COPD (r = – 0,255, diff. < 0,05) which

The table shows that among the tested patients of the clinical groups B, С and D, most of the patients were diagnosed with osteoporosis. Structural and functional disorders of the done system, and the most frequent detection of osteoporosis were observed in patients in clinical group D that is characterized by the most severe clinical symptoms, the lowest values of functional performance and the highest risk of potential complications of COPD.

Therefore, among the patients diagnosed with osteoporosis (36,5 ± 6,1) % of all the examined were patients of the clinical group D, which was significantly statistically different from the same value in clinical groups В – (19,0 ± 4,9) %, diff. < 0,05 and С (14,3 ± 4,4) %, diff. < 0,05.

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<table>
<thead>
<tr>
<th>Densitometry Values</th>
<th>I Group (n = 63)</th>
<th>Clinical groups of COPD patients</th>
<th>II Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (n = 22)</td>
<td>C (n = 12)</td>
<td>D (n = 29)</td>
</tr>
<tr>
<td>Z</td>
<td>-1,03 ± 0,13*</td>
<td>-0,78 ± 0,23*</td>
<td>-0,93 ± 0,29*</td>
</tr>
<tr>
<td>T</td>
<td>-3,19 ± 0,14*</td>
<td>-2,79 ± 0,26*</td>
<td>-3,26 ± 0,27*</td>
</tr>
</tbody>
</table>

Note: * – The difference from II group is statistically significant (diff. <0,001).
speaks of an increase in the risk of osteoporosis if COPD is developing over an extended period of time. Note that the conducted study calculated the duration of COPD development beginning at the time of diagnosing. In the clinical group B the duration of COPD was (8,0 ± 2,0) years, in the group C – (14,0 ± 1,0) years, in the group D – (11,1 ± 0,9) years.

It should also be noted that many of the patients encountered first symptoms of the disease many years earlier than the official diagnosis, and some of the patients were treated for other diseases until they received their final diagnoses of COPD. Thus tracking the real term of COPD development in these patients remains unlikely. Resolving the problem of hypo diagnosis and establishing the diagnosis at earlier stages when the clinical symptoms are less evident or not apparent is only possible by means of screening tests (with the help of spirometry).

Timely diagnosis and treatment of COPD are the main preventive measures against development of secondary systemic osteoporosis.

Conclusion
1. It has been proven that osteoporosis in COPD patients was detected 6 times more often than in practically healthy individuals of the same age and gender, which allows for considering the presence of COPD a major risk factor for secondary systemic osteoporosis.
2. Structural and functional disorders of the done system were observed in patients in the clinical group D that is characterized by severe clinical symptoms, low values of functional performance and the highest risk of potential complications of COPD. Osteoporosis was detected the most in patients of this clinical group – 79,3 % of patients.
3. The duration of the course of the disease raises the risk of osteoporosis in COPD patients. Timely diagnosis and treatment of COPD are the main preventive measures against development of secondary systemic osteoporosis.

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ОРИГІНАЛЬНІ СТАТТІ

АСТМА ТА АЛЕРГІЯ, № 4 • 2013

VIWИВЛЕННЯ ОСТЕОПОРОЗУ В КЛІНІЧНИХ ГРУПАХ ХВОРИХ НА ХРОНІЧНЕ ОБСТРУКТИВНЕ ЗАХВОРЮВАННЯ ЛЕГЕНЬ

Гуменюк М. І., Ігнатьєва В. І., Гуменюк Г. Л., Линник М. І., Харченко–Севрюкова Г. С., Куз В. В.

Резюме

Мета дослідження – дослідити частоту виявлення остеопорозу в різних клінічних групах хворих на хронічне обструктивне захворювання легень.

Об’єкт дослідження – 63 хворих на ХОЗЛ, які склали І групу, із них 41 чоловік і 22 жінки, у віці від 40 до 80 років, середній вік – (63,8 ± 1,1) роки. ОФВ1 до пробы з бронхосклетом становив (46,2 ± 0,2) %; ОФВ1/ЖЄЛ – (78,0 ± 0,6), які добровільно погодилися взяти участь у дослідженні.

Методи дослідження: анкетування, клініко-функціональні методи дослідження, кількісна комп’ютерна денситометрія (3D QCT), статистичні.

Результати. В результаті проведеного обстеження майже у всіх хворих на ХОЗЛ було виявлено симптоми патологічних змін кісткової тканини. У 18 (28,6 ± 5,7) % хворих із 63 було виявлено остеопеороз, а у 44 (63,8 ± 5,8) % – остеопороз, що 6 разів перевищував частоту діагностики остеопорозу в контролії групі.
У хворих контрольної групи остеопороз було діагностовано лише у 3 (10,0 ± 5,5) % пацієнтів, що статистично достовірно відрізнялося від групи хворих на ХОЗЛ, де остеопороз спостерігался у 44 (63,8 ± 5,8) % хворих (р < 0,01). Остеопороз у II групи було виявлено лише у 2 хворих, які значно можна було вважати в постменопаузальному періоді. 14 (46,7 ± 9,1) % осіб контрольної групи мали прояви остеопенії, які були обумовлені переважно похилим віком пацієнтів і навіть інволюційними процесами, що відповідало загальномузостатистичним дослідженням в популяції.

Серед обстежених 22 (34,9 %) хворих були віднесено до клінічної групи В, 12 (19,1 %) — до клінічної групи С, 29 (46,0 %) — до клінічної групи D. Визначення остеопенії або остеопорозу відрізнялося за клінічними групами.

Серед хворих, які діагностували остеопороз (36,5 ± 6,1) % від усіх обстежених складали хворі клінічної групи D, що статистично значимо відрізнялося від цього показника в клінічних групах В - (19,0 ± 4,9) %, р < 0,05 і С (14,3 ± 4,4) %, р < 0,05.

Всередині клінічних груп визначено, що остеопороз діагностували достовірно частіше в клінічних групах С і D. У хворих клінічної групи В досить часто діагностували остеопенію та остеопороз.

За критеріями Z і T основна і контрольна групи достовірно відрізнялися між собою. Так, Z-критерій в I групі становив (-1,03 ± 0,13), а в II групи - (0,59 ± 0,23), р < 0,001. T-критерій в I групі становив (-3,19 ± 0,14), а в II групі - (-1,29 ± 0,17), р < 0,001.

При аналізі Z і T критеріїв у клінічних групах хворих на ХОЗЛ також виявлена статистично значима їх різниця в порівнянні з аналогічними показниками у практично здорових осіб. Встановлено кореляційний слабкий від’ємний зворотній зв’язок між Т-критерієм і логічними показниками у практично здорових осіб. Встановлено також виявлено статистично значиму різницю в порівнянні з аналігічними групами.

Т-критерій в I групі ставив (-3,19 ± 0,14), а в ІІ групі – (0,59 ± 0,23), р < 0,001. T-критерій в І групі становив (-1,03 ± 0,13), а в II групі – (-1,29 ± 0,17), р < 0,001.

Висновки. Доведено, що остеопороз у хворих на ХОЗЛ являється в 6 разів частіше, ніж у практично здорових осіб того ж віку і статі, що дозволяє вживати названість ХОЗЛ головним фактором ризику вторинного системного остеопорозу.

Найбільш чисельною групою, де спостерігаються структурно-функціональні порушення кісткової системи є клінічна група D, яка характеризується тяжким вираженням клінічних симптомів, низькими значеннями функціональних показників і високим рівнем можливих ускладнень ХОЗЛ. В цій клінічній групі найбільш часто виявляється остеопороз у 79,3 % пацієнтів.

Ризик виникнення остеопорозу у хворих на ХОЗЛ підвищується з часом в 6 разів, ніж у практично здорових осіб того ж віку і статі, що відповідає загальностатистичним дослідженням в популяції.

ІНТЕРВ'Ю З АСТМА ТА АЛЕРГІЯ, № 4 • 2013

Об'єкт дослідження: 63 хворих з ЧКЗЛ, які були включени до досліду.

Методи: гістологічний, біохімічний, функціональний, імунологічний.

Результати: У хворих з ЧКЗЛ було виявлено значні відставання у відростанні, розвитку і репаруванні кісткової тканини.

Висновки. Остеопороз у хворих з ЧКЗЛ є важливим фактором ризику вторинного системного остеопорозу.

Ключові слова: хронічна обструктивна хвороба легень, клінічна група, остеопороз.