SMOKING AND ALCOHOL ABUSE AS RISK FACTORS CAUSING LOW-ENERGY FRACTURES IN MALES SUFFERING FROM PRIMARY OSTEOPOROSIS

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Osteoporosis is a persistent social and medical issue taking into account moral and material losses related to bone fractures occurring against its background. The disease is more frequently examined in women than in men; still, according to EVOS (European Spinal Osteoporosis Study) 13.5 % men older than 50 and 26 % men older than 60 run high risks of fractures in case they have osteoporosis. Risk factors that cause both the disease itself and fractures as its complications have not been examined profoundly, even though men run 1.6 times higher risk of death after a fracture than women. There is an assumption that a reason for this higher mortality is lack of knowledge about risk factors that cause the disease and a fracture as one of its complications. Growing morbidity with osteoporosis among men indicates it is necessary to perform activities aimed at persuading them to pursue healthy lifestyle. Given that, it seems important to assess impacts exerted by smoking and alcohol abuse on risks of fractures among patients with primary osteoporosis bearing in mind prevention of the disease and fractures as its complications.

We examined a relation between smoking and alcohol abuse and risks of fractures as osteoporosis markers in 231 patients suffering from primary osteoporosis. We revealed that fractures were authentically more frequent among smoking patients, 90.5 % against 68.1 % (р˂0.001). It was primarily true for fractures of the proximal section in the thigh bone and fractures of vertebral bodies: 20.2 % against 8.8 % and 44.1 % against 27.3 % accordingly. Alcohol abuse also resulted in authentically higher risks of fractures, 89.8 % against 66.2 % accordingly (р˂0.001). Authentic discrepancies were detected only for fractures of vertebral bodies, 43.9 % against 23.6 % accordingly among those who didn’t abuse alcohol (р˂0.001).

Therefore, we have evidence that there is an authentic relation between smoking and alcohol abuse and risks of fractures of the proximal section in the thigh bone and vertebral bodies. Inclusion of our research results into educational programs may lead to a reduction in frequency of fractures that have the gravest outcomes for health and cause the highest economic losses.

Key words: primary osteoporosis in men, risk factors of fractures, fractures of vertebral bodies, fractures of the proximal section in the thigh bone, smoking, alcohol abuse, an increase in morbidity with osteoporosis, prevention of the disease.

Osteoporosis (OP) is a metabolic disease that occurs in bones making them loss their tissue, impairing their structure and strength thus resulting in elevated risks of bone fractures [1]. Annually osteoporosis causes more than 8.9 million bone fractures in various parts of the skeleton [2]. Number of patients that are put into hospital due to osteoporosis is growing and it is already higher than a number of people put into hospital due to cardiac infarction, stroke, and breast cancer [3]. According to some forecasts [4] in 2020 50 % women in menopause will have various bone fractures due to osteoporosis, including 25 % with vertebral bodies’ fractures and 15 % with thigh bone fractures. A number of bone fractures caused by osteoporosis in men will also increase; thus, in 2025 a number of thigh bone fractures will be equal to that in women in 1990; by 2050 the figure will grow by 310 % whereas it will rise by 240 % for women [5]. Economically, a growth in num-
ber of bone fractures means that there will be a constant growth in social expenses on treating, hospitalizing, and rehabilitating patients with fractures caused by osteoporosis as well as in expenses related to their temporary or constant disability (social pensions). Given that, a study on risk factors that can cause osteoporosis and related bone fractures is a vital component in prevention activities aimed at reducing moral and economic expenses borne by both a patient and a society as a whole.

Such bad habits as smoking and alcohol abuse are distinctive among risk factors that cause osteoporosis and related bone fractures. They are modifiable ones since negative effects produced by them on bone tissue can be reduced [6]. However, impacts exerted by these factors are, as a rule, discussed only when it comes to patients suffering from secondary osteoporosis while there are practically no researches that dwell on assessing their role played in pathological bone fractures occurrence among men with primary osteoporosis.

Our research goal was to estimate contribution made by smoking and alcohol abuse into occurring deficiency of bone mineral density (BMD) and a correlation between these bad habits and risks of bone fractures as markers in men suffering from primary osteoporosis.

Data and methods. We accomplished as open comparative controlled examination; men suffering from primary OP took part in it. The examination was performed in full conformity with ethical principles and Good Clinical Practice rules fixed in Helsinki Declaration. All the patients gave their informed consent to be examined and have their clinical data processed. Overall, we examined 231 patients suffering from primary osteoporosis; they were aged from 17 to 92 and were treated in the Center for Osteoporosis of the N.N. Pirogov’s National Medical Research Center for Traumatology and Orthopedics from 2008 to 2018. As our research focused only on primary osteoporosis, we excluded all patients with pathologies that could cause secondary osteoporosis (we examined case histories in order to reveal diseases or prescribed medications that could influence bone tissue). We also excluded patients with hypogonadism from our research (to do that, we assessed sex hormones, examined family case histories, and performed a clinical examination; also, patients had consultations with endocrinologists). Osteomalacia was excluded basing on peculiarities detected via x-ray examinations and assessed homeostasis parameters of calcium, phosphor, and calcium-regulating hormones; hypophosphatasia was excluded as per alkaline phosphatase levels and genetic examinations results.

Primary osteoporosis was diagnosed basing on occurring low energy fractures of vertebral bodies or peripheral bones including fractures in the proximal section of the thigh bone, or on BMD losses being equal to <-2.5 SD as per T-criterion for people older than 50, or <-2.0 SD as per Z-criterion for people younger than 50 [7].

People who were included into the research only basing on a relevant decrease in BMD had first degree relatives who turned out to have low energy fractures. As for patients aged 17–20, 7 out of 26 didn’t have any fractures; nevertheless, we took into account an apparent decrease in BMD (higher than -2.0 SD as per Z-criterion) and occurrence of osteoporosis with low energy fractures in their first degree relatives (father or mother); therefore, they were included into our research group. Another reason for including patients aged 17–19 into our research was the fact that healthy men in Russia have their peak bone tissue mass in the lumbar spine and femoral neck completely formed by the age of 15. BMD in these localizations has no authentic discrepancies in young males aged 16–19 whereas there were significant discrepancies revealed between them and 15–year old young males1. Bearing these data in mind, we excluded any possibility that BMD could

change in young people aged 17–20 due to their skeletons still growing; any revealed decrease in BMD against a physiological standard for this age was considered to result from disorders in peak bone mass formation due to osteoporosis.

We applied X-ray densitometry (LUNAR Prodigy) to estimate BMD in L1–L4 and the femoral neck (we took a database collected for this device obtained in NHANES research). To detect symptomless fractures in the vertebral bodies, we performed X-ray examinations of the thoracic and lumbar spine; the examination was performed on each patient included into our research group.

Patients were divided into 3 age groups (Table 1) that corresponded to the following primary OP types: age 17–20 years, juvenile OP; age 21–50 years, idiopathic OP; age 51 and older, both idiopathic and senile primary OP.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Number of patients</th>
<th>Average age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17–20</td>
<td>26</td>
<td>18.02±1.43</td>
</tr>
<tr>
<td>2</td>
<td>21–50</td>
<td>103</td>
<td>33.68±9.3</td>
</tr>
<tr>
<td>3</td>
<td>51 and older</td>
<td>102</td>
<td>63.5±8.1</td>
</tr>
</tbody>
</table>

We examined such bad habits as smoking and alcohol abuse in each patient included into our research group.

A patient was considered to abuse alcohol in case he daily consumed 30 grams of spirit or totally 200 grams of spirit per week [8].

Smoking was considered to be a habit in case a patient had been smoking for more than three months prior to the research (this term was taken as a minimal one to judge on whether the examined patients actually had this bad habit).

To assess impacts exerted by a bad habit on BMD, we compared its absolute values in g/cm² in patients who had this bad habit and their counterparts who didn’t.

To assess effects produced by the same factors on risks of fractures, we divided all the patients into 5 groups, 4 out of them according to fracture localizations, and 1 group included patients without any fractures and was denominated Group 0. Group 1 included patients with low energy fractures of foot and hand bones; Group 2, patients with fractures in the proximal section of the humeral bone, shin bones, forearm bones, and ribs; Group 3, patients with fractures in the proximal section of the thigh bone; Group 4, patients with fractures in the vertebral bodies. We sequentially assessed bad habits of patients included into these groups that could cause a pathologic fracture in patients with various primary OP types.

**Statistical analysis.** We applied contingency tables to estimate interval variables and exact Fischer’s test to reveal any correlations between the examined parameters. Critical significance was taken as 0.05 [9, 10].

**Results and discussion.** Tables 2 and 3 contain the results of influence exerted by bad habits on BMD.

The performed analysis didn’t reveal any authentic discrepancies in BMD deficiency between smoking and non-smoking patients in these groups.

We also didn’t detect any effects produced by alcohol abuse on BMD deficiency value.

Therefore, we didn’t reveal any correlations between absolute BMD values (g/cm²) and such bad habits as alcohol abuse and smoking. Table 4 contains data on effects produced by smoking on risk of fractures.
Table 3

Influence exerted by alcohol abuse on BMD (g/cm²) in L1–L4 and the femoral neck (Mann–Whitney test)

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Number of patients</th>
<th>BMD L1–L4 (g/cm²)</th>
<th>Neck BMD (g/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abusing alcohol</td>
<td>91</td>
<td>0.93±0.16</td>
<td>0.93±0.16</td>
</tr>
<tr>
<td>Percentiles</td>
<td></td>
<td>25 % 0.84</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 % 0.93</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75 % 1.02</td>
<td>0.89</td>
</tr>
<tr>
<td>Not abusing alcohol</td>
<td>140</td>
<td>0.81±0.15</td>
<td>0.83±0.15</td>
</tr>
<tr>
<td>Percentiles</td>
<td></td>
<td>25 % 0.82</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 % 0.90</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75 % 1.00</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Table 4

Estimating correlations between fractures and smoking (exact Fischer’s test, p < 0.001)

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Division into groups as per fractures</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>0 9 13 17 37 84</td>
<td>100 %</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>47 17 30 13 40 147</td>
<td>100 %</td>
</tr>
</tbody>
</table>

As we can see from the Table, smoking patients tended to have more frequent fractures in the proximal section of the thigh bone, 20.2% against 8.8% accordingly, and fractures in the vertebral bodies, 44.1% against 27.3% accordingly. 31.9% non-smoking patients didn’t have any fractures whereas only 9.5% of their smoking counterparts managed to avoid them. Discrepancies between smoking and non-smoking patients were authentic (p < 0.001).

To get more precise data on a correlation between fracture localizations and smoking, we sequentially divided patients into three groups for each localization; it was done in the following way: Group 1 included patients without fractures; Group 2, patients with fractures of all localizations except the one being estimated in this contingency table; Group 3 included patients with the fracture localization being estimated.

Sequential analysis revealed that there were authentic discrepancies between patients without fractures (their number was authentically (p < 0.001) higher among non-smokers) and patients with fractures of the vertebral bones (their number was authentically higher among smokers (p < 0.001). These data are given in Table 5.

Table 5

Contingency of vertebral bodies fractures with smoking (exact Fischer’s test, p < 0.001)

<table>
<thead>
<tr>
<th>Groups of patients depending on smoking status</th>
<th>Division into gorups as per fractures</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>1 2 3</td>
<td>84</td>
</tr>
<tr>
<td>Non-smoking</td>
<td>47 60 40 27.3%</td>
<td>147</td>
</tr>
</tbody>
</table>

We didn’t reveal any correlations between other localizations of fractures and smoking.

Table 6 contains data on a correlation between fractures and alcohol abuse.

Table 6

Assessing a correlation between fractures and alcohol abuse (exact Fischer’s test, p < 0.001)

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Division into gorups as per fractures</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abusing alcohol</td>
<td>10 14 16 15 43 98</td>
<td>100 %</td>
</tr>
<tr>
<td>Not abusing alcohol</td>
<td>45 12 27 15 34 133</td>
<td>100 %</td>
</tr>
</tbody>
</table>

We assessed a correlation between fractures and alcohol abuse and revealed that fractures occurred among alcohol abusers authentically more frequently than among those who didn’t have this bad habit (p < 0.001). There were only 10.2% patients without any fractures among those who abused alcohol.
whereas there were 33.8% patients without fractures among those who didn’t do it.

The next stage was to get more precise data on a correlation between fracture localizations and alcohol abuse. Patients were divided into groups in the same way as it was done when assessing influence exerted by smoking. Group 1 were patients without fractures; Group 2, patients with fractures of all localizations except the one being estimated in this contingency table; Group 3 included patients with the fracture localization being estimated.

We sequentially assessed all fracture localizations and revealed authentic discrepancies only for fractures of the vertebral bodies (Table 7). Fractures of the vertebral bodies authentically more frequently occurred among patients who abused alcohol, 43.9% against 23.6% accordingly ($p < 0.001$).

Table 7
 Assessing a correlation between fractures of the vertebral bodies and alcohol abuse (exact Fischer’s test, $p < 0.001$)

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Division into groups as per fractures</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Abusing alcohol</td>
<td>10</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>10.2%</td>
<td>45.9%</td>
</tr>
<tr>
<td>No abusing alcohol</td>
<td>45</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>33.8%</td>
<td>40.6%</td>
</tr>
</tbody>
</table>

At present osteoporosis holds a very specific place among non-communicable diseases due to high prevalence and significant risks of fractures; prior to their occurrence the disease is mostly symptomless and its clinical picture is not at all apparent. Frequently fractures not only give a clear signal the disease has already developed but also cause grave health disorders or even death [11]. Over many years, the disease has been considered as being exceptionally a female one. However, over the last 20 years, it has become quite obvious that 30% low energy fractures of the thigh bone among men occur due to osteoporosis; its prevalence among men older than 50 varies from 2 to 8%, and additionally from 33 to 47% men in this age group can be put a diagnosis «decreased bone mineral density» and it also results in higher risks of low energy fracture [12, 13]. 1 out of 5 male patients has a fracture associated with OP [14]. When analyzing risk factors that can cause fractures, experts mostly discuss secondary osteoporosis cases without giving special attention to influence exerted by these factors on risks of fractures in case of primary osteoporosis [15–17]. At the same time, according to certain data [18] 80% osteoporosis cases among men older than 50 are exactly primary osteoporosis. These are the cases when it is impossible to reveal any somatic pathology or intake of medications that could cause metabolic changes in the bone tissue [19]. Primary osteoporosis among men can be juvenile, idopathic, or senile depending on age at which the disease is detected [20]. Our research group included 231 patients with different types of primary osteoporosis; some patients had fractures of different localizations. In all cases fractures were spontaneous or low energy ones and were considered to be pathologic fractures caused by osteoporosis.

Fractures caused by OP occur among male patients 10 years later than among female ones but they tend to have much graver outcomes [21]. According to available data, risks of such fractures and mortality due to them is higher among men older than 60 than among women from the same age group [22, 23]. Thus, in case of thigh bone fractures mortality among men during the $1^{\text{st}}$ year after a fracture was 2 times higher than among women [24–26]. As life expectancy grows both among men and women, a number of fractures also increases and this growth is considered to be related not only to age but also to bad habits. Thus, in the research work by Mariola Janiszewska [27] that concentrated on risk factors causing osteoporosis, 71.25% respondents mentioned alcohol abuse, and 56.6% stated they were smokers. In another research work that also dwelled on issues related to osteoporosis among male patients [28], 38% respondents mentioned smoking as a risk factor that can cause osteoporosis and more than one third of
respondents considered alcohol abuse to be another risk factor. Negative effects produced by smoking on BMD deficiency are also being discussed, among other things, in relation to BMI and physical activity [6]. Thus, a decrease in BMD among men aged 40–80 varied from 14 % (non-smoking and physically active men with BMI equal to 30 kg/m²) to 30 % (smoking and not physically active men with BMI starting from 18 kg/m²). A separate analysis of BMD among men older than 80 revealed that non-smoking and physically active men (4 hours of physical activity per week) had BMD that was by 1–2.0 SD higher than BMD among their smoking and not physically active counterparts from the same age group. However, among other modifiable causes of osteoporosis, smoking has long been accepted as a factor that, regardless of any other reason, produces negative effects on a balance between bone resorption and bone formation and it results in an increase in BMD deficiency [29]. Disorders in bone tissue metabolism influenced by smoking are also thought to be related to influence exerted on calcium homeostasis (calcium absorption declines) and on parathyrin-D-hormone endocrine chain [30]. Previously, P.D. Broulik et al. [31] made a point on a direct impacts exerted by nicotine on bones. There are some data on smoking exerting more adverse effects on bone tissue among men than among women [32]. Thus, smoking causes a 13 % increase in risks of spine fractures among women and a 32 % increase in the same risks among men; a 31 % and 40 % increase accordingly in risks of thigh bone fracture.

We didn’t dwell on influence exerted by smoking on BMD value; still, we obtained some evidence that this bad habit authentically caused elevated risks of fractures for those who had it against those who didn’t; 31.9 % non-smoking patients didn’t have any fractures whereas there were only 9.5 % smoking patients who managed to avoid them, discrepancies being authentic at \( p < 0.001 \). Smoking patients more frequently had fractures in the proximal section of the thigh bone, 20.2 % against 8.8 % accordingly, and fractures of the vertebral bodies, 44.1 % against 27.3 % accordingly; discrepancies in frequency of vertebral bone fractures were authentic (\( p < 0.001 \)).

When it comes to such bad habit as alcohol abuse, we should mention that effects produced by alcohol on risks of osteoporosis and fractures caused by the disease are considered to be related both to calcium homeostasis disorders and pathological changes in the liver that result in D-hormone metabolism disorders. Besides, alcohol abuse makes people more prone to falling [33]. In our research alcohol abuse, just as smoking, wasn’t revealed to exert any influence on BMD deficiency value but it had certain influence on risk of fractures. Only 10.2 % patients among those who abused alcohol didn’t have fractures whereas there were 33.8 % patients without any fractures among those who didn’t do it; discrepancies between two groups were authentic (\( p < 0.001 \)). First of all, it was the case with frequency of vertebral bodies’ fractures, 43.9 % alcohol abusers against 23.6 % of those who didn’t have this bad habit (\( p < 0.001 \)).

Therefore, despite absence of any direct influence exerted by smoking and alcohol abuse on BMD value, our research allowed obtaining certain evidence that there was a correlation between these bad habits and fractures frequency; first of all, it was true for fractures of the vertebral bones and it was similar to effects produced by these bad habits on risks of fractures in case of secondary osteoporosis. These data are significant for working out measures aimed at preventing fractures in patients with primary osteoporosis hence previously several cross-over studies included into meta-analysis by D. Kenneth et al. [32] contained data on ex-smokers having BMD similar to BMD of those people who never smoked. In the authors’ opinion, these data indicate that giving up smoking produces favorable effects on BMD. And though mechanisms of these effects are still not clear, we can assume that it is quite advisable to promote healthy lifestyle among men with primary osteoporosis who have such bad habits as smoking and alcohol abuse. Such promotion can result in lower risks of fractures in the prox-
mal section of the thigh bone and vertebral bodies. There is other evidence that this trend in prevention is significant; it is related to people being hardly aware of smoking and alcohol abuse as risk factors that can cause osteoporosis and related fractures. It is especially vital when it comes to teenagers. Thus, the research work [27] contains a reference to the work by S. Wahba et al. [34], mentioning results of a questioning with 494 participants aged 16–24 living in Cairo; only 6 % teenagers and young people knew that smoking can cause osteoporosis. And though 41.7 % adult women [35] among the examined ones realized that smoking was a risk factor that could cause osteoporosis, more than a half questioned women didn’t see any relations between the disease and this bad habit.

Since reducing risks of fractures is a vital component in a healthcare strategy aimed at improving life quality of patients suffering from osteoporosis, we believe that our data on contributions made by smoking and alcohol abuse should be included into educational programs for patients with the disease. It will result in lower frequency of pathologic fractures in the proximal section of the thigh bone and vertebral bodies; these fractures have the gravest consequences for patients’ health and result in the highest economic costs.

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**References**


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