Osteoporosis and sleep: a modern view of the problem (literature review)


Abstract. This article presents a review of the literature on the problem of osteoporosis in chronic sleep deprivation. Sleep is a periodic functional physiological state of the human body, which is characterized by the exclusion of consciousness and a decrease in the ability of the nervous system to respond to external irritation. The main hormones that regulate sleep include: melatonin, which is responsible for circadian rhythms, normalizes the hormonal background and has a positive effect on the immune, cardiovascular system; somatotropin — growth hormone, which has a positive effect on cell regeneration, participates in the formation of bone tissue, strengthens the immune system; testosterone — a sex hormone, the maximum of which is produced during sleep; follicle-stimulating and luteinizing hormones that affect women's reproductive function, as well as leptin, ghrelin and cortisol. Lack of sleep not only damages the nervous, endocrine, immune, cardiovascular systems, but also adversely affects the musculoskeletal system, often leading to osteoporosis — a disease that is accompanied by a decrease in bone mineral density. It was found that the duration of sleep less than 5 hours a day in women in postmenopausal period contributes to a decrease in bone mineral density and the development of osteoporosis. Obstructive sleep apnea is associated with vitamin D deficiency, increased bone resorption, and decreased bone mineral density. Chronic sleep disturbance in patients with obstructive sleep apnea leads to hormonal failure, which disrupts all metabolic processes in the body.

Keywords: osteoporosis; sleep; bone mineral density; review

The modern era and the progress of scientific achievements interpret new rules of life and behavior to the humanity, which, in its turn, negatively influences the health of the population. Scientists from all over the world are actively discussing the problem of chronic lack of sleep and socioeconomic factors that influence the prevalence of sleep disorders. Today, scientists attribute problems with sleeping to a modern view of the problem — walking while sleeping. The main function of sleep is responsible for all the necessary life processes of the body. Today, scientists attribute problems with sleeping to a global epidemic that threatens the health deprivation of up to 45% of the world’s population.

A sleeping is a periodic physiological state of the human body, which is characterized by the exclusion of consciousness and a decrease in the ability of the nervous system to respond to external irritants. In 1870, M. M. Manasein, who was a student of the physiologist I. R. Tarkhanov, studied on puppies the importance of sleeping for the body. Thanks to her works, the scientist is called the founder of the "science of sleeping". Modern ideas about the nature of sleeping have appeared in the second half of the 20th century with the invention of methods of recording of bioelectrical activity of the brain (electroencephalography), muscles (electromyography) and eyes (electrooculography). The word "sleeping" comes from the Latin word "somnus", which explains the names of the most of pathological conditions: somnolence — oppression of the consciousness; somnambulism — walking while sleeping. The main function of sleep-
The relevance of the studying the influence of sleeping on bone tissue was also confirmed by the American scientists S. Upala, A. Sanguankeo, S. Congrete, having published the journal "Bone and Mineral Research" in 2020 published an article titled "Short sleeping is associated with low BMD and osteoporosis in the group Women's Health Initiative" (Women's Health Initiative), which presented the results of their own research of the relationship between the duration and quality of sleeping with BMD of different areas of the skeleton, as well as the prevalence of osteopenia and osteoporosis in this group of patients [3]. They noted that short duration of the sleeping is recognized as a public health epidemic and is associated with a deterioration of the quality of life of the population, but is known a little about the connections between sleeping and bone health, so they decided to test whether sleeping behavior affects the development of osteoporosis. 11,084 women in postmenopausal period from the "Women's Health Initiative" group were examined. The average age of the examined was 63.3 ± 7.4 years. Duration and quality of the sleeping were assessed with the use of special questionnaires, and BMD was determined using two-photon X-ray absorptiometry at the level of the entire skeleton, lumbar spine, and femoral neck. The results had been evaluated taking into account the following factors: smoking, body mass index, alcohol consumption, physical activity, the use of sleeping pills. The result of the research showed that women who had slept less than 5 hours a day had 0.012-0.018 g/cm² lower BMD of the whole skeleton, lumbar spine and femoral neck compared to women who had slept 7 hours a day. In addition, women who had slept less than 5 hours a night had an increased risk of having low BMD and osteoporosis at the femoral neck: Odds Ratio (OR, odds ratio, 95 % confidence interval (CI)): 1.22 (1.03-1.45) and 1.63 (1.15-2.31), respectively. There were similar results at the level of the lumbar spine: (95 % CI): 1.28 (1.02-1.60). However, the authors hadn’t found reliable links between the quality of sleeping and BMD. In such a way, the scientists have made the conclusions that sleeping less than 5 hours a day among postmenopausal women is associated with low BMD and an increased risk of developing osteoporosis. The scientists did not accidentally have chosen a group of women in the postmenopausal period for the research, because this period in a woman's life is considered to be dangerous for a woman in terms of the risk of bone fractures and the development of osteoporosis because of hormonal changes in the body. They wanted to emphasize the need to provide the recommendations in time for the healthy sleeping to the women in postmenopausal period [3].

For today, the scientists from many countries around the world have noticed that lack of sleeping harms not only the activity of the nervous, endocrine, immune, and cardiovascular systems, but also negatively affects the state of the musculoskeletal system, that often is leading to the development of osteoporosis — a disease that is accompanied by a decrease bone mineral density (BMD) and an increase of the risk of fractures, as evidenced by a large number of foreign scientific publications [3-5, 8, 11].

Thereby, American scientists H. M. Ochs — Balcom, K.M. Hovey, C. Andrews and others in the journal "Bone and Mineral Research" in 2020 published an article titled “Short sleeping is associated with low BMD and osteoporosis in the group “Women's Health Initiative” (Women's Health Initiative)”, which presented the results of their own research of the relationship between the duration and quality of sleeping with BMD of different areas of the skeleton, as well as the prevalence of osteopenia and osteoporosis in this group of patients [3]. They noted that short duration of the sleeping is recognized as a public health epidemic and is associated with a deterioration of the quality of life of the population, but is known a little about the connections between sleeping and bone health, so they decided to test whether sleeping behavior affects the development of osteoporosis. 11,084 women in postmenopausal period from the "Women's Health Initiative" group were examined. The average age of the examined was 63.3 ± 7.4 years. Duration and quality of the sleeping were assessed with the use of special questionnaires, and BMD was determined using two-photon X-ray absorptiometry at the level of the entire skeleton, lumbar spine, and femoral neck. The results had been evaluated taking into account the following factors: smoking, body mass index, alcohol consumption, physical activity, the use of sleeping pills. The result of the research showed that women who had slept less than 5 hours a day had 0.012-0.018 g/cm² lower BMD of the whole skeleton, lumbar spine and femoral neck compared to women who had slept 7 hours a day. In addition, women who had slept less than 5 hours a night had an increased risk of having low BMD and osteoporosis at the femoral neck: Odds Ratio (OR, odds ratio, 95 % confidence interval (CI)): 1.22 (1.03-1.45) and 1.63 (1.15-2.31), respectively. There were similar results at the level of the lumbar spine: (95 % CI): 1.28 (1.02-1.60). However, the authors hadn’t found reliable links between the quality of sleeping and BMD. In such a way, the scientists have made the conclusions that sleeping less than 5 hours a day among postmenopausal women is associated with low BMD and an increased risk of developing osteoporosis. The scientists did not accidentally have chosen a group of women in the postmenopausal period for the research, because this period in a woman’s life is considered to be dangerous for a woman in terms of the risk of bone fractures and the development of osteoporosis because of hormonal changes in the body. They wanted to emphasize the need to provide the recommendations in time for the healthy sleeping to the women in postmenopausal period [3].

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article "The connections between obstructive apnea during sleeping and osteoporosis: a systematic review and meta-analysis" in the scientific journal "International journal of endocrinology and metabolism" [7]. It is known that patients with obstructive sleep apnea syndrome often stop breathing during their sleeping, as the brain sends a signal to wake up for a few minutes to restore the supply of oxygen. Accordingly, such people practically do not have a deep phase during sleeping, which is necessary for the synthesis of the most of hormones that are responsible for the assimilation of calcium and maintaining the balance between the processes of formation and destruction of bone tissue. Chronic hypoxia reduces the number of osteoblasts, which leads to a decrease in BMD. The main sources that were used by the scientists for the analysis were PubMed / MEDLINE and EMBASE databases. A systematic review and meta-analysis of published single-point studies that have assessed the frequency or prevalence of osteoporosis or BMD in the conditions of obstructive apnea during the sleeping versus controls was conducted. There were included the studies that have involved the individuals at the age from 18 years and over who did not have osteoporosis at baseline. The subjects underwent polysomnography and the disorders of the sleeping were assessed. The data were obtained from 7 studies that had involved 113,558 people. Among cohort studies, the overall odds ratio of the development of osteoporosis in patients with obstructive apnea during sleeping was 1.92 (95% CI: 1.24-2.97) compared with controls, but in cross-sectional studies, the odds of osteoporosis were higher in controls compared with the patients with obstructive apnea during sleeping (OR = 0.60; 95% CI: 0.42-0.87). Thus, in studies with a cohort design, there was a significant connection between obstructive apnea during sleeping and osteoporosis. The scientists have noted that in order to determine whether obstructive apnea during sleeping is a risk factor for the development of osteoporosis, further prospective studies with a large number of patients, taking into account the influence of age, sex, or body mass index, are needed [7, 8].

The publication of the Japanese scientist D. Inoue also testifies to the importance of studying of this problem, who concluded that obstructive apnea during sleeping is associated with vitamin D insufficiency, increased bone tissue resorption, and a decrease in BMD indicators. The scientist concludes that obstructive apnea during sleeping should be considered as a risk factor for the development of osteoporosis [9].

In addition, one of the prospective studies showed an increased risk of vertebral body fractures in women with an obstructive apnea during sleeping in anamnesis, but no reliable connection between femoral neck fracture and obstructive apnea during sleeping was found. The results of these studies were published in 2020 by the scientists T. Huang, S. S Tworoger, S. Redline in the article "Obstructive apnea during sleeping and the risk of vertebral and femur fractures in women" [11]. Chronic disturbance of sleeping in patients with obstructive apnea during sleeping requires the attention of the doctors and scientists, because it leads to hormonal disturbances in the body, which affects all metabolic processes, therefore, due to this imbalance, BMD decreases faster than it has time to recover, which leads to the development of osteoporosis [7-9].

There are some scientific data about the connection between disturbance of the sleeping and premature aging. It has been proven that telomeres, which are the end sections of chromosomes and perform a protective function, have a short length in some diseases, which is associated with premature aging and the risk of developing a cancer. It has been established that patients with obstructive apnea during sleeping have shorter telomeres, and therefore their problem with sleeping is one more factor of premature aging of cells [12-15].

Another scientific study that was published in the journal "Orthopedic Trauma" in 2015 by the scientists B.S. Shulman, F.A. Liporace, R. I. Davidowitch and others, demonstrated the importance of the studies of sleeping for the patients who have already had bone fractures [16]. After all, in this situation, not only the functional disturbance of sleeping as a risk factor for osteoporosis is important, but also the emotional impact of the already established fracture on the patient's mood and his quick recovery. A prospective study was conducted among 1095 individuals with the fractures of the proximal part of the humerus (n = 111), distal part of the radius (n = 440), tibia (n = 109), and a fracture in the area of the ankle-foot joint (n = 435). Patient-reported difficulties with the sleeping were compared with each patient's overall functional and emotional state 3, 6, and 12 months later after treatment. Difficulties in sleeping after 3 months of the observation had been found in 41% of the patients with a fracture of the proximal part of the humerus, in 25% of the people with a fracture of the distal part of the radius, in 36% of the patients with a fracture of the tibia, and in 19% of the patients with a fracture in the area of the ankle-foot joint. After 12-months of the supervision, less than 20% of the patients with the fractures have informed about difficulties with sleeping. During 12-months supervision, the indices of the mental health of the patients with the fractures of the distal part of the radius (p = 0.001) and the indices of the emotional state of the patients with the fractures of tibia (p = 0.024) and the fractures of ankle-foot joint (p ≤ 0.001) were independent predictors of the development of disorders of sleeping. Thus, the scientists showed that during the 12-months supervision, unsatisfactory sleeping was associated with a disturbed emotional state, but there was no connection with an impaired functional state, so it is necessary to evaluate carefully the mental health indicators of the patients with the problems of sleeping at the last stages of the treatment of bone fractures. This will allow orthopedists and traumatologists to refer in time the patients with disorders of sleeping after acute fractures for the consultation to neurologists or psychotherapists in order to prevent the development of depressive states in such patients due to chronic insomnia [16, 17].

In 2020, in China, an article titled "Connection between quality of sleeping and bone mineral density in urban residents" was published in the Journal "Medical Sciences" of Zhejiang University, which presented the results of the researches that have been conducted at the Management Center of Health Control in South Western University of
China. A retrospective analysis was conducted from 2012 to 2019 that assessed a quality of sleeping and BMD using two-photon X-ray absorptiometry among 28756 adults (14,355 men and 14,401 women). The quality of sleeping was assessed using the Pittsburgh Sleep Quality Index (PSQI). A $t$ test and a multiple regression model were used for statistical analysis between quality of sleeping and BMD indicators. Among the examined patients, taking into account the Pittsburgh index, the following data were obtained: 15,936 people — without a sleep disorder (55.4 %), 5,965 people — with a mild one (20.7 %), 4,897 people — with a moderate one (17.0 %) and 1958 people — with severe sleep disorder (6.8 %). It was found that the frequency of osteoporosis in the group of moderate sleep disorders was higher than in the group with mild disorders ($t = 525.6, p < 0.01$), and the frequency of osteopenia and osteoporosis in the group of severe sleep disorders was significantly higher than in the group of patients with moderate disorders ($t = 1124.9, p < 0.01$). In accordance with the data of multiple regression it was revealed that individuals who smoked, engaged in heavy mental work, and had higher scores of Pittsburgh Index had lower BMD scores, while moderate and intensive daily physical activity was associated with higher BMD scores ($p < 0.05$). Thus, according to the authors, sleep disturbance may be one of the main risk factors of loss of BMD by urban residents, which indicates the need of the correction of sleeping to prevent the development of osteoporosis [10].

The conducted analysis of the results of the literature sources regarding the connection of osteoporosis with the possible sleep disorders had demonstrated that in one of the research works, where the analysis of cohort and cross-sectional studies was conducted, that only in the cohort studies, patients with obstructive apnea during sleeping had higher rates of osteoporosis compared to the controls, and in cross-sectional studies, the likelihood of osteoporosis was higher in the controls compared with the patients with obstructive apnea during sleeping. Therefore, taking into account, that only in the studies with a cohort design there was a significant association between obstructive apnea during sleeping and osteoporosis, further prospective studies with a large number of patients taking into account the influence of age, sex, or body mass index are needed. In the studies for the assessment of the state of BMD, the presence of somatic pathology of the patient, in particular, diabetes mellitus, hyperparathyroidism, hepatitis, rheumatoid arthritis and oncological diseases, which can contribute to the development of osteoporosis, was not taken into account. It is also important to indicate whether the patients have taken certain medications, including sleeping pills, antiepileptics, glucocorticoids, bisphosphonates, calcium preparations with vitamin D, and others. Moreover, up to this moment, there are not enough research scientific works as for the study of the problems of sleeping and osteoporosis among men, so, in further researches it is necessary to pay attention to the gender peculiarities of this problem. Regarding the researches that have studied the risks of the fractures in patients with sleep disorders, the results were ambiguous, because no reliable data were found between femoral neck fracture and obstructive apnea during sleeping, and only an increased risk of vertebral body fractures was observed in women with obstructive apnea during sleeping in the anamnesis. All this indicates the need for the further study of this problem.

**Conclusions**

Healthy sleeping is the key to the successful functioning of all organs and systems of the human body. It prevents premature aging, improves the quality of life and is the most valuable “treasure” of the humanity for achieving longevity. Most of the sleep disorders can be prevented or treated, the main thing is to start it in time. Chronic lack of sleeping leads not only to the development of obesity, diabetes, hypertension, depression, metabolic syndrome, oncological pathology and exacerbation of chronic diseases, but also contributes to the changes in the musculoskeletal system. In particular, hormonal imbalance and disruption of circadian rhythms contribute to bone metabolic changes, which lead to a decrease in BMD, a decrease of the level of vitamin D in blood serum, which, in its turn, leads to the development of osteoporosis. It has been proven that duration of sleeping less than 5 hours a day in postmenopausal women is associated with low BMD and an increased risk of osteoporosis. Chronic hypoxia during obstructive apnea during sleeping reduces the number of osteoblasts, which contributes to the occurrence of fractures of the vertebral bodies in women and the development of osteoporosis. This problem is extremely relevant and requires further study.

In their practice, when taking an anamnesis, doctors should always ask the patients about sleeping mode and refer patients for insomnia treatment in time in order to prevent the progression of BMD loss, premature bone fractures, and the development of osteoporosis.

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В даній статті наведений огляд літературних джерел щодо проблеми розвитку остеопорозу за умов хронічної недостатності сну. Сон — це періодичний фізіологічний стан світу, який характеризується виключенням світлю та зниженням здатності нервоївої системи відповідати на зовнішні подразники. До основних гормонів, що регулюють сон, відносять мелатонін, який відповідає за циркадні ритми, нормалізує гормональний фон і позитивно впливає на імунну та серцево-судинну системи; соматотропін — гормон росту, який позитивно впливає на регенерацію клітин, бере участь у формуванні кісткової тканини та зміцнює гистокомпозицію, а також впливає на імунну та серцево-судинну системи; тестостерон — статевий гормон, максимум якого досягається в періоди сну, впливає на клітинну та зосередження репродуктивних ритмів, адаптацію до зовнішніх чинників.

Остеопороз і сон: сучасний погляд на проблему (огляд літератури)

Резюме. У даний статті наведений огляд літературних джерел щодо проблеми розвитку остеопорозу за умов хронічної недостатності сну. Сон — це періодичний фізіологічний стан світу, який характеризується виключенням світлю та зниженням здатності нервоївої системи відповідати на зовнішні подразники. До основних гормонів, що регулюють сон, відносять мелатонін, який відповідає за циркадні ритми, нормалізує гормональний фон і позитивно впливає на імунну та серцево-судинну системи; соматотропін — гормон росту, який позитивно впливає на регенерацію клітин, бере участь у формуванні кісткової тканини та зміцнює гистокомпозицію, а також впливає на імунну та серцево-судинну системи; тестостерон — статевий гормон, максимум якого досягається в періоди сну, впливає на клітинну та зосередження репродуктивних ритмів, адаптацію до зовнішніх чинників.

Ключові слова: остеопороз; сон; мінеральна щільність кісткової тканини; огляд

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