Type 2 diabetes and bone mineral density in postmenopausal women

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Abstract: The article gives information about type 2 diabetes and bone mineral density in postmenopausal women.

Keywords: diabetes mellitus, calcitonin, parathyroid hormone, calcium-regulating hormones, calcitriol, glucocorticoids, insulin

INTRODUCTION. The progressively increasing prevalence of type 2 diabetes mellitus (T2DM) in recent years is characterized as a non-infectious pandemic[1-3]. Chronic hyperglycemia in diabetes is accompanied by dysfunction of various organs and systems, and not only cardiovascular, which determines morbidity and mortality, but also bone tissue (CT), the dysfunction of which, in addition to urgent aspects caused by fractures, makes a significant contribution to the progression of diabetic macro- and microangipathies[4-6].

RELEVANCE. The relevance of the problem of CT status in T2DM is due to the increase in life expectancy, since the peak incidence of both DM and osteoporosis (OP) occurs in old age. The problems of AP as a cause of disability and mortality in patients from bone fractures (especially the proximal femur) occupy fourth place among non-communicable diseases, behind diseases of the cardiovascular system, cancer and diabetes [14-15]. This is due to the wide prevalence of AP, its multifactorial nature, late diagnosis and untimely initiation of treatment[5-9]. Based on data from a number of large prospective studies, T2DM was only recently included in the clinical recommendations of the FDAUz as a risk factor for osteoporotic fractures, especially the dramatic consequences of hip fractures [16-17]. The formation of estrogen deficiency in women brings special emphasis to the interaction of these two nosologies. After menopause, bone loss accelerates to 2-5% per year, in contrast to age-related physiological loss from 35-40 years of age, which is 0.3-0.5%. Women lose bone mass earlier and faster than men: during life, on average, up to 35% cortical and about 50% trabecular CT [18-19]. AP is a systemic

skeletal disease characterized by a decrease in CT mass per unit volume and disruption of CT microarchitecture, leading to increased bone fragility and a high risk of fractures. Bone is a complex dynamic system in which processes of bone remodeling constantly and simultaneously occur due to the interaction of two cell lines: osteoblasts, which ensure bone formation (synthesis of collagen and other organic bone matrix proteins, calcium deposition and metabolism), and osteoclasts, which destroy CT [20-21]. CT remodeling is regulated by numerous factors [22]. Among them: calcium-regulating hormones - parathyroid hormone (PTH), calcitonin, calcitriol; systemic hormones - sex and thyroid hormones, glucocorticoids, insulin, somatotropic hormone; growth factors and the RANK/RANKL/OPG cytokine system [22-23], as well as local factors produced by the bone cells themselves (prostaglandins, leukotrienes, lysosomal enzymes, etc.). Disruption of the remodeling cycle at any stage can lead to pathology of bone formation. Since insulin, as a systemic hormone, has a complex relationship with various remodeling regulators, there is every reason to believe that the pathogenesis of osteopenia and AP in diabetes is complex[24-27].

PURPOSE OF THE STUDY: Study of bone structure in postmenopausal women with diabetes mellitus.

MATERIALS AND METHODS OF RESEARCH: We examined 52 women with type 2 diabetes mellitus. The age of the examined patients was 52.12 ± 3.8, who were in the postmenopausal period of menopause. 8 women had normal body weight, 24 were overweight, 18 were obese; BMI ranged from 24 to 37 kg/m2. All women were postmenopausal, lasting from 2 years to 20 years (median 16 years). The duration of the disease ranged from 6 to 25 years (median 8 years). The average age was 57.89-+3.63 years. Concomitant pathologies included arterial hypertension (n=77), coronary heart disease (n=28). Exclusion criteria were: age over 70 years; a history of endocrine system diseases (hypercorticism, thyrotoxicosis, hypopituitarism, polyglandular syndromes); rheumatic diseases (rheumatoid arthritis, ankylosing spondylitis, diffuse connective tissue diseases); diseases of the digestive system (malabsorption syndrome, conditions after gastrectomy, bypass surgery on the gastrointestinal tract, liver failure); kidney diseases of non-diabetic nature; diseases of the blood system; alcoholism and drug addiction; anamnestic indications for taking glucocorticoids, immunosuppressants, thiazolidinediones, bisphosphonates, calcitonin, strontium preparations; postmenopausal replacement therapy, indications in the anamnesis of the presence of stroke, heart attack. The study also did not include persons with proteinuric stage of nephropathy and proliferative retinopathy. During the examination period, patients did not receive medications that could affect bone density. The mandatory scope of diagnostic studies complied with the methodological recommendations of the WHO Expert Committee - and included

clinical blood and urine tests, biochemical blood tests, instrumental research methods - blood pressure measurement, ECG, chest x-ray, ultrasound of the abdominal cavity and kidneys. All patients were examined by an ophthalmologist and a neurologist to identify symptoms of retinopathy and neuropathy. The history of the disease, features of the course, and the age at which diabetes mellitus debuted were studied in detail. The degree of compensation of diabetes mellitus, the presence of acute complications of diabetes mellitus - ketoacidosis, hypoglycemic conditions - were retrospectively assessed. Along with the typical symptoms of diabetes mellitus, complaints from the skeletal system were actively detected. Attention was paid to the lifestyle of the patients - compliance with the treatment regimen prescribed by the endocrinologist, dietary habits, physical activity, the presence of bad habits, factors of osteoporosis. When studying the medical history, such features were revealed as the age at which diabetes mellitus manifested, compliance with the treatment regimen (as perceived by the patient), family history of diabetes mellitus, osteoporosis, and the presence of bad habits - smoking, alcohol abuse. Complications of diabetes mellitus occurred: diabetic polyneuropathy in 100% of cases; diabetic retinopathy 37.5%. Of the 50 women represented in this group, 4 (8%) had a history of early menopause, 2 (4%) had menstrual irregularities. All patients received therapy with hypoglycemic drugs: drugs of the biguanide group and sulfonylureas. Results and discussions: The degree of compensation for diabetes mellitus in this group of patients was different. Only 14 women (28%) had type 2 diabetes in a state of compensation, the level of glycated hemoglobin was 6.5%, 20 women (40%) had subcompensated diabetes (glycated hemoglobin - up to 7.5%) and 16 women had diabetes mellitus. diabetes was in a decompensated state - glycated hemoglobin >7.5%. When studying heredity, a high frequency of family history of diabetes mellitus (35 (70%)) and osteoporosis (15 (30%)) was revealed. The presence of bad habits - smoking, drinking alcohol - was noted with equal frequency: 5 patients were smokers - 10%, 5 patients drank alcohol - 10%. The results of a biochemical examination of this group of patients included determination of the lipid spectrum and the state of phosphorus-calcium metabolism. When examining lipid metabolism, the following data were obtained: total cholesterol - 5.81-+0.5 mmol/l; LDL - 1.52 -+ 0.02 mmol/l; HDL - 1.78-+0.03 mmol/l; triglycerides - 1.12-+0.02 mmol/l; atherogenic coefficient - 1.87-+0.04 mmol/l. In addition to determining the biochemical analysis of total calcium, phosphorus and alkaline phosphatase, the level of parathyroid hormone, osteocalcin. Thyroid dysfunction was not detected in this group of patients. Background hormone levels: TSH -2.47-+0.1 μIU/ml; total T4 - 107.31-+1.5 pmol/l; total T3 -3.93-+ 0.58 pmol/l. It is known that impaired renal function can significantly affect the state of bone metabolism. In this regard, we conducted a study of the functional state of the kidneys: total protein - 73.79±1.57 g/l, creatinine 84.13±1.75 μmol/l, urea - 5.4±1.12

mmol/l , potassium - 4.2±1.2 mmol/l, sodium - 136.4±1.1 mmol/l. Bone loss was assessed by dual-energy x-ray absorptiometry using DXA (QDR-4500 Elite device from Hologic, USA. The study was performed in three standard sections of the skeleton (lumbar spine, proximal femur, forearm). For statistical processing of the obtained data, an applied statistical program was used analysis "StatSoft Statistica v.6". 20 women (40%) had subcompensated diabetes mellitus (glycated hemoglobin - up to 7.5%) and 16 women had decompensated diabetes mellitus - glycated hemoglobin >7.5%. When studying heredity, a high frequency of family history of diabetes mellitus (35 (70%)) and osteoporosis (15 (30%)) was revealed. The presence of bad habits - smoking, drinking alcohol - was noted with equal frequency: 5 patients were smokers - 10%, 5 patients drank alcohol - 10%. The results of a biochemical examination of this group of patients included determination of the lipid spectrum and the state of phosphorus-calcium metabolism. When examining lipid metabolism, the following data were obtained: total cholesterol - 5.81-+0.5 mmol/l; LDL - 1.52 -+ 0.02 mmol/l; HDL - 1.78-+0.03 mmol/l; triglycerides - 1.12-+0.02 mmol/l; atherogenic coefficient - 1.87-+0.04 mmol/l. In addition to determining the biochemical analysis of total calcium, phosphorus and alkaline phosphatase, the level of parathyroid hormone, osteocalcin. Thyroid dysfunction was not detected in this group of patients. Background hormone levels: TSH -2.47-+0.1 μIU/ml; total T4 - 107.31-+1.5 pmol/l; total T3 -3.93-+ 0.58 pmol/l. It is known that impaired renal function can significantly affect the state of bone metabolism. In this regard, we conducted a study of the functional state of the kidneys: total protein - 73.79±1.57 g/l, creatinine 84.13±1.75 μmol/l, urea - 5.4±1.12 mmol/l , potassium - 4.2±1.2 mmol/l, sodium - 136.4±1.1 mmol/l. Bone loss was assessed by dual-energy x-ray absorptiometry using DXA (QDR-4500 Elite device from Hologic, USA. The study was performed in three standard sections of the skeleton (lumbar spine, proximal femur, forearm). For statistical processing of the obtained data, an applied statistical program was used analysis "StatSoft Statistica v.6". 20 women (40%) had subcompensated diabetes mellitus (glycated hemoglobin - up to 7.5%) and 16 women had decompensated diabetes mellitus - glycated hemoglobin >7.5%. When studying heredity, a high frequency of family history of diabetes mellitus (35 (70%)) and osteoporosis (15 (30%)) was revealed. The presence of bad habits - smoking, drinking alcohol - was noted with equal frequency: 5 patients were smokers - 10%, 5 patients drank alcohol - 10%. The results of a biochemical examination of this group of patients included determination of the lipid spectrum and the state of phosphorus-calcium metabolism. When examining lipid metabolism, the following data were obtained: total cholesterol - 5.81-+0.5 mmol/l; LDL - 1.52 -+ 0.02 mmol/l; HDL - 1.78-+0.03 mmol/l; triglycerides - 1.12-+0.02 mmol/l; atherogenic coefficient - 1.87-+0.04 mmol/l. In addition to determining the biochemical analysis of total calcium,

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RESEARCH RESULTS. In all patients included in the study, in three parts of the skeleton, the severity of bone mineral density deficiency (proportions of osteopenia: -2.5<T<-1.0 and osteoporosis - T <-2.5) occurs in 26 patients (65%). At the same time, the percentage of patients diagnosed with osteoporosis (T < - 2.5) is 42% - 21 patients. Moreover, the severity of bone mineral density deficiency in different parts of the skeleton is distributed unevenly. Osteoporosis most often occurs in the lumbar spine - 19 patients (90.5%); This is followed by the proximal femur - 14 patients (66.7%) and osteoporosis is least often detected in the distal forearm - 7 patients (33.3%). The most typical changes in BMD are in 2 standard sections

(lumbar spine) - in 11 patients (52.5%), or in 1 standard section - 8 (38%) (in the lumbar spine), much less often in 3 standard study areas (lumbar spine and forearm) - in 2 patients (9.5%). Assessing the results of the study, we assessed diabetes mellitus as the main factor determining the further progression of bone tissue pathology. In this regard, we assessed the influence of some qualitative and quantitative indicators in the development of changes in bone mineral density. At the same time, we divided all patients into 2 groups: patients with osteoporosis and patients without osteoporosis. In patients with osteoporosis, a significant ($p < 0.001$) presence of bad habits was revealed ($p < 0.05$). A direct correlation between changes in bone mineral density and the level of glycated hemoglobin was revealed ($r = 0.32$; $p = 0.02$). We also obtained a positive correlation between complications of diabetes mellitus and bone mineral density ($r = 0.38$; $p = 0.03$). A positive correlation was also revealed between the duration of diabetes mellitus and the state of bone mineral density. Our examination of 52 postmenopausal women with type 2 diabetes revealed changes in BMD in 42%. In most cases, this category of patients has normal BMD values. Only 21 (42%) had a decrease in BMD - osteopenia (30%) and 12% had osteoporosis. The changes we found in BMD in women with type 2 diabetes are similar to the data obtained by Nicodemus K. K et al., Rakic V. et al. and Gerdhem P. [12,13]. However, the first team of authors did not study BMD of the spine, and the other two studies were carried out on a contingent of elderly and senile women. We also found that women with altered BMD values had an average body weight of 7.8 kg less than women with normal BMD values. Our study of phosphorus-calcium metabolism did not reveal changes in these parameters. A major role in the regulation of calcium and phosphorus homeostasis belongs to parathyroid hormone (PTH). In our study, we did not detect any changes in PTH levels. Our study revealed a positive correlation of BMD with the level of glycated hemoglobin, which confirms that hyperglycemia may be a leading pathogenetic factor. A positive correlation with the duration and complications of diabetes mellitus was also revealed. It was also found that a postmenopausal duration of more than 1.5 years contributes to the risk of developing osteoporosis. Considering that hyperglycemia is now recognized as the main pathogenetic factor that negatively affects bone tissue in diabetes, adequate glucose-lowering therapy may be one of the measures to prevent osteoporosis in patients with type 2 diabetes [14]. In addition to glucose-lowering therapy, physical activity is often recommended for patients with diabetes. Diabetes, especially with type 2 diabetes, may also play a role in the prevention of osteoporosis. Thus, there is evidence of improved microcirculation of bone tissue during physical activity. Thus, today, improving glycemic control, moderate physical activity and preventing diabetes complications are undoubtedly preventive measures against fractures in patients with type 2 diabetes.

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