

FEATURES OF BONE MINERAL DENSITY IN PATIENTS WITH DISEASES OF THE DIGESTIVE SYSTEM

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Abstract *The population (age, gender) has been established, decrease in body mass index, menopause), clinical and laboratory factors indicating a high risk of a decrease in bone mineral density in this category of patients. The data on the frequency of occurrence of bone mineral density disorders in patients with chronic pancreatitis, cirrhosis of the liver, cholelithiasis, inflammatory bowel diseases, as well as diseases accompanied by malabsorption syndrome (gluten enteropathy, short small intestine syndrome) are presented. The article is devoted to the study of the clinical features of the course of diseases of the gastrointestinal tract and liver in the formation of osteopenia and osteoporosis.*

Keywords: *violation of bone mineral density; densitometry; biliary insufficiency; gallstone disease; chronic pancreatitis; malabsorption syndrome; cirrhosis of the liver.*

INTRODUCTION

Hypocalcemia leads to activation of the parathyroid glands and secondary hyperparathyroidism. An absolute or relative deficiency of vitamin D, moreover, causes a violation of the mineralization of organic the matrix.. All these diseases can provoke a decrease in calcium absorption, often combined with impaired vitamin D metabolism and protein deficiency. The result of these complex disorders is in most cases osteopenia. One of the pathogenetic links in the development of osteoporosis is a violation of the oxidation of vitamin D in the liver. The spectrum of pathology of the gastrointestinal tract, fraught with the development of disorders of bone mineral density (osteoporosis, osteopenia), is very wide: diseases of the liver, intestines, pancreas, biliary tract According to the literature, it is known that 90% of vitamin D synthesis takes place in the liver, where the first hydroxylation reaction of cholecalciferol and calciferol is carried out with the participation of the microsomal enzyme 25-hydroxylase. Particular importance is attached to bile acids, the main physiological significance of which lies in the emulsification of fats, the formation of lipid-bile complexes. In addition, bile acids activate pancreatic lipase, and therefore facilitate the absorption of fat-soluble vitamins, in particular vitamin D. The nature of pathological processes in the digestive organs, their severity and duration determine the predominance of one or another type of metabolic osteopathy and its severity. Mechanisms of pathogenetic disorders of bone remodeling processes in gastroenterological patients according to the literature They are represented by a violation of the absorption processes of vitamin D, calcium, proteins, fats, which in turn is accompanied by a violation of vitamin D metabolism. The high activity of inflammatory cytokines and the disconnection of bone remodeling processes lead to a change in the synthesis of parathyroid hormone and thyroid hormones. Accompanying changes in the form of a decrease in estrogen and testosterone levels, as well

as ongoing glucocorticoid therapy, cause violations of bone mineralization. Due to the objectification of the diagnosis of metabolic pathology of the bone system (that is, methods that allow assessing bone mineral density, such as densitometry, biochemical markers of bone resorption and osteogenesis), it is now possible to more accurately determine the prevalence of osteopenia in gastroenterological diseases and assess this problem from the point of view of evidence-based medicine. All of the above served as the basis for the purpose of the study — to develop criteria for the prognosis of metabolic disorders of bone tissue and improve the effectiveness of prevention and treatment of osteopenia in gastroenterological patients based on the pathogenetic features of its development.

MATERIALS AND METHODS OF RESEARCH

100 patients with chronic pancreatitis were examined: 47 (47%) men and 53 (53%) women, the average age was 51.0 ± 10.2 years. In 52% of patients, CP was associated with alcohol intake, and 48% were diagnosed with biliary pancreatitis. Of the 53 women surveyed, there were significantly more menopausal women — 40 (75.5%), and 13 (24.5%) women had preserved menstrual function ($\chi^2 = 21.7$, $p < 0.001$). The duration of menopause ranged from 1 year to 15 years. The study included 56 (56%) people with uncomplicated CP. 44 (44%) patients had complications of CP (postnecrotic cysts, calcification, pseudotumor pancreatitis, pancreatic resection). 75 patients suffering from cirrhosis of the liver of various etiologies and duration of the disease were examined. There are 54 women among them ($72 \pm 6,1\%$), 39 ($72 \pm 7,2\%$) of them were menopausal, and 21 male ($28 \pm 9.8\%$). The average age was 56.4 ± 12.3 years for women and 51.2 ± 7.9 years for men. The etiology of liver cirrhosis among the examined patients was distributed as follows: primary biliary cirrhosis was detected in 27 patients ($36 \pm 9.2\%$), alcoholic cirrhosis — in 34 ($45.3 \pm 8.5\%$), cirrhosis of the liver of other etiology (viral, mixed (alcoholic and viral), Wilson's disease — Konovalov, of unspecified etiology) — in 14 ($18.7 \pm 10,4\%$). The duration of the disease in 28 ($37.3 \pm 9.1\%$) patients was more than 5 years, in 47 ($62.7 \pm 7.1\%$) — less than 5 years. In the analysis of hepatic cell insufficiency on the Child-Pugh scale, class A was established in 44 ($58.7\% \pm 7.4$) patients, class B in 16 ($21.3 \pm 10.2\%$), class C in 15 ($20 \pm 10.3\%$). 60 people with diseases accompanied by impaired absorption syndrome were examined (gluten enteropathy, short thin syndrome intestinal diseases) and inflammatory bowel diseases (Crohn's disease, ulcerative colitis) at the age of 20 to 70 years with a disease duration of one to 20 years. The average age of the patients was 47.4 ± 7.3 years, among them there were 50 (83%) women and 10 (17%) men. About half of all the examined patients were female patients with gluten enteropathy, half of whom were menopausal. The group of patients with postresection syndromes numbered 18.3%, with inflammatory bowel diseases — 26.7%. 68 patients with pathology of the biliary system were examined, including 31 (45.6%) with GI and 37 (54.4%) who underwent cholecystectomy. Among the surveyed, 63 ($92.6 \pm 3.1\%$) were women and 5 ($7.4 \pm 3.1\%$) of men.

Have been studied indicators of phosphorous-calcium metabolism (calcium, phosphorus in blood and urine), the level of parathyroid hormone, calcitonin, testosterone, a marker of bone resorption — CrossLaps, TNF-2, the level of vitamin D metabolites (25OHD3 and 1,25 (OH) 2 D3). Bone mineral density was determined by dual-energy X-ray absorptiometry on the

Lunar DPX 21200 apparatus. The state of the BMD was assessed according to the criteria of the Ti Z-scale and in g / cm^2 . Statistical processing of the results was performed using Statistica statistical programs 6.0 and Biostat. The significance level of the error (probability of error of the first kind) was considered reliable at $\alpha \leq 0.05$ with sensitivity (probability of error Type II) $\beta = 0.8$.

THE RESULTS AND THEIR DISCUSSION

The results of the study demonstrated a high prevalence of BMD disorders among patients with chronic pancreatitis (CP). Osteopenia occurred in 57% of patients (47.2 – 66.8; 95% CI), and in 32% (19.9 – 44.1; DI 95%) of them showed a decrease in BMD to the values of criterion T, which are classified like osteoporosis. During densitometry, a decrease in BMD to the level of osteopenia was most often noted — in 39% of cases. Of these, in 18% of cases, there was a combined lesion of the spine both the hips and 14% of patients have an isolated lesion of the spine. In 17% of cases, there were changes in BMD before osteoporosis in the spine, and in 6% — osteoporosis in the hip area. Thus, there was no characteristic localization of osteoporosis and osteopenia in patients with CP.

The incidence of osteopenia among the examined women with preserved menstrual function was 61.5% (35-88; CI 95%), among menopausal women — 65% (50.3 – 79.7; CI 95%), and among men — 48.9% (34.6 – 63.2; CI 95%) of patients. The confidence intervals of the frequency of osteopenia overlap each other. This indicates that there is no significant difference between men and women in the prevalence of osteopenia in patients with CP. According to the tasks set, the patients were divided into two groups depending on the severity of external secretory pancreatic insufficiency. The criterion for assessing the degree of exocrine insufficiency was the level of pancreatic elastase E1 in the stool. The first group consisted of 59 patients with CP with reduced elastase levels (below 200 mcg / g), and 41 patients in the second group HP with normal levels of fecal elastase (from 200 mcg / g and above). The average level of fecal elastase E1 in the 1st group of patients was 65 ± 41.2 mcg / g and was significantly lower than in the second group: 361 ± 142 mcg / g ($p = 0.002$). The average age of patients in groups 1 and 2 did not significantly differ ($p = 0.916$). Men prevailed in group 1 ($\chi^2 = 10$, $p = 0.002$), and women in group 2. Significantly, the complicated course of CP was more common among patients with CP with exocrine pancreatic insufficiency ($\chi^2 = 14.6$, $p < 0.001$) and the alcoholic etiology of CP ($\chi^2 = 9.3$, $p = 0.002$). There was no significant difference between the groups in terms of the duration of CP and BMI. The level of calcium and phosphorus in the blood of the patients included in the study was within the normal range, but its level differed depending on the state of the external secretory function of the pancreas. Patients with BPH had significantly lower levels of calcium and significantly higher levels of phosphorus in the blood.

The level of $1,25(OH)_2 D_3$ — calcitriol was also significantly lower in extracretory pancreatic insufficiency, but the number of patients. There was no significant difference with calcitriol deficiency. The level of CrossLaps protein was significantly higher in the group of patients with preserved function Pancreas, its average values exceeded the norm in 76% of patients, which was significantly more common than in patients with BPH. The average values of TNF α in the blood did not differ significantly. TNF α was elevated in 15% of

patients with BPH and in 12% of patients with preserved pancreatic exocrine function, which had no significant differences.

There was no correlation between BMD and TNF content. Thus, in the patients we examined, there was no effect of sex hormones and the proinflammatory cytokine TNF on the risk of osteopenia.

In men, one of the risk factors is a decrease in BMD is a decrease in testosterone levels. Among the men we examined, only 3 (6.3%) there was a decrease in testosterone levels below normal. Two of them had osteopenia, and one had a normal BMD. The data we obtained do not allow us to establish a relationship between osteopenia and a decrease in testosterone in men, there was no correlation between BMD and testosterone levels. In the examined men, BPH was observed in 76% of patients, and osteopenia — in 48.9%. Secondary hyperparathyroidism was observed in 17 (74%) patients with osteopenia, of which 15 (88%) developed against the background of vitamin D deficiency, in 3 (12%) secondary hyperparathyroidism was not associated with vitamin D deficiency, but increased excretion of fatty acid salts (soaps) with feces was noted. Thus, out of 23 men with osteopenia, the main cause in 17 (74%) patients was secondary hyperparathyroidism, and in 2 (9%) patients the most likely factor that led to a decrease in MPCT was hypogonadism, which was confirmed by a decrease in testosterone levels. In 4 (17%) patients in our study, it was not possible to find the causes of a decrease in BMD, they can be considered as patients with idiopathic osteoporosis.

Among menopausal women with CP, 24-54% have postmenopausal osteoporosis, which is not associated with pancreatic disease, and 46-76% of menopausal women may have a combined variant of osteoporosis – postmenopausal, burdened with secondary osteoporosis. In the process of analyzing the obtained MPCT data in patients with cirrhosis of the liver, all the examined patients were divided into three groups. The first group included patients with osteoporosis in at least one of the studied departments, the second group included patients with osteopenia, respectively, and the third group included patients without BMD disorders.

During the examination, osteopenia was detected in 35 ($46.7 \pm 8.4\%$) patients, osteoporosis in 19 ($25.3 \pm 10\%$), and no changes in bone mineral density were found in 21 ($28 \pm 9.8\%$) patients. Thus, in patients with cirrhosis of the liver, a decrease in BMD was found in 72% ($62.2 - 81.8$; CI 95%). Osteopenia and osteoporosis in women were found in 77.8% of the surveyed, which was significantly more common than among men — 42.8%, $p = 0.01$. Among women, a decrease in BMD was most often observed in the group of menopausal women — 82%, but the difference between the group of women with preserved menstrual function, in whom a decrease in BMD was found in 66.7%, was not significant. The etiology of liver cirrhosis significantly influenced the prevalence of osteoporosis and osteopenia. Among patients with PBC, a decrease in bone mineral density was found in 96.2% of the examined patients, while among patients with alcoholic cirrhosis of the liver, osteoporosis and osteopenia were found in 47% ($p = 0.0008$). It was not possible to find a relationship between the degree of Child-Pugh liver failure and a decrease in bone mineral density. But there was a significant relationship between the duration of the disease and the frequency of osteoporosis and osteopenia. Thus, among patients with cirrhosis lasting less

than 5 years, a decrease in BMD was found in 63.8% of cases, and with a duration of more than 5 years — already in 85.7% of patients ($\chi^2 = 5.3$; $p = 0.021$). An increase in the prevalence of osteoporosis and osteopenia in patients with cirrhosis of the liver, depending on BMI, was not detected, perhaps this is caused by an increase in the weight of patients due to the presence of edematous ascitic syndrome, which leads to incorrect calculation of BMI. In patients with cirrhosis of the liver, loss of bone density in the lumbar vertebrae was observed in 85.2% of patients with reduced BMD, isolated osteopenia of the lumbar spine was diagnosed in 18 (33.3%) patients with cirrhosis of the liver, the average T criterion was -1.4 ± 0.3 ; in combination with hip osteopenia in 9 (16.7%) patients, the average criterion T of the spine was -1.8 ± 0.4 ; the average criterion of T of the femoral neck was -1.7 ± 0.5 . In 31.5% of patients with CP, BMD decreased to the level of osteoporosis. 5 (9.3%) of them had a combination of spinal osteoporosis with hip osteoporosis, the average criterion of T vertebrae was -4.1 ± 0.2 , the average criterion of T of the femoral neck was -3.1 ± 0.3 ; in 8 (14.8%) osteoporosis of the spine developed simultaneously with osteopenia of the femoral neck, the average criterion of T vertebrae was -3.0 ± 0.4 , the average criterion of T of the femoral neck was -1.6 ± 0.3 ; and 4 (7.4%) patients suffered from osteoporosis of the spine without a decrease in BMD in the hip area, the average criterion of T vertebrae is -3.1 ± 0.2 .

Thus, in the group of patients with cirrhosis of the liver, such population risk factors for osteopenia as age, decreased BMI, and the postmenopausal period in women are relevant. Osteopenia prevails in this pathology of the liver and osteoporosis in the spine compared to changes in bone mineral density in the femoral neck. In women suffering from cirrhosis of the liver, a decrease in bone mineral density is significantly more common than unchanged indicators. Metabolic pathology of bone tissue prevails in patients with primary biliary cirrhosis of the liver compared with cirrhosis of a different etiology. The degree of bone loss increases as the underlying disease progresses. About half of all examined patients with diseases accompanied by malabsorption syndrome were female patients with gluten enteropathy ($55 \pm 0.087\%$). During densitometry in this group, BMD was not changed in $27.2 \pm 0.148\%$ of patients. Changing the MPCT it was detected in $72.8 \pm 0.091\%$ of cases. The second largest group consisted of patients with inflammatory bowel diseases (IBD), among them $56 \pm 0.165\%$ of BMD was normal, and $44 \pm 0.188\%$ — reduced. And finally, the group of patients with postresection turned out to be the smallest syndromes, among which $82 \pm 0.128\%$ of all examined patients had signs of osteopenia / osteoporosis and only $18 \pm 0.272\%$ did not. When studying the localization of a violation of the BMD patients with celiac disease have a predominant lesion of the spine. A decrease in BMD by type of osteopenia and/or osteoporosis of the spine was significantly more common ($p = 0.045$) in 72.8% of patients with celiac disease, while hip neck osteopenia was observed in 45.5% of patients. In patients with postresection syndromes, combined spinal and hip lesions of the type of osteopenia were most common and/or osteoporosis — in 7 patients. Isolated hip osteopenia was found in only one person, as well as isolated spinal osteopenia.

The duration of menopause in women with normal BMD was significantly lower ($p = 0.015$). The prevalence of osteoporosis and/or osteopenia in patients with PCES was higher than in patients GI with preserved gallbladder, but the values were not statistically significant

($p = 0.266$). The number of patients with a history of fractures there were more in the group of patients with reduced BMD. The number of fractures per patient in both groups did not differ. When analyzing the correlation relationships, a significant correlation was found between BMI and the T criterion in the lumbar vertebrae and the T criterion in the hip region ($r = 0.32$; $p = 0.009$).

CONCLUSIONS

According to the data obtained, chronic pancreatitis, cirrhosis of the liver, cholelithiasis, inflammatory bowel diseases, as well as diseases accompanied by malabsorption syndrome (gluten enteropathy, short small intestine syndrome), exacerbate the risk of osteopenia / osteoporosis in patients with population risk factors. A decrease in BMD in patients with certain diseases of the digestive system occurs equally in both cortical and trabecular bone tissue, which indicates

the polyethologicity of osteopenia in this group of patients. The main population risk factors for certain diseases of the digestive system are female gender, menopause, and the clinical risk factor is the duration of the disease for more than 10 years. In some women, osteopenia is caused by menopause (primary postmenopausal osteoporosis); at the same time, osteoporosis occurs against the background of physiological menopause, as well as against the background of early or premature menopause due to diseases of the gastrointestinal tract. Some women have a combination of postmenopausal and secondary osteoporosis. For men in the vast majority, secondary osteopenia is detected (against the background of a decrease in testosterone levels due to diseases of the gastrointestinal tract) or idiopathic.

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