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Postmenopausal osteoporosis – clinical, biological and histopathological aspects

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Abstract

Osteoporosis is one of the most common disorders in postmenopausal women, affecting the quality of life and increasing the risk for fractures in minor traumas. Changes in the bone microarchitecture causes static changes in the body and affects motility. In this study, we analyzed two groups of women, one with physiological menopause and one with surgically induced menopause. The diagnosis of osteoporosis was suspected based on the clinical symptoms and confirmed by assessing bone mineral density by the dual-energy X-ray absorptiometry (DEXA). Comparing some clinical and biological aspects there was noted that a much higher percentage of women with surgically induced menopause exhibited increases in body mass index, changes in serum lipids, cholesterol, triglycerides, blood glucose, serum calcium, magnesemia and osteocalcin. In contrast, no significant differences were observed in the histopathological aspects of bone tissue examined from these two groups. In all patients, there was identified a significant reduction in the number of osteocytes and osteoblasts, the expansion of haversian channels, reducing the number of trabecular bone in the cancellous bone with wide areola cavities often full of adipose tissue, non-homogenous demineralization of both the compact bone and the cancellous bone, atrophy and even absence of the endosteal, and the presence of multiple microfractures. Our study showed that early surgically induced menopause more intensely alters the lipid, carbohydrate and mineral metabolism, thus favoring the onset of osteoporosis.

Keywords: osteoporosis, menopause, osteocalcin, body mass index, osteoporotic fracture, microfracture.

Introduction

Osteoporosis (OP) is defined as a systemic disease characterized by low bone mass, deterioration of bone microarchitecture, increased bone fragility and risk of fracture at mild trauma [1, 2]. It is an insidious, progressive systemic disease and affects both women and men [3]. Most often, it affects postmenopausal women. According to some authors [3], almost half of all postmenopausal women will have a fracture related to osteoporosis [4]. The most common fractures caused by osteoporosis are located in the proximal femur, humerus, neck, radio-carpal joint, ribs, vertebrae or pelvis [5–7].

Changes of the bone microarchitecture causes changes of the body, with the onset of scoliosis, thoracic kyphosis or lumbar lordosis and disorders of body movements, particularly of the spine, pelvis and legs. Most often, patients experience diffuse pain at the back, spine and legs, caused by bone changes and muscle atrophy [8].

Currently, osteoporosis is one of the most common problems, thus becoming a public health problem [9]. Statistical studies have shown that over 50% of adults over age 50 suffer from osteoporosis, and of these about 70% are postmenopausal women [9].

The most feared complications of osteoporosis are represented by fractures. For their treatment, the social costs are very high. Thus, worldwide, the direct and indirect costs for hip fractures in 1990 was estimated at 34.8 billion US dollars, and these costs are expected to rise up to 131.5 billion US dollars in 2050 [10]. In 2010, the EU countries spent about 67.7 billion euro for treating osteoporotic fractures [11, 12].

The mortality of osteoporotic fractures is quite high. According to studies in 2012, in the European Union, the number of deaths caused by osteoporotic fractures was estimated at 43 000 [12], of which 50% were due to hip fractures, 28% of vertebral fractures and 22% of other types of fractures [2].

Given the fact that the most common forms of osteoporosis are those that occur in postmenopausal women, in this study we aimed to evaluate certain clinical, histopathological and biological aspects at women with postmenopause osteoporosis.

Materials and Methods

The study group included 97 patients aged between 45 and 80 years old, admitted to the Department of Endocrinology, Emergency County Hospital of Craiova, Romania, between 2011 and 2015, clinically and ima-

gistically (dual-energy X-ray absorptiometry – DEXA) diagnosed with postmenopausal osteoporosis. The studied cases were selected in the Ambulatory of Endocrinology of the same Hospital by the specialist physicians, being directed to this consultation by family doctors.

In the study, 75 patients had physiological menopause, and 22 (including six patients with early surgical menopause) had surgically induced menopause. Clinically, all patients had signs and symptoms of menopause (at least 12 months of amenorrhea associated with vegetative lability, vasomotor disturbances, emotional lability, signs of desexualisation due to estrogen deficiency). The physical examination was completed by laboratory investigations aiming at: complete blood count (CBC), urea, creatinine, glucose, urine analysis exam, lipidogram (assessment: cholesterol, serum lipids, triglycerides), serum calcium (total and ionic), magnesemia.

For the assessment of bone metabolism, there were determined the serum osteocalcin (marker of bone formation) and serum carboxy-terminal type I collagen telopeptide-CrossLaps (marker of bone resorption); hormonally, there were determined the following serum hormones: thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), thyroxine (FT4), anti-thyroid peroxidase antibodies (ATPO), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), estradiol, progesterone.

The evaluation of bone mineral density for the diagnosis of osteoporosis was made by DEXA (MEDIX 90).

The histopathological (HP) examination was made on fragments of bone harvested from a total of eight patients (six patients with physiological menopause and two patients with surgical menopause) who were diagnosed with hip osteoporosis fracture and requiring hip replacements. The patients were hospitalized in the Department of Orthopedics, Emergency County Hospital of Craiova, between 2009 and 2011. The biological material obtained following surgery or head and femoral neck were immediately put into 10% neutral formalin-fixing solution. Then, to facilitate the process of the histological fixing, the head and femoral neck were fragmented using a small saw with a blade smooth, in longitudinal sections of 2–4 mm thickness. After this, the process was continued for fixing neutral formalin for seven days at room temperature in the laboratory. After fixation, the biological material was washed using tap water for 24 hours, to remove any residual formaldehyde from the tissue. The bone fragments were then subjected to a decalcifying process time of 25–30 days, in a 5% trichloroacetic acid solution. The decalcifying solution was replaced by a fresh one every 4–5 days. After a complete decalcification, when the bone pieces have become soft, elastic and flexible, they were taken about 2/2 cm fragments that have been washed in tap water for 24 hours to remove the decalcifying solution. Then, the biological material embedded in paraffin, by using the classical histological techniques. Using a microtome, there were made 4–5 μm thick sections, which were stained with Hematoxylin–Eosin (HE) and green light Goldner–Szekely (GS) trichromic. The HP examination was performed at Nikon Eclipse 55i optical microscope (Nikon, Apidrag, Romania) equipped with integrated 5 megapixels charge-coupled device (CCD) camera for the handling and processing of microscopic images.

Results

In our study, we identified two categories of osteoporosis according to the mechanism of menopause onset:

- physiological menopause, present in 75 (77.32%) patients, eight (8.24%) patients with early menopause (menopause before the age of 40 years), and 67 (69.08%) with physiological menopause;
- the surgical menopause was present in 22 (22.68%) patients, of which six (6.19%) patients had surgically induced menopause until the age of 40 years and 16 (16.49%) patients with surgical menopause onset over the age of 40 years (Figure 1).

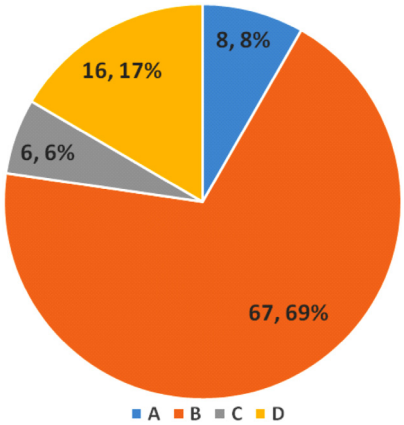

Figure 1 – ***Graphical representation of the distribution of different types of menopause found in women from our study group: A – Early physiological menopause; B – Physiological menopause; C – Surgical menopause after 40 years old; D – Surgical menopause below 40 years old.***

Of the 75 patients with osteoporosis and physiological menopause, 11 (14.66%) patients had a history of osteoporotic fracture, and of the 22 patients with surgical menopause and osteoporosis, four (18.18%) patients had already historical presence of osteoporotic fracture. From these data, it appears that a higher percentage of women with osteoporosis and surgically induced menopause had induced osteoporotic fractures than women with physiological menopause.

The diagnosis of osteoporosis was suspected based on clinical symptoms presented by patients on clinical examination and confirmed by assessing bone mineral density using DEXA technique. By this method, there was assessed the T-score representing the comparison result in bone mineral density (BMD) of the patient with the average young adults, and specifically the number of standard deviations that the patient's BMD is different compared to a reference population: young people of the same race and sex with the assessed patient. All the studied patients had T-scores $\leq$-2.5.

The clinical examination showed that most patients have a higher BMI (body mass index) than normal. Thus, of the 97 patients with osteoporosis, only 35 (36%) had

a normal body weight, while the remaining 62 (64%) patients were overweight or obese. The number of patients with physiological menopause, overweight or obese was 43 (57.33%), of which 22 overweight patients, 13 patients with first-degree obesity and eight patients with second-degree obesity. The number of overweight or obese patients with surgically induced menopause was 19 (83.66%), of which 12 were overweight patients, six patients with first-degree obesity and one patient with second-degree obesity (Figure 2). From these data, it may be observed that a much higher percentage of women with surgical menopause (83.66%) were overweight or obese, compared to the group of women with physiological menopause (57.33%).

The increase of body mass index was accompanied by changes in the lipid metabolism. Thus, of the 75 patients with physiological menopause, 45 (60%) of the patients had cholesterol values above 200 mg/dL, 41 (54.66%) had higher triglyceride levels than normal, and lipemia presented values increased over 42 (56%). Of the 22 patients with osteoporosis and surgical menopause, 17 (77.27%) had elevated cholesterol, triglycerides and lipemia.

Most patients who had high serum lipids, simultaneously presented both high triglycerides and cholesterol, all of which showing a major alteration of the lipid metabolism in patients with osteoporosis.

Regarding the carbohydrate metabolism, only nine patients had elevations of blood glucose "fasting" (115–189 mg/dL): six (8%) patients with physiological menopause and three (13.63%) patients with surgical menopause. All these patients were diagnosed with diabetes before study admission and had a specific antidiabetic treatment.

The assessment of the serum calcium in osteoporotic individuals showed that only 14 (14.43%) patients had hypocalcemia values (repeated during hospitalization) ≤8.8 mg/dL, with nine (12%) patients of the group with physiological menopause and five (22.72%) patients with surgical menopause.

Serum magnesium levels had low values (≤1.6 mg/dL) in 13 (13.4%) patients, eight (8.24%) patients with physiological menopause and five (5.15%) patients with surgical menopause.

Serum osteocalcin had normal values (15–46 ng/mL) in a total of 44 (45.36%) osteoporotic patients, with 36 (48%) patients in the group with physiological menopause and eight (36.36%) patients in the group with surgical menopause. A total of 53 (54.64%) patients had high levels of osteocalcin (>46 ng/mL), of which 39 (52%) patients were in the physiological osteoporosis group and 14 (63.63%) patients were in the group with surgical menopause (Figure 3).

Assessing bone resorption, performed by analyzing the carboxy-terminal type I collagen telopeptide (β-CrossLaps) serum showed the following: 78 (80.41%) patients had normal values (0.251±0.761 ng/mL) of which 57 (76%) were patients with osteoporosis and physiological menopause, and 21 (95.45%) patients had osteoporosis associated with surgical menopause. A total of 19 (19.59%) patients showed high values (>1.005 ng/mL) of serum β-CrossLaps, of which 18 (24%) patients had physiological menopause and only one patient (4.54%) had osteoporosis and surgical menopause (Figure 4).

Some patients were identified with osteoporosis and other disorders. Thus, 40 patients were diagnosed with hypertension, 28 with chronic autoimmune thyroiditis, 27 with hyperthyroidism, 18 with hypothyroidism, nine patients with diabetes, five patients with depression, four patients with various malignancies and three patients with rheumatoid arthritis (Figure 5).

Histopathological aspects of bone tissue in patients with osteoporotic hip fractures

In our study, we analyzed fragments of haversian bone and fragments of cancellous bone, from both physiological menopausal women and women with surgical menopause. We must mention that there were not observed any histopathological differences between the two groups.

In the compact bone tissue, there was observed a significant reduction of the number of osteoblasts and osteocytes and, particularly, at osteons internal blades (Figure 6). Also, most osteocytes appeared weak or absent, with a stained pyknotic nucleus and a weak acidophil cytoplasm, thus betraying a significant reduction in cell organelles. Some of the osteoblasts appeared empty because of a process of osteocyte lysis. The Havers channels occurred most often much wider with poor vascularity. Inside the Havers channels, there were found partially degraded scraps of bone and bone microfractures between blades (Figure 7). At the level of the interhaversian systems, the microfracture lines were more abundant, with tracks and various sizes (Figure 8). However, both haversian systems and interhaversian systems showed processes of bone demineralization, more or less accentuated, extremely variable as intensity and extending from one area to another and from one patient to another, characterized by reduction of histological staining intensity. Sometimes, bone demineralization was associated with changes in the collagen structure of bone blades (Figures 9 and 10).

In the cancellous tissue of the epiphysis of the femoral head, there was found a thinning of the bone trabeculae, with large areola cavities, often filled with fat and fibrous tissue (Figure 11). Here, there are highlighted more intense phenomena of bone demineralization, as compared with cancellous bone, and the presence of trabecular microfracture lines (Figures 12 and 13).

The trabecular bone was often lined by endosteal atrophy (Figure 14), sometimes even absent, the collagen fibers of areola inserting them and continuing with the collagen fibers in the bone trabeculae structure (Figure 15).

In the trabecular bone, there has been rarely identified the presence of osteogenic reactive endosteal cells (Figures 16 and 17), which shows that the turnover bone from osteoporosis is not completely and irreversibly prone to osteolysis, but there may be phenomena of osteogenesis by reactivating the endosteal cells. Unfortunately, in our study there were rarely observed any bone forming processes.

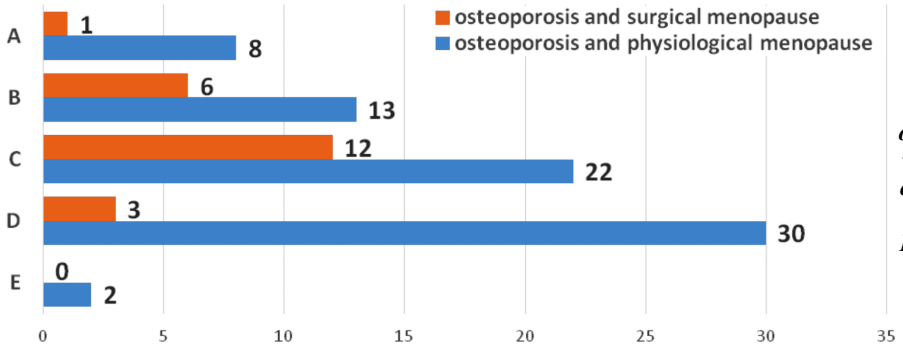

Figure 2 – ***Distribution of types of menopause according to weight in our study group: A – No. of women with second-degree obesity; B – No. of women with first-degree obesity; C – No. of overweight women; D – No. of normoponderal women; E – No. of underweight women.***

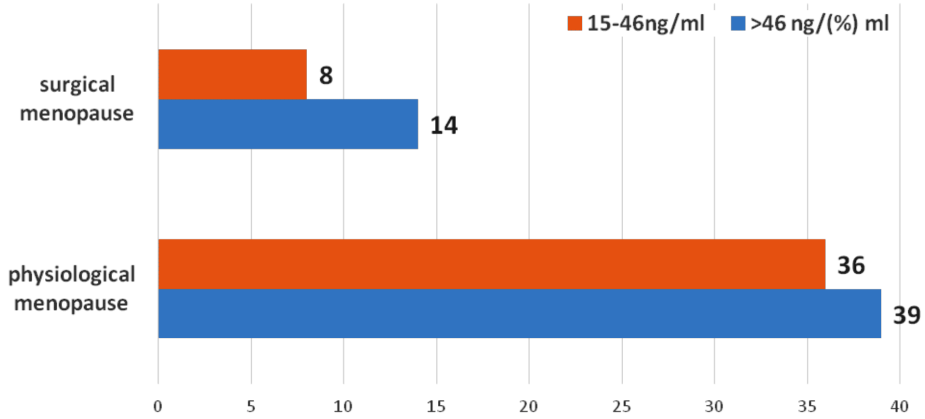

Figure 3 – ***Distribution of types of menopause according to a cut-off value for serum osteocalcin.***

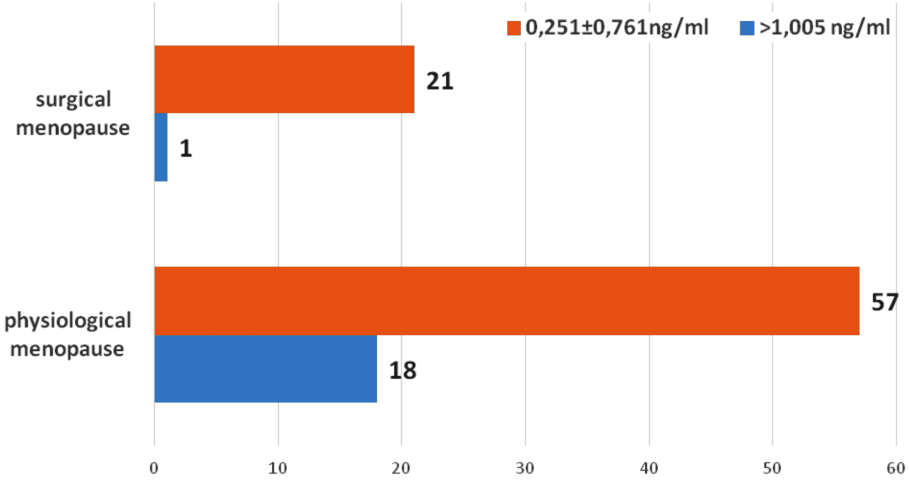

Figure 4 – ***Distribution of types of menopause according to a cut-off value for serum β-CrossLaps.***

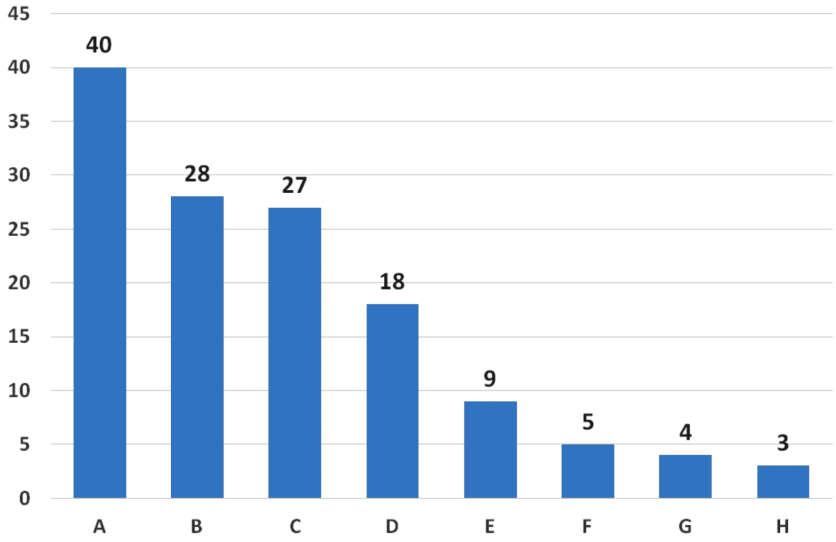

Figure 5 – ***Co-morbidities in our study group: A – Arterial hypertension; B – Autoimmune thyroiditis; C – Hyperthyroidism; D – Hypo-thyroidism; E – Diabetes mellitus; F – Depression; G – Neoplasia; H – Rheumatoid arthritis.***

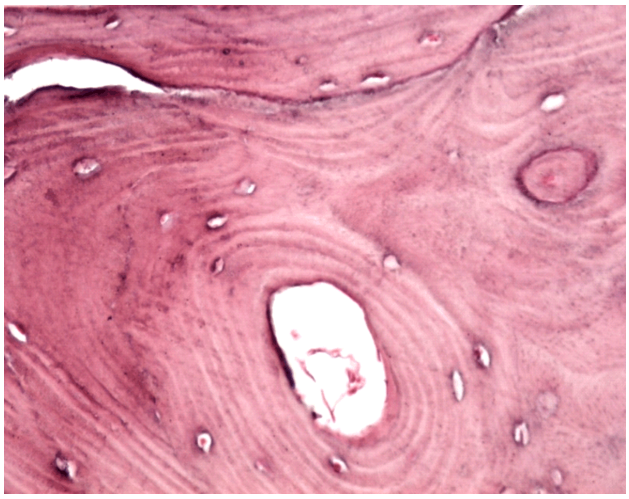

Figure 6 – ***Osteon with Havers channel widened, with rare osteocytes in the bone blades. HE staining, ×200.***

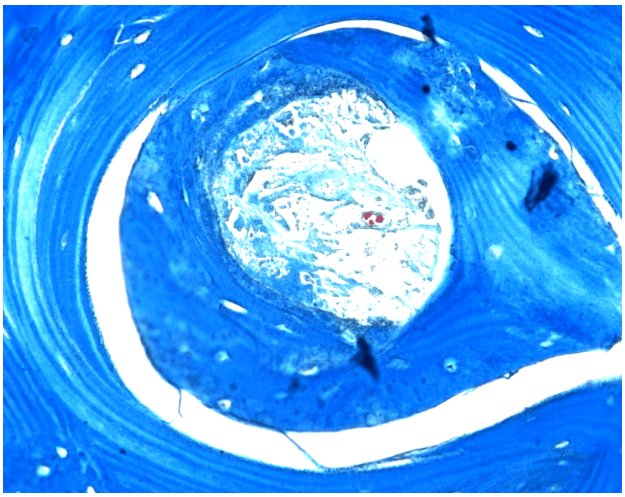

Figure 7 – ***Microscopic image of a cross-sectioned osteon showing a widened Havers channel, with reduced vasculature and lumen, occupying most of the bone, partially degraded. Among the bone blades there highlights a line of a microfracture. GS trichromic staining, ×200.***

Figure 8 – ***Microfracture lines at interhaversian systems. GS trichromic staining, ×200.***

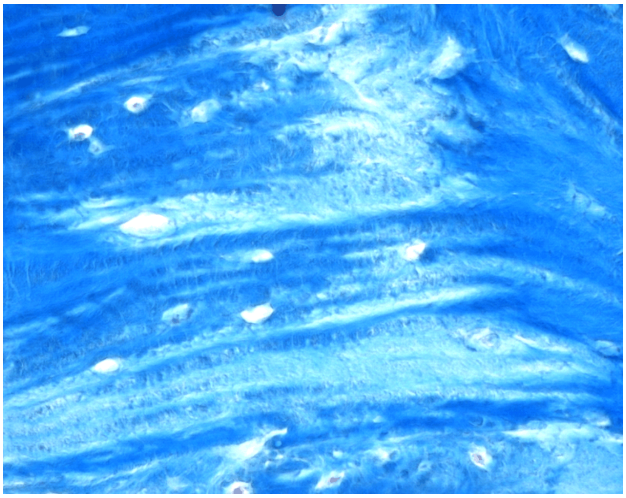

Figure 9 – ***Lamellar bone with diffuse inhomogeneous demineralization. GS trichromic staining, ×400.***

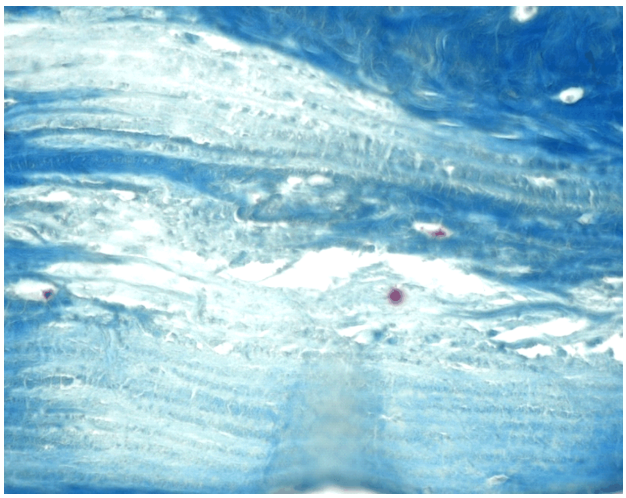

Figure 10 – ***Lamellar bone with massive demineralization associated with disorganization of collagen structures. GS trichromic staining, ×400.***

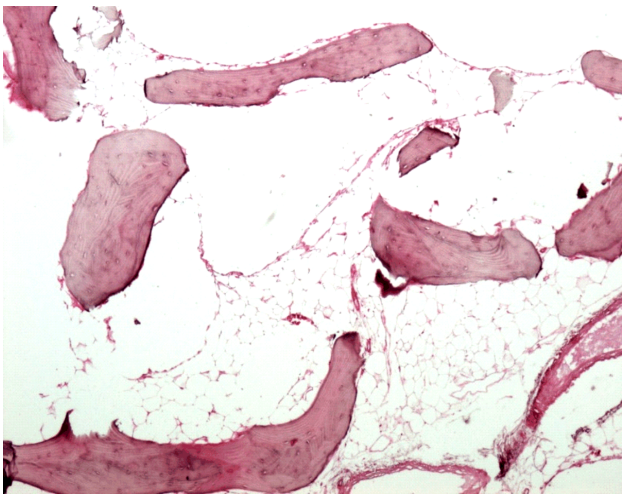

Figure 11 – ***Overview of the cancellous bone from the femoral neck with rarefaction of bone trabeculae and widening of the areola spaces. HE staining, ×40.***

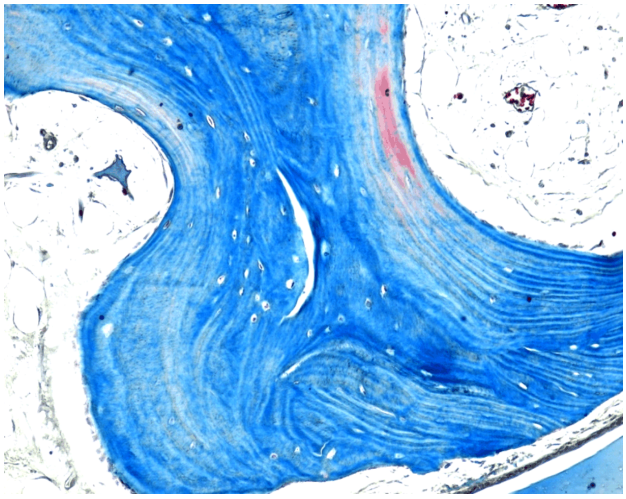

Figure 12 – ***Trabecular bone with diffuse homogeneous demineralization and the presence of microfracture lines. GS trichromic staining, ×100.***

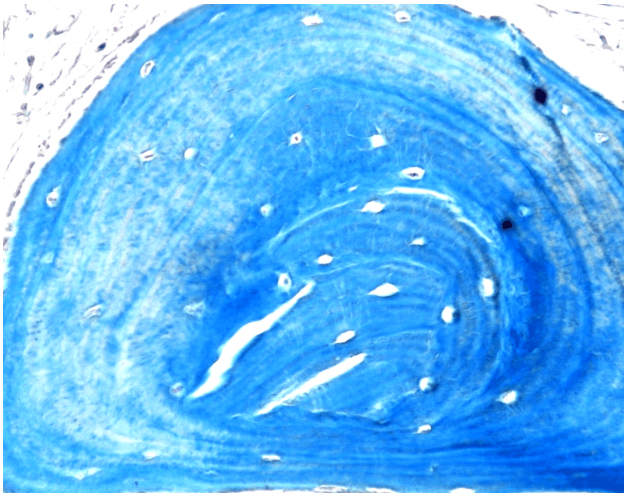

Figure 13 – ***Trabecular bone with massive demineralization and presence of two lines of microfracture. GS trichromic staining, ×200.***

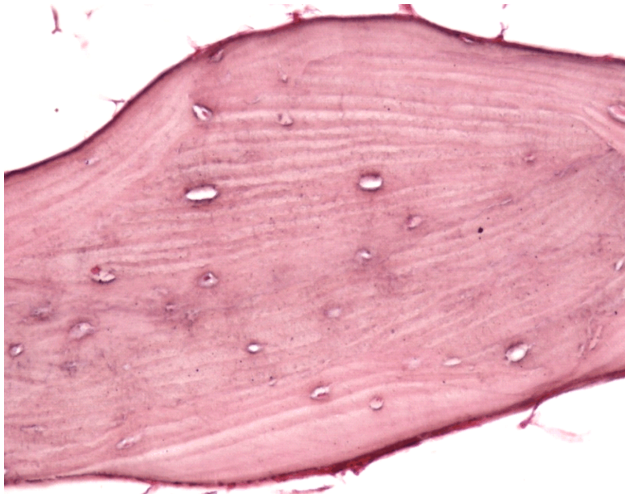

Figure 14 – ***Trabecular bone bordered by an atrophic endosteal. HE staining, ×200.***

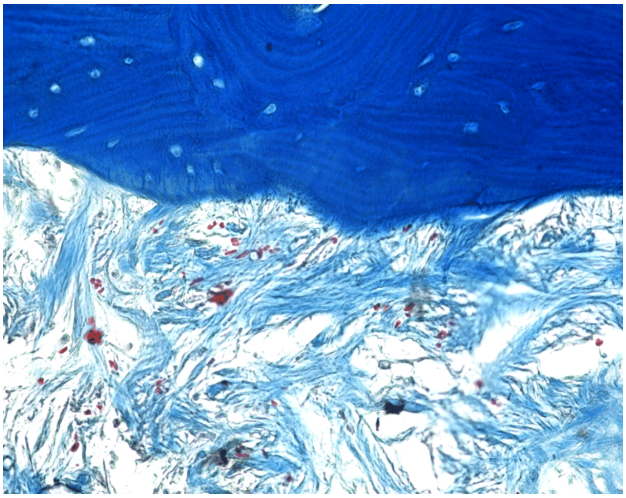

Figure 15 – ***Microscopic image of the trabecular highlighting a lack of the endosteal, which allowed the collagenous fibrous tissue to insert on the collagen matrix of the trabeculae. GS trichromic staining, ×200.***

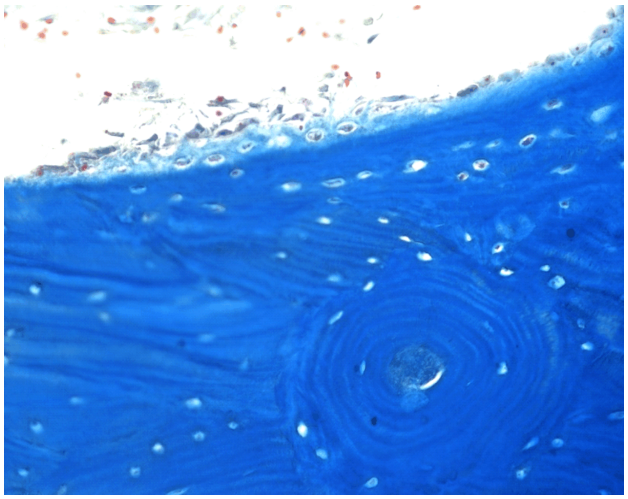

Figure 16 – ***Trabecular bone covered by a reagent, osteogenic endosteal area, with large, hypertrophied cells. GS trichromic staining, ×200.***

Figure 17 – ***Detail of the previous figure with osteogenic activity of the endosteal. GS trichromic staining, ×400.***

Discussion

Osteoporosis is one of the most important health problems affecting worldwide women in postmenopausal age [13]. According to some studies, the prevalence of osteoporosis is higher in industrialized countries, affecting about 13–18% of the adult population. Thus, in the major industrialized countries of the European Union, about 21% of women aged between 50 and 84 years old suffer from osteoporosis [2, 12]; in Sweden and the US, the osteoporosis prevalence is about 21.2% [14], while in China the prevalence of osteoporosis is estimated to be 15.7% [15]. Taking into account the increasing life expectancy and aging of the population, we can say that osteoporosis is, and will continue to be, a public health problem [16].

Based on the etiology, osteoporosis was divided into two categories: postmenopausal osteoporosis (type I) and senile osteoporosis (type II). Recent studies have suggested that estrogen deficiency is one of the most important factors intervening in the pathogenesis of osteoporosis, both women and men [17, 18].

Our study evaluated the two groups of women with postmenopausal osteoporosis: physiological menopause with surgically induced menopause, to evaluate the clinical, biological or histopathological possible differences.

The clinical examination showed that a very high percentage (64%) of people with osteoporosis were overweight or obese. Also, it was noted that there were significant differences between the two groups in terms of body mass index: in the patients with physiological menopause only 57.33% were overweight or obese, and in the patients with surgical menopause, the percentage of overweight or obese was 83.66%.

Our data are in accordance with other studies that have shown that the concomitant osteoporosis and obesity affect millions of women. Obesity may be a risk factor for osteoporosis localized at different levels [19–23]. For a long time there was considered that there was no link between the two conditions; however, clinical and experimental data in the last decades have shown that there is a complex relationship between the adipose tissue and the bone [24]. Clinical and experimental studies in the last 20 years have shown that the adipose tissue is not "tank passive energy" but it is a true active endocrine organ involved in the metabolism of the bone tissue, secreting various inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) [25] and adipokines (a variety of pro-inflammatory peptides), with negative effects on the bone tissue [26]. It also synthesizes a series of adipocyte hormones, such leptin and adiponectin, with varying effects on the bone tissue. If adiponectin stimulates the growth of the bone, by increasing the production of bone cells and bone matrix [27], leptin leads to a reduced bone mass [28].

The clinical data of our patients make us believe that osteoporosis has a complex pathogenesis and multifactorial etiology and the main risk factors are represented by the menopausal hormonal changes caused by it, reduced physical activity, excess food with obesity and corticosteroids. The involvement of risk factors in the development of osteoporosis is currently difficult to determine. Also, the clinical non-specific symptoms of osteoporosis make this condition proper diagnose and treatment to be a relatively late one. However, recent studies have shown that an increase in the abdominal fat may be considered a risk factor for the decrease in bone mineral density and the development of osteoporosis, both in women and in men, which suggests that an increase in the abdominal circumference would be an early clinical sign for reduced bone mineral density [29–31].

Body mass index increase in the patients with osteoporosis has been accompanied by a change in the lipid metabolism with increased serum serum lipids, triglycerides and cholesterol. The most affected were women with surgically induced menopause, where it was recorded a higher percentage of patients with elevated serum lipids, compared with the group of women with physiological menopause. We can say that early surgical menopause induced disruption of lipid metabolism characterized by increased serum lipids and obesity.

Increased lipids in the blood may be due to an increased intake of fat and other metabolic disorders that accompany menopause. It is known that adipocytes secrete leptin, a hormone that is involved in regulating appetite and bone remodeling [28, 32, 33]. According to some studies, the reduction in plasma level of leptin stimulates food ingestion, inhibiting energy consumption, which leads to the development of obesity, via increased expression of Y neuropetide synthesized by the neurons of the hypothalamus [34].

It should be noted that a rich in fat diet is often a cause for obesity and hypocalcemia, because fat interferes with the intestinal calcium absorption. It has been shown that free fatty acids can form insoluble salts, non-absorbable calcium and, therefore help to reduce calcium absorption in the intestine [35–37].

The relationship between osteoporosis and carbohydrate metabolism in our study appeared to be insignificant, being recorded only nine patients with type 2 diabetes, *i.e.*, 9.27% of the entire group patients. Given that the prevalence of diabetes can reach values of 35–37% in persons aged between 60 and 69 years old [38], we believe that osteoporosis is not correlated with changes in the carbohydrate metabolism. However, some authors have demonstrated that the metabolic changes that occur in type 2 diabetes mellitus, can impair calcium homeostasis with a negative impact on bone mass [39, 40].

Several studies support that osteoporosis is a serious complication in patients with diabetes [41, 42], because these patients have an increased risk of bone fractures [43–45] through the early onset of osteopenia or osteoporosis [46], which will lead to progressive decline in the bone volume [47], showing changes in the calcium and phosphate metabolism and delayed fracture healing [48].

The investigation of bone metabolism in our patients, by determining serum osteocalcin showed a total of 53 patients, accounting for only 54.64% had elevated levels of this biochemical marker, the rest having normal values for postmenopausal osteoporosis (increased to normal values in premenopausal).

Osteocalcin is a hormone secreted only by the osteoblasts. It stimulates the osteoblast proliferation, interferes with the homeostasis of calcium ions and speeds bone matrix mineralization. It also intervenes in the regulation of glucose metabolism in beta cells of the pancreas by

stimulating insulin release [49]. According to some studies, serum osteocalcin present low levels in women aged between 20 and 49 years, showing a progressive increase after the age of 50 years and even after 60 years [50].

Regarding serum β-CrossLaps, only 19 (19.59%) patients had this biochemically high parameter, the rest having normal values for postmenopause (increased to normal values in premenopause). Although they were recognized as markers of formation and bone remodeling, the data we have obtained confirm that the major biochemical markers of bone turnover (osteocalcin and β-CrossLaps) does not provide sufficient data for the diagnosis of osteopenia and osteoporosis [51, 52], its dosing them should be dynamically performed, more useful in assessing the treatment response.

Serum calcium and magnesium were not significantly correlated with osteoporosis, the majority of the patients with osteoporosis having normocalcemia and magnesemia.

The HP changes in bone tissue seen in patients who have suffered hip fractures were significant for osteoporosis. Both the Haversian compact bone tissue and the cancellous bone had a significantly low number of osteocytes, degenerate osteocytes with pyknotic nucleus or even the lack of osteocytes in osteoblast. These microscopic aspects reflect lower bone formation process and increased bone resorption, osteoporosis being characterized by an imbalance of the processes of bone formation and bone resorption [53, 54]. Bone demineralization, both in the compact and cancellous bone tissue, was totally heterogeneous, which makes us believe that osteocytes are the main cells responsible for the quality of bone protein matrix and for its mineralization. Therefore, we believe that the degeneration and apoptosis of osteocytes are the main causes for the loss of calcium salts of ossein. Similar microscopic aspects were also found by other authors, who obtained osteoporosis on experimental animals, caused by the induction of type 2 diabetes [55–58].

Another microscopic aspect presented by us was the atrophy, or even the disappearance, of the endosteal that defines bays of cancellous bone. We believe that endosteal atrophy or apoptosis contributes to the installation and progression of osteoporosis, these cells being a part of bone formation. At present there are not known the factors acting on endosteal and producing a reduction in the activity of these cells. In one case, on a limited area of trabecular bone cells, we identified a hypertrophied endosteal with osteogenic activity. Some authors, managing corticosteroid hormones in large doses in experimental animals have shown that the osteoblast cells from endosteal reduces their number and decreases their ability of synthesis of ossein and bone mineralization capacity [59, 60].

In our study, lack of bone formation and intensification processes of bone resorption caused enlargement of cortical bone Havers channels and areolas of cancellous bone with increased bone porosity. In the cancellous bone tissue, we found large amounts of adipocytes and sometimes-fibrous bones. According to some studies in women during post-menopause, there appeared a high bone turnover associated to a decreased bone mineral density and microarchitecture deterioration, resulting in an inefficient remodeling that decreases bone strength and increases fracture risk [61–64]. In this process of bone deterioration there are involved local adipocytes who secrete numerous endocrine and paracrine factors (adipokines, interleukin-6, TNF-α) that influence the activity of neighboring or more remote cells [65], including the processes of resorption and bone remodeling. Other studies have shown that the stromal cells in the bone marrow of the patients with osteoporosis express markers of differentiation into adipocytes at the expense of markers of differentiated osteoblasts, all of which suggesting that these patients have more pronounced bone resorption processes and osteosynthesis [66, 67].

The physiological processes of bone remodeling and resorption involved the osteoclasts, cells originating in the bone red marrow and in blood monocytes. In our study, we did not find the presence of these cells in large quantities, which makes us believe that they are less involved in the process of resorption and bone remodeling in osteoporosis. Relatively recent experimental data support that osteocytes inside bone structures and from the endosteal are capable of osteolysis (osteocytic osteolysis) [68–70] and are consistent with our observations on human subjects.

Another HP aspect commonly observed in our study was the presence of microfractures in the structure of osteons and trabecular bone of cancellous bone. We believe that they occur due to the loss of resistance and elasticity of bone caused by processes of bone resorption and bone remodeling. Some authors [71, 72] consider that microfractures represent a subclinical pathological response to microtraumas or excessive load exerted on bone tissue.

Conclusions

Our study group consisted of 97 patients with postmenopausal osteoporosis, of which 75 had physiological menopause, and 22 early surgically-induced menopause. In the group, 64% of patients with osteoporosis had higher body mass index, but the percentage of overweight women was much higher in the group with surgically-induced menopause. The increased body mass index was accompanied by changes in lipid metabolism to about 55% of the group of women with osteoporosis and physiological postmenopausal osteoporosis and about 75% of the group of women with osteoporosis and surgical menopause. The relationship between osteoporosis and carbohydrate metabolism appeared to be insignificant, only 9.27% of the patients being diagnosed with type 2 diabetes. In the patients, hypocalcemia was recorded at 14.43% and hypomagnesemia at 13.4%. Relative to the actual number of patients in each group, it was noted that a higher percentage of women with osteoporosis and surgical menopause presented hypocalcemia and hypomagnesemia compared to the group of women with osteoporosis and physiological menopause. Serum osteocalcin high levels were found in 52% of the patients with osteoporosis and physiological menopause and in 63.63% of patients with osteoporosis and surgical menopause, while serum β-CrossLaps levels were high in 24% of people with osteoporosis and physiological menopause and only 4.54% of the patients with osteoporosis and surgical menopause. The histopathological changes in bone tissue seen in patients with osteoporosis who had suffered hip fractures were represented by a significantly reduced number of osteocytes and osteoblasts, the presence of degenerate osteocytes with pyknotic nucleus, inhomogeneous demi-

neralization of bone tissue, atrophy or even disappearance of the endosteal, widening of the Havers channel, a reduction of the trabecular bone to cancellous bone with the emergence of large areola cavities often filled with fat and the presence of multiple microfractures, of various sizes, both in the compact bone tissue and at trabecular level of the cancellous bone tissue.

Conflict of interests

The authors declare that they have no conflict of interests.

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