

### CLINICAL AND EPIDEMIOLOGICAL FEATURES OF COMPLEX APPROACHES IN THE TREATMENT OF OSTEOPOROSIS IN SYSTEMIC SCLERODERMA

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### Annotation

Diseases of osteoporosis and the assessment of the patient is taken from the degree of fracture as a marker of many diseases. But bone mineral density (SMZ) is also associated with disease and the risk of fracture. Metabolic disorders associated with secondary osteoporosis are 2-3 times higher in women and in men with hip fractures and vertebral fractures. Globally, osteoporosis is the most common metabolic, bone disease, affecting more than 200 million people worldwide. In Europe, the United States and Japan, 75 million people are diagnosed with osteoporosis. As SMZ decreases, osteoporosis increases with age. Senile osteoporosis is more common in people over 70 years of age. Secondary osteoporosis can occur in any person. Although bone loss in women begins gradually, it accelerates menopause, with delivery at age 50 and beyond. The incidence of postmenopausal osteoporosis is highest in 50-70 women. Women are higher on osteoporosis. Half of postmenopausal women have fractures associated with life and osteoporosis; Ush develops a spinal deformity in 25% of women, and 15% experience hip fractures. Hip fractures are similar in different ethnicities.

**Keywords**: Osteoporosis, systemic scleroderma, vasculopathy, cellular, humoral autoimmune, densitometry, simple venipuncture, hormonal, diabetes mellitus, pregnancy.

## Introduction

Systemic scleroderma (TSD) is a disease of unknown connective tissue of unknown etiology, clinically heterogeneous and chronically progressive. It is based on three pathological processes: vasculopathy, cellular and humoral autoimmune conditions, and progressive visceral and vascular fibrosis in many organs. In the United States, the disease causes 9 to 19 cases per 1 million people each year. [2,33]

According to the National Osteoporosis Foundation (MOF), in 2010, more than 10 million adults over the age of 50 in the U.S. had osteoporosis, and more than 43 million had low bone mineral density. In 2015, there were 2.3 million osteoporotic



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fractures from nearly 2 million Medicare in the United States. Within 12 months of experiencing a new osteoporotic fracture, approximately 15 percent of patients experienced one or more subsequent fractures, and nearly 20 percent died. Mortality was highest in patients with hip fractures, with 30 percent dying within 12 months.

Many studies evaluating the prevalence and morbidity of osteoporosis use the degree of fracture as a marker of disease. But bone mineral density (SMZ) is also associated with risk of disease and fracture.

The risk of hip fracture and spinal fracture is 2-3 times higher in women and men with metabolic disorders associated with secondary osteoporosis.

Globally, osteoporosis is the most common metabolic bone disease, affecting more than 200 million people worldwide. [5] Approximately 75 million people in Europe, the United States, and Japan are diagnosed with osteoporosis. [11]

The risk of osteoporosis increases with age as SMZ decreases. Senile osteoporosis is more common in people over 70 years of age. Secondary osteoporosis can occur in people of any age. Although bone loss in women begins gradually, it accelerates during menopause, usually around the age of 50 and beyond. The incidence of postmenopausal osteoporosis is highest in women aged 50–70 years.

Women are at higher risk for osteoporosis. Half of postmenopausal women have fractures associated with osteoporosis throughout their lives; 25% of these women develop a spinal deformity, and 15% experience a hip fracture. Risk factors for hip fractures are similar in different ethnic groups. [6]

2.2.2. Instrumental methods

In addition to these methods, a portable densitometer (SONOST 3000) (Korea) was used to assess bone density in all patients. In assessing bone density, the ankle portion of the patient's body was selected and the results were expressed on the T and Z criteria.

The computer software of the device includes a database of normative indicators of age and age, calculated on the basis of population samples. The results of bone mass measurements were compared with people's data on gender, age, race, anthropometric indicators, as well as gynecological status in women.

The results of the study are presented in the form of conclusions in absolute values: bone mineral content and mineral density, as well as, for comparison, as a standard deviation from the norms calculated on the basis of population samples: Z-index, Tindex.

Bone mineral component - The mass of bone tissue indicates the amount of mineralized tissue scanned by the bones.





Bone mineral content is determined by the length of the scanning path (g/cm). Bone mineral density is the amount of mineralized bone tissue (g/cm) in the scanned area, the most optimal indicator for clinical practice.

The Z-index indicates the current state of the skeletal system, which represents the amount of standard deviations (SD) that are higher or lower than the average Bone mineral density for people of the same age as the patient compared to men and women. The indicator takes into account the variability of bone mass and bone density among healthy populations and their decrease with age. The mean Z-criterion in any age group is 0. The Z-criterion in patients whose bone mineral density is significantly lower than that of other people of the same age is -1.

The densitometry results recommended by the WHO working group used the Tcriterion. The T-criterion is the amount of SD bone mineral density that is average and lower for the highest bone mass of young (30–35-year-old) subjects of the corresponding sex. The T-criterion is independent of age and decreases at the same time as bone mass decreases with age.

Ultrasound examination of bone tissue. The control device emits ultrasonic waves with a frequency higher than 3 MHz. In the process, the speed of the wave passing through the bone tissue varies depending on its density. All information about this velocity change is recorded and then used for diagnostics and comparison with normal values. The procedure is absolutely painless and harmless and is suitable for pregnancy or other restrictions related to exposure. Encryption of analysis results. According to the results of the examination, the doctor receives two main types of data: T-score. Its value is formed by comparing bone density with a normal ratio of 1 point and above.

If it is less than indicated, then: -1 to -2.5 - a decrease in mineral density, Below -2.5 - osteoporosis with high fractures Z-ball. This is determined by comparing bone mass to the average norm for the patient's age. Negative value low bone density.

Ultrasonic bone densitometry is a diagnostic method that allows accurate diagnosis as well as evaluation of the effectiveness of subsequent treatment and therapy. The painless and non-invasive diagnostic method allows to determine the effectiveness of treatment aimed at determining bone fractures, calcium density in bone tissue, mineral density of bone tissue, determining the risk of osteoporosis and slowing bone demineralization.

Densitometry is the only way to reliably detect osteoporosis at an early stage of development, as well as to evaluate the effectiveness of its treatment.

Currently, the number of patients with diseases of the musculoskeletal system is increasing. X-ray and ultrasound diagnostic methods can detect bone erosion -



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osteopenia. Osteopenia is more commonly seen in pregnant and lactating women, so ultrasound densitometry is an important assessment of bone tissue in this category of patients.

This procedure is absolutely painless and does not require prior preparation. The densitometer operator records the result, passes the conclusion and images to the patient. Another specialist (rheumatologist, orthopedist-traumatologist) interprets the results and makes a definite diagnosis.

When performing a quantitative ultrasound densitometry, a contact hypoallergenic gel-stained recording sensor is placed over the calcaneus or patella, tibia, or phalanges of the hands. Using a densitometer, the ultrasonic wave characteristics are recorded by processing the data later on a computer.

This diagnostic procedure is able to record even minimal bone loss. Densitometry is able to detect osteoporosis at the earliest stage of development, when osteopenia is present.

Quantitative ultrasound densitometry is a promising new method that characterizes bone tissue in terms of the rate of passage through ultrasound and its broad-spectrum decrease. Ultrasound velocity characterizes the loss of ultrasound intensity during its propagation, is expressed in dB / MHz, and reflects the volume and spatial orientation of trabecular bone tissue. From other indicators, in particular, a combination of SOS and BUA-stability parameters reflecting the percentage of young adults is used.

WHO has developed the following diagnostic criteria for assessing bone density:

1. Normal bone density is higher than the mean (SD) at the time of age-related "peak" of bone mass in women (T-criterion is higher - 1);

2. Osteopenia - in women during the "peak" of bone mass decreased by 1-2.5 SD compared to the average of this indicator (T-criterion -1 to -2.5 SD);

3. Osteoporosis is a bone mineral density in women during the "peak" period of bone mass that is at least 2.5 SD lower than the average of this figure. Currently, a decrease in the T-criterion is a generally accepted definition of osteoporosis greater than 2.5 SD.

Laboratory research methods

Blood samples were taken from all patients to determine erythrocyte sedimentation rate and C-reactive protein. Plasma 25OH-vitamin D was assessed by ELISA.

The reference concentration of calcitriol in adult serum is 16-65 ng / ml (42-169 nmol / 1). Vitamin D3 (cholecalciferol) is formed from 7-dehydrocholesterol in the skin under the influence of sunlight or enters the body through food. The synthesized and derived vitamin D3 is transported to the liver through the blood, where it is converted to 25-hydroxyvitamin in the mitochondria [25 (OH) D3].



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This interval is converted to either 1.25 (OH) 2D3, or 24.25 (OH) 2D3. Calcitriol [1.25 (OH) 2D3] is formed in the mitochondria of kidney cells under the action of 1hydroxylase, which is the most active form of vitamin D3. 1.25 (OH) 2D3 is actually a hormone that has a direct effect against rickets, its mechanism of action is similar to hormones. After synthesis in the kidneys, it is transported through the blood to the intestines, where in the cells of the mucous membrane it stimulates the synthesis of protein, which binds calcium that comes with food (this is the main function of vitamin D). As a result of these processes, the concentration of calcium in the blood rises.

Calcium and phosphorus in food affect the formation and secretion of 1.25 (OH) 2D3 in the kidneys. Excess 1.25 (OH) inhibits 2D3 parathyroid hormone synthesis. An increase in the concentration of calcium in the blood above 1.25 (OH) 2D3 also inhibits parathyroid hormone output. Prolactin and somatotropin are important regulators of vitamin D metabolism during pregnancy and growth. Deficiency of 1.25 (OH) 2 D3 leads to hypocalcemia, osteomalacia and similar diseases. Low blood concentrations of 1.25 (OH) 2 D3 in rickets, postmenopausal osteoporosis, osteomalacia, hypoparathyroidism, in adolescents with type 1 diabetes, bone metastases, chronic renal failure. Concentrations of 1.25 (OH) 2 D3 in the blood are detected in primary hyperparathyroidism, sarcoidosis, tuberculosis, calcification, in normally growing children, pregnant and lactating women.

Laboratory tests are needed to determine the level of the major metabolites of vitamin D in the blood.

It is preferable to submit on an empty stomach at least 4 hours after the last meal, there are no mandatory requirements. Alcohol and fatty foods should be excluded 12 hours before the study. Refuse to smoke 1-2 hours before blood donation, do not drink juice, tea, coffee (water can be drunk). It is recommended to rest for 15 minutes before donating blood.

Data values (Standards)

1. <10 ng / ml - severe deficiency

2. <20 - kamomad

3. 20-30 - failure

4. 30–100 - sufficient level (targets for the correction of vitamin D deficiency - 30– 60)

5. 150 - may have toxic effects

Factors influencing research results

1. Drugs that reduce the level of 25-hydroxycalciferol in the blood: phenytoin, phenobarbital, rifampicin, oral anticoagulants.



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2. Pregnancy

3. Excessive consumption of pFreparations containing vitamin D.

There are currently several analyzes available to measure the amount of 25 (OH) D in serum. Each of them has its strengths and weaknesses.

Antibody-based analysis has been available since the early 1980s. Since then, various antibody-based methods have been used, including radioimmunoanalysis (RIA), enzyme-linked immunosorbent assay (ELISA), and chemiluminescent assays.

The first liquid chromatography (LC) based method was introduced in 1977. It was based on the specific ultraviolet (UV) spectral absorption peak of the vitamin D metabolite at 265 nm. By detecting ultraviolet light, this analysis made it possible to directly quantify not only the total 25 (OH) D, but also 25 (OH) D2 and 25 (OH) D3. Over the years, this LC-based method has evolved into the newest LC-chromatography - tandem mass spectrometry (LC-MS / MS), which is now considered the benchmark standard for vitamin D analysis. In this method, the mass spectrometer acts as a detector of metabolites instead of UV rays.

It measures 25 (OH) D2 and 25 (OH) D3 with much higher sensitivity and specificity than traditional LC methods. Despite advances in methodology over the past 40 years, the still wide and unacceptable interassay and laboratory variability may influence physicians 'clinical decisions. This intensified the call for standardization of analyzes. To address this issue, an external vitamin D quality assurance scheme (DEQAS; Charing Cross Hospital, London, UK) was developed to monitor and ensure the reliability of vitamin D assays.

However, until a single method is developed, physicians should be careful in interpreting vitamin D results.

Collection and panels

Sample: blood (0.25 ml of room temperature serum)

Container: Red top tube, serum separator tube (if whey separator tube is used, allow to cool at room temperature; remove from centrifuge and gel within 48 hours).

Collection method: Simple venipuncture

Other instructions: Collect blood in a red upper tube; allow blood to clot at room temperature; immediately separate the serum from the cells in a centrifuge.

Panels: 25-hydroxyvitamin D (25 (OH) D) is not routinely included in comprehensive metabolic panels, it should be ordered as a separate blood test.

Methods of statistical processing

Statistical analysis of the obtained results was performed using Microsoft Excel 2007 program. To describe the distribution of the analyzed parameters, the frequencies occurring for discrete variables or constant parameters were calculated using the





standard representation  $M \pm m$ , where M is the arithmetic mean, the statistical error of its determination (standard deviation). group average), as well as other parameters, including percentages. The distribution of continuous random variables was graphically represented in the form of distribution functions as well as a frequency histogram.

The significance of differences in the division of continuous variables into different groups was determined using non-parametric Kolmogorov-Smirnov and Mann-Whitney criteria. In the comparison of group averages, a difference analysis was used, taking into account the dimensions of the compared groups and their eccentricity coefficients. In doubtful cases, comparisons were made between groups using similar non-parametric methods.

The analysis of the correlation between the continuous variables was performed using the Fisher correlation coefficient and the non-parametric - Spearman correlation coefficient. The significance of the differences in the correlation coefficients in the different groups was determined using the Fisher conversion. to compare the mean power, the average value of the Fisher conversion was calculated from the sample correlation coefficient adjusted to the group size.

Where it is necessary to analyze the true significance of the risk factor in relation to certain clinical manifestations, perhaps due to age (or the presence of other factors), partial correlation coefficients are calculated under the control of age (or the presence of another factor). reviewed and analyzed.

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