**Summary**

**Objective:** Questions of the relationship between the structural and functional condition of periodontal and bone tissue still remain disputable. A correlation between the mineral density of the skeletal bones and the course of periodontal diseases has been revealed in post-menopausal women. The actuality of this problem is obvious because grounding of such relationship would enable to substantiate pathogenically the possibility and necessity of osteotropic therapy in patients with generalized periodontitis.

**Materials and methods:** Roentgenological and periodontological examination was performed to 165 patients (87 women and 78 men) with generalized periodontitis grade II–III of severity. The mineral density of bone tissue was measured using an Achilles+ ultrasound densitometer. Metabolic processes in bone tissue were evaluated by the serum levels of biochemical indexes (such as calcium-tropic hormones, i.e. parathyroid hormone and calcitonin, biochemical markers reflecting bone tissue formation, i.e. osteocalcin, bone-specific alkaline phosphatase and bone tissue resorptive markers such as C-terminal telopeptide of type 1 collagen and deoxypiridinolin).

**Results:** Influence of functional bone system condition on the structural and metabolic processes in periodontal tissues and alveolar bone was confirmed in this study. Pathologic processes in periodontal tissues were observed in 47% of women with a decreased bone density and in 72% of men with a normal and high bone mineral density indexes. Disorders of bone tissue metabolism and dissociation in the processes of bone tissue remodeling (i.e. prevalence of bone resorption and depression of bone formation) were noted in patients with general periodontitis.

**Conclusion:** Disturbed metabolism of bone tissue in patients with generalized periodontitis was determined independently of the bone tissue density. Therefore, a normal index of bone density by itself isn’t yet the evidence of normal bone tissue metabolism and of coordinated bone tissue remodeling processes. The results suggest the necessity of correcting bone tissue metabolism in patients with generalized periodontitis by osteotropic medications.

**Keywords:**
periodontal diseases, bone mass, bone density, bone turnover
Objective

Multiple studies were performed during the last 20 years to reveal a relationship between bone mineral density and periodontal diseases [2, 7, 13], but the investigators still didn’t come to a common opinion about this problem. This disagreement may be caused by different methods used for the evaluation of periodontal state and bone mineral density and also by the various age criteria for the analysed persons. It should also be noted that periodontal diseases and osteoporosis are chronic health disorders developing and progressing with the aging. They are both characterized by gradual loss of bone mass [6]. At present, the number of elderly people with a higher incidence of osteopenia and osteoporosis than in general population constantly increases [13]. Disorders in mineral turnover and systemic mineral density loss in the skeletal bone are the risk factor for periodontal diseases, however, this relationship isn’t yet conclusively determined. The studies revealed no difference in bone density between healthy persons and patients with periodontitis [3, 4, 11]. This enabled the authors of these studies to deny the influence of osteoporosis on the pathogenesis of periodontitis [10]. However, other investigators determined a correlation between bone mineral density and the severity of generalized periodontitis in the peri- and post-menopausal period [1, 8]. M. C. Jeffcoat in his studies [6, 8] considered osteopenia and osteoporosis to be a risk factor of periodontal diseases both in men and in women. A decrease of bone mineral density may have a negative influence on the state of periodontal tissues [12]. Age-related bone tissue loss and its metabolic disturbances accelerate resorptive processes in the alveolar bone and lead to premature loss of teeth [2].

Studies of the relationship between the structural and functional condition of bone tissue and the course of generalized periodontitis are necessary for determining alveolar bone loss pathogenesis in the case of periodontal diseases and for the substantiation of pathogenetic therapy.

The aim of this study was to analyse the relationship between periodontal tissue state and the structural-functional condition of bone tissue, its mineral density and features of the bone tissue metabolism in patients of different age and sex with generalized periodontitis.

Materials and methods

165 patients (87 women and 78 men) with generalized periodontitis II–III° of severity were examined clinically, roentgenologically and using laboratory and instrumental tests. Data on their medical history and co-existing diseases were noted in a special questionnaire on general health and stomatologic condition. Clinical methods of examination included visual inspection of the oral cavity, estimation of the periodontal state and evaluation of paraclinical indexes (such as PMA index, Fiodorov–Volodkina oral hygiene index, Ramfied’s index and periodontal index). Roentgenological methods (such as orthopantomography, intra-oral radiography and radiovisiography) were used for examination of periodontal tissues.

Laboratory investigation aimed to estimate the biochemical markers reflecting the condition of bone tissue metabolism. Serum parathyroid hormone level was determined by the immunological enzyme-intensified double-stage method using a DSL-10-80 ACTIVLE I-PTH laboratory kit. The normal values of the parathyroid hormone level ranged from 16 to 62 pg/ml. Serum calcitonin level was evaluated by enzyme-linked immunoabsorptive analysis with monoclonal antibodies to human calcitonin using the DRG Calcitonin ELISA (EIA-3648) test. Its normal values varied from 0.68 to 30.26 pg/ml for men and from 0.07 to 12.97 pg/ml for women.

Evaluating serum osteocalcin level, the double-centered Osteometer BioTech A/S N-MID Osteocalcin One Step ELISA enzyme-linked immunological test (Denmark) was used. The normal values for osteocalcin levels ranged from 5 to 55.8 ng/ml for men, from 4.9 to 30.5 ng/ml for pre-menopausal women and from 9.5 to 48.3 ng/ml for post-menopausal women.

Serum bone-specific alkaline phosphatase level was determined by the enzyme-linked immunological method using a Metra BAP ELA kit (USA). The normal values for the level of this enzyme ranged from 15 to 41.3 U/ml for men, from 11.6 to 29.6 U/ml for pre-menopausal women and from 14.2 to 42.7 U/ml for post-menopausal women.

Evaluating serum C-terminal telopeptide of type 1 collagen level, the enzyme-linked immunological test Serum CrossLaps ELISA (Denmark) was used. The normal values for it ranged from 0.142 to 0.522 ng/ml for men, from 0.166 to 0.476 ng/ml for pre-menopausal women and from 0.251 to 0.761 ng/ml for post-menopausal women.

Deoxypyridinolin level was determined by its ratio to creatinine level in urine, using enzyme-linked immunological method and a Metra DPD ELA kit (USA). The normal values for this ratio ranged from 3 to 7.4 nmolDpD/mmolCr for women (aged 25–44 years) and from 2.3 to 5.4 nmolDpD/mmolCr for men (aged 25–55 years). Cre-
Relationships between periodontal status, periodontitis and structural and functional condition of bone system

Carnitine level was evaluated in the first portion of morning urine; the normal values for the creatinine level ranged from 2.47 to 19.2 mmol/l for women and from 3.45 to 22.9 mmol/l for men.

To evaluate the functional condition of bone tissue (its elasticity, density, bone quality and firmness) an ultrasound Achilles+ densitometer was used. In accordance with ultrasound densitometry data, all the patients were divided into four groups: patients with osteoporosis, osteopenia, normal bone tissue condition and patients with osteosclerosis (i.e. increased bone density). According to the WHO recommendations, osteoporosis is determined in case of T-score lower than –2.5 SD. T-score from –2.5 to –1 SD is evaluated as osteopenia. The criterion of normal bone tissue is T-score from –1 to +1 SD. In this study, patients with a T-score higher than +1SD were distinguished to a separate group of osteosclerotic bone tissue. Persons of this group had specific features of periodontal tissue state (such as a pathologic scuffing of teeth, hyperesthesia of the paracervical site, erosions and wedge-shaped defects). Their roentgenograms revealed a thickening of the spongy bone septa.

Statistical analysis was performed using parametrical and non-parametrical criteria (such as Student’s, Fisher’s criteria and other) and also using multiplex methods of mathematical research (such as step-by-step progressive, dispersive and factorial analyses). The results obtained were processed using Statgraphics and Statistika 5.0 computer programs.

**Results**

Examining women with periodontal diseases whose average age was 45.9 ± 2.3 years, a decreased bone tissue density was stated in 41 patients (47% of all women); 6 women (7%) had osteoporosis and 35 women (40%) had osteopenia (Fig. 1). Normal bone tissue density was determined for 40 women (46%), and in 6 of them (7%) ultrasound densitometry revealed osteosclerosis. Thus, in 53% of the women periodontal diseases were associated with normal and increased indexes of bone tissue density.

Examining men with periodontal diseases whose average age was 45.9 ± 3.4 years, normal bone density was determined in 42 patients (54%) and osteosclerosis was stated in 14 persons (18%); 22 men had a decreased bone density: 19 of them (24%) had osteopenia and 3 men (4%) had osteoporosis (Fig. 2).

Metabolic processes of bone tissue in patients with different values of bone mineral density (i.e. with osteoporosis, osteopenia, normal and osteosclerotic bone tissue) were analysed in this study.

The results revealed a reliable (p < 0.01) decrease of parathyroid hormone level in women with osteopenia and osteoporosis (39.05 ± 3.60 pg/ml) in comparison with those who had normal or increased bone density. The mean level of parathyroid hormone in women with normal bone tissue was 52.62 ± 5.67 pg/ml. Women with osteosclerotic bone tissue had a reliably higher moderate parathyroid hormone level (81.87 ± 5.67 pg/ml versus the highest normal value for this index 62 pg/ml). On the other hand, a reliably lower mean serum calcitonin level (0.51 ± 0.21 pg/ml) was noted in this group of women. A decreased calcitonin level accompanied by a high level of parathyroid hormone in women with osteosclerosis is an evidence of dissociation in calcium metabolism regulating hormones. Women with a normal bone density had a rather high mean calcitonin level (1.54 ± 0.65 pg/ml). This study revealed
no essential variation of calcium level in women with different values of bone mineral density.

Analysis (Table 1) of the serum levels of parathyroid hormone and calcitonin in women revealed a close reverse correlation ($r = -0.687$, $p < 0.001$).

Activity of bone tissue remodellation slackens with increasing bone density and reflect changes in the levels of biochemical bone remodellation markers. Decreased levels of bone formation reflecting markers, i.e. bone-specific alkaline phosphatase (its average value was $16.77 \pm 2.01$ U/l) and osteocalcin (average value $18.27 \pm 2.10$ ng/ml) were found in women with osteosclerosis in comparison with those who had a normal bone tissue density (mean values in these women were $22.88 \pm 0.90$ U/l and $20.68 \pm 1.07$ ng/ml, respectively, $p < 0.05$). Levels of bone resorption markers, i.e. C-terminal telopeptide of type 1 collagen (its mean value was $0.294 \pm 0.060$ ng/ml) and deoxypyridinolin (mean value $4.62 \pm 0.94$ nmolDpD/mmolCr) in women with osteosclerosis decreased almost twice as compared with those who had a normal bone tissue density (mean values for them were $0.402 \pm 0.020$ ng/ml and $9.42 \pm 1.13$ nmolDpD/mmolCr, respectively). Accelerated rates of bone tissue remodellation (i.e. increased activity of bone tissue formation and reliably accelerated bone resorption processes) were determined in women with osteopenia and osteoporosis. Increased levels of bone-specific alkaline phosphatase (its mean value was $25.78 \pm 1.18$ U/l) and osteocalcin (mean value $23.77 \pm 1.42$ ng/ml) were found in this group of women in comparison with those who had a normal bone tissue density ($p < 0.05$). In women with osteopenia, like in those who had a normal bone density, an increased serum deoxypyridinolin level was noted (its average value was $10.80 \pm 0.89$ nmolDpD/mmolCr, i.e. significantly exceeded the highest normal value of this index for women). Thus, the results indicated a dissociation of the processes of bone tissue remodellation and a significant prevalence of bone resorption in women with a decreased bone tissue density.

Analysis of the main indexes of bone tissue metabolism in women demonstrated a close relation of biochemical bone formation reflecting markers with serum parathyroid hormone level (Table 1). Increased parathyroid hormone secretion inhibits bone formation processes and is reflected in decreased levels of osteocalcin ($r = -0.687$, $p < 0.001$) and bone-specific alkaline phosphatase ($r = -0.557$, $p < 0.001$). Calcitonin level influences bone tissue resorption processes: a decrease in its value caused a rise of deoxypyridinoline level ($r = -0.544$, $p < 0.001$). Reduction of bone density in women is mainly caused by accelerated bone tissue resorption. A reverse correlation has been revealed between the indexes of bone tissue strength and biochemical bone resorption markers: the correlative coefficient with deoxypyridinoline was $-0.432$ ($p < 0.01$) and with C-terminal telopeptide of type 1 collagen $-0.691$ ($p < 0.01$). Reduced bone tissue density correlated with increased calcium levels ($r = -0.784$, $p < 0.01$).

Thus, bone tissue metabolic processes in women with osteosclerosis are characterized by a dissociation of the main calcium-regulating hormones (i.e. a probable increase of parathyroid hormone and a decrease of calcitonin level). Bone tissue resorption rate in this group of women is normal, but bone formation processes are suppressed. An insignificant depression of bone tissue formation processes and probably an increased bone resorption reflecting markers accompanying an augmented parathyroid hormone level were noted in women with a normal bone density. In women with osteopenia and osteoporosis, bone tissue formation rate was normal and bone resorption was reliably accelerated.

Studying bone tissue metabolic processes in men with periodontal diseases, a decrease of parathyroid hormone level (its mean value was $20.98 \pm 4.53$ pg/ml) and an increase of calcitonine level (mean value $12.48 \pm 1.32$ pg/ml) was stated in case of osteopenia and osteoporosis versus those who had a normal bone tissue density (moderate values

<table>
<thead>
<tr>
<th>Indexes of structural and functional bone system condition</th>
<th>Coefficient of correlation, $r$</th>
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<th>Reliability of correlative coefficient, $p$</th>
</tr>
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<tbody>
<tr>
<td>Parathyroid hormone</td>
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for them were 46.12 ± 3.65 pg/ml and 5.25 ± 1.56 pg/ml respectively, p < 0.05). In men with osteosclerosis decreased parathyroid hormone level (40.01 ± 2.76 pg/ml) was noted (p < 0.05). Analysing calcium level in men with different values of bone density, an increasing tendency for this mineral was found in patients with osteopenia (mean value 2.48 ± 0.09 mmol /l) versus those who had normal indexes of bone density (2.43 ± 0.07 mmol/l). High calcium levels in men with osteopenia result in increased calcitonine secretion and inhibition of parathyroid hormone synthesis, this has a protective value for the bone tissue. At the same time, depression of bone formation was revealed in this group of men: the mean osteocalcine value in them was 18.64 ± 0.19 ng/ml and the average value of bone-specific alkaline phosphatase 18.37 ± 1.32 U/l. Markers of bone tissue resorption, i.e. deoxypiridinoline (its mean value was 10.82 ± 1.21 nmolDpD/mmolCr) and C-terminal telopeptide of type 1 collagen (mean value 0.943± 0.05 ng/ml) were reliably higher than in men with a normal bone density (5.49 ± 0.98 nmolDpD/mmolCr and 0.532 ± 0.04 ng/ml, respectively, p < 0.01).

A reliable increase of serum parathyroid hormone level accompanying a decreased level of calcitonin was noted in men with normal bone tissue. Hypersecretion of parathyroid hormone results in accelerated bone tissue resorption rates and is manifested by increased biochemical markers of bone resorption. Bone tissue formation reflecting markers react ambiguously: this study revealed inhibition of osteocalcin secretion and a high activity of bone-specific alkaline phosphatase. This is an evidence of a high differentiation of the osteoblasts, however, organic matrix formation rate isn’t high.

No significant changes in parathyroid hormone and calcitonin levels were noted in men with osteosclerosis. Bone tissue formation rate reflected by osteocalcine (its mean value was 21.94 ± 1.03 ng/ml) and bone-specific alkaline phosphatase (mean value 30.42 ± 1.76 U/l) was normal in this group of men; however, bone resorption processes were significantly accelerated: increased levels of C-terminal telopeptide of type 1 collagen (mean value 0.598 ± 0.1 ng/ml) and deoxypiridinoline (mean value 7.92 ± 1.08 nmolDpD/mmolCr) were found in men with osteosclerosis as compared with those who had a normal bone density (p < 0.01).

Analysis of the main indexes of bone tissue metabolism in men showed an increased parathyroid hormone level to result in bone matrix synthesis depression (Table 2). A reverse correlation has been revealed between the levels of parathyroid hormone and osteocalcin (r = 0.323, p < 0.01) and also between calcitonin and C-terminal telopeptide of type 1 collagen levels (r = −0.641, p < 0.001). Accelerated bone tissue resorption rate is caused by suppressed osteocalcin secretion. Reduced bone mineral density is closely associated with the levels of biochemical bone formation markers: a correlation has been revealed between bone strength value and osteocalcine level (r = 0.472, p < 0.001) and also between bone strength and the level of bone-specific alkaline phosphatase (r = 0.781, p < 0.001).

Thus, features of bone tissue metabolism in men with generalized periodontitis in case of various bone density values were determined in this study. In men with osteosclerosis bone metabolism is characterized by accelerated bone resorption while the bone formation rate is normal. In men with normal bone density, non-significant inhibition of bone matrix formation accompanied by a high activity of osteoblasts and an increased bone resorption reflecting markers with a high parathyroid hormone level were noted.

In men with osteopenia and osteoporosis, increased serum calcium and calcitonine levels were determined. Dissociation in bone tissue remodelation processes (i.e. depression of bone formation and a reliably accelerated resorption) were noted in this group of patients.

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Discussion

A study of 135 women aged 41–70 years, performed by Hildebolt et al. [5], demonstrated a relationship between clinical attachment loss level in the periodontal tissues and the number of lost teeth. At the same time, no correlation between clinical attachment loss level in the periodontal tissues and bone mineral density measured in spine or femur was determined. In later studies performed by Pilgram, Hildebolt et al. [14], a statistically non-reliable correlation ($r = 0.06, p < 0.75$) between these two parameters was stated in post-menopausal women with a good periodontal tissue condition and a good oral hygiene skills. Longitudinal analysis performed during the period of three years demonstrated a lower loss of the alveolar bone height in women with high bone tissue density than in those whose bone density was low.

A weak correlation between clinical attachment loss level and bone density was determined by Weyant [15] in a study of 292 women of the average age 75.5 years. This fact enabled the investigators to consider osteopenia and osteoporosis as an indicator of periodontal disease risk. No correlation between the activity of inflammatory-destructive processes in periodontal tissues and bone mineral density was revealed in this study. Pathologic processes in periodontal tissues were found in 47% of women with a decreased bone density and in 72% of men with normal and high bone mineral density indexes. Disorders of bone tissue metabolism and a dissociation in the processes of bone tissue remodeling (i.e. prevalence of bone resorption and depression of bone formation) were noted in all patients with general periodontitis. The results suggest the necessity to correct bone tissue metabolism in patients with generalized periodontitis by osteotropic medications.

Conclusions

Inflammatory and destructive processes in periodontal tissue were noted independently of bone density: pathologic processes in periodontal tissues were observed in 47% of women with a decreased bone density and in 72% of men with normal and high bone mineral density indexes. Disorders of bone tissue metabolism and a dissociation in the processes of bone tissue remodeling (i.e. prevalence of bone resorption and depression of bone formation) were noted in all patients with general periodontitis. The results suggest the necessity to correct bone tissue metabolism in patients with generalized periodontitis by osteotropic medications.

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PERIODONTO BŪKLĖS, PERIODONTITO IR KAUĻŲ SISTEMOS STRUKTŪRINĖS IR FUNKCINĖS BŪKLĖS RYŠYS

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Santrauka
Tikslas: Įvertinti periodonto būklės ir generalizuoto periodontito sąsajas su kaulinio audinio pokyčiais.

Duomenys (medžiaga) ir metodai: 165 pacientams (87 moterims ir 78 vyrams) su generalizuoto 2–3 laipsnio periodontitu atlikti rentgenologiniai ir periodontologiniai tyrimai. Kaulinio audinio mineralų tankis buvo matuotas naudojant Achilles+ ultragarso densitometrą. Kaulinio audinio apykaita buvo vertinta pagal biocheminius žymenis, kurie atspindin kaulinio audinio formavimąsis (osteokalcinas, kaulų specifinė šarminė fosfatė) arba kaulinio audinio rezorbciją (C-terminalinis telopeptido 1 tipo kolagenas, deoksipiridinolinas).

Rezultatai: Šio tyrimo metu patvirtinta funkcinės kaulų sistemos būklės įtaka periodonto audinių ir alveoliarinių kaulų struktūriniams ir metaboliniams procesams. Patologiniai procesai periodonto audiniuose buvo aptikti 47% moterų, kurioms sumažėjęs kaulų tankis, ir 72% vyrų, kurių kaulų mineralų tankis normalus ir didelis. Pacientams su generalizuotu periodontitu buvo nustatyta kaulinio audinio mineralų apykaitos sutrikimas bei kaulinio audinio remodeliacijos disociacija.


Raktažodžiai:
periodonto ligos, kaulų masė, kaulų mineralų tankis, kaulinio audinio apykaita