VILNIUS UNIVERSITY

STATE RESEARCH INSTITUTE CENTRE FOR INNOVATIVE MEDICINE

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RELATIONSHIP OF BONE TURNOVER AND STRUCTURE INDICES WITH SERUM LIPIDS AND COMPONENTS OF METABOLIC SYNDROME

Summary of doctoral dissertation
Biomedical Sciences, Medicine (06 B),
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VILNIAUS UNIVERSITETAS

VALSTYBINIS MOKSLINIŲ TYRIMŲ INSTITUTAS INOVATYVIOS MEDICINOS CENTRAS

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KAULINIO AUDINIO APYKAITOS IR STRUKTŪROS RODIKLIŲ SĄSAJOS SU KRAUJO LIPIDAIS BEI METABOLINIO SINDROMO KOMPONENTĖMIS

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ABBREVIATIONS

ABP – arterial blood pressure
BMI – body mass index
BMD – bone mineral density
BTM – biochemical markers of bone turnover
FM – bone formation markers
HDL – high density lipoprotein cholesterol
LDL – low density lipoprotein cholesterol
PINP – procollagen type I N propeptide
PTH – parathyroid hormone
RM – bone resorption markers
s-CTX-I – serum C-terminal cross-linking telopeptide of type I collagen
TCh – total cholesterol
TG – triglycerides
WHO – World Health Organization

1. INTRODUCTION

Biochemical markers of bone turnover are products of osteoblast and osteoclast activity: enzymes, body matrix proteins and other materials, which can be found in the body's blood or urine. At present it is believed that bone tissue quality can be assessed by identifying biochemical markers of bone turnover reflecting the bone metabolism. It is expected that the test of biochemical markers used as an extra information may show the metabolic activity of bone tissue. However, bone turnover rate, as reflected by biochemical markers, may vary significantly among different age groups. As it has been proven, healthy women aged 30–39 years with the same biochemical markers of bone turnover, had lower rates, compared to women over the age of 40 years. In women biochemical markers of bone turnover and age relation research showed conflicting results: one study confirms the existence of such dependence, and others – not.

For more than 20 years scientists are looking for relation between bone biochemical markers and bone mineral density, but studies have shown variable correlation, or indicators of the bone remodeling associations could not be found.

In the mechanism of bone metabolism the same immunological and inflammatory pathophysiological factors are involved, as in the atherogenesis process, which is closely related to a change of metabolism (glucose, cholesterol), obesity and arterial blood pressure problems. The clinical symptom complex of these changes is known as the metabolic syndrome. At an average, 11–30% of persons older than 20 years are found with symptoms consistent to criteria of the metabolic syndrome, and almost twice as likely metabolic syndrome determined to the persons of 40 years and older. Obesity during the syndrome causes chronic inflammation, which is a key component of insulin resistance and the metabolic syndrome itself. It is estimated that during obesity mediated inflammation released cytokines activates bone resorption thus disrupting its metabolism. Hyperglycemia resulting from insulin resistance may lead to changes in bone markers, as well as hyperlipidemia it stimulates osteoclast activity, as evidenced by in vitro studies. All of this suggests that biochemical markers of bone turnover may be associated with metabolic disorder indicators, complex of which is defined as a metabolic syndrome. However, the data of the studies that analyze a variety of relationships of biochemical bone turnover and structure parameters with blood hyperglycemia, dyslipidemia, hypertension and obesity, is inconsistent and often investigated only in women.

1.1. The aim of the research

To investigate and evaluate the association of bone turnover and structure characteristics, serum lipids and the metabolic syndrome components.

1.2. The objectives of the research

1. To analyze bone turnover (C-terminal cross-linking telopeptide of type I collagen and procollagen type I N propeptide) and structural (bone mineral density) parameters and serum

lipids (total cholesterol, high-and low-density lipoprotein cholesterol and triglyceride) features by age, in men and in women.

2. Identify the C-terminal cross-linking telopeptide of type I collagen, and procollagen type I N propeptide, bone mineral density links with total cholesterol, high-and low-density lipoprotein cholesterol and triglycerides.

3. To evaluate the links between bone turnover and structure indices and the components of the metabolic syndrome.

4. Determine the prognostic value of serum lipids and the metabolic syndrome components providing bone turnover and structure changes.

1.3. Scientific novelty

So far there is no proven bone turnover and structure parameters with serum lipids. Studies that analyzed such correlations are not numerous, and there is especially small amount of publications on research involving persons of both sexes or only males. In addition, studies carried out the unequal bone turnover and structure parameters with serum lipids.

This investigation is one of the few in which the bone turnover markers analyzed in the population with different genders and evaluated the metabolism of individual components within the metabolic syndrome, and their groups statistical relationships with bone turnover and structure parameters. We managed to find only single scientific publications on the impact of metabolic syndrome and male bone metabolism and structure, so this study will complement the knowledge of the relations between metabolic syndrome components and bone turnover and structure parameters.

For the first time serum lipids and individual components of metabolic syndrome were comprehensively investigated by providing predictive value of changes in bone turnover and structure. This is especially important now, when general metabolism and bone turnover indicators are increasingly gaining the prognostic significance of risk of the chronic non-infectious diseases and conditions.

2. SUBJECTS AND METHODS

2.1. Study population

The sample size was calculated by G Power 3.1.2 statistical program. It was offered to participate in the study for all persons of forty years and older who have applied to the National Center for Osteoporosis for the bone mineral density test. Exclusion from the study criteria: an objection to any procedure, pregnancy, large dose of radiation received over the past 12 months, bone fracture in the past 12 months, malignant tumours, metabolic bone diseases, early menopause in women (under 45 years of age). Also excluded from the study those who have used medicine affecting bone turnover and the medicine for treatment of dyslipidemia. Re-

gional Biomedical Research Ethics Committee provided permission to carry out this study (No. 158200–10–209–056LP26 (2010–10–06).

2.2. Methods

Each person was interviewed during the visit, the investigator recorded the results of the research in questionnaire. Demographic data, social and lifestyle factors – smoking, alcohol consumption were registered.

While collecting medical history subjects were interviewed about former or current disease. Women asked about menstruation, menopause. If a woman did not remember the last cycle of menstruation last menstrual date was considered 50 years of age.

Data was also gathered on previously used medicine or currently in use which is affecting bone turnover. Test of physical activity was assessed using the International Physical Activity Questionnaire short form (called IPAQ_SHOT_SELF_ADM_Lithuanian).

The measurement of blood pressure. Blood pressure was measured on both of the upper arms, with mechanical manometer, using measuring equipment in accordance with Riva-Rocci / Korotkoff and 2007 European Society of Cardiology guidelines. It was assumed that blood pressure is elevated when the final measurement of systolic blood pressure was 130 mmHg or greater, or diastolic 85 mm Hg or more.

Waist, height and weight measurements. Waist was measured according to the World Health Organization (WHO) recommendations. Also, the height measured with accuracy of one millimetre and body weight with accuracy of 50 g, using electronical medical scales. Body mass index (BMI) was calculated with the SPSS statistical program, the body weight in kilograms divided by height in meters squared.

Bone turnover biochemical markers, serum lipids, glucose, vitamin D and PTH research. Blood samples were taken from the elbow vein into two tubes – one for biochemical markers of bone turnover, vitamin D and PTH testing, the other – for the examination of glucose, cholesterol and its fractions.

Venous blood samples for biochemical markers, vitamin D and PTH were taken in the mornings between 8 and 11 hours into serum vials with an isolating gel. After the blood had clotted at room temperature but not more than 1 hour after the collection of sera samples for 15 min. were centrifuged at room temperature and 1500 rev./min. with Labofuge centrifuge. Immediately after the separation of serum, the samples were stored at -20 ^{0} C till examination, but no more than a week. After thawing, samples were immediately examined for the biochemical markers of bone, vitamin D and PTH. To research bone resorption marker C-terminal cross-linking telopeptide of type I collagen (s-CTX-I) and bone formation marker procollagen type I N propeptide (PINP) and 25-hydroxyvitamin D (25 (OH) D and bone turnover affecting parathyroid hormone (PTH) , Roche Diagnostics Cobas immunological analyzer E411 was used. Analysis was carried out by fully automated electrochemical luminescence immunoassay method using the original reagents, and in accordance with the manufacturer's instructions, regular calibration and quality

control applied on a daily basis. Metabolic indicators such as total cholesterol (TCh), its fractions (HDL, LDL, triglycerides) and glucose concentrations in plasma, were analyzed by an enzymatic method, with a fully automated ADVIA 1800 (Siemens Medical Solution) analyzer, in a certified laboratory.

Evaluation of the bone mineral density. Bone mineral density was analyzed by Dual-energy x-ray absorptiometry (iDXA, GE Lunar, USA). Bone mineral density of a total body was measured in the areas of proximal left side of femur, and the lumbar spine (L_1–L_4) the anterior-posterior direction.

BMD was expressed in absolute numbers (g/cm^2), as well as the T-score. Examined persons were divided by BMD T-score into three groups according to WHO guidelines: 1) normal BMD group consisted of individuals with the T-score in any of the studied areas ≥ -1; 2) the low BMD group of subjects the T- score was between -1 and -2.5; 3) very low BMD group consisted of subjects with a T-score equal to -2.5 or less.

Metabolic syndrome and its components. The criteria of the metabolic syndrome and its components were chosen according to NCEP ATP III recommendations. Components of metabolic syndrome are as follows: central obesity (waist circumference greater than 102 cm for men and more than 88 cm for women), elevated arterial blood pressure (systolic blood pressure of 130 mmHg or greater, or diastolic blood pressure of 85 mmHg or greater), glycemia in fasting persons 6.1 mmol/l and higher, triglycerides 1.7 mmol/l or more, high-density lipoprotein less than 1.03 mmol/l in men and less than 1.29 mmol/l in women. When the studied subjects was associated with three or more components of metabolic syndrome, they were assigned to a group of individuals with metabolic syndrome.

2.3. Statistical methods

Statistical analysis were performed using Windows software package SPSS 18.0. Mean of variables, standard deviation (SD) were calculated. To assess normality of distribution of interval variables Kolmagorov-Smirnov test was applied. Mean differences of interval variables were compared using Student t-test, the difference between age groups was checked by Fisher's least significant difference test – LSD criteria. To calculate relations between the interval variables Pearson's correlation coefficient (r) was used.

For the assessment of effect of independent factors to the evaluation of dependent variable and prediction of the values of the dependent variable we used multivariate linear regression analysis, after checking whether the independent variables are not multicollinear. In order to determine the suitability of the model the coefficient of determination was calculated.

The differences were considered statistically significant if the probability of error p value was less than 0.05.

3. RESULTS

3.1. Characteristics

In this study the data of 541 persons was analyzed, including 241 (44.5%) men and 300 (55.5%) women. The youngest man and the woman was 40 years old, the oldest man was 95 years, woman – 89 years. Menopausal age of women studied had a mean of 49.06 ± 6.46 years. The basic characteristics of subjects analyzed is provided in Table 1.

Table 1. Baseline characteristics (mean ± SD)

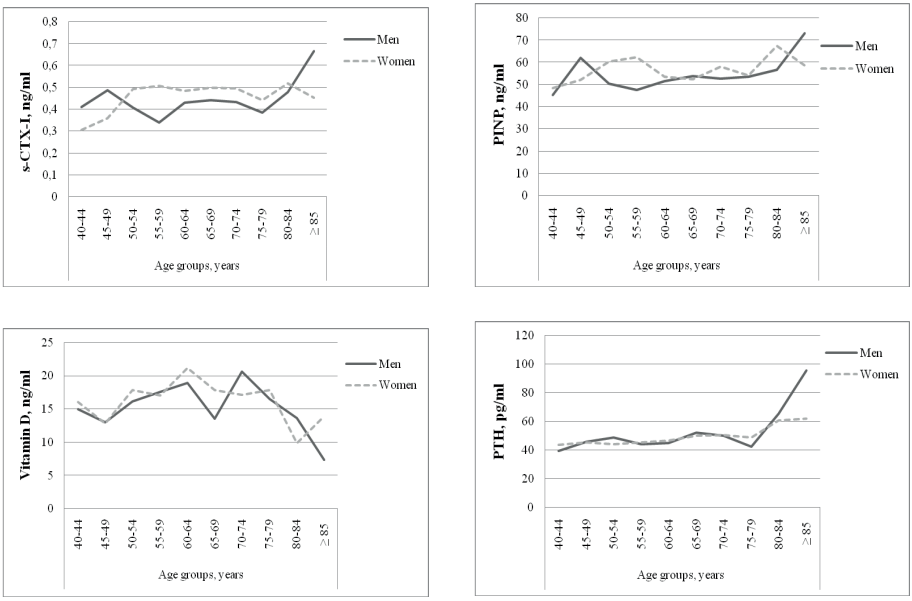
Parameters	Men (n=241)	Women (n=300)	p
Age, years	62.84±12.76	61.68±13.3	0.304
Height, cm	174.95±6.78	161.41±6.71	<0.0001
Body mass, kg	84.39±13.48	71.8±14.01	<0.0001
BMI, kg/m^2	27.55±4.02	27.72±5.78	0.686
Waist circumference, cm	97.85±11.8	89.44±14.27	<0.0001
Systolic ABP, mm/Hg	137.63±18.98	130.76±19.2	<0.0001
Diastolic ABP, mm/Hg	82±9.75	78.11±9.53	<0.0001
Glucose, mmol/l	5.47±0.8	5.16±0.75	<0.0001
TCh, mmol/l	5.47±1.12	5.87±1.17	<0.0001
HDL, mmol/l	1.44±0.34	1.74±0.49	<0.0001
LDL, mmol/l	3.42±1.01	3.59±1.05	0.049
TG, mmol/l	1.38±0.72	1.29±0.63	0.094
s-CTX-I, ng/ml	0.43±0.202	0.456±0.226	0.159
PINP, ng/ml	53.14±24.87	56.9±23.29	0.071
Vitamin D, ng/ml	16.08±9.62	16.2±8.41	0.881
PTH, pg/ml	49.67±23.06	48.77±19.17	0.622
Total body BMD, g/cm^2	1.204±0.133	1.078±0.141	<0.0001
Spinal BMD, g/cm^2	1.249±0.217	1.136±0.199	<0.0001
Femoral neck BMD, g/cm^2	1.049±0.159	0.952±0.174	<0.0001

p – value calculated using Student t-test. SD – standard deviation; BMI – body mass index; ABP – arterial blood pressure; TCh – total cholesterol; HDL – high density lipoprotein cholesterol; LDL – low density lipoprotein cholesterol; TG – triglycerides; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; PTH – parathyroid hormone; BMD – bone mineral density.

The data from the table show that male and female age, body mass index did not differ, but the men's height, weight and waist circumference were significantly higher in males than females. Also, men had significantly higher arterial blood pressure. It was found that men's blood glucose were significantly higher and total cholesterol, HDL and LDL – significantly lower than women, but triglycerides, s-CTX-I, PINP, vitamin D and PTH had no differences among the sexes. Significantly higher total body, spine and femoral neck BMD had been found in men's group.

3.2. Bone turnover, structure factors and serum lipids in different age groups, and their interface parameters

In order to analyze the BTM, vitamin D and PTH in the blood by age, study subjects were divided into groups ranging every 5 years. In both sexes 40–44 years of age and with normal bone mineral density (T-score was -1 and more) have been chosen as the reference group. Reference group of men consisted of eighteen persons, and in the reference group of women there were twenty-four women before menopause. The results of male and female biochemical markers of bone turnover of vitamin D and parathyroid hormone levels are shown in Figure 1.



s-CTX-I – C-terminal cross-linking telopeptide of type I collagen;
PINP – procollagen type I N propeptide;
PTH – parathyroid hormone.

Figure 1. Bone turnover markers, vitamin D and parathyroid hormone depending on age and sex

Application of Fisher's least significant difference criteria (LSD), found that in men and women of reference groups s-CTX-I (males 0.412 ± 0.146 ng/ml and 0.305 ± 0.141 ng/ml for females), PINP (males 45.43 ± 15. 87 ng/ml and 48.37 ± 15 females ng/ml) and PTH (males 39.27 ± 11.73 pg/ml and 43.67 ± 14.6 pg/ml for females) concentration was the lowest. Statistical analysis showed that in both men and women in each older age group s-CTX-I, PINP, PTH were higher than concentration indicated in reference group. In reference groups of men and

women the vitamin D levels also differed from vitamin D levels in other age groups: the lowest vitamin D levels found in men 85 years and older age group (7.33 ± 4.31 ng/ml), but the difference is negligible, because the highest concentration was in – 70–74 year age group (20.65 ± 12.97 ng/ml, $p < 0.04$), for women lowest vitamin D levels were in 80–84 age group (9.84 ± 4.9 ng/ml, $p < 0.007$), the highest – in the age group of 60–64 years (21.14 ± 9.75 ng/ml, $p < 0.02$).The highest concentration of s-CTX-I (0.667 ± 0.39 ng/ml), PINP (73.15 ± 22.95 ng/ml), PTH (95.60 ± 74.44 pg/ml) in men was in 85 years old and the older age group, compared with the reference group (for all of these indicators, $p < 0.05$). In women's 80–84 age group s-CTX-I (0.518 ± 0.221 ng/ml), PINP (67.43 ± 26.05 ng/ml) and in 85 years of age and older group PTH (62.22 ± 34. 8 pg/ml) were higher than in a reference group – s-CTX-I, PINP, and PTH ($p < 0.05$).

Evaluating the results obtained, it can be said that 40–45 year reference groups in which were pre-menopausal women and those with normal BMD had the lowest s-CTX-I, PINP, PTH compared to other age groups. Although in older than a reference age group, CTX-I, PINP, PTH were not increased in each older age group, but it didn't went below the concentration of reference groups.

We also compared serum lipids (total cholesterol, HDL, LDL and triglycerides) by age and gender. The results are presented in Table 2.

Table 2. Serum lipids, by gender and age

Age groups	Serum lipids (mean ± SD)			
	TCh, mmol/l	HDL, mmol/l	LDL, mmol/l	TG, mmol/l
Men				
40–49 (n=43)	5.56±1.08 [e]	1.45±0.27	3.43±0.93 [e]	1.43±0.67
50–59 (n=64)	5.7±1.04 [d,e]	1.43±0.31	3.58±1.01 [d,e]	1.59±0.87 [c,d,e]
60–69 (n=56)	5.76±1.22 [e]	1.47±0.39	3. 71±1.1 [d,e]	1.33±0.52
70–79 (n=46)	5.16±1.16	1.48±0.38	3.14±0.99	1.29±0.86
≥80 (n=32)	4.82±0.72	1.33±0.3	2.97±0.74	1.15±0.41
Women				
40–49 (n=74)	5.36±0.93 [b,c,d]	1.84±0.48 [e]	3.02±0.83 [b,c,d,e]	1.13±0.56
50–59 (n=66)	6.01±1.27	1.88±0.59 [e]	3.64±1.08	1.29±0.74
60–69 (n=60)	6.32±1.18	1.68±0.35	4.03±1.05	1.33±0.59
70–79 (n=62)	5.96±1.17	1.66±0.46	3.78±1.07	1.4±0.68
≥80 (n=38)	5.77±1.17	1.52±0.42	3.65±1.05	1.32±0.44

p – calculated using the LSD test. SD – standard deviation; TCh – total cholesterol, HDL – high density lipoprotein cholesterol, LDL – low density lipoprotein cholesterol, TG – triglycerides.

a – $p < 0.05$ compared with the 40–49 years age group;

b – $p < 0.05$ compared with the 50–59 years age group;

c – $p < 0.05$ compared with the 60–69 year age group;

d – $p < 0.05$ compared with the 70–79 year age group;

e – $p < 0.05$ compared with 80 years of age and older age group.

We found that men had the lowest total cholesterol, HDL, LDL and triglycerides were in the 80 years of age and older age group. Total cholesterol and LDL in 40–49, 50–59, 60–69 age groups were higher than in 80 years and older group. HDL levels were not such a difference, but the triglycerides in the age group of 50–59 years was higher than triglycerides of the age groups of 60–69, 70–79 and 80 years of age and older.

Women's triglycerides, total cholesterol and LDL were lowest in the age group of 40–49 years. This age group total cholesterol and LDL were lower than those of the 50–59, 60–69, 70–79 age groups. With triglycerides such differences were not found, but women had HDL in 80 years and older age group were lower compared to the 40–49 and 50–59 age groups.

Summing up the results of statistical analysis, we suggest that the researched men and women, total cholesterol, LDL, HDL and triglyceride concentrations were different depending on gender: men with the lowest serum lipid levels were observed in the oldest age group, in women – the youngest age group, except for HDL. Also, men and women, serum lipids differed at the same age groups.

We also compared total body, spine and femoral neck BMD in men and women, by the age groups (see Table 3).

Table 3. Bone mineral density in relation to gender, age and area of skeleton

Age groups	Indices (mean ± SD)		
	Total body BMD, g/cm²	Spine BMD, g/cm²	Femoral neck BMD, g/cm²
Men			
40–49 (n=43)	1.231±0.142 [e]	1.229±0.211	1.089±0.172 [e]
50–59 (n=64)	1.21±0.105 [e]	1.242±0.149	1.084±0.135 [e]
60–69 (n=56)	1.209±0.126 [e]	1.226±0.233	1.064±0.141 [e]
70–79 (n=46)	1.221±0.158 [e]	1.309±0.256	1.047±0.179 [e]
≥80 (n=32)	1.125±0.121	1.249±0.249	0.904±0.107
Women			
40–49 (n=74)	1.149±0.132 [c,d,e]	1.238±0.181 [b,c,d,e]	1.024±0.183 [c,d,e]
50–59 (n=66)	1.125±0.105 [c,d,e]	1.157±0.159 [c,d]	1.014±0.137 [c,d,e]
60–69 (n=60)	1.064±0.118 [d,e]	1.072±0.168	0.908±0.177
70–79 (n=62)	1.017±0.129	1.079±0.204	0.892±0.147
≥80 (n=38)	0.974±0.161	1.094±0.247	0.873±0.165

p – value calculated between age groups using LSD test. SD – standard deviation; BMD – bone mineral density.
a – p <0.05 compared with the 40–49 years age group;
b – p <0.05 compared with the 50–59 years age group;
c – p <0.05 compared with the 60–69 year age group;
d – p <0.05 compared with the 70–79 year age group;
e – p <0.05 compared with 80 years of age and older age group.

The data show that men and women had the highest total body and femoral neck BMD was in 40–49 years age group, the same age group for women with the highest spine BMD. Men's spine BMD was highest in the age group of 70–79 years, but it did not differ statistically significantly from the other age groups. Male and female spine BMD, total body BMD of women in each older age group was lower and the lowest for both men and women total body and spine BMD were in 80 years of age and older age groups. In women of the 60–69 and 70–79 age groups total body, spine and femoral neck BMD was lower compared to the 50–59 years age group, in men of the same age groups, BMD was not significantly different.

The BMD of total body, spine and femoral neck is lower in older age groups than in the youngest age groups, but BMD in men and women in some age groups varies differently.

In order to assess and compare bone turnover and structure indicators with serum lipid concentrations studies, we have analyzed the BTM of both sexes and bone structure parameters correlation with serum lipids. The results are provided in Table 4.

Table 4. Bone turnover and structure parameters and serum lipids Pearson's correlation between the genders

Serum lipids	s-CTX-I	PINP	Total body BMD	Spine BMD	Femoral neck BMD
Men					
TCh	-0.06	-0.15*	0.06	-0.06	0.12
HDL	0.03	0.03	-0.06	-0.08	-0.06
LDL	-0.02	-0.12	-0.04	-0.08	-0.09
TG	-0.23**	-0.2**	0.16*	0.09	0.19**
Women					
TCh	0.08	-0.08	0.02	-0.06	-0.01
HDL	0.01	0.08	-0.08	-0.15*	-0.1
LDL	0.08	-0.09	0.01	-0.04	-0.02
TG	-0.1	-0.13*	0.02	0.12*	0.11

TCh – total cholesterol; HDL – high density lipoprotein cholesterol; LDL – low density lipoprotein cholesterol; TG – triglycerides; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; BMD – bone mineral density.
For the s-CTX-I, PINP, HDL and TG concentration logarithmic transformation was used. * $p < 0.05$, ** $p < 0.01$.

It was found that in men the s-CTX-I and PINP had a weak negative association with triglycerides, as well as triglycerides were associated with total body and femoral neck BMD in men, but the identified correlation was negative. Such relation with spine BMD was not observed in men. In women spine BMD was associated with triglycerides and negatively with HDL also there was no women's total body and femoral neck BMD correlation with serum lipids. However, PINP had negative correlation with triglycerides. Women's s-CTX-I correlations with serum lipids were not found.

Since the BMD correlation with serum lipids in men and women was different, also our previously performed statistical analysis showed that BTM, serum lipids and BMD differ between age groups, we evaluated bone turnover and structure indicators statistical relations with serum lipids in age groups (Table 5).

Table 5. Pearson correlation between bone mineral density, bone turnover markers and serum lipids, depending on sex and age

Serum lipids	Men					Women				
	s-CTX-I	PINP	Total body BMD	Spine BMD	Femoral neck BMD	s-CTX-I	PINP	Total body BMD	Spine BMD	Femoral neck BMD
40-49 (n=43)						**40-49 (n=74)**				
TCh	0.11	-0.01	0.02	-0.04	0.08	-0.18	-0.12	-0.05	0.06	-0.11
HDL	0.3*	0.44**	-0.2	-0.16	-0.25	0.12	-0.03	-0.3**	-0.24*	-0.24*
LDL	0.07	-0.02	0.1	-0.01	0.14	-0.22	-0.12	0.01	0.13	-0.13
TG	-0.2	-0.4**	0.09	0.02	0.13	-0.14	-0.01	0.24*	0.24*	0.36**
50-59 (n=64)						**50-59 (n=66)**				
TCh	0.02	0.05	-0.12	-0.19	0.05	-0.11	-0.24	0.26*	0.08	0.22
HDL	0.08	0.03	-0.2	-0.02	-0.26*	0.16	0.21	-0.35**	-0.15	-0.33**
LDL	0.06	0.11	-0.13	-0.29*	0.04	-0.11	-0.3*	0.27*	-0.09	0.26*
TG	-0.11	-0.11	0.23	0.22	0.29*	-0.08	-0.09	0.19	0.15	0.31*
60-69 (n=56)						**60-69 (n=60)**				
TCh	-0.1	-0.25	0.07	0.08	0.04	0.08	-0.24	-0.05	-0.04	-0.02
HDL	-0.04	0.12	0.24	0.31*	0.18*	0.1	0.31*	-0.11	-0.27*	-0.18
LDL	0.01	-0.23	-0.01	-0.02	-0.05	0.06	-0.3	0.02	0.01	0.05
TG	-0.45**	-0.38**	0.07	-0.01	0.2	-0.13	-0.39**	-0.09	0.14	0.01
70-79 (n=46)						**70-79 (n=62)**				
TCh	-0.03	-0.14	0.08	-0.05	-0.01	0.16	-0.08	0.16	0.02	0.19
HDL	0.02	-0.09	-0.19	-0.38*	-0.16	-0.1	0.04	-0.23	-0.3*	-0.2
LDL	-0.05	-0.13	0.13	0.04	0.03	0.09	-0.11	0.19	0.11	0.25
TG	-0.23	-0.15	0.06	0.1	-0.01	-0.33**	-0.24	0.08	0.23	0.14
≥80 (n=32)						**≥80 (n=38)**				
TCh	-0.17	-0.36*	-0.03	-0.11	-0.14	0.16	0.38*	0.09	-0.03	-0.03
HDL	-0.12	-0.28	-0.26	-0.22	-0.17	-0.06	0.07	-0.09	-0.18	-0.11
LDL	-0.1	-0.26	-0.05	-0.05	-0.17	0.24	0.4*	0.14	0.02	0.05
TG	-0.02	0.17	0.46**	0.15	0.35	-0.13	-0.07	0.1	0.19	-0.09

TCh – total cholesterol; HDL – high density lipoprotein cholesterol; LDL – low density lipoprotein cholesterol, TG – triglycerides; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP - procollagen type I N propeptide; BMD – bone mineral density.

For variables s-CTX-I, PINP, HDL and TG concentrations we used logarithmic transformation. * $p < 0.05$, ** $p < 0.01$

The table shows that men in 40–49 years age group s-CTX-I concentration weakly and PINP concentration moderately related to HDL and the concentration of PINP is moderately negatively associated with triglycerides. The same age group of women s-CTX-I and PINP and serum lipids were not related, but in women total body, spine and femoral neck BMD a weak correlation with triglycerides and a weak negative correlation with HDL were found. This BMD relation was not found in 40–49 years age group of men. In men 50–59 years age group, spine BMD was weakly negatively associated with LDL, femoral neck BMD with HDL and there was a weak positive correlation observed between femoral neck BMD and triglycerides. In the women of the same age femoral neck BMD also was weakly associated with triglycerides and negatively with HDL, but unlike men, women 50–59 years age group femoral neck BMD was weakly associated with LDL. Women spine BMD does not show such links, but the 50–59 years age group of women total body BMD had a weak correlation with total cholesterol and LDL and a weak negative correlation with HDL. The negative LDL relation with PINP was found in the women's 50–59 age group, but for women and men in this age group s-CTX-I was not associated with serum lipids. In men 50–59 years age group serum lipids relation with PINP had not been found as well. In the 60–69 year age group of men moderate negative correlation of s-CTX-I with triglycerides and a weak negative – PINP and triglycerides. There was the same PINP – triglyceride concentration and correlation in the women's 60–69 age group, but in this group of women s-CTX-I concentrations were not associated with serum lipids. For both men and women in 60–69 years age groups, total body BMD is not associated with serum lipids, for women at this age and femoral neck BMD was also not associated with serum lipids, but the female spine BMD had a weak negative correlation with HDL and the male spine BMD weak positive correlation with HDL. Male femoral neck BMD also had a very weak association with HDL. Both men and women in 70–79 years age group, where found with a weak negative correlation of spinal BMD and HDL, both men and women in this age group total body and femoral neck BMD had not been associated with serum lipids. 70–79 year age groups both genders PINP was not associated with total cholesterol, LDL, HDL and triglycerides, but the women s-CTX-I was weakly negatively related to triglycerides. In men's 70–79 age group s-CTX-I levels such relations had not been found. In both men and women 80 years and older age group s-CTX-I correlation with the serum lipids was not present. In this age group, total cholesterol was weakly associated with women PINP and weakly negatively with male PINP concentration. Women PINP was also moderately related to LDL. In groups of 80 years and older of both sexes the spine and femoral neck BMD, and total body BMD in women, correlation with serum lipids were not found, however, the total body BMD in men showed moderate relation with triglycerides.

Thus, after evaluating BTM and BMD relations with serum lipids, the different BMD correlations between men and women were found, those were different in age groups too. This led to analysis of serum lipids in separate groups of subjects, depending on the T-score. The results are presented in Table 6.

Table 6. Serum lipids and biochemical markers of bone turnover (mean + SD) depending on the T-score

Serum lipids	Male groups by T-score, T				Female groups by T-score, T			
	T ≥ -1 (n=151)	-1 > T > -2.5 (n=72)	T ≤ -2.5 (n=18)	p	T ≥ -1 (n=156)	-1 > T > -2.5 (n=110)	T ≤ -2.5 (n=34)	p
TCh,mmol/l	5.52±1.11	5.35±1.2	5.49±0.86	0.569	5.8±1.14	5.94±1.25	5.94±1.12	0.611
HDL, mmol/l	1.43±0.32	1.44±0.36	1.53±0.34	0.457	1.75±0.51	1.73±0.47	1.72±0.4	0.957
LDL, mmol/l	3.45±1.01	3.37±1.1	3.36±0.66	0.83	3.52±1.05	3.68±1.03	3.66±1.08	0.405
TG, mmol/l	1.45±0.73	1.26±0.66	1.3±0.81	0.16	1.29±0.65	1.29±0.6	1.23±0.61	0.976
s-CTX-I, ng/ml	0.4±0.189	0.475±0.213	0.504±0.223	0.01	0.405±0.190	0.513±0.238	0.508±0.284	<0.0101
PINP, ng/ml	50.71±26.28	55.91±20.97	62.45±24.94	0.088	53.93±21.02	60.8±23.54	57.93±30.23	0.058

p – calculated by ANOVA test; p – value of between different BMD groups, calculated using the LSD test; TCh – total cholesterol; HDL – high density lipoprotein cholesterol; LDL – low density lipoprotein cholesterol; TG – triglycerides; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP –procollagen type I N propeptide.

It was found that men's total cholesterol and HDL where higher in each group which had a lower BMD, LDL – lower, in women's groups HDL levels where lower in each group with lower BMD, LDL – is higher, but in both male and female groups, these differences are insignificant. Triglyceride level differences for both men and women were also insignificant in BMD groups. However, men and women in the normal BMD group had s-CTX-I statistically significantly lower than in the low and very low BMD groups. Also, women whose BMD was normal, PINP statistically significantly lower than in the low BMD group. Because serum lipids were not different in areas of the central skeleton BMD groups, while searching for the spine, femoral neck and total body BMD relations to serum lipids in individual BMD T-score group, we performed correlation analysis. These results are presented in Table 7.

It was found that in men of the normal BMD group, spine BMD had a very weak negative association with LDL, in women of the normal BMD group, spine BMD had a weak negative correlation with HDL, as well as women's total body and femoral neck BMD had weak negative association with HDL. In the group of women with normal BMD, a weak correlation between femoral neck BMD and triglycerides was found. In group of men with normal BMD, total body and femoral neck BMD was not associated with serum lipids. However, the total body and femoral neck BMD weakly correlated with triglycerides and femoral neck BMD had a weak correlation with total cholesterol in men with low BMD. In women with low BMD the femoral neck BMD relationship with serum lipids were not found, however, same as in a group of men, women, spine BMD was weakly positively associated with triglycerides, and in contrast to

Table 7. Pearson correlation between bone mineral density and serum lipids in men and women, by BMD groups

Serum lipids	Men			Women		
	Total body BMD	Spine BMD	Femoral neck BMD	Total body BMD	Spine BMD	Femoral neck BMD
Normal BMD (T-score ≥ -1)						
TCh	0.02	-0.14	0.04	0.07	-0.01	0.11
HDL	-0.04	-0.1	-0.06	-0.24**	-0.23**	-0.22**
LDL	0.03	-0.16*	0.04	0.08	0.03	0.12
TG	0.04	-0.01	0.04	0.1	0.11	0.27**
Low BMD (-1 >T-score > -2.5)						
TCh	0.1	-0.07	0.24*	0.02	-0.08	-0.11
HDL	-0.03	0.08	-0.11	0.09	-0.22*	-0.03
LDL	0.08	-0.07	0.23	-0.02	-0.02	-0.1
TG	0.25*	-0.04	0.29*	-0.21*	0.26**	-0.11
Very low BMD (T-score ≤ -2.5)						
TCh	-0.14	-0.05	0.61**	0.32	-0.04	0.12
HDL	-0.09	-0.38	0.35	-0.12	-0.26	-0.08
LDL	-0.29	0.15	0.25	0.33	-0.01	0.11
TG	0.11	-0.07	0.72**	0.15	0.09	0.11

* $p < 0.05$, ** $p < 0.01$.

BMD – bone mineral density; TCh – total cholesterol; HDL – high density lipoprotein cholesterol; LDL – low density lipoprotein cholesterol; TG – triglycerides.

men – the weak negative link of total body BMD with triglycerides. In women's group with low BMD the spine BMD also has a slight negative association with HDL. Both in men and women groups with very low BMD, total body, spine and femoral neck BMD in women was not associated with serum lipids, but the same group of men in BMD at the femoral neck BMD moderate correlation with total cholesterol and strong correlation with triglycerides.

3.3. Association of bone turnover and bone structural parameters with metabolic syndrome and it components

We have analyzed men and women NCEP ATPIII criteria corresponding to metabolic syndrome components, BTM and the bone structure rates inequalities between people with and without metabolic syndrome. One hundred nineteen people (21.9% of all investigated individuals) had the metabolic syndrome. Increased waist circumference was in 338 (62.4%) cases, elevated ABP was found in 355 (65.6%) individuals, hyperglycemia – 63 (11.6%), hypertriglyceridemia – 108 (19.9%) and a decrease in the concentration of HDL in 54 (9.9%) of examined subjects. The frequency of metabolic syndrome and its separate components within the examined groups of both sexes presented in Table 8.

Table 8. The frequency of metabolic syndrome and its components in men's and women's groups

Parameters	Men (%)	Women (%)	p
Metabolic syndrome	66 (27.4)	53 (17.7)	0.009
Metabolic syndrome components: Increased waist circumference (male >102 cm, female >88 cm)	187 (77.6)	151 (50.3)	<0.0001
Increased ABP (systolic ≥130 mm/Hg or diastolic ≥85 mm/Hg)	181 (75.1)	174 (58.0)	<0.0001
Hyperglycemia (glucose ≥6.1 mmol/l)	38 (15.8)	25 (8.3)	0.01
Hypertriglyceridemia (TG ≥1.7 mmol/l)	56 (23.2)	52 (17.3)	0.104
Decreased HDL (male <1.03 mmol/l; female <1.29 mmol/l)	19 (7.3)	35 (11.7)	0.079

p – calculated using $\chi 2$ test.
ABP – arterial blood pressure; TG – triglycerides; HDL – high density lipoprotein cholesterol;

It was found that the metabolic syndrome, increased waist circumference, elevated ABP and hyperglycemia were more often male group. Frequency of hypertriglyceridemia in male and female groups did not differ, and the occurrence of decreased HDL levels were significantly higher in women.

We had compared s-CTX-I, PINP and total body, spine and femoral neck BMD readings in groups of men with and without metabolic syndrome. The results of statistical analysis are presented in Table 9.

In men with metabolic syndrome, s-CTX-I and PINP concentration was lower than in men without metabolic syndrome and total body, spine and femoral neck BMD was greater in men with metabolic syndrome group. In women with metabolic syndrome, s-CTX-I and PINP concentrations were also lower than that of women without metabolic syndrome, but that was not statistically significant. In women with metabolic syndrome, the spine and femoral neck BMD was higher compared to women without the metabolic syndrome in the field of BMD.

Because, unlike men, women's age, with and without metabolic syndrome, differed significantly (women with metabolic syndrome had a mean age of 67.49 ± 13.23, and without the metabolic syndrome – 60.43 ± 13, $p < 0.0001$), after doing an analysis of covariance we assessed the s-CTX-I, PINP concentration and total body, spine and femoral neck BMD differences between women in the groups with and without metabolic syndrome, set aside the effect of age (Table 10).

Table 9. Bone turnover markers and bone mineral density readings (mean ± SD) depending on gender and metabolic syndrome

Parameters	Men			Women		
	With metabolic syndrome (n=66)	Without metabolic syndrome (n=175)	p	With metabolic syndrome (n=53)	Without metabolic syndrome (n=247)	p
s-CTX-I, ng/ml	0.371±0.208	0.452±0.196	0.005	0.418±0.225	0.464±0.226	0.173
PINP, ng/ml	46.35±22.88	55.7±25.17	0.009	54.48±22.74	57.42±23.41	0.403
Total body BMD, g/cm^2	1.246±0.139	1.189±0.128	0.003	1.096±0.162	1.074±0.136	0.289
Spine BMD, g/cm^2	1.315±0.242	1.225±0.203	0.004	1.23±0.214	1.116±0.189	<0.001
Femoral neck BMD, g/cm^2	1.118±0.162	1.023±0.151	<0.001	1.004±0.197	0.941±0.167	0.034

p – calculated using Student t-test. s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; BMD – bone mineral density.

Table 10. Women with and without metabolic syndrome s-CTX-I, PINP concentration and total body, spine and femoral neck BMD averages, set aside the effect of age

Parameters	With metabolic syndrome (n=53)	Without metabolic syndrome (n=247)	p
s-CTX-I, ng/ml	0.4	0.47	0.039
PINP, ng/ml	53.41	57.65	0.238
Total body BMD, g/cm^2	1.13	1.07	0.002
Spine BMD, g/cm^2	1.26	1.11	<0.0001
Femoral neck BMD, g/cm^2	1.0	0.94	<0.0001

Averages adjusted taking into account the average age, which was 61.68 years. P – calculated by ANCOVA. S-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; BMD – bone mineral density.

It was found that women with the metabolic syndrome, had s-CTX-I significantly lower, while the total body, spine and femoral neck BMD compared with the larger group of women without metabolic syndrome.

We investigated differences of s-CTX-I, PINP and BMD of total body, spine and femoral neck across the age groups in men and women with metabolic syndrome. Statistical analysis is presented in the eleventh table.

Table 11. s-CTX-I, PINP concentration and total body, spine and femoral neck BMD averages of individuals with metabolic syndrome, according to sex and age

Age groups	Indices (mean ± SD)				
	s-CTX-I, ng/ml	PINP, ng/ml	Total body BMD, g/cm²	Spine BMD, g/cm²	Femoral neck BMD, g/cm²
Men with metabolic syndrome(n=66)					
40–49	0.401±0.213	42.24±13.42	1.259±0.158	1.279±0.2	1.153±0.187
50–59	0.307±0.138	41.78±15.58	1.248±0.097	1.314±0.147	1.149±0.12
60–69	0.347±0.189	43.71±15.49	1.212±0.128	1.249±0.232	1.126±0.156
70–79	0.407±0.299	54.66±39.55	1.297±0.19	1.401±0.35	1.115±0.202
≥80	0.472±0.163	54.46±18.77	1.182±0.091	1.341±0.289	0.963±0.055
p	0.371	0.407	0.378	0.539	0.098
Women with metabolic syndrome(n=53)					
40–49	0.262±0.077	56.91±27.88	1.286±0.109 [d,e]	1.396±0.191 [c]	1.238±0.163 [c,d,e]
50–59	0.413±0.279	54.27±25.39	1.226±0.049 [d,e]	1.351±0.116	1.152±0.069 [d,e]
60–69	0.427±0.181	47.09±15.07	1.103±0.149	1.209±0.172 [a]	0.975±0.172
70–79	0.439±0.282	51.68±14.45	1.025±0.118	1.148±0.236	0.946±0.164
≥80	0.459±0.17	62.03±30.97	1.003±0.169	1.185±0.22	0.899±0.195
p	0.488	0.626	<0.0001	0.043	<0.0001

p – calculated by ANOVA test, finding differences between age groups applied the criteria of LSD. s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; BMD – bone mineral density.
a – p <0.05 compared with the 40–49 years age group;
b – p <0.05 compared with the 50–59 years age group;
c – p <0.05 compared with the 60–69 year age group;
d – p <0.05 compared with the 70–79 year age group;
e – p <0.05 compared with 80 years of age and older age group.

After comparison of data in different age groups of men with metabolic syndrome, statistically significant differences in s-CTX-I, PINP concentration and total body, spine and femoral neck BMD were not found. In women with metabolic syndrome, the lowest s-CTX-I concentrations were in 40–49 years age group, the highest – 80 years of age and older women, but the difference was not statistically significant. There was no significant difference between PINP in age groups also. In women with metabolic syndrome, total body and femoral neck BMD was highest in 40–49 years age group, the lowest – 80 years and older age group. In each older than the previous age group BMD was lower, but the 40–49 and 50–59 year old women total body BMD was significantly higher compared to 70–79 years and 80 years of age and older women's groups. 40–59 years old women with metabolic syndrome, femoral neck BMD was statistically

significantly higher than the 60–69, 70–79 years and 80 years of age and older groups of women, as well as groups of women 40–49 years BMD at the femoral neck was higher than BMD of women in 60–69 age group. Bone mineral density T-score in men and women with and without metabolic syndrome presented in Table 12.

Table 12. Distribution of men and women with and without metabolic syndrome, by T-score

Examined area, T-score	Men (%)			Women (%)		
	With metabolic syndrome	Without metabolic syndrome	p	With metabolic syndrome	Without metabolic syndrome	p
Spine or femoral neck						
T-score ≥-1	103 (58.9)	48 (72.7)	0.023	127 (51.4)	29 (54.7)	0.151
-1 >T-score > -2.5	57 (32.6)	15 (22.7)	0.137	90 (36.4)	20 (37.7)	0.394
T-score ≤-2.5	15 (8.6)	3 (4.5)	0.412	30 (12.1)	4 (7.5)	0.474
Spine						
T-score ≥-1	131 (74.9)	54 (81.8)	0.254	147 (59.5)	39 (73.6)	0.056
-1 >T-score > -2.5	36 (20.6)	10 (15.2)	0.34	74 (30)	10 (18.9)	0.103
T-score ≤-2.5	8 (4.6)	2 (3)	0.732	26 (10.5)	4 (7.5)	0.621
Femoral neck						
T-score ≥-1	118 (67.4)	56 (84.8)	0.007	172 (69.6)	37 (69.8)	0.98
-1 >T-score > -2.5	49 (28)	9 (13.6)	0.02	65 (26.3)	15 (28.3)	0.736
T-score ≤-2.5	8 (4.6)	1 (1.5)	0.451	10 (4.0)	1 (1.9)	0.696

p – calculated by ANOVA test.

It was found that in men in the central areas of the skeleton and femoral neck BMD T-score-1 SD and higher, and was significantly more frequent in groups with the metabolic syndrome compared to the men without metabolic syndrome groups, but femoral neck BMD T-score between -1 and -2.5 more frequent in the men without the metabolic syndrome than in men with the metabolic syndrome. This difference was not found when compared BMD in women with and without metabolic syndrome.

Bone turnover markers and BMD of men and women with different number of metabolic syndrome components were compared (Table 13).

Table 13. s-CTX-I, PINP and BMD of total body, spine and femoral neck (the mean ± SD), according to gender and the number of components of metabolic syndrome

Parameters	1 component	2 components	3 components	4 and more components	p
	Men (n=59)	Men (n=101)	Men (n=49)	Men (n=17)	
s-CTX-I, ng/ml	0.489±0.206	0.431±0.186	0.397±0.208	0.297±0.194	0.003
PINP, ng/ml	56.02±23.6	55.23±26.74	47.41±24.61	43.32±17.25	0.085
Total body BMD, g/cm^2	1.186±0.126	1.199±0.13	1.238±0.143	1.269±0.128	0.044
Spine BMD, g/cm^2	1.228±0.207	1.245±0.199	1.303±0.231	1.35±0.278	0.082
Femoral neck BMD, g/cm^2	1.018±0.161	1.032±0.14	1.11±0.17	1.142±0.14	0.001
	Women (n=81)	Women (n=90)	Women (n=37)	Women (n=16)	p
s-CTX-I, ng/ml	0.521±0.261	0.431±0.189	0.433±0.206	0.383±0.268	0.021
PINP, ng/ml	59.26±22.97	54.54±20.45	56.94±25.66	48.76±12.79	0.266
Total body BMD, g/cm^2	1.061±0.154	1.081±0.136	1.082±0.161	1.129±166	0.403
Spine BMD, g/cm^2	1.085±0.195	1.137±0.207	1.211±0.222	1.273±0.192	0.001
Femoral neck BMD, g/cm^2	0.932±0.138	0.954±0.172	0.991±0.198	1.034±0.197	0.085

p – calculated by ANOVA test. s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; BMD – bone mineral density.

In men with four or more components of metabolic syndrome, s-CTX-I concentrations were low, and statistically significantly different from men, with one component of metabolic syndrome ($p \leq 0.0001$) and two components of metabolic syndrome ($p = 0.01$). PINP concentration difference between groups, depending on the number of components of metabolic syndrome was not observed. Total body, spine, femoral neck BMD of men with metabolic syndrome, was higher in each of a larger number of components of metabolic syndrome group. Total body BMD was the lowest of men, with one component of metabolic syndrome, the total body BMD of these men was 0.052 g/cm^2 significantly lower than in men, with three components of metabolic syndrome ($p = 0.044$) and 0.083 g/cm^2 lower than of men with four or more components of metabolic syndrome ($p = 0.023$). Spinal BMD was lowest in men who have a metabolic syndrome components, and 0.123 g/cm^2 lower than of men with four or more components of metabolic syndrome ($p = 0.039$). The femoral neck BMD was the lowest in men, with one component of metabolic syndrome, their femoral neck BMD was 0.091 g/cm^2 significantly lower than that of men, with three components of metabolic syndrome ($p = 0.002$) and 0.123 gcm^2 lower than that of men with four or more components of metabolic syndrome ($p = 0.004$). Men with two metabolic syndrome components had femoral neck BMD 0.077 g/cm^2 significantly lower than men,

with three components of metabolic syndrome ($p = 0.004$) and 0.11 g/cm^2 lower than men with four or more components of metabolic syndrome ($p = 0.007$).

Women PINP and total body and femoral neck BMD statistically significant differences between groups according to the number of components of metabolic syndrome were not observed. In women with one metabolic syndrome component, s-CTX-I were highest and significantly different from that of women with two ($p = 0.01$), three ($p = 0.049$) or four or more components of metabolic syndrome ($p = 0.026$). Spinal BMD was lowest for women with one component of metabolic syndrome, these women had spine BMD 0.127 g/cm^2 lower than women, with three components of metabolic syndrome ($p = 0.002$) and 0.188 g/cm^2 lower than that of women with four or more metabolic syndrome component ($p = 0.001$).

Between the two genders we did not find any statistically significant s-CTX-I, PINP concentration and total body, spine or femoral neck BMD differences related to the metabolic syndrome component: comparison of the participants with metabolic syndrome who's glycemia was ≥ 6.1 mmol/l, with the metabolic syndrome in persons who's glycemia was < 6.1 mmol/l, as well as those with metabolic syndrome, with systolic ABP ≥ 130 mm/Hg or diastolic ≥ 85 mm Hg, with those with systolic ABP < 130 mm/Hg or diastolic < 85 mm/Hg and people with metabolic syndrome, with triglyceride concentrations > 1.7 mmol/l, with those with the metabolic syndrome and triglyceride concentrations < 1.7 mmol/l, and persons who have decreased HDL levels, with individuals with HDL of ≥ 1.03 mmol/l (men) or ≥ 1.29 mmol/l (women).

Men with metabolic syndrome, one of which components of the metabolic syndrome were an increased waist circumference (> 102 cm), had no statistically significant differences of BTM and total body, spine and femoral neck BMD from men with the metabolic syndrome and a waist circumference of ≤ 102 cm. Meanwhile, for women with metabolic syndrome and increased waist circumference (> 88 cm), total body BMD and spine BMD was significantly higher than in women whose waist circumference ≤ 88 cm, but these women were 10.52 years younger. After the assessment of the impact of women's age, the BMD differences disappeared.

Bone turnover and structure rates depending on the correlation of the metabolic syndrome are presented in Table 14.

It was found that men and women with and without metabolic syndrome, had s-CTX-I significantly weakly negatively associated with total body BMD, as well as men with metabolic syndrome and men and women without metabolic syndrome had weak statistically significant negative s-CTX-I levels in relation to the femoral neck BMD. In a group of women without metabolic syndrome, s-CTX-I had significant negative correlation with spine BMD. Men and women without metabolic syndrome PINP concentration had significantly negative association with total body BMD, also men group without metabolic syndrome PINP concentration had statistically significant weak negative correlation with femoral neck BMD. In group of men and women with the metabolic syndrome PINP concentration relation with the total body, spine or femoral neck BMD was not observed.

Table 14. Correlation between biochemical markers of bone turnover and bone mineral density in two gender groups, depending on the metabolic syndrome

Parameters	s-CTX-I		PINP	
	r	p	r	p
Men with metabolic syndrome (n=66)				
Total body BMD	-0.31	0.011	-0.1	0.406
Spine BMD	-0.1	0.449	0.05	0.699
Femoral neck BMD	-0.31	0.011	-0.12	0.341
Men without metabolic syndrome (n=175)				
Total body BMD	-0.2	0.008	-0.19	0.013
Spine BMD	-0.1	0.179	-0.1	0.185
Femoral neck BMD	-0.26	0.001	-0.2	0.009
Women with metabolic syndrome (n=53)				
Total body BMD	-0.32	0.022	-0.14	0.302
Spine BMD	-0.22	0.108	-0.09	0.514
Femoral neck BMD	-0.19	0.182	-0.09	0.517
Women without metabolic syndrome (n=247)				
Total body BMD	-0.31	<0.0001	-0.21	0.001
Spine BMD	-0.23	<0.0001	-0.08	0.203
Femoral neck BMD	-0.22	<0.0001	-0.11	0.09

r – Pearson's correlation coefficient. s-CTX-I and PINP logarithmic transformation was applied. s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide. BMD – bone mineral density.

3.4. Predictive value of serum lipids and the metabolic syndrome components providing data of bone mineral density

For the analysis of total body BMD dependence on bone turnover markers, serum lipids and metabolic syndrome components we used stepwise multivariate linear regression analysis. The initial regression model included the dependent variable – total body BMD and independent variables which are: s-CTX-I and PINP, glucose, total cholesterol, HDL, LDL, triglycerides, systolic and diastolic ABP, waist circumference and age. In order to create an optimal model, that is to say such, which has the highest adjusted coefficient of determination, we applied backward analysis. Independent variables entering into the final model presented in Table 15.

In 12.2% of men changes in total body BMD is lead by a linear influence of s-CTX-I concentration, waist circumference and age. Men who has s-CTX-I concentrations higher by 1 ng ml, total body BMD is 0.169 g/cm^2 lower, without changing other factors.

Table 15. Relationship between total body BMD and waist circumference, s-CTX-I, serum lipids and age (multiple linear regression)

Parameters	adjR^2	β	95% PI	p
Men (n=241)				
Waist circumference	0.122	0.225	0.001 – 0.004	<0.0001
s-CTX-I		-0.169	-0.193 – -0.029	0.008
Age		-0.173	-0.003 – -0.001	0.005
Women (n=300)				
Waist circumference	0.379	0.313	0.002 – 0.004	<0.0001
s-CTX-I		-0.184	-0.173 – -0.056	<0.0001
TCh		0.097	0.001 – 0.023	0.036
HDL		-0.11	-0.06 – -0.004	0.024
Age		-0.557	-0.007 – -0.005	<0.0001

adjR2 – adjusted coefficient of determination; PI – 95 % regression coefficient confidence interval; β – the standardized regression coefficient; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; TCh – total cholesterol; HDL – high density lipoprotein cholesterol.

In 37.9% of women changes in total body BMD is lead by a linear influence of s-CTX-I, total cholesterol, HDL, waist circumference and age. For women with s-CTX-I concentrations higher by 1 ng/ml, total body BMD is 0.184 g/cm^2 lower, without changing other factors. In women with total cholesterol levels higher by 1 mmol/l, total body BMD was of 0.097 g/cm^2 higher, and in those women with HDL cholesterol levels higher by 1 mmol/l, total body BMD was lower by 0.11 g/cm^2 lower, without changing other factors.

In both the absence and presence of metabolic syndrome we haven't found dependence of the men's total body BMD on serum lipids. BTM, serum lipids, ABP, waist circumference, age, resulted only in a small part of changes of total body BMD (12.3% in cases of metabolic syndrome and 11.1% in cases of the absence of the metabolic syndrome). In the presence of metabolic syndrome there was noted statistically significant negative dependence of total body BMD on s-CTX-I, and a positive dependence on PINP concentration, in cases of the absence of metabolic syndrome dependence on the s-CTX-I, waist circumference and age.

Metabolic syndrome in women changes of total body BMD in 55.5% resulted by s-CTX-I, serum lipids (LDL and triglyceride), diastolic blood pressure, waist circumference, age. The statistically significant correlation was found between total body BMD and LDL, diastolic blood pressure and waist circumference.

Table 16. Relationship between total body BMD and waist circumference, bone turnover biochemical markers, serum lipids, components of metabolic syndrome and age (multiple linear regression)

Parameters	adjR²	β	95% PI	p
Men with metabolic syndrome (n=66)				
s-CTX-I	0.123	-0.537	-0.59 – -0.127	0.003
PINP		0.433	0.001 – 0.005	0.016
Systolic ABP		0.211	0.001 – 0.004	0.077
Men without metabolic syndrome (n=175)				
s-CTX-I	0.111	-0.16	-0.198 – -0.01	0.03
Waist circumference		0.184	0.001 – 0.004	0.012
Age		-0.216	-0.004 – -0.001	0.003
Women with metabolic syndrome (n=53)				
s-CTX-I	0.555	-0.198	-0.287 – 0.002	0.053
LDL		0.237	0.003 – 0.066	0.032
Triglycerides triglycerides		-0.179	-0.081 – 0.002	0.065
Diastolic ABP		0.196	0.0001 – 0.008	0.045
Waist circumference		0.272	0.001 – 0.007	0.015
Age		0.001	-0.01 – -0.005	<0.0001
Women without metabolic syndrome (n=247)				
s-CTX-I	0.339	-0.175	-0.17 – -0.041	0.001
HDL		-0.111	-0.066 – -0.001	0.042
Waist circumference		0.308	0.002 – 0.004	<0.0001
Age		-0.518	-0.0007 – -0.004	<0.0001

adjR2 – adjusted coefficient of determination; PI – 95% regression coefficient confidence interval; β – the standardized regression coefficient; ABP – arterial blood pressure; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; HDL – high density lipoprotein cholesterol.

Women's total body bone mineral density dependence on low-density lipoprotein cholesterol in metabolic syndrome was calculated using partial regression and presented in Figure 2.

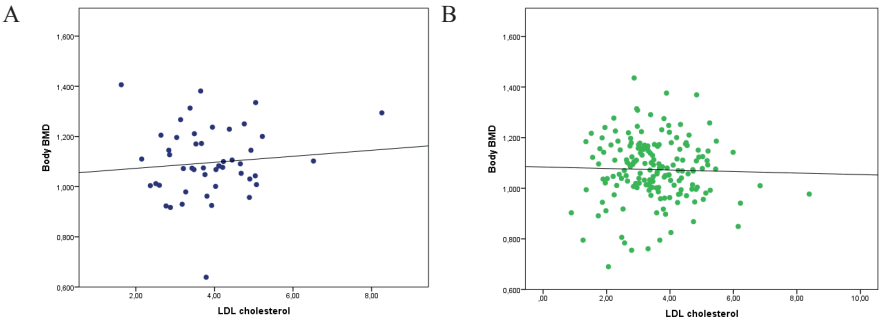


Figure 2. The total body bone mineral density and low-density lipoprotein cholesterol of women with metabolic syndrome (A) and without metabolic syndrome (B)

Graphic expression of results suggests that women with higher levels of LDL 1 mmol/l, has total body BMD 0.034 g/cm^2 higher, without changing other factors. In the absence of metabolic syndrome in women s-CTX-I, serum lipids (HDL), waist circumference and age resulted in 33.9% of total body BMD changes. In the absence of metabolic syndrome in women total body BMD dependence on s-CTX-I and HDL, waist circumference and age was observed.

Step and multivariate linear regression analysis applied to analyze lumbar spine BMD dependence on the biochemical markers of bone turnover, serum lipids and metabolic syndrome components. The initial regression model included the dependent variable – the spine BMD, and the same independent variables as well as in the analysis of total body BMD dependence: s-CTX-I and PINP, glucose, total cholesterol, HDL, LDL, triglycerides, systolic and diastolic ABP, waist circumference and age. In order to create an optimal model, that is to say such, which has the highest adjusted coefficient of determination, we applied backward analysis. Men's spine BMD dependence did not fit the model – the adjusted coefficient of determination was very low 0.045, so analysis was limited to women's spinal BMD dependence. Independent variables entering into the final model presented in Table 17.

In 24.5% of women changes in spine BMD are lead by a linear s -CTX-I, HDL cholesterol, waist circumference and age influence. For women with s-CTX-I concentrations above 1 ng/ml, spine BMD is 0.217 g/cm^2 lower, without changing other factors. For women with HDL cholesterol levels higher than 1 mmol/l, the spinal BMD is 0.116 g/cm^2 lower, those women whose waist circumference higher by 1 cm, spine BMD is 0.302 g/cm^2 higher, without changing other factors. For women with metabolic syndrome, spinal bone mineral density is significantly negatively influenced by the concentration of triglycerides (β = -0.068, p = 0.004) and age (β = -0.007, p = 0.001).

Table 17. Relationship between spine BMD and waist circumference, bone turnover biochemical markers, serum lipids, components of metabolic syndrome and age in women (multiple linear regression)

Parameters	adjR²	β	95% PI	p
s-CTX-I	0.245	-0.217	-0.318 – -0.063	0.004
PINP		0.13	0.001 – 0.002	0.072
Glucose		0.101	-0.001 – 0.054	0.056
HDL		-0.116	-0.091 – -0.004	0.033
Waist circumference		0.302	0.003 – 0.006	<0.0001
Age		-0.399	-0.008 – -0.004	<0.0001

adjR2 – adjusted coefficient of determination; PI – 95% regression coefficient confidence interval; β – the standardized regression coefficient; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; PINP – procollagen type I N propeptide; HDL – high density lipoprotein cholesterol.

Diagram shows that in women with higher levels of triglycerides by 1 mmol/l, lumbar BMD is 0.068 g/cm² lower, without changing other factors (Figure 3).

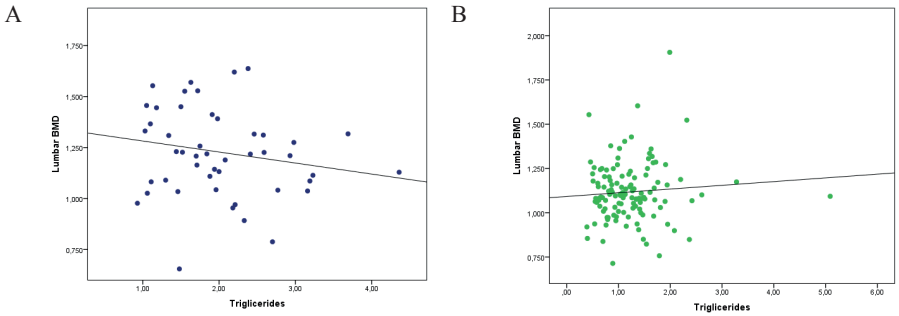


Figure 3. Spine $L_1 – L_4$ bone mineral density and triglyceride levels of women with metabolic syndrome (A) and without metabolic syndrome (B)

Multivariate linear regression analysis applied to the analyze of the dependence of femoral neck BMD on the biochemical markers of bone turnover, serum lipids and metabolic syndrome components. The initial regression model included the dependent variable – the femoral neck BMD and the same independent variables as well as the analysis of total body BMD dependence: s-CTX-I and PINP, glucose, total cholesterol, HDL, LDL, triglycerides, systolic and diastolic ABP, waist circumference and age. In order to create an optimal model, that is to say such,

which has the highest adjusted coefficient of determination, we applied backward analysis. Independent variables entering into the final model presented in Table 18.

Table 18. Relationship between femoral neck BMD and waist circumference, s-CTX-I, serum lipids and age (multiple linear regression)

Parameters	adjR²	β	95% PI	p
Men (n=241)				
s-CTX-I	0.202	-0.178	-0.233 – -0.047	0.003
Waist circumference		0.246	0.002 – 0.005	<0.0001
Age		-0.297	-0.005 – -0.002	<0.0001
Women (n=300)				
s-CTX-I	0.229	-0.104	-0.16 – -0.001	0.049
HDL		-0.096	-0.073 – 0.004	0.077
Waist circumference		0.28	0.002 – 0.005	<0.0001
Age		-0.438	-0.007 – -0.004	<0.0001

adjR2 – adjusted coefficient of determination; PI – 95 % regression coefficient confidence interval; β – the standardized regression coefficient; s-CTX-I – C-terminal cross-linking telopeptide of type I collagen; HDL – high density lipoprotein cholesterol.

Dependence of the femoral neck BMD on s-CTX-I, waist circumference and age found for both women and men: 20.2% in men and 22.9% in women femoral neck BMD changes are determined by a linear influence of s-CTX-I, waist circumference and age.

Dependence of femoral neck BMD in men with the metabolic syndrome on the s-CTX-I levels ($\beta = -0.331$, $p = 0.015$), PINP ($\beta = 0.003$, $p = 0.008$), waist circumference ($\beta = 0.004$, $p = 0.043$) and age ($\beta = -0.005$, $p = 0.002$) was found. Women with metabolic syndrome had their femoral neck BMD statistically significantly influenced by diastolic arterial blood pressure ($\beta = 0.01$, $p < 0.0001$) and age ($\beta = -0.009$, $p < 0.0001$).

So men's and women's total body, femoral neck and lumbar spine L_1–L_4 bone mineral density are associated with three factors – s-CTX-I, waist circumference and age, but with the metabolic syndrome, this relationship changes, and highlights other factors – LDL cholesterol, triglycerides, diastolic arterial blood pressure, influencing bone mineral density.

4. CONCLUSIONS

1. Men had the lowest serum lipids observed in 80 years and older age group, women – in 40–49 years age group. In post-menopausal women, bone markers s-CTX-I and PINP concentrations are higher than in pre-menopausal women.
2. In men, s-CTX-I and PINP negatively correlated with triglycerides, and in women, PINP negatively correlated with total cholesterol.
3. In women with T-score between -1 and -2.5, spine bone mineral density correlated with triglycerides and negatively correlated with high-density lipoprotein cholesterol. In men with T-score -2.5 and lower, femoral neck bone mineral density correlated with total cholesterol and triglycerides.
4. BMD is higher and bone turnover markers are lower in subjects of both genders with three and more components of metabolic syndrome.
5. In both genders, the bone mineral density statistically significant dependence on the bone resorption marker s-CTX-I, waist circumference and age was found. In presence of metabolic syndrome, there are also other factors affecting bone mineral density – low density lipoprotein cholesterol and triglycerides. In women with LDL levels higher by 1 mmol/l, the total body BMD is higher by 0.237 g/cm^2, and those with higher triglyceride concentration by 1 mmol/l had a lower spine BMD by 0.179 g/cm^2.

SUMMARY IN LITHUANIAN

ĮVADAS

Kaulinio audinio apykaitos biocheminiai žymenys yra osteoblastų ir osteoklastų veiklos produktai: fermentai, organizmo matrikso baltymai ir kitos medžiagos, kurių galima rasti organizmo kraujyje arba šlapime. Šiuo metu manoma, kad kaulinio audinio kokybė gali būti vertinama nustačius kaulinio audinio metabolizmą atspindinčius biocheminius kaulinio audinio apykaitos žymenis. Tikimasi, kad biocheminių žymenų tyrimas, naudojamas kaip papildoma informacija, gali parodyti kaulinio audinio apykaitos aktyvumą. Tačiau kaulinio audinio apykaitos greitis, kurį rodo biocheminiai žymenys, skirtingų amžiaus grupių labai varijuoja. Įrodyta, kad visiškai sveikų 30–39 metų moterų tų pačių kaulinio audinio apykaitos biocheminių žymenų normos mažesnės, palyginti su vyresnių nei 40 metų moterų. Moterų kaulinio audinio apykaitos biocheminių žymenų ir amžiaus sąsajų tyrimų skelbiami rezultatai yra prieštaringi: vienų tyrimų duomenys tokios priklausomybės buvimą patvirtina, o kitų – ne.

Daugiau nei 20 metų ieškoma kaulinio audinio biocheminių žymenų ir kaulų mineralų tankio ryšių, tačiau tyrimais nustatyta nevienoda koreliacija arba šių kaulinio audinio remodeliacijos rodiklių ryšio nerandama.

Kaulinio audinio apykaitos mechanizme dalyvauja tie patys imunologiniai ir uždegimo patofiziologiniai veiksniai, kaip ir aterogenezės procese, kuri glaudžiai susijusi su pakitusia medžiagų (gliukozės, cholesterolio) apykaita, nutukimu ir arterinio kraujo spaudimo sutrikimais. Šių pokyčių klinikinių simptomų kompleksas vadinamas „metaboliniu sindromu“. Vidutiniškai 11–30 proc. vyresnių nei 20 metų asmenų nustatomi simptomai, atitinkantys metabolinio sindromo kriterijus, ir beveik dvigubai dažniau metabolinis sindromas nustatomas sulaukusiems 40 metų bei vyresniems žmonėms. Esant šiam sindromui, nutukimas sukelia lėtinio uždegimo procesą, kuris yra atsparumo insulinui bei paties metabolinio sindromo pagrindinis komponentas. Manoma, kad nutukimo sukelto uždegimo metu išskiriami citokinai aktyvina kaulinio audinio rezorbciją ir taip sutrikdo šio audinio apykaitą. Hiperglikemija, išsivysčiusi dėl atsparumo insulinui, gali sukelti kaulinio audinio žymenų pokyčius, o hiperlipidemija skatina osteoklastų veiklą, kaip matyti iš *in vitro* atliktų tyrimų rezultatų. Visa tai leidžia manyti, kad kaulinio audinio apykaitos biocheminiai žymenys gali būti susiję su medžiagų apykaitos sutrikimo rodikliais, kurių kompleksas įvardijamas kaip „metabolinis sindromas“. Tačiau įvairius biocheminių kaulinio audinio apykaitos ir struktūros rodiklių ryšius su hiperglikemija, dislipidemija, hipertenzija ir nutukimu analizuojančių tyrimų duomenys yra nevienareikšmiai, dažnai tirtos tik moteriškosios lyties asmenų grupės.

Darbo tikslas

Ištirti ir įvertinti kaulinio audinio apykaitos ir struktūros rodiklių, kraujo lipidų ir metabolinio sindromo komponenčių tarpusavio sąsajas.

Darbo uždaviniai

1. Nustatyti vyrų ir moterų kaulinio audinio apykaitos (I tipo kolageno C telopeptido ir I tipo prokolageno N propeptido) ir struktūros (kaulų mineralų tankio) rodiklių bei kraujo lipidų (bendrojo cholesterolio, didelio ir mažo tankio lipoproteinų cholesterolio ir trigliceridų) koncentracijos amžinius ypatumus.
2. Įvertinti I tipo kolageno C telopeptido, I tipo prokolageno N propeptido ir kaulų mineralų tankio sąsajas su bendrojo cholesterolio, didelio ir mažo tankio lipoproteinų cholesterolio bei trigliceridų koncentracija kraujyje.
3. Įvertinti kaulinio audinio apykaitos ir struktūros rodiklių sąsajas su metabolinio sindromo komponentėmis.
4. Nustatyti prognostinę kraujo lipidų ir metabolinio sindromo komponenčių vertę numatant kaulinio audinio apykaitos ir struktūros rodmenis.

Darbo mokslinis naujumas

Šiame moksliniame darbe pateikiami kaulinio audinio apykaitos ir struktūros ryšiai su kraujo lipidų koncentracija vyresnio amžiaus asmenims. Pirmą kartą buvo ištirti 80 metų ir vyresni vyrai bei moterys.

Mažai mokslinių darbų nagrinėja vyrų kaulinio audinio apykaitos biocheminių žymenų sąsajas su kraujo lipidais. Mūsų atliktas mokslinis darbas yra originalus tuo, kad skirtingo kaulų mineralų tankio T-lygmens vyrų grupėse nustatytos kaulų mineralų tankio sąsajos su kraujo lipidų koncentracija.

Mokslinėje literatūroje yra pavienės publikacijos apie metabolinį sindromą ir kaulinio audinio apykaitą. Šiame tyrime įvertinti vyrų ir moterų kaulinio audinio apykaitos ir struktūros rodiklių ryšiai su metabolinio sindromo komponenčių skaičiumi.

Pirmą kartą nustatyta kraujo lipidų ir metabolinio sindromo komponenčių prognostinė vertė numatant kaulinio audinio apykaitos ir struktūros rodmenis.

TIRTI ASMENYS IR TYRIMO METODAI

Imties dydis apskaičiuotas „G Power 3.1.2“ statistine programa remiantis anksčiau atliktų tyrimų pateiktais kaulinio audinio apykaitos biocheminių žymenų įverčiais, įvertinant 5 proc. statistinę paklaidą bei siekiant 95 proc. patikimumo. Gautas Vilniaus regioninio biomedicininių tyrimų etikos komiteto leidimas atlikti šį tyrimą (Nr. 158200–10–209–056LP26 (2010–10–06).

Dalyvauti tyrime buvo pasiūlyta visiems 40 metų ir vyresniems asmenims, kurie nuo 2010 m. spalio mėn. iki 2011 m. gegužės mėn. kreipėsi į Nacionalinį osteoporozės centrą dėl kaulų mineralų tankio nustatymo. Į tyrimą buvo įtraukti savanoriškai sutikę dalyvauti tyrime ir pasirašę informuoto asmens sutikimo formą asmenys. Neįtraukimo į tyrimą kriterijai: nesutikimas atlikti kurios nors tyrimo procedūros, nėštumas, per pastaruosius 12 mėnesių gauta didelė jonizuojančiosios apšvitos dozė, kaulų lūžis per pastaruosius 12 mėnesių, piktybiniai navikai, kaulų metabolinės ligos, ankstyva moterų menopauzė (iki 45 metų). Taip pat į tyrimą neįtraukti asmenys, vartoję kaulinio audinio apykaitą veikiančius vaistus ir dislipidemijai gydyti skirtus vaistus.

Kiekvienas asmuo per apsilankymą buvo apklaustas tyrėjo, o apklausos rezultatai buvo fiksuojami anketoje. Registruoti demografiniai duomenys, socialiniai ir gyvensenos veiksniai – rūkymas, alkoholio vartojimas.

Renkant medicininę anamnezę tiriamieji buvo apklausti dėl persirgtų ar esamų ligų. Moterų klausta apie menstruacijas. Taip pat rinkti duomenys apie vartotus ir vartojamus vaistus, galinčius turėti įtakos kaulinio audinio apykaitos būklei. Tiriamųjų fizinis aktyvumas vertintas taikant Tarptautinio fizinio aktyvumo klausimyno sutrumpintą formą (angl. IPAQ_SHOT_SELF_ADM_Lithuanian). Arterinis kraujospūdis matuotas abiejų rankų žasto srityje, mechaniniu manometru, taikant seniai žinomą Riva-Rocci / Korotkoff matavimo techniką. Radus skirtumą, kitiems dviem matavimams buvo pasirenkama ranka, vadovaujantis 2007 m. Europos kardiologų draugijos gairėmis. Laikyta, kad kraujo spaudimas yra padidėjęs, kai galutinis išmatuotas sistolinis kraujo spaudimas buvo 130 mm Hg ir daugiau arba diastolinis 85 mm Hg ir daugiau.

Juosmens apimtis matuota vadovaujantis Pasaulio sveikatos apsaugos organizacijos (PSO) rekomendacijomis. Taip pat išmatuotas ūgis ir kūno masė, kūno masės indeksas (KMI) skaičiuotas su SPSS statistine programa, kūno masę kilogramais padalijus iš ūgio metrais, pakelto kvadratu.

Kaulinio audinio apykaitos biocheminių žymenų, vitamino D, PTH ir medžiagų apykaitos parametrų, tokių kaip gliukozė, cholesterolis ir jo frakcijos, tyrimams kraujas imtas ryte tarp 8 ir 11 val. iš alkūninės venos tiriamiesiems nevalgius dvylika valandų, į du mėgintuvėlius. Mėginiai, paruošti kaulinio audinio rezorbcijos žymens I tipo kolageno karboksitelopeptido (s-CTX-I) ir kaulinio audinio formacijos žymens I tipo prokolageno N propeptido (PINP) bei 25-hidroksivitamino D (25(OH)D ir paratiroidinio hormono (PTH) tyrimams, buvo laikomi -20 ºC, ne ilgiau kaip savaitę. Atšildžius mėginius, nedelsiant buvo atliktas tyrimas „Roche Diagnostic“ imunologiniu analizatoriumi „Cobas E411“. Bendrasis cholesterolis (BCh), jo frak-

cijos (DTL, MTL, trigliceridai) bei gliukozė plazmoje, tirti fermentiniu metodu, visiškai automatizuotu ADVIA 1800 („Siemens Medical Solution“) analizatoriumi.

Kaulų mineralų tankis tirtas dvisrautės radioabsorbciometrijos (DXA) metodu, viso kūno, kairiosios pusės šlaunikaulio proksimalinės dalies ir stuburo juosmeninių 1–4 slankstelių srityse, priekine-užpakaline kryptimi.

Tyrime analizuoto metabolinio sindromo ir jo komponenčių kriterijai pasirinkti vadovaujantis NCEP ATP III rekomendacijomis. Kai tirtiems asmenims buvo nustatyti trys ar daugiau metabolinio sindromo komponenčių, jie priskirti metabolinio sindromo grupei.

Statistinei duomenų analizei naudotas „SPSS 18.0 for Windows“ programų paketas. Buvo skaičiuoti kintamųjų vidurkiai, vidutinis kvadratinis nuokrypis (standartinis nuokrypis, SN). Kiekybinių kintamųjų vidurkių skirtumai buvo palyginti naudojant Stjudento t testą, skirtumas tarp amžiaus grupių vertintas *post hoc* ir LSD (angl. *Least Significant Difference*) metodikomis. Sąsajoms tarp kiekybinių kintamųjų nustatyti apskaičiuotas Pearson koreliacijos koeficientas (r).

Veiksnių įtaka analizuota taikant daugiaveiksnės tiesinės regresijos modelį, prieš tai patikrinus, ar nepriklausomi kintamieji nėra multikolinearūs. Modelio tinkamumui nustatyti skaičiuotas determinacijos koeficientas.

Tikrinant statistines hipotezes, skirtumai laikyti statistiškai reikšmingais, jeigu paklaidos tikimybės p reikšmė buvo mažesnė nei 0,05.

REZULTATAI

Analizuoti 541 asmenų tyrimų duomenys, tarp jų 241 (44,5 proc.) vyras ir 300 (55,5 proc.) moterų. Tyrimo duomenimis, jauniausias vyras ir moteris buvo 40 metų, vyriausias vyras buvo 95 metų, moteris – 89 metų. Tirtų moterų menopauzės vidutinis amžius buvo 49,06 ± 6,46 metų.

Vyrų ir moterų amžius, kūno masės indeksas nesiskyrė, tačiau vyrų ūgis, kūno masė ir juosmens apimtis buvo statistiškai reikšmingai didesni negu moterų. Taip pat reikšmingai didesnis buvo vyrų arterinis kraujo spaudimas. Nustatyta, kad vyrų gliukozės koncentracija kraujyje buvo statistiškai reikšmingai didesnė, o bendrojo cholesterolio, DTL ir MTL koncentracija – reikšmingai mažesnė nei moterų, tačiau triglicerido, s-CTX-I, PINP, vitamino D ir PTH koncentracijos skirtumo tarp lyčių nebuvo. Reikšmingai didesnis viso kūno, stuburo ir šlaunikaulio kaklo KMT nustatytas vyrų grupėje.

Analizuojant kraujo lipidų, KŽ, KMT rodiklius amžiaus grupėse, vyrai ir moterys buvo suskirstyti į amžiaus grupes kas 5 metus.

Įvertinus gautus rezultatus, galima teigti, kad 40–45 metų tirtų asmenų grupių, kuriose buvo moterys iki menopauzės ir asmenys su normaliu KMT, buvo mažiausia s-CTX-I ir PINP koncentracija palyginus su kitomis amžiaus grupėmis. Nors s-CTX-I ir PINP koncentracija vyresnių amžiaus grupių nei 40–44 metų nebuvo didesnė kiekvienoje vyresnio amžiaus grupėje, tačiau ji nesiekė 40–44 metų amžiaus grupės koncentracijos lygio.

Siekiant įvertinti ir tarpusavyje palyginti kaulinio audinio apykaitos ir struktūros rodiklius

su kraujo lipidų koncentracijos tyrimais, išanalizuoti abiejų lyčių KŽ ir kaulinio audinio struktūros rodiklių koreliaciniai ryšiai su kraujo lipidų koncentracija.

Nustatyta, kad vyrų 40–49 metų amžiaus grupės s-CTX-I koncentracija silpnai ir PINP koncentracija vidutiniškai stipriai buvo susijusi su DTL koncentracija bei PINP koncentracija vidutiniškai stipriai neigiamai susijusi su trigliceridų koncentracija kraujyje. Neigiamas MTL koncentracijos ryšys su PINP nustatytas moterų 50–59 metų amžiaus grupėje. 60–69 metų amžiaus grupės vyrų vidutiniškai stiprus neigiamas ryšys buvo s-CTX-I koncentracijos su trigliceridų koncentracija ir silpnas neigiamas – PINP koncentracijos su trigliceridų koncentracija. Tokia pati PINP koncentracijos ir trigliceridų koreliacija nustatyta moterų 60–69 metų amžiaus grupėje. 70–79 metų amžiaus abiejų lyčių grupių PINP koncentracija nebuvo susijusi su bendrojo cholesterolio, MTL, DTL ar trigliceridų koncentracija, tačiau moterų s-CTX-I buvo silpnai neigiamai susijusi su trigliceridais. 80 metų ir vyresnio amžiaus grupėje bendrojo cholesterolio koncentracija silpnai siejosi su moterų PINP koncentracija ir silpnai neigiamai su vyrų PINP koncentracija.

Taigi, įvertinus KŽ ir KMT ryšius su kraujo lipidų koncentracija kraujyje, nustatyta skirtinga vyrų ir moterų KMT koreliacija, kuri skyrėsi ir amžiaus grupėse. Tai paskatino išanalizuoti kraujo lipidų koncentraciją atskirose tiriamų asmenų grupėse, priklausomai nuo T-lygmens.

Nustatyta, kad vyrų normalaus KMT grupėje stuburo KMT labai silpnai neigiamai siejosi su MTL koncentracija, moterų normalaus KMT grupėje stuburo KMT silpnai neigiamai siejosi su DTL koncentracija, taip pat moterų viso kūno ir šlaunikaulio kaklo KMT buvo silpnai neigiamai susijęs su DTL koncentracija. Moterų su normaliu KMT grupėje šlaunikaulio kaklo KMT silpna koreliacija nustatyta su trigliceridų koncentracija. Vyrų grupės su mažu KMT buvo viso kūno ir šlaunikaulio kaklo KMT silpna koreliacija su trigliceridų koncentracija ir šlaunikaulio kaklo KMT silpna koreliacija su bendrojo cholesterolio koncentracija. Mažo KMT moterų grupėje, kaip ir vyrų grupės, stuburo KMT buvo silpnai teigiamai susijęs su trigliceridų koncentracija ir, priešingai nei vyrų, nustatyta silpna neigiama moterų viso kūno KMT sąsaja su trigliceridų koncentracija. Mažo KMT moterų grupėje stuburo KMT taip pat silpnai neigiamai siejosi su DTL koncentracija. Labai mažo KMT tiek vyrų, tiek moterų grupėse viso kūno ir stuburo KMT bei moterų šlaunikaulio kaklo KMT nebuvo susiję su kraujo lipidų koncentracija, tačiau nustatyta tos pačios KMT grupės vyrų šlaunikaulio kaklo KMT vidutinio stiprumo koreliacija su bendrojo cholesterolio ir labai stipri su trigliceridų koncentracija kraujyje.

Buvo išanalizuoti metabolinio sindromo komponenčių ir KŽ bei kaulinio audinio struktūros rodiklių skirtumai, esant metaboliniam sindromui ir jo nesant.

Metabolinį sindromą turinčių vyrų s-CTX-I ir PINP koncentracija buvo mažesnė nei metabolinio sindromo neturinčių vyrų, o viso kūno, stuburo ir šlaunikaulio kaklo KMT didesnis buvo metabolinio sindromo vyrų grupėje. Metabolinį sindromą turinčių moterų stuburo ir šlaunikaulio kaklo KMT buvo didesnis, palyginti su metabolinio sindromo neturinčių moterų atitinkamos srities KMT. Taip pat nustatyta, kad esant metaboliniam sindromui moterų s-CTX-I koncen-

tracija buvo statistiškai reikšmingai mažesnė, o viso kūno, stuburo ir šlaunikaulio kaklo KMT didesnis, palyginti su metabolinio sindromo neturinčių moterų grupe.

Analizuojant viso kūno KMT priklausomybę nuo kaulinio audinio apykaitos žymenų, kraujo lipidų koncentracijos ir metabolinio sindromo komponenčių, buvo atlikta daugiaveiksnė žingsninė tiesinės regresijos analizė.

Nustatyta, kad esant metaboliniam sindromui, moterų s-CTX-I, kraujo lipidų (MTL ir trigliceridų) koncentracija, diastolinis arterinis kraujospūdis, juosmens apimtis, amžius lėmė 55,5 proc. viso kūno KMT pokyčių. Taip pat nustatyta viso kūno KMT statistiškai reikšminga teigiama priklausomybė nuo MTL koncentracijos, diastolinio AKS ir juosmens apimties.

Dalinės regresijos metodas parodė, kad moterų, kurių MTL koncentracija didesnė 1 mmol/l, viso kūno KMT yra 0,237 g/cm^2 didesnis, nesikeičiant kitiems veiksniams. Nesant metabolinio sindromo moterų s-CTX-I, kraujo lipidų (DTL) koncentracija, juosmens apimtis ir amžius lėmė 33,9 proc. viso kūno KMT. Nesant metabolinio sindromo pastebėta moterų viso kūno KMT priklausomybė nuo s-CTX-I, DTL koncentracijos, juosmens apimties ir amžiaus.

Vyrų stuburo KMT priklausomybei modelis netiko, todėl analizuota tik moterų stuburo KMT priklausomybė. Nustatyta, kad moterų, kurių trigliceridų koncentracija didesnė 1 mmol/l, stuburo juosmens slankstelių KMT yra 0,068 g/cm^2 mažesnis, nesikeičiant kitiems veiksniams.

Analizuojant šlaunikaulio kaklo KMT priklausomybę nuo kaulinio audinio apykaitos žymenų, kraujo lipidų koncentracijos ir metabolinio sindromo komponenčių, nustatyta metabolinį sindromą turinčių vyrų šlaunikaulio kaklo KMT priklausomybė nuo s-CTX-I koncentracijos ($\beta = -0{,}331$, $p = 0{,}015$), PINP ($\beta = 0{,}003$, $p = 0{,}008$), juosmens apimties ($\beta = 0{,}004$, $p = 0{,}043$) ir amžiaus ($\beta = -0{,}005$, $p = 0{,}002$). Metabolinį sindromą turinčių moterų šlaunikaulio kaklo KMT statistiškai reikšmingai veikė diastolinis arterinis kraujospūdis ($\beta = 0{,}01$, $p < 0{,}0001$) ir amžius ($\beta = 0{,}009$, $p < 0{,}0001$).

Taigi vyrų ir moterų viso kūno, šlaunikaulio kaklo ir stuburo juosmens L_1–L_4 slankstelių kaulų mineralų tankis priklauso nuo trijų pagrindinių veiksnių – s-CTX-I koncentracijos, juosmens apimties ir amžiaus, tačiau esant metaboliniam sindromui ši priklausomybė pakinta, išryškėja ir kiti veiksniai – MTL cholesterolio, trigliceridų koncentracija, diastolinis arterinis kraujo spaudimas, veikiantys kaulų mineralų tankį.

IŠVADOS

1. Tirtų vyrų mažiausios kraujo lipidų koncentracijos nustatytos 80 metų ir vyresnio amžiaus grupėje, moterų – 40–49 metų amžiaus grupėje. Moterų po menopauzės kaulinio audinio apykaitos biocheminių žymenų s-CTX-I ir PINP koncentracija kraujyje yra didesnė negu moterų iki menopauzės.

2. Vyrų s-CTX-I ir PINP koncentracija kraujyje silpnai neigiamai koreliuoja su trigliceridų koncentracija, o moterų PINP koncentracija neigiamai koreliuoja su bendrojo cholesterolio koncentracija kraujyje.

3. Moterų, kurių T-lygmuo tarp –1 ir –2,5, stuburo kaulų mineralų tankis koreliuoja su trigliceridų koncentracija ir neigiamai koreliuoja su didelio tankio lipoproteinų cholesterolio koncentracija kraujyje. Vyrų, kurių T-lygmuo –2,5 ir mažesnis, šlaunikaulio kaklo kaulų mineralų tankis koreliuoja su bendrojo cholesterolio ir trigliceridų koncentracija kraujyje.

4. Abiejų lyčių asmenims, turintiems tris ir daugiau metabolinio sindromo komponenčių, kaulų mineralų tankis didesnis, o kaulinio audinio apykaitos biocheminių žymenų koncentracijos mažesnės, nei metabolinio sindromo neturintiems.

5. Nustatyta statistiškai reikšminga kaulų mineralų tankio priklausomybė nuo biocheminio rezorbcijos žymens s-CTX-I koncentracijos, juosmens apimties ir amžiaus abiejų lyčių asmenims. Esant metaboliniam sindromui išryškėja ir kiti veiksniai, turintys įtakos kaulų mineralų tankiui, – mažo tankio lipoproteinų cholesterolio ir trigliceridų koncentracija. Moterų, kurių MTL koncentracija didesnė 1 mmol/l, viso kūno KMT yra 0,237 g/cm^2 didesnis, o 1 mmol/l didesnė trigliceridų koncentracija atitinka 0,179 g/cm^2 mažesnį stuburo KMT.

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