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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

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Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

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ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

გაღიზიანება, რასაც მოსდევს სხვადასხვა ჰუმორული ფაქტორის აქტივაცია და დუოდენური აფერენტაცია. ამასთან, შერეული საკვების მიღებიდან 20-30 წთ-ში ტკივილისადმი მგრძნობელობის დაქვეითებაში ერთ-ერთ სავარაუდო მექანიზმად ავტორები განიხილავენ თორმეტგოჯა ნაწლავში ქოლეცისტოკინინის გამოყოფას, რასაც, სავარაუდოდ, ანტინოციცეპციური გავლენა აქვს ენდოგენური ოპიოიდების სინთეზის გამო.

FEATURES OF BONE METABOLISM AND THEIR INFLUENCE ON ARTERIAL WALL STIFFNESS IN POSTMENOPAUSAL WOMEN WITH CONTROLLED UNCOMPLICATED HYPERTENSION

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Cardiovascular disease occupies a leading place in the structure of morbidity and mortality [29]. With the global aging of the population, osteoporosis and cardiovascular diseases have become a major issue with considerable medical and socioeconomic burdens [13]. Age is an important determinant in the development of arterial hypertension (AH), which is largely associated with arterial consolidation due to the age-related changes and other risk factors [6]. Observational studies have reported an association between low serum vitamin D levels and elevated risk of cardiovascular disease (CVD), though such studies may not prove causation because of possible unmeasured confounding. Some findings concern the patients with osteoporosis who frequently suffer from vascular calcification, which was shown to predict both cardiovascular morbidity/mortality and osteoporotic fractures. Various common risk factors and mechanisms have been suggested to cause both bone loss and vascular calcification, including aging, estrogen deficiency, vitamin D and K abnormalities, chronic inflammation, oxidative stress, metabolic syndrome [24]. Major breakthroughs in molecular and cellular biology of bone metabolism and characterization of knockout animals with deletion of bone-related genes have led to the concept that common signaling pathways, transcription factors and extracellular matrix interactions may account for both skeletal and vascular abnormalities [12].

However, there seems to be a current lack of information on the nature of bone metabolism in patients with various diseases of the cardiovascular system, for example, arterial hypertension and arterial wall stiffness.

The aim of this study was to examine the features of bone metabolism and their influence on arterial wall stiffness in postmenopausal women with a controlled uncomplicated hypertension.

Material and methods. The study involved 44 women (main group) with the mean age of 69.04±0.72 years and a postmenopausal duration of 18.4±0.85 years, with uncomplicated arterial hypertension (AH) grade 2, and 30 healthy patients (control group), their mean age 69.3±1.21 years and postmenopausal duration of 19.4±1.18 years ($p>0.05$).

Inclusion criteria: females over 65 y.o. with a controlled AH of 1-2 grades, according to the office BP morning measurements. They took an antihypertensive therapy based on indapamide-retard + amlodipine at a dose of 1.5/5 mg /d or 1.5/10 mg/d with target blood pressure levels (<140/90 mm Hg).

Exclusion criteria: the presence of secondary hypertension; previous history of myocardial infarction and/or stroke; heart failure with NYHA above a functional class (FC) II signs of stable angina of the III-IV FC; left ventricular ejection fraction (LVEF)<50%; diabetes; congenital heart diseases; peripheral vascular disease; heart rhythm disturbances (permanent and persistent form of atrial fibrillation, frequent extrasystolic arrhythmia, ventricular paroxysms or ventricular tachycardia in the medical history, persistent sinus tachycardia); violation of atrioventricular conduction or sinus bradycardia (heart rate< 50 bpm) or weakness syndrome of the sinus node; impossibility to withdraw previous AHT; obesity with body mass index (BMI)>35 kg/m²; chronic kidney disease with GFR for EPI<60 ml/min/1.73 m2 and any other clinically relevant concomitant pathology; hyper- (> 5.5 mmol/L) and hypopotassemia (< 3.5 mmol/L).

Questionnaire-survey method was used to assess a nutritional status. Furthermore, patients were examined by a general clinical examination, routine laboratory clinical and biochemical studies, measurements of office bBP (brachial systolic, diastolic, pulse, mean BP (bSBP, bDBP, bPP, mean bBP) using a mechanical tonometer Microlife BP AG1-30. Applantation tonometry was performed using the SphygmoCor device AtCor Medical (Australia) and Doppler-Echo by the ultrasound diagnostic system of the Hitachi ALOKA Medical.

According to the pulse wave analysis by applanation tonometry [3], we determined central systolic, diastolic, pulse, and mean BP (respectively, cSBP, cDBP, cPP, mean cBP), augmentation pressure (AP), augmentation index (AIx), augmentation index, normalized for a pulse rate of 75 beats/min (AIx75), amplification pressure (PP ampl.), and measured carotid-radial (PVW rad.) and carotid-femoral pulse wave velocity (PWV fem.). The amplification pressure was calculated as the ratio between bPP and cPP (%) [19].

The FRAX-all and FRAX-hip technique was used to calculate the 10-year risk of hip fracture and major osteoporotic fractures (the Ukrainian version was developed under the guidance of Prof. Povoroznyuk V.V. at www.sheffield.ac.uk/FRAX/tool.aspx) [23].

Bone turnover markers in the peripheral blood (procollagen type 1 propeptide (P1NP), collagen type 1 cross-linked C-telopeptide (β-CTx)), parathyroid hormone (PTH) and vitamin D were defined by electrochemiluminescence method Eleksys 2010 analyzer (Roche Diagnostics, Germany), Cobas test systems. Levels of ionized calcium, phosphorus in serum (hexokinase method0 were assayed by the automatic biochemical analyzer Integra 400/800 ("Roche", Germany).

Vitamin D status was evaluated according to the latest classification [21,24], based on which vitamin D deficiency is diagnosed at 25 (OH) D in serum below 20 ng/ml, vitamin D deficiency at 25 (OH) D 20-30 ng/ml. A concentration of 25 (OH) D in the range of 30–50 ng/ml indicates an optimum level, and 50–100 ng/ml - a high level.

The bone mineral density (BMD) was examined using the "Hologic Discovery" apparatus. The following parameters of bone mineral density (BMD, g/cm^2) were determined: T score of the total body, lumbar spine L1-L4, femoral neck, radial bone. To assess the quality of bone tissue (Trabecular Bone Score - TBS), the TBS iNsight technique, developed by Med-Imaps (Bordeaux, France), was used.

Results and discussion. Within the framework of risk factor analysis for bone fractures, it was found that the calcium content in the actual diet (according to the questionnaires) in the main group was on average 245±21 mg/day, and in the control group - 268±23 mg/day. Thus, it was significantly reduced in both groups compared to the generally accepted norms.

At the time of the inclusion at this stage of the study, the target levels of blood pressure were reached, that is, the effect of elevated blood pressure on bone metabolism was excluded. Patients with hypertension and control group were compared by age, BMI, brachial and central blood pressure (Table 1).

bSBP, bDBP, bPP, mean bBP - brachial systolic, diastolic, pulse, mean blood pressure; cSBP, cDBP, cPP, mean cBP - central systolic, diastolic, pulse, and mean BP; AP-augmentation pressure; AIx-augmentation index; AIx75 - augmentation index, normalized for a pulse rate of 75 beats/min; PP ampl.- amplification pressure ; PWV rad., PWV fem. - carotid-radial and carotid-femoral pulse wave velocity.

At the time of inclusion, we revealed a significant increase in AP, AIx, AIx75 in the main group by 37.7%, 57.5%, 58.2% (Table 1, $p<0.001$) and a decrease in PPampl. by 20.8% (Table 1, $p<0.001$) compared to the control, which reflects the increase of the central PP due to the influence of the reflected wave, and characterizes the increased stiffness of arteries.

Patients of the main group, compared with the control group, at the time of inclusion in the study, had PWV rad. which was higher by 31% and PWV fem. by 32%, respectively (Table 1, all $p<0.001$). In hypertensives, PWV is an independent risk factor for cardiovascular death and all causes [30].

Table 1. Baseline data of BP and pulse wave indices in two groups of patients

Parameter	Main group n=44	Control group n=30
Age, years	69.04±0.72	69.3±1.21
Postmenopausal duration (PD), years	18.4±0.85	19.4±1.18
Duration of AH, years	17.0±0.86	–
BMI, kg/m²	28.9±0.55	27.6±1.11
bSBP, mm hg	123.6±1.95	121.2±1.85
bDBP, mmHg	78.3±1.28	79.3±1.51
bPP, mmHg	45.7±1.71	41.8±1.27
cSBP, mm Hg.	117.1±1.84	113.7±1.73
cDBP, mmHg	78.6±1.22	79.3±1.51
cPP, mmHg	38.4±1.53	35.1±1.15
HR (heart rates), bpm	66.0±1.09	72.7±1.34***
AP, mm Hg	14.5±0.87	9.03±0.59***
Alx, %	34.2±1.12	14.5±1.38***
Alx75, %	30.6±1.15	12.8±1.19***
PPampl, %	120.1±1.79	152.9±2.19***
PWV rad., m/s	10.0±0.28	6.89±0.26***
PWV fem., m/s	11.6±0.37	7.9±0.24***

*Statistically relevant difference in the scores between two groups * $p<0.05$; ** $p<0.01$; *** $p<0.001$*

Table 2. Baseline data of the examined groups

Parameter	Main group n=44	Control group n=30
TCh, mmol/l	6.28±0.18	4.6±0.1*
LDL cholesterol, mmol/l	3.83 ±0.17	1.73±0.14*
P1NP, ng/ml	55.12±4.45	58.32±3.24
Total vitamin D, ng/ml	23.21±1.1	29.18±2.12*
β – CTx, ng/ml	0.57±0.03	0.45±0.03*
PTH, ng/ml	67.9±3.75	39.56±1.14*
Ca++, mmol/l	1.27±0.02	1.3±0.02
Phosphorus, mmol/l	1.17±0.02	1.10±0.02

** - statistically relevant difference in the scores between two groups $p<0.05$*

The analysis of bone metabolism manifested the level of markers PINP, ionized calcium, phosphorus which did not differ in the comparison groups, whereas a significantly higher level of PTH was observed in patients of the main group, possibly as a result of vitamin D deficiency, more pronounced in patients with an AH.

Note the increase of the resorption marker activity in the main group, which was reflected by a likely increase in the marker β-CTx. This suggests the need for choosing osteoporosis treatment tactics.

The average level of vitamin D in patients with AH was lower by 20.7% compared to the healthy women. Vitamin D deficiency was found in 21 (47.7%) patients of the main group, deficiency - in 16 (36.4%), normal level - in 7 (15.9%), whereas in the control group, vitamin D deficiency was found in 6 (20.0%), insufficiency - in 4 (13.3%) patients. Secondary hyperparathyroidism was determined in the patients in the main group with vitamin D deficiency. Thus, patients with hypertension suffer a secondary hyperparathyroidism against the background of vitamin D deficiency, which may explain the additional negative effect on the alterations in blood vessel stiffness [5,18].

To evaluate the relationship between arterial stiffness, phosphorus-calcium metabolism, vitamin D, we conducted the Spearman correlation analysis. We found statistically significant correlations between the PWV fem. and the level of PTH, the PTH and the Alx, the PTH and the Alx 75%, the LDL level and Alx 75% (Table 3).

The main group results indicate the presence of hypercholesterolemia, a more pronounced deficiency of vitamin D, secondary hyperparathyroidism and accelerated bone tissue metabolism.

BMD disorders were found in 33 (75%) patients of the main group, 25 (56.8%) of them being women had osteopenia and 8 (18.2%) - osteoporosis. In the control group, BMD disorders

Table 3. Correlation between changes in BP and pulse wave values, arterial stiffness and bone metabolism in main group patients

Parameter	r
PPampl. – HR	0.44*
PTH – bPP	0.46*
PTH – PWV fem.	-0.44*
PTH - Alx	-0.31*
PTH – Alx 75%	-0.36*
P1NP- TCh	0.30**
P1NP- LDL	0.37**
Vitamin D - Age	-0.42*
Vitamin D - PD	-0.37*
Vitamin D – FRAX all	-0.4*
PPamp - LDL	0.36*
LDL – Alx 75%	-0.36*
LDL - AP	0.31*

** - the correlation is significant at the level of 0.05*

Table 4. Baseline data analysis of bone mineral density, FRAX of the examined groups

Parameter	Main group n=44	Control group n=30
FRAX all, %	5.94±0.44	4.44±0.12*
FRAX hip, %	1.72±0.27	1.13±0.09*
TBS, SD	1.27±0.02	1.30±0.03
BMD (L1-L4), g/sm^2	1.07±0.03	1.20±0.03*
T-score L1-L4, SD	-0.62±0.27	-0.20±0.24*
BMD femoral neck right, g/sm^2	0.84±0.02	0.97±0.03*
T-score femoral neck right, SD	-0.84±0.14	-0.23±0.17*
BMD femoral neck left, g/sm^2	0.84±0.02	1.02± 0.02*
T-score femoral neck left, SD	-0.8±0.15	-0.05± 0.2*
BMD Total body, g/sm^2	1.09±0.01	1.15±0.02*
T-score Total Body, SD	-0.5±0.16	-0.08±0.23
BMD Radius , g/sm^2	0.67±0.01	0.83±0.02*
T- score radius, SD	-1.04±0.18	-0.35±0.13*

** - statistically relevant difference in the scores between two groups p<0.05*

were found in 11 (36.7%) women: osteopenia in 7 (23.3%), osteoporosis in 4 (13.3%) (Table 3).

Average FRAX-all and FRAX-hip of the main group were significantly higher compared to the control group. This is explained by the presence of fractures in the anamnesis of 9 women (20.4%), included in the main group. Patients in the control group had no history of fractures.

Patients of the main group had a decrease in BMD at all the skeletal sites in (Table 4), compared with women without hypertension. The TBS bone quality index did not differ in the comparison groups.

To evaluate the relationship between arterial stiffness and BMD we conducted a Spearman correlation analysis (Table 5).

As revaled by the findings, the value of BMD total body, BMD radius, BMD femoral neck left, TBS, FRAX all were significantly decreased and associated with the increased parameters of applanation tonometry, in particular AP, AIx, AIx 75 (Table 5).

Correlation analysis in the control group did not reveal a significant correlation between the elastic-elastic properties of the arteries and the BMD indices.

Many epidemiological studies have shown that a low BMD and atherosclerosis appear to be related. However, their correlation is not completely clear after a full adjustment of shared confounders of atherosclerosis and bone metabolism [28].

Osteoporosis and vitamin D deficiency cause the impairments of bone density, strength and microarchitecture in older patients and increased risk of fragility fractures, and cause a significant morbidity and mortality [28].

Certain studies showed that vitamin D supplementation was not associated with reduced risks of MACE, myocardial infarction, stroke, cardiovascular mortality, or all cases of mortality. Additional trials of a higher-dose vitamin D supplementation, perhaps targeting members of older age groups and focusing on the CVD endpoints, such as heart failure, are of interest [4].

It was revealed in the studies [16] of older adults that vitamin D deficiency is associated with myocardial infarction and mortality. PTH excess is associated with heart failure. Vitamin D and PTH might influence cardiovascular risk through divergent pathways [10].

One of the studies [11] showed that in the older, predominantly postmenopausal South African women, BP, large artery stiffness and IMT were associated with calciotropic hormones and bone resorption, indicating a predisposition to arterial calcification. It is known that recombinant osteoprotegerin is a bioactive protein intended for use in the cell culture applications. Osteoprotegerin is an osteoblast-secreted decoy receptor that functions as a negative regulator of bone resorption. This protein specifically binds itself to its ligand, osteoprotegerin ligand, both of which are key extracellular regulators of osteoclast development. Studies of the mouse counterparts also suggest that this protein and its ligand play a role in lymph-node organogenesis and vascular calcification [26].

The study [17] confirmed an association between arterial stiffness and BMD in women. The other recent studies [20] showed a significant correlation between a vascular calcification and BMD.

There is a lack of data on the above-mentioned association in patients with CVD, namely with AH, for the possibility of substantiating common pathogenetic mechanisms between the development of osteoporosis and calcification of vessels, the role of secondary hyperparathyroidism.

Researchers have shown [7] that the arterial stiffness, as assessed by PWV, independently increased both with BP and with PTH, but BP remains the main driver of arterial stiffening.

Regarding the association between osteoporosis and atherosclerosis, the study [25] showed that the low BMD is associated with coronary atherosclerosis in the healthy postmenopausal women, independent of age and cardiovascular risk factors. Postmenopausal women with a decreased BMD may have a higher risk of developing coronary atherosclerosis.

The correlations we observed between PTH and PWVfem in women may indicate a possible relationship between media calcification (arteriosclerosis) and aortic atherosclerosis with the development of osteoporosis. This mechanism may be related to a violation of vitamin D. It is known that vitamin D deficiency is an important risk factor for the development of not only metabolic bone disease, but also of hypertension, obesity, diabetes, and its additional intake may significantly reduce the incidence of cardiovascular complications [5].

The key link in these processes is probably the disruption of the formation of the active metabolite of vitamin D, since the target organs for hypertension, diabetes are kidneys, and their lesion reduces the synthesis of 1α-hydroxylase - an enzyme through which 25-hydroxycholecalciferol (25 (OH) D3, calcidiol) in the kidneys is converted to the active form of vitamin D3-

Table 5. Correlation among pulse wave values, arterial stiffness and BMD in main group

Parameter	cPP, mmHg	AP, mmHg	Alx, %	Alx75, %	PPampl, %	PWV rad, m/s	PWV fem, m/s
FRAX all, %	**0.39***	**0.32***	**0.36***	0.37	**–0.44***	0.29	0.12
TBS, SD	–0.42	0.12	0.10	0.19	**0.32***	0.30	0.22
BMD (L1-L4), g/sm^2	0.26	0.01	–0.20	–0.18	0.19	0.14	**0.3***
T-score L1-L4, SD	–0.18	–0.18	**–0.57 ***	–0.13	0.28	0.02	0.24
BMD femoral neck right, g/sm^2	0.02	–0.02	0.11	0.30	0.21	0.14	0.22
T-score femoral neck right, SD	–0.18	–0.35	–0.27	–0.22	–0.09	0.15	–0.03
BMD femoral neck left, g/m^2	–0.04	–0.11	0.02	**0.36***	0.31	0.33	0.10
T-score femoral neck left, SD	–0.27	–0.16	–0.10	–0.27	0.01	0.03	–0.11
BMD Total body, g/sm^2	0.08	–0.09	**–0.41***	**–0.36***	0.12	0.24	0.14
T-score Total Body, SD	–0.26	–0.19	–0.10*	–0.12	0.18	–0.12	0.05
BMD Radius , g/sm^2	0.23	0.26	**-0.32**	**-0.32**	**-0.37***	0.15	0.12
T- score radius, SD	–0.29	–0.25	–0.30	–0.21	–0.04	–0.23	–0.13

** - the correlation is significant at the level of 0.05*

1,25 by dihydroxycholecalciferol (1,25 (OH) 2D3, calcitriol - D-hormone) [25]. Due to the hypovitaminosis of the D-hormone, hypocalcemia develops, which in turn leads to the development of secondary hyperparathyroidism, increasing the rate of bone tissue resorption, results in the development of OP and enhances calcium exit from the depot, increases its absorption in the intestine, and flow into the intestine. Alkaline phosphatase exchange is central in this process as a molecular marker of vascular calcification [22]. The production of endothelial cell vesicle matrix, which regulates mineralization in vascular intimacy and the media, stimulates smooth muscle cells (MMCs) [1]. Other cell types (eg. microvascular pericytes and adventitial fibroblasts) have the ability to generate a mineralized matrix and stimulate osteoblasts to differentiate, resulting in an increased calcification [22]. Arterial calcification may occur in the intimacy and media. Proinflammatory mediators cause an increase in LDL cholesterol concentration due to osteogenic differentiation of MMCs. Media calcification is associated with an advanced age, diabetes and chronic kidney disease, contributes to arterial stiffness, which increases the risk of adverse cardiovascular events [15]. In our study, we also obtained data on the deficiency of vitamin D, secondary hyperparathyroidism in patients with an uncomplicated hypertension, which may explain the mechanism of increase in the level of bone tissue resorption marker. Correlation between arterial stiffness (AP, AIx, AIx75) and BMD may indicate an association of media calcification, i.e. arteriosclerosis, and aortic atherosclerosis with development of OP [15]. In our opinion, the explanation for this phenomenon may be a disorder of vitamin D metabolism in the elderly women with hypertension, which we found in the study. It is known that vitamin D deficiency is an important risk factor for the development of not only metabolic bone disease, but also hypertension, obesity, diabetes, and its supplemental intake may significantly reduce the frequency of cardiovascular events [5]. We found statistically significant correlations between the PWVfem. and PTH levels. The value of BMD total body, BMD radius, BMD femoral neck left, TBS, FRAX-all were significantly decreased and associated with the increased parameters of applanation tonometry, in particular AP, AIx, AIx 75 . This probably indicates an association between vitamin D metabolism disorders due to the secondary hyperparathyroidism, progression of arterial rigidity and calcification of elastic fibers in women postmenopausal women with a controlled uncomplicated hypertension [2]. Correlations between total cholesterol (TCh), low density lipoprotein (LDL), and P1NP levels indicate the likelihood of hypercholesterolemia among bone turnover markers activity in the elderly patients with an uncomplicated hypertension.

Conclusions. The data obtained from the study of the parameters of applanation tonometry and the structural and functional state of bone tissue in patients with an uncomplicated hypertension, aged 69±3.30 years reveals the possibility of joint pathogenetic mechanisms of development the atherocalcinosis, increased vascular stiffness, developing osteoporosis. These processes were associated with the reduced level of 25(OH) D, hypercholesterolemia, secondary hyperparathyroidism, and determine the necessary selection of therapy for correcting the revealed disorders.

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SUMMARY

FEATURES OF BONE METABOLISM AND THEIR INFLUENCE ON ARTERIAL WALL STIFFNESS IN POSTMENOPAUSAL WOMEN WITH CONTROLLED UNCOMPLICATED HYPERTENSION

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The aim of this study was to investigate the features of bone metabolism and their influence on the arterial wall stiffness in postmenopausal women with a controlled uncomplicated arterial hypertension (AH).

The study involved 44 women (main group) with the mean age of 69.04±0.72 years and a postmenopausal duration of 18.4±0.85 years, suffering from an AH grade 2, and 30 healthy patients (control group), their mean age being 69.3±1.21 years, postmenopausal duration 19.4±1.18 years (p>0.05). All patients underwent general clinical and laboratory examination with determination of lipid level in blood. Pulse wave analysis (SphygmoCor) parameters , Bone mineral density (BMD) were assessed. The levels of 25(OH) D, parathyroid hormone, propeptide procollagen of type 1 aminoterminal (P1NP), b-isomerized C-terminal telopeptides (b-CTx), ionized calcium and phosphorus in serum were assessed.

The data obtained from the study of the parameters of applanation tonometry and the structural and functional state of bone tissue in patients with an uncomplicated hypertension at the age of 69±3.30 years manifest the likelihood of joint pathogenetic mechanisms of developing atherocalcinosis, increased vascular stiffness and impending osteoporosis.

Keywords: hypertension, arterial stiffness, osteoporosis.

РЕЗЮМЕ

ОСОБЕННОСТИ КОСТНОГО МЕТАБОЛИЗМА И ЕГО ВЛИЯНИЕ НА ЖЕСТКОСТЬ АРТЕРИАЛЬНОЙ СТЕНКИ У ЖЕНЩИН В ПОСТМЕНОПАУЗЕ С КОНТРОЛИРУЕМОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Цель исследования - изучить особенности метаболизма костной ткани и его влияние на жесткость артериальной стенки у женщин в постменопаузе с контролируемой неосложненной артериальной гипертензией.

В исследовании приняли участие 44 женщины (основная группа), средний возраст - 69,04±0,72 года, длительность постменопаузы 18,4±0,85 г., с артериальной гипертензией (АГ) 2 степени. Группу сравнения составили 30 здоровых женщин, средний возраст - 69,±1,21 г., длительность постменопаузы 19,4±1,18 г. (p>0,05). Исследуемым проведено общеклиническое и лабораторное обследование с определением уровня липидов в крови. Оценены параметры пульсовой волны (SphygmoCor), минеральная плотность костной ткани, уровни 25 (OH) D, паратиреоидного гормона, пропептида проколлагена аминотерминального типа 1, b-изомеризованных С-концевых телопептидов, ионизированного кальция и фосфора в сыворотке крови.

Данные, полученные при изучении параметров аппланационной тонометрии и структурно-функционального состояния костной ткани у пациентов с неосложненной АГ в возрасте 69±3,30 г., свидетельствуют о вероятности совместных патогенетических механизмах развития атерокальциноза, повышения жесткости сосудов и развития остеопороза.

რეზიუმე

ძვლოვანი მეტაბოლიზმის თავისებურებები და მოქმედება არტერიული კედლის სიმტკიცეზე მენოპაუზის ასაკის ქალებში კონტროლირებული არტერიული ჰიპერტენზიით

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კვლევის მიზანს წარმოადგენდა ძვლოვანი ქსოვილის თავისებურებების და მათი გავლენის შეფასება არტერიული კედლის სიმტკიცეზე მენოპაუზის ასაკის

ქალებში კონტროლირებული გაურთულებელი არტერიული ჰიპერტენზიით.

კვლევაში მონაწილეობა მიიღო 44 ქალმა (ძირითადი ჯგუფი) არტერიული ჰიპერტენზიის II ხარისხით, საშუალო ასაკი - 69,04±0,72 წ., მენოპაუზის ხანგრძლივობა - 18,4±0,85 წ. შედარების ჯგუფი შეადგინა 30 ჯანმრთელმა ქალმა, საშუალო ასაკი – 69±1,21 წ., მენოპაუზის ხანგრძლივობა - 19,4±1,18 წ. (p>0,05). პაციენტებს ჩაუტარდა ზოგადი კლინიკური და ლაბორატორიული კვლევა ლიპიდების დონის განსაზღვრით სისხლში. შეფასებულია პულსური ტალღის პარამეტრები (SphygmoCor), ძვლოვანი ქსოვილის მინერალური სიმკვრივე, 25 (OH) D-ის, პარა-თიროიდული ჰორმონის, ტიპი 1 ამინოტერმინალური პროკოლაგენის პროპეპტიდის, ხ-ი ზომერიზებული C–ტელოპეპტიდების, იონიზებული კალციუმის და ფოსფორის დონე სისხლის შრატში.

პარამეტრების შესწავლით მიღებული მონაცემები მიუთითებს ათეროკალცინოზის, არტერიული კედლის სიმტკიცის მომატების და ოსტეოპოროზის ერთობლივი პათოგენეზური მექანიზმების არსებობის შესაძლებლობის შესახებ.

CHARACTERISTICS OF DRUG RESISTANT TUBERCULOSIS IN GEORGIA (2015-2020)

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In 2019, an estimated 10 million people fell ill with tuberculosis (TB) worldwide (5.6 million men, 3.2 million women and 1.2 million children). A total of 1.4 million people died from TB in 2019 (including 208 000 people with HIV). Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. A global total of 206 030 people with multidrug- or rifampicin-resistant TB (MDR/RR-TB) were detected and notified in 2019, a 10% increase from 186 883 in 2018. Worldwide, only 57% of MDR-TB patients are currently successfully treated [1,2].

According to the World Health Organization (WHO), in 2018, the total number of notified TB Cases in Georgia was 2 590 (incidence – 65 cases per 100 000 population).

MDR-TB was diagnosed in 12% of new, and in 31% of previously treated cases. The treatment outcome was defined as successful in 65% of MDR/RR-TB and in 56% of XDR-TB cases started on second-line treatment in 2016 (cohorts – 339 and 55, respectively) [3].

For three decades, drug-resistant tuberculosis (TB) has posed grave challenges to patients, communities and global TB control efforts. Treatment of multidrug-resistant (MDR)-TB and extensively drug-resistant (XDR)-TB was relied on medications that are less potent and more toxic than first-line TB therapy, which is used for treatment of drug susceptible TB. Consequently, prolonged drug-resistant TB treatment was associated with frequent and severe side-effects. This led to the high rate of unfavorable treatment outcomes. Fortunately, in recent years TB world globally has several key innovations that, together, have brought us to a tipping point in revolutionizing the care of patients with MDR- and XDR-TB. In 2012, bedaquiline, the first new TB medication in more than 40 years, was approved by the US Food and Drug Administration (FDA). Approximately 6 months later, delamanid, in yet another new drug class, was approved by the European Medicines Agency [4]. Since 2019, based on WHO's recommendations toxic injectable agents (Kanamycin and Capreomycin) are removed from the DR-TB regimens and patients has the access to the shorter fully oral regimens [5-6]. From 2020, the new treatment regimen with next new drug - Pretomanid is recommended for treatment of XDR-TB patients [6].

Georgia as the part of TB world has always had access to the all previously and newly recommended treatment regimens and today, at the stage of transition from old to new DR-TB treatment, it's important to compare general characteristics of different DR-TB cohorts and to assess possibility to raise the effectiveness of DR-TB treatment in the future.

Material and methods. A retrospective cohort study was conducted with individual data of >18 years old DR-TB patients from 2015 -2020 cohorts, whose treatment outcome was defined until August 2020.

Considering the inclusion criteria, 1581 DR-TB patients (n=503[2015 cohort] + n=387[2016 cohort] + n=345[2017 cohort] + n=229[2018 cohort] + n=113[2019 cohort] + n=4[2020 cohort]), with known treatment outcomes were selected as study participants.

The study was conducted at the National Center for Tuberculosis and Lung Disease as a part of the Georgian National TB Programme. During the study period the treatment of DR-TB patients was provided based on latest WHO's recommendations and in different cohorts the different combinations of old, repurposed or new II line drugs with different duration was used.

Data variables were collected in relation to study objectives and included socio-demographic characteristics, laboratory data, data about susceptibility to the anti-TB drugs, treatment regimens and treatment outcomes.

Treatment was defined as successful in case of "Cured" and "Completed" treatment. "Failure", "Default", "Not Evaluated" and "Death" was defined as unsuccessful outcomes.

The data collected were analyzed by using of EasyStat (https://easystat.app). A descriptive analysis was performed for socio-demographic, behavioral and clinical characteristics. Bivariate and multivariate logistic regression analysis was used to measure the link between these characteristics and treatment outcomes. Odds ratios and their 95% confidence intervals were calculated. All the variables significant at $p<0.05$ in the bivariate analysis were included in the adjusted model.