УДК: 616.12-008.331.1-07-008.9:575.113.2

ASSOCIATION OF THE ALLELIC STATE OF THE GNB3 (RS5443) AND AGT (RS4762) GENES WITH ANTHROPOMETRIC, METABOLIC-HORMONAL PARAMETERS AND INDICATORS OF MINERAL METABOLISM IN PATIENTS WITH ESSENTIAL ARTERIAL HYPERTENSION

K. O. Voroniuk, L. P. Sydorchuk

Bukovinian State Medical University, Chernivtsi, Ukraine

The aim of research – *to analyze the dependence of changes in metabolic-hormonal parameters and indicators of mineral metabolism depending on the allelic state of the AGT (rs4762) and GNB3 genes in patients with essential arterial hypertension (EAH).*
Material and methods. *The case-control study involved 100 patients with EAH stage II, 1-3 degrees of blood pressure (BP), high and very high cardiovascular risk. Among the patients there were 21% (21) men, 79% (79) women. The mean age of patients was 59.86±6.22y.o. The control group consisted of 60 almost healthy individuals, relevant in age (49.13±6.28y.o.) and gender distribution (63% – women, 37% – men). To study AGT (rs4762) and GNB3 (rs5443) genes polymorphism a qualitative polymerase chain reaction (PCR) was performed in real time. The lipid panel parameters, such as: Total cholesterol (TC), Triglycerides (TG), Low-density and High-density lipoprotein cholesterol (LDL-C, HDL-C) were investigated in the blood plasma, using diagnostic kits «Accent 200» (Poland). The atherogenic index (AI) was calculated by the equation: (TC – HDL-C)/ HDL-C. All recruited subjects were tested for serum levels of fasting glucose, ionized calcium, parathyroid (PTH) hormone, 25-hydroxyvitamin D.*
Results. *The activity of certain metabolic processes is associated with the allelic state of the AGT (rs4762) and GNB3 (rs5443) genes in patients with EAH: carriers of the T-allele of the AGT gene (rs4762) have a glucose level 27.36% higher than that of owners of the CC genotype (P CC = 0.032), while KA, on the contrary, is lower 14.41% (P CC =0.047) with a probable difference in women – 14.90% (P CC =0.046); the presence of the TT-genotype of the GNB3 gene (rs5443) in patients with EAH is associated with hypercholesterolemia: the content of cholesterol probably exceeds that of homozygous owners of the wild C-allele 13.95% (P CC =0.037). Hormonal-messenger indicators of the regulation of mineral metabolism do not depend on the allelic state of the GNB3 gene (rs5443), while in the owners of the T-allele of the AGT gene (rs4762) a lower level of total metabolites of vitamin D in the blood (at the " deficiency" level) was established – 14, 97% (P CC =0.002), against a background of a compensatory increase in PTH concentration – 29.18% (P CC =0.025).*
Conclusions. *The mutated T-allele of the AGT gene (rs4762) is associated with hyperglycemia, hypovitaminosis D and a compensatory increase in PTH, and the TT-genotype of the GNB3 gene (rs5443) is associated with hypercholesterolemia in patients with EAH.*

Key words:
arterial hypertension, polymorphism of AGT (rs4762) and GNB3 (rs5443) genes, lipid metabolism, glucose, mineral metabolism.

Clinical and experimental pathology 2022. Vol.21, № 4 (82). P. 65-70.

DOI:10.24061/1727-4338.XXI.4.82.2022.10

E-mail:
lsydorchuk@ukr.net

АСОЦІАЦІЯ АЛЕЛЬНОГО СТАНУ ГЕНІВ GNB3 (RS5443) ТА AGT (RS4762) З АНТРОПОМЕТРИЧНИМИ, МЕТАБОЛІЧНО-ГОРМОНАЛЬНИМИ ПАРАМЕТРАМИ І ПОКАЗНИКАМИ МІНЕРАЛЬНОГО ОБМІНУ У ХВОРИХ НА ЕСЕНЦІЙНУ АРТЕРІАЛЬНУ ГІПЕРТЕНЗІЮ

К. О. Воронюк, Л. П. Сидорчук

Буковинський державний медичний університет, м. Чернівці, Україна

Мета дослідження – *проаналізувати залежність змін метаболічно-гормональних параметрів і показників мінерального обміну від алельного стану генів AGT (rs4762) та GNB3(rs5443) у хворих на есенційну артеріальну гіпертензію (ЕАГ).*
Матеріали і методи. *В одномоментному дослідженні взяло участь 100 хворих на ЕАГ II стадії, 1-3 ступенів підняття артеріального тиску (АТ), високого та дуже високого серцево-судинного ризику. Серед хворих було 21% (21) чоловіків, 79% (79) жінок. Середній вік пацієнтів – 59,86±6,22 років. Група контролю – 60 практично здорових осіб, зіставних за віком (49,13±6,28 років) та статевим розподілом (63% – жінок, 37% – чоловіків). Для дослідження поліморфізму генів AGT (rs4762) та GNB3 (rs5443) виконали якісну полімеразну ланцюгову реакцію (ПЛР) в режимі реального часу. Показники ліпідограми: загальний холестерин (ЗХ), тригліцериди (ТГ), ліпопротеїни низької щільності (ХСЛПНЩ), ліпопротеїни високої щільності (ХСЛПВЩ) досліджували в плазмі крові, використовуючи діагностичні набори фірми*

Ключові слова:
артеріальна гіпертензія, поліморфізм генів AGT (rs4762), GNB3 (rs5443), метаболізм ліпідів, глюкоза, мінеральний обмін.

Клінічна та експериментальна патологія 2022. Т.21, №4 (82). С. 65-70.

«Accent 200» firm (Poland). Індекс атерогенності (ІА) розраховували за формулою: ЗХ-ХСЛПВШ)/ХСЛПВШ. Також обстежуваним визначали рівень глюкози натщесерце, іонізованого кальцію, паратиреоїдного гормону (ПТГ) та 25-гідроксивітаміну D.

Результати. *Активність окремих метаболічних процесів у хворих на ЕАГ асоціює з алельним станом гена AGT (rs4762) та GNB3 (rs5443): у носіїв Т-алеля гена AGT (rs4762) рівень глюкози перевищує цей показник у власників СС-генотипу на 27,36% (P_{CC} =0,032), а коефіцієнт атерогенності, навпаки, нижчий на 14,41% (P_{CC} =0,047) з вірогідною різницею у жінок (на 14,90%, P_{CC} =0,046); наявність у хворих на ЕАГ ТТ-генотипу гена GNB3 (rs5443) асоціює з гіперхолестеролемією: вміст ЗХС вірогідно переважає над відповідним показником у гомозиготних власників дикого С-алеля – на 13,95% (P_{CC} =0,037). Гормонально-месенджерні показники регуляції мінерального обміну не мають залежності від алельного стану гена GNB3 (rs5443), тоді як у власників Т-алеля гена AGT (rs4762) встановили нижчий рівень сумарних метаболітів вітаміну D крові (на рівні " дефіцит") – на 14,97% (P CC = 0,002), на тлі компенсаторного зростання концентрації ПТГ – на 29,18% (P CC = 0,025).*

Висновки. *Гормонально-месенджерні показники регуляції мінерального обміну не мають залежності від алельного стану гена GNB3 (rs5443), тоді як у власників Т-алеля гена AGT (rs4762) встановили нижчий рівень сумарних метаболітів вітаміну D крові (на рівні «дефіцит») – на 14,97% (PCC=0,002), на тлі компенсаторного зростання концентрації ПТГ – на 29,18% (PCC=0,025).*

Introduction

Hypertension is a major modifiable risk factor for cardiovascular diseases (CVD) morbidity and mortality.

The genetic component determines the elevation of blood pressure only 20-30%, the rest is the result of the influence of epigenomic structures, environment, lifestyle, access to medical care, etc. Importantly, both EAH and left ventricular hypertrophy (LVH) are modifiable risk factors. However, the choice of treatment in both cases is much more complicated than simply controlling blood pressure [1]. At the same time, questions arise that point to a genetic predisposition to the development of LVH: why do some patients with EAH with moderate hypertension develop LVH, while others do not; why some patients respond more effectively to antihypertensive drugs with LVH reversal, while others do not. A number of mutated genes encoding sarcomere proteins, actin filaments connecting myofibrils of cardiomyocytes (MYH7, MYBPC3, genes encoding β-myosin heavy chain and myosin-bound protein C), have a direct etiological relationship in patients with hypertrophic cardiomyopathy (HCM) and LVH for other pathologies [1]. But in almost 40% of patients with HCM, the causative genes have to be established yet. Therefore, genetic testing and preclinical identification of pathology in family members is an important progress in understanding the molecular pathogenesis of myocardial hypertrophy, its early diagnosis, prognosis and finding ways for genetically determined treatment.

Materials and methods

Study design and patients

The study was conducted in full compliance with the main ethical principles of the European Convention on Human Rights and Biomedicine, according to the standards of the Helsinki Declaration, GLP and GCP, EUC directive #609 and other EU and international legislations on bioethics. The Research Protocol was approved by the Ethics' Committee of the Bukovinian State Medical University. Each participant signed a consent form to participate in the study. The Research is defined as prospective, cohort, case-control study.

Diagnosis. Inclusion / Exclusion criteria.

Hypertension was defined according to European Societies of Hypertension and Cardiology (ESH/ESC) recommendations: office systolic BP (SBP) values ≥140 mmHg and/or diastolic BP (DBP) values ≥90 mmHg at least for three measurements during a month.

The study enrolled EAH patients with hypertensive-mediated organ damage (HMOD) estimated according to European Societies of Hypertension and Cardiology recommendations (ESH/ESC 2018, 2021): target-organs damage – 2nd stage (asymptomatic EAH), moderate-high CV risk, from the 1st through to the 3rd grade of BP elevation.

Exclusion criteria were as follows: EAH patients with complicated /symptomatic HMOD (coronary heart disease, heart attack, stroke, heart failure, aneurysm, chronic kidney diseases, thickened, narrowed or torn blood vessels in the eyes, carotid arteries intima-media thickness enlargement, peripheral artery disease, etc.); secondary arterial hypertension; malignant or uncontrolled arterial hypertension; diabetes mellitus type I (DM 1), sub- and decompensated diabetes mellitus (DM) type 2 (with diabetic target-organ damage); sub- and decompensated liver diseases; bronchial asthma, chronic obstructive pulmonary disease of III-IV stage with C or D risk value (GOLD 2019); exacerbated infectious diseases or during unstable remission of any location, including systemic immune system diseases; severe dementia; psychological/psychiatric disorders/ diseases; malignancies of any location; multiple organ failure; use of oral corticosteroids or contraceptives; pregnancy or lactation.

100 patients were selected for further examination after screening of matching inclusion and exclusion criteria: 79% women, 21% men, mean age 59,86±6,22 years old. The control group included 60 practically

healthy individuals who were not relatives of the patients, without reliable differences in age (49,13±6,28) and gender distribution (63% – women, 37% – men) with the study group.

Laboratory, anthropometric and clinical data collection

All enrolled patients underwent a complex of basic clinical examinations: clinical anamnesis recording, anthropometric parameters, body mass index (BMI, kg/m^2), complete blood count, total cholesterol level, low / high density level cholesterol (LDL-, HDL-C), serum uric acid, office SBP, DBP and heart rate (HR) measurement, ECG in 12 leads, EchoCG, kidneys' ultrasound examination and Daily Holter BP monitoring in undetermined conditions as well as consultations of ophthalmologist and neurologist according to Ukrainian standards (2019) and European recommendations ESC/ESH (2018, 2021). All recruited patients were observed by general physicians, cardiologists. Patients were tested for serum level of fasting glucose (enzymatic method, «CORMAY», Poland), ionized calcium (Ca^{2+}) (potentiometry, «SINNOWA», China), parathyroid hormone (PTH) and *25-hydroxyvitamin D* (Vit D) (immune luminescent test «MAGLUMI», «SNIB», China), as well as genetic testing (qualitative real-time polymerase chain reaction (qRT-PCR, PCR)) for the detection of GNB3 (rs5443) and AGT (rs4762) gene polymorphism was done.

Research results and their discussion

Our study showed that the level of venous blood glucose in patients with EAH, carriers of the T-allele of the AGT gene, probably exceeded that of owners of the CC-genotype 27.36% (P_{CC}=0,032) (table 1).

Table 1

Glucose and blood lipid panel indicators in the examined depending on the genotypes of the AGT gene (rs4762, 521 C>T)

Values		AGT gene genotypes in the control group		AGT gene genotypes in the group under study	
				CC-	CT-, TT-
Glucose, mmol/l		CC-	5,20±0,18	6,87±0,63 P=0,002	8,75±0,96 P=0,007 P_{CC}=0,032
		CT-	4,85±0,16		
TC, mmol/l		CC-	5,60±0,21	5,77±0,30	5,52±0,34
		CT-	5,15±0,23		
TG, mmol/l		CC-	1,78±0,20	2,08±0,28	1,76±0,19
		CT-	1,89±0,08		
LDL-C, mmol/l		CC-	3,98±0,22	4,29±0,27	4,03±0,34
		CT-	3,86±0,15		
HDL-C, mmol/l		CC-	1,44±0,10	1,24±0,07 P=0,009	1,31±0,06
		CT-	1,19±0,11		
HDL-C, mmol/l	w	CC-	1,54±0,07	1,29±0,06 P=0,007	1,37±0,06
		CT-	1,35±0,08		
HDL-C, mmol/l	m	CC-	1,24±0,11 Рж=0,039	1,11±0,06 Рж=0,009	1,13±0,04 Рж=0,043
		CT-	1,05±0,09 Рж=0,048		
IA, cu		CC-	3,24±0,39	3,81±0,30	3,33±0,19 P_{CC}=0,047
		CT-	3,29±0,10		
IA, cu	w	CC-	2,64±0,30	3,47±0,18	3,02±0,16 P_{CC}=0,046
		CT-	2,81±0,17		
	m	CC-	3,52± 0,28 Рж=0,039	4,20±0,23 Рж=0,037	3,88±0,15 Рж=0,006
		CT-	3,90±0,19 Рж=0,049		

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC} – the probability of differences in indicators among carriers of the CC-genotype in the corresponding group; Pw – the probability of differences in indicators with women in the corresponding group.

However, in individuals with the CC-genotype, against a background of slightly higher hypercholesterolemia and a lower content of HDL-C, a statistically significant increase in IA by 14.41% was established (P_{CC}=0,047) regardless of gender, with a probable difference only in women – 14,90% (P_{CC}=0,046). At the same time, the level of LDL-C in men is significantly lower than the indicator in women, regardless of the allelic state of the AGT gene – 13.95% (Pw=0,009) and 17,52% (Pw=0,043), which was also accompanied by a proper growth of IA – 21.04% (Pw=0,037) and 28,48% (Pw=0,006), respectively.

Owners of the T-allele of the AGT gene (rs4762) were found to have a lower content of total metabolites of vitamin D in the blood (at the «deficiency» level) – 14,97% (P_{CC}=0,002), against a background of a higher concentration of PTH – 29.18% (P_{CC}=0,025), respectively (table 2).

We also did not establish the dependence of the fasting blood glucose level on the polymorphism of the GNB3 gene (rs5443, *825 C>T*) (table 3). However, the content of TC was probably higher in EAH patients with the TT-genotype of the GNB3 gene than in homozygous owners of the wild C-allele – 13,95% (P_{CC}=0,037).

Hormonal-messenger indicators of regulation of mineral metabolism did not depend on the allelic state of the gene *GNB3* (rs5443) (table 4).

Blood pressure levels and individual anthropometric parameters do not depend on polymorphic variants of the AGT gene (rs4762, *521 C>T*) (table 5).

Table 2

Hormonal-messenger indicators of regulation of mineral metabolism depending on the allelic state of the gene *AGT* (rs4762)

Values	AGT gene genotypes in the control group		AGT gene genotypes in the group under study	
			CC-	*CT+TT*-
Ionized calcium concentration, mmol/l	CC-	1,16±0,015	0,17±0,01	0,17±0,02
	CT+TT-	1,16±0,02		
Vit D concentration, ng/ml	CC-	24,15±1,66	21,24±1,63 P=0,042	18,06±1,53 P=0,015 P_{CC}=0,002
	CT+TT-	29,12±1,07		
Parathormone concentration, pg/ml	CC-	55,91±4,33	55,0±5,59	71,05±1,91 P=0,051 P_{CC}=0,025
	CT+TT-	62,48±6,30		

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC} – the probability of differences in indicators with carriers of the CC-genotype in the corresponding group.

Table 3

Glucose and blood lipid panel indicators in subjects depending on the genotypes of the GNB3 gene (rs5443, *825 C>T*)

Values		GNB3 gene genotypes in the control group		GNB3 gene genotypes in the group under study		
				CC-	CT-	TT-
Glucose, mmol/l		CC-	5,13±0,21	7,38±0,78 P=0,011	7,16±0,68 P=0,019	6,32±0,33
		CT-	5,19±0,16			
		TT-	5,65±0,10			
TC, mmol/l		CC-	5,44±0,34	5,52±0,26	5,91±0,38	6,29±0,23 P=0,049 P_{CC}=0,037
		CT-	5,68±0,23			
		TT-	5,65±0,15			
TG, mmol/l		CC-	1,99±0,21	2,11±0,29	1,74±0,20	2,41±0,32 P=0,041 P_{CT}=0,055
		CT-	1,53±0,17 P_{CC}=0,048			
		TT-	1,22±0,15 P_{CC}=0,046			
LDL-C, mmol/l		CC-	3,83±0,33	4,03±0,30	4,50±0,37	4,56±0,24 P=0,051
		CT-	4,03±0,20			
		TT-	4,10±0,12			
HDL-C, mmol/l		CC-	1,35±0,14	1,22±0,12	1,28±0,10 P=0,038	1,29±0,05
		CT-	1,45±0,11			
		TT-	1,29±0,09			
HDL-C, mmol/l	w	CC-	1,52±0,12	1,29±0,09 P=0,034	1,34±0,08	1,28±0,02 P_{CT}=0,004
		CT-	1,53±0,09			
		TT-	1,35±0,10			
	m	CC-	0,83±0,09 Рж=0,005	1,07±0,08 Pw=0,01	1,13±0,04 Pw=0,019	1,14±0,02 Pw=0,046
		CT-	1,35±0,15			
		TT-	1,18±0,07			
IA, cu		CC-	3,44±0,40	3,65±0,28	3,71±0,33	3,86±0,30 P=0,038
		CT-	3,15±0,35			
		TT-	3,02±0,19			

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC}, P_{CT} – the probability of differences in indicators in individuals with CC-, CT- genotypes in the corresponding group; Pw – the probability of differences in indicators with women in the corresponding group.

Table 4

Hormonal-messenger indicators of regulation of mineral metabolism depending on the allelic state of the gene *GNB3* (rs5443)

Values	GNB3 gene genotypes in the control group		GNB3 gene genotypes in the group under study	
			CC-	*CT+TT*-
Ionized calcium concentration, mmol/l	CC-	1,16±0,02	0,17±0,02	0,17±0,01
	CT+TT-	1,17±0,01		
Vit D concentration, ng/ml	CC-	23,61±2,55	20,56±1,69	22,72±1,30
	CT+TT-	25,03±1,46		
Parathormone concentration, pg/ml	CC-	60,91±5,71	63,59±9,0	57,44±6,18
	CT+TT-	54,09±4,55		

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC} – the probability of differences in indicators with carriers of the CC genotype in the corresponding group

Table 5

Individual anthropometric parameters and the level of blood pressure in the examined depending on the genotypes of the AGT gene (rs4762, *521 C>T*)

Values	AGT gene genotypes in the control group		AGT gene genotypes in the group under study	
			CC-	CT-, TT-
SBP, mmHg	CC-	117,14±1,80	152,25±4,0 P<0,001	157,10±2,52 P<0,001
	CT-	116,50±1,0		
DBP, mmHg	CC-	76,67±2,21	94,31±2,23 P<0,001	95,0±1,85 P<0,001
	CT-	72,50±088		
BMI, kg/m²	CC-	26,18±1,27	31,43±1,52 P<0,001	32,17±1,46 P<0,001
	CT-	26,41±0,39		
WC, sm	CC-	89,33±3,61	102,23±2,71 P<0,001	102,11±4,65 P=0,049
	CT-	92,50±1,89		
WHR, cu	CC-	0,85±0,04	0,91±0,03 P=0,001	0,93±0,04
	CT-	0,91±0,03		

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC} – the probability of differences in indicators with the control group according to the corresponding genotype.

The dependence of hemodynamic indicators and individual anthropometric parameters on gene genotypes was also not established *GNB3* (rs5443, *825 C>T*) (table 6).

Table 6

Individual anthropometric parameters and the level of blood pressure in the examined depending on the genotypes of the AGT gene GNB3 (rs5443, 825 C>T)

Values	GNB3 gene genotypes in the control group		GNB3 gene genotypes in the group under study		
			CC-	CT-	TT-
SBP, mmHg	CC-	116,35±2,52	153,05±3,53 P<0,001	152,67±5,0 P<0,001	154,17±2,62 P<0,001
	CT-	116,59±2,22			
	TT-	118,80±1,05			
DBP, mmHg	CC-	75,42±2,29	93,87±1,85 P<0,001	94,50±2,71 P<0,001	95,0±3,07 P=0,001
	CT-	76,65±2,21			
	TT-	78,90±2,0			
BMI, kg/m²	CC-	26,18±1,27	31,43±1,52 P<0,001	32,17±1,46 P<0,001	33,23±0,9 P=0,013
	CT-	26,41±0,39			
	TT-	25,97±0,57			
WC, sm	CC-	89,33±5,98	101,39±3,27 P=0,016	102,27±3,12 P=0,001	108,83±2,90 P=0,048
	CT-	90,17±2,62			
	TT-	97,09±2,0			
WC/HC, cu	CC-	0,84±0,03	0,91±0,02 P=0,017	0,92±0,02 P=0,013	0,94±0,02 P=0,045
	CT-	0,86±0,02			
	TT-	0,88±0,015			

Notes: P – the probability of differences in indicators with the control group according to the corresponding genotype; P_{CC}, P_{CT} – the probability of differences in indicators among carriers of the CC-and TT-genotypes in the corresponding group.

Conclusions

1. The activity of certain metabolic processes in patients with EAH is associated with the allelic state of the AGT (rs4762) and GNB3 (rs5443) genes: carriers of the T-allele of the AGT gene (rs4762) have a glucose level 27.36% higher than that of owners of the CC-genotype 27,36% (P_{CC}=0,032), at the same time, the atherogenicity coefficient, on the contrary, is lower – 14.41% (P_{CC}=0,047) with a probable difference in women – 14,90% (P_{CC}=0,046); the presence of the TT-genotype of the GNB3 gene (rs5443) in patients with EAH is associated with hypercholesterolemia: the content of cholesterol probably exceeds that of homozygous owners of the wild C-allele by 13.95% (P_{CC}=0,037).

2. Hormonal-messenger indicators of the regulation of mineral metabolism do not depend on the allelic state of the GNB3 gene (rs5443), while in the owners of the T-allele of the AGT gene (rs4762) a lower level of total metabolites of vitamin D in the blood (at the «deficiency» level) was established – 14, 97% (P_{CC}=0,002), against a background of a compensatory increase in the concentration of PTH – on 29,18% (P_{CC}=0,025). The obtained results indicate that the hypocalcemia present in patients with EAH, although it does not have a statistically significant dependence on the allelic state of the genes analyzed by us, is caused in part and potentiated by a pronounced deficiency of 25-hydroxycholecalciferol 25(ON)D3 in the blood, especially in patients with EAH carriers of T- allele of the AGT gene (rs4762), which led to an increase in PTH in them to maintain calcium homeostasis at the proper level.

Prospects for further research

In the future, we will investigate the association of hypertrophic geometric models of the left ventricle with changes in clinical and anthropometric parameters.

References

1. Sciarretta S, Paneni F, Palano F, Chin D, Tocci G, Rubattu S, Volpe M. Role of the renin-angiotensin-aldosterone system and inflammatory processes in the development and progression of diastolic dysfunction. Clin Sci (Lond), 2009;116(6):467-77. doi: 10.1042/CS20080390

2. Marian AJ, Braunwald E. Hypertrophic Cardiomyopathy: Genetics, Pathogene-sis, Clinical Manifestations, Diagnosis, and Therapy. Circ Res, 2017;121(7):749-770. doi: 10.1161/CIRCRESAHA.117.311059

3. Repchuk, Y., Sydorchuk, L. P., Sydorchuk, A. R., Fedonyuk, L. Y., Kamyshnyi, O., Korovenkova, O., … & Sydorchuk, R. I. (2021). Linkage of blood pressure, obesity and diabetes mellitus with angiotensinogen gene (AGT 704T> C/rs699) polymorphism in hypertensive patients. Bratislavske Lekarske Listy, 122(10), 715-720.

4. Sydorchuk A, Sydorchuk L. The severity of essential hypertension in terms of blood pressure values does not depend on NOS3 (rs2070744) and GNB3 (rs5443) genes polymorphisms in the West-Ukrainian population. Journal of Education, Health and Sport, 2021;11(10):332-341. DOI: https://doi.org/10.12775/JEHS.2021.11.10.032

5. Ghafouri-Fard S, Gholipour M, Taheri M. The Emerging Role of Long Non-coding RNAs and Circular RNAs in Coronary Artery Disease. Front Cardiovasc Med, 2021;8:632393. doi: 10.3389/fcvm.2021.632393.

6. Global Burden of Disease Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet, 2018; 392:1923-1994.

7. Gregoire Wuerzner, Murielle Bochud, Carole Zweiacker, et al. Step Count is Associated with Lower Nighttime Systolic Blood Pressure and Increased Dipping. Am J Hypertens, 2013; 26(4):527-534. doi:10.1093/ajh/hps094

8. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. NCHS Data Brief, no 360. Hyattsville, MD: National Center for Health Statistics, 2020. https://www.cdc.gov/nchs/products/databriefs/db360.htm.

9. Hall ME, Cohen JB, Ard JD, Egan BM, Hall GE, Lavie CJ et al. Weight-Loss Strategies for Prevention and Treatment of Hypertension: A Scientific Statement From the American Heart Association. Hypertension. 2021;78: e38-e50. https://doi.org/10.1161/HYP.0000000000000202

10. Miranda VPN, Dos Santos Amorim PR, Bastos RR, et al. Association of Lifestyle and Body Composition on Risk Factors of Cardiometabolic Diseases and Biomarkers in Female Adolescents. Mediators Inflamm, 2020, 2020:9170640. doi:10.1155/2020/9170640.

Information about authors:
Sydorchuk L. P. – Doctor of Science, Professor, Head of the Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.
E-mail: lsydorchuk@ukr.net
ORCID ID: https://orcid.org/0000-0001-9279-9531
Voroniuk K. O. – postgraduate student, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.
E-mail: ksju2605@ukr.net
ORCID ID: https:// orcid.org/0000-0002-7233-5112

Відомості про авторів:
Сидорчук Л. П. – д.мед.н., професор, завідувач кафедри сімейної медицини, Буковинський державний медичний університет, м. Чернівці, Україна.
E-mail: mail: lsydorchuk@ukr.net
ORCID ID: https://orcid.org/0000-0001-9279-9531
Воронюк К. О. – аспірант кафедри сімейної медицини, Буковинський державний медичний університет, м. Чернівці, Україна.
E-mail: ksju2605@ukr.net
ORCID ID: https:// orcid.org/0000-0002-7233-5112

Стаття надійшла до редакції 29.11.2022