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Features of hemodynamics in the comorbid course of essential hypertension and type 2 diabetes in men, residents of Podillia, carriers of polymorphic variants of the brain natriuretic peptide gene

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Essential hypertension (EH) and type 2 diabetes (T2D) are important risk factors for the development of chronic heart failure (CHF). The early detection of CHF, especially under comorbidity, remains a challenge. To solve it in today's conditions are used not only instrumental diagnostic methods (Echo-CG), but also the assessment of plasma levels of biomarker - brain natriuretic peptide (BNP), the expression of which is determined by the corresponding gene (locus T-381C) and may depend on its structural organization. It is proved that deregulation of the natriuretic peptide system (NP) is an important factor in the initiation and progression of myocardial dysfunction and energy imbalance, but the role of genetic preconditions for these disorders, including the peculiarities of polymorphic variants of the most physiologically significant gene is still not enough clear. The aim of the work was to investigate the presence of associations between indicators of systemic and intracardiac hemodynamic and the carrier of polymorphic variants of the BNP gene (T-381C) in men, residents of Podillia with the comorbid course of EH 2 and type 2 diabetes mellitus. We examined 132 middle-age men: 62 patients with EH 2 and chronic heart failure (CHF) 0-I functional classes (FC) according to NYHA Classification and 70 - with EH 2 combined with T2D and CHF FC I-II. Patients with EH 2 included in the first group and patients with EH 2 and T2D included in the second group of comparison. Parameters of intracardiac hemodynamics were determined on the basis of pulsed Doppler echocardiography. The genomic DNA of the BNP gene (T-381C) for the determination of its alleles was isolated by PCR. The mathematical processing was performed using the standard statistical package Statistica 10. We calculated the primary statistical indicators, identified differences between groups on statistical signs, performed correlation and discriminant analysis. The calculation of the relative risk with a 95% confidence interval was performed using an online calculator (<https://medstatistic.ru/calculators/calcrisk.html>). Among men living in Podillya with EH, both in the presence and absence of diabetes mellitus 2, the T381C genotype of the BNP gene ($p > 0.05$) dominates. In the group of comorbid patients diastolic dysfunction of the left ventricle (DD LV) was diagnosed in 90% of people ($n=63$), while in the isolated course of EH it was found only in 43.55% ($n=28$). Although among homozygotes T381T BNP gene its symptoms were 100% ($n=24$), and among carriers of the C allele - in 84.78% ($n=39$) of patients. Carriers of the T381T genotype of the BNP gene dominated among persons with DD grade II: 41.66% against 10.87% of carriers of the C allele ($p < 0.05$), while among persons with DD LV grade I there were more carriers of the C allele. Homozygous T381T genotype with EH 2 and T2D had a higher level of pulse blood pressure ($p < 0.01$), a higher probability of developing eccentric left ventricular hypertrophy ($p > 0.05$) and more pronounced diastolic changes in the myocardium, as compared with carriers of the C allele and can be allocated to the priority group of observation for the organization of targeted measures aimed at preventing the development and progression of CHF.

Keywords: essential hypertension, type 2 diabetes, the brain natriuretic peptide gene polymorphism, diastolic dysfunction.

Introduction

The combination of essential hypertension (EG) and type 2 diabetes (T2D) as an additional factor of specific adverse effects on the myocardium several times increases the risk of cardiovascular complications due to the mutually aggravating course of the disease and damage to common target organs, including blood vessels and heart [13, 22, 24]. The inevitable end and the leading cause of death, as in almost all cardiovascular diseases and T2D is the development of chronic heart failure (CHF), the course of which in comorbid patients is more severe and characterized by a worse prognosis [12, 13, 16, 23].

In order to improve the individual strategy for the prevention of CHF, especially in the comorbid course of EG and T2D, there is an urgent need to use effective diagnostic biomarkers of myocardial dysfunction at the stage of reverse changes [33, 36]. Natriuretic peptides (NP) are considered to be important markers, as well as biological properties of direct antagonists of RAAS activity and regulators of heart structure and function [21]. Currently, the assessment of the informativeness of brain natriuretic peptide (BNP) remains relevant, the plasma level of which may depend on hereditary, sexual, age characteristics of patients and metabolic changes in T2D [5, 10, 15, 32]. It is known that the genotype is an important determinant of BNP levels in the general community and explains some variability in its plasma concentration [8, 11, 17]. That is why there is a need to clarify the diagnostic significance of allelic polymorphism of the BNP gene (locus T-381C-SNPs 198389) in left ventricular hypertrophy (LVH) and the detection of early signs of CHF. This clarification seems especially important in patients with T2D, because it is proved that the violation of the regulation of the NP system is a significant factor not only in the initiation and progression of myocardial dysfunction, but also energy imbalance [6, 33, 39].

The growing number of genetic and epidemiological studies in recent years suggests that BNP involved in cardiac stress is inversely associated with risk factors for diabetes - with metabolic syndrome and insulin resistance, but the expected association remains unclear [3, 7, 19]. Because metabolic processes, in turn, are closely linked to the development of cardiovascular disease, interest in the study of humoral agents that combine them has not abated. That is why the role of BNP in the development of remodeling and myocardial dysfunction, as well as the genetic polymorphism of the gene, which may cause its regulation, requires further evaluation under the conditions of comorbidity of EG and T2D.

Studies conducted in this area in Ukraine are few. In previous works, employees of the Department of Internal Medicine of the Medical Faculty №2 National Pirogov Memorial Medical University, Vinnytsia evaluated the features of the structural and functional state of the myocardium in carrying different variants of the BNP gene

in men, residents of Podillya in the isolated course of EG II with different stages of CHF, but patients with T2D were not included in the study [2, 25, 26, 27].

Continuing research to improve understanding of pathogenetic mechanisms as a possible individual basis for the development of CHF, taking into account genetic, sex and population differences in the combined course of EG and T2D may complement existing data and provide new perspectives for early detection, timely and rational treatment of these comorbid patients.

Purpose of study: to investigate the presence of associations between indicators of systemic and intracardiac hemodynamics and the carrier of polymorphic variants of the BNP gene (T-381C) in men, residents of Podillya with the comorbid course of EG II and T2D.

Materials and methods

The study was approved by the local ethics commission, as well as the informed consent of all patients. Surveyed 132 middle-aged men living in the Podillya region of Ukraine in the third generation, at a distance of more than 5 km from each other and which are not relatives. A comprehensive clinical-anamnestic, anthropometric and laboratory-instrumental examination was performed, on the basis of which the diagnosis of EG II and CHF was established in accordance with the recommendations of the European and Ukrainian Association of Cardiologists for the diagnosis and treatment of hypertension and CHF [29, 31, 37].

Verification of the diagnosis of T2D was performed according to the WHO criteria and according to the Order of the Ministry of Health of Ukraine dated 21.12.2012 №1118 [9, 34]. The parameters of intracardiac hemodynamics were determined on the basis of echocardiography. The criterion of LVH for men was considered to be $LV\ weight/height^{2.7} > 50\ g/m^{2.7}$ according to the recommendations of the European Association of Cardiologists for the diagnosis and treatment of hypertension (2018) [37]. Diastolic LV function was assessed according to current guidelines using pulsed Doppler echocardiography [18]. Exclusion criteria were: symptomatic hypertension, severe CHF (III-IV FC according to NYHA) with reduced left ventricle ejection fraction ($<40\%$), T1D, T2D decompensation, insulin therapy, diabetic nephropathy 4-5 degree, chronic kidney disease of non-diabetic origin, liver failure, chronic obstructive pulmonary disease and bronchial asthma, acquired heart disease, tumors, diseases of the blood system, concomitant inflammatory and other endocrine diseases, except T2D.

Patients were divided into 2 groups. 62 individuals with EG II and CHF 0-I FC according to NYHA were included in the first, and 70 men with EG II in combination with T2D and CHF I-II FC - in the second comparison group. The genomic DNA of the BNP gene for the determination of alleles of the polymorphic region (T-381C) was isolated by

PCR in collaboration with the Research Institute of Genetic and Immunological Basis of Pathology and Pharmacogenetics of the Ukrainian Medical Dental Academy, Poltava (Head of Laboratory - Doctor of Medicine, Professor I.P.Kaidashev).

Mathematical processing of the results was performed using the standard statistical package Statistica 10. Primary statistical indicators were calculated, differences between groups on statistical features were revealed, correlation and discriminant analysis was performed. Relative risk (RR) with a 95% confidence interval is calculated using an online calculator (<https://medstatistic.ru/calculators/calcrisk.html>).

Results

The frequency distribution of polymorphic genes in the population was checked in accordance with Hardy-Weinberg equilibrium law. Analysis of the frequency distribution of genotypes of the BNP gene revealed the dominance of the T381C variant ($p \leq 0.05$) in both comparison groups in the absence of a significant difference between the number of carriers of individual polymorphic variants in each group. For greater accuracy of comparative analysis due to the small number of individuals - homozygotes C381C they are combined with carriers of the genotype T381C to one common group - carriers of the C allele of the BNP gene (Fig. 1). In order to identify hereditary preconditions for myocardial remodeling and dysfunction

Fig. 1. Frequency of distribution of alleles of the BNP gene in comparison groups among men living in Podillya (%). The difference is significant ($p \leq 0.05$) when compared with * - carriers of the C allele within the group.

in men with EG II in the presence of comorbid T2D, the parameters of systemic hemodynamics and structural and functional parameters of the myocardium in comparison groups depending on the structural organization of the BNP gene were determined (Table 1).

The Kendall rank correlation method was used to investigate the possible relationship between the carrier of polymorphic variants of the BNP gene and the values of

Table 1. Systemic hemodynamic parameters and structural and functional parameters of the myocardium in men with EG II, and EG II in combination with T2D, carriers of different genotypes of the BNP gene, ($M \pm m$).

Indicator	1. Patients with EG II, homozygotes T381T (n=22)	2. Patients with EG II, carriers of the C allele (n=40)	3. Patients with EG II and T2D, homozygotes T381T (n=24)	4. Patients with EG II and T2D, carriers of the C allele (n=46)	p
SBP, mm Hg	159.80±1.11	141.60±2.05	173.96±2.32	166.48±1.80	$p_{2-1}^*, p_{3-1}^\#, p_{4-2}^\#, p_{4-3}^*$
DBP, mm Hg	91.25±1.39	84.60±1.06	103.25±1.37	100.46±0.79	$p_{2-1}^*, p_{3-1}^*, p_{4-2}^\#, p_{4-3}^*$
Pulse pressure, mm Hg	68.55±1.23	57.00±1.99	70.71±1.15	66.02±1.29	$p_{2-1}^*, p_{3-1}^*, p_{4-2}^\#, p_{4-3}^*$
Heart rate, for 1 min.	78.16±0.12	74.37±1.43	83.00±2.74	78.43±1.82	p_{3-1}^*, p_{4-3}^*
Left ventricular posterior wall thickness, cm	1.32±0.02	1.18±0.02	1.36±0.04	1.17±0.03	p_{2-1}^*, p_{4-3}^*
Interventricular septal wall thickness, cm	1.36±0.03	1.22±0.02	1.33±0.03	1.26±0.04	$p_{2-1}^*, p_{4-2}^\#$
Relative wall thickness, c.u.	0.54±0.03	0.51±0.01	0.51±0.03	0.52±0.02	p_{3-1}^*, p_{4-2}^*
LVMI, g/m ^{2.7}	62.35±2.81	60.89±2.32	71.41±3.06	66.22±1.92	$p_{3-1}^*, p_{4-2}^\#, p_{4-3}^*$
End diastolic volume index, mL/m ²	61.07±1.67	53.20±0.92	56.29±2.65	55.52±1.97	$p_{2-1}^*, p_{3-1}^*, p_{4-2}^\#$
End systolic volume index, mL/m ²	26.28±1.26	21.14±0.80	21.71±1.61	21.36±1.31	p_{2-1}^*, p_{4-2}^*
Emission fraction, %	60.29±1.24	62.06±1.83	58.34±1.38	62.39±1.43	p_{4-3}^*
Left atrium, cm	3.82±0.10	3.58±0.08	4.00±0.05	3.80±0.08	$p_{2-1}^*, p_{4-2}^\#, p_{4-3}^*$
E/A, c.u.	0.89±0.07	0.83±0.06	1.09±0.13	0.73±0.05	$p_{3-1}^*, p_{4-2}^*, p_{4-3}^*$
E/E', c.u.	7.77±0.38	6.25±0.24	10.13±0.50	7.69±0.23	$p_{2-1}^\#, p_{3-1}^\#, p_{4-2}^\#, p_{4-3}^\#$
DT, ms	249.02±3.43	254.07±4.27	194.79±6.37	255.07±5.12	$p_{3-1}^\#, p_{4-3}^\#$
IVRT, ms	95.35±2.09	91.46±2.14	109.15±2.82	119.11±2.23	$p_{2-1}^*, p_{3-1}^*, p_{4-2}^\#, p_{4-3}^\#$

Notes: * - difference of indicators is statistically significant at ($p < 0.05$); # - difference of indicators is statistically significant at ($p < 0.01$).

Fig. 2. Types of LV remodeling in men with EG II in combination with T2D. Carriers of different genotypes of the BNP gene (%). The difference was significant ($p < 0.05$) when compared with # - individuals with eccentric LVH in different study groups.

Fig. 3. Distribution of variants of transmitral blood flow in men with EG II in combination with T2D. Carriers of different variants of the BNP gene (%). The difference is significant ($p < 0.05$) when comparing: * - with persons with DD I degree within one genotype/allele; # - with persons with DD II degree in carriers of other genotypes/alleles of the BNP gene.

individual indicators of systemic and intracardiac hemodynamics. In men with a comorbid course of EG II and T2D, the presence of a correlation between the carrier of polymorphic genotypes of the BNP gene and the level of DBP ($\tau = -0.53$, $p < 0.05$), interventricular septal wall thickness indicators ($\tau = 0.17$, $p < 0.05$), size of left atrium ($\tau = 0.19$, $p < 0.05$), LVMI ($\tau = 0.18$, $p < 0.05$), E/A ($\tau = -0.42$, $p < 0.05$), DT ($\tau = 0.62$, $p < 0.01$), IVRT ($\tau = 0.41$, $p < 0.01$), E/E' ($\tau = -0.60$, $p < 0.01$) was found. The obtained data indicate that the carrier of different variants of the BNP gene is to some extent associated with indicators that characterize systemic hemodynamics, the degree of myocardial remodeling and the severity of LV DD.

Analysis of systemic hemodynamic parameters (Table 1) showed that the level of pulse blood pressure was higher

in T381T homozygotes than in carriers of the 381C allele of the BNP gene: 70.71 ± 1.15 mm Hg against 66.02 ± 1.29 mm Hg ($p < 0.05$). In addition, the mean values of systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure among carriers of the T381T genotype were higher in the group of comorbid patients ($p < 0.05$, $p < 0.01$).

Among men with EG II and T2D, carriers of the T381T genotype had higher values of left ventricular posterior wall thickness, left atrium, LVMI, and E/A and E/E' indices ($p < 0.01$), while the IVRT was lower than that of C allele carriers. ($p < 0.01$), which may be a sign of more pronounced disorders of the structural and functional state of the myocardium. The emission fraction index in carriers of the T381T genotype was lower than in carriers of the 381C allele of the BNP gene ($p < 0.05$).

When analyzing the distribution of individuals by types of LV remodeling, it was found (Fig. 2) that in the comorbid course of EG II and T2D, regardless of the inheritance of a particular variant of the BNP gene, individuals with concentric LVH ($p < 0.05$) predominated, but among T381T homozygotes found more people with eccentric LVH, which is characterized by a less hemodynamically effective type of remodeling - 33.33% vs. 8.7% in the group of carriers of the C allele ($p < 0.05$).

In the group of comorbid patients DD LV was diagnosed in 90% of people ($n = 63$), while in men with isolated EG II only in 43.55% of people ($n = 28$), although among homozygotes T381T its signs had 100% ($n = 24$), and among carriers of the C allele - 84.78% of patients ($n = 39$).

The next step was to study the presence of associations between the polymorphism of the BNP gene and variants of transmitral blood flow (TBF) among men with a combined course of EG and T2D (Fig. 3).

It should be noted that among persons with DD of the II degree carriers of the T381T genotype of the BNP gene prevailed: 41.66% against 10.87% of carriers of the C allele ($p < 0.05$), while among persons with less pronounced disorders of LV diastolic function carriers predominated allele C.

In order to assess the significance of the impact of the studied indicators on the risk of structural and functional changes of the heart in men, residents of Podillya with EG II in combination with T2D relative risk (RR), which also indicates that the carrier of the T381T genotype higher risk of formation of eccentric LVH and LV DD than the carrier of the C allele (Fig. 4).

The obtained results can confirm the presence of associations between the corresponding genetic component - the carrier of the T381T genotype of the BNP gene and the tendency to more pronounced negative structural and functional changes of the myocardium under the conditions of comorbidity of EG and T2D.

Thus, among men living in Podillya, carriers of the T381T genotype of the BNP gene constitute a special cohort with a high risk of myocardial remodeling and an unfavorable course of CHF. Such patients with EG and T2D can be

Fig. 4. Relative risk of development of structural and functional changes of the heart on the background of EG II and T2D among men, residents of Podillya (RR=1 - no association. RR>1 - increased risk of pathology. RR<1 - negative association).

assigned to the priority group of observation with the organization of targeted measures aimed at preventing the development of CHF and premature mortality.

The above data suggest that taking into account genotype, in addition to age and sex, when using biomarkers may improve their test characteristics to detect LV dysfunction in men with comorbid pathology and increase the effectiveness of screening among asymptomatic individuals and in expert cases.

Discussion

For many years, the focus of numerous scientific studies remains the system of natriuretic peptides, one of which is the brain natriuretic peptide. In addition to the classic hemodynamic effects, they have been shown to regulate many physiological functions that control energy metabolism: they can activate lipolysis, lipid oxidation and mitochondrial respiration, darkening of white adipose tissue, protect against obesity, caused by diet, and insulin resistance. These metabolic processes, in turn, are closely linked to the development of cardiovascular disease. Today it is believed that due to the secretion of NP the heart can play a central role in regulating the energy balance [20, 35]. Given the above, the scientific interest in terms of studying the role of BNP in the regulation of cardiohemodynamic and energetic processes is a cohort of patients with mutually aggravating comorbid pathology, namely with EG in combination with T2D. A number of authors note that the reasons for the increase in the level of circulating BNP in patients with T2D, even without concomitant heart failure and clinically significant decrease in renal function, are not

fully understood [30]. Of great interest are the population and sexual characteristics of the inheritance and expression of BNP, which led to the involvement in the study of persons with comorbid pathology only in males and residents of one region of Ukraine.

We did not find a statistically significant difference in the distribution of genotyping and frequency of alleles between groups of patients, which coincides with the results of researchers from Iran in 70 cardiac patients (acute coronary syndrome, etc.) and in the control group of healthy [1]. The authors also indicate that the T-381C polymorphism in the BNP gene affects the plasma level of the biomarker, where the CC genotype and the C allele are associated with its higher levels.

The results of our study of comorbid patients with EG II and T2D with signs of LV DD and early stages

of CHF indicate the presence of associations between carriers of polymorphic variants of the BNP gene and certain parameters of intracardiac and systemic hemodynamics. Based on the obtained data, we can predict that the presence of the T-allele of the T-381C polymorphism of the BNP gene may adversely affect the course of disease and progression of HF.

Similar data were obtained by E.N.Berezikova in the Russian population of patients with coronary heart disease. It is noted that the T allele and the TT genotype of the T-381C polymorphic locus of the BNP gene were associated with a high risk of development, severity and adverse course of CHF, and the C allele and the CC genotype proved to be protective factors [4]. In the South Chinese population, it was also found that the rs198389 polymorphism of the BNP locus may be an additional additive genetic factor influencing the progression of LV dysfunction in patients with coronary heart disease and dyslipidemia [38]. The association of genetic variations in the NP system with cardiovascular effects and T2D in the New Zealand population was studied. Variants of rs198388 and rs198389 of the BNP gene were found to be associated with decreased blood pressure, decreased remodeling, improved LV function, and lower incidence of T2D [14].

Interesting but ambiguous correlations have been obtained in a number of studies on the plasma level of BNP and associations with the carrier of certain genotypes of the corresponding gene in individuals living in different areas. A mixed cohort of North Americans with EG found that inheritance of BNP genotypes with the presence of the 381C allele was associated with high plasma peptide

concentrations [11]. However, a large, prospective EPIC-Norfolk study (USA) in a mixed cohort of individuals found no significant association between rs198389 genotypes and the risk of CHF. The mean follow-up was 12.6 years. The results did not differ significantly in the presence of hypertension, obesity and coronary heart disease. According to the authors, a possible explanation may be that the physiological activation of BNP in conditions of enhanced mechanical deformation of the heart may block small genetically determined differences in biomarker levels. In addition, it is possible that a slight genetic influence on certain subtypes of heart failure syndrome, which is associated with polymorphism of the gene, may not affect the risk of its development as a whole [28].

As the literature data differ markedly, a further study of the determining role of the BNP gene polymorphism involved in the coding of the corresponding biomarker and determining the need to take into account genetic features in the diagnostic process in EG, including comorbid T2D is a promising approach.

Continuation of population studies to establish patterns between the carrier of polymorphic variants of the BNP gene, the plasma level of the biomarker and the structural and functional state of the myocardium in different variants of

comorbid diseases will further provide additional information that may be particularly useful for improving individual diagnosis and diagnosis. appropriate secondary prevention measures.

Conclusions

1. Carrying of the T381T genotype of the BNP gene, in middle-aged men, residents of Podillya with comorbid EG II and T2D, is associated with a significantly higher level of pulse blood pressure ($p < 0.01$), a higher probability of developing eccentric LVH ($p \leq 0.05$) and with more pronounced diastolic changes in the myocardium, compared with the carrier of the allele C.

2. Among comorbid male patients with EG and T2D, residents of Podillya carriers of the T381T genotype of the BNP gene can be allocated to the priority observation group with the organization of targeted measures aimed at preventing the development of CHF and premature mortality.

3. Taking into account the genotype, in addition to age and sex, the use of biomarkers can improve their test characteristics to detect LV dysfunction in men with comorbid pathology and increase the effectiveness of screening among asymptomatic individuals and in expert cases.

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ОСОБЛИВОСТІ ГЕМОДИНАМІКИ ЗА КОМОРБІДНОГО ПЕРЕБІГУ ЕСЕНЦІАЛЬНОЇ ГІПЕРТЕНЗІЇ ТА ЦУКРОВОГО ДІАБЕТУ 2 ТИПУ У ЧОЛОВІКІВ, МЕШКАНЦІВ ПОДІЛЛЯ, ПРИ УСПАДКУВАННІ ПОЛІМОРФНИХ ВАРІАНТІВ ГЕНА МОЗКОВОГО НАТРІЙУРЕТИЧНОГО ПЕПТИДУ

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Есенціальна гіпертензія (ЕГ) та цукровий діабет 2 типу (ЦД 2) є визнаними вагомими факторами ризику хронічної серцевої недостатності (ХСН) раннє виявлення якої, особливо за умов коморбідності, залишається складним завданням. Сьогодні для його вирішення поряд з інструментальними методами діагностики (Ехо-КГ), застосовують оцінку плазматичного рівня біомаркера - мозкового натрійуретичного пептиду (МНУП), експресія якого детермінується відповідним геном (локус Т-381С) і може залежати від його структурної організації. Доведено, що порушення регуляції системи натрійуретичних пептидів є вагомим фактором в ініціації, прогресуванні міокардіальної дисфункції та енергетичного дисбалансу, однак роль генетичних передумов цих порушень, в тому числі особливостей носійства поліморфних варіантів найбільш фізіологічно значимого гена МНУП, до цього часу залишається не до кінця зрозумілою. Метою роботи було: дослідити наявність асоціацій між показниками системної і внутрішньосерцевої гемодинаміки та носійством поліморфних варіантів гена МНУП (Т-381С) у чоловіків, мешканців Поділля, за умов коморбідного перебігу ЕГ II та ЦД 2. Обстежили 132 чоловіки середнього віку: 62 особи з ЕГ II і ХСН 0-ІФК за НУНА склали першу, а 70 - з ЕГ II у комбінації з ЦД 2 і ХСН І-ІІФК другу групу порівняння. Параметри внутрішньосерцевої гемодинаміки визначали на основі імпульсної доплер-ЕхоКГ. Геномну ДНК гена МНУП для визначення алелів поліморфної ділянки (Т-381С) виділяли методом ПЛР. Математичне опрацювання виконали, використовуючи стандартний статистичний пакет Statistica 10. Розраховано первинні статистичні показники, виявлено відмінності між групами за статистичними ознаками, здійснено кореляційний та дискримінантний аналіз. Відносний ризик з 95% довірчим інтервалом розраховано за допомогою онлайн-калькулятора (<https://medstatistic.ru/calculators/calcrisk.html>). Встановлено, що серед чоловіків, мешканців Поділля з ЕГ як за наявності, так і за відсутності ЦД 2 домінує генотип Т381С гена МНУП ($p > 0,05$). У групі коморбідних хворих діастолічну дисфункцію лівого шлуночка (ДД ЛШ) діагностовано у 90% осіб ($n=63$), тоді як за ізольованого перебігу ЕГ лише у 43,55% ($n=28$) при тому, що серед гомозигот Т381Т гена МНУП її ознаки мали 100% ($n=24$), а серед носіїв алелю С - 84,78% ($n=39$) пацієнтів. Серед осіб із ДД II ступеня переважали носії генотипу Т381Т гена МНУП: 41,66% проти 10,87% носіїв алелю С ($p < 0,05$), тоді як серед осіб з ДД ЛШ I ступеня було більше носіїв алелю С. Чоловіки, гомозиготи Т381Т гена МНУП з ЕГ II в сполученні з ЦД 2, вирізняються вищим рівнем пульсового АТ ($p < 0,01$), більшою ймовірністю розвитку ексцентричної гіпертрофії ЛШ ($p \leq 0,05$) та більш вираженими діастолічними змінами в міокарді, порівняно з носіями алелю С і можуть бути виділені у пріоритетну групу спостереження для організації цільових заходів, спрямованих на профілактику розвитку і прогресування ХСН.

Ключові слова: есенціальна гіпертензія, цукровий діабет 2 типу, поліморфізм гена мозкового натрійуретичного пептиду, діастолічна дисфункція.

ОСОБЕННОСТИ ГЕМОДИНАМИКИ ПРИ КОМОРБИДНОМ ТЕЧЕНИИ ЭСSENЦИАЛЬНОЙ ГИПЕРТЕНЗИИ И САХАРНОГО ДИАБЕТА 2 ТИПА У МУЖЧИН, ЖИТЕЛЕЙ ПОДОЛЬЯ, ПРИ НАСЛЕДОВАНИИ ПОЛИМОРФНЫХ ВАРИАНТОВ ГЕНА МОЗГОВОГО НАТРИЙУРЕТИЧЕСКОГО ПЕПТИДА

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Эссенциальная гипертензия (ЭГ) и сахарный диабет 2 типа (СД 2) являются признанными весомыми факторами риска хронической сердечной недостаточности (ХСН), раннее выявление которой, особенно в условиях коморбидности, остается сложной задачей. Для ее решения в современных условиях, наряду с инструментальными методами диагностики (ЭхоКГ), применяется оценка плазменного уровня биомаркера - мозгового натрийуретического пептида (МНУП), экспрессия которого детерминирована соответствующим геном (локус Т-381С) и может зависеть от его структурной организации. Доказано, что нарушение регуляции системы натрийуретических пептидов является важным фактором в инициации и прогрессировании миокардиальной дисфункции и энергетического дисбаланса, однако роль генетических предпосылок этих нарушений, в том числе особенностей носительства полиморфных вариантов наиболее физиологически значимого гена МНУП до сих пор остается не до конца понятной. Целью работы было: исследовать наличие ассоциаций между показателями системной и внутрисердечной гемодинамики и носительством полиморфных вариантов гена МНУП (Т-381С) у мужчин, жителей Подолья, в условиях коморбидного течения ЭГ II и СД 2. Обследовали 132 мужчин среднего возраста: 62 человека с ЭГ II и ХСН 0-ІФК по НУНА составили первую, а 70 - с ЭГ II в сочетании с СД 2 и ХСН І-ІІФК вторую группу сравнения. Параметры внутрисердечной гемодинамики определяли на основе импульсной доплер-ЭхоКГ. Геномную ДНК гена МНУП для определения аллелей полиморфного участка (Т-381С) выделяли методом ПЦР. Математическую

обработку выполнили, используя стандартный статистический пакет Statistica 10. Рассчитаны первичные статистические показатели, выявлены различия между группами по статистическим признакам, осуществлен корреляционный и дискриминантный анализ. Расчет относительного риска с 95% доверительным интервалом осуществлен с помощью он-лайн калькулятора (<https://medstatistic.ru/calculators/calcrisk.html>). Установлено, что среди мужчин, жителей Подолья с ЭГ как при наличии, так и при отсутствии СД 2 доминирует генотип T381C гена МНУП ($p > 0,05$). В группе коморбидных больных диастолическая дисфункция левого желудочка (ДД ЛЖ) диагностирована у 90% лиц ($n=63$), тогда как при изолированном течении ЭГ только у 43,55% ($n=28$) при том, что среди гомозигот T-гена МНУП ее признаки имели 100% ($n=24$), а среди носителей аллели C - 84,78% ($n=39$) пациентов. Среди лиц с ДД II степени преобладали носители генотипа T381T гена МНУП: 41,66% против 10,87% носителей аллели C ($p < 0,05$), тогда как среди лиц с ДД ЛЖ I степени было больше носителей аллели C. Мужчины, гомозиготы T381T гена МНУП с ЭГ II в сочетании с СД 2, отличаются высоким уровнем пульсового АД ($p < 0,01$), большей вероятностью развития эксцентрической гипертрофии ЛЖ ($p \leq 0,05$) и более выраженными диастолическими изменениями в миокарде по сравнению с носителями аллели C и могут быть выделены в приоритетную группу наблюдения для организации целевых мероприятий, направленных на профилактику развития и прогрессирования ХСН.

Ключевые слова: эссенциальная гипертензия, сахарный диабет 2 типа, полиморфизм гена мозгового натрийуретического пептида, диастолическая дисфункция.