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S.M. Pyvovar, Yu.S. Rudyk, T.V. Lozyk, V.Yu. Galchinska
SI "L.T. Malaya National Institute of Therapy, NAMS of Ukraine", Kharkiv

POLYMORPHISM OF C825T (RS5443) G-PROTEIN β3-SUBUNIT GENE AND THE LONG-TERM PROGNOSIS FOR PATIENTS WITH HEART FAILURE

E-mail: sn_p@ukr.net

Forecasting of an unfavorable course in heart failure is very relevant. The purpose of the work was to determine the effect of the G protein β3-subunit C825T (RS5443) gene polymorphism on the long-term prognosis for patients with heart failure. The study included 170 patients with heart failure on the background of post-infarction cardiosclerosis. The G protein β3-subunit C825T (RS5443) gene polymorphism was determined by means of the polymerase chain reaction. Daily monitoring of ECG, Doppler echocardioscopy were carried out. The observation period was 3 years, whereby the course of the disease was evaluated, the atrial fibrillation paroxysms development, the frequency of hospitalizations due to the disease decompensation, and mortality were taken into account. The frequencies of the C825T (RS5443) polymorphic variants of the G protein β3-subunit gene were determined in the patients. 47% of patients are homozygous carriers of C825 alleles, 47% of patients are heterozygotes (C825T), 11 out of 170 patients are homozygous by the T genome. Homozygous patients with T genome are younger by 7.5 years, compared to homozygous C-allele patients and by 6 years younger compared to heterozygotes (CT) ($p < 0.01$). For 3 years, in the patients homozygous by the T-allele, an increase in the left ventricle end-diastolic volume (by 6%, $p < 0.05$) and a decrease in the amount of left ventricular ejection fraction (by 11%, $p < 0.05$) was observed. In 5 out of 11 patients with heart failure who are homozygous by the T allele (TT), in the third year of observation, a pathological number of ventricular extrasystoles is recorded. Among the homozygous by the C-allele (CC) and heterozygous (CT) patients, this type of rhythm disorder is statistically reliably less frequent ($\chi 2 = 6.854$; $p < 0.05$). The tendency was revealed towards a higher frequency of hospitalization in patients due to the disease decompensation for 3 years in the group of homozygous patients with T-allele.

Key words: heart failure, clinical course, atrial fibrillation, C825T (RS5443) polymorphism, gene, β3 subunit of G protein.

The study is a fragment of the research project "Development of methods for preventing the unfavorable course of chronic heart failure with account of the pharmacological and genetic profile of patients and concomitant pathology", state registration No. 0116U003038.

The result of heart diseases is heart failure (HF). This pathology is an actual medical and social problem in our country [2]. The prevalence of HF among the adult population ranges from 1.5 to 5.5% and grows pro rata with age [1]. The fact that about half of the patients die within 4 years is also a sign of the HF prognosis severity [2]. Prediction of an unfavorable HF flow is important for a number of reasons. One of them is selection of patients requiring more intensive observation and treatment [5, 6].

The β-adrenergic receptors (β-AR) are paired transmembrane proteins, which are found in cells throughout the body, including cardiomyocytes and blood vessels smooth myocytes. There are three subclasses of AR (β1, β2, β3). β1- and β2-AR affect the of the cardiovascular system's (CVS) physiology. β-AR stimulates catecholamines on intracellular processes through the cytosolic G protein, i.e. heterotrimer consisting of three subunits: α, β, and γ. G-proteins are expressed in all human cells. The most frequent C825T polymorphism of the β3-subunit gene (GNB3) is associated with an increase in the activity of signaling pathways. In the CVS, this polymorphism primarily affects vascular reactivity and cardiomyocytes growth [14].

However, whether the indicated genomic variation affects the HF course, according to previous studies, remains unclear [14]. T-allele has a high prevalence among the black race representatives, compared to europoids [9]. Approximately 50% of Africans are homozygotes by the GNB3 TT genotype. Meanwhile, only 10% of Europeans are alike. In the genetic study "African-American Heart Failure Trial" (AHeFT), homozygote by T allele (GNB3 TT) patients had the most adverse pathogeny in the placebo group and received the most benefit from therapy [9]. Despite the clear racial differences in the mutations frequency, there are only stand-alone and quite contradictory results of studies on the GNB3 TT genotype impact on the HF progression in Europeans. This inspires to new studies in this field.

The purpose of the study was to determine the G-protein β3-subunit's C825T (RS5443) gene polymorphism influence on the long-term prognosis for patients with HF.

Material and methods. The study included 170 patients with HF (100 women and 70 men) of the European race. The involvement criteria were: signing the Patient Informed Consent, the left ventricle (LV) systolic dysfunction on the background of post-infarction cardiosclerosis. HF diagnosis and treatment of patients were carried out in accordance with the recommendations of the European Society of Cardiologists and the Ukrainian Association of Cardiologists [10, 3]. The observation period lasted 3 years, whereby the

HF course was evaluated, with account of the atrial fibrillation paroxysms development, the frequency of hospitalizations for the disease decompensation and mortality.

Doppler echocardioscopy was performed using the VIVID-3 ultrasonic diagnostic system, (General Electric, USA). The calculations of the left ventricle end-diastolic volume (LVEDV) values, left ventricle end-systolic volume (LVESV), left ventricle ejection fraction (LVEF) were performed. The diameter of the left atrium (LA), the right ventricle (RV) and other parameters were determined [4].

Types of cardiac rhythm and conduction disorders and their daily number were studied by daily ECG monitoring using the CardioSens computerized system for ECG monitoring (CDS, Ukraine). The pathology of the Extra Systoles Ventriculaire (ESV) daily number was evaluated according to the criteria given in the European Society of Cardiology recommendations (2015) [11].

Molecular genetic study of the G protein β3- subunit C825T (RS5443) gene (GNB3) polymorphism was performed by means of the polymerase chain reaction (PCR). The material for the genetic study was leukocytes of the patients' peripheral blood. Peripheral blood was obtained by blood sampling from the cubital vein in fasting state in the amount of 4 ml in a vacuum collection tube with EDTA (8.4 mg K3-EDTA). The genomic DNA isolation from blood leukocytes for molecular genetic studies was carried out using the "DNA-sorb-B" commercial kit (AmpliSens, Russia) in accordance with the instructions for the kit. Samples were stored at minus 20oC prior to the amplification.

Amplification of the isolated DNA was carried out automatically in the TP4-PCR-01 – "Tercyk" thermocycler using the "GenePak PCR Core" commercial reagents kit ("IzoGen" Laboratory, Russia) and specific primers ("Thermo Scientific", Lithuania). To the final PCR mixture, "GenePak PCR Core", 50 ng of genomic DNA and 20 pmoles of each specific primers pair were introduced (the total volume of the mixture was 20 μl). The primer sequences specified in the paper were applied [14].

Testing the equality of means hypothesis in the two groups was carried out using the two-sample t-test. When comparing data in the monitoring dynamics, the one-sample t-test was used. When analyzing data in more than two patients' groups simultaneously, one-factor dispersion analysis (ANOVA - Analysis of variance, deviation analysis) was used. Assessment of the difference in the signs frequencies in the groups was carried out according to Pearson's $\chi 2$ criterion (with the Yates correction for the signs number less than 10). The data are presented in the formula M ± SD, where M is the mean value, SD is the standard deviation. The calculations were performed using the SPSS statistical package for Windows.

Results of the study and their discussion. While analyzing the data, it was found that among 170 patients with HF, 80 (47%) were homozygous carriers of the C825 (CC) allele. The total of 11 out of 170 patients had two T825 (TT) alleles. The total of 79 (475%) patients with HF were heterozygotes (CT).

Clinical profiles of the patient groups, depending on the specified gene polymorphism, are demonstrated in table 1.

Table 1

Clinical profiles of patients with different G protein gene β_3-subunit C825T (RS5443) polymorphisms at baseline

Parameter	C825T (RS5443) polymorphism			p
	CC (n = 80)	CT (n = 79)	TT (n = 11)	
Age, years	66.8 ± 10.8	65.3 ± 9.8	59.3 ± 7.8 *	< 0.01
FC NYHA (% I/II/III/IV)	10.0/40.0/35.0/15.0	12.7/34.2/35.5/17.6	9.1/36.5/36.4/18	> 0.05
HR, min.$^{-1}$	65.3 ± 17.5	68.7 ± 15.9	67.6 ± 11.3	> 0.05
SAP, mm Hg	128.4 ± 26.3	120.2 ± 25.3	122.5 ± 27.1	> 0.05
DAP, mm Hg	74.1± 11.9	72.9± 11.5	75.5 ± 13.1	> 0.05
ACE inhibitors	68 (85.0 %)	71 (89.9 %)	10 (90.9 %)	> 0.05
Aldosterone receptor antagonists	32 (40.0 %)	30 (38.0 %)	4 (36.4 %)	> 0.05
β-adrenergic blockers	72 (90 %)	73 (92.4 %)	10 (90.9 %)	> 0.05

Note: * - probability of difference in homozygous patients by T-allele, compared to homozygous patients by C-allele and heterozygotes.

At baseline, the group of patients probably did not differ against each other according to the HF functional classes (NYHA), heart rate (HR), systolic (SAP) and diastolic arterial pressure (DAP), angiotensin converting enzyme inhibitors, β-blockers and spironolactone. Meanwhile, at baseline, homozygous patients with T-alleles were younger by 7.5 years compared to homozygous patients with C allele and by 6 years compared to heterozygotes. The difference was significant ($p < 0.01$).

At baseline, patients with a different G-protein β_3-subunit C825T (RS5443) gene polymorphism did not differ in the main parameters of the intracardiac hemodynamics (table 2).

Table 2

Parameters of intracardiac hemodynamics in patients with different G protein gene β_3-subunit C825T (RS5443) polymorphism

Parameter	C825T (RS5443) polymorphism			p
	CC (n = 80)	CT (n = 79)	TT (n = 11)	
	1	2	3	
Baseline period				
EDV, ml	190.4 ± 42.5	201.2 ± 45.8	193.9 ± 36.2	> 0.05
ESV, ml	118.8 ± 31.7	123.8 ± 33.1	118.2 ± 28.8	> 0.05
LVEF, %	37.6 ± 8.8	38.5 ± 8.6	39.04 ± 5.9	> 0.05
LA, cm	4.3 ± 1.5	4.5 ± 1.5	4.4 ± 1.2	> 0.05
RV, cm	3.2 ± 1.1	3.1 ± 1.0	3.4 ± 0.9	> 0.05
3 years after the baseline				
EDV, ml	193.2 ± 38.2	198.5 ± 40.2	205.9 ± 15.1$^{*(3\text{-}1 \text{ та } 3\text{-}2)}$	< 0.05
ESV, ml	120.0 ± 32.1	119.3 ± 32.9	134.4 ± 21.5	> 0.05
LVEF, %	37.9 ± 9.2	39.9 ± 7.0	34.7 ± 4.6$^{\S; *(3\text{-}1 \text{ та } 3\text{-}2)}$	< 0.05
LA, cm	4.4 ± 1.6	4.3 ± 1.7	4.5 ± 1.0	> 0.05
RV, cm	3.2 ± 1.5	3.2 ± 1.3	3.5 ± 1.1	> 0.05

Note: $^{*(3\text{-}1 \text{ and } 3\text{-}2)}$ - probability of difference between groups 3 and 1, groups 3 and 2; § - probability of difference in the monitoring dynamics.

While analyzing the parameters of intracardiac hemodynamics, obtained in the 3rd year of observation, it was found that in the homozygous patients with T allele, an increase in left ventricular EDV was observed, compared to the baseline (by 6%, $p < 0.05$), and a decrease in the left- ventricle ejection fraction (LVEF) value (11%, $p < 0.05$) (see table 2). Similar probability patterns were not found in the group of homozygous by C allele (CC) and heterozygous (CT) patients.

In the third year of observation, LVEDV in the group of homozygous patients with T-allele (TT) were significantly higher compared to that in patients homozygous by C allele (CC) and heterozygotes (CT) (7% and 4% respectively, at $p < 0.05$). The left ventricular ejection fraction in patients with TT genotype was 8% lower compared to that in homozygous patients with C allele (SS) and 9% compared to those with CT genotype ($p < 0.05$).

Analysis of the rhythm disorders development frequency within 3 years was carried out. The observation showed no reliable difference in the rate of atrial fibrillation (AF) development in patients with HF with a different G protein gene β_3-subunit C825T (RS5443) polymorphism (table 3).

Table 3

Frequency of rhythm disorders development in patients with HF during 3 years of observation (n = 170)

Rhythm disorder	C825T (rs5443) polymorphism		
	CC (n = 80)	CT (n = 79)	TT (n = 11)
AF (n = 49)	22 (28 %)	25 (32 %)	2
AF not found (n = 121)	58 (73 %)	54 (68 %)	9
$\chi^2 = 0.982$; $p > 0.05$			
ESV (n = 29)	13	11	5
ESV not found (n = 141)	67 (84 %)	68 (86 %)	6
$\chi^2 = 6.854$; $p < 0.05$			

Herewith, in the group of patients who are homozygous by the T-allele in the third year of observation, 5 of 11 patients are registered with ESV in a pathological amount. Meanwhile, in the groups of patients homozygous by the C-allele and heterozygous (CT), this type of rhythm disorder was detected in 16% and 14%, respectively (table 3). The difference is statistically reliable ($\chi 2 = 6.854$; $p < 0.05$).

Further analysis has shown that the highest incidence of hospitalization for 3 years due to the pathology decompensation was observed in patients with HF, which were homozygotes for the T-allele (in 6 of 11 patients) (table 4), comparing to that among homozygous and heterozygous patients for the C-allele (26% and 22%, respectively). But the difference does not reach the statistically significant level ($\chi 2 = 5{,}501$; $p = 0{,}064$) and becomes biased.

There was no reliable correlation between the 3-year mortality with the polymorphism of this gene among patients with HF (see table 4). Three-year mortality among homozygous T-alleles in patients with HF was 18% (2 out of 11 patients), in patients homozygous by the C-allele - 19%, among heterozygotes - 17% ($\chi 2 = 0.146$; $p > 0.05$).

Table 4

HF course during 3 years of observation (n = 170)

HF course	C825T (RS5443) polymorphism		
	CC (n = 80)	CT (n = 79)	TT (n = 11)
Hospitalization due to HF decompensation (n = 44)	21 (26 %)	17	6
Hospitalization not registered (n = 126)	59 (74 %)	62 (79 %)	5
$\chi^2 = 5.501$; $p = 0.064$			
Unfavourable course (mortality) (n = 30)	15	13	2
Favourable course (n = 140)	65 (81 %)	66 (84 %)	9
$\chi^2 = 0.146$; $p > 0.05$			

Although genetic predisposition is increasingly considered as a risk factor for cardiovascular diseases, the role of the genomic factor in the development and progression of HF remains largely unexplored. In our study, it has been demonstrated that in patients homozygous by the T-allele of the C825T (RS5443) polymorphism of the G protein gene β3-subunit, an increase in LVEDV (by 6%, $p < 0.05$) and a reduction of LV ESV value (11 %, $p < 0.05$) have been observed for 3 years. Similar regularities were not found in the group of homozygous by the C-allele (CC) and heterozygote (CT) patients.

In spite of the fact that T-polymorphism is functionally inactive, it leads to truncated (alternative) splicing of exon 9 (GNB3) and ultimately to the “truncated” β3 subunit of G-protein. This "truncated" subunit increases α-adrenergic activation. Frequently, this mutation is the cause for an early manifestation (from 17 years of age) of the low-renin variant of arterial hypertension in African Americans [13]. We have not established the dependence of the AP level on this polymorphism, although the correlation could be distorted by using both the ACE inhibitors and β-blockers in most of these patients.

The influence of GNB3 polymorphism on the HF course was studied in the AHeFT genetic study involving African Americans [8]. In the trail, patients with the GNT3 TT genotype in the placebo group had a high mortality rate compared to the C-allele carriers. Also, homozygotes by the T-allele were in the most fortunate position due to the combination of isosorbide dinitrate and hydralazine in a fixed combination. These data may indicate that the GNB3 genotype affects the pharmacotherapy efficacy in African Americans with HF. We note that although nearly all the patients in our study were treated with β-blockers and ACE inhibitors, we did not prescribe the combination of isosorbide dinitrate with hydralazine. Could the use this combination to improve the course of HF in Europeans in the presence of GNT3 TT genotype, remains uncertain.

The genotypes’ effect on cardiac remodeling and LVEF in patients with HF was studied in AHeFT and in small trails. The studied genotypes referred to the genes encoding renin-angiotensin aldosterone systems [8], nitric oxide synthesis [8] and adrenoreceptors. These genes have been studied as potentially affecting myocardial remodeling and the therapy efficacy. On the contrary, the AHeFT study did not obtain data on the effects of the GNB3 TT genotype on myocardial remodeling in patients with HF [9]. In addition to the data obtained in the AHeFT study, another report has demonstrated that the GNB3 T-allele may be associated with an increase in arrhythmic events in patients with HF [7]. In Schmitz B, et al (2014) [12], the GNB3 gene mutation was associated with an reverse remodeling after resynchronizing device implantation in patients with HF [12].

The data obtained by us, on the fact that in 5 out of 11 patients with HF, homozygous by the T-allele (TT), in the third year of observation, ESV is recorded in a pathological amount, comparing to the frequency of this rhythm disorder development among homozygous by the C-allele (CC) and heterozygous (CT) patients ($\chi 2 = 6.854$; $p < 0.05$), probably agree with the results of a study performed by Chemello D. at al. (2010) [7]. The authors have demonstrated that the G protein gene β3-subunit T825 polymorphism is associated with a higher rate of discharge in patients with HF having a defibrillator cardioverter implanted for ventricular tachycardia.

Conclusions

1. Frequency of G-protein β_3-subunit C825T (RS5443) gene polymorphous variants among patients with HA was determined. The amount of 47% patients are homozygous carriers of C825 allele, 47% of patients are heterozygotes (C825T), 11 of 170 patients are homozygotes by the T-allele.

2. Homozygous patients by the T-allele are younger by 7.5 years compared to homozygous patients by the C allele and by 6 years younger compared to heterozygotes ($p < 0.01$).

3. For 3 years, in HF patients with homozygous T-allele, a growth in the diastolic volume of the left ventricle (LVEDV) (by 6%, $p < 0.05$) and a decrease in the size of the left ventricular ejection fraction

(LVEF) (by 11%, p <0, 05) were observed. Similar regularities were not found in the group of homozygous by the C allele (CC) and heterozygous (CT) patients.

4. In 5 out of 11 HF patients, homozygous by the T-allele (TT), in the third year of observation, ESV is registered in a pathological amount. Among the homozygous by the C-allele (CC) and heterozygous (CT) patients, this type of rhythm disorder is reported to be reliably less frequent ($\chi 2 = 6.854$; $p < 0.05$).

5. The tendency towards a higher rate of hospitalization has been revealed for patients with HF decompensation for the 3 years period in the group of patients homozygous by the T allele (6 out of 11 patients), comparing to that among homozygous and heterozygous patients with C-allele (26 and 22%, respectively) ($\chi 2 = 5.501$; $p = 0.064$).

6. Our study is confined to a small number of patients, which reduces the strength of data on the genetic association between the GNB3T allele and left ventricular myocardial remodeling in HF patients with post-infarction cardiosclerosis. But the probable patterns of GNB3 TT influence on the HF course can demonstrate the strong influence of this mutation and indicate that this allele is not only a race marker. The results are likely to require further research involving a large cohort of patients.

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Реферати

ПОЛІМОРФІЗМ С825Т (RS5443) ГЕНА β_3-СУБОДИНИЦІ G-ПРОТЕЇНУ ТА ВІДДАЛЕНИЙ ПРОГНОЗ ХВОРИХ З СЕРЦЕВОЮ НЕДОСТАТНІСТЮ

Пивовар С.М., Рудик Ю.С., Лозик Т.В., Гальчінська В.Ю.

Прогнозування несприятливого плину серцевої недостатності є вельми актуальним. Метою роботи було визначення впливу поліморфізму С825Т (RS5443) гена β_3-субодиниці G-протеїну на віддалений прогноз хворих з серцевою недостатністю. До дослідження включено 170 хворих з серцевою недостатністю на фоні після інфарктного кардіосклерозу. За допомогою полімеразної ланцюгової реакції визначали поліморфізм С825Т

ПОЛИМОРФИЗМ С825Т (RS5443) ГЕНА β_3-СУБЪЕДИНИЦЫ G-ПРОТЕИНА И ОТДАЛЕННЫЙ ПРОГНОЗ БОЛЬНЫХ С СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ

Пивовар С.Н., Рудык Ю.С., Лозик Т.В., Гальчинськая В.Ю.

Прогнозирование неблагоприятного течения сердечной недостаточности является весьма актуальным. Целью работы было определение влияния полиморфизма С825Т (RS5443) гена β_3-субъединицы G-протеина на отдаленный прогноз больных с сердечной недостаточностью. В исследование включено 170 больных с сердечной недостаточностью на фоне послеинфарктного кардиосклероза. С помощью полимеразной цепной реакции определяли полиморфизм

(RS5443) гена β3-субодиниці G-протеїна. Проводили добове моніторування ЕКГ, Допплер-ехокардіоскопію. Період спостереження склав 3 роки, протягом якого оцінювали перебіг захворювання, враховували розвиток пароксизмів фібриляції передсердь, частоту госпіталізацій з приводу декомпенсації захворювання, смертність. Визначено частоту поліморфних варіантів C825T (RS5443) гена β3-субодиниці G-протеїну серед хворих. 47 % пацієнтів є гомозиготними носіями алелі C825, 47 % пацієнтів – гетерозиготи (C825T), 11 з 170 хворих є гомозиготами за Т алелем. Гомозиготні хворі за Т алелем молодші на 7,5 років, порівняно до гомозиготних пацієнтів за С алелем та на 6 років порівняно з гетерозиготами ($p < 0,01$). На протязі 3 років у гомозиготних за Т алелем хворих спостерігається збільшення кінцево-діастолічного об'єму лівого шлуночка (на 6 %, $p < 0,05$) та зменшення величини фракції викиду лівого шлуночка (на 11 %, $p < 0,05$). У 5 з 11 хворих з серцевою недостатністю, що є гомозиготними за Т алелем (ТТ) на третій рік спостереження у реєструється патологічна кількість шлуночкової екстрасистолії. Серед гомозиготних за С алелем (СС) та гетерозиготних (СТ) пацієнтів даний вид порушення ритму реєструється вірогідно рідше ($\chi 2 = 6,854$; $p < 0,05$). Виявлено тенденцію до більшої частоти госпіталізації хворих з приводу декомпенсації серцевої недостатності протягом 3 років в групі пацієнтів, що є гомозиготами за алелем Т.

Ключові слова: серцева недостатність, клінічний перебіг, фібриляція передсердь, C825T (RS5443) поліморфізм, ген, β3-субодиниця G-протеїна.

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C825T (RS5443) гена β3-субъединицы G-протеина. Проводили суточное мониторирование ЭКГ, Допплер-эхокардиоскопию. Период наблюдения составил 3 года, в течение которого оценивали течение заболевания, учитывали развитие пароксизмов фибрилляции предсердий, частоту госпитализаций в связи с декомпенсацией заболевания, смертность. Определены частоты полиморфных вариантов C825T (RS5443) гена β3-субъединицы G-протеина среди больных. 47% пациентов - гомозиготные носители аллели C825, 47% пациентов - гетерозиготы (C825T), 11 из 170 больных является гомозиготами по Т геному. Гомозиготные больные с Т геном моложе на 7,5 лет, по сравнению с гомозиготных пациентов по С алели и на 6 лет по сравнению с гетерозиготами (СТ) ($p < 0,01$). На протяжении 3 лет в гомозиготных по Т алели больных наблюдается увеличение конечного диастолического объема левого желудочка (на 6%, $p < 0,05$) и уменьшение величины фракции выброса левого желудочка (на 11%, $p < 0,05$). В 5 из 11 больных с сердечной недостаточностью, которые является гомозиготными по Т аллели (ТТ) на третий год наблюдения регистрируется патологическое количество желудочковой экстрасистолии. Среди гомозиготных по С аллели (СС) и гетерозиготных (СТ) пациентов данный вид нарушения ритма регистрируется достоверно реже ($\chi 2 = 6,854$; $p < 0,05$). Выявления тенденции к большей частоте госпитализации больных в связи с декомпенсации заболевания на протяжении 3 лет в группе гомозиготных больных по Т аллели.

Ключевые слова: сердечная недостаточность, клиническое течение, фибрилляция предсердий, C825T (RS5443) полиморфизм, ген, β3-субъединица G-протеина.

Рецензент Катеренчук І.Г.

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[1]Р.О. Стефанчук, [2]А.О. Янчук, [3]М.М. Стефанчук, [4]М.О. Стефанчук
[1]Харківський національний університет ім. В. Н. Карабіна, Харків
[2]Міністерство охорони здоров'я України, Київ
[3]Київський національний економічний університет ім. Вадима Гетьмана, Київ
[4]Київський національний університет імені Тараса Шевченка, Київ

ЗДОРОВ'Я ЯК ПРАВОВА КАТЕГОРІЯ

E-mail: alya.kozhushko@gmail.com

У статті розкривається зміст терміну «здоров'я» з правової точки зору. Аналізуються різні підходи до висвітлення поняття здоров'я фізичної особи як немайнового блага. Окрема увага приділена з'ясуванню змісту поняття «здоров'я» відповідно до відкритої концепції здоров'я. Окрім того, у статті наводиться критика чинного легального визначення здоров'я з точки зору його використання у правовій сфері. Обґрунтовано необхідність включення у зміст поняття здоров'я не лише соматичної, а й психічної складової. Зроблено висновок, що здоров'я як особисте немайнове благо повинно охоплюватись наявним соматичним та психічним станом життєдіяльності організму, який визначається системою якісних та кількісних медичних показників.

Ключові слова: здоров'я, психічне здоров'я, соматичне здоров'я, немайнове благо, право на здоров'я, правозастосування.

Відповідно до статті 3 Конституції України життя та здоров'я людини є вищою соціальною цінністю. Таке високе визнання цього фундаментального особистого немайнового блага людини обумовлює його глибоку інтеграцію до правової матерії, створюючи людині низку правових можливостей, які спрямовані на використання та охорону вказаного блага.

Правова регламентація можливостей у сфері власного здоров'я фізичної особи на сьогодні визначається закріпленням низки прав, що пов'язані із здоров'ям, зокрема, право на усунення небезпеки, яка загрожує здоров'ю (ст. 282 ЦК України), право на охорону здоров'я (ст. 283 ЦК України), право на медичну допомогу (ст. 284 ЦК України), право на інформацію про стан свого здоров'я (ст. 285 ЦК України), право на таємницю про стан здоров'я (ст. 286 ЦК України) тощо. Переважно така правова регламентація є фактичним калькуванням відповідних положень Конституції України (ст. 49), або положень іншого законодавства.