**DOI 10.26724/2079-8334-2022-1-79-85-90**
**UDC 616.12-008.318.4: 616.12-008.331.1**

**N.V. Kuzminova, A.V. Ivankova, S.E. Lozinsky, I.I. Knyazkova[1], A.O. Gavrylyuk, Yu.L. Shkarivskyi, O.M. Kulchytska**
**National Pirogov Memorial Medical University, Vinnytsia**
**[1]Kharkiv National Medical University, Kharkiv**

# CHANGES OF APELIN-13 AND CYSTATIN C LEVELS AND METABOLIC PROFILE IN PATIENTS WITH HYPERTENSION AND FREQUENT VENTRICULAR EXTRASYSTOLE

e-mail: Kuzminova5517@gmail.com

We examined 82 patients with stage II hypertension. 50 of them had frequent ventricular arrhythmias according to Holter electrocardiogram monitoring. 32 patients had verified stage II hypertension without any heart rhythm disorders, another 30 healthy individuals were included in the control group. It was found that in patients with ventricular arrhythmias, the level of apelin-13 was significantly ($p<0.0001$) lower than in healthy individuals and even in patients with hypertension but without arrhythmias. In turn, the level of cystatin C in patients with ventricular arrhythmias was significantly ($p <0.001$) higher than the corresponding level in patients with stage II hypertension without arrhythmias and in the control group. Patients with frequent ventricular arrhythmias also had more pronounced proatherogenic shifts in the blood lipid spectrum and higher levels of uric acid ($p<0.05$) compared with patients with hypertension of the second stage but without arrhythmias. In patients with stage II hypertension, a significant decrease in glomerular filtration rate was observed compared with control ($p <0.001$), while in patients with stage II hypertension and ventricular arrhythmias, the level of glomerular filtration rate (both by creatinine- and cystatin-calculated) not only the lowest but also less than 60 ml/min/1.73 m $^2$.

**Key words:** apelin-13, cystatin C, glomerular filtration rate, metabolic cardiovascular risk factors.

**Н.В. Кузьмінова, А.В. Іванкова, С.Е. Лозинський, І.І. Князькова, А.О. Гаврилюк, Ю.Л. Шкарівський, О.М. Кульчицька**

# ОСОБЛИВОСТІ ЗМІН РІВНІВ АПЕЛІНУ-13 І ЦИСТАТИНУ С ТА ПОКАЗНИКІВ МЕТАБОЛІЧНОГО ПРОФІЛЮ У ХВОРИХ НА ГІПЕРТОНІЧНУ ХВОРОБУ З ЧАСТИМИ ШЛУНОЧКОВИМИ ЕКСТРАСИСТОЛАМИ

Обстежено 82 хворих на гіпертонічну хворобу II стадії. За даними холтерівського моніторування електрокардіограми, 50 з них, мали часту шлуночкову екстрасистолію. У 32 пацієнтів верифікована гіпертонічна хвороба II стадії без будь-яких порушень серцевого ритму та ще 30 практично здорових осіб увійшли до групи контролю. Встановлено, що у пацієнтів із шлуночковим варіантом екстрасистолії рівень апеліну-13 був достовірно ($p<0,0001$) нижчим від відповідного показника не тільки у здорових осіб, але і порівняно з хворими на гіпертонічну хворобу без аритмій. В свою чергу, рівень цистатину С у пацієнтів з шлуночковою екстрасистолією достовірно ($p<0,001$) перевищував відповідний рівень у хворих на гіпертонічну хворобу II стадії без аритмій та у групи контролю. У хворих з частою шлуночковою екстрасистолією визначені більш виражені проатерогенні зсуви ліпідного спектру крові та більш високі рівні сечової кислоти ($p<0,05$) порівняно з пацієнтами з гіпертонічною хворобою II ст. без порушень ритму. У хворих на гіпертонічну хворобу II стадії зафіксовано достовірне зниження швидкості клубочкової фільтрації порівняно з контролем ($p<0,001$), при чому у пацієнтів з гіпертонічною хворобою II стадії та шлуночковою екстрасистолією рівень швидкості клубочкової фільтрації (як за креатиніном, так і за цистатином С) був не тільки найнижчим, а й менше 60 мл/хв/1,73 м$^2$.

**Ключові слова:** апелін-13, цистатин С, швидкість клубочкової фільтрації, метаболічні чинники серцево-судинного ризику.

*The study is a fragment of the research project "Metabolic risk factors, cardiovascular remodeling and functional status of the kidneys in patients with cardiovascular disease. Possibilities of pharmacological correction", state registration number 0119U101849.*

In recent years, the role of arterial hypertension (AH), in particular, essential hypertension (EH) in the progression of various cardiac arrhythmias has been actively studied. Left ventricular hypertrophy in patients with EH is a pathomorphological basis for the progression of electrical instability of the myocardium and cardiac arrhythmias. Increased myocardial stress on the background of hypertension, along with excessive after-load, stimulates myocardial hypertrophy, its structural remodeling with a disproportionate increase in fibrous tissue, reduction of coronary blood flow, and the progression of myocardial diastolic dysfunction. Today, atrial fibrillation is the most studied cardiac arrhythmia in patients with EH while the mechanisms of the most common cardiac arrhythmia – extrasystolic arrhythmia are studied insufficiently [1, 2]. It has been shown that ventricular extrasystole arrhythmia (VE) may be a predictor of ventricular paroxysmal tachycardia, which in turn significantly increases the risk of sudden arrhythmic death [11].

AH rarely occurs in isolation and often forms clusters with other cardiometabolic risk factors, such as decreased glucose tolerance, hyperuricemia, and dyslipidemia [3, 4]. Various metabolic risk markers for cardiovascular (CV) complications are being actively studied around the world today. We want to

emphasize apelin-13 (AP 13) and cystatin C (Cys C). Apelin belongs to the adipokines family, its receptors have been found in cardiomyocytes in high concentrations, as well as in vascular endothelium, smooth muscle cells, brain, kidneys, and adrenal glands [10]. Apelin-13 positively affects the CV system, as it has an antagonism to the renin-angiotensin system. It has antihypertensive, positive inotropic, and cardioprotective properties (reduces myocardial ischemia, improves myocardial contractility, and prevents the formation of hypertrophy of the heart) [7]. In addition, AP13 may affect the progression of diseases associated with obesity, but its role in this area requires further research [14].

In its turn, cystatin C today plays the role of an early and most informative marker of renal function. Cys C is freely filtered through the glomerular membrane, due to low molecular weight. It is a more sensitive marker of decreased glomerular filtration rate than creatinine because such factors as age, sex, muscle mass, nutrition, physical activity, race factors do not affect its level [5]. At the same time, it serves as an effective predictor for early detection of renal failure, even at normal creatinine levels, which is very important for patients with cardiovascular disease and, in particular with hypertension [13, 15].

**The purpose** of the study was to evaluate the peculiarities of changes in apelin-13 and cystatin C serum levels as well as metabolic profile in patients with essential hypertension and frequent ventricular extrasystole arrhythmia.

**Materials and methods.** The total of 82 patients with stage II EH were involved in the study. The main group consisted of 50 persons, aged 27 to 75 years (mean age 60.5±1.3) with stage II EH and frequent VE. In addition, we examined 32 patients with stage II EH without any cardiac arrhythmias aged 32 to 72 years (mean age 55.9±1.7), who entered the comparison group. Among the patients with VE, there were 22 men (44.0 %) and 28 women (56.0 %). The comparison group included 15 (46.9 %) men and 17 (53.1 %) women. We also examined 30 people without any cardiovascular and renal pathology, including 16 (53.3 %) men and 14 (46.7 %) women, mean age of 53.1±0.3 years, who were included in the control group. The statistical analysis did not show any significant inter-group differences ($p>0.05$) of mean age and sex values, which indicated the age and gender homogeneity of patients [8].

Inclusion criteria were as followed:

1) age from 25 to 75 years; 2) EH stage II according to the unified clinical protocol; 3) frequent (>30 extrasystoles per 1 h study) ventricular extrasystole verified by the daily Holter electrocardiogram monitoring (DM ECG); 4) patients naive to antiarrhythmic treatment at the time of inclusion.

Exclusion criteria:

1) age younger than 25 and older than 75 years; 2) EH I or III stages, symptomatic hypertension; 3) concomitant coronary disease; 4) heart failure of III-IV functional class according to NYHA and the presence of systolic myocardial dysfunction; 5) the history of persistent (>30 sec) and permanent atrial fibrillation or paroxysmal tachycardia, dominant supraventricular extrasystole; 6) diabetes mellitus or impaired carbohydrate tolerance, clinically significant concomitant diseases of the internal organs with impaired function.

All patients underwent full comprehensive clinical, laboratory, and instrumental examination to verify the underlying diagnosis and concomitant conditions: 1) general clinical examination, measurement of blood pressure (BP); 2) electrocardiography (ECG) in 12 standard leads; 3) DM ECG; daily blood pressure monitoring (DBPM); 4) echocardiography (EchoCG); 5) laboratory methods: the level of serum lipid spectrum, uric acid level, the level of apeline-13; 6) assessment of the kidneys' functional state (cystatin C and blood creatinine level with the calculation of glomerular filtration rate).

Daily monitoring of ECG and BP was carried out using hardware and software of the "DiaCard" complex system (JSC "Solvaig", Ukraine) according to the standard protocol.

EchoCG studies were performed in one-dimensional and two-dimensional modes with color, pulse, and constant-wave Doppler using "My Lab 25" (Italy) equipment.

Apelin-13 and cystatin C levels in blood serum were determined by enzyme-linked immunosorbent assay using the kits "Human AP13" and "Human Cystatin C" according to the manufacturer's instructions.

Serum lipid spectrum level was determined by a spectrophotometric method using standard reagent kits "Cholesterin-F", "Triglycerid-F" "HDL-cholesterin-F" produced by "Philisit–Diagnostics" (Ukraine).

The level of uric acid (UA) and creatinine were determined using a colorimetric enzyme method on a Cobas 6000 analyzer using a "Roche Diagnostics" test system (Switzerland).

The glomerular filtration rate was calculated using online calculators according to the CKD-EPI formula: https://boris.bikbov.ru/2013/07/21/kalkulyator-skf-rascheta-skorosti-klubochkovoy-filtratsii (for creatinine) and https:/ /medlabdiag.ru/calculators/clearance_cys (for cystatin C).

Statistical processing of the data was performed using the software StatSoft "Statistica" v. 12.0 according to the recommendations for medical and biological studies. The results were presented as the

median and interquartile range (25 and 75 percentiles) for quantitative values, and percentages (%) – for relative values. Comparison of relative values (%) was performed using criterion $\chi^2$, of quantitative values for independent samples – using Kruskal-Wallis ANOVA test & Median test [8, 9].

**Results of the study and their discussion.** The variation of AP13 and Cys C levels in EH patients was determined. The concentration of AP13 was significantly lower in patients with EH and VE, compared to patients without arrhythmias (814 (730; 987) versus 1045 (823; 1425) pg/ml, p<0.0001) and patients in the control group (814 (730; 987)) pg/ml versus 1311 (882; 1754) pg/ml, p<0.0001) (fig. 1).

In turn, the highest level of Cys C was recorded in patients with frequent VE, which was significantly different from the corresponding level of Cys C in patients without arrhythmias (1.25 (1.10; 1.38) mg/l vs. 1.01 (0.86; 1.24) mg/ml, p=0.001) and the control group (1.25 (1.10; 1.38) mg/l vs. 0.89 (0.63; 1.04) mg/l, respectively, p<0.0001) (fig. 2).

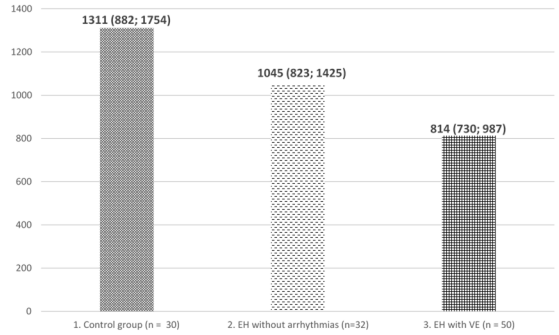


Fig. 1. Levels of apeline-13 in blood serum (in pg/ml) in patients with EH.

Note: the significance of intergroup differences of apeline-13 levels in serum was calculated by Kruskal-Wallis ANOVA test & Median test (P 1–2 < 0.0001; P1–3 <0.0001; P2–3 <0.0001)

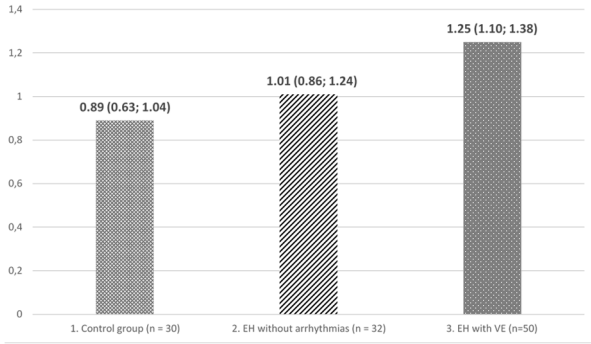


Fig. 2. Serum cystatin C levels (in mg/l) in patients with EH.

Note: the significance of intergroup differences in serum cystatin C levels was calculated by Kruskal-Wallis ANOVA test & Median test (P 1–2=0.04; P1–3 <0.0001; P2–3=0.001).

Besides apelin-13 and cystatin C levels, we also evaluated such well-known cardiometabolic risk factors as serum lipid spectrum, presence of hyperuricemia, uric acid, and creatinine levels (with subsequent calculation of glomerular filtration rate (GFR)) in our patients (table 1).

□□bl□1

**Levels of lipid spectrum, uric acid, and GFR in patients with stage II hypertension**

| Indices | Patients with EH without extrasystole | Patients with EH and frequent VE | R |
|---|---|---|---|
| | n=32 | n=50 | |
| TC, mmol/l | 5.60 (4.65; 6.07) *** | 5.45 (5.06; 6.28) ** | NS |
| TC > 5 mmol/l, abs. number (%) | 21 (65.6 %) | 42 (84.0 %) | *0.05* |
| TG, mmol/l | 1.45 (1.20; 1.95) | 1.73 (1.43; 1.94) * | 0.01 |
| TG > 1.7 mmol/l, abs. number (%) | 9 (28.1 %) | 27 (54.0 %) | 0.02 |
| HDL-C, mmmol/l | 1.17 (0.99; 1.50) | 1.18 (1.09; 1.28) | NS |
| HDL-C <1.2 in men and <1.1 in women | 13 (40.6 %) | 20 (40.0 %) | NS |
| LDL-C, mmol/l | 3.20 (2.60; 3.88) * | 4.04 (3.49; 4.33) *** | 0.002 |
| LDL-C > 3 mmol/l, abs . number (%) | 19 (59.4 %) | 47 (94.0 %) | 0.0001 |
| LDL-C > 4 mmol/l, abs. number (%) | 6 (18.8 %) | 26 (52.0 %) | 0.003 |
| VLDL-C, mmol/l | 0.72 (0.58; 0.87) * | 0.89 (0.80; 0.98) *** | 0.008 |
| LDL-C > 3 + TG > 1.7, abs. number (%) | 5 (15.6 %) | 26 (52.0 %) | 0.0009 |
| LDL-C > 3 + HDL-C <1.2/1.1 + TG> 1.7, abs. number (%) | 2 (6.3 %) | 9 (18.0 %) | 0.001 |
| AI | 3.35 (2.45; 4.47) * | 3.86 (3.31; 4.57) ** | NS |
| AI > 3 | 19 (59.4 %) | 44 (88.0 %) | NS |
| UA, mmol/l | 318 (267; 347) | 381 (342; 419) *** | 0.001 |
| HU, abs. number (%) | 3 (9.4 %) | 24 (48.0 %) | NS |
| TG> 1.7 + HU, abs. number (%) | 0 (0) | 11 (22.0 %) | 0.005 |
| Creatinine, мmol/l | 74 (58; 97) | 89 (82; 94) * | NS |
| GFR by creatinine, ml/min/1.73 m $^2$ | 64 (42; 87) *** | 50 (44; 60) *** | 0.04 |
| GFR by Cys C, ml/min/1.73 m $^2$ | 74 (55; 94) *** | 54 (48; 65) *** | 0.002 |

Notes: 1. NS – not significant, p> 0.05; 2. VE – ventricular extrasystole; UA – uric acid; HU – hyperuricemia (UA>420 in men and > 360 μmol/l in women); AI – atherogenicity index; GFR – glomerular filtration rate; 3. Significance of intergroup differences of absolute meanings is calculated by Kruskal-Wallis ANOVA test & Median test, and percentages – by criterion $\chi^2$; the sign "*" indicates the significance of the difference from the control group (n=30), p<0.05; "**" – p <0.01, and "***" – p<0.001.

The results of the analysis showed that the average level of TC exceeded 5 mmol/l in all groups of patients with EH, with no significant difference within them but it differed from the control group (5.60 mmol/l in patients without arrhythmias, 5.45 mmol/l in patients with VE vs 4.60 mmol/l, p<0.01). The number of patients with a level of TC > 5 mmol/l was higher in the group of patients with frequent VE, which tended to be significant (84.1 % vs. 65.6 %, p=0.05). The average level of low-density lipoprotein cholesterol (LDL-C) exceeded 3 mmol/l in both groups of patients with EH, and its highest values were recorded in patients with frequent VE (4.04 mmol/l), which was statistically different from patients without arrhythmias (3.2 mmol/l, p<0.008) and persons without cardiovascular and renal pathology (2.8 mmol/l, p<0.001). The level of LDL-C higher than 3 mmol/l was determined in 94.0 % of patients with VE, which was significantly different from patients without arrhythmias (59.4 %, p<0.0001). Moreover, the level of LDL-C> 4 mmol/l was noted in 52.0 % of patients with VE, which was significantly different compared to patients without arrhythmias: 18.8 % (p<0.05). Very low-density lipoprotein cholesterol (VLDL-C) was also higher in patients with extrasystoles, compared to hypertensive patients without cardiac arrhythmias (p<0.01) and healthy individuals (p<0.001).

High-density lipoprotein cholesterol (HDL-C) below 1.2 mmol/l in men and below 1.1 mmol/l in women was recorded in 40.6 % of patients with EH without extrasystole and in 40.0 % of patients with EH and VE.

The largest number of patients with TG> 1.7 mmol/l was recorded in patients with frequent VE (54.0 % vs. 28.1 % in patients without arrhythmias, p=0.02).

More than half of the subjects with VE (52.0 %) had the combination of LDL-C>3 mmol/l and TG> 1.7 mmol/l, which was significantly less (15.6 %, p<0.0009) than in patients without arrhythmias. In addition, 18.0 % of patients with EH and VE had dyslipidemia in the form of a combination of LDL-C>3 mmol/l and HDL-C <1.2 mmol/l in men and <1.1 mmol/l in women and TG level>1.7 mmol/l, which was significantly different from patients with EH without extrasystole (6.3 %, p=0.001).

It was noted that the average value of the atherogenicity index (AI) exceeded 3 units in all groups of patients with EH, which was significantly different from the control group (2.97 units, p<0.05). The largest number of patients with AI>3 was noted in patients with frequent VE (88.0 %). It was significantly higher than in patients without extrasystole (59.4 %, p<0.007).

The level of uric acid in patients with frequent VE was significantly higher than in patients without arrhythmias (381 μmol/l vs. 318 μmol/l, p=0.001) and persons without cardiovascular and renal pathology (303 μmol/l, p<0.001). In turn, the number of patients with hyperuricemia (HU), determined when UA level was higher than 420 μmol/l in men and 360 μmol/l in women, was also highest in patients with ventricular extrasystolic arrhythmia (48.0 %), which was significantly different compared with patients without arrhythmias, where the number of patients with HU was only 9.4 % (p<0.0003). A combination of HU and elevated LDL-C (>3 mmol/l) was reported in 44.0 % of patients with EH and VE, while the percentage of such patients in the comparison group was significantly lower (6.3 %, p<0.001). A combination of HU and hypertriglyceridemia was met in 22.0 % of patients with VE, which was statistically different from patients without arrhythmia, where no cases of such combination were found (p=0.004).

The mean creatinine level in patients with extrasystole did not exceed the reference values and differed significantly only from the control group (89 μmol/l in patients versus 70 μmol/l, p<0.04). Mean GFR, calculated by creatinine, was significantly lower in the groups of patients with EH compared to healthy individuals (64 ml/min/1.73 m $^2$ in patients without extrasystole and 50 ml/min/1.73 m $^2$ in patients with VE against 91 ml/min/1.73 m $^2$ respectively, p<0.001). The lowest GFR was recorded in patients with VE. It was significantly different from patients without extrasystoles (50 vs. 64 ml/min/1.73 m $^2$, p=0.04). It was noted that the mean GFR calculated by Cys C was higher than the corresponding values of GFR calculated by creatinine, but the differences were not significant. The GFR calculated by Cys C in all patients with EH was significantly lower than in the control group (with healthy individuals) (74 ml/min/1.73 m$^2$ in patients without extrasystole and 54 ml/min/1.73 m $^2$ in patients with VE against 94 ml/min/1.73 m$^2$ respectively, p<0.001). The mean GFR by Cys C in patients with VE was significantly lower than in patients without arrhythmias (54 ml/min/1.73 m $^2$ vs. 74 ml/min/1.73 m $^2$, p<0.03).

Considering the great scientific interest in various metabolic markers of risk of cardiovascular complications, we compared the mean levels of apelin-13 and cystatin C in patients with essential hypertension stage II without cardiac arrhythmias and in patients with EH and frequent ventricular extras. Our data demonstrated that lower levels of AP13 were associated with the presence of frequent VE and to some extent echo the results of some researchers who emphasized the ability of AP13 to change the electrophysiological characteristics of the heart muscle [7, 12]. In addition, the lowest AP13 in the group of patients with VE confirms the opinion of scientists that the damages of AP13 production lead to the progression of life-threatening arrhythmias and progression of heart failure, which in turn worsens the prognosis [14].

Patients with frequent VE had significantly higher levels of Cys C than those without arrhythmias (p=0.001). Hypertension and extrasystole (especially ventricular) are known to lead to heart remodeling and dysfunction. It is known that heart remodeling is accompanied by certain inflammatory changes (apoptosis, atrial fibrosis, disorders of calcium transfer and regulation of connexin, etc.). Cys C is often referred to as a marker of inflammation because it is produced during inflammation by cells containing the nucleus [5, 13, 15]. This may explain the increase in the level of this peptide in patients with hypertension and extrasystole.

Our study demonstrated a decrease in GFR in patients with stage II EH had compared with healthy individuals. In turn, the lowest GFR (both, by creatinine and cystatin C calculated) was recorded in patients with stage II EH and frequent VE probably due to more severe hemodynamic and metabolic disorders in ventricular extrasystolic arrhythmia. Our assumption agrees with some literature sources but requires further study [1].

An increase in the level of LDL-C, VLDL-C, TG, and UA should be considered as a possible predictor of arrhythmias in patients with EH. To date, dyslipidemia as a manifestation of metabolic syndrome is undoubtedly one of the main CV risk factors. There is evidence that excessive accumulation of LDL-C and VLDL-C has a direct cytotoxic effect on the left atrium, disrupts calcium regulation, and slows the rate of pulse conduction. Electrical remodeling and structural changes in the heart result in an increased risk of extrasystole and atrial fibrillation [1, 2, 4, 6]. In addition, there is strong evidence of an association of elevated serum UA levels (even at lower levels than required for clinical manifestations of gout) and endothelial dysfunction: inhibition of nitric oxide production, vascular smooth muscle cell proliferation and inflammation activation), as well as with activation of the sympathoadrenal and renin-angiotensin systems, diabetes mellitus, hyperinsulinemia and insulin resistance, disorders of lipid metabolism, progression of hypertension, target organ damage and worsening of patients' prognosis.

Thus, the results of our study indicate more severe disorders of the cardiometabolic profile in patients with stage II hypertension with frequent VE compared with patients with those without cardiac arrhythmias. They are accompanied by definite changes in the concentration of additional markers of cardiovascular risk, namely a decrease in the level of apelin-13 and an increase in cystatin C level.

## Conclusions

1. Patients with stage II hypertension had a significant decrease in the level of AP13 compared to the control (37.9 %, p<0.0001). Patients with VE had a significantly lower level of AP13 than patients with EH without arrhythmias (22.1 %, p <0.0001).

2. The level of Cys C in patients with VE was 40.4 % (p<0.0001) higher than the corresponding level in the control group and 23.8 % (p<0.001) than patients with stage II EH without arrhythmias.

3. Patients with stage II EH and frequent VE had more pronounced proatherogenic shifts in the blood lipid spectrum and a significantly higher level of uric acid (p<0.05).

4. Patients with stage II EH had a significant decrease in GFR compared to the control group (p<0.001). Moreover, patients with stage II EH and VE had GFR (both by creatinine and Cys C calculated) not only the lowest but also less than 60 ml/min/1.73 m $^2$ (50 (44; 60) and 54 (48; 65) ml/min/1.73 m $^2$).

## References

1. Zharinov OI, Talaieva TV, Lishchyshyna OM, Bozhko LI, Hetman TV, Zalevskyi VP, et al. Adaptovana klinichna nastanova, zasnovana na dokazakh. Fibryliatsiia peredserd. Rekomendatsii Robochoi hrupy z porushen rytmu sertsia Asotsiatsii kardiolohiv Ukrainy. 2016; 11–7. [in Ukrainian]

2. Nykyforov VS, Marsalskaia OA, Metso KV, Palahutyn MA. Arteryalnaya hypertenziya i narushenyiya rytma serdtsa. Zdorovye – osnova chelovecheskogo potentsiala: problemy i puti ikh resheniya. 2016. 2; 594–96. [in Russian]

3. Sirenko YuM. Recomendatsii ESC I ESH z likuvannya arterialnoyi hipertenziyi. K.: Zaslavskyi OYu. 2019; 22–23. [in Ukrainian]

4. Trybrat TA, Shut SV, Trybrat AA, Kazakov YuM. Shliakhy korektsiyi asotsiiovanoho metabolichnoho syndromu u khvorykh na hipertonichnu khvorobu. Visnyk problem biolohiyi i medytsyny. 2018; 1 (142): 197–201. [in Ukrainian]

5. Dangle PP, Ayyash O, Kang A. Cystatin C-calculated glomerular filtration rate-a marker of early renal dysfunction in patients with neuropathic bladder. Urology. 2017; 100: 213–17. https://doi.org/10.1016/j.urology.2016.08.011

6. Hoogendijk MG, Geczy T, Yap S, Szili-Torok T. Pathophysiological mechanism of premature ventricular complexes. Front Physiol. 2020; 11: 406. https://doi.org/10.3389/fphys.2020.00406

7. Hu G, Wang Z, Zhang R, Sun W, Chen X. The Role of Apelin/Apelin Receptor in Energy Metabolism and Water Homeostasis: A Comprehensive Narrative Review. Front Physiol. 2021; 12. https://doi.org/10.3389/fphys.2021.632886

8. Ivankova AV, Kuzminova NV, Lozinsky SE, Havryliuk AO, Knyazkova II, Ivanova EI. Peculiarities of daily ECG changes in patients with essential hypertension of the second stage. World of medicine and biology. 2021; 1 (75): 59–63. https://doi.org/10.26724/2079-8334-2021-1-75-59-63

9. Kuzminova NV, Ivankova AV, Ivanov VP, Lozinsky SE, Knyazkova II, Gavriluk AO. Daily blood pressure pattern disorders in patients with stage II essential hypertension and frequent premature beats. World of medicine and biology. 2020; 1(71): 72–7. https://doi.org/10.26724/2079-8334-2020-1-71-72-77

10. Marcus GM. Evaluation and Management of Premature Ventricular Complexes. Circulation. 2020; 141 (17): 1404–18. https://doi.org/10.1161/CIRCULATIONAHA.119.042434
11. Purmah Y, Proietti M, Laroche C, Mazurek M, Tahmatzidis D, Boriani G. [et al.] EORP-AF General Pilot Registry Investigators. Rate vs. rhythm control and adverse outcomes among European patients with atrial fibrillation. Europace. 2018; 20 (2): 243–52. https://doi.org/10.1093/europace/euw421
12. Tian Y, Chen R, Jiang Y, Bai B, Yang T, Liu H. The Protective Effects and Mechanisms of Apelin/APJ System on Ischemic Stroke: A Promising Therapeutic Target. Frontiers in neurology. 2020; 11: 75. https://doi.org10.3389/fneur.2020.000755
13. Yang S, Song L, Zhao L, Dong P, Lai L, Wang H. Predictive value of cystatin C in people with suspected or established coronary artery disease: A meta-analysis. Atherosclerosis. 2017; 263: 60–7. https://doi.org/10.1016/j.atherosclerosis.2017.05.025
14. Zaki M, Kamal S, Ezzat W, Hassan N, Yousef W, Ryad H. [et al.] Serum apelin levels and metabolic risk markers in obese women. J Genet Eng Biotechnol. 2017; 15 (2): 423–29. https://doi.org10.1016/j.jgeb.2017.05.002
15. Zhu Z, Zhong C, Xu T, Wang A, Peng Y, Xu T. [et al.] Prognostic significance of serum cystatin C in acute ischemic stroke patients according to lipid component levels. Atherosclerosis. 2018; 274: 146–51. https://doi.org/10.1016/j.atherosclerosis.2018.05.015

Стаття надійшла 17.01.2021 р.

**DOI 10.26724/2079-8334-2022-1-79-90-93**
**UDC 617.557-007.43-089-06:539.55**

**R.A. Lutkovskyi, A.L. Chelischvili[1]**
**National Pirogov Memorial Medical University, Vinnytsia**
**[1]Poltava State Medical University, Poltava**

# TRANSABDOMINAL PREPERITONEAL ALLOPLASTY OF INGUINAL HERNIAS USING A NANOMODIFIED MESH IMPLANT

e-mail: lutkovskiruslan@gmail.com

Surgical treatment of 142 patients with inguinal hernias who underwent transabdominal preperitoneal allohernioplasty was analyzed. The author's mesh was used in group I patients, and in group II patients, a classical polypropylene mesh was used. Statistically, significantly better results were obtained in patients of group I compared with group II: seroma was found in 1.4 % and 7.0 % of patients, respectively. Chronic pain was observed in 5.6 % of patients in group II compared to group I, with no such complications, hernia recurrence – in 8.5 % and 1.4 % of patients, respectively. The duration of inpatient treatment in group I was 2.3±1.2 days, in group II – 5.2±1.1 days. Surgical treatment of inguinal hernias using nanomodified polypropylene mesh was more effective than using classical polypropylene mesh, as evidenced by a decrease in the seroma frequency from 7.0±1.3 to 1.4±0.3 %, chronic postoperative pain – from 5.6±0.2 to 0 %, hernia recurrence – from 8.5±0.3 to 1.4±0.2 %.

**Key words:** inguinal hernia, nanomodified polypropylene mesh, postoperative wound complications.

**Р.А. Лутковський, А.Л. Челішвілі**

# ТРАНСАБДОМІНАЛЬНА ПРЕПЕРИТОНЕАЛЬНА АЛОПЛАСТИКА ПАХВИННИХ ГРИЖ ЖИВОТА З ВИКОРИСТАННЯМ НАНОМОДИФІКОВАНОГО СІТЧАСТОГО ІМПЛАНТАТУ

Проведено аналіз хірургічного лікування 142 пацієнтів з пахвинними грижами живота в яких виконували операцію трансабдомінальну препериторнеальну алогерніопластику. У хворих групи І використовували розроблену сітку, у хворих групи ІІ класичну поліпропіленову сітку. Статистично значущо кращі результати отримано у хворих групи І порівнянно з групою ІІ: серому виявлено відповідно у 1,4 % та 7,0 % хворих. Хронічний біль спостерігався у 5,6 % хворих групи ІІ на відміну від групи І де таких ускладнень не було, рецидиви грижі – відповідно у 8,5 % і 1,4 % хворих. Тривалість стаціонарного лікування в групі І становила 2,3±1,2 доби, в групі ІІ – 5,2±1,1 доби. Хірургічне лікування пахвинних гриж живота з використання наномодифікованої поліпропіленової сітки є ефективнішим порівняно з використанням класичної поліпропіленової сітки, про що свідчило зменшення частоти сероми з 7,0±1,3 до 1,4±0,3 %, хронічного післяопераційного болю – з 5,6±0,2 до 0 %, рецидиву грижі – з 8,5±0,3 до 1,4±0,2 %.

**Ключові слова:** пахвинна грижа живота, наномодифікована поліпропіленова сітка, післяопераційні ранові ускладнення.

*The study is a fragment of the research project "Damages: mechanical, physical, chemical and biological causes. Mechanisms of development, diagnosis and treatment", state registration No. 0121U110669.*

In recent years, transabdominal pre-peritoneal (TAPP) alloplasty has become more widely used in surgical practice for inguinal hernias (IH). This is due to low trauma, speed of surgery, a short length of stay in the hospital and faster postoperative rehabilitation compared to open surgery [1, 3, 8, 9]. However, it should be noted that the recurrence rate of inguinal hernias after transabdominal preperitoneal alloplasty is 5.3–10.0 % [2]. The causes of recurrent inguinal hernias after transabdominal preperitoneal alloplasty surgery are insufficient overlap of the medial and lateral inguinal fossae with a mesh implant due to the small size of the implant and the lack of fixation at the level of the iliac vessels.