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Реферати

**ОСОБЕННОСТИ ВЕДЕНИЯ ПАЦИЕНТОВ
С ПОЗДНО ДИАГНОСТИРОВАННЫМ ВРОЖДЕННЫМ
ПОРОКОМ СЕРДЦА**

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Разнообразие проявлений врожденных пороков сердца затрудняет их своевременную диагностику. Но несмотря на это, понимание принципов развития данной патологии у пациентов старшей возрастной группы, профессиональная осведомленность врачей, в том числе благодаря информации, полученной при ознакомлении с материалами приведенного клинического случая, позволят сформировать современные подходы к дифференцированному лечению с использованием консервативных и хирургических методов, положительно повлияет на качество жизни пациентов, оптимизирует прогноз.

Ключевые слова: врожденный порок сердца, поздняя диагностика, методы лечения, оптимизация прогноза.

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**FEATURES OF MANAGEMENT OF PATIENTS
WITH LATE DIAGNOSTED CONGENITAL
HEART DISEASE**

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The variety of manifestations of congenital heart defects complicates their timely diagnosis. But, despite this, understanding the principles of pathology development in patients of the older age group, the professional awareness of doctors, including thanks to the information obtained in acquaintance with the materials of the given clinical case, will allow to form modern approaches to differentiated treatment using conservative and surgical methods, will affect positively the quality of patients' life, should optimize the prognosis.

Keywords: congenital heart disease, late diagnostics, treatment methods, prognosis optimization.

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**FEATURES OF THE HYPERTENSIVE HEART DEVELOPMENT
IN MINeworkERS WITH ARTERIAL HYPERTENSION**

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The purpose of the research project was to study the clinical and structural-functional features of hypertensive heart (HH) in miners with arterial hypertension (AH) with experience of over 10 years and to develop clinical and functional criteria for its diagnosis. The examined mineworkers included 127 underground miners and 58 surface profession workers aged 35-55 years, with experience in mining conditions exceeding 10 years, with normal high blood pressure (AP), stages I and II hypertension, which constituted respectively the main and the auxiliary groups. The total of 30 virtually healthy men, who did not work under harmful conditions, made control group 1, and 30 practically healthy miners of superficial occupations formed the control group 2. The general-clinical examination of patients, electrocardiography (ECG), daily monitoring of blood pressure were carried out. The structural and functional heart status was studied using one- and two-dimensional echocardiography (ECHO-CG) by means of "PHILIPS-HDI 1500" apparatus according to the standard procedure. The types of left ventricle (LV) geometry according to Framingham criteria were studied. The methodological approach to studying the LV weight was based on the Devereux formula (Pen Convention). The examination data testify to the predominant development of concentric remodeling in healthy miners, and in 25.2% of them - the physiological left ventricular hypertrophy (LVH). Unlike pathological LVH, the physiological "working" LVH is not accompanied by the formation of diastolic dysfunction of the LV (LVDD). In 98.5% of the miners there is a concentric structural-functional type of hypertensive heart, based on the development of concentric LVH and the concentric LV remodeling. In 14.7% of the main group miners with the II stage hypertensive disease (HD), the right ventricle hypertrophy develops. The peculiarity of hypertensive heart in miners of underground jobs is its development against the background of the physiological "working" LVH. The following types of LV remodeling are prevalent in miners: concentric left ventricular hypertrophy (86.2%) and concentric remodeling (12.3%). At the early stages of the hypertensive heart development, the left ventricular diastolic dysfunction is formed in miners, which at later stages is transformed into diastolic heart failure with the subsequent attachment of systolic heart failure. In miners with hypertensive heart, the structural-functional status of the right ventricle undergoes early disorders, which is manifested by diastolic dysfunction.

Key words: arterial hypertension, hypertensive heart, left ventricle remodeling.

The present study is a fragment of the research project "Justification of comprehensive approaches to clinical laboratory diagnostics, prevention and treatment of the cardiorespiratory system diseases and comorbid conditions in the age aspect" (state registration No. 0117 U 004728).

Arterial hypertension (AH) remains one of the most common diseases of the cardiovascular system worldwide, it is a predictor of myocardial infarction, stroke, renal failure, significantly impairs the survival prognosis of these patients, is accompanied by the growing frequency of hospitalizations and treatment costs [2, 7]. According to the official statistics, over 12 million patients with arterial hypertension (AH) have been registered in Ukraine, accounting for about 31.5% of the adult population [3, 4]. Changing of

the geometry and growing weight of the myocardium are among the earliest signs of left ventricular (LV) injury [5]. Moreover, the presence of left ventricular hypertrophy (LVH) in patients with AH significantly increases the risk of complications [5, 1].

Hypertensive heart (HS) is a cardioghemodynamic anomaly that develops at the formation and stabilization stages of hypertension and determines the high level of vascular catastrophes, development of heart failure, increased risk of sudden death [1]. Among the workers of the mining industry, the prevalence of hypertension is 30.4%, increasing with age and work experience in the underground conditions [1]. In this contingent of patients a progressive course of the disease with relatively frequent development of severe complications is observed, leading to losses of working capacity and mortality in young age [1]. Therefore, the study of the hypertensive heart (HH) development features in miners with AH remains a very topical problem which needs to be solved.

The purpose of the paper was to study the clinical and structural-functional features of the HH in miners with hypertension and the working experience exceeding 10 years and to develop clinical and functional criteria for its diagnosis.

Material and methods. The research was carried out on the basis of the therapeutic department at the Krivoy Rog City Clinical Hospital No. 8 of the Dnipropetrovsk Regional Council. The total of 215 miners with AH working at the mining industry enterprises of the Kryvyi Rih city, were examined. Among these, 127 miners of underground (machine drillers, shaft sinkers, shaft timbermen) and 58 men of surface (service-men, electricians) occupations aged 35-55 years, with experience in mining conditions exceeding 10 years, with normal high arterial pressure (AP), I and II stage hypertension, respectively, formed the main and auxiliary groups. Whereas, 30 virtually healthy men who do not work under harmful conditions, constituted control group 1 and 30 practically healthy miners of superficial occupations formed control group 2. The groups are comparable according to age, anthropometric indices, and the main and auxiliary groups – according to the disease duration and the hypertension degree.

The inclusion criteria were: age 35-55, experience in the underground conditions exceeding 10 years, systolic arterial pressure (AP) ≥ 130 mm Hg, diastolic AP = 80 mm Hg. The *exclusion criteria* were: comorbid conditions, working experience less than 10 years, secondary arterial hypertension.

All the patients were examined and treated in accordance with the clinical protocol of medical care in compliance with the Order of the MOH of Ukraine dated May 24, 2012 No. 384 “On Approval and Implementation of Medical and Technology Documents for the Medical Assistance Standardizing in Arterial Hypertension” (Order of the MOH No. 384, 2012), clinical AH guidelines of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) of 2013, guidelines for the European Society of Cardiology and the European Society for the Hypertension (AH) Treatment [9, 10].

A general-clinical examination of patients, determination of thyroid stimulating hormone and blood electrolytes content was carried out. Electrocardiography (ECG), diagnosis of left ventricular hypertrophy (LVH) was carried out according to Sokolov-Lyon voltage ECG-criteria: $SV1 + RV5 > 35$ mm $RaVL \geq 11$ mm and the Cornell voltage $SV3 + RaVL > 28$ mm [10]. The daily monitoring of AP (DMAP) was carried out. The structural and functional heart status was studied using one- and two-dimensional echocardiography (ECHO-CG) with “PHILIPS-HDI 1500” apparatus according to the standard procedure. The end-systolic (ESV, ml) and end diastolic (EDV, ml) volume of the left ventricle (LV) and the index of global LV contractility - ejection fraction (EF, %) were taken into account.

To assess the LV diastolic function, the velocity of the transmitral flow in the early and late diastole (E, A, m / sec) and their ratio (E/A) was determined. The myocardial weight (LVMW, g) was calculated using R. Devereux formula, the LV myocardial weight index (LVMWI) and the relative LV wall thickness (RLVWT) were determined. The LV geometry was considered normal at the LVMWI values of < 130 g / m² and the RLVWT values < 0.44 .

The LVMWI value of > 130 g / m² and RLVWT value of > 0.44 indicated the concentric LVH development. At the LVMWI values of > 130 g / m² and the RLVWT values of < 0.44 , an eccentric LVH was diagnosed. In cases when the LVMWI values were < 130 g / m² and the RLVWT values were > 0.44 , the concentric LV remodeling was diagnosed. The criterion for a moderate LVH was considered to be LVMWI value of 130-180 g / m². The pronounced LVH was diagnosed with the LVMWI value of > 180 g / m².

The results were statistically analyzed using STATISTICA® 6.0 for Windows (license No. AGAR909E415822FA) with parametric methods applied. The values are given in the form of the mean value (M) \pm standard error of the mean (m). Statistically significant were considered the differences with p not exceeding 0.05.

Results of the study and their discussion. Patients complained of headache, dizziness, noise in the head, pain in the heart area, palpitations, interruptions in cardiac activity. Individual patients reported shortness of breath with physical loads.

It is known that heart rhythm disorder is a topical problem of clinical practice [8]. According to literature sources, patients with hypertension often have both ventricular and supraventricular rhythm disorders [6]. In miners at ECG-study on the background of ECG-signs of LVH, we diagnosed the rhythm disorders of the ventricular and supraventricular genesis, short paroxysms of atrial fibrillation. In the main group, rhythm disorders were diagnosed in 39.5% of patients, 94.2% of them being of ventricular genesis. In the auxiliary group, rhythm disorders were recorded in 6.7% of the miners.

The study of the structural and functional LV status with the I stage hypertensive disease (HD) showed that the mean values of linear and volumetric indices tended to increase, compared to these indices in healthy miners. In patients with II stage HD of the main and auxiliary groups a significant growth of these indices was recorded.

The structural and functional heart status in miners of underground occupations and that of hypertensive heart in miners is represented by different variants of the left ventricle geometry: normal geometry, concentric remodeling, concentric and eccentric LVH (fig. 1).

In the control group of healthy men, LVMWI and RLVWT were $93.7\% \pm 1.27 \text{ g / m}^2$ and 0.41 ± 0.01 respectively. In the group of healthy miners, the LVMWI was equal to $117.6\% \pm 8.52 \text{ g / m}^2$, and RLVWT was 0.44 ± 0.01 . These data indicate the predominant development of concentric remodeling in healthy miners, and in 25.2% of them - physiological LVH. Unlike pathological LVH, the physiological "working" LVH is not accompanied by the formation of LV diastolic dysfunction (DD). In 98.5% of the miners there is a concentric structural-functional type of hypertensive heart, which is based on the development of concentric LVH and the concentric LV remodeling. Concentric LV hypertrophy was diagnosed in 86.2% of miners, concentric remodeling - in 12.3% of patients. In 1.5% of the miners in the main group, the eccentric type of hypertensive heart was recorded, which is based on the development of eccentric LVH. In the development of a concentric LVH, significantly larger values of the LVMWI were recorded, compared to those with an eccentric form. The formation of concentric hypertrophy and concentric remodeling in the miners of the main group is accompanied by the LV diastolic dysfunction. In 85.5% of the miners in the main group, the left ventricle DD was recorded. Formation of LVH in miners of underground occupations begins with high normal blood pressure.

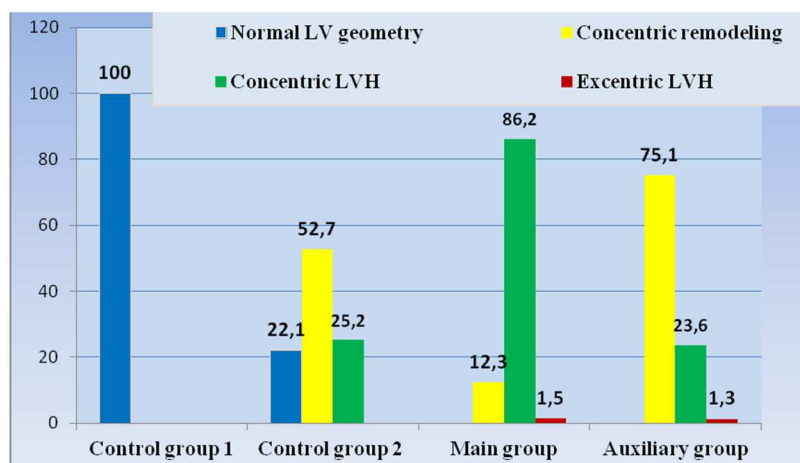


Fig. 1. Variants of the left ventricular geometry in the studied groups.

At the early stages of DD, disorders of diastolic relaxation and LV filling were recorded. The growth in the isometric relaxation phase duration (IRPD), the phase of slow LV filling (DT), the increase in the ratio of the slow LV filling phase to the phase of rapid LV filling (SFP/RFP), and the reduction in the RFP duration was considered as early signs of LVDD. The E/A ratio was <1 . In all cases, with the increase of left atrium (LA) end-diastolic size (EDS), the

LVMWI increase was recorded. Hyperfunction and dilatation of the left atrium against the background of LVH were recorded already at high normal blood pressure and at stage I of HD.

In healthy miners, the maximum LA EDS was 3.1cm. In patients with HH, LA EDS exceeded 3.2 cm and was highly correlated with ECG-criteria for the LA hypertrophy. The compensatory LA hyperfunction was evidenced by changes in the left atrium ejection fraction (LAEF). With an increase in the LA EDS up to 4.5 cm, a proportional increase in the ejection fraction exceeding 82% was registered in miners. With LA EDS growth up to 4.9 cm, the LAEF value decreased and amounted to $<82\%$.

The graduated exercise test was used for differential diagnosis of LVDD with its diastolic failure (DF). The delimitation criterion was the LAEF value in response to physical load. At stage I DD, LAEF was $>82\%$. At stage II DD, LAEF was $<82\%$. DF was diagnosed in cases when DD was accompanied by the heart failure clinical manifestations.

In 14.7% of the miners of the main group with stage II HD, the right ventricle hypertrophy develops, which is confirmed by the data of electrocardiography (predominance of the S-wave potentials in V5 and V6 branches). In 7.3% of patients with II stage HD, according to instrumental study methods, in response to the graduated exercise, signs of the right ventricle latent heart failure occurred.

Thus, hypertensive heart is a structural and functional impairment of all (right and left) heart organs with early development of diastolic dysfunction, diastolic heart failure with a preserved ejection fraction.

The study identified three stages of hypertensive heart. The first stage is characterized by the absence of heart failure clinical manifestations with significant physical load. LVH is registered with ECG. In the Echo-CG study, there was LV EDS up to 3.5 cm, concentric hypertrophy and concentric LV remodeling, the ratio of the LV slow filling phase to the fast filling phase of 3.0-3.5, the LAEF value of $> 82\%$.

At the second stage, clinical manifestations of diastolic dysfunction occur at significant physical load. In the Echo-CG study the concentric hypertrophy of the LV, LA EDS up to 4.0 cm are recorded. The compensatory possibilities of LA- LAEF are reduced $<82\%$. The ratio of the LV slow filling phase to the rapid filling phase was > 3.5 , the LAEF value was $> 82\%$. There were signs of diastolic dysfunction of the right ventricle: the ratio of the right ventricle slow filling phase to the rapid filling phase was > 3.35 .

The third stage is characterized by the presence of heart failure clinical manifestations, which occur at normal physical load. An electrocardiogram shows the P-mitral with signs of LV overload. In the Echo-CG study, the LVH is expressed (concentric or eccentric), the LA EDS is increased up to 4.5-5.0 cm. The value of the left atrial ejection fraction (LAEF) was $<82\%$, the ratio of the of slow filling phase to the fast filling phase (SFP/FFP) was > 3.5 cm. With LVEF values of $> 40\%$, the predominance of the LV diastolic heart failure was diagnosed, and with LV values of $<40\%$ the predominance of systolic heart failure was established.

The present study has expanded the views on heart remodeling in patients with arterial hypertension. The study on the features of hypertensive heart development permitted to distinguish clinical variants and structurally-functional types of hypertensive heart in miners of various professional groups. The compensatory possibilities of the left atrium in the formation of the left ventricle diastolic dysfunction have been determined. Structurally-functional status of the right ventricle in the development of hypertensive heart was studied. The criteria for diagnosing the left ventricle diastolic dysfunction, criteria for diagnosing the stages of hypertensive heart in miners have been developed.

The results of our study are confirmed by research data of the recent years and suggest that the risk of cardiovascular events is connected not with the blood pressure level, but with the severity of hypertensive heart manifestations and with its key indicator: the left ventricle myocardium mass (LVMM) [2, 5]. Other numerous clinical studies have shown that effective long-term antihypertensive treatment is accompanied by a reduction in LVMM and, as a result, a reduction of cardiovascular risk [4, 5]. However, no major study or meta-analysis has shown a reduction in risk due to the blood pressure lowering [9]. Consequently, hypertensive heart may be a structural and functional link between growing of the blood pressure and the growing risk of death and dangerous cardiovascular events.

The information, accumulated as of today, on the hypertensive heart formation requires further systematization and generalization.

Conclusions

1. The peculiarity of hypertensive heart in miners of underground professions is its development against the background of the physiological "working" LVH.

2. In underground miners, the following variants of LV remodeling are predominant: concentric left ventricular hypertrophy (86.2%) and concentric remodeling (12.3%).

3. In the early stages of the hypertensive heart development in miners, the left ventricle diastolic dysfunction is formed, which in later stages is transformed into diastolic heart failure with the subsequent attachment of systolic heart failure.

4. Early stages of HH formation are characterized by the left atrium hyperfunction with an increase in left ventricular ejection fraction, which compensates the left ventricle diastolic dysfunction.

5. In miners with HH, the right ventricle structural-functional status is impaired, which manifests itself as diastolic dysfunction.

Prospects for further research lie in the fact that the right heart compartments changes in miners of the underground occupations with arterial hypertension need further study.

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Реферати

**ОСОБЛИВОСТІ РОЗВИТКУ
ГІПЕРТЕНЗИВНОГО СЕРЦЯ У ГІРНИКІВ
З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ**
Шейко С.О., Колб Н.О.

Метою дослідження було вивчити клінічні і структурно-функціональні особливості ГС у гірників з АГ зі стажем роботи більше 10 років і розробити клініко-функціональні критерії його діагностики.

Обстежено 127 гірників підземних та 58 чоловіків поверхневих професій віком 35-55 років, зі стажем роботи в гірничих умовах понад 10 років, з нормальним високим артеріальним тиском (АТ), гіпертонічною хворобою І і ІІ стадії, які склали відповідно основну та допоміжну групу. 30 практично здорових чоловіків, які не працюють в шкідливих умовах, склали контрольну групу №1. 30 практично здорових гірників поверхневих професій склали контрольну групу №2. Проведено загально-клінічне обстеження хворих, електрокардіографію (ЕКГ), добове моніторування АТ. Структурно-функціональний стан серця вивчали за допомогою одно- і двомірної ехокардіографії (ЕХО-КГ) на апараті «PHILIPS-HDI 1500» за стандартною методикою. Вивчено типи геометрії лівого шлуночка (ЛШ) за критеріями Фреймінгама. Методологічний підхід до вивчення ваги ЛШ базувався на формулі Devereux (Pen Convention). Дані експертизи свідчать про переважаючий розвиток концентричного ремоделювання у здорових гірників, а у 25,2% - фізіологічна гіпертрофія лівого шлуночка (ЛШ). На відміну від патологічної ГЛШ, фізіологічна "робоча" ГЛШ не супроводжується формуванням діастолічної дисфункції ЛШ (ЛШДД). У 98,5% шахтарів відмічено концентричний структурно-функціональний тип гіпертонічного серця, заснований на розвитку концентричної ГЛШ та концентричної реконструкції ЛШ. У 14,7% шахтарів основної групи з ІІ стадії гіпертонічної хвороби (ГХ) розвивається гіпертрофія правого шлуночка.

Особливістю гіпертонічного серця у шахтарів підземних спеціальностей є його розвиток на тлі фізіологічної «робочої» ГЛШ. У гірників переважають такі типи реконструкції ЛШ: гіпертрофія концентричної лівого шлуночка (86,2%) та концентричне ремоделювання (12,3%). На ранніх стадіях гіпертонічного розвитку серця у гірників формується діастолічна дисфункція лівого желудочка, яка на більш

**ОСОБЕННОСТИ РАЗВИТИЯ ГИПЕРТЕНЗИВНОГО
СЕРДЦА У ГОРНЯКОВ С АРТЕРИАЛЬНОЙ
ГИПЕРТЕНЗИЕЙ**
Шейко С.А., Колб Н.А.

Целью исследования было изучить клинические и структурно-функциональные особенности ГС у горняков с АГ со стажем работы более 10 лет и разработать клинико-функциональные критерии его диагностики.

Обследованы 127 горняков подземных и 58 мужчин поверхностных профессий в возрасте 35-55 лет, со стажем работы в горных условиях более 10 лет, с нормальным высоким артериальным давлением (АД), гипертонической болезнью І и ІІ стадии, которые составили соответственно основную и вспомогательную группы. 30 практически здоровых мужчин, которые не работают во вредных условиях, составили контрольную группу №1. 30 практически здоровых горняков поверхностных профессий составили контрольную группу №2. Проведены: клиническое обследование больных, электрокардиография (ЭКГ), суточное мониторирование АД. Структурно-функциональное состояние сердца изучали с помощью одно- и двухмерной эхокардиографии (ЭХО-КГ) на аппарате «PHILIPS-HDI 1500» по стандартной методике. Изучены типы геометрии левого желудочка (ЛЖ) по критериям Фреймингама. Методологический подход к изучению веса ЛЖ базировался на формуле Devereux (Pen Convention). Данные экспертизы свидетельствуют о преобладающем развитии концентрического ремоделирования у здоровых горняков, а у 25,2% - физиологическая гипертрофия левого желудочка (ЛЖ). В отличие от патологической ГЛЖ, физиологическая «рабочая» ГЛЖ не сопровождается формированием диастолической дисфункции ЛЖ (ЛЖДД). У 98,5% шахтеров отмечено концентрический структурно-функциональный тип гипертонического сердца, основанный на развитии концентрической ГЛЖ и концентрической реконструкции ЛЖ. В 14,7% шахтеров основной группы со ІІ стадии гипертонической болезни (ГБ) развивается гипертрофия правого желудочка.

Особенностью гипертонического сердца у шахтеров подземных специальностей является его развитие на фоне физиологической «рабочей» ГЛЖ. У горняков преобладают следующие типы реконструкции ЛЖ: гипертрофия концентрическая левого желудочка (86,2%) и концентрическое ремоделирование (12,3%). На ранних стадиях развития гипертонического сердца у горняков формируется

пізніх стадіях перетворюється на діастолічну серцеву недостатність з наступним приєднанням систолічної серцевої недостатності. У шахтарів з гіпертонічним серцем структурно-функціональний статус правого шлуночка зазнає ранніх порушень, що виявляється за діастолічної дисфункції.

Ключові слова: артеріальна гіпертензія, гіпертензивне серце, ремоделювання лівого шлуночка.

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діастоліческая дисфункція левого желудочка, которая на более поздних стадиях превращается в диастолическую сердечную недостаточность с последующим присоединением систолической сердечной недостаточности. У шахтеров с гипертоническим сердцем структурно-функциональный статус правого желудочка испытывает ранние нарушения, проявляющиеся диастолической дисфункцией.

Ключевые слова: артериальная гипертензия, гипертензивное сердце, ремоделирование левого желудочка.

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PATHOGENETIC EFFECTS IN THE TREATMENT OF COMBINED CARDIORESPIRATORY PATHOLOGY

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Study of the possibility to correct endothelial dysfunction (ED), structural changes in peripheral arteries and synthesis of metabolic-waste products of nitric oxide (NO) (nitrites NO_2^- / nitrates NO_3^-) by means of including the combination of roflumilast and quercetin to the background therapy has been investigated. In 6 months, the use of complex therapy, in contrast to the background one, has resulted in a statistically significant increase of the initial rate by 18.76% from (0.61 ± 0.04) m/s to (0.75 ± 0.04) m/s ($t=2.47$; $p<0.05$) and in a statistically significant decrease of the initial diameter of a brachial artery to 3.74 ± 0.28 mm ($t=2.49$; $p<0.05$). Administration of complex therapy after 6 months has showed that the concentration of NO metabolites in the blood has gone up 1.3 times, up to 10.35 ± 1.89 $\mu\text{mole/l}$ ($t=1.00$; $p>0.1$) with the norm of 12.05 ± 2.11 $\mu\text{mole/l}$. Administration of complex therapy for patients with a severe stage of chronic obstructive pulmonary disease (COPD) in an exacerbation phase accompanied with a stable coronary artery disease and stable effort angina (SCAD SEA) of the 2nd FC helps restore endothelial function, improves peripheral arterial structural changes and has a stimulating effect on the synthesis of NO.

Key words: stable coronary artery disease, chronic obstructive pulmonary disease, endothelial dysfunction, oxidative stress.

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It is well-known nowadays, that oxidative stress is the most important pathogenetic factor of a wide range of disorders, including cardiovascular diseases, transient ischemic attack, COPD, diabetes mellitus etc. Moreover, it is oxidative stress that initiates the development and progression of mitochondrial diseases, bronchopulmonary dysplasia, atopy and many other conditions [1].

According to contemporary views, oxidative stress, regarded as an imbalance between the production and degradation of free oxygen forms, plays an important role in many physiological processes (tissue growth and maturation, cell differentiation, antineoplastic activity, natural cytotoxicity, immune response, repair) and basic pathological conditions such as blood clotting, inflammation, apoptosis etc. [7-8]. In addition, the main biological role of oxidative stress is renewal of cell membranes, membrane-associated receptors, enzymes, signaling molecules, ionic pumps [1] and accumulation of free radicals that lead to the oxidation of unsaturated fatty acids in cell membranes, proteins and DNA as well as the formation of polar permeable channels, which increases passive permeability of the membrane for Ca^{2+} ions, the excess of which is deposited in mitochondria, inducing its dysfunction [5].

As a result of this process, a deficiency of energy-rich products occurs, which is accompanied by the activation of peroxidation, which reflects different by severity damages of target organs through the process of ischemia/reperfusion, apoptosis/necrosis. It is assumed that oxidative stress significantly reduces the bioavailability of NO [10], which is responsible for adequate vasodilatation, both through a direct suppression of its products and by increasing the production of superoxide and peroxide anions [3]. The latter can react rapidly with NO and form a by-product peroxynitrite (ONOO⁻), which is modified to peroxynitric acid, which in its turn forms a hydroxyl radical (O⁻) [4]. This reaction forms the basis for the processes of lipid oxidation of vascular wall membranes and of blood corpuscles. Moreover, accumulation of endoperoxides in the endothelium due to mononuclear angiotensin 2 mediated activation leads to vascular remodeling; and the concomitant activation of the local renin-angiotensin system through the mobilization of cellular adhesion molecules determines the increasing anticoagulation potential [9].