UDC [616.12-005.4-07:616.24-002-052](1-17)

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# FORECASTING CORONARY EVENTS BASED ON THE ANALYSIS OF THE DYNAMICS OF MORPHOFUNCTIONAL PARAMETERS OF THE CARDIOVASCULAR SYSTEM IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE NORTH

## Abstract

Modern science has relatively recently identified chronic obstructive pulmonary disease (COPD) as an independent nosologic unit. COPD along with cardiovascular diseases (CVD) makes up the major group of the socially significant chronic diseases and is one of the most urgent medical and social issues in pulmonology.

The **objective of the study** was to determine the possibility of predicting and early diagnosis of ischemic heart disease in patients with chronic obstructive pulmonary disease living in the North on the basis of evaluation of morphofunctional parameters of the cardiovascular system.

**Materials and methods**. During the prospective five-year observation, an extended instrumental examination of 182 patients with chronic obstructive pulmonary disease was performed to identify the five-year dynamics of the morphofunctional parameters of the cardiorespiratory system at various levels of coronary risk taking into account gender differences. In 66 patients (mean age 64.0 ± 1.1 years) (comparison group), nonfatal coronary events were registered during the observation.

**The conclusion**. 1. In the North, cardiac remodeling in patients with chronic obstructive pulmonary disease includes changes in the right chambers due to persistent obstructive disorders and a decrease in pulmonary volumes, as well as an enlargement of left chambers, a decrease in myocardial contractility, and progressive left ventricular hypertrophy. 2. In the course of prophylaxis in case of outpatient examination of patients with chronic obstructive pulmonary disease, it is necessary to determine the criteria for predicting high and very high coronary risks according to the formula d = 0.000108 (Systematic Coronary Risk Evaluation × "Northern Experience" × frequency of exacerbations of chronic obstructive pulmonary disease × end-diastolic dimension of the left ventricle (mm) × systolic blood pressure in the pulmonary artery (mm)) for women and d = 0.000078 (Systematic Coronary Risk Evaluation × frequency of exacerbations of chronic obstructive pulmonary disease × end-diastolic dimension (mm) × expiratory reserve volume (%)) for men. A high and very high risk can be determined at d≥ 27.5 for women; and at d≥ 16.2 for men.

***Key words:*** *chronic obstructive pulmonary disease, coronary risk, ischemic heart disease, comorbidity.*

**For citation:** Dolgopolova D.A., Popova M.A., Terentyeva N.N. FORECASTING CORONARY EVENTS BASED ON THE ANALYSIS OF THE DYNAMICS OF MORPHOFUNCTIONAL PARAMETERS OF THE CARDIOVASCULAR SYSTEM IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE NORTH. The Russian Archives of Internal Medicine. 2018; 8(1): 36-44. [In Russian]. DOI: 10.20514/2226-6704-2018-8-1-36-44

**DOI:** 10.20514/2226-6704-2018-8-1-36-44

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SCORE — Systematic Coronary Risk Evaluation, BP — blood pressure, Ao — aortic diameter, IC — inspiratory capacity, VC — vital capacity of lungs, $PW_{LV}$ — posterior wall of the left ventricle, IHD — ischemic heart disease, PA — pulmonary artery, LV — left ventricle, IVS — interventricular septum, MEF — maximum expiratory flow, $FEV_1$ — forced expiratory volume in 1 second, PEF — peak expiratory flow, ERV — expiratory reserve volume, SPAP — systolic pulmonary arterial pressure, CVD — cardiovascular diseases, SV — stroke volume, $EF_{LV}$ — ejection fraction of the left ventricle, FVC — forced vital capacity of lungs, COPD — chronic obstructive pulmonary disease, ECG — electrocardiogram

## Introduction

Modern science has relatively recently identified chronic obstructive pulmonary disease (COPD) as an independent nosologic unit. COPD along with cardiovascular diseases (CVD) makes up the major group of the socially significant chronic diseases and is one of the most urgent medical and social issues in pulmonology [1, 2].

Currently, the problem of COPD and CVD comorbidity is becoming extremely relevant. It has been established that the main cause of lethality in patients with COPD is not only respiratory failure, but also CVD [3, 4, 5]. Patients suffering COPD are at 2 to 3 fold higher risk of cardiovascular mortality [6]. And this risk is 5 to 6-fold higher in the northern regions [7] and contributes approximately 50% of the total number of deaths [6]. Chronic obstructive pulmonary disease and ischemic heart disease (IHD) are considered to be mutually aggravating and often concomitant diseases: 62% of elder patients with COPD suffer IHD [8]. Based on the Systematic Coronary Risk Evaluation score (SCORE), every second patient (47.6%) is at very high coronary risk, a high coronary risk is observed in every eighth patient (12.7%) and a moderate risk is observed in 33.6% of patients among patients with COPD [9, 10]. Therefore, early diagnosis of IHD in COPD patients remains relevant. However, it is complicated due to similarity of the symptoms, low diagnostic value of routine electrocardiogram (ECG) examination, peculiarities of clinical signs when one disease leaves another in "the shadow" [11, 12]. It is considered relevant to search for more distinct CVD risk markers in patients with COPD. The detection of such risk at the early stage of CVD before the cardiovascular accident occurs shall be considered one of the issues of predictive diagnostics [13].

Current literature data are contradictory concerning myocardial remodeling in isolated COPD and insufficient concerning peculiarities of cardiovascular dysfunction development in case of cardiorespiratory impairment. They do not reflect issues of cardiorespiratory impairment relation with systemic inflammation and endothelial dysfunction; insufficiently cover data on clinical outcomes and early markers of cardiovascular accident development in patients suffering COPD. Thus, further studies are required.

**The objective of the study was** to identify the possibility of prediction and early diagnosis of IHD in patients with COPD in the North based on the evaluation of morphofunctional parameters of the cardiovascular system.

## Materials and Methods

In the course of a prospective five-year observation, an extended instrumental examination of 182 patients with COPD was performed in order to identify a five-year trend of morphofunctional parameters of the cardiorespiratory system at different levels of coronary risk while taking into consideration gender differences. During the period of observation, non-fatal coronary events (IHD) were registered in 66 patients (mean age (64.0 ± 1.1) years) (Table 1). Among 116 patients making up the main study group, we examined 20 females (mean age (55.4 ± 2.8) years) and 96 males (mean age (61.8 ± 1.0) years) ($p = 0.140$). In the control group of 66 patients the male to female ratio was 10:1: 60 males (mean age (64.0 ± 1.2) years) and 6 females (mean age (75.0 ± 0.9) years) ($p = 0.005$). Based on the five-year trend results of the cardiac remodeling in patients suffering isolated COPD and COPD registered at the time of IHD observation, we detected predictors of coronary events. Echocardliography and spirometry were performed at the beginning of the study and five years later.

An inclusion criterion was the presence of confirmed COPD (Global Initiative for Chronic Obstructive Lung Disease ((GOLD) 2014). Exclusion criteria

***Table 1.*** *Clinical characteristics of patients*

| Parameter | COPD n=116 | IHD + COPD n=66 | ρ-value | $\chi^2$ |
|---|---|---|---|---|
| Men | 96 | 60 | ρ=0,761 | $\chi^2$=0,092 |
| Women | 20 | 6 | ρ=0,271 | $\chi^2$=1,214 |
| Mean age, years | 60,7±1,00 | 64,0±1,18 | **ρ=0,040** | |
| Duration of COPD, years | 8,83±0,61 | 8,59±1,40 | ρ=0,857 | |
| «North» experience, years | 30,9±1,47 | 33,81±3,86 | ρ=0,407 | |

**Note:** the reliability of the differences by criterion $\chi^2$

were: IHD at the time of the beginning of the study, concomitant diseases of the respiratory system, cancer and hematologic diseases, end-stage kidney or liver failure, congestive heart failure of functional classes 3 and 4, and diabetes mellitus types 1 and 2. The study used data of patients' medical history. In all patients with COPD, complaints were assessed using the survey method, which makes it possible to identify the leading clinical syndromes, as well as the age, duration of COPD and smoking status. This information was obtained during history taking. The history of smoking was evaluated for each patient as a present or absent factor. Presence of this risk factor implied smoking at least one cigarette a day. The clinical examination included blood pressure (BP) assay as well as the evaluation of the degree of manifestation of major clinical syndromes of COPD and IHD by means of physical examination. General (complete blood count) and biochemical (total cholesterol, lipid profile) tests were performed. Instrumental examination methods included ECG, spirometry, echoCG, and plain X-ray of the chest. EchoCG parameters were obtained using Vivid 7 Pro ultrasound system (USA) in M- B- and Doppler modes using 3.5 mHz transducers following the standard procedure and taking into consideration the guidelines of the American Society of Echocardiography [14]. The standardized study included patients with satisfactory visualization of cardiac structures. We determined linear dimensions of the right atrium (RA, mm), right ventricle (RV, mm), left atrium (LA, mm), end diastolic dimension of the left ventricle ($EDD_{LV,}$ mm), end systolic dimension of the left ventricle ($ESD_{LV,}$ mm), end diastolic volume of the left ventricle ($EDV_{LV,}$ mm) and end systolic volume of the left ventricle ($ESV_{LV,}$ mm). Systolic and diastolic volumes were calculated using Simpson's method of discs.

The following systolic function parameters of the left ventricle were determined: stroke volume (SV, ml) and ejection fraction of the left ventricle ($EF_{LV}$, %). SV was calculated by blood flow velocity integral in the LV outflow tract. $EF_{LV}$ was calculated as a percentage ratio of $SV_{LV}$ to $EDV_{LV.}$ We determined the diameter of ascending aorta (Ao, mm) and diameter of the pulmonary artery (PA, mm), area of the aortic valve ($S_{AV,}$ $cm^2$), blood flow velocity at the aortic valve ($V_{AV,}$ $m•s^{-1}$), peak pressure gradient at the aortic valve ($P_{AV,}$ mm Hg), area of the mitral valve ($S_{MV,}$ $cm^2$), blood flow velocity at the mitral valve ($V_{MV,}$ $m•s^{-1}$), peak pressure gradient at the mitral valve ($P_{MV,}$ mm Hg), area of the tricuspid valve ($S_{TV,}$ $cm^2$), blood flow velocity at the tricuspid valve ($V_{TV,}$ $m•s^{-1}$), peak pressure gradient at the tricuspid valve ($P_{TV,}$ mm Hg), blood flow velocity at PA valve ($V_{PA,}$ $m•s^{-1}$), peak pressure gradient at PA valve ($P_{LA,}$ mm Hg), and systolic pressure in PA (SPAP, mm Hg). We measured thickness of the interventricular septum (IVS, mm), thickness of the left ventricle posterior wall ($PV_{LV,}$ mm).

We evaluated parameters of the respiratory function using spirometry and bronchial challenge test software of the Jager Master Lab diagnostic complex (Germany). The following parameters were measured: vital capacity of lungs (VC, l; %); forced VC (FVC, l; %); forced expiratory volume per 1st second ($FEV_{1,}$ l; %); Tiffeneau index ($FEV_1$/VC, %); maximum expiratory flow rate at level of 25%, 50% and 75% from the forced vital capacity of the lungs — $MEF_{25}$, $MEF_{50}$ and $MEF_{75}$ (l/s; %); inspiratory capacity (IC, l; %); expiratory reserve volume (ERV, l; %); peak expiratory flow rate (PEF, l/s; %) i.e. maximum air flow rate achieved in the process of expiration. Based on the guidelines of the European Respiratory Society, the obstruction degree and dynamics were evaluated based on $FEV_1$. During general clinical examination, all

the patients underwent X-ray of the chest in frontal view performed via Siemens Multix Pro system (Germany).

The obtained data were systematized using the Microsoft Excel 2007 spreadsheet package, and statistical calculations were made using the IBM SPSS Statistics 22 software package. Student's t-test was used to evaluate differences between the groups. The sampling was tested for normal data distribution using Kolmogorov-Smirnov's test. We used $c^2$ Pearson's *z*-test to analyze contingency tables. The differences were considered significant at $p < 0.05$. The contribution of the factors to the risk of coronary accident development was determined using multifactor analysis: a cluster analysis based on classification tree construction and K-means as well as a factor analysis of the principal components. We used a stepwise discriminant analysis to predict cardiovascular events. The grouping factor was $EDD_{LV.}$ In 82% of cases the grouped initial observations were classified correctly when predicting coronary risk for males. The same was true in 76% of cases for females.

## Results and Discussion

It is known that cardiovascular diseases are observed more frequently as the bronchial obstruction progresses. The cohort of the studied patients included patients with moderate bronchial obstruction (54%, n = 62, 95% CI 51.3 to 56.6% (study main group); 50%, n = 33, 95% CI 48.3 to 56.7% (control group) ($p > 0.05$)), whose number was 6-fold higher than the number of patients experiencing the extremely severe disease (8.6%, n = 10, 95% CI 6.9 to 10.5% (study main group); 7.3%, n = 5, 95% CI 4.2 to 9.4% (control group) ($p > 0.05$)) ($p < 0.001$). The smallest percentage of the patients had mild course of the disease (4.2%, n = 5, 95% CI 2.9 to 5.5%) (main group); 3.8%, n = 3, 95% CI 1.8 to 4.4%) (control group) ($p > 0.05$). Every third of the studied patient had severe disease (33.2%, n = 39, 95% CI 30.2 to 36.2% (study main group); 38.9%, n = 25, 95% CI 34.2 to 39.3% (control group)) ($p > 0.05$). Thus, the bronchial obstruction degree was comparable in the study groups (Table 2).

The rate of the systemic hypertension occurrence in the chronic pulmonary patients varies from 4.0 to 38.8% [4] and even increases two-fold in combination with IHD. Based on the results of the in-office measurements, every second COPD patient from the main group had an increase in BP correspondent to hypertension (n = 59, 51.2%). This parameter was comparable with the control group (n = 40, 60%) ($p > 0.05$), which is correspondent to general population level. Mean BP value was (128.7 ± 1.51) mm Hg in the main group and (132.72 ± 1.63) mm Hg in the control group ($p > 0.05$). Thus, the hypertension occurrence rate was the same in the main group and the control group.

Table 3 presents EchoCG parameters in groups of COPD patients and in groups of COPD patients with confirmed IHD at the study onset.

Differences are found in the values of the pressure gradient at AV ($p = 0.005$), blood flow rate and pressure gradient at MV ($p = 0.001$). These differences were significant in patients with confirmed

***Table 2.*** *Respiratory function parameters in patients with COPD and COPD + IHD diagnosed during the study (M±m)*

| Parameters | Patients with COPD n=116 | Patients with IHD and COPD n=66 |
|---|---|---|
| VC, l | 3.09 ± 0.11 | 2.89 ± 0.09 |
| VC, % | 81.82 ± 2.53 | 78.14 ± 2.86 |
| FVC, l | 2.83 ± 0.10 | 2.60 ± 0.09 |
| FVC, % | 76.09 ± 2.35 | 73.02 ± 2.93 |
| $FEV_1$, l | 2.21 ± 0.48 | 1.33 ± 0.08 |
| $FEV_1$, % | 50.79 ± 2.13 | 47.72 ± 2.76 |
| Tiffeneau index, % | 61.43 ± 1.73 | 58.60 ± 2.24 |
| $MEF_{25}$, l/s | 1.67 ± 0.66 | 0.31 ± 0.03 |
| $MEF_{25}$, % | 21.58 ± 1.78 | 22.90 ± 2.85 |
| $MEF_{50}$, l/s | 2.15 ± 0.76 | 0.75 ± 0.08 |
| $MEF_{50}$, % | 20.23 ± 1.66 | 18.08 ± 1.76 |
| $MEF_{75}$, l/s | 1.94 ± 0.18 | 1.62 ± 0.18 |
| $MEF_{75}$, % | 26.66 ± 1.97 | 23.43 ± 2.45 |
| IC, l | 4.76 ± 1.80 | 2.15 ± 0.09 |
| IC, % | 81.89 ± 3.63 | 80.15 ± 3.92 |
| ERV, l | 1.14 ± 0.16* | 0.73 ± 0.05 |
| ERV, % | 90.83 ± 4.98* | 74.08 ± 5.08 |
| PEF, l/s | 3.55 ± 0.21 | 3.44 ± 0.22 |
| PEF, % | 47.14 ± 2.46 | 44.86 ± 2.64 |

**Note:** * $p < 0.05$ — the reliability of differences between COPD and COPD and CHD

***Table 3.*** *EchoCG parameters in patients with COPD and COPD + IHD diagnosed during the study (the beginning of the study) (M ± m)*

| Parameters | Patients with COPD (the beginning of the study) n=116 | Patients with IHD and COPD (the beginning of the study) n=66 |
|---|---|---|
| Aorta, mm | 31.31 ± 1.13 | 30.66 ± 0.61 |
| $S_{AV,}$ $cm^2$ | 18.48 ± 0.98 | 18.13 ± 0.45 |
| $V_{AV,}$ $m•s^{-1}$ | 1.89 ± 0.39 | 1.46 ± 0.12 |
| ΔP, AV | 5.47 ± 0.46* | 10.28 ± 2.08 |
| RA, mm | 30.30 ± 1.17** | 36.00 ± 0.60 |
| RV, mm | 27.94 ± 0.75*** | 30.69 ± 0.98 |
| LA, mm | 29.81 ± 0.69** | 35.30 ± 0.70 |
| $EDD_{LV}$, mm | 43.54 ± 1.43** | 47.84 ± 0.83 |
| $ESD_{LV}$, mm | 28.92 ± 0.90 | 31.30 ± 0.80 |
| EDV, ml | 95.77 ± 5.56 | 99.16 ± 3.47 |
| ESV, ml | 34.55 ± 2.61 | 37.00 ± 1.97 |
| SV, ml | 58.12 ± 3.45 | 59.50 ± 3.24 |
| $PW_{LV}$, mm | 9.00± 0.37** | 10.69 ± 0.18 |
| IVS, mm | 9.36 ± 0.30* | 10.61 ± 0.20 |
| $EF_{LV,}$ % | 63.72 ± 1.05 | 61.50 ± 0.99 |
| $S_{MV,}$ $cm^2$ | 24.89 ± 0.97 | 27.40 ± 0.26 |
| ΔP, MV | 2.22 ± 0.24** | 3.46 ± 0.27 |
| $V_{Av}$ $m•s^{-1}$ | 0.74 ± 0.02** | 1.15 ± 0.12 |
| ΔP, TV | 1.36 ± 0.12 | 1.50 ± 0.12 |
| $V_{TV}$ $m•s^{-1}$ | 0.92 ± 0.12 | 0.85 ± 0.07 |
| $ρ_{PA,}$ mm Hg | 22.86 ± 1.77** | 38.75 ± 2.34 |
| $V_{PA}$ $m•s^{-1}$ | 0.94 ± 0.03 | 1.01 ± 0.03 |
| PA, mm | 21.90 ± 0.67 | 20.90 ± 0.42 |
| ΔP, PA | 3.81 ± 0.36 | 4.32 ± 0.31 |

**Note:** : * ρ<0,01; **ρ<0,001; ***ρ<0,05 — The reliability of the differences between COPD and COPD and IHD at the beginning of the study.

***Table 4.*** *EchoCG parameters in patients with COPD and COPD + IHD diagnosed during the study (the end of the study) (M ± m)*

| | Patients with COPD (the end of the study) n=116 | Patients with IHD and COPD (the end of the study) n=66 |
|---|---|---|
| Aorta, mm | 32.12 ± 1.17 | 32.27 ± 0.79 |
| $S_{AV,}$ $cm^2$ | 17.75 ± 0.85 | 17.40 ± 0.53 |
| $V_{AV,}$ $m•s^{-1}$ | 1.76 ± 0.33 | 1.55 ± 0.10 |
| ΔP, AV | 5.99 ± 0.67 | 9.90 ± 1.62 |
| RA, mm | 34.36 ± 0.78** | 36.92 ± 1.10 |
| RV, mm | 31.01 ± 0.78 | 32.61 ± 1.09 |
| LA, mm | 31.66 ± 0.60*** | 37.35 ± 0.78 |
| $EDD_{LV}$, mm | 47.74 ± 0.81 | 50.23 ± 1.47 |
| $ESD_{LV}$, mm | 32.21 ± 0.76** | 34.97 ± 1.08 |
| EDV, ml | 107.40 ± 4.47 | 118.41 ± 10.50 |
| ESV, ml | 42.36 ± 2.27 | 50.66 ± 5.19 |
| SV, ml | 65.61 ± 2.87 | 67.00 ± 7.56 |
| $PW_{LV}$, mm | 10.64 ± 0.29 | 10.78 ± 0.22 |
| IVS, mm | 11.02 ± 0.28 | 10.76 ± 0.26 |
| $EF_{LV,}$ % | 60.15 ± 0.91* | 56.61 ± 0.80 |
| $S_{MV,}$ $cm^2$ | 21.66 ± 1.50 | 24.38 ± 1.32 |
| ΔP, MV | 2.91 ± 0.29 | 3.13 ± 0.33 |
| $V_{Av}$ $m•s^{-1}$ | 0.78 ± 0.03* | 1.14 ± 0.15 |
| ΔP, TV | 1.52 ± 0.21 | 1.33 ± 0.08 |
| $V_{TV}$ $m•s^{-1}$ | 0.73 ± 0.04 | 0.81 ± 0.07 |
| $ρ_{PA,}$ mm Hg | 28.09 ± 2.14** | 35.12 ± 3.02 |
| $V_{PA}$ $m•s^{-1}$ | 0.96 ± 0.03 | 0.96 ± 0.02 |
| PA, mm | 23.44 ± 0.69 | 25.27 ± 1.08 |
| ΔP, PA | 4.14 ± 0.29 | 4.07 ± 0.27 |

**Note:** * ρ <0,01; ** ρ <0,05; *** ρ <0,001 — the reliability of differences between COPD and COPD and IHD at the end of the study.

IHD. They also showed significant differences in the linear dimensions of RA (ρ < 0.001) and RV (ρ = 0.028). Pulmonary hypertension was observed in patients with confirmed IHD (ρ < 0.001). Beside the increased linear dimensions of right chambers, the left heart was also remodeled, namely LA, which remodeling degree was significant in the control group (ρ < 0.001) as well as the thickness of $PW_{LV}$ and IVS (ρ = 0.001 and ρ = 0.004, respectively). After the five-year period of the observation, the pressure gradient at the aortic valve (ρ = 0.01), blood flow velocity at the mitral valve (ρ = 0.003), and RA (ρ = 0.050) and LA (ρ < 0.001) dimension values were higher in patients of the control group. The LV systolic function impairment progressed in all patients. $EF_{LV}$ value was lower in the group of patients with confirmed IHD (ρ = 0.009), and conversely SPAP values were higher (ρ = 0.050) (Table. 4).

Therefore, during the five-year period of observation, remodeling of right chambers was observed in COPD patients. These changes were conditioned by a natural increase of SPAP value as the result of persistent obstructive impairments and reduced lung volumes (ρ < 0.05), as well of cardiac dysfunction progress.

The process of cardiac remodeling in COPD also has an effect on the left heart, particularly on LV, and the literature has indicated this fact more frequently in recent years. At a particular stage of chronic cor pulmonale (CP) development in COPD patients, the process of cardiac remodeling naturally involves its left chambers, where changes imply diastolic dysfunction of LV, which is often restrictive, a confident increase in the LV sphericity index and systolic myocardial strain (MS) as well as a trend to increase in LV mass, index of LV EDV, index of LV ESV and sizes of LA. Patients with decompensated CP show not only more pronounced signs of LV remodeling as compared to the patients with the compensated CP, but also a decrease of its systolic function leading to additional loss of life quality and an increase in the risk of death. The major cause of structural and functional changes in the left chambers of the heart in CP patients is the restricted diastolic function of LV conditioned by interventricular interaction disorder, increased asynchronism in RV and LV interaction, and paradoxic motion of IVS [15].

An important feature of this study was also the detection of left chamber remodeling, and mainly LV hypertrophy development. We also noted a decrease of LV contractility, which did not reach the values of the systolic dysfunction in most cases ($p < 0.05$). In addition, the values of EDD did not increase during the period of observation. Thus, we can suppose presence of diastolic dysfunction (Figure 1), which, along with the progressing bronchial obstruction, causes the left chamber remodeling in examined patients.

Analysis of EchoCG parameters in the group of COPD patients according to the coronary risk degree showed more apparent changes of the main parameters when there was higher risk. Most of mean values of EchoCG were comparable in males and females (n = 116) among the COPD patients if no coronary event was observed. Nevertheless, it should be noted that we found the highest values of SPAP levels as well as LV eccentric hypertrophy in the group of COPD males at high coronary risk. Most of the females demonstrated normal LV model and concentric hypertrophy. The most apparent changes in EchoCG parameters were detected among the females with a moderate coronary risk. A rate of IHD occurrence determined on the basis of prospective observation of this group was comparable to high risk in males.

An analysis of EchoCG data in patients of control group demonstrated, along with right chambers remodeling, a significant increase of left chambers dimensions, decreased myocardial contractility, and more pronounced LV hypertrophy as compared to the cases of isolated COPD ($p < 0.05$). It should be noted that the dynamics of respiratory function parameters in these patients were less pronounced as compared to the patients with isolated COPD (Figure 2).

When predicting the risk of coronary accident development in COPD patients taking into consideration the results of the expanded instrumental

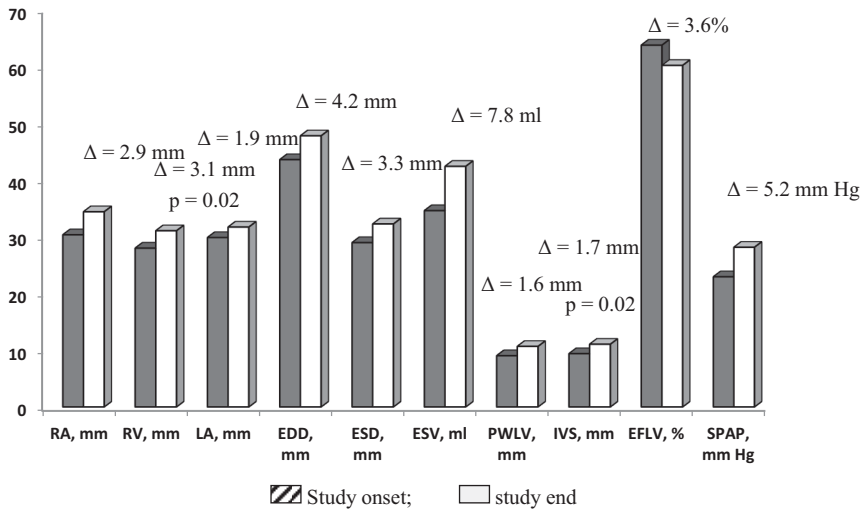


***Figure 1.*** *Dynamics of echocardiographic parameters in patients with COPD over a five-year period (n = 116)*

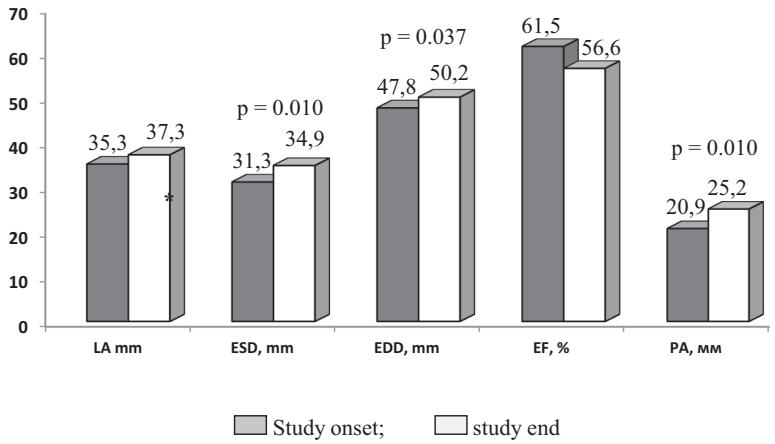


***Figure 2.*** *Dynamics of echocardiographic parameters in patients with COPD and IHD, over a five-year follow-up period (n = 66)*

examination (spirometry, echoCG), we can identify high and very high risk groups to provide primary prevention of cardiovascular disease.

The stepwise discriminant analysis used for predicting cardiovascular events in COPD patients shall consider medical history data (annual number of aggravation episodes requiring hospitalization, period of employment in northern regions), age, total cholesterol, systolic blood pressure and EchoCG data ($EDD_{LV}$, SPAP) and spirometry data (expiratory reserve volume, ERV). High and very high risk of a cardiovascular event requiring preventive care can be calculated for females using the formula:

**D = 0.000108 (SCORE × period of employment in the northern regions × × occurrence of COPD aggravation episodes × $EDD_{LV}$ (mm) × SPAP (mm)**

The high and very high risk may be determined at *D ≥ 27.5*.

It should be noted, that in case of males, the length of stay in the North is less critical then the annual rate of COPD aggravation episodes. A high or very high risk of cardiovascular event requiring preventive care can be calculated for males using the formula:

**D = 0.000078 (SCORE × occurrence of COPD aggravation episodes × × $EDD_{LV}$ (mm) × ERV (%)**

A high or very high risk may be determined at *D ≥ 16.2*.

Thus, predicting coronary risk while taking into consideration EchoCG data allows us to identify high and very high risk groups which require prevention of cardiovascular diseases with a set of medications affecting the myocardial remodeling process.

## Conclusion

The issue of the cardiorespiratory system remodeling in patients with COPD remains relevant. There are different points of view on cardiac remodeling in cases of isolated COPD. According to the classical understanding, in case of CP development, the right ventricle is remodeled following generally the same pattern as it happens with the left ventricle in case of IHD. Initially, in pulmonary hypertension, hypertrophy of the right ventricle develops, and then its cavity dilates. Some authors do not rule out that right ventricle dilatation develops long before the onset of RV heart failure [16], and RV hypertrophy is a very late and non-compulsory stage of its development [17]. Discussions of CP have not covered the state of left heart chambers over a long period of time. No clear understanding of these stages of CP development has been presented. However, the data from the latest studies do not exclude involvement of the left ventricle in the cardiac remodeling process in COPD patients [18]. Our study confirms CP development in COPD patients in the course of the disease progression: dimensions of the right ventricle increased somewhat earlier. The pulmonary artery remodeling

process and pulmonary hypertension development process reached the acceptance thresholds at the end of the five-year observation period. Beside the right chambers, the left ventricle was also involved in the remodeling process in our patients. LV hypertrophy development was observed [19].

At the same time, one of the typical cardiovascular complication in cases of COPD is increased pressure in the pulmonary artery system contributing CP development. There are data evidencing an increase in the percentage of patients with pulmonary hypertension and increased pulmonary vascular resistance among patients with COPD and IHD. In fact, pulmonary hypertension was observed in patients who developed comorbid IHD on the background of COPD, and this hypertension led to remodeling and an increase in pulmonary artery diameter ($p = 0.010$). Probably, the signs of cardiac remodeling that were not detected in time and the presence of pulmonary hypertension gave rise to IHD onset in these patients. Taking into consideration the progressing restrictive respiratory dysfunction, which is probably conditioned by a postcapillary pulmonary hypertension, and taking into consideration the remodeling of LV myocardium in COPD patients, the presence of "silent" LV dysfunction in COPD patients cannot be excluded.

In cases of concomitant IHD and COPD, cardiac remodeling is more complex and is manifested in hypertrophy and dilatation. Changes to the heart diastolic function are more pronounced, and pressure in the pulmonary artery system increases. These facts were confirmed by our study. It should be noted that diastolic function of the heart is impaired while the global diastolic function remains within the normal range. It has been established that when two diseases occur together, the rate of myocardial remodeling processes is higher. It is one more piece of evidence of the negative influence of COPD on the course of IHD in general, and particularly on myocardium [20].

However, there is an opinion that LV dysfunction in patients with CP can be explained by concomitant cardiovascular diseases (IHD, essential hypertension, etc.). In our study, we had observed comparable groups of COPD patients suffering from essential hypertension and of COPD patients developed IHD during the observation period. The available data obtained by a retrospective analysis of COPD patient post-mortem examination data demonstrate an aggravating comorbid background of COPD: in 85% of cases we observe essential hypertension with target organ lesions, in 64% of cases we observe significant coronary atherosclerosis, and in 19% of cases there was an ischemic stroke in the medical history. As the study results show, sclerotic changes of aorta and aortic valve were noted in patients who developed IHD during the observation period. These changes are manifestations of coronary atherosclerosis not detected at the outpatient stage of the examination. Based on the current literature, myocardial injury often remains undetected and, thus, we observe an underdiagnosis of IHD in COPD patients [21].

Furthermore, arterial hypoxemia has a particular influence on LV functional status, and this may be the one of the major causes of the vascular remodeling onset and the basis of cardiovascular changes. Our opinion is confirmed by the observation of some authors that LV remodeling in patients with COPD influences the development of restrictive LV diastolic dysfunction.

Therefore, cardiac remodeling in COPD patients in the North includes changes in right chambers of the heart as the result of persistent obstructive impairments and decreased lung volumes as well as a decrease of the myocardial contractility and progressing LV hypertrophy. During the preventive medical examination of COPD patients it is required to evaluate criteria predicting the high and very high risk of the coronary event using the formulas: $d = 0.000108$ *(SCORE × period of employment in the northern regions × occurrence of COPD aggravation episodes ×* $EDD_{LV}$ *(mm) × SPAP (mm) for females and* $d = 0.000078$ *(SCORE × occurrence of COPD aggravation episodes ×* $EDD_{LV}$ *(mm) × ERV (%)) for males*. A high and a very high risk may be determined at $d \geq 27.5$ for females, and at $d \geq 16.2$ for males.

## Conflict of interests

The authors declare no conflict of interests.

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Article received on 08.10.2017
Accepted for publication on 13.11.2017