

O.V. Kniazieva,  
V.A. Potabashnii\*,  
V.I. Fesenko

## REMODELING OF HEART IN PATIENTS WITH STABLE ISCHEMIC HEART DISEASE COMBINED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS A BASIS FOR DEVELOPMENT OF HEART FAILURE

Dnipro State Medical University

30-ty richchia Peremohy sq., 2, Kryvyi Rih, Dnipropetrovsk region, 50056, Ukraine

Дніпровський державний медичний університет

пл. 30-ти річчя Перемоги, 2, Кривий Ріг, Дніпропетровська область, 50056, Україна

\*e-mail: [kafterfpodma@i.ua](mailto:kafterfpodma@i.ua)

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**Key words:** ischemic heart disease, chronic obstructive pulmonary disease, echocardiography, comorbidity, heart failure

**Ключові слова:** ішемічна хвороба серця, хронічне обструктивне захворювання легень, ехокардіографія, коморбідність, серцева недостатність

**Ключевые слова:** ишемическая болезнь сердца, хроническое обструктивное заболевание легких, эхокардиография, коморбидность, сердечная недостаточность

**Abstract.** Remodeling of heart in patients with stable ischemic heart disease combined with chronic obstructive pulmonary disease as a basis for development of heart failure. Kniazieva O.V., Potabashnii V.A., Fesenko V.I. The aim of this study was to determine phenotypes of remodeling of heart and the status of systolic and diastolic function in patients with ischemic heart disease (IHD) combined with chronic obstructive pulmonary disease (COPD) with early symptoms and signs of heart failure (HF). We enrolled 108 males with stable IHD and spirometrically confirmed COPD which preceded the manifestations of IHD – the main group (group 1). As comparison groups 30 males with stable IHD (group 2) and 30 males with COPD (group 3) were examined. Control group included 30 males without IHD and respiratory diseases. All groups were comparable in age, groups 1 and 2 – in the duration of IHD, groups 1 and 3 – in the duration of COPD. The patients of the group 1 were divided into 3 subgroups: subgroup 1 – 45 patients with stable angina, subgroup 2 – 27 patients with postinfarction cardiosclerosis, subgroup 3 – 36 patients with combination of stable IHD and arterial hypertension (AH) without history of myocardial infarction. The patients of group 1 had different phenotypes of heart remodeling, which depended on the clinical forms of IHD, the presence of concomitant AH, the severity of bronchial obstruction. The patients of subgroup 1 in 60.0% cases had concentric remodeling and concentric left ventricular hypertrophy (LVH), in 26.7% – normal LV geometry, in all these cases ejection fraction (EF) was preserved. Only in 13.3% of cases eccentric LVH with mildly reduced EF was found. 59.3% of patients in subgroup 2 had eccentric LVH, left atrium dilatation and 55.6% had reduced EF. All patients of subgroup 3 had concentric direction of LV remodeling. The phenotypes of HF with reduced and mildly reduced EF were accompanied by impaired LV diastolic function. In assessing the likelihood of HF with preserved EF the HFA-PEFF score showed better accuracy. Pulmonary hypertension had a mixed cause with predominance of postcapillary component.

**Реферат.** Ремоделювання серця в пацієнтів зі стабільною ішемічною хворобою серця в поєднанні з хронічним обструктивним захворюванням легень як основа формування серцевої недостатності. Князева О.В., Потабашній В.А., Фесенко В.І. Мета дослідження – визначити фенотипи ремоделювання серця і стан систолічної та діастолічної функції в пацієнтів зі стабільною ішемічною хворобою серця (ІХС) в поєднанні з хронічним обструктивним захворюванням легень (ХОЗЛ) з ранніми проявами серцевої недостатності (СН). До дослідження включено 108 чоловіків зі стабільною ІХС та спірометрично підтвердженим ХОЗЛ, що передувало ІХС, - основна група (група 1). В якості груп порівняння обстежено 30 чоловіків зі стабільною ІХС (група 2) та 30 чоловіків з ХОЗЛ (група 3). Група контролю – 30 чоловіків без ІХС та хвороб органів дихання. Усі групи зіставні за віком, групи 1 та 2 – за тривалістю ІХС, групи 1 та 3 – за тривалістю ХОЗЛ. Пацієнти групи 1 розподілені на 3 підгрупи: підгрупа 1 – 45 пацієнтів зі стабільною

стенокардією напруги (ССН), підгрупа 2 – 27 пацієнтів з постінфарктним кардіосклерозом (ПІК), підгрупа 3 – 36 пацієнтів з поєднанням стабільної ІХС та артеріальної гіпертензії (АГ) без інфаркту міокарда в анамнезі. Виявлено, що пацієнти групи 1 мають різні фенотипи ремоделювання серця залежно від клінічної форми ІХС, наявності супутньої АГ, тяжкості бронхіальної обструкції. У пацієнтів підгрупи 1 у 60,0% випадків зареєстровано концентричне ремоделювання та концентричну гіпертрофію лівого шлуночка (ГЛШ), а в 26,7% – нормальну геометрію ЛШ, у всіх випадках фракція викиду (ФВ) була збереженою. Лише в 13,3% мала місце ексцентрична ГЛШ з помірно зниженою ФВ. У 59,3% пацієнтів підгрупи 2 встановлено ексцентричну ГЛШ, дилатацію лівого передсердя та в 55,6% знижену ФВ. У всіх пацієнтів підгрупи 3 мав місце концентричний напрям ремоделювання ЛШ. Фенотипи СН з низькою та помірно зниженою ФВ супроводжувалися порушенням діастолічної функції ЛШ. В оцінці ймовірності СН зі збереженою ФВ кращу точність продемонструвала шкала HFA-PEFF. Легенева гіпертензія мала змішане походження з переважанням посткапілярного компонента.

At a certain period of the cardiovascular continuum in patients with ischemic heart disease (IHD) chronic heart failure (HF) develops. The phenotypes of HF are divided by the left ventricular ejection fraction (EF) to HF with reduced EF (HF<sub>r</sub>EF), HF with mildly reduced EF (HF<sub>mr</sub>EF) and HF with preserved EF (HF<sub>p</sub>EF) [12,15]. Some studies demonstrated that right ventricular (RV) dysfunction and pulmonary hypertension (PH) are widespread in the cohort of patients with HF and associated with the worse prognosis [10]. Lung diseases have a significant impact on the development of HF<sub>p</sub>EF [15].

Among patients with HF, the prevalence of comorbid COPD reaches 32% [5]. Patients with mild to moderate COPD are 8-10 times more likely to die from cardiovascular disease than from respiratory failure, and the risk of cardiovascular mortality increases by 28% with each 10% reduction in the forced expiratory volume in 1 second (FEV1) [14]. The patients with COPD mainly have remodeling of the pulmonary vessels and heart with developing of precapillary PH and cor pulmonale [1]. Comorbid IHD is one of the causes of structural and functional disorders of the left ventricular (LV) and left atrium (LA). In recent years, the interest of researchers is focused on the problem of mechanisms of HF in patients with IHD combined with COPD [3, 5, 14]. However, there are few data about phenotypes of the whole heart remodeling in accordance with clinical forms of chronic IHD and COPD, which should determine the directions of therapy personification.

The aim of this study is to determine phenotypes of remodeling of heart and the status of systolic and diastolic function in patients with different forms of stable ischemic heart disease combined with chronic obstructive pulmonary disease and early symptoms and signs of heart failure.

#### MATERIALS AND METHODS OF RESEARCH

We conducted an initial examination of patients after 10-days wash-out period included in the

prospective study that was carried out in Kryvyi Rih City Clinical Hospital N 2 according to the principles of bioethics set out in the WMA Declaration of Helsinki – “Ethical principles for medical research involving human subjects”, the Convention on Human Rights and Biomedicine of the Council of Europe, Ukraine legislation.

Inclusion criteria were: stable IHD – stable effort angina functional classes (FC) II-III according to the Canadian Cardiovascular Society, anginal equivalents (dyspnea), myocardial infarction (MI) more than 6 months ago, HF stage I-IIA (stages B and C [12]) NYHA II-III FC; males aged  $\geq 40$  years, COPD, which is spirometrically confirmed before the manifestation of IHD.

Exclusion criteria were: stable effort angina FC IV, acute coronary syndrome, MI up to 6 months ago, postinfarction LV aneurysm, stroke up to 6 month ago, HF stage IIB-III (stage D [12]) NYHA IV FC, COPD not confirmed by spirometry, asthma, suspicion of pulmonary arterial hypertension, chronic kidney disease, anaemia, refusal of the patient to participate in the study.

The main group (group 1) consisted of 108 males with stable IHD combined with COPD aged 43 to 69 years, mean age 61.5 (58;67) years. As comparison groups there were examined 30 males with stable IHD, a mean age – 63.5 (59; 68) years (group 2) and 30 males with COPD, mean age – 60.5 (58; 64) years (group 3). Control group included 30 males without IHD and respiratory diseases mean aged 59.5 (57;63) years. All groups were comparable in age ( $p > 0.05$ ). Groups 1 and 2 are comparable in the duration of IHD – 6.5 (5;9) years and 6 (4;10) years respectively ( $p > 0.05$ ). Groups 1 and 3 are comparable in the duration of COPD – 9.5 (6; 11) and 8.5 (6; 10) years, respectively ( $p > 0.05$ ). Stable angina (SA) FC II was diagnosed in 70 patients (64.8%) of group 1, FC III – in 27 patients (25.0%). 11 patients (10.2%) after MI had silent IHD. In group 1 comorbid COPD of group B was

in 54 patients (50,0%), group C – 12 (11,1%), group D – 42 (38,9%).

Stable IHD was diagnosed according to order of the Ministry of Health of Ukraine dated March 2, 2016 N152 [4], taking into account 2019 European Society of Cardiology (ESC) Guidelines [13]. Verification and stratification of HF was performed based on ESC Guideline (2021) [15]. COPD was diagnosed according to Adapted evidence-based clinical guideline “Chronic obstructive pulmonary disease” of National Academy of Medical Sciences (2020) [1]. In the diagnosis of HF combined with COPD the recommendations of the Ukrainian Association of Cardiology (2020) were used [5]. The structural and functional status of the heart and LV remodeling phenotypes were determined using transthoracic echocardiography according to standard methods [8]. The studies were carried out on ESAOTE MyLabClassC using a 3.5 MHz mechanical sensor. LV and LA volumes were measured by Simpson's rule, and were indexed to body surface area calculated by Dubois formula. LV systolic function was determined by the level of EF. RV systolic function was determined by tricuspid annular plane systolic excursion in M-mode (TAPSE). LV mass in overweight and obese patients was indexed to height raised to 2.7 power. LV diastolic function was evaluated by continuous-wave and color Doppler with measurement of parameters of diastolic transmitral flow (peak E-wave velocity ( $V_{max} E$ ), peak A-wave velocity ( $V_{max} A$ ), E/A ratio). Tissue Doppler was used to determine early diastolic mitral annulus velocity septal and lateral ( $e'$ ), average E/ $e'$  ratio [9]. The systolic pulmonary artery pressure (SPAP) was calculated based on the tricuspid regurgitation (TR) velocity plus right atrial (RA) pressure, determined by the diameter and percentage of inferior vena cava collapse during the inspiration. To assess the possibility of contribution of the precapillary component of pulmonary hypertension, the TAPSE/SPAP ratio was calculated. Velocity measurements of airway patency (FEV1, Forced vital capacity (FVC), FEV1/FVC ratio) were determined by computer spirometry system “Pulmowind” “Sensor-systems” LTD.

According to the algorithm for the diagnosis of chronic HF [15], at the first step, clinical features with an emphasis on dyspnea were evaluated. Taking into account the presence of dyspnea due to airflow obstruction associated with COPD preceding IHD, and the possibility of cardiac origin of dyspnea, the level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) was determined by the

fluorescent immunoassay with the Finecare™ FIA System. All patients of group 1 had NT-proBNP levels exceed 125 pg/ml (261.5 (174.6; 326.2) pg/ml ( $p < 0.01$ )). In the comparison groups, the level of NT-proBNP corresponded to the reference values and only in certain cases reached the threshold (group 2 – 104.4 (89.4; 112.4) pg/ml, group 3 – 65.5 (58.9; 69.3) pg/ml, control – 53.9 (47.1; 56.7) pg/ml). Thus, all patients in group 1 had chronic HF according to universal definition of HF [12] stage B ( $n=79$ ; 73.1%) and stage C ( $n=29$ ; 26.9%).

The patients of group 1 were divided into 3 subgroups. Subgroup 1 – 45 patients with SA, subgroup 2 – 27 patients with postinfarction cardiosclerosis (PIC), subgroup 3 – 36 patients with combination of stable IHD and arterial hypertension (AH) without a history of MI.

Statistical analysis was performed with the licensed program STATISTICA 6.1 (StatSoftInc., serial No AGAR909E415822FA). The analysis of the normality of the data distribution was carried out according to the Kolmogorov-Smirnov and Shapiro-Wilk tests. The quantitative data were presented as median and its interquartile range (Me (25;75%)). The Kruskal-Wallis test was used for comparison multiple independent groups with Bonferroni correction for post-hoc test, Mann-Whitney test – for two independent groups. We used Spearman's rank correlation coefficient ( $r_s$ ) to assess the relationship between quantitative variables. The results were considered statistically significant at  $p < 0.05$  [2].

## RESULTS AND DISCUSSION

Different phenotypes of LV remodeling are observed in patients with stable IHD combined with COPD (Fig. 1). For patients with SA, concentric remodeling and concentric LV hypertrophy (LVH) was in 60.0%. Eccentric LVH was found in patients with PIC without concomitant AH, and concentric LVH was predominant in patients with PIC and AH.

In patients of subgroup 3 with SA in combination with AH, but without a history of MI, there was only a concentric direction of LV remodeling. In group 1, in general, all variants of EF were registered, but preserved EF prevailed (Fig. 2). In group 2, the vast majority of patients had preserved EF, in group 3 it was in all patients.

In the literature it is emphasized that patients with IHD on the background of lung diseases are characterized by HFpEF presence [15]. But our data indicate that patients with stable IHD combined with COPD have all phenotypes of chronic HF (Fig. 3). In patients of subgroup 1 preserved LVEF

dominated. In subgroup 2, 55.6% of patients had HFmrEF and HFrEF. And patients with PIC and concomitant AH had HFpEF. In patients of sub-

group 3 with stable IHD with concomitant AH, but without a history of MI HFpEF dominated, and only in 13.9% cases they had mildly reduced LVEF.

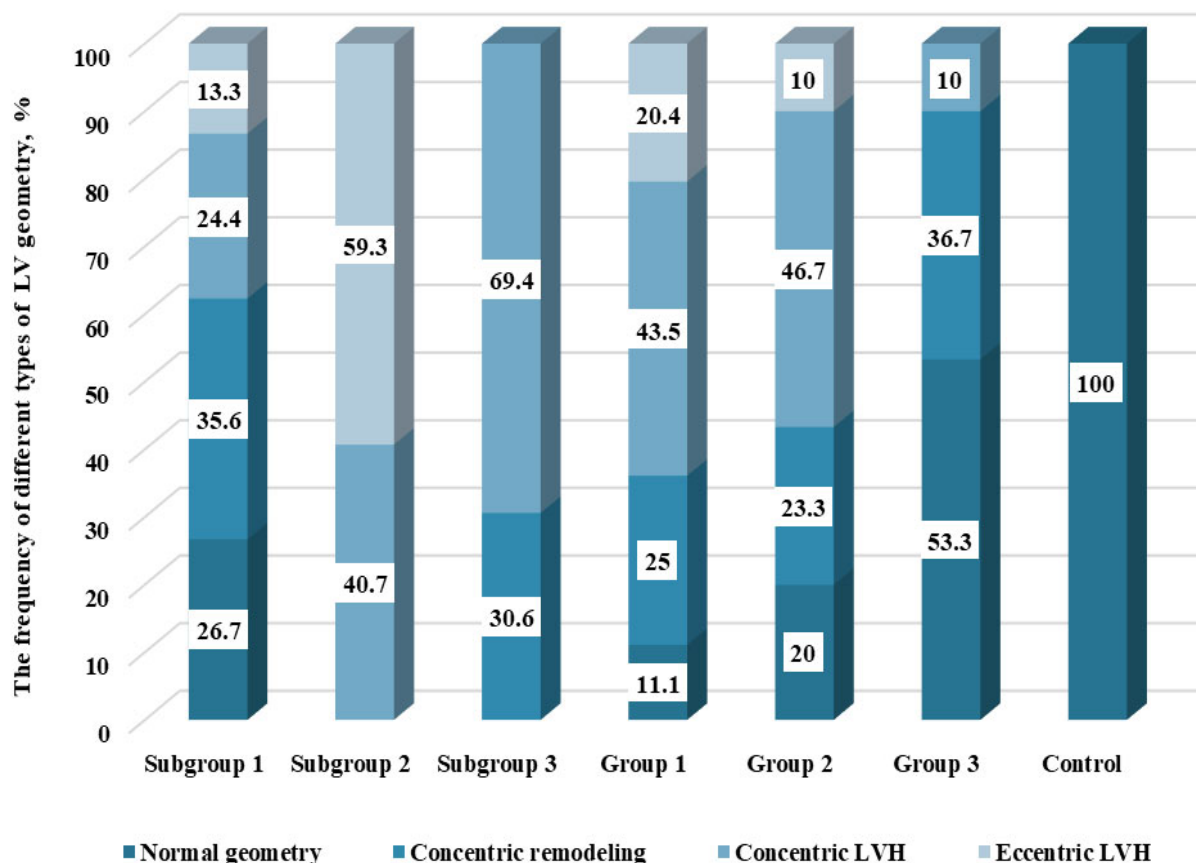


Fig. 1. Phenotypes of left ventricular remodeling in the examined patients

As it is shown in Table 1, in patients of group 1, the E/A ratio was significantly different comparing to group 3 and the control group, but did not differ from group 2. A similar direction of changes was observed relative to the maximum volume of LA (LAVI). In contrast, the parameters of diastolic mitral annulus velocity septal and lateral (e') were significantly lower in patients of group 1, not only compared with control, but also compared with groups 2 and 3. The ratio E/e' in group 1 was higher than in the control group, as well as in group 3, but did not differ from group 2. The level of TR velocity was the highest in group 1. Analysis of parameters of LV diastolic function in 26 patients with mildly reduced and reduced EF revealed that all these patients had LV diastolic dysfunction: grade I – in 6 cases (23.1%), grade II – in 18 cases (69.2%), grade III – in 2 cases (7.7%).

In order to diagnose HFpEF, we evaluated its probability by the HFA-PEFF score [7]. Among the 82 patients with stable IHD combined with COPD and preserved LVEF, 70 (85.4%) had a score  $\geq 5$  points, which allows to diagnose HFpEF, and 12 patients (14.6%) had 3-4 points (intermediate probability), but HF was confirmed by NT-proBNP test. Recent publications [6] have proposed the H2FPEF score as a probable sign of HFpEF. According to this score, only 9 (10.9%) of these 82 patients scored 6-9 points, indicating a high probability of HFpEF, 62 patients (75.7%) scored 2-5 points, indicating the necessity for additional examination, and 11 patients (13.4%) scored 0-1 points, which allows to exclude HFpEF. At the same time, among 70 patients in whom, according to the HFA-PEFF score, the probability of HFpEF was determined as high, it was confirmed by the H2FPEF score in 9 cases (12.8%),

in 54 cases (77.1%), the probability was determined as intermediate, and in 7 cases (10.1%) HFpEF should be excluded. Our data are similar to the

results of the study [11], but in this study the proportion of patients with IHD and COPD was limited.

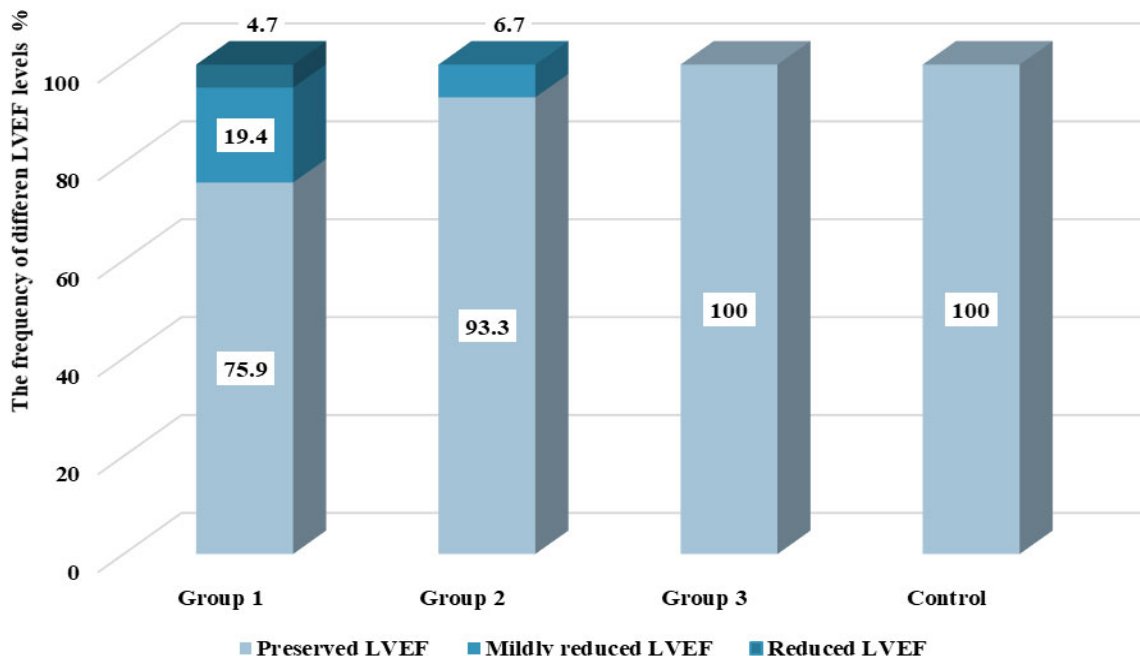


Fig. 2. Left ventricular systolic function in examined groups of patients

In our opinion, such discrepancies in assessing the likelihood by HFpEF by two scores in patients with stable IHD in combination with COPD may be explained by the fact that the H2FPEF score includes clinical variables (age, AH, atrial fibrillation, obesity) and only 2 echocardiographic findings – SPAP and E/e' ratio. Among 61 patients for whom

there were discrepancies in assessment, 59 (96.7%) had a sinus rhythm, concomitant AH – 29 cases (47.5%), and obesity – 27 cases (44.3%). The HFA-PEFF score, which considers structural, functional parameters and diagnostic biomarkers, were found to be more accurate in patients with stable IHD combined with COPD.

Table 1

The main parameters of left ventricular diastolic function

Parameter	Group 1 IHD+COPD (n=108)	Group 2 IHD (n=30)	Group 3 COPD (n=30)	Control group (n=30)	p
Vmax E, cm/s	72 (61;84.5)	70 (62;92)	84 (72;87)	76 (70;82)	0.09
Vmax A, cm/s	74.5 (65;83)^	83.2 (76;92)*	74.5 (62;86.1)^	71 (63;77)	<0.01
E/A	0.81 (0.68;0.90) <sup>†*</sup>	0.70 (0.60;1.00) <sup>†*</sup>	1.1 (0.82;1.4)^	1.1 (0.96;1.2)	<0.01
LAVI, ml/m <sup>2</sup>	35 (33;36) <sup>†*</sup>	34 (31;39) <sup>†*</sup>	27 (26;29)^	27.5 (26;30)	<0.01
Septal e', cm/s	5.3 (4.3;6.2) <sup>^†*</sup>	6.4 (5.4;7.3) <sup>†*</sup>	8.1 (7.4;9.6)^	8.0 (7.2;8.6)	<0.01
Lateral e', cm/s	7.2 (6.2;8.9) <sup>^†*</sup>	9.9 (8.2;10.6) <sup>†*</sup>	12.2 (10.9;13.2)^	12.4 (10.8;13.2)	<0.01
Average E/e'	8.3 (6.9;14.1) <sup>†*</sup>	8.25 (7.2;10.2) <sup>†*</sup>	7.0 (6.3;7.6)^	6.4 (5.7;7.5)	<0.01
TR velocity, m/s	2.7(2.4;2.9) <sup>^†*</sup>	2.35 (2.2;2.5)*	2.5 (2.4;2.6)*	2.2 (2.0;2.3)	<0.01

Notes: p – the level of statistical significance of differences between groups (according to Kruskal-Wallis test), ^ – significant difference with group 2, † – significant difference with group 3, \* – significant difference with control group.





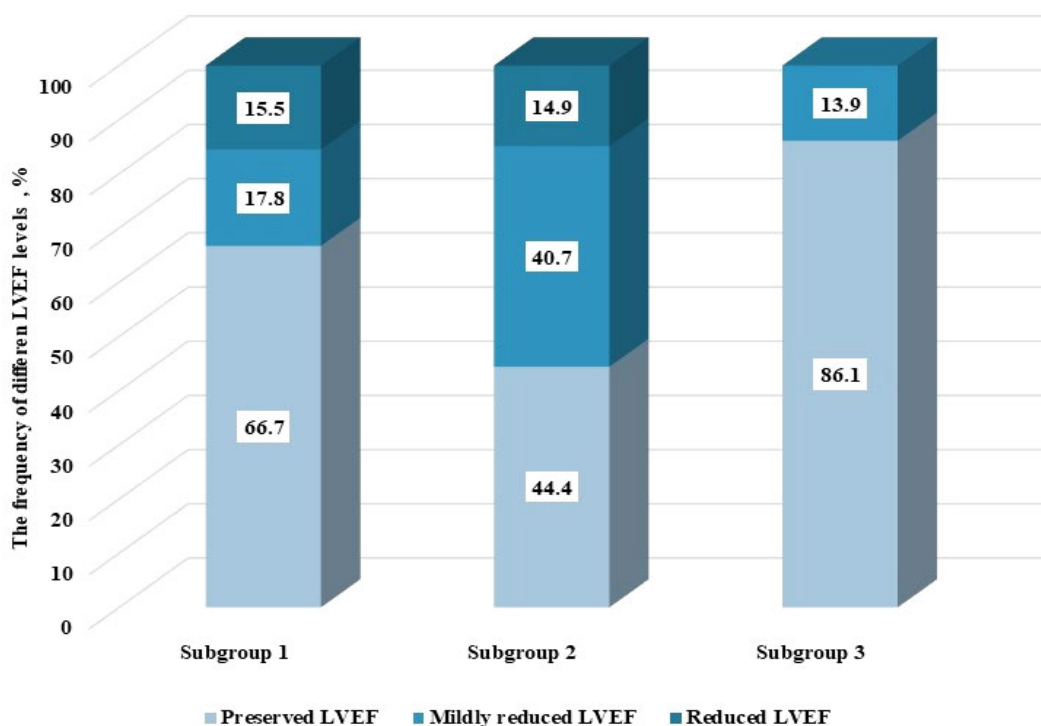


Fig. 3. Left ventricular systolic function in patients with different forms of IHD combined with COPD

In patients of group 1, the linear sizes of RA and RV, SPAP were significantly higher relative to group 2, and the RV systolic function was significantly lower compared to group 2, however TAPSE

was within reference values (Table 2). TAPSE/SPAP ratio was significantly lower in group 1 than in group 2. This data could be explained by higher level of postcapillar PH.

Table 2

Structural and functional parameters of the right ventricle

Parameter	Group 1 IHD+COPD (n=108)	Group 2 IHD (n=30)	Group 3 COPD (n=30)	Control group (n=30)	P
RA, cm <sup>2</sup>	16 (15;18,5) <sup>†*</sup>	14(13;15)	15 (14;16)*	13 (12;14)	<0.01
RV, mm	28 (25;31) <sup>^*</sup>	22 (20;25) <sup>†</sup>	26 (25;28) <sup>^*</sup>	21 (20;23)	<0.01
SPAP, mm Hg	35 (28;38) <sup>^†*</sup>	27,5 (25;31) <sup>†*</sup>	31 (29;32) <sup>^*</sup>	25 (24;26)	<0.01
TAPSE, mm	23 (21;23) <sup>^*</sup>	24 (24;25) <sup>†</sup>	22.5 (21;24) <sup>^*</sup>	25 (24;27)	<0.01
TAPSE/SPAP, mm/mm Hg	0.67 (0.58;0.82) <sup>^*</sup>	0.90 (0.77;1.03)*	0.73 (0.68;0.79)*	1.04 (0.96;1.13)	<0.01

Notes: – p - the level of statistical significance of differences between groups (according to Kruskal-Wallis test), ^ – significant difference with group 2, † – significant difference with group 3, \* – significant difference with control group.

According to the results of the assessment of structural and functional parameters of the right heart depending on the severity of airflow obstruction (Table 3), more severe course of COPD (GOLD III and IV) was associated with an increase of RV size, significantly higher SPAP (indirect correlation

between RV size and FEV1 ( $r_s = -0.23$ ;  $p < 0.05$ ), SPAP and FEV1 ( $r_s = -0.27$ ;  $p < 0.05$ ), direct correlation between SPAP and duration of COPD ( $r_s = 0.24$ ,  $p < 0.05$ ) and trend to decrease TAPSE/SPAP ratio, which indicates RV afterload. So, PH had mixed cause, but postcapillar component dominated.

**Structural and functional parameters of the right ventricle in patients with IHD combined with COPD depending on airflow obstruction**

Parameter	GOLD II (n=56)	GOLD III (n=36)	GOLD IV (n=16)	p
RA, cm <sup>2</sup>	15 (15;17)	17 (15;19.5)	16.5 (15.5;18.5)	0.34
RV, mm	27 (23;29) <sup>†</sup>	29 (27.5;31.5) <sup>^</sup>	29.5 (25;31.5)	0.01
SPAP, mm Hg	32 (26.5;36.5) <sup>†*</sup>	37 (30;39) <sup>^</sup>	37 (34;41) <sup>^</sup>	<0.01
TAPSE, mm	22 (21;23)	23 (21.5;23)	23 (21;24)	0.72
TAPSE/SPAP, mm/mm Hg	0.72 (0.58;0.87)	0.62 (0.54;0.77)	0.63(0.57;0.71)	0.06

Notes: p – the level of statistical significance of differences between groups (according to Kruskal-Wallis test), ^ – significant difference with GOLD II, † – significant difference with GOLD III, \* – significant difference with GOLD IV.

### CONCLUSIONS

1. Patients with stable IHD combined with COPD have different phenotypes of heart remodeling. The vast majority of patients with stable angina had concentric phenotype of left ventricular remodeling and normal geometry with preserved ejection fraction. In patients with postinfarction cardiosclerosis eccentric left ventricular hypertrophy and reduced systolic function dominated. All patients with combination of stable IHD and arterial hypertension had concentric direction of left ventricular remodeling with dominating preserved ejection fraction.

2. In patients with stable IHD combined with COPD and the phenotypes of heart failure with reduced and mildly reduced ejection fraction, functional changes are not limited to systolic dysfunction, but are also accompanied by left ventricular diastolic dysfunction.

3. In patients with stable IHD combined with COPD in the early stages of heart failure, the systolic function of right ventricle does not exceed the reference values, but in comparison with the control

group trends to decrease. Systolic pulmonary artery pressure in these patients was higher than in isolated IHD and COPD. However, pulmonary hypertension had mixed cause, but its postcapillar component dominated.

4. In assessing the likelihood of heart failure with preserved ejection fraction in patients with stable IHD combined with COPD, the HFA-PEFF score, which is based on heart remodeling parameters and diagnostic biomarkers showed better accuracy.

#### Contributors:

Kniazieva O.V. – investigation, writing – original draft;

Potabashnii V.A. – conceptualization, methodology;

Fesenko V.I. – investigation, writing – review & editing.

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### REFERENCES

1. [Adapted evidence-based clinical guideline “Chronic obstructive pulmonary disease”]. Kyiv: National Academy of Medical Sciences. 2020. p. 70. Ukrainian. Available from:

[http://www.ifp.kiev.ua/ftp1/metoddoc/nastanova\\_hozl\\_2020.pdf](http://www.ifp.kiev.ua/ftp1/metoddoc/nastanova_hozl_2020.pdf)

2. Antomonov MYu. [Mathematical processing and analysis of biomedical data]. 2nd ed. MITC “Medinform”; 2018. p. 579. Russian.

3. Potabashnii VA. [The phenotypes of chronic heart failure in patients with ischemic heart disease combined with chronic obstructive pulmonary disease]. *Medicni perspektivi*. 2018;23(3):161-71. Ukrainian. doi: [https://doi.org/10.26641/2307-0404.2018.3\(part1\).142364](https://doi.org/10.26641/2307-0404.2018.3(part1).142364)

4. [Order of the Ministry of Health of Ukraine dated March 2, 2016 No. 152 “On Approval and Implementation of Medical-Technological Documents for the Standardization of Medical Assistance in Stable Ischemic Heart Disease”]. Kyiv; 2016. Ukrainian. Available from: [https://www.dec.gov.ua/wp-content/uploads/2019/11/2016\\_152\\_ykpm\\_d\\_ihs.pdf](https://www.dec.gov.ua/wp-content/uploads/2019/11/2016_152_ykpm_d_ihs.pdf)

5. [Recommendations of the Ukrainian Association of Cardiology. Comorbidity in chronic heart failure. Chronic obstructive pulmonary disease in chronic heart failure]. *Sertseva nedostatnist. Klinichna praktyka*. 2020;2:45-53. Ukrainian. Available from: <https://www.researchgate.net/publication/346463261>

6. Reddy Y, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. *Circulation*. 2018;138:861-70. doi: <https://doi.org/10.1161/CIRCULATIONAHA.118.034646>
7. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association of the European Society of Cardiology. *Eur Heart J*. 2019;40:3297-317. doi: <https://doi.org/10.1093/eurheartj/ehz641>
8. Recommendations for cardiac chamber quantification by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1-39. doi: <https://doi.org/10.1016/j.echo.2014.10.003>
9. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2016;29:277-314. doi: <https://doi.org/10.1016/j.echo.2016.01.011>
10. Gorter TM, van Veldhuisen DJ, Bauersachs J, Borlaug BA, Celutkiene J, Coats AJS, et al. Right heart dysfunction and failure in heart failure with preserved ejection fraction: mechanisms and management. Position statement on behalf of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2018;20(1):16-37. doi: <https://doi.org/10.1002/ejhf.1029>
11. Sanders-van Wijk S, Aizpurua AB, Brunner-La Rocca HP, Henkens M, Weerts J, Knackstedt C, et al. The HFA-PEFF and H2FPEF scores largely disagree in classifying patients with suspected heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021;23(5):838-40. doi: <https://doi.org/10.1002/ejhf.2019>
12. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. *Eur J Heart Fail*. 2021;23:352-80. doi: <https://doi.org/10.1002/ejhf.2115>
13. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. 2020;41:407-77. doi: <https://doi.org/10.1093/eurheartj/ehz425>
14. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J*. 2021;00:1-111. doi: <https://doi.org/10.1093/eurheartj/ehab484>
15. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;00:1-128. doi: <https://doi.org/10.1093/eurheartj/ehab368>

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