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PROBLEMS OF DIAGNOSIS AND TREATMENT OF CHRONIC ISCHAEMIC HEART DISEASE COMBINED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ACCORDING TO RETROSPECTIVE ANALYSIS

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Ключові слова: *ішемічна хвороба серця, хронічне обструктивне захворювання легень, коморбідність, прихильність до лікування, шкала Моріскі-Гріна*

Ключевые слова: *ишемическая болезнь сердца, хроническая обструктивная болезнь легких, коморбидность, приверженность к лечению, шкала Мориски-Грина*

Abstract. Problems of diagnosis and treatment of chronic ischaemic heart disease combined with chronic obstructive pulmonary disease according to retrospective analysis. Potabashnii V.A., Kniazieva O.V., Markova O.Ya. Ischaemic Heart Disease (IHD) and Chronic Obstructive Pulmonary Disease (COPD) are common diseases that rank highest in the Global Burden of Disease Study (2019). IHD and COPD are often combined, making diagnosis and treatment of patients difficult in actual clinical practice. The aim of the study was to identify problems in the diagnosis and treatment of patients with a combination of chronic IHD and COPD, based on a retrospective analysis of medical records. Patient's adherence to treatment was also assessed with the Moriski-Green Scale (MMAS-8). The analysis of 108 inpatient charts with a combination of chronic IHD and COPD was carried out. The quality of diagnosis and treatment of IHD was evaluated in accordance with the order of the Ministry of Health of Ukraine N152 dated March 02 2016, considering the recommendations of the European Society of Cardiology (2019). It was found that smoking history was in 23.1% of patients, a body mass index (BMI) was calculated in 51.9%, and a carotid ultrasound examination was carried out in 7.4% of cases. The total cholesterol level was determined in 59.2% of patients, while the level of low-density lipoprotein cholesterol (LDL-C) was determined in only 43.5%. Transthoracic echocardiography (TTE) was performed in 62.9 % of patients, but stress-echocardiography and exercise ECG were not performed. Daily ECG monitoring was performed in 60.2% of cases. The levels of brain natriuretic peptide (BNP) or N-terminal proBNP (NT-proBNP) were not determined to precise etiology of dyspnea. It was also found that beta-blockers (29.6% of patients), ivabradine (11.1% of patients) and statins (65.7% of patients) are seldom administered to patients with IHD and COPD. The targeted doses of these drugs are not reached. Fixed combinations of long-term bronchodilators were insufficiently used in therapy of COPD. However, patients' adherence to basic IHD and COPD therapy is weak. 45.4 % of patients were non-adherent to treatment, 43.5% were medium-adherent, and only 11.1% of patients were adherent to treatment.

Реферат. Проблемы диагностики и лечения хронической ишемической болезни сердца в сочетании с хроническим обструктивным заболеванием легких по данным ретроспективного анализа. Потабашний В.А., Князева Е.В., Маркова Е.Я. Ишемическая болезнь сердца (ИБС) и хроническое обструктивное заболевание легких (ХОЗЛ) – распространенные заболевания, занимающие ведущие места в рейтинге Глобального бремени заболеваний (2019). ИБС и ХОЗЛ часто сочетаются, что создает трудности в диагностике и лечении пациентов в реальной клинической практике. Целью исследования было выявить проблемы в диагностике и лечении пациентов с сочетанием хронической ИБС с ХОЗЛ на основании ретроспективного анализа медицинской документации. Также была оценена приверженность пациентов к лечению на основании шкалы Мориски-Грина (MMAS-8). Проведен анализ медицинских карт стационарного больного 108 пациентов с сочетанием хронической ИБС и ХОЗЛ, находившихся на лечении в КП «Криворожская городская клиническая больница № 2» КМР. Было оценено качество диагностики и лечения ИБС в соответствии с приказом МЗ Украины № 152 от 02.03.2016 г., с учетом рекомендаций Европейского кардиологического общества 2019 года. Установлено, что анамнез курения собран у 23,1% пациентов, индекс массы тела (ИМТ) определен в 51,9%, ультразвуковое исследование сонных артерий проведено в 7,4% случаев. Уровень общего холестерина определен у 59,2% пациентов, а уровень холестерина липопротеидов низкой плотности (ХСЛПНП) – только у 43,5%. Трансторакальная эхокардиография (ЭхоКГ) выполнена у 62,9% пациентов, но ни в одном случае не проведена стресс-ЭхоКГ и тесты с дозированной физической нагрузкой. Суточное мониторирование ЭКГ выполнено в 60,2% случаев. Определение уровня мозгового натрийуретического пептида (BNP) или его предшественника (NT-proBNP) для уточнения генеза одышки не проводилось. Также выявлено, что пациентам с сочетанием ИБС и ХОЗЛ редко назначаются бета-адреноблокаторы (29,6% пациентов), ивабрадин (11,1% пациентов) и статины (65,7% пациентов). В базисной терапии ХОЗЛ недостаточно использовались фиксированные комбинации бронходилататоров длительного действия. При этом приверженность пациентов к базисной терапии ИБС и ХОЗЛ является недостаточной – неприверженными к лечению оказались 45,4% пациентов, частично приверженны – 43,5%, и только 11,1% пациентов были приверженны к лечению.

Ischemic heart disease (IHD) ranks first in the Global Burden of Disease (2019) ranking in people over 50, and chronic obstructive pulmonary disease (COPD) ranks 4th in people aged 50-74 and 3rd, place in people 75 years and older [14].

IHD is one of the most common diseases of the cardiovascular system, which affects almost 24% of the adult population of Ukraine, and its structure is dominated by chronic forms [8, 9]. Chronic (IHD) is

often combined with COPD, which is not a stochastic phenomenon, but is considered as a comorbidity primarily due to such common risk factors as smoking, age, systemic inflammation [4, 7, 16].

In some studies, emphasis is placed on the fact that patients with a combination of ischemic heart disease and COPD have a more severe course of the disease, poorer quality of life, increased risk of chronic heart failure (CHF) and death than patients

without COPD [3, 12, thirteen]. In 2019, experts from the European Society of Cardiology (ECT) [18] included shortness of breath as the equivalent of angina pectoris, which is a common symptom of COPD. This requires a careful differential diagnosis between cardiac and pulmonary dyspnea. There are difficulties in assessing ischemic changes in the myocardium according to electrocardiography (ECG) at rest and technical errors in the registration of transient thoracic echocardiography (EchoCG), which complicates the timely diagnosis of IHD [12]. Unfortunately, there are currently no international and national guidelines for the diagnosis and treatment of chronic IHD in combination with COPD. Even in the latest ECT guideline on chronic coronary syndromes (2019) there are no recommendations for the diagnosis and treatment of IHD on the background of COPD. On the other hand, the international guide GOLD (2020) [15] and the national guidelines for COPD (2020) [1] emphasize that there is a hypodiagnosis of IHD in combination with COPD.

In the treatment of patients with chronic IHD on the background of COPD there are a number of problems associated with polypragmatism, the need to take into account the interaction between prescribed drugs, quality of life and patient adherence to treatment [1, 3, 11]. The latest national guideline on COPD draws attention to the possibility of using β_1 -blockers in combination with IHD and warns against prescribing ultra-high doses of β_2 -agonists. To date, the effectiveness and safety of long-term use of inhaled cholinolytics of prolonged action in patients with COPD have been proven [6].

The effectiveness of therapy is largely determined by the patient's commitment to treatment. A systematic review of epidemiological studies on cardiovascular disease has shown that the level of adherence to treatment depends on numerous factors, including the complexity of treatment regimens, the number of drugs prescribed, which is associated with worse clinical consequences [10]. Therefore, the assessment of the patient's adherence to treatment is essential. One of the approaches for assessing adherence to treatment is the validated Moriski-Green scale (MMAS-8), which has a high level of sensitivity [5, 17].

The aim of the study was to identify problems in the diagnosis and treatment of patients with chronic IHD in combination with COPD in the inpatient care based on retrospective analysis and to assess patients' adherence to treatment.

MATERIALS AND METHODS OF RESEARCH

The study was conducted in the therapeutic departments of ME "Kryvyi Rih City Clinical Hos-

pital No. 2" Kryvyi Rih City Council, which is the clinical base of the Department of Therapy, Cardiology and Family Medicine FPE Dnipro State Medical University.

Inclusion criteria: chronic forms of IHD – angina pectoris II-III functional class, equivalents of angina (shortness of breath, arrhythmias); suffered myocardial infarction more than 6 months; heart failure I-IIA stage II-III functional class according to NYHA; men over the age of 40; COPD diagnosed (confirmed by spirometry) before the manifestation of IHD.

Exclusion criteria: angina pectoris functional class IV, acute coronary syndrome, myocardial infarction up to 6 months old; acute cerebrovascular accident (ACA) or transient ischemic attack (TIA) less than 6 months ago; heart failure stage IIB-III; diagnosis of COPD, not confirmed by spirometry; bronchial asthma; refusal of the patient to participate in the study.

For the purpose of retrospective analysis according to the inclusion criteria, medical cards of 108 inpatients with a combination of IHD and COPD, who were on inpatient examination and treatment during 2017-2020, were selected. Indications for hospitalization were substantiated by the provisions of the order of the Ministry of Health of Ukraine № 152 from 02.03.2016, which provides for the provision of medical care at the secondary and tertiary levels using complex methods of research and risk assessment and examination of performance, which can not be performed in an outpatient setting .

Quality of diagnosis and treatment of IHD was evaluated in accordance with the order of the Ministry of Health of Ukraine No. 152 from 02.03.2016 [8], taking into account the recommendations of the EAC 2019 [18]. Diagnosis and treatment of COPD were assessed in accordance with the Adapted Clinical Guidelines, based on the evidence of "Chronic obstructive pulmonary disease", approved by the NAMS of Ukraine in 2020 [1], taking into account the recommendations of GOLD 2020 [15]. Adherence to treatment was determined by a validated Moriski-Green scale (MMAS-8). 1 point was awarded for each answer "No", except for the question about taking all drugs for yesterday (1 point for the answer "Yes"). In the question with ranked answers, 1 point was awarded only for the answer "Never". Patients who scored 8 points were considered highly supportive, 6-7 points were considered moderately supportive, and those who scored less than 6 points were considered poorly supportive.

Statistical analysis of the results of the study was performed using the software product

STATISTICA 6.1 (StatSoftInc., Serial No. AGAR909E415822FA). The analysis of the normality of data distribution was performed according to the Shapiro-Wilk criterion. The results of descriptive statistics for the normal type of distribution of quantitative features are presented as the arithmetic mean (M) and the standard error of the arithmetic mean (m). When the distribution of quantitative traits other than normal was determined by the median and interquartile range (Me (25.0%; 75.0%)). The Mann-Whitney (U) test was used to compare two unrelated samples with an abnormal distribution. The significant level of statistical significance (p) was <0.05 [2].

RESULTS AND DISCUSSION

The mean age of patients with IHD in combination with COPD was 61.4±8.04 years, exclusively males. In all cases, IHD was diagnosed after a clinical manifestation of COPD, confirmed by spirometry. The average duration of IHD was 6.5 (5; 9) years, the average duration of COPD was 9.5 (6; 11) years (p<0.05). Stable angina pectoris (SAP) without a history of myocardial infarction was diagnosed in 81 (75.0%) patients, of which SAP of II functional class (FC) in 65 patients (80.2%), and SAP of III FC – in 16 patients (19.8%). Postinfarction cardiosclerosis occurred in 27 patients (25.0%). In 16 (59.3%) of them SAP was detected, which in 7 cases (43.8%) corresponded to SAP II FC and in 9 (56.2%) – SAP III FC. Concomitant hypertension was detected in 49 patients (45.4%). Chronic heart failure stage I according to the classification of MD Strazheska – V.Ch. Vasylenko was diagnosed in 79 patients (73.1%), stage IIA – in 29 patients (26.9%). In the analyzed data of medical cards of inpatients in no case the pretest probability of obstructive form of IHD was determined.

It was found that a history of smoking was collected in only 25 patients (23.1%), body mass index (BMI) was calculated in 51.9% of cases, and waist circumference was measured in 8.3%. A general blood test, blood glucose, blood pressure, and resting ECG were performed in all cases. Transthoracic echocardiography was performed in 68 patients (62.9%), but in no case stress echocardiography was performed. Ultrasound examination of the carotid arteries as a marker of coronary atherosclerosis was performed in only 8 patients (7.4%). Coronary angiography was performed in 6 (22.2%) patients after myocardial infarction, of which stenting – in 3.

The study of total cholesterol (TC) was performed in 64 patients (59.2%), and low-density lipoprotein cholesterol (LDL) – in only 43.5%.

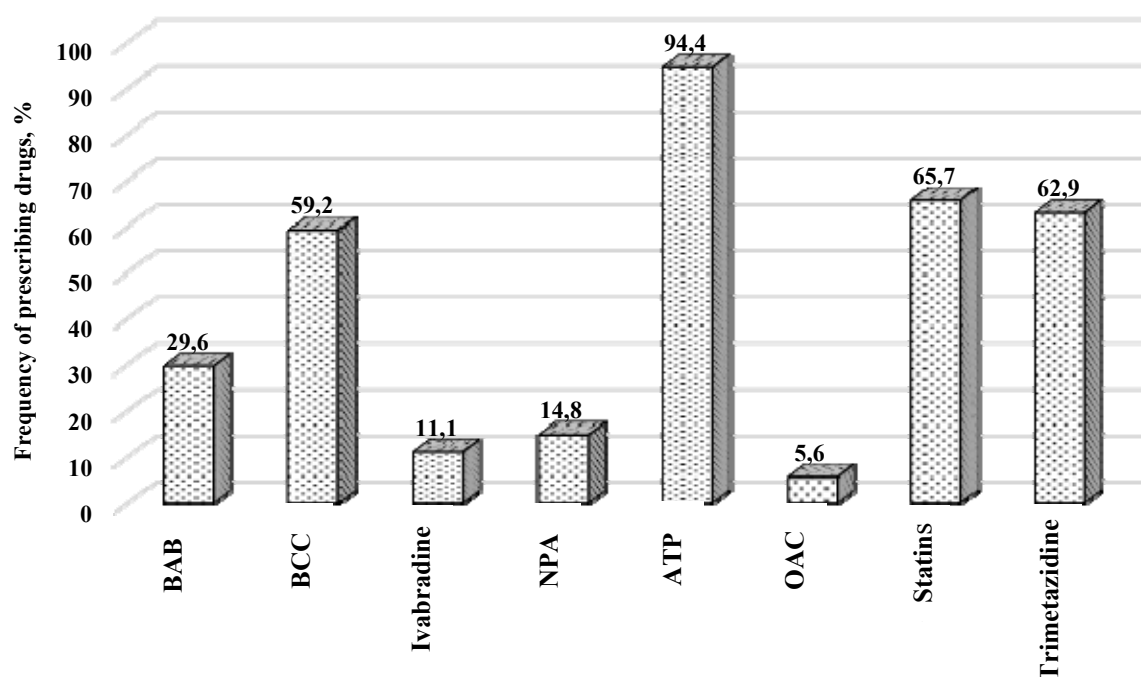
Creatinine levels were determined in 49.1% of cases. The level of brain natriuretic peptide (BNP) or its precursor (NT – proBNP) was not determined in any patient in order to clarify the genesis of dyspnea.

Tests with dosed physical activity (bicycle ergometry, treadmill test) were not performed at all, and the test with a 6-minute walk in combination with pulse oximetry to determine the level of desaturation was used in 7 (6.5%) cases. Daily ECG monitoring was performed in 65 patients (60.2%).

The general analysis of basic anti-ischemic therapy of IHD received by patients is shown in Figure 1. Beta-blockers (BAB) were prescribed to 32 patients (29.6%), of whom nebivolol (2.5-5 mg) was taken by 12 patients (37.5%), bisoprolol (2.5-5 mg) – 15 patients (46.9%), and 7 (15.6%) patients received non-selective BAB carvedilol (12.5-25 mg), which was considered undesirable on the background of COPD. Ivabradine (10-15 mg) was prescribed in 12 cases (11.1%). Among calcium channel blockers (BCC), 64 patients (59.2%) received amlodipine 5-10 mg. Nitrates of prolonged action (NPA) were taken by 16 patients (14.8%), and trimetazidine – 68 patients (62.9%). Antiplatelet drugs were received by 102 patients (94.4%), of which acetylsalicylic acid – 76 patients (74.5%), clopidogrel – 26 patients (25.5%). Oral anticoagulants (warfarin, rivaroxaban) were prescribed to 6 (5.6%) patients due to atrial fibrillation.

Out of 65 patients with SAP IIFC 19 (29.3%) received BAB, 45 (69.2%) – BCC, 4 (6.2%) – ivabradine and 25 (38.5%) – trimetazidine. Patients with SAP III FC in 6 (37.5%) cases out of 16 were prescribed BAB, in 10 (62.5%) – BCC, 4 (25.0%) patients were prescribed ivabradine, 7 (43.8%) patients – NPA. All patients in this group were prescribed trimetazidine. Of the 27 patients with postinfarction cardiosclerosis, including in combination with SAP, 7 (25.9%) were prescribed BAB, 9 (33.3%) – BCC, 4 (14.8%) – ivabradine, 9 (33.3%) – NPA and all patients – trimetazidine. Thus, among the drugs that improve the quality of life and have a positive effect on the prognosis in patients with chronic IHD, BAB in combination with COPD were prescribed in only 29.6% of cases.

Only 71 patients (65.7%) received statins (atorvastatin 20 mg, rosuvastatin 10 mg). At the same time, in no case at their long-term reception the target levels of cholesterol or LDL-C provided in the recommendations on dyslipidemia of the All-Ukrainian Association of Cardiologists (2020) are reached.



Notes: BAB – beta-adrenoblockers, BCC – calcium channel blockers, NPA – nitrates of prolonged action, ATP – antiplatelet drugs, OAC – oral anticoagulants.

Fig. 1. Basic anti-ischemic therapy of patients with IHD in combination with COPD (n=108)

Among 49 patients with concomitant arterial hypertension (AH), 28 patients (57.1%) received angiotensin-converting enzyme (ACE) inhibitors. Of these, enalapril (10-20 mg) was prescribed to 6 patients (21.4%), lisinopril (10 mg) – to 7 patients (25.0%), perindopril (5-10 mg) – to 5 patients, ramipril (2.5-10 mg) – 10 patients (35.7%). Angiotensin II Receptor Blockers (ARBs) were prescribed to 21 patients (42.9%), of which valsartan (80-160 mg) was administered to 14 patients (66.7%), and candesartan (4-16 mg) to 3 patients (14.3%), losartan (50-100 mg) – 4 patients (19.0%).

Mineralocorticoid receptor antagonist (MRA) spironolactone was taken by 32 patients (29.6%). Thiazide or thiazide-like diuretics (indapamide 1.25-2.5 mg, hydrochlorothiazide 12.5 mg) were given to 15 patients (13.9%) and loop diuretics (torasemide 5-10 mg) to 26 patients (24.1%).

The diagnosis of COPD was spirometrically confirmed in all cases at the stage of clinical diagnosis. In addition, all patients at the inpatient stage, whose medical records were analyzed, underwent spirometry. It was not possible to evaluate COPD clinical groups due to the lack of questionnaires on the COPD assessment test (AT) and

the Modified Respiratory Scale of the Medical Research Council (MRC).

Figure 2 presents an analysis of the basic therapy of COPD depending on the severity of bronchial obstruction in patients with chronic IHD. According to the results of postbronchodilation spirometry performed in the hospital, the 2nd degree of bronchial obstruction by GOLD was registered in 56 patients (51.8%), in whom the level of forced expiratory volume in the first second (FEV₁) was 62.4 (54.9; 68.4)% of the appropriate, the ratio of FEV₁/FJEL – 0.64 (0.60; 0.67). Of these 56 patients, 39 (69.6%) were prescribed long-acting β 2-agonist (LABA) formoterol, 10 patients (17.9%) – long-acting cholinolytics (LACL) tiotropium bromide, 7 patients (12.5%) – a combination of LABA salmeterol with inhaled corticosteroid (ICS) fluticasone propionate. In 36 patients (33.4%) the 3rd degree of bronchial obstruction was established, the level of FEV₁ – 40.5 (32.1; 46.1)% of the proper, FEV₁/FVEL – 0.55 (0.46; 0.60). Of these, 20 (55.6%) patients were prescribed LACL, 3 patients (8.3%) – a fixed combination of LACL and LABA (umeclidinium bromide + vilanterol), 8 (22.2%) patients – a combination of LABA and ICS, and 5 (13.9%)

patients with a combination of LACL, LABA and ICS. 16 patients (14.8%) were diagnosed with the 4th degree of bronchial obstruction by GOLD, the level of FEV1 in them was 27.7 (29.7; 22.9)% of normal, FEV1/FVEL – 0.48 (0.39; 0.63). 3 (18.7%) of them were prescribed a combination of LABA

and LACL, 13 (81.3%) – triple therapy with LACL, LABA and ICS. Among patients with grade 2 bronchial obstruction, 32 (57.1%) received basic therapy drugs irregularly, among 36 patients with grade 3 – 13 (36.1%), and among 16 patients with grade 4 – 4 (25.0%).

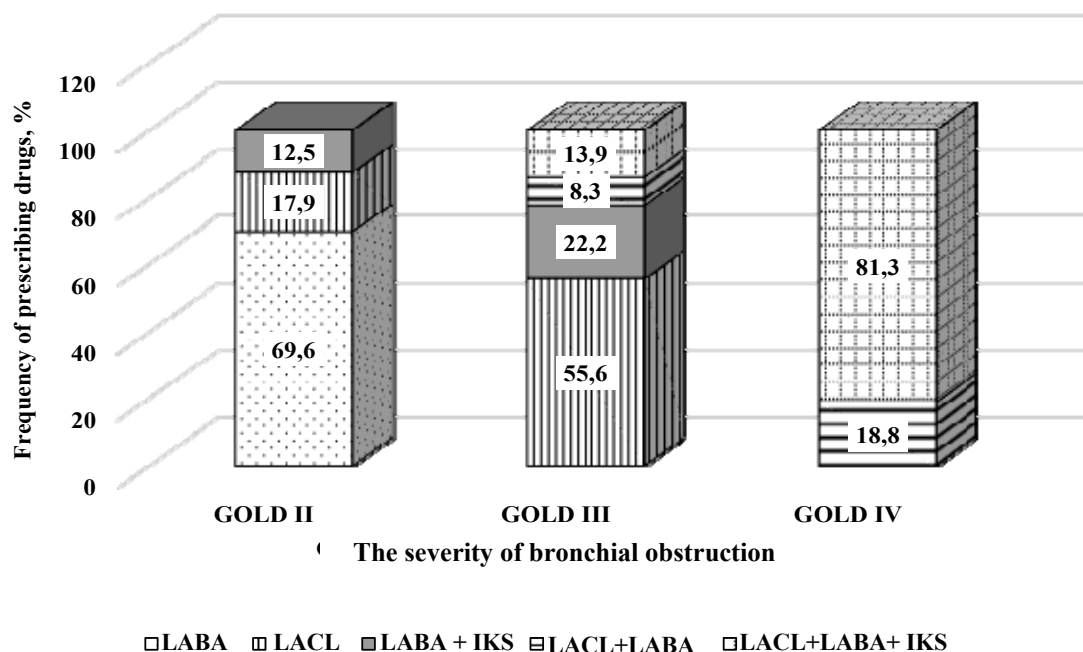


Fig. 2. Basic therapy of COPD in patients with a combination of IHD and COPD (n=108)

To relieve symptoms as needed, in 86 (79.6%) cases, patients received a combination of short-acting inhaled cholinolytic (SAIC) ipratropium bromide and β 2-agonist (SABA) fenoterol. In 22 (20.4%) cases, salbutamol was prescribed by the KGBA as needed.

In general, the average number of drugs prescribed to one patient was 6 (4; 9). Only 12 patients (11.1%) showed high adherence, 47 patients (43.5%) showed moderate adherence, and 49 patients (45.4%) were reluctant to treat.

CONCLUSIONS

1. Problems in the diagnosis of chronic coronary heart disease in combination with COPD are associated with the lack of determination of the test probability of obstructive coronary heart disease according to clinical data, insufficient use of echocardiography, Holter ECG monitoring, carotid ultrasound, determination of tolerance to exercise. changes in the coronary arteries according to coronary angiography and NT-proBNP to clarify the origin of shortness of breath.

2. In chronic coronary heart disease in patients with comorbid COPD, b-blockers, the alternative drug ivabradine in case of contraindications or insufficient dose of b-blockers, protocol drugs of metabolic action (trimetazidine and ranolazine), as well as statins are insufficiently prescribed.

3. In determining the clinical group of COPD in patients with chronic coronary heart disease, no questionnaire is used on the COPD assessment test and the Modified Respiratory Scale of the Medical Research Council (MDRC). In the basic therapy of stable COPD, fixed combinations of inhaled cholinolytics and long-acting B2 agonists prescribed by protocols are insufficiently prescribed, and inhaled corticosteroids without eosinophilia are additionally used in the treatment of severe COPD.

4. In real practice, patients with chronic coronary heart disease in combination with COPD have a low adherence to treatment, which requires the definition of quality of life parameters that prevent adherence to treatment.

Conflict of interest. The authors declare no conflict of interest.

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