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ARTERIAL HYPERTENSION WITH COMORBID CHRONIC OBSTRUCTIVE PULMONARY DISEASE: RELATIONSHIP BETWEEN OF TOLERANCE TO PHYSICAL EXERCISE AND STRUCTURAL AND FUNCTIONAL STATE OF THE HEART

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Abstract. Arterial hypertension with comorbid chronic obstructive pulmonary disease: relationship between tolerance to physical exercise and structural and functional state of the heart. Burtniak T.Z., Potabasniy V.A., Fesenko V.I. *The aim of the study was to establish the relationship between tolerance to exercise, oxygen saturation, and structural and functional cardiac status in patients with hypertension in combination with COPD. This study included 120 patients with primary arterial hypertension of stage I-II, grade 1, 2, and 3 in combination with COPD of grades 2 and 3 and clinical groups A, B, C, D, consisting group 1; group 2 – 30 patients with primary hypertension, and group 3 – 30 patients with COPD; group 4 – 30 practically healthy people representative by age and sex. Research methods included general clinical examination (collection of complaints, anamnestic data) and instrumental research methods: electrocardiography (ECG), echocardiography, measurement of ambulatory blood pressure (BP) profile (ABPM), spirometry, pulsoxymetry (SpO_2), 6-minutes walking test (6MWT). On examination of 120 patients with stage I-II, grade 1 hypertension was established in 19 (15.8%), grade 2 was in 83 (69.2%) and grade 3 was in 18 (15%) patients, respectively. COPD in clinical group A was diagnosed in 10 (8.3%), B – in 51 (42.5%), C – in 18 (15%) and D - in 41 (34.2%) patients, respectively. The most common was AH stage 2 with COPD in clinical group B – 35 (29.2%) cases and D – 31 (25.8%) cases. The 24-hour average systolic BP (SBP) in patients of the main group was 165 [144;178] mmHg, and the diastolic BP (DBP) was 103 [94;111] mmHg. The daytime average SBP was 160 [140;180] mmHg, and the DBP was 105 [93;117] mmHg accordingly. The night-time average SBP was 165 [155;175] mmHg, DBP – 100 [95;105] mmHg, heart rate (HR) – 83 [76;88] minutes, respiration rate (RR) – 21 [19;24] minutes. Decreases in index of chronotropic reserve (ICR) and the index of inotropic reserve (IIR) and load index indicate an increase in myocardial oxygen demand during exercise. There was an inverse correlation of IIR with SBP at rest ($r= –0.42$; $p<0.05$) and a direct correlation with age ($r=0.28$; $p<0.05$), which is significantly different from the control group. A direct correlation was found between the double product (DP) before and after exercise ($r=0.43$; $p<0.05$), which indicated an increase in consumption of oxygen by the myocardium. We found a direct correlation between left atrium (LA) and the ratio of expiratory volume per 1 sec (FEV_1) to the forced lung capacity (FEV) – FEV_1/FVC ($r=0.32$; $p<0.05$), which indicates the effect of the severity of bronchial obstruction on the level of left ventricular (LV) overload in patients with hypertension combined with COPD. The inverse correlation between thickness of the posterior wall of the LV (RVWT) and FEV_1/FVC ($r= -0.32$; $p<0.05$) indicates the contribution of disorders of bronchial patency and intrathoracic pressure with the level of BP to the development of concentric remodeling and LV hypertrophy. The inverse correlation between SV and COPD Assessment Test (CAT) ($r= -0.32$; $p<0.05$) indicates an additional effect of COPD clinical severity on central hemodynamics in patients with hypertension. This relationship between the ventilatory and hemodynamic parameters is confirmed by the inverse* *correlation of HR and FVC (r= –0.33; p<0.05)), left ventricular internal dimension (LVEDD) of LV and CAT (r= –0.24; p<0.05)), stroke volume (SV) and Modified British Medical Research Questionnaire (mMRC) (r= –0.42; p.00.05), CAT and pack years (r=0.33; p<0.05), inverse correlation between CAT and mMRC and FEV_1, FVC and FEV_1/FVC (r= -0.40;p<0.05 and r= -0.45; p<0.05), respectively. Linear regression analysis showed that changes in SV LV, LVEDD and SpO_2 were dependent predictors of patient's worsening state according to CAT (p<0.05). The direct correlation was established between the desaturation (ΔSpO_2) and ΔDP (r=0.48) and the inverse of ΔSBP (r= -0.29), 6MWT (r= -0.45), ICR (r= -0.34) and IIR (r= -0.29), which indicates a pronounced effect of hypoxemia on hemodynamics in patients with hypertension in combination with COPD. Comprehensive determination of cardiorespiratory reserve by 6-minute walk test, pulse oximetry and ambulatory blood pressure monitoring in patients with hypertension in combination with COPD makes it possible to establish disadaptation of the body to physical activity due to hypoxemia, decrease in the index of chrono- and inotropic reserves, which is an indication for administering appropriate therapy. In patients with hypertension combined with COPD, the degree of desaturation, stroke volume, end-diastolic parameters of the left ventricle, maximal size and volume of the left atrium, as well as remodeling of the left heart sections in the concentric direction can be considered as independent predictors of prognosis. The 6-minute walk test with desaturation can be used as an additional method of personalizing rehabilitation measures in patients with hypertension in combination with COPD.*

Реферат. Артеріальна гіпертензія з коморбідним хронічним обструктивним захворюванням легень: взаємний зв'язок між толерантністю до фізичного навантаження і структурно-функціональним станом серця. Буртняк Т.З., Потабашній В.А., Фесенко В.І. *Метою дослідження було встановити взаємозв'язок між толерантністю до фізичного навантаження, сатурацією крові киснем та структурно-функціональним станом серця у пацієнтів з артеріальною гіпертензією (АГ) у поєднанні з хронічним обструктивним захворюванням легень (ХОЗЛ). До дослідження включено 120 пацієнтів з АГ I-II стадії 1, 2 та 3 ступеня у поєднанні з ХОЗЛ 2 і 3 ступеня та клінічними групами A, B, C, D, які склали групу 1; група 2 – 30 пацієнтів з есенціальною АГ та група 3 – 30 пацієнтів з ХОЗЛ; 4 група – 30 практично здорових осіб, репрезентативних за віком та статтю. Методи дослідження включали загальноклінічне обстеження (збір скарг, анамнестичні дані) та інструментальні методи дослідження: електрокардіографію (ЕКГ), ехокардіографію (ЕхоКГ), офісне вимірювання артеріального тиску (АТ) та його добовий моніторинг (АМАТ), спірометрію, пульсоксиметрію (SpO2), тест 6-хвилинної ходьби (6-ХТзХ). Обстежено 120 осіб з АГ I-II стадії, АГ 1 ступеня встановлена в 19 (15,8%), 2 ступеня – у 83 (69,2%) і 3 ступеня – у 18 (15%) пацієнтів відповідно. ХОЗЛ клінічної групи А діагностована в 10 (8,3%), В – у 51 (42,5%), С – у 18 (15%) і D – у 41 (34,2%) пацієнта відповідно. Найбільш поширеними були АГ 2 ступеня з ХОЗЛ клінічної групи В – 35 (29,2%) випадків та D – 31 (25,8%) випадок. Середньодобовий систолічний АТ (САТ) у пацієнтів основної групи становив 165 [144;178] мм рт. ст., а діастолічний АТ (ДАТ) – 103 [94;111] мм рт. ст. Середньоденний САТ становив 160 [140;180] мм рт. ст., а ДАТ – 105 [93;117] мм рт. ст. відповідно. Середньонічний САТ – 165 [155;175] мм рт. ст., ДАТ – 100 [95;105] мм рт. ст., ЧСС 83 [76; 88] хв., ЧД 21 [19;24] хв. Зниження індексів хронотропного резерву (ІХР) та інотропного резерву (ІІР) та індексу навантаження свідчать про підвищення потреби міокарда в кисні при фізичному навантаженні. Наявна зворотня кореляція ІІР з САТ у спокої (r= –0,42; p<0,05) та пряма кореляція з віком (r=0,28; p<0,05), що достовірно відрізняється від показників контрольної групи. Виявлено пряму кореляцію між подвійним добутком (ПД) до і після навантаження (r=0,43; p<0,05), що вказує на зростання споживання міокардом кисню. Виявили пряму кореляцію між ЛП і ОФВ1/ФЖЄЛ (r=0,32; p<0,05), що може свідчити про вплив вираженості бронхіальної обструкції на рівень переднавантаження ЛШ у пацієнтів з АГ у поєднанні з ХОЗЛ. Зворотня кореляція між відносною товщиною стінки ЛШ (ВТСЛШ) і ОФВ1/ФЖЄЛ (r= –0,32; p<0,05) вказує на внесок порушень бронхіальної прохідності і внутрішньогрудного тиску з рівнем АТ, у розвиток концентричного ремоделювання і гіпертрофії ЛШ. Зворотня кореляція між ударним об'ємом (УО) і тестом оцінки ХОЗЛ (ТОХ) (r= –0,32; p<0,05) вказує на додатковий вплив клінічної тяжкості ХОЗЛ на центральну гемодинаміку в пацієнтів з АГ. Цей взаємозв'язок між вентиляційними та гемодинамічними параметрами підтверджується зворотньою кореляцією ЧСС і ФЖЄЛ (r= –0,33; p<0,05)), кінцево-діастолічним розміром (КДР) ЛШ і ТОХ (r= –0,24; p<0,05)), УО і модифікованою шкалою задишки (мМДР) (r= –0,42; p<0,05), ТОХ і тривалістю пачко-років (r=0,33; p<0,05), зворотньою кореляцією між ТОХ та мМДР та показниками ОФВ1, ФЖЄЛ та ОФВ1/ФЖЄЛ (r= –0,40; p<0,05 та r= –0,45; p<0,05) відповідно. Лінійний регресійний аналіз показав, що зміни УО ЛШ, КДР ЛШ та SpO_2 є незалежними предикторами погіршення стану пацієнта згідно з ТОХ (p<0,05). Пряма кореляція встановлена між десатурацією (ΔSpO_2) та ΔПД (r=0,48) та зворотня з ΔСАТ (r=-0,29), 6-ХТзХ (r=-0,45), ІХР (r=-0,34) та ІІР (r=-0,29), що свідчить про виражений вплив гіпоксемії на стан гемодинаміки в пацієнтів з АГ у поєднанні з ХОЗЛ. Комплексне визначення кардіореспіраторного резерву за тестом 6-хвилинної ходьби, пульсоксиметрією та амбулаторним добовим моніторуванням артеріального тиску в пацієнтів з АГ у поєднанні з ХОЗЛ дає можливість встановити дезадаптацію организму до фізичних навантажень за рахунок гіпоксемії, зменшення індексів хроно- та інотропного резервів, що є показанням для призначення відповідної терапії. У пацієнтів з АГ у поєднанні з ХОЗЛ рівень десатурації, ударний об'єм, кінцево-діастолічні параметри лівого шлуночка, максимальний розмір і об'єм лівого передсердя, а також ремоделювання лівих відділів серця у концентричному напрямку можуть розглядатися в якості незалежних предикторів прогнозу. Тест 6-хвилинної ходьби з визначенням десатурації можна використовувати як додатковий метод персоналізації реабілітаційних заходів у пацієнтів з АГ у поєднанні з ХОЗЛ.*

The modern trend in the development of internal medicine and family medicine clinics is the study of comorbid conditions. Comorbidity should be understood as a combination of several diseases, which includes the development of new pathogenetic mechanisms, the appearance of the clinical picture, complications and course, which is not characteristic of the underlying disease [12]. Among the comorbid conditions arterial hypertension (AH) and chronic obstructive pulmonary disease (COPD) occupy significant place in the practice of therapist and family doctor. Even a separate subspecialty – cardiopulmonology developed. The combination of cardiovascular and bronchopulmonary pathology in the general population leads to unfavorable prognosis and disability [14, 17]. COPD is diagnosed in every fourth patient with hypertension between the age of 25 and 64 years, so early diagnosis, treatment and rehabilitation of a patient with a combination of hypertension and COPD is required [1, 3, 4].

The use of ambulatory blood pressure monitoring (ABPM) allowed us to evaluate the variability of blood pressure (BP), the effectiveness of antihypertensive therapy and to determine the predictors of cardiovascular mortality. Disorder of the daily profile of BP in patients with hypertension in combination with COPD is characterized by the predominance of "non-dipper" and "night-peaker" types, which increases the risk of damage to target organs and adversely affect the prognosis [9]. A direct correlation was found between hypoxemia, the grade of BP elevation, sympathetic activity and a correlation between a decrease in FEV_1, desaturation, and variability in the BP night profile [4, 18]. However, the question of the relationship between exercise tolerance and hypoxemia in patients with hypertension combined with stable COPD remains unclear. The answer lies in the plane of study of the cardiovascular system as a whole.

It is believed that impaired structural and functional status of the heart in patients with hypertension in combination with COPD is associated with the development of left ventricular hypertrophy (LV), its systolic, diastolic dysfunction and subsequent involvement of the right ventricular, which creates the basis for cardiac insufficiency, as a key mechanism for reducing exercise tolerance [4, 15, 19]. It is believed that impaired structural and functional status of the heart in patients with hypertension in combination with COPD is associated with the development of left ventricular hypertrophy (LV), its systolic, diastolic dysfunction and subsequent involvement of the right ventricle, which creates the basis for the development of heart failure (HF) as a key mechanism for reducing exercise tolerance [4, 15, 19]. The COSYCONET study [17] demonstrated that one of five COPD patients had cardiovascular pathology. The relationship between the LV remodeling profile, the ejection fraction (EF) stage and the chronic HF phenotype (CHF) was established [7, 16].

The SCOTT study found that COPD patients had a more pronounced desaturation during physical activity due to hyperinflation, inadequate cardiac output, and increased peripheral oxygen extraction [11]. That is, the level of tolerance to physical activity, as a criterion of the general functional state, is determined as a whole by the cardiorespiratory system [2]. Therefore, in the combination of hypertension with COPD, it is important to identify the leading mechanism that limits the physical activity of the patient. Transient hypoxemia in patients with COPD associated with exercise, exacerbation, and increased bronchial obstruction at night adversely affect the cardiovascular system (CVS) [18].

The 6-minute walk test (6MWT) is the most affordable, low-cost method of study that does not require sophisticated equipment but correlates with maximal physical activity and oxygen absorption ($maxVO_2$) [2]. This test has a certain prognostic value and implies increased risk of hospitalization and mortality of patients with cardiovascular disease (CVD) [6].

The aim of the study is to establish the relationship between exercise tolerance, oxygen saturation, and structural and functional cardiac status in patients with hypertension in combination with COPD.

MATERIALS AND METHODS OF RESEARCH

The study included 120 patients with primary arterial hypertension of stage I-II, grade 1, 2, and 3 in combination with COPD of grades 2 and 3 and clinical groups A, B, C, D; group 2 – 30 patients with primary arterial hypertension of stage II grade 2, and group 3 – 30 patients with COPD of grade 2 and clinical groups – B 15 (50%) patients and D – 15 (50%) patients and 30 practically healthy age- and the sex- representative people. The mean age of the patients in the main group was 58±7 years. The duration of hypertension was on average 13 [8;19] years, and COPD – 12 [6;19] years. Among the smokers surveyed, 60 (50%) persons with a smoking period of 26 [15;40] pack-years were found. The study was carried out in the outpatient clinic No 2CPMSH No 4 in Kryvyi Rih.

Criteria for inclusion in the study: primary (essential) hypertension, COPD, voluntary consent to participate in the study according to the 2000 Helsinki Declaration.

Exclusion criteria are secondary AH, ischemic heart disease, heart failure above grade I according to the All-Ukrainian Association of Cardiologists (2017) and II Class according to New York Heart Association (NYHA), cerebral circulation disorders, chronic kidney disease, diabetes mellitus.

Research methods included general clinical examination (complaint collection, anamnestic data) and instrumental research methods: electrocardiography (ECG), echocardiography, measurement of ambulatory BP profile (ABPM), spirometry, pulsoxymetry (SpO_2), 6MWT. The stage and grade of hypertension were determined according to the recommendations of the European Society of Cardiologists (2018) and the Ukrainian Association of Cardiologists (2018) [4, 12]. ABPM was performed with the help of a portable monitor "Cardiotehnika-4000 AD". Daily average heart rate (HR), average heart rate before and after exercise, daily average SBP and DBP, daytime average systolic (SBP) and diastolic (DBP) BP, night-time average SBP and DBP were calculated. Threshold levels of office BP – ≥140/90 mmHg; day ABPM – ≥135/85 mmHg, night ABPM – ≥120/70 mmHg, daily blood pressure – ≥130/80 mmHg.

The structural and functional state of the heart was examined using Echocardiography by a standard technique. The studies were performed on a ZONAR Z.ONE PRO using a 3.5 MHz mechanical sensor. The thickness of the posterior wall of the LV (PWTD) and the interventricular septal (SWTD), left ventricular internal dimension, end-diastole (LVEDD) and index (LVEDVI), left ventricular internal dimension end-systolic (LVESD), left ventricular mass of the myocardium (LVM) (gram), left ventricular mass index (LVMI)(g/m^2), stroke volume (SV) were determined. The relative wall thickness (RVWT) was calculated (2×PWT)/LVEDD. Left ventricular mass (g):=0.8×1.04×[$(LVEDD+PWTD++SWTD)^3-LVEDD^3$]+0.6. The dimensions were established in accordance with the recommendations of the American Society of Echocardiography (ASE) and the European Echocardiography Association (EEA) [2].

To quantify the adaptive capacity of patients the double-product method (DP), or Robinson's index, DP reserve index DP= (HR×SBP)/100 were used. Chronotropic cardiac function was determined using the index of chronotropic reserve (ICR, %): ICR = (load HR - rest HR)×100%/rest HR. Expected maximum HR – (exp max HR, beats/min) = = (208-0.7×age). Expected CR – (exp CR) = = (exp max HR-HR)/HR. A chronotropic incompetence (CI) was established at a level of XP ≤62%. The state of inotropic cardiac function during physical activity was determined by calculating the index of inotropic reserve (IIR, %): IIR = (load SBP - rest SBP)×100%/rest SBP. For analysis, the average daily blood pressure and heart rate before and after loading according to the ABPM data were used.

External respiration function was determined by computer spirometry “Pulmowind” “Sensorsystems” LTD. The calculated expiratory volume per 1 sec (FEV_1), the forced lung capacity (FEV) and their ratio (FEV_1/FVC) were calculated. According to the Adapted Clinical Guideline 2019 and the GOLD 2019 Guideline, stratification of patients by COPD severity changed from an isolated assessment of the degree of bronchial obstruction by GOLD (FEV_1/FVC and FEV_1 index) to a polyparametric integral assessment of the degree of shortness of breath, cough, amount of sputum, exercise tolerance and risk of exacerbation or death of COPD. In accordance with these parameters, according to the GOLD 2019 guidelines, criteria for individual COPD clinical groups were developed [8, 15].

The Modified British Medical Research Questionnaire (mMRC) and the COPD Assessment Test (CAT) were used to assess patients' symptoms. Patients underwent standard pulse oximetry continuously while walking using a hand pulse oximeter, with desaturation criteria of SpO_2 <90% or ≥4%. Analysis and statistical processing of the material as performed using Excel (Microsoft Office 2016). Mathematical and statistical analysis of the results of the study was performed using the licensed program STATISTICA (version 10.0) using determination of mean values (M), standard deviation (SD), errors of mean value (m), (M±SD), and the interquartile range medians (Me [25-75%]). Univariate and stepwise multivariate logistic regression analysis was performed to determine the independent predictors of the combined endpoint. Significant differences were assumed to be $p<0.05$. All surveyed patients consented to the processing of personal data.

RESULTS AND DISCUSSION

On examination of patients with AH of stages I-II, grade 1 was established in 19 (15.8%), grade 2 – in 83 (69.2%) and grade 3 – in 18 (15%) patients, respectively. COPD in clinical group A was diagnosed in 10 (8.3%), B – in 51 (42.5%), C – in 18 (15%) and D – in 41 (34.2%) patients, respectively. The most common was grade 2 hypertension with COPD in clinical group B – 35 (29.2%) cases and D – 31 (25.8%) cases.

The 24-hour average SBP in patients of the main group was 165 [144;178] mmHg, and the DBP was 103 [94;111] mmHg. The daytime average SBP was

160 [140;180] mmHg, and the DBP was 105 [93;117] mmHg in accordance. The night-time average SBP is 165 [155;175] mmHg, DBP – 100 [95;105] mmHg, HR 83 [76;88] minutes, respiration rate (RR) 21 [19;24] minutes. Comparative clinical characteristics of the groups is shown in table 1.

Table 1

Clinical characteristics of patients

Parameters	Group 1 (n=120)	Group 2 (n=30)	Group 3 (n=30)	Control group (n=30)
Age, years	58±7	56±6	57±5	59±6
Sex, men/women (n)	55/15	19/11	20/10	22/8
Smoking duration, n	26 [15;40]	15 [9;20]	21 [7;31]	17[8;25]
Current smoker, n (%)	60 (50%)	18 (60%)	19 (63.3%)	16 (53.3%)
Duration of hypertension, years	13 [8;19]	5 [2;8]	-	-
Duration of COPD, years	12 [6;19]	-	7 [3;10]	-
Exacerbations with hypertension per year, (n)	2.2 [2;3]	2 [1;3]	-	-
Exacerbations with COPD per year, (n)	2 [1;3]	-	2 [1;2]	-
CAT, b.	20 [12;32]	-	19 [15;23]	-
mMRC, b.	3 [3;4]	-	2 [2;3]	-
FEV_1, %	48 [36;60]	92 [86;98]	50 [41;63]	90 [80;100]
FVC, %	58 [46;69]	96 [89;100]	66 [60;70]	95 [90;100]
FEV_1/FVC	0.57[0.49;0.65]	0.80 [0.75;0.85]	0.62 [0.53;0.69]	0.83 [0.77;0.90]
HR, min.	83 [76; 88]	76 [68;82]	79 [76;84]	72 [70;78]
RR, min.	21 [19;24]	15 [13;18]	18 [16;20]	16 [15;16]
24-hour average, mm Hg				
SBP	165 [144;178]	152 [140;164]	130 [115;129]	119 [110;125]*
DBP	103 [94;111]	95 [90;105]	81 [75;87]	80 [75;85]*
Daytime average, mm Hg				
SBP	160 [140;180]	159 [150;172]	128 [120;139]	125 [120;130]*
DBP	105 [93;117]	100 [90;110]	84 [80;89]	83 [75;89]*
Night-time average, mm Hg				
SBP	165 [155;175]	126 [121;132]	115 [110;120]	110 [105;115]*
DBP	100 [95;105]	79 [73;85]	65 [60;70]	60 [55;70]*

Note. *p<0.05

SBP at a rest was at 150 [140;160] mmHg. A direct correlation was found between SBP before exercise and HR after (r=0.30; p<0.05), reflecting a positive response to exercise. SBP after loading – 170 [160;180] mmHg. The increase was 15 [8;25] accordingly. When performing 6MWT, it was found that SpO_2 before loading in the main group was 94 [92;96]%, and in the control – 97 [96;97]%, the pulse respectively 80 [76;86]/min and 72 [70;77]/min SpO_2 after loading – 88 [85;91]% and 99 [96;101]%. HR – 105 [93;114]/min and 90 [86;95]/min. The inverse correlation between CAT and O_2 saturation to load was found (r= -0.28; p<0.05).

The resting DPs are 164 [91;250] and 126 [114;134], respectively. Post-load DPs were 193 [144;242] and 137.9 [130.2;142.5]. Increase in DP (IDP) is 45 [19;72]. Load index 0.39 [0.13;0.66] (Table 2). According to our study, a direct correlation was found between HR and DP before loading (r = 0.31; p<0.05) and HR and DP (r = 0.43; p<0.05) after loading, indicating a change DP is due to the difference of the HR, not the SBP. Studies have shown that desaturation has a significant inverse correlation with FEV_1, initial oxygen saturation, and a 6-minute walking distance, indicating a higher degree of airflow obstruction and lower SpO_2 tolerance at rest, which is confirmed by less time walking.

It was found that the ICR was 0.19 [0.14; 0.26], the inverse correlation between the HR before loading and the ICR (r= –0.47; p<0.05), ICR and LA (r= –0,24; p<0.05). ICR and RR (r=0.33; p<0.05). There is an inverse correlation of IIR with SBP at rest (r= –0.42; p<0.05) and a direct correlation with age (r=0.28; p<0.05), which is significantly different from the control group. Decreases in ICR and IIR and load index indicate an increase in myocardial oxygen demand during exercise. A low increase in IIR in group 1 – 0.08 [0.05;0.12] indicates a decrease in myocardial reserves and adaptive capacity of the functional coronary reserve of the organism, which exacerbates hypoxemia in patients with combined pathology of AH and COPD. CI is 0.56 [0.42;0.65], indicating a decrease in cardiac output due to tachycardia.

Table 2

Indicators of cardiorespiratory reserve in the main and control groups

Indicator	Group 1 (n=120)	Group 2 (n=30)	Group 3 (n=30)	Control group (n=30)
FEV_1, %	48 [36;60]	92 [86;98]	50 [41;63]	90 [80;100]
FEV_1/FVC	0.57 [0.49;0.68]	0.80 [0.75;0.85]	0.62 [0.53;0.70]	0.83 [0.77;0.90]
SpO_2 , % before physical activity	94 [92;96]	97 [96;98]	95 [94;96]	97 [96;97]
SpO_2 , % after physical activity	88 [85;91]	96 [94;97]	92 [90;95]	99 [96;101]
ΔSpO_2, %	-6 [-7;-5]	-1 [-2;1]	-3 [-4;-1]	2 [0;4]*
Δ PD	45 [19;72]	24 [20;28]	29 [22;34]	15.1 [0.75;18.9]*
Δ SBP	15 [8;25]	17 [10;19]	19 [18;20]	20 [15;20]*
6MWT, m	290 [250;340]	403 [384;415]	386 [361;400]	450 [390;510]*
Load index	0.32 [0.25;0.37]	0.35 [0.29;0.41]	0.38 [0.36;0.40]	0.40 [0.35;0.51]*
ICR, %	0.19 [0.14;0.27]	0.23 [0.18;0.27]	0.25 [0.21;0.29]	0.28 [0.25;0.35]*
IIR, %	0.08 [0.05;0.12]	0.09 [0.08;0.11]	0.1 [0.09;0.12]	0.14 [0.10;0.15]*

Note. *p<0.05

An indirect correlation was found between SpO_2 and HR (r=-0.31; p<0.05) between SpO_2 and RR (r=-0.36; p<0.05), between SpO_2 and the average DBP (r=0.62; p<0.05), between SpO_2 and the average daytime DBP (r =-0.52; p<0.05), SpO_2 and the average daytime DBP (r =-0.64, p<0.05), which is explained by the response of peripheral vascular resistance to exercise.

External respiratory function in patients with hypertension in combination with COPD was FEV_1 48 [36;60]%, FVC 58 [46;69]%, FEV_1/FVC 0.57 [0.49;0.68]. During Echocardiography (Table 3), a significant increase in LVEDVI, RVWT, EF LV compared to the control and comparison groups was found. Concentric LV hypertrophy was most pronounced when combined with hypertension and COPD and was found in 26 (21.6%) patients, concentric remodeling was found in 40 (33.3%) patients, eccentric hypertrophy in 11 (9.2%) patients. In group 2, concentric remodeling was established in 11 (36.6%) patients, concentric LV hypertrophy in 10 (33.3%) patients, and eccentric LV hypertrophy in 1 (3.3%) patients. In group 3, concentric remodeling was established in 5 (16.6%) patients. The severity of LV hypertrophy in combined pathology is significantly higher than in hypertension and COPD without comorbidity, which is caused by hypertrophy and dilation of the right ventricle. The peculiarities of changes in the geometry of the LV in the combined diseases depend on both the level of blood pressure and the hypertrophy of the LV and the severity of hypoxia [19].

We found a direct correlation between LA and the FEV_1/FVC (r=0.32; p<0.05), which indicates the effect of the severity of bronchial obstruction on the level of LV overload in patients with hypertension combined with COPD. The inverse correlation between RVWT and FEV_1/FVC (r=-0.32; p<0.05) indicates the contribution of disorders of bronchial patency and intrathoracic pressure with the level of BP to the development of concentric remodeling and LV hypertrophy. The inverse correlation between SV and CAT (r= –0.32; p<0.05) indicates an additional effect of COPD clinical severity on central hemodynamics in patients with hypertension. This relationship between the ventilatory and hemodynamic parameters is confirmed by the inverse correlation of HR and FVC (r= –0.33; p<0.05)), LVEDD of LV and CAT (r= –0.24; p<0.05)), SV and mMRC (r= –0.42; p.00.05), CAT and pack of years (r=0.33; p<0.05), inverse correlation between CAT and mMRC and FEV_1, FVC and FEV_1/FVC (r= –0.40; p<0.05 and r= –0.45; p<0.05), respectively.

Table 3

Structural and functional indicators of the heart according to Echocardiography

Indicator	Group 1 (n=120)	Group 2 (n=30)	Group 3 (n=30)	Control group (n=30)
LVEDD, sm	4.9 [4.5;5.1]	4.3 [4.2;4.4]	4.5 [4.4;4.6]	4.2 [4.1;4.3]*
LVEDDI, ml/m^2	2.3 [2;2.5]	1.9 [1.7;2.0]	2.1 [1.9;2.2]	1.7 [1.6;1.8]*
LVESD, sm	3.2 [3.0;3.6]	2.9 [2.8;3.0]	2.9 [2.8;3.1]	2.7 [2.6;2.8]*
LVEDVi, ml	136 [119;179]	94 [90;98]	99 [96;104]	87 [77;97]*
LVESVi, ml	60 [54;89]	38 [37;41]	42 [40;44]	37.5 [31;44]*
LVEDVI, ml/m^2	84 [79;97]	52 [50;56]	58 [50;67]	53 [50;55]*
RVWT, sm	0.49 [0.46;0.52]	0.39 [0.35;0.46]	0.35 [0.30;0.41]	0.34 [0.23;0.40]*
SV, mm	65 [60;69]	54 [51;57]	60 [57;62]	50.5 [46;55]*
E/A	0.8 [0.69;0.9]	0.9 [0.7;1.2]	1.0 [0.8;1.3]	1.6 [1.4;1.8]*
EFLV, %	58 [56;60]	60 [57;63]	61 [58;64]	67 [65;68]*
LVM, g	259 [196;301]	152 [134;170]	134 [122;153]	103 [93;113]*
LVMi , g/m^2	146 [115;180]	102 [87;118]	65 [53;79]	58 [48;73]*
Types of left ventricular geometry				
Concentric remodeling of the LV, n (%)	40 (33.3%)	5 (16.6%)	11 (36.6%)	-
Eccentric LV remodeling, n (%)	-	-	-	-
Concentric hypertrophy of the LV, n (%)	26 (21.6%)	10 (33.3%)	-	-
Eccentric LV hypertrophy, n (%)	11 (9.2%)	1 (3.3%)	-	-

Note. *p<0,05.

Assessment of cardiorespiratory reserve in patients with combined pathology revealed a relationship between impaired bronchial obstruction and indicators of cardiorespiratory reserve, namely, a direct correlation of FEV_1 with ΔSBP (r=0.32), 6MWT (r=0.44), ICR (r=0.25) and IIR (r=0.38). FEV_1/FVC with ΔSBP (r=0.27), 6MWT (r=0.35), ICR (r=0.32), and IIR (r=0.20).

The direct correlation was established between the desaturation (ΔSpO_2) and ΔDP (r=0.48) and the inverse of ΔSBP (r= -0.29), 6MWT (r= -0.45), ICR (r= -0.34) and IIR (r= -0.29), which indicates a pronounced effect of hypoxemia on hemodynamics in patients with hypertension in combination with COPD (Table 4).

Table 4

Correlation relationships of indicators of the main group

	FEV_1, %	FEV1/ FVC	ΔSpO_2, %	Δ PD	Δ SBP	6-MWT, m	ICR, %	IIR, %
FEV_1, %	-	0.56	-0.55	-0.26	0.32	0.44	0.25	0.38
FEV1/FVC	0.56	-	-0.41	-0.20	0.27	0.35	0.32	0.20
ΔSpO_2, %	-0.55	-0.41	-	0.48	-0.29	-0.45	-0.34	-0.29
Δ PD	-0.26	-0.20	0.48	-	0.52	-0.36	-0.46	-0.31
Δ SBP	0.32	0.27	-0.29	0.52	-	-0.30	0.33	0.45
6-MWT, m	0.44	0.35	-0.45	-0.36	-0.30	-	0.35	0.47
ICR, %	0.25	0.32	-0.34	-0.46	0.33	0.35	-	0.30
IIR, %	0.38	0.20	-0.29	-0.31	0.45	0.47	0.30	-

Linear regression analysis showed that changes in SVLV, LVEDD, and SpO_2 were dependent predictors of patient's state worsening according to CAT ($p<0.05$) (Table 5).

The inverse correlation between IP before and after loading and the size of the right atrium (r= -0.26; p<0.05 and respectively r= -0.27; p<0.05), PD and SWTD (r= -0,30; p<0.05), between the increase in DP and PWTD (r= -0.29; p<0.05), the increase in DP and LVESD (r= -0.24; p<0.05), which indicates the systolic ability of the myocardium to respond to exercise in hypoxemia in patients with hypertension in combination with COPD.

Table 5

Results of multivariate analysis of CAT and load index in patients with hypertension combined with COPD

	CAT			LOAD INDEX	
	SV	LVEDD	SpO_2	LVESD	LVEDD
β	-0.28	-0.264781	-0.292091	0.345957	0.326191
Stand.error β	0.11	0.112864	0.111937	0.118208	0.119097
B	-0.30974	-0.17034	-0.07171	15.27918	14.68884
Stand.error	0.123667	0.072609	0.027479	5.220673	5.363114
t (70)	-2.50462	-2.34603	-2.6094	2.92667	2.73886
p	0.014491	0.021693	0.010996	0.004761	0.008007
R	0.281306389	0.264781409	0.292091175	0.345957	0.326190829
R2	0.0791332845	0.0701091944	0.0853172542	0.119686246	0.106400457
Correct R2	0.066518672	0.0573709642	0.0727873536	0.105713012	0.0922163372
F(1,73)	6.27314428	5.50384106	6.80909265	8.56539326	7.50137893
Standard error of estimation	6.56820936	0.0216931012	0.0109964563	0.00476052566	0.00800726563
The regression equation for the dependent variable	y= 75.4127-0.3097×x	y= 53.9682-0.1709×x	y= 97.3798-0.0717×x	y= 31.0387+15.2792×x	y= 46.6937+14.6888×x

The direct mean correlation was found between the load index and RV size (r=0.25; p<0.05), between the load index and the LVEDD (r=0.37; p<0.05), the LVEDD (r=0.35; p<0.05) and SV (r=0.26; p<0.05). According to the regression analysis, only the LVEDD and the LVEDD are independent indicators of load index, indicating the direct effect of hypoxemia on LV remodeling under load conditions at 6MWT. This, in turn, confirms the relationship between exercise tolerance and structural and functional state of the heart.

CONCLUSIONS

1. Comprehensive determination of cardio-respiratory reserve by the test of 6-minute walk, pulse oximetry and ambulatory monitoring of blood pressure in patients with hypertension in combination with COPD makes it possible to establish disadaptation of the body to physical activity due to hypoxemia, decrease in the index of chrono- and inotropic reserves, which is an indication for administering appropriate therapy.
2. In patients with hypertension combined with COPD, the degree of desaturation, stroke volume, end-diastolic parameters of the left ventricle, maximal size and volume of the left atrium, as well as remodeling of the left heart sections in the concentric direction can be considered as independent predictors of prognosis.
3. The 6-minute walk test with desaturation can be used as an additional method of personalizing rehabilitation measures in patients with hypertension in combination with COPD.

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