ORIGINAL ARTICLE

CLINICAL PECULIARITIES AND PATHOGENETIC DETERMINANTS OF DEVELOPMENT AND PROGRESSION OF CHRONIC PULMONARY HEART WITH ARTERIAL HYPERTENSION

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ABSTRACT

The aim: To investigate the clinical and pathogenetic peculiarities of formation and course of CCP and the relationship between clinical, hemodynamic and neurohumoral factors of comorbidity development in COPD combined with arterial hypertension (AH).

Materials and methods: The object of the study were 484 patients with COPD. Among them, 350 patients with CCP as a result of cardiac insufficiency/severe congestive heart failure (COPD III-IV) out of aggravation, combined with AH II stage (non-symptomatic organ damage) and 1 - 3 grades, including 55 patients (43 men, 12 women) with compensated CCP (average age 43.7 ± 3.4 years), and 295 patients (212 men and 83 women) with decompensated CCP and chronic heart failure (CHF), average age 63.2 ± 8.9 years.

Results: It was found that the development and progression of the left and right CHF in patients with CCP combined with AH occurs due to the disorders of the central hemodynamic, progression of pulmonary hypertension, bronchial obstruction syndrome, neurohumoral and systemic immunoinflammatory activation, disorders of endothelial regulation of vascular tension, overproduction of epithelial and mitogenic growth factors, inducers of apoptosis, and is accompanied by increasing levels of natriuretic peptides.

Conclusions: The main pathogenetic formation mechanisms of the heart failure on the background of CCP combined with AH are: neurohumoral and systematic immune-inflammatory activation with the development of endothelial dysfunction and (neo)angiogenesis, induction of pathological apoptosis, increase in the intrathoracic pressure, and deposition of blood in the extrathoracic tissues, which result in pulmonary and systemic hypertension, metabolic and hemodynamic remodelling and heart dysfunction.

KEY WORDS: chronic cor pulmonale, neurohumoral activation, inflammation, mitogenic growth factors, apoptosis

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains one of the most challenging problems of internal medicine. According to WHO, more than 600 million people suffer from COPD worldwide today. According to the prognoses, by 2020, this number is expected to be doubled, resulting in the COPD being on a third place among the causes of death [1, 2].

The main cause of mortality in patients with COPD is heart failure as a result of the CCP. Prognosis is less favorable for those with decompensated CCP [3, 4].

Interfering syntrophy, during which the disease, that occurs on the ground of previous diseases, aggravates its course (polymorbid and comorbid states), is currently not studied well. It was found that 60.1% of patients with COPD suffered from AH, and 19.7% from chronic heart failure (CHF) [5].

AH belongs to the most common diseases of the cardiovascular system in the world [6]. According to the statistics, currently, there are more than 1 billion people with AH. This number is expected to be increased to 1.5 billion in 2015 [7].

One of the most frequent and dangerous complications of AH is chronic heart failure (CHF) [8]. The results of the Framingham Heart Study demonstrated conclusively that in people with high blood pressure (BP) the risk of CHF is 2 - 4 times higher compared to the people with normal blood pressure [9].

On the other hand, COPD and CHF are global epidemics, each of which affects more than 10 million patients, resulting in significant morbidity and mortality [10]. According to National Scientific Center "M.D. STRAZHESKO INSTITUTE OF CARDIOLOGY, MAS OF UKRAINE", the 31% of CHF patients have concomitant COPD [11]. It is known, that in the EU, the combination frequency of COPD and CHF ranges from 19% to 41% of cases [12].

The evidence indicates that the activation of the renin-angiotensin-aldosterone system (RAAS) influences the development of cardiovascular remodelling and cardiac dysfunction, pathological apoptosis, the formation of pulmonary arterial hypertension (PAH) and right ventricular CHF in patients with COPD [13-15].

On the other hand, the activation of the RAAS through a series of neurohormonal factors, such as angiotensin II, aldosterone, and production of proinflammatory cytokines as the components of the immunoinflammatory system activation, is one of the main mechanisms of hypertension and CHF formation [16, 17].

Consequently, a significant prevalence of COPD and its complication (CCP), which are the leading cause of mortality and comorbid conditions, associated with hypertension, justifying the need for a detailed study of new clinical and pathogenetic aspects of the development and course of CCP in combination with AH.

THE AIM

To investigate clinical and pathogenetic peculiarities of the formation and progress of CCP, and the relationship between clinical, hemodynamic and neurohumoral factors of comorbid disease development in COPD combined with AH.

MATERIALS AND METHODS

The object of the study were 484 patients with COPD. Among them, 350 patients with CCP as a result of COPD III - IV stage without exacerbation and combined with AH 1-3 grades and non-symptomatic organ damage, including 55 patients (43 men, 12 women) with compensated CCP (age 43.7 ± 3.4 years), and 295 patients (212 men and 83 women) with decompensated CCP and CHF-NYHA IV (age 63.2 ± 8.9 years). Also, 95 patients were examined (64 men, 31 women) with compensated CCP as a result of COPD III stage in the remission with AH II stage (non-symptomatic organ damage) and 1 – 3 grades, (age 54.7 ± 9.5 years). The group for comparison included 39 (30 men and 9 women) COPD patients I- II stage without clinical and instrumental signs of CCP (age 32.5 ± 4.2 years). AH II stage (non-symptomatic organ damage) and 1 – 3 grades was present in 423 (87.4%) of 484 patients. The remaining 61 (12.6%) patients had "high-normal blood pressure". The reference group consisted of 27 healthy people with no cardiovascular and bronchopulmonary diseases (age 28.4 ± 2.9 years).

The diagnosis of COPD is based on the Global initiative for Chronic Obstructive Lung Disease (GOLD) "Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease" (Updated 2015) [2] and CCP - based on WHO criteria (1963). [18]

The diagnosis and the stage of congestive heart failure are based on the recommendations for the diagnosis and treatment of acute and chronic heart failure (2012) from European Society of Cardiology. [19]

According to conventional methods, the structural and functional state of the right and left heart and intracardiac and systemic hemodynamics were evaluated with two-dimensional echocardiography and pulsed doppler echocardiography using machines "Logiq 500" (Kranzbühler, Germany) and "Logiq E" (China) with 2.5 and 3.5 MHz sensors [20]. Volumetric parameters of the right and left heart, systolic function in terms of ejection fraction (EF), and diastolic function by the ratio of maximum flow rate of early and late diastolic filling (E /A), were studied separately for the right (RV) and left (LV) heart ventricles. Systolic pressure in the pulmonary artery (SPPA) was measured using Doppler method, by the size of systolic trans-tricuspid pressure gradient. [21]

According to international recommendations ASE / EAE [20] and "2013 ESH / ESC Guidelines for the management of arterial hypertension" [22], based on parameters of the left ventricular mass index (LVMI) and relative wall thickness (RWTLV), the following LV geometry types were established: normal (NHLV), concentric remodelling (KRLV), concentric hypertrophy (KHLV), and eccentric hypertrophy (EHLV).

Vasoconstriction, vasodilatation and status of peripheral blood flow in the brachial artery (BA) were determined based on the indicators of endothelium-dependent vasodilation of BA in the probe with reactive hyperaemia (RH), applying the method, described by D.S. Celermajer, K.E. Sorensen et al., using the ultrasonic apparatus "Logiq 500", (Kranzbühler, Germany) with linear sensor 7.5 MHz.

Daily blood pressure monitoring (DBPM) was conducted using the instruments AVRM-04 ("Meditech", Hungary) and EBPM ("Innomed", Hungary). The daily index (DI) was calculated using the ratio of daytime and nighttime blood pressure. Daily arterial hypertension of examined patients was characterized as "Dipper" (DI - 10-22%), "Non-dipper" (DI <10%), "Over-dipper" (DI> 22%) and "Night-peaker" (DI has negative value), depending on the values of DI using common methodology. [24]

Aortic stiffness index (ASI, mmHg/ml) was evaluated according to technique from G. D. Radchenko, Y. M. Sirenko [25].

ELISA method (analyzer "Stat Fax 303 Plus", "Awareness Techology Inc", USA) was used for the detection of serum levels of aldosterone ("DSL", USA), endothelin-1 - ET-1 ("Peninsula Laboratories", USA), vascular endothelial growth factor - VEGF ("Cytimmune", USA), basic fibroblast growth factor - bFGF ("Biosource", USA) tumor nekrose faktor -α - TNF-α ("Diaclone", USA), apoptosis inducer Fas-Ligand - FasL ("Diaclone", USA) and N-terminal fragment of natriuretic peptide - NT-proBNP ("Peninsula Laboratories", USA).

Statistical analysis of the research results was carried out using spreadsheets Microsoft Excel 2013, statistical software packages Statistica v8.0 ("Stat Soft", USA) and Clin Tools v4.1 ("Psytek Ltd", Australia).

RESULTS

During the study of clinical and hemodynamic peculiarities of CCP combined with AH, mainly increase in diastolic blood pressure (BP), an increase in pulse BP (> 40mm Hg) and variability of BP, and prevalence of unfavorable profiles BP ("Non-dipper" (38.5%) and "Night-peaker" (32.9%)) were observed. It was found that the compensated CCP and decompensated CCP combined with CHF-NYHA II and associated with AH, is the typical first (hyperplastic-hypertrophic) type of RV remodelling, during which the concentric hypertrophy of the RV with the initial extend in the longitudinal size (41.1%) takes place. In case of the development of more severe CHF-NYHA III coupled with

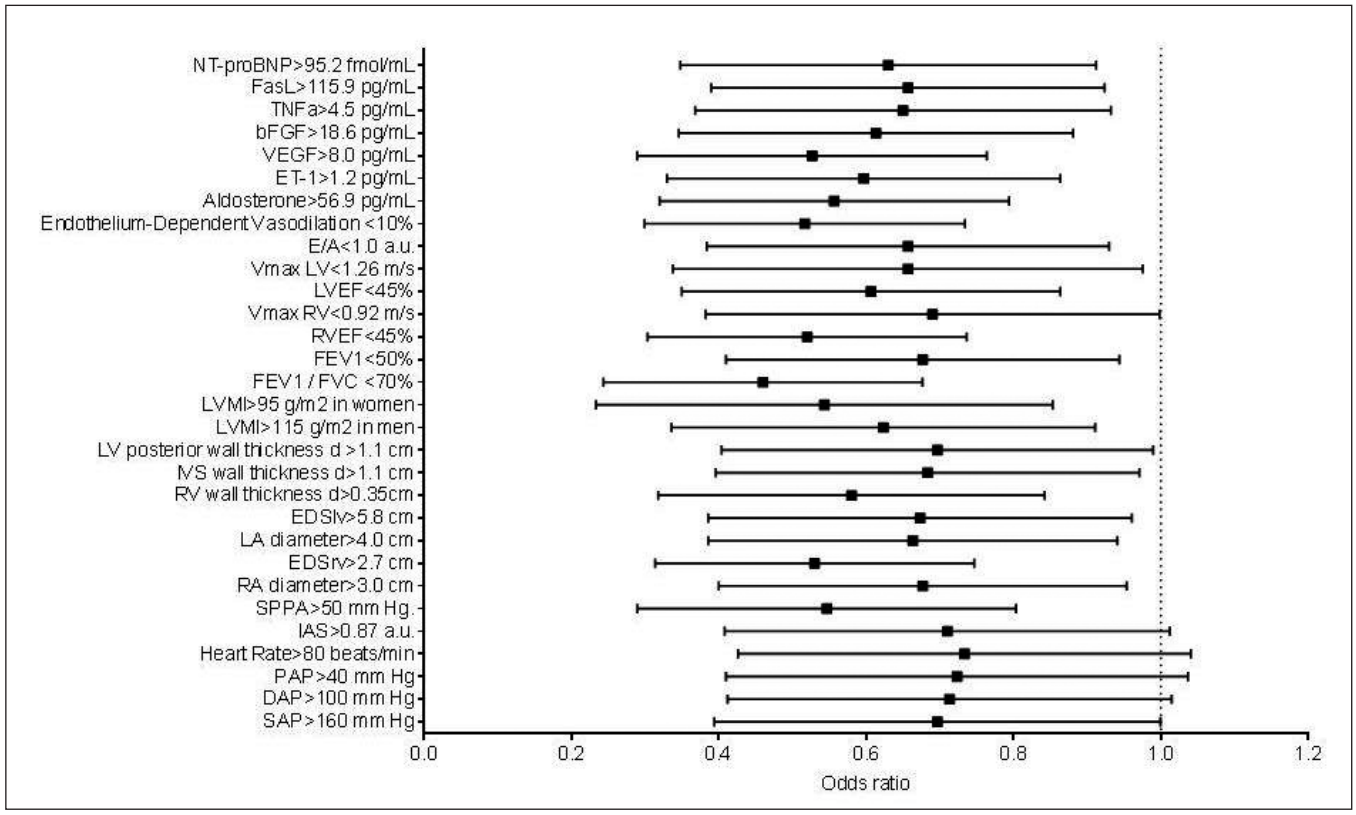

Fig. 1. Clinical and pathogenetic predictors of adverse course, early development of decompensation and rapid progression of CHF during CCP with AH, according to the analysis of the odds ratio of positive / negative prognosis

decompensated CCP with AH, remodelling of the right heart takes a path of the second (hypertrophic dilated) type with eccentric hypertrophy and myogenic cavity dilation of RV, combined with an increase in the right atrium (PP), representing 30% cases. If patients with decompensated CCP and AH have severe CHF-NYHA IV, the process of the RV dilatation predominate over hypertrophy and accompanied by widespread of RA (28.9%).

In the patients with decompensated CCP with AH and CHF-NYHA II, concentric remodelling (31.5%) and concentric hypertrophy (68.5%) are the prevailing changes of the LV geometry. In case of CCP decompensation with AH and CHF-NYHA III, remodelling of the LV develops mainly following the pathway of eccentric (76.2%) and, less often, concentric hypertrophy (23.8%). In a combination of CCP decompensation with AH and CHF-NYHA IV, the most common type of remodelling is eccentric hypertrophy of LV (81.2%).

At the same time, in 76.4% of patients with compensated CCP and AH are observed: structural, functional and hemodynamic changes of the left heart, caused by concentric remodeling of the LV with the development of its diastolic dysfunction (DD) of "hypertrophic" type.

In case of decompensated CCP with AH, as the CHF progress to DD LV, also expressive systolic dysfunction (SD) LV is getting involved. In particular, in case of decompensated CCP with AH and CHF-NYHA III, development of "hypertrophic" (76.2%) is observed more often, and less often - "pseudonormal" (23.8%) type of DD LV. DD LV forms a "pseudonormal" (41.6%) and "restrictive" (58.4%) types if CCP with AH are combined with CHF-NYHA IV.

Analysis of a Pulmonary arterial hypertension (PAH) pathogenic role in the formation and progression of decompensated CCP on the background of AH, allowed to reveal the existence of the correlation between the levels of SPPA and Vmax in right ventricular outflow ($r = 0.85$; $p < 0.001$), RVEF ($r = 0.82$; $p < 0.001$), EDSrv ($r = 0.79$; $p < 0.01$), EDVrv ($r = 0.80$; $p < 0.01$), ESVrv ($r = 0.62$; $p < 0.05$), RV wall thickness ($r = 0.53$; $p < 0.05$), IVTRrv ($r = 0.75$; $p < 0.05$), E / A ($r = -0.79$; $p < 0.01$), and RA diameter ($r = 0.59$; $p < 0.05$).

Based on our data, PAH plays the most significant role in the formation of CCP, what confirms the results from other studies [21, 25]. Conducted study of the diameter of the inferior vena cava (IVC) reveals that in case of healthy individuals it was (18.65 ± 1.22) mm broad, in combination with uncomplicated COPD and AH - (19.20 ± 1.05) mm ($p > 0.05$), in the presence of compensated CCP and AH - (20.38 ± 1.11) mm ($p < 0.05$), decompensated CCP with AH and CHF-NYHA II - (22.46 ± 1.37) mm ($p < 0 01$), decompensated CCP with AH and CHF-NYHA III - (23.51 ± 1.45) mm ($p < 0.001$), and decompensated CCP with AH and CHF-NYHA IV - (24.60 ± 1.58) mm ($p < 0.001$). It should be noted, that patients who are suffering from compensated CCP combined with AH, and decompensated CCP with AH and CHF-NYHA II, decrease of IVC during inspiration by 50% has been observed. However, there was no inspiratory collapse of the

Table I. Multiple Regression Analysis (MANOVA) for the dependent factor "SPPA" in patients with CCP combined with AH

R = 0,82213483; R2 = 0,67590567; adjasted R2 = 0,63749450					
F (16,135) = 17,597; p<0,00003; standard error of the estimate: 0,08330					
Analysis factors	**Beta**	**Standard error for Beta**	**B**	**Standard error for B**	**p**
Interscept			2,50420	1,403066	0,007653
1	2	3	4	5	6
Vmax in right ventricular outflow	0,15824	0,207436	0,08015	0,105074	0,044688
Vmax in BA	-0,42267	0,263358	-0,21680	0,135083	0,011045
RVEF	0,39141	0,313497	0,20317	0,162730	0,021399
EDSrv	0,27877	0,180101	0,06665	0,043059	0,012399
NT-proBNP	0,01277	0,175307	0,00312	0,042798	0,942049
Aldosterone	0,19375	0,086314	1,8053	0,804380	0,026815
IVRT	0,44982	0,174249	0,10533	0,040800	0,010904
wall thickness RVd	0,38061	0,235323	0,14709	0,090939	0,108123
EDVrv	0,84971	0,343834	0,00182	0,000735	0,024785
Endothelium-dependent vasodilation (Drg, %)	0,54406	0,416287	0,00108	0,000828	0,019345
FasL	0,55978	0,380091	2,15864	1,465709	0,143138
Vmax in BA during RH	-1,07431	0,360369	-3,71190	1,245125	0,034085
bFGF	0,29772	0,145410	4,47065	2,183524	0,042559
VEGF	0,42178	0,150055	6,25040	2,223673	0,005677
E/A	-0,07821	0,521588	-0,00014	0,000958	0,008136
ET-1	0,40084	0,486469	0,00070	0,000844	0,004152
TNFα	1,05573	0,394113	0,00179	0,000669	0,073084

Notes:
1. Intercept – estimate of the multiple regression coefficient B0.
2. Beta – standardized coefficient of multiple regression.
3. B – unstandardized coefficient of multiple regression.
4. R – coefficient of multiple correlation.
5. R2 – coefficient of multiple determination.
6. Adjusted R2 – ratio of R2 to its error.
7. p – probability coefficient.

IVC noticed in the case of severe decompensation CCP with AH and CHF-NYHA III-IV.

Based on the results of IVC diameter survey, the conclusion can be made that the increase of intrathoracic pressure and RA pressure takes place already at the stage of compensated CCP, which progress as the CCP and CHF worsening, what is in a good agreement with data of others authors [11, 18].

It was found, that together with the progression of CCP and CHF in patients with CCP in combination with AH, significant increase of serum aldosterone level ($p<0.05$), endothelial (ET-1, $p<0.05$) and mitogenic growth factors, neoangiogenesis (VEGF, $p<0.05$; bFGF, $p<0.05$), proinflammatory cytokines (TNFα, $p<0.05$), inducers of apoptosis (Fas-Ligand, $p<0.05$) and natriuretic peptides (NT -proBNP, $p<0.05$) takes place.

The formation of the endothelial dysfunction in patients with CCP combined with AH is characterized by progressing dysfunction of the brachial artery, depending on the type of CHF. Dysfunction of the BA is accompanied by the decrease in the initial maximum speed of blood flow to the BA, its growth after reactive hyperemia, and decrease of EDVD, and is associated with the increase of serum levels of ET-1 > 1.2 pg/ml (OR = 0.56; 95% CI = 0.35-0.88) and VEGF> 8.0 pg / ml (OR = 0.49; 95% CI = 0.31- 0.78).

Also important are the results of the research were the stiffness of the vascular wall was determined by the index of arteryal stiffness (IAS). In case of compensated CCP and AH, IAS exceeded the referent norm by 1.9 times ($p<0.05$). In case of decompensated CCP with AH and CHF-NYHA II, 2.2-fold increase ($p<0.05$) was observed, decompensated CCP with AH and CHF-NYHA III - 2.5-fold increase ($p<0.01$), decompensated CCP with AH and CHF-NYHA IV - 2.7-fold increase ($p<0.001$). These changes indicate an increase in the aortic stiffness and decrease in the flexibility of the major vessels in patients.

According to G.D. Radchenko and Y. M. Sirenko [25], if IAS index exceeds 1.5 mm Hg / ml, the risk of fatal endpoints of cardiovascular disease is 1.54-fold higher.

The multivariate analysis of variance (MANOVA) of the data (tab.I) reveals, that during combination CCP and AH, the level of SPPA get influenced by such factors as Vmax in the right ventricular outflow tract (RVOT) (p=0.0447), EFrv (p=0.0214) EDVD (p=0.0193), Vmax in BA (p = 0.0110), Vmax in BA during RH (p = 0.0340), (end-diastolic size) EDSrv (p = 0.0124), EDVrv (p = 0 , 0248), RV wall thickness d (p = 0.1081), IVRT (p = 0.0109), E / A (p = 0.0081), serum aldosterone levels (p = 0.0268), ET-1 (p = 0.0041), VEGF (p = 0.0057), bFGF (p = 0.0426), TNFα (p = 0.0730), FasL (p = 0.1431) and NT-proBNP (p = 0.9420).

Conducted nonparametric tests using Odds Ratio (Fig. 1) and the Pearson's chi-squared test (χ^2) allowed to identify the major pathogenic factors of negative prognosis, early development of decompensation and rapid progression of CHF combined with CCP and AH, which include: increase of systolic pressure ≥160 mm Hg (OR = 0.65; 95% CI = 0.42-1.02; χ^2 = 3.56; p = 0.030); diastolic pressure ≥100 mmHg (OR=0.68; 95% CI = 0.43-1.07; χ^2 = 2.81; p = 0.047); pulse pressure > 40 mmHg (OR=0.67; 95% CI = 0.44-1.06; χ^2 = 2.89; p = 0.044); increase in heart rate> 80 beats / min. (OR=0.69; 95% CI = 0.45-1.06; χ^2 = 2.88; p = 0.045); IAS> 0.87 cu (OR=0.67; 95% CI = 0.43-1.03; χ^2 = 3.29; p = 0.035); SPPA≥50 mmHg (OR=0.51; 95% CI = 0.31-0.82; χ^2 = 7.90; p = 0.002); RA diameter> 3.0 cm (OR=0.64; 95% CI = 0.42-0.97; χ^2 = 4.37; p = 0.018); EDSrv> 2.7 cm (OR=0.50; 95% CI = 0.33-0.76; χ^2 = 10.37; p = 0.001); LA diameter> 4.0 cm (OR=0.62; 95% CI = 0.41-0.96; χ^2 = 4.71; p = 0.015); EDSlv> 5.8 cm (OR=0.63; 95% CI = 0.41-0.98; χ^2 = 4.31; p = 0.019); RV wall thickness d > 0.35 cm (OR=0.54; 95% CI = 0.34-0.86; χ^2 = 6.92; p = 0.004); IVS wall thickness d > 1.1 cm (OR=0.64; 95% CI = 0.42-0.99; χ^2 = 4.13; p = 0.021); LV posterior wall thickness d> 1.1 cm (OR=0.65; 95% CI = 0.43-1.01; χ^2 = 3.76; p = 0.026); LVMI> 115 g / m^2 in men (OR=0.58; 95% CI = 0.36-0.93; χ^2 = 5.20; p = 0.011) and LVMI / m^2 in women (OR=0.48; 95% CI = 0.27-0.88; χ^2 = 5.74; p = 0.008) and a decrease in FEV1 / FVC <70% from average values (OR=0.43; 95% CI = 0.26-0.69; χ^2 = 12.36; p = 0.0002); FEV1 <50% from average values (OR=0.64; 95% CI = 0.43-0.96; χ^2 = 4.69; p = 0.015); RVEF ≤ 45% (OR=0.49; 95% CI = 0.32-0.75; χ^2 = 11.03; p = 0.0004); Vmax in RV outflow tract <0.92 m / s (OR=0.64; 95% CI = 0.41-1.02; χ^2 = 3.57; p = 0.030); LVEF ≤ 45% (OR=0.57; 95% CI = 0.37-0.88; χ^2 = 6.68; p = 0.004); Vmax in LV outflow tract <1.26 m / s (OR=0.60; 95% CI = 0.37-1.00; χ^2 = 3.90; p = 0.032); E / A <1.0 (OR=0.61; 95% CI = 0.41-0.95; χ^2 = 4.93; p = 0.013); EDVD <10% (OR=0.48; 95% CI = 0.32-0.75; χ^2 = 10.87; p = 0.0005) and aldosterone increase in blood > 56.9 pg / ml (OR=0.52; 95% CI = 0.34-0.81; χ^2 = 8.62; p = 0.002); ET-1> 1.2 pg / ml (OR=0.56; 95% CI = 0.35-0.88; χ^2 = 6.30; p = 0.006); VEGF> 8.0 pg / ml (OR=0.49; 95% CI = 0.31-0.78; χ^2 = 9.21; p = 0.001); bFGF> 18.6 pg / ml (OR=0.57; 95% CI = 0.37-0.90; χ^2 = 6.03; p = 0.007); TNFα> 4.5 pg / ml (OR=0.61; 95% CI = 0.39-0.95; χ^2 = 4.89; p = 0.013); FasL> 115.9 pg / ml (OR=0.62; 95% CI = 0.41-0.94; χ^2 = 5.10; p = 0.012); NT-proBNP> 95.2 fmol / ml (OR=0.59; 95% CI = 0.37-0.93; χ^2 = 4.,94; p = 0.014).

DISCUSSION

Our results on neurohumoral and systemic immunoinflammatory activation, which result in the endothelial dysfunction, apoptosis induction, and production of growth factors and natriuretic peptides in patients with CCP in combination with AH, are in a good agreement with the results from other authors [11, 13, 14, 15].

As a result of this research, the main factors of development and progression mechanisms of CHF, based on CCP combined with AH, were identified. These factors include: disorders of the central and intracardial hemodynamics, subclinical damage, impaired structural and functional condition of the heart, increased intrathoracic pressure and extrathoracic deposition of blood, neurohumoral and immunoinflammatory activation, PAH and AH, endothelial dysfunction, hyperproduction of endothelial and mitogenic growth factors, neoangiogenesis potentiation, induction of pathological apoptosis, accompanied by increased production of natriuretic peptides.

CONCLUSIONS

1. Typical peculiarities of the clinical course, hemodynamic, structural and functional changes in the myocardium during CCP, combined with AH, are: increase in diastolic blood pressure, high pulse pressure (> 40 mm Hg) and blood pressure variability, the prevalence of adverse BP profiles ("Non-dipper "(38.5%) and" Night-peaker "(32.9%)), the development of diastolic, or, in case of decompensation CCP, also systolic dysfunction of LV and RV, which are progressing as the formation of decompensated CCP and the increase in the severity of CHF.
2. Depending on the stage of compensation or decompensation of CCP, and the type of CHF, which are developed on the background of AH, the types of right and left heart remodeling were distinguished. In the compensation or decompensation stage of CCP, combined with AH and CHF-NYHA II (41.1%), first type (hypertrophic–hyperplastic) of RV remodeling with concentric hypertrophy takes place; in case of CHF-NYHA III (30.0%) and CHF-NYHA IV (28.9%), the second (hypertrophic, dilated) type RV remodeling with eccentric hypertrophy and myogenic dilatation of its cavity take place.

In patients with decompensated CCP and AH, combined with CHF-NYHA II, the characteristic changes in the left ventricular geometry are concentric remodeling (31.5%) and concentric hypertrophy (68.5%), in case of CHF-NYHA III - the eccentric (76.2%) and concentric hypertrophy (23.8%), and in the case of CHF-NYHA IV - eccentric hypertrophy (81.2%). It was found that structural, functional and hemodynamic changes of the left heart in patients with CCP on the background of AH depend on the stage of CHF, and left ventricular diastolic dysfunction of "hypertrophic" type (83.1%) can be observed in the decompensated type

of CCP with CHF-NYHA II, in case of CHF-NYHA III - "hypertrophic" (76.2%), and, less often, "pseudonormal" (23.8%) types, and in CHF-NYHA IV - the "pseudonormal" (46.6%) or " restrictive "(58.4%) types.

3. Development and progression of right- and left ventricular CHF in patients with CCP in combination with essential AH is due to disorders of the central hemodynamic, progression of pulmonary hypertension, bronchial obstruction syndrome, neurohumoral and systemic immunoinflammatory activation, endothelial vasoregulation disorders, overproduction of endothelial and mitogenic growth factors, inducers of apoptosis, and is accompanied by the increase of the natriuretic peptides level. Systolic pressure level in pulmonary artery of the CCP patients with essential AH, is determined by the next factors: Vmax in the outflow tract of RV ($p = 0.045$), RVEF ($p = 0.021$), Vmax in shoulder artery ($p = 0.011$), EDSrv ($p=0.012$), EDVrv ($p=0.025$), RV wall thickness d ($p=0.108$), IVRT ($p=0.011$), E/A ($p=0.008$), serum aldosterone levels ($p=0.027$), ET-1 ($p=0.004$), VEGF ($p=0.006$), bFGF ($p=0.043$), TNFα ($p=0.073$), FasL ($p=0.143$) та NT-proBNP ($p=0.942$).

4. The characteristic signs of the endothelial dysfunction in patients with CCP with essential AH is a progressing decrease of the vasomotoric function of the brachial artery, violation of elastic properties of the aorta on the background of the pronounced increase in serum levels of endothelin-1 (OR=0.56; 95% CI=0.35–0.88), vascular and endothelial growth factors (OR=0.49; 95% CI=0.31–0.78), which are dependent on the compensation or decompensation face of CCP and the type of CHF.

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