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ESTIMATION OF SYSTOLIC AND DIASTOLIC FUNCTION OF THE RIGHT VENTRICULAR MYOCARDIUM AMONG PATIENTS WITH CHRONIC COR PULMONALE OF BRONCHO-PULMONARY GENESIS IN COMBINATION WITH HYPERTENSIVE DISEASE

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Abstract

Chronic obstructive lung disease is the main reason for the development of chronic cor pulmonale. Comorbidity of chronic obstructive lung disease with cardiovascular pathology is very important and reflects the unity of cardiorespiratory system. It becomes a summary integral factor of a negative prognosis. Chronic obstructive lung disease and cardiovascular diseases are considered as "criminal partners".

The aim of the study was to investigate the functional state of right ventricular myocardium in patients with chronic cor pulmonale of broncho-pulmonary genesis combined with hypertensive disease.

Objects of the study were 96 patients with chronic cor pulmonale in combination with hypertensive disease depending on the disease severity. Among them 32 patients were without signs of circulatory insufficiency – compensation stage, and 64 were with signs of circulatory insufficiency of II stage – decompensation stage – forming the main group. The comparative group included 64 patients with chronic cor pulmonale without hypertensive disease, among whom 32 patients without signs of circulatory insufficiency and 32 patients with signs of circulatory insufficiency of II stage. The control group was consisted of 15 practically healthy individuals. All groups were of the same sex and age.

It was established that systolic dysfunction of the right ventricle worsens in case of adding of hypertensive disease to chronic cor pulmonale. This fact can be connected with the development of both precapillary pulmonary hypertension, which is typical for chronic cor pulmonale, and postcapillary one as a result of the left ventricular insufficiency in case of hypertensive disease. It has been manifested by the dependence of the average degree between the diameter of the right ventricle and left ventricular ejection fraction, systolic pressure of the pulmonary artery and left atrial size.

It is known, that diastolic dysfunction appears already on the background of chronic cor pulmonale formation in patients with chronic obstructive pulmonary disease and changes significantly in case of adding of hypertensive disease, particularly due to the development of circulatory insufficiency. It is caused not only by cardiomyopathy in conditions of chronic hypoxia that is revealed in patients with chronic cor pulmonale, but also by hypertensive disease which is characterized by myocardial stiffness. Right ventricular diastolic dysfunction occurs as a result of slowing-down of the hypertrophied myocardium relaxation and afterload increase. Interconnection between the systolic pressure of the pulmonary artery and peak early filling velocity of the right ventricle, between the peak early filling velocity and thickness of the myocardium during diastolic period, and between the ratio of early to late filling and thickness of the right ventricular myocardium during diastole testifies about it.

Keywords: *lungs, obstruction, cor pulmonale, hypertensive disease, hypoxia, ventricular functions.*

Introduction

Epidemiological researches conducted in different parts of the world for many years have revealed that diseases of respiratory organs have a great percentage because the morbidity remains high and it has no tendency to the reduction despite the developed therapeutic complexes [*Chuchalin A, 2008; Gavrysiuk V, 2011*].

Chronic cor pulmonale is formed among patients with kyphoscoliosis, obesity, recurrent pul-

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monary embolism during many years, but the main reason of chronic cor pulmonale development is chronic obstructive lung disease. According to the definition of Ukrainian Association of Phthisiatricians and Pulmonologists [*Gavrysiuk V, 2007*], chronic cor pulmonale is a syndrome of circulatory insufficiency with development of peripheral edemas that complicates the course of many diseases with lesion of lungs' structure or function itself. The formation of chronic cor pulmonale is the most severe complication of pulmonary diseases, which significantly decreases life quality of the patient and determines unfavorable clinical outcome in many respects [*Rakhimova D, 2012*].

Chronic obstructive lung disease is one of the most severe medico-social and economic problems both in Ukraine and in the whole world. First of all its actuality is caused by very high prevalence, disability and death rates [*Gavrysiuk V, 2011; Feshchenko Yu, 2012*]. According to the data of WHO, 600 million people in the world suffer from obstructive lung disease and the amount of these patients will be doubled by 2020. Morbidity which is caused by this pathology is rapidly increasing year after year. According to experts, this disease will be shifted to the 3rd place in the structure of general mortality and on the 5th place by social-economic losses by 2020. According to GOLD (2011) more than 3 million patients died from chronic obstructive lung disease. The annual direct expenses reach 38.6 milliard euros. The approximate calculation shows that hourly 340 people die due to the reason connected to obstructive disease [*Gibson G et al., 2013*]. In the near future the disease will become not only one of the most widespread forms of the human pathology, but it also will be among the leading reasons of deaths along with the expected reduction of fatal cases from myocardial infarction, oncological diseases [*Order No 555, MH of Ukraine, 2013*]. Every year 5-7 new cases are diagnosed among 30-45 cases of obstructive disease [*Shmelev Ye, 2003*]. This disease leads to disability on the average in 10 years after diagnosing it. Unfavorable prognoses concerning the increase in frequency of chronic obstructive lung disease are based both on the researches in Europe and in the regions of the American continent [*Yakovleva O et al., 2012; Boutou A et al., 2013*]. The data which were published in the European Lung White Book in 2013 [*Gibson G et al., 2013*] once again confirm this regularity. Thus, among 28 European countries 23 million people who are over 40 years are diagnosed with chronic obstructive lung disease, among them 1.1 million people are hospitalized, and 150 thousand die annually. This situation promotes the constant audit of obstructive disease in Europe.

In this connection, the amount of patients with chronic corn pulmonale (as a complication of chronic obstructive lung disease) has increased, lethality among them is 67% and it takes the third place after arterial hypertension and ischemic heart disease, particularly among causes of death of individuals over 50 years [*Konoplyova L, Rudenko Yu, 2009*]. A majority of experts claim that obstructive lung disease must be considered only as a polymorbid state [*Cavailles A et al., 2013; Nesen A et al., 2015*], and that it is often manifested on the background of arterial hypertension [*Yachnik A, 2009; Fabbri L et al., 2011*], ischemic heart disease [*Boyev S et al., 2015*] and metabolic disorders [*Kaydashev I, 2012*]. Different comorbid conditions are supposed to have stronger influence on clinical outcome among patients with chronic obstructive lung disease than indirectly disorders of bronchial patency and reduction of pulmonary function [*Mannino D et al., 2008*]. Comorbidity of obstructive disease with cardiovascular pathology remains the most important, reflecting the unity of cardiorespiratory system, becoming a summary integral factor of a negative prognosis: chronic obstructive lung disease and cardiovascular diseases are considered as "criminal partners". So, patients often die from cardiovascular reasons – 25% causes [*Berezin A, 2009*]. It is the comorbidity that remains the first among the risk factors of frequent exacerbations of obstructive disease, and every exacerbation is known to approximate the irreversible outcome. Thus, after the second severe exacerbation, the lethality increases in 1.9 times in comparison with the first one and after the fifth one – in 3 times [*Suissa S et al., 2012*]. That is why the risk prediction of the future exacerbation is very desirable, as it allows performing a complex of prophylactic actions in patients and evading deterioration in their condition [*Simoens S et al., 2013*]. The major epidemiological research Lung Health Study established that car-

diovascular diseases are the main reasons for the hospitalization of patients with obstructive disease in 42% cases, whereas respiratory complications are only in 14%.

Development of cor pulmonale in patients with chronic obstructive lung disease is an unfavorable prognostic factor. Myocardial lesion occurs as a result of the action of hypoxia, intoxication, development of pulmonary hypertension, which leads to the disorders of its contractile ability. Even insignificant pulmonary hypertension is an additional pathogenic factor in the appearance of myocardial pump function disorders. It essentially changes intracardial hemodynamics, increases myocardial ischemia and afterloads on the right ventricle [*Borisova O et al., 2001*]. Adding of hypertensive disease provokes progressing of disorders in pulmonary circulation that promotes the deterioration of bronchial patency and development of chronic heart failure [*Lyzogub V et al., 2007*]. L.I. Dvoretsky (2001) informs that prevalence of arterial hypertension in patients with obstructive disease ranges from 6.8% to 76.3%, on average 34.3%. Similar data are registered in Ukraine – about 35.0% [*Sirenko Yu, 2004*].

Thus, significant prevalence, frequent exacerbations and involvement into pathological process of adjacent internal organs determine the actuality of studying the problems of the development of chronic cor pulmonale.

The aim of the study was to investigate the functional state of right ventricular myocardium in patients with chronic cor pulmonale of broncho-pulmonary genesis combined with hypertensive disease.

Material and methods

For the solution of this question systolic and diastolic functions of the right ventricular myocardium were studied in 96 patients with chronic cor pulmonale combined with hypertensive disease depending on the disease severity, among them 32 patients (33.3%) without signs of circulatory insufficiency –compensation stage (I group), 64 (66.7%) – with signs of circulatory insufficiency of II stage –decompensation stage (II group). The number of males was 58 (60.4%) and females – 38 (39.6%), the mean age was 55.6±2.2 years. These patients formed the main group. Obtained results were compared with identical groups of patients with chronic cor pulmonale without hypertensive disease, among whom 32 (50.0%) patients without signs of circulatory insufficiency – compensation stage (III group), 32 (50.0%) patients with signs of circulatory insufficiency of II stage –decompensation stage (IV group). There were 40 males (62.0%) and 24 females (38.0%) with the mean age of 53.5±1.2 years. These patients formed the comparative group. The control group was consisted of 15 practically healthy individuals. All groups were of the same sex and age.

Diagnosis of chronic cor pulmonale was established based on clinical and instrumental signs of right ventricular hypertrophy and/or dilatation of right ventricular cavity and right atrium [*Roytberg G, Strutynsky* A*, 2003; Gavrysiuk V, 2007*].

Estimation of morphological changes and functional condition of right parts of the heart was carried out by means of two-dimensional echocardiography by apparatus Toschiba SSA, 380A Powerwission (Japan) with determination of common indices characterizing systolic and diastolic function of right ventricle. The following indices of diastolic function of right ventricle were estimated: end-diastolic dimension, isovolumic relaxation time, early diastolic filling velocity (E) and late diastolic filling velocity (A), ratio E/A by indices of transtricuspidal blood flow, diameter of the right atrium.

End-systolic dimension, blood peak flow (V_{max}) in the outflow tract of the right ventricle by indices of transpulmonary blood flow, shortening fraction, paradoxical movement of interventricular septum, collapse of inferior vena cava, its diameter were determined with the aim of estimation of systolic function of the right ventricle.

Systolic pressure in pulmonary artery was determined by the value of transtricuspidal gradient with the presence of tricuspid regurgitation. The following formula was used for the calculation:

SPPA=DP+pressure in RA, where SPPA is systolic pressure in pulmonary artery, DP – transtricuspidal gradient, RA – right artery;

$DP=4v^2$, v – maximal regurgitate velocity.

In the case when the collapse of inferior vena cava after full inspiration was more than 50%, the pressure of right atrium was 5 *mm Hg*, and if the collapse of inferior vena cava was less than 50% – 15 *mm Hg* [*Louie E et al., 1992*].

Three degrees were used for the estimation of pulmonary hypertension: 1 – mild (25-45 *mm Hg*), 2 – moderate (46-65 *mm Hg*), 3 – severe (> 65 *mm Hg*) [*Simonneau G et al., 2004*]. The classification of the work group of Ukrainian Association of Phthisiatricians, Pulmonologists and Cardiologists was used for the estimation of circulatory insufficiency in patients with chronic cor pulmonale [*Gavrysiuk V, Yachnik A, 2005*].

Parameters of systolic and diastolic blood pressure were measured by Korotkov's method; the value of arterial hypertension was estimated according to the classification of hypertensive disease accepted in Ukraine in 1992 (the order of Ministry of Health of Ukraine, No 206 from 30.12.92). Informed consent for participation in the research signed by the patient was the obligatory condition in order to let the patient take part in the research.

Statistical analysis of the results was carried out by parametric statistics. Student's t-test was used to estimate the significance of differences. The difference of indices was significant in case of $p<0.05$, and also by means of nonparametric Kolmogorov-Smirnov test. Correlation analysis was realized by method of Pearson correlation coefficient (r) on Celeron 650 computer with SPSS 11.0 software.

Results and discussion

The indices of right ventricular myocardium obtained during echocardiographic study in patients with chronic cor pulmonale combined with hypertensive disease and without hypertensive disease are shown in table.

The table demonstrates the presence of a number of peculiarities in the indices of systolic and diastolic function of right ventricular myocardium in patients with chronic cor pulmonale combined with hypertensive disease (I and II groups) in comparison with patients with chronic cor pulmonale without hypertensive disease (III and IV groups).

While estimating systolic function a natural increase of right ventricular size was revealed in both groups, peculiarly among patients with accompanying hypertensive disease in case of decompensation (3.6±0.3 and 4.2±0.6, $p<0.05$). Par-

Table

Indices of systolic and diastolic function of the right ventricle in examined patients and healthy individuals

Indices	Control group n=15	Main group		Comparative group	
		I (n=32)	II (n=32)	III (n=32)	IV (n=64)
Systolic pressure in pulmonary artery (*mm Hg*)	19.5±0.6	32.4±0.9*	34.4±1.2*	29.2±1.1	32.5±1.0
End-diastolic dimension of the right ventricle (*cm*)	1.93±0.6	3.6±0.3	4.2±0.6*	3.0±0.03	3.4±0.2
Thickness of right ventricular myocardium (diastolic), (*mm*)	0.48±0.1	0.6±0.003	0.8±0.004*	0.4±0.001	0.5±0.002
V_{max}, in the outflow tract (*m/sec*)	0.9±0.03	0.6±0.003	0.4±0.002*	0.5±0.003	0.7±0.002
Diameter of the right atrium (*cm*)	32.9±0.8	4.0±0.03*	4.2±0.04*	3.6±0.2	3.9±0.4
Shortening fraction (%)	23.5±0.6	19.8±0.7*	16.6±0.3*	22.5±0.8	20.4±0.6
Diameter of inferior vena cava (*mm*)	14.8±0.8	21.2±0.6*	22.3±0.8	18.1±0.6	20.3±0.9
Collapse of inferior vena cava after inspiration (%)	38.4±1.6	20.4±0.8*	18.2±0.6	25.6±1.2	23.2±0.8
Isovolumic relaxation time (*sec*)	0.05±0.03	0.08±0.02*	0.12±0.002*	0.06±0.003	0.07±0.004
E (*m/sec*)	0.59±0.04	0.5±0.003*	0.4±0.001*	0.6±0.04	0.4±0.003
A (*m/sec*)	0.41±0.03	0.7±0.002*	0.8±0.02*	0.4±0.002	0.5±0.003
E/A (*c.u.*)	1.72±0.11	0.7±0.001*	0.5±0.001*	1.5±0.01	0.8±0.02

Note: ** – significance of differences of indices among patients of I, III groups in compensation stage and II, IV groups in decompensation stage; $p<0.05$.*

ticularly, the increase of end-diastolic dimension of the right ventricle in 0.6±0.003 *cm* (25.8%) was observed during decompensation stage and in 0.4±0.002 *cm* (12.5%) during compensation stage. Increase of the thickness of right ventricular myocardium wall is marked. It indicates a significant increase of the load on right ventricle. Systolic pressure of pulmonary artery also increases, peculiarly in patients of II group (Figure).

This fact can be connected with the development of both precapillary pulmonary hypertension, which is typical for chronic cor pulmonale, and postcapillary one, as a result of the left ventricular insufficiency in case of hypertensive disease. It is shown between moderate right ventricular diameter and left ventricular ejection fraction (r=062, p<005), as well as systolic pressure of pulmonary artery and left atrial size (r=0.58, p<0.05).

Shortening fraction of the right ventricle as the main index of its systolic function is decreased in patients of I group by 2.7±0.2% and by 3.8±0.4% among patients of II group.

Diastolic right ventricular dysfunction is caused not only by cardiomyopathy in conditions of chronic hypoxia, which is revealed among patients with chronic cor pulmonale, but also by hypertensive disease, which is characterized by myocardial stiffness [*Viner G et al., 2008*].

Thus, almost the double increase of isovolumic relaxation time and decrease of early (E) diastolic filling velocity was marked. Preponderance of late diastolic filling velocity (A) compared with early one (A>E), increase of isovolumic relaxation time to 0.12±0.002 *sec* gives possibility

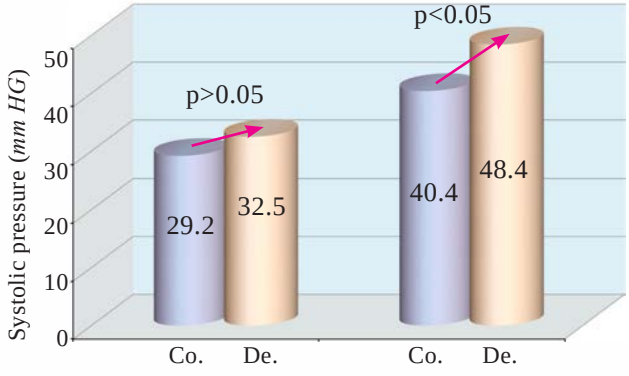

FIGURE. *Level of systolic pressure in pulmonary artery in patients with chronic cor pulmonale (left columns) and in combination with hypertensive (right columns) disease. Co and De* compensation and decompensation stages correspondently

for the type of diastolic filling to be related to "hypertrophic" (relaxation failure), which is similar with the data obtained by R.A. Nishimura and Tajik A.J. (1997). Disorder of the structure of right ventricular diastolic filling was accompanied by dilatation of the right atrium by 0.4±0.002 *cm* during compensation stage and by 0.3±0.003 *cm* during decompensation stage.

Right ventricular diastolic dysfunction is due to the slowdown of the hypertrophied myocardium relaxation and afterload increase. Interconnection between the systolic pressure of the pulmonary artery and peak early filling velocity (E) of the right ventricle (r=-0.56, p<0.001), between the peak early filling velocity and thickness of the myocardium during diastolic period (r=-0.60, p<0.01), and between the ratio of early to late filling (A) – E/A and thickness of the right ventricular myocardium during diastole testifies about it.

Revealed disorders of right ventricular diastolic filling, especially in patients with chronic cor pulmonale with accompanying hypertensive disease, indicates an increase of passive stiffness, decrease of myocardial compliance and increase contribution of the right atrium into the process of right ventricular diastolic filling. These disorders can be connected with hypoxia of cardiac muscle, elevation of pressure in the pulmonary artery on the background of progressive lung failure.

Lesions of the left ventricle due to chronic hypoxia, recurrent inflammatory process are also formed in patients with chronic cor pulmonale, which leads to the development of cardiomyopathy.

Obtained results are consistent with the data of early conducted researches. It is established that myocardial changes occur with progressing of chronic cor pulmonale. At the beginning they are as metabolic remodeling, later – with the change of ventricular geometry by development of hypertrophy, dystrophy, atrophy and necrosis of cardiac hystiocytes (mainly of the right ventricle). Myocardial pressure overload and volume overload is accompanied by remodeling of both ventricles [*Zadionchenko V et al., 2003; Adamyan K et al., 2013*], which occurs under the influence of complex of factors including toxic factor which is connected with bacterial agents. Moreover hypoxic factor is also important. It leads to cardiac ventricular dystrophy [*Seredyuk V, 2013*]. Adding

of hypertensive disease also leads to ischemia, dystrophy, necrosis of cardiac hystiocytes. In case of combined pathology (ischemic heart disease, hypertensive disease) cardiac ventricles are overloaded with volume, but the right ventricle unlike the left one, also works simultaneously in conditions of pressure overload due to pulmonary hypertension [*Gavrysiuk V, 1997*]. Contractile ability of myocardium decreases [*Amosova Ye, Konoplyova L, 2003*].

Thus, the analysis of obtained results demonstrates that systolic dysfunction of right ventricle worsens in case of adding of hypertensive disease to cor pulmonale. Not only elevated blood pressure, decreased contractile ability of myocardium, but also hypoxia, myocardial dystrophy, which are typical for the patients with chronic cor pulmonale of broncho-pulmonary genesis, have influence on the changes of cardiac ventricles.

Diastolic dysfunction occurs on the background of forming chronic obstructive lung disease and significantly intensifies in case of adding of hypertensive disease, and especially due to development of circulatory insufficiency.

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