



## ESTIMATION OF SYSTOLIC AND DIASTOLIC FUNCTION OF THE LEFT VENTRICULAR MYOCARDIUM AMONG PATIENTS WITH CHRONIC COR PULMONALE OF BRONCHOPULMONARY 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 this disease with cardiovascular pathology is 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".*

*The aim of the study was to investigate the functional state of left ventricular myocardium in patients with chronic cor pulmonale of bronchopulmonary 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 2<sup>nd</sup> 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 2<sup>nd</sup> stage. The control group was consisted of 15 practically healthy individuals. All groups were of the same sex and age.*

*It was established the systolic dysfunction of the left ventricle worsens in case of adding of hypertensive disease to chronic cor pulmonale. Revealed significant decrease of the stroke and cardiac indices, acceleration of blood flow through aortic valve, that resulted in decrease of ejection fraction, testifies about it. These differences were the most evident in patients of decompensation stage, when also increased hypertrophy of the left ventricular posterior wall and, particularly, interventricular septum was revealed.*

*Diastolic dysfunction appears already on the background of chronic cor pulmonale formation in patients with chronic obstructive pulmonary disease and intensifies significantly in case of adding of hypertensive disease, in development of circulatory insufficiency particularly. It was confirmed by revealed changes of the left ventricular diastolic function of relaxation type among all the patients. They were reflected in diminishing of early diastolic filling velocity, ratio of early to late filling velocity, increase of isovolumic relaxation time, particularly in presence of hypertensive disease and signs of circulatory insufficiency. Significant thickening of interventricular septum also testifies about forming of left ventricular diastolic dysfunction.*

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

### INTRODUCTION

Diseases of respiratory organs have a great percentage, and morbidity remains high despite the de-

veloped therapeutic complexes [Gavrysiuk V, Feshchenko Yu, 2011]. Chronic cor pulmonale is a widespread pathology in the practice of therapist, geriatrician, cardiologist. According to the definition of Ukrainian Association of Phthisiatricians and Pulmonologists [Gavrysiuk V, Merenkova Ye, 2014], chronic cor pulmonale is a syndrome of circulatory insufficiency with development of peripheral edemas that

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complicates the course of many diseases with lesion of lung's structure or function itself. In the most frequent cases chronic cor pulmonale is a result of forming and steady progressing of chronic obstructive lung disease, particularly among elderly and old people. The rate of increase of chronic obstructive lung disease is worthy of a peculiar note. So, in 1990 chronic obstructive lung disease took the 12<sup>th</sup> place in the structure of morbidity, according to experts of WHO prognosis it will have entered into the first five pathologies (after ischemic heart disease, depression, traumas which are results of accidents and diseases of cerebral vessels) by 2020. Moreover, chronic obstructive lung disease took the 4<sup>th</sup> place among ten leading causes of death in 2008, but this disease will be shifted to the 3<sup>rd</sup> place by 2020. It can cause 6 million deaths [GOLD, 2011; Gibson G et al., 2013]. Every year 5-7 new cases are diagnosed among 30-45 cases of obstructive disease [Shmelev Ye, 2003]. Thereby, morbidity in absolute figures makes approximately 100 million per year. Annually 3 million people die from chronic obstructive lung disease [Feshchenko Yu, 2012]. 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 [Vestbo J et al., 2013; Yakovleva O, Masloyed T, 2014], different variants of phenotypes are taken into account. Problem becomes complicated in condition of comorbidity of chronic obstructive lung disease [Nesen A et al., 2015]. The amount of patients with chronic cor pulmonale as a result of complicated chronic obstructive lung disease has increased. Lethality among them takes the 3<sup>rd</sup> place after arterial hypertension and ischemic heart disease, particularly among causes of death of individuals over 50 years [Konoplyova L, Rudenko Yu, 2009].

Today chronic obstructive lung disease is considered as a multidisciplinary problem [Avdeyev S, Baymakanova G, 2008; Cavailles A et al., 2013] owing to its frequent combination with obesity, metabolic disorders, cachexia, dementia. But it is comorbidity of this disease with cardiovascular pathology, which is the most important, it reflects 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". Comorbidity often remains the first among the risk factors of frequent exacerbations of chronic obstructive lung disease, and every exacerbation approximates the irreversible outcome. So, combination of bronchitis with ischemic heart disease increases death risk by 50%, moreover, the decrease of forced expiratory volume per 1 second by every 10% causes the growth of death risk by 14 % or cardiac death by 28% [Cavailles A et al., 2013].

The major epidemiological research Lung Health Study established that cardiovascular diseases are the main reasons for the hospitalization of patients with obstructive disease in 42% cases, whereas respiratory complications are only in 14%.

According to the data of N.A.Karoli and A.P. Rebrov (2005), the pathology of cardiovascular system is revealed in 61,8% patients with chronic obstructive pulmonary disease, besides frequency of arterial hypertension varies in a wide diapason – from 6.8 to 76.3%, on average making 34.3%. Other authors inform that prevalence of combination of chronic obstructive lung disease and arterial hypertension makes 28% [Mannino D et al., 2008; Yachnik A, 2009]. It is considered that chronic hypoxia, caused by chronic obstructive lung disease, promotes to elevation of blood pressure by means of worsening of endothelium-dependent vasodilating mechanisms [Chuchalin A, 2010]. In case of variation in intrathoracic pressure which appears during episodes of bronchial obstruction, sympathetic nervous system activates and vasoconstriction develops. It is accompanied by elevation of blood pressure.

The formation of chronic cor pulmonale in patients with chronic obstructive lung disease is an unfavorable factor for prognosis

*To overcome it  
is possible, due to the  
uniting the knowledge and  
will of all doctors in the world*



[Rakhimova D, 2012]; myocardial lesion develops as result of hypoxia, intoxication, pulmonary hypertension's development, that causes disorder of its contractile ability [Adamyan K et al., 2013]. Even insignificantly expressed pulmonary hypertension is additional pathogenic factor of myocardial pump function's disorders rise. Adding of hypertensive disease provokes progressing of disorders in pulmonary circulation, promotes to worsening of bronchial patency and development of chronic heart failure.

Thus, significant prevalence, frequent exacerbations and involvement into pathological process of adjacent organs determine the actuality of studying the problem of the development of chronic cor pulmonale of bronchopulmonary genesis. Combination of chronic cor pulmonale in patients with chronic obstructive lung disease and hypertensive disease causes peculiar clinical interest.

The aim of the study was to investigate the functional state of the left ventricular myocardium in patients with chronic cor pulmonale of bronchopulmonary genesis combined with hypertensive disease.

#### MATERIAL AND METHODS

For the solution of this question systolic and diastolic functions of the left 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 (1<sup>st</sup> group), 64 (66.7%) – with signs of circulatory insufficiency of 2<sup>nd</sup> stage – decompensation stage (2<sup>nd</sup> group). The number of males was 58 (60.4%) and females – 38 (39.6%), the mean age was  $55.6 \pm 2.2$  years. These patients formed the main group. Obtained results were compared with identical group of patients with chronic cor pulmonale without hypertensive disease, among whom 32 (50.0%) patients without signs of circulatory insufficiency – compensation stage (3<sup>rd</sup> group), 32 (50.0%) patients with signs of circulatory insufficiency of 2<sup>nd</sup> stage – decompensation stage (4<sup>th</sup> group). There were 40

males (62.0%) and 24 females (38.0%) with the mean age of  $53.5 \pm 1.2$  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 left parts of the heart was carried out by means of two-dimensional echocardiography by apparatus Toshiba SSA, 380A Powerwision (Japan) with determination of common indices characterizing systolic and diastolic function of left ventricle. The following indices of diastolic function of left ventricle were estimated: early diastolic filling velocity (E) and late diastolic filling velocity (A), ratio E/A, isovolumic relaxation time by indices of transmitral blood flow.

Diameter of the left atrium, cardiac index, stroke index, thickness of left ventricular posterior wall, ejection fraction were determined with the aim of estimation of systolic function of the left ventricle [Kazakov YuM, et al., 2016].

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.

TABLE

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

Indices	Control group (n=15)	Main group		Comparative group	
		1 <sup>st</sup> (n=32)	2 <sup>nd</sup> (n=64)	3 <sup>rd</sup> (n=32)	4 <sup>th</sup> (n=32)
Systolic blood pressure (mm Hg)	130.0±1.5	145.0±1.5*	160.0±2.5*	120.0±2.0	120.0±2.0
Diastolic blood pressure (mm Hg)	80.0±1.0	90.0±1.2	95.0±1.3	85.0±2.0	80.0±2.0
Heart rate per 1 min	72.1±1.9	88.0±1.5*	95.0±3.0*	78.0±2.0	80.0±2.0
Stroke index (ml/m <sup>2</sup> )	43.7±1.9	36.5±1.2*	30.0±1.4*	42.0±1.3	40.0±1.2
Cardiac index (l/min/m <sup>2</sup> )	3.1±0.1	2.4±0.4	2.1±0.6	3.0±0.3	2.8±0.2
Ejection fraction (%)	65.7±0.6	50.0±2.5*	40.5±1.0*	63.4±1.2	58.5±2.0
Thickness of left ventricular posterior wall (mm)	9.1±0.2	9.6±0.4	9.8±0.3*	8.2±0.4	8.7±0.3
Interventricular septum (mm)	8.9±0.2	10.4±0.6	11.5±0.5*	8.0±0.3	9.2±0.3
V <sub>max</sub> (m/sec)	1.2±0.03	0.8±0.002	0.5±0.003*	1.0±0.02	0.9±0.003
Acceleration of blood flow through aortic valve, (m/sec <sup>2</sup> )	18.7±0.9	9.2±0.3*	7.5±0.2*	16.8±0.4	14.2±0.2
Diameter of the left atrium (mm)	28.1±0.7	34.0±0.8	37.0±1.2*	29.0±1.0	32.0±0.9
E (m/sec)	0.84±0.04	0.6±0.002	0.4±0.001*	0.8±0.003	0.7±0.002
A (m/sec)	0.5±0.04	0.4±0.001	0.3±0.002*	0.5±0.002	0.5±0.003
E/A (c.u.)	1.74±0.06	1.5±0.02	1.3±0.03	1.6±0.02	1.4±0.01
Isovolumic relaxation time (sec)	0.07±0.001	0.13±0.002*	0.16±0.004*	0.09±0.001	0.11±0.002

NOTE: \* - significance of differences of indices among patients of 1<sup>st</sup>, 3<sup>rd</sup> groups in compensation stage and 2<sup>nd</sup>, 4<sup>th</sup> groups in decompensation stage; p < 0.05.

## RESULTS AND DISCUSSION

The indices of left 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 that significant decrease of the stroke and cardiac indices, acceleration of blood flow through aortic valve were revealed in patients with chronic cor pulmonale combined with hypertensive disease even during compensation stage (p<0.05). It resulted in decrease of ejection fraction in 1.3 times in comparison with healthy individuals, but this index was within limits of normal value (50.0±2.5%). These changes indicate additional contribution of hypertensive disease to development of systolic function's decrease on the back-

ground of hypoxia, toxic-infectious and metabolic influences of chronic obstructive lung disease. These differences are more evident in patients of 2<sup>nd</sup> group, that was reflected in the figures 1. All indices (stroke and cardiac indices, V<sub>max</sub>, acceleration of blood flow through aortic valve, diameter of the left atrium) were changed significantly. It resulted in decrease of ejection fraction to 40.5±1.0%. Increasing hypertrophy of the left ventricular posterior wall and interventricular septum, particularly, were revealed. But they didn't reach values, which are typical of isolated hypertensive disease. Pathogenesis of these changes can be explained by diminishing of blood flow to the left part of the heart due to increase of total pulmonary resistance, pulmonary hypertension in pulmonary circulation and right ventricular failure.

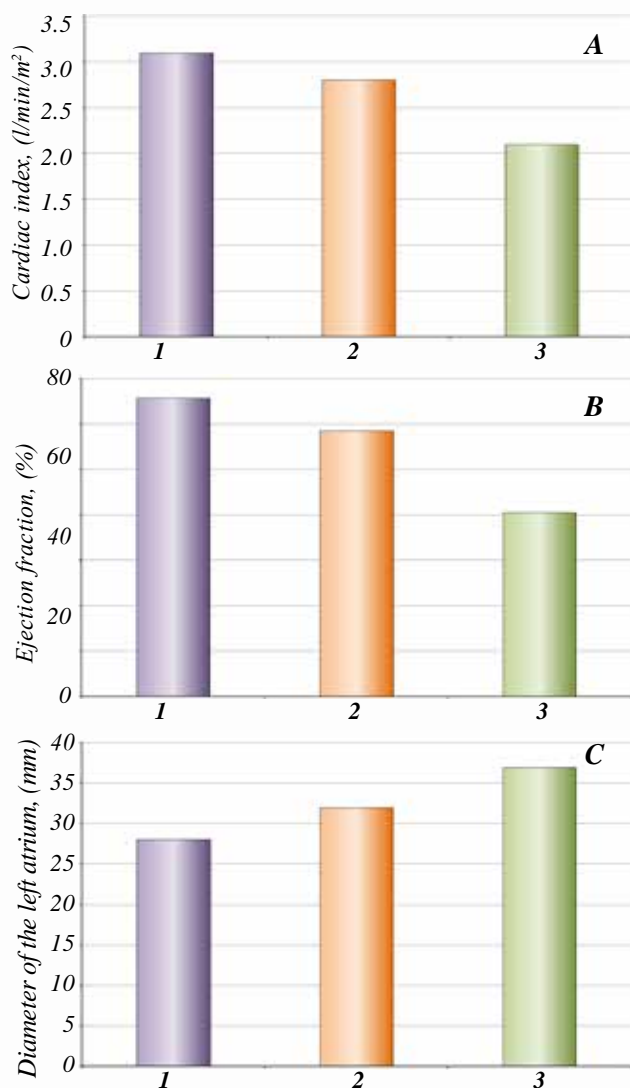


Figure 1. Cardiac index (A), Ejection fraction (B) and Diameter of the left atrium (C) in healthy individuals and patients with chronic cor pulmonale (during decompensation stage) depending on presence of hypertensive disease.

NOTES: 1 - healthy individuals, 2- chronic cor pulmonale without hypertensive disease (IV gr.), 3- chronic cor pulmonale combined with hypertensive disease (II gr.)

Changes of the left ventricular diastolic function by a relaxation type were revealed in 100% patients. They were reflected in diminishing of early diastolic filling velocity (E), ratio of early to

late filling velocity (E/A), particularly among the patients of 2<sup>nd</sup> group. The difference of indices was, correspondingly,  $0.3 \pm 0.001$  m/sec ( $p < 0.05$ ) and  $0.1 \pm 0.001$  c.u. in comparison with 4<sup>th</sup> group of patients. Index of isovolumic relaxation time increased from  $0.11 \pm 0.002$  sec in patients of 4<sup>th</sup> group to  $0.16 \pm 0.04$  sec in patients of 2<sup>nd</sup> group ( $p < 0.05$ ). Significant thickening of interventricular septum also testifies about forming of the left ventricular diastolic dysfunction. It is necessary to mention that disorder of left ventricle's filling together with changes of systolic function was accompanied by its dilatation by 7.6%.

The obtained results testify that not only the right ventricular myocardium's lesion (see our preceding works [Kazakov Yu et al., 2016] but also left ventricular myocardium's lesion play significant role in development of chronic cor pulmonale. The simultaneous course of chronic obstructive lung disease and hypertensive disease is accompanied by syndrome of "mutual burden".

Thus, the analysis of obtained results demonstrates that systolic dysfunction of left ventricle (like one of right ventricle) increases 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 of the patients with chronic obstructive lung disease, that is confirmed by data of other scientists [Amosova K et al., 2008], have influence on the changes of cardiac ventricles.

Diastolic dysfunction occurs on the background of forming of chronic cor pulmonale in patients with chronic obstructive lung disease and significantly intensifies in case of adding of hypertensive disease, particularly in development of circulatory insufficiency.

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