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COMPARATIVE CHARACTERISTICS OF SOME HOMEOSTASIS INDICES IN PATIENTS WITH CHRONIC COR PULMONALE IN DECOMPENSATION STAGE AND IN CONDITIONS OF ITS COMORBIDITY WITH STABLE CORONARY HEART DISEASE

PETROV YE.YE.^{1*}, KAZAKOV YU. M.¹, BURMAK YU. H.², IVANYTSKA T. A.¹, CHEKALINA N. I.¹, TRYBRAT T. A.¹

¹ Department of Propedeutics of Internal Medicine, Poltava State Medical University, Poltava, Ukraine

² Department of Internal Medicine N3, Bohomolets National Medical University, Kyiv, Ukraine

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ABSTRACT

The analysis of literature data indicates a high frequency of the combination of chronic obstructive pulmonary disease and coronary heart disease. The aim of the study is to investigate and analyze the peculiarities of changes in some indicators of hemostasis system, lipid metabolism and endothelial function and to determine their possible role in the formation of vascular lesions in patients with chronic cor pulmonale of broncho-pulmonary genesis in the decompensation stage and in conditions of a comorbid course with stable coronary heart disease.

All the patients (96) were divided into 2 groups: the main group (chronic cor pulmonale combined with coronary heart disease, 64 patients) and comparative group (chronic cor pulmonale, 32 patients). Endothelial function indicators were studied and analyzed in 32 patients of the main group and 10 patients of the comparative group (identical sex-age structure). The obtained research results in the patients of the main and comparative groups were compared between themselves and also with the indices of practically healthy individuals (n=15) who were of the same sex and age.

The analysis of the changes of the hemostasis system indices in patients with chronic cor pulmonale indicates the presence of an increase of coagulation potential: the most significant changes with suppression of fibrinolytic activity are typical of the patients with comorbid coronary heart disease. The direction of changes in lipid metabolism in patients with chronic cor pulmonale reflects generally their proatherogenic orientation, the changes are combined with significant violations of the regulatory function of the endothelium, and the greatest expressiveness of such changes is typical of patients with comorbid coronary heart disease.

KEYWORDS: chronic cor pulmonale, coronary heart disease, comorbidity

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ADDRESS FOR CORRESPONDENCE:

Yevhen Ye. Petrov; PhD, Associate Professor
Poltava State Medical University
23 Shevchenko Street, Poltava 36000, Ukraine
Tel.: +38 (097) 8214020
E-mail: ye.petrov.2017@gmail.com

INTRODUCTION

During last time significant attention has been paid all over the world to an extremely topical problem, namely, the problem of chronic obstructive pulmonary disease [Feshchenko YuI et al., 2022]. It is noted that prevalence of this pathology is constantly and rapidly growing: according to the forecasts of the World Health Organization experts, the next decade will be marked by an increase in the incidence of this disease by another 30%, if certain preventive measures are not taken [Ilashchuk TO et al., 2021]. Chronic obstructive pulmonary disease is the leading factor in the development of chronic cor pulmonale, and the presence of chronic cor pulmonale is a factor that determines the development of adverse consequences. Besides, according to mortality rates, this disease continues to be the third leading cause of death in the world [Global initiative for chronic obstructive lung disease (GOLD) Global Strategy for Diagnosis, Management and Prevention of COPD. 2020].

Comorbid pathology and, first of all, cardiovascular diseases adversely affect the course of chronic obstructive pulmonary disease. It is also emphasized by the works of recent years [Morgan AD et al., 2018; Trinkmann F et al., 2019]. Besides, in almost of a quarter of cases, the fatal outcome in such patients is caused by cardiovascular causes [Caughey GE et al., 2010]. The analysis of literature data indicates a high frequency of the combination of chronic obstructive pulmonary disease and coronary heart disease, which, depending on the age and duration of the disease, varies from 20 to 60% [Bolotnova TV et al., 2016; Ostroumova OD, Kochetkov AI., 2018]. The high degree of such comorbidity is explained, first of all, by presence of a number of common risk factors and pathogenetic factors, but a certain number of them and possible mechanisms of “mutual burden” need to be clarified [Voynarovs'ka HP, Asanov EO, 2020]. The existing problem, thus, needs a more detailed study of various mechanisms involved in the formation of foregoing comorbid pathology.

The importance of changes in the state of the hemocoagulation link of homeostasis in patients with chronic obstructive pulmonary disease was reflected in number of publications, sometimes contradictory in their results, as we reminded in one of our past works [Petrov YeYe et al., 2021].

The data on changes in the coagulation potential of blood in patients with pathology of the cardiovascular system, particularly coronary heart disease, are well known [Fedotova LA, 2014; Wu W et al., 2016; Pastushyna AI., 2021]. It was noted that in patients with coronary heart disease the presence of significant hypercoagulation was accompanied by depression of the fibrinolysis system, which eventually led to the formation of an imbalance between these components [Fedotova LA et al., 2013] and significantly increased the risk of thrombogenic complication developing. It was noted that the inhibition of both enzymatic and non-enzymatic fibrinolysis was diagnosed in patients with coronary heart disease, which correlated with the severity of the clinical manifestation of the disease [Sokolov YeI et al., 2013]. In our recent work, it was shown the increase of changes in the indicators of the hemostasis system in patients with compensated chronic cor pulmonale of broncho-pulmonary genesis in the case of comorbidity with stable coronary heart disease [Petrov YeYe et al., 2023]. However, in this context, we did not consider the issue of patients with chronic cor pulmonale in the stage of decompensation.

It is known that significant disturbances in lipid metabolism lead to the progressive development of atherosclerosis, play an important role in the formation of coronary heart disease, which was reflected in numerous publications [Dalen JE et al., 2014; Reiner Ž, 2017]. It is also known that lipid metabolism disorders play a significant role in increasing the severity of chronic obstructive pulmonary disease, especially in presence of metabolic syndrome [Poulain M et al., 2008; Treumova SI et al., 2015], including obesity when level of systemic inflammation increases [Savchenko L et al., 2018]. Significant attention is paid to the development of endothelial dysfunction in chronic obstructive pulmonary disease and coronary heart disease [Chekalina NI et al., 2016; Medina-Leyte DJ et al., 2021; Theodorakopoulou MP et al., 2021]. It is noted that endothelial dysfunction is present among the triggering factors on the path to the formation of these pathologies and contributes to their mutual aggravation in the case of comorbidity [Tudorache E et al., 2022].

Despite the fact that the combination of chronic obstructive pulmonary disease and coronary heart

disease is of great interest to a certain number of researches and practitioners, works on the study of hemostasis, lipid metabolism and endothelial function in patients with chronic cor pulmonale in the decompensation stage in combination with coronary heart disease are not numerous. It caused carrying out of this research.

The aim of the study is to investigate and analyze the peculiarities of changes in some indicators of hemostasis system, lipid metabolism and endothelial function and to determine their possible role in the formation of vascular lesions in patients with chronic cor pulmonale of broncho-pulmonary genesis in the decompensation stage and in conditions of a comorbid course with stable coronary heart disease.

MATERIAL AND METHODS

For the solution of this question, indicators of the hemostasis system and lipid metabolism were studied and analyzed in 96 patients with chronic obstructive pulmonary disease and chronic cor pulmonale in the stage of decompensation with signs of circulatory insufficiency of the II stage, among whom 64 patients have comorbid stable coronary heart disease (angina pectoris, functional class II-III, postinfarction or atherosclerotic cardiosclerosis). The diagnoses of chronic obstructive pulmonary disease and stable coronary heart disease were made in accordance with following International recommendations, Ukrainian guidelines and orders of Ministry of Health of Ukraine: Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease, 2020; The order of Ministry of Health of Ukraine N555 dated 27.06. 2013; Adapted clinical guideline: chronic obstructive pulmonary disease, 2020; The order of Ministry of Health of Ukraine N2857 dated 23.12.2021.

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].

In patients with chronic obstructive pulmonary disease and chronic cor pulmonale, the severity of circulatory insufficiency was assessed according to the classification of the Association of Phthisiologists and Pulmonologists of Ukraine (2003): patients

are grouped according to the presence of insufficiency manifestations only in the systemic circulation.

The number of males was 62 (64,6%) and females – 34 (35,4%), the mean age was $58,6 \pm 2,2$ years. All the patients were divided into 2 groups: the main group (chronic cor pulmonale combined with coronary heart disease) and comparative group (chronic cor pulmonale). The representatives of the both groups were of the same sex, age and duration of the disease. Endothelial function indicators were studied and analyzed in 32 patients of the main group and 10 patients of the comparative group (identical sex-age structure). The carrying out treatment of both chronic cor pulmonale of broncho-pulmonary genesis and coronary heart disease met the requirements of the protocol.

Evaluation of the vascular-platelet and plasma components of hemostasis was determined by the number of platelets, indicators of thrombin time, prothrombin time, antithrombin-III, tolerance plasma to heparin, plasmin lysis, fibrinogen, soluble fibrin.

The blood lipid spectrum was studied by total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, their ratio, and triglycerides.

The endothelial function was assessed by the spectrophotometric method based on the total content of nitrogen oxide metabolites in blood serum (Total NO, RL-system (USA)) and endothelin-1 by the immunoenzymatic method (BIG Endothelin-1 (HUMAN) Peninsula Laboratories inc. Division of Bachem).

The obtained research results in the patients of the main and comparative groups were compared between themselves and also with the indices of practically healthy individuals ($n=15$) who were of the same sex and age.

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.

RESULTS AND DISCUSSION

The results of the carried out study revealed (Figure 1) changes in all analyzed indicators of hemostasis in patients with chronic cor pulmonale

of broncho-pulmonary genesis in decompensation stage. Thus, compared to practically healthy individuals, there was significant increase of thrombin time (23.2 ± 0.9 to 14.6 ± 0.8 s), fibrinogen content (5.6 ± 0.4 g/l to 2.4 ± 0.2 g/l) ($p < 0.001$ in both cases). Significant ($p < 0.05$) increase in the content of soluble fibrin (SF) – to 1.2 ± 0.2 conditional units (control group – 0.52 ± 0.02 conditional units) and the number of platelets, $10^9/l$ (320.0 ± 13.0 to 270.0 ± 10.0 , $p < 0.05$), significant decrease in plasma tolerance to heparin (240.0 ± 3.2 s to 360.0 ± 12.0 s, $p < 0.001$) and antithrombin III (17.2 ± 0.5 % to 20.9 ± 0.4 %, $p < 0.001$) was also observed. At the same time only a trend towards an increase in prothrombin time and plasmin lysis was noted. The detected changes in the analyzed indicators of blood coagulation of patients with chronic cor pulmonale of broncho-pulmonary genesis in the stage of decompensation generally reflected the presence of a significantly increased thrombogenic potential of the hemostasis system.

The changes in the indicators of the hemostasis system in patients with chronic cor pulmonale in the stage of decompensation with comorbid coronary heart disease were more significant. While among significantly increased (compared to practically healthy individuals) there were also thrombin time – 2.1 times (30.0 ± 1.4 s), the content of fibrinogen – 3.5 times (8.4 ± 0.6 g/l), the amount of platelets, $10^9/l$ (390.0 ± 4.0) and, in contrast to patients with isolated chronic cor pulmonale, plasmin lysis (270.0 ± 13.0 s) and prothrombin time (34.4 ± 0.6 s) – 2.1 times ($p < 0.001$ in all cases). There was also a significant (by 2.1 times) decrease in plasma tolerance to heparin (170.0 ± 3.0 s) and antithrombin III (by 1.9 times – to 11.0 ± 0.6 %) ($p < 0.001$ in all cases) and, at the same time, a fivefold increase in the content of soluble fibrin (2.6 ± 0.3 conditional units, $p < 0.002$), which indicated the activation of intermediate links of thrombus formation. It should be emphasized that in patients with comorbid pathology in comparison with patients of comparative group the following indicators were significantly increased: prothrombin time (2.0 times, $p < 0.001$), plasmin lysis (2.0 times, $p < 0.001$), platelets count (1.2 times, $p < 0.001$), soluble fibrin (2.2 times, $p < 0.002$), thrombin time (1.3 times, $p < 0.002$), the content of fibrinogen (1.5 times, $p < 0.002$). Plasma tolerance to heparin was

1.4 times as little as among patients of comparative group ($p < 0.001$), and antithrombin III was 1.6 times as little as among patients of comparative group ($p < 0.001$).

The obtained results indicated the presence of a significant increase of coagulation potential (the changes of indices of platelets, fibrinogen, plasma tolerance to heparin, antithrombin III, and SF) and activation of fibrinolysis system (thrombin time) and, simultaneous, its more pronounced depression (plasmin lysis) and increase of prothrombin time in case of presence of comorbid coronary heart disease in the patients with chronic cor pulmonale (decompensation stage) in conditions of chronic inflammatory process. Comorbidity promoted the formation of disbalance of systemic correlation hemocoagulation and fibrinolysis. Our results confirm to a certain extent the following ideas of scientists: there are hypercoagulation and “exhaustion of the anticoagulant system potential” in case of combination of coronary heart disease and chronic obstructive pulmonary disease [Malchevska TY, 2015]; hypercoagulation together with the oxidative stress and chronic systemic inflammation are general pathogenic mechanisms of chronic obstructive pulmonary disease and cardiovascular diseases, particularly of the coronary heart disease [Austin V et al., 2016; Zirlik A et al., 2017]. It is certainly reflected in the case of their comorbid course as an important component of the “syndrome of mutual burden”.

The results of the study showed (Figure 2) an increase in the content of triglycerides, to a greater extent – in total cholesterol, LDL cholesterol and LDL cholesterol/ HDL cholesterol ratio in patients with chronic cor pulmonale of broncho-pulmonary genesis in decompensation stage in comparison with practically healthy individuals. But all these changes were not significant and had the nature of a trend. And only the content of HDL cholesterol was significantly reduced (by 1.2 times, $p < 0.001$).

On the other hand, changes in lipid metabolism indicators in patients with chronic cor pulmonale in the stage of decompensation with comorbid coronary heart disease were more significant – the cholesterol content was 7.6 ± 0.5 mmol/l, LDL cholesterol – 6.5 ± 0.4 mmol/l. They were, accordingly, 1.8 times ($p < 0.01$) and 2.0 times ($p < 0.002$) as large as among practically healthy individuals,

and exceeded the same indicators of comparative group by 1.4 ($p<0.01$) and 1.6 ($p<0.001$) times. In addition, in the patients of the main group there was a significant decrease in the content of HDL cholesterol (1.0 ± 0.02 mmol/l) – 1.8 times as little as among practically healthy individuals ($p<0.001$) and 1.5 times as little as among comparative group (1.5 ± 0.02 mmol/l, $p<0.001$).

In contrast to patients with decompensated chronic cor pulmonale of broncho-pulmonary genesis, whose LDL cholesterol/ HDL cholesterol ratio (2.2 ± 0.2) had only a tendency to increase compared to practically healthy individuals (1.7 ± 0.3), LDL cholesterol/ HDL cholesterol ratio in patients of the main group was increased by 3.8 times (6.5 ± 0.2) compared to control group and by 2.5 times ($p<0.001$) – compared to patients of the comparative group. It quantitatively and qualitatively reflected proatherogenic direction of changes in lipid metabolism. The level of triglycerides in patients of the main group also was significantly increased in comparison with the comparative group ($p<0.001$).

As mentioned above, significant lipid metabolism disorders play an important role in the development of atherosclerosis and coronary heart disease. Particularly, LDL cholesterol, especially its oxidized forms, inhibits the expression of endothelial nitroxide synthase, reducing the level of nitric oxide [Kazakov YuM et al., 2016]. Experimental and clinical studies showed that endothelial dysfunction in the presence of hyperlipidemia precedes the development of intimal damage, i.e. endothelial dysfunction occurs much earlier than atherosclerotic vascular damage [Kazakov YuM et al., 2016]. In this sense, the fact that there are correlations between indicators of the blood lipid spectrum (particularly, LDL cholesterol and total cholesterol) and endothelial function is also indicative [Kolomiyets VV et al., 2006].

And what did the indicators of endothelial function “look like” in patients with chronic cor pulmonale in decompensation stage, and what was the impact of comorbid coronary heart disease? We had to find out later.

Results of our subsequent study of the total content of nitroxide metabolites in the blood showed their significant decrease in both patients of comparative group (21.2 ± 1.0 mcmol/l) and patients

with comorbid pathology (12.2 ± 0.8 mcmol/l) in comparison with practically healthy individuals (35.3 ± 2.8 mcmol/l) (accordingly, $p<0.01$ and $p<0.001$). Besides, the content of nitroxide in patients of the main group was 1.7 times as little as in patients of the comparative group ($p<0.001$).

On the other hand, the direction of change in the content of endothelin-1 was the opposite – its highest value was observed in patients with chronic cor pulmonale of broncho-pulmonary genesis in the stage of decompensation with comorbid coronary heart disease (8.2 ± 0.2 pmol/l), which is 1.6 times ($p<0.001$) exceeded this indicator of the comparative group’s patients (5.2 ± 0.3 pmol/l) and by 2.2 times ($p<0.001$) – the indicator of practically healthy individuals (3.8 ± 0.5 pmol/l).

The detected changes in endothelial function indicators (decrease in nitrogen oxide content and increase in endothelin-1) in patients with decompensated chronic cor pulmonale of broncho-pulmonary genesis reflected a violation of the regulatory function of the endothelium and evidenced their greatest expressiveness in patients with a comorbid course of chronic cor pulmonale with coronary heart disease. We would like emphasize once more that endothelial dysfunction is not only an important pathogenetic link in the development of coronary heart disease, but also in development of chronic obstructive pulmonary disease [Lemko OI, Vantyukh NV, 2017; Polverino F et al., 2017].

Thus, taking into account the above, the statement of the greatest expressiveness of changes in hemostasis system and unfavourable in lipid metabolism and endothelial function in patients with comorbid pathology, in our opinion, is fully justified. It allows us to draw the following conclusions.

CONCLUSION

The analysis of the changes of the hemostasis system indices in patients with chronic cor pulmonale of broncho-pulmonary genesis in decompensation stage indicates the presence of an increase of coagulation potential; the most significant changes with suppression of fibrinolytic activity are typical of the patients with comorbid coronary heart disease.

The direction of changes in lipid metabolism in patients with chronic cor pulmonale of broncho-pulmonary genesis in stage of decompensation re-

flects generally their proatherogenic orientation, the changes are combined with significant violations of the regulatory function of the endothelium, and the greatest expressiveness of such changes is typical of patients with comorbid coronary heart disease.

The nature and direction of changes in the hemostasis system, lipid metabolism and endothelial function in the patients with decompensated chronic cor pulmonale of broncho-pulmonary gen-

esis should be considered as markers of the unfavorable development of vascular sclerosis and increased risk of the thrombogenic vascular complications, which must be taken into account during forming of medical-diagnostic strategy (both in the isolated course of chronic cor pulmonale and in the conditions of comorbidity with coronary heart disease).

REFERENCES

1. Austin V, Crack PJ, Bozinovski S, Miller AA, Vlahos R (2016). COPD and stroke: are systemic inflammation and oxidative stress the missing links? *Clin Sci (Lond)* 2016; 130:1039-50. doi: 10.1042/CS20160043
2. Bolotnova TV, Okonechnikova NS, Andreyeva OV, et al (2016). [Clinical peculiarities of ischemic heart disease and arterial hypertension in conditions of comorbidity with chronic obstructive pulmonary disease in elderly patients] [Published in Russian]. *Meditinskaya nauka i obrazovaniye Urala*. 2016; 17 (4): 5-9
3. Caughey GE, Ramsay EN, Vitry AI, Gilbert AL, Luszc MA, Ryan P, et al (2010). Comorbid chronic diseases, discordant impact on mortality in older people: a 14-year longitudinal population study. *J Epidemiol Community Health*. 2010 Dec; 64(12):1036-1042. doi: 10.1136/jech.2009.088260
4. Chekalina NI, Kazakov YM, Mamontova TV, Vesnina LE, Kaidashev IP (2016). Resveratrol more effectively than quercetin reduces endothelium degeneration and level of necrosis factor α in patients with coronary artery disease. *Wiad Lek*. 2016; 69(3 pt 2):475-479
5. Dalen JE, Alpert JS, Goldberg RJ, Weinstein RS (2014). The epidemic of the 20(th) century: coronary heart disease. *Am J Med*. 2014 Sep;127(9):807-812. doi: 10.1016/j.amjmed.2014.04.015.
6. Fedotova LA, Zorin VN, Plastun MYu (2013). [Haemostasis and fibrinolysis in ischemic heart disease and hypertension] [Published in Russian]. *Tavrisheskiy mediko-biologicheskiy vestnik*. 2013; 4 (64):183-186.
7. Fedotova LA (2014). [Functional activity of hemostasis and fibrinolysis in patients with ischemic heart disease in the course of cardiocyte protective therapy] [Published in Russian]. *Circulation and hemostasis*. 2014; 1/2: 110-114.
8. Feshchenko YuI, Ostrovs'kyy MM, Makoyda IYa (2022). [Modification of clinical course of chronic obstructive pulmonary disease: a myth or essential reality of present?] [Published in Ukrainian]. *Ukr Pulmon Zh*. 2022; 30 (1): 47-51. doi: 10.31215/2306-4927-2022-30-1-47-51
9. Gavrysiuk VK (2007). [Chronic cor pulmonale: mechanisms of pathogenesis and principles of the therapy] [Published in Russian]. *Ukrainian Pulmonological Journal*. 2007; 1: 9-10.
10. Global initiative for chronic obstructive lung disease (GOLD) Global Strategy for Diagnosis, Management and Prevention of COPD. 2020 Available from: <https://goldcopd.org/wp-content/uploads/2019/11/GOLD-2020-REPORT-ver1.0wms.pdf>
11. Ilashchuk TO, Mykytyuk OP, Chobanu YaV(2021). [The peculiarities of the combined course of chronic obstructive pulmonary disease and coronary heart disease (Literature review)] [Published in Ukrainian]. *Klinichna ta eksperymental'na patolohiya*. 2021; 2 (76): 96-104. doi:10.24061/1727-4338.XX.2.76.2021.14
12. Kazakov YuM, Treumova SI, Petrov YeYe (2016). [The role of endothelial dysfunction in the development of chronic cor pulmonale] [Published in Ukrainian]. *Poltava: TOV «Firma«Tekhservis»*; 2016. 146 p.
13. Kolomiyets VV, Vankhanen NV, Bobrova YeV, Bekker PF, Sulayeva TA (2006). [The effect of atorvastatin on endothelial function in patients with ischemic heart disease and arterial hypertension] [Published in Russian]. *Ukrainian Journal of Cardiology*. 2006; 3:83-87
14. Medina-Leyte DJ, Zepeda-García O, Domínguez-Pérez M, González-Garrido A, Villarreal-Molina T, Jacobo-Albavera L (2021). Endothelial Dysfunction, Inflammation and Coronary Artery Disease: Potential Biomarkers and Promising Therapeutical Approaches. *Int J*

- Mol Sci.* 2021; 22(8): 3850. doi:org/10.3390/ijms22083850
15. Morgan AD, Zakeri R, Quint JK (2018). Defining the relationship between COPD and CVD: what are the implications for clinical practice? *Ther Adv Respir Dis.* 2018; 12: 1-16. doi: 10.1177/1753465817750524
 16. Ostroumova OD, Kochetkov AI (2018). [Chronic obstructive pulmonary disease and comorbid cardiovascular disease: in the context of guidelines] [Published in Russian]. *Consilium Medicum.* 2018; 20 (1): 54–61. doi: 10.26442/2075-1753_2018.1.54-61
 17. Pastushyna AI (2021). [Activity of coagulation processes with comorbid hypertension and coronary heart disease] [Published in Ukrainian]. *Liky Ukrayiny.* 2021; 5(251): 35–38. doi: 10.37987/1997-9894.2021.5(251).238140
 18. Petrov YeYe, Burmak YuG, Treumova SI, Ivanyts'ka TA (2021). [Comparative characteristics of some hemostasis system indices in the patients with compensated chronic cor pulmonale of broncho-pulmonary genesis and in conditions of its comorbidity with hypertensive disease] [Published in Ukrainian]. *Bulletin of Problems in Biology and Medicine.* 2021;1(159):109- 112. doi: 10.29254/2077-4214-2021-1-159-109-112
 19. Petrov YeYe, Burmak YuH, Ivanytska TA, Pogoryelova IA, Nyemchenko LB (2023). [Characteristics of Some Hemostasis System Indices in Patients with Compensated Chronic Cor Pulmonale of Broncho-Pulmonary Genesis and Peculiarities of Their Changes in Conditions of Comorbidity with Stable Coronary Heart Disease] [Published in Ukrainian]. *Ukrainian Journal of Medicine, Biology and Sport.* 2023; 8 (1): 140-145. doi: 10.26693/jmbs08.01.140
 20. Poulain M, Doucet M, Drapeau V, Fournier G, Tremblay A, Poirier P, et al (2008). Metabolic and inflammatory profile in obese patients with chronic obstructive pulmonary disease. *Chron Respir Dis.* 2008; 5(1):35-41. doi: 10.1177/1479972307087205.
 21. Reiner Ž (2017). Hypertriglyceridaemia and risk of coronary artery disease. *Nat Rev Cardiol.* 2017 Jul; 14 (7): 401–411. doi: 10.1038/nrcardio.2017.31.
 22. Roytberg GY, Strutyncky AV (2003). [Internal diseases. Cardio-vascular system] [Published in Russian]. Moscow: Binom; 2003. 865 p.
 23. Savchenko L, Mykytiuk M, Cinato M, Tronchere H, Kunduzova O, Kaidashev I (2018). IL-26 in the induced sputum is associated with the level of systemic inflammation, lung functions and body weight in COPD patients. *Int J Chron Obstruct Pulmon Dis.* 2018 Aug 24; 13:2569-2575. doi: 10.2147/COPD.S164833.
 24. Sokolov YeI, Grishina TI, Shtin SR (2013). [The effect of von Willebrandt factor and endothelin-1 on the formation of thrombotic status in ischemic heart disease] [Published in Russian]. *Kardiologiya.* 2013; 53 (3): 25-30.
 25. Theodorakopoulou MP, Alexandrou ME, Bakaloudi DR, Pitsiou G, Stanopoulos I, Kontakiotis T, Boutou AK (2021). Endothelial dysfunction in COPD: a systematic review and meta-analysis of studies using different functional assessment methods. *ERJ Open Res.* 2021 Jun 28;7(2):00983-2020. doi: 10.1183/23120541.00983-2020
 26. Treumova SI, Petrov YeYe, Boryak VP (2015). [Clinical-laboratory peculiarities of the course of chronic obstructive pulmonary disease in combination with coronary heart disease on the background of metabolic syndrome] [Published in Ukrainian]. *Visnyk problem biolohiyi i medytyny.* 2015;1(3):218-222
 27. Trinkmann F, Saur J, Borggreffe M, Akin I (2019). Cardiovascular Comorbidities in Chronic Obstructive Pulmonary Disease (COPD)—Current Considerations for Clinical Practice. *J Clin Med.* 2019 Jan 10; 8 (1):69. doi:10.3390/jcm8010069
 28. Tudorache E, Fira-Mladinescu O, Traila D, Marc M, Rajnoveanu RM, Tofolean DE, Fildan AP (2021). Endothelial dysfunction: The possible link between cardiovascular comorbidities and phenomenon of inflammaging from COPD. *Medicine (Baltimore).* 2022 Aug 19;101(33): e30078. doi: 10.1097/MD.00000000000030078
 29. Voynarova'ska HP, Asanov EO (2020). [Ischemic heart disease and chronic obstructive pulmonary disease: actual problem of comorbidity in internal medicine] [Published in Ukrainian]. *Scientific Journal «ScienceRise: Medical Science».* 2020; 3(36):20-24. doi: 10.15587/2519-4798.2020.203968
 30. Wu W, Liu R, Chen L, Chen H, Zhang S (2016). Disequilibrium of Blood Coagulation and Fibrinolytic System in Patients with Coronary Artery Ectasia. *Medicine (Baltimore).* 2016 Feb; 95 (8): 2779. doi: 10.1097/MD.0000000000002779
 31. Zirlik A, Bode Ch, Gawaz M (2017). Platelets, Haemostasis and Inflammation. Springer; 2017. 300 p. doi: 10.1007/9783-319-66224-4



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Armen A. **MURADYAN**

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU

(+37493 588697 Editor-in-Chief

Fax: (+37410) 582532

E-mail: namj.ysmu@gmail.com, ysmiu@mail.ru

URL: <http://www.ysmu.am>

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