DOI: https://doi.org/10.30841/2786-720X.1.2026.353785
UDC 616.151.5-02:[616.24-007.272-06:617.37-002.2

Hemostasis system disorders on the background of external respiratory function in the comorbid course of chronic obstructive pulmonary disease and chronic pancreatitis

I. V. Dudka
Bukovinian State Medical University, Chernivtsi

The comorbidity course of chronic obstructive pulmonary disease (COPD) and chronic pancreatitis (CP) can exacerbate the clinical manifestations of both diseases and increases the frequency of relapses of the pathological process due to disturbances of hemocoagulation.
The objective: **to establish the features of the external respiratory function and the state of selected hemostasis factors and fibrinolytic activity in patients with COPD and concomitant CP.**
Materials and methods**. 144 patients with COPD and CP were examined. The external respiratory function, total coagulation potential of blood plasma, enzymatic and non-enzymatic fibrinolysis, total fibrinolytic activity were investigated.**
Results**. CP contributes to the progression of bronchial obstructive syndrome with a maximum reduction in forced expiratory volume in the first second compared to the normal values (1.4 times, $p < 0.05$) and vital capacity (1.2 times, $p < 0.05$) observed in patients with comorbid COPD and CP. The prothrombin time was significantly shortened in all patient groups compared with the practically healthy individuals (PHI): in patients of group 1 – by 20.1%, in group 2 – by 26.3%, in group 3 – by 38.8% ($p_{1-3} < 0.05$). Plasma concentration of fibrinogen was significantly reduced across all patient groups in group 1 – by 12.3%, in group 2 – by 18.6%, in group 3 – by 29.2% ($p_{1-3} < 0.05$). Thrombin time was also reduced in all groups of patients with the greatest decline in group 3 – by 36.3% ($p < 0.05$) compared with group of PHI. Activation of systemic proteolysis was confirmed by changes in the activity of antithrombin III (AT III), the activity of which in patients of group 3 was reduced compared to the normative values by 29% ($p < 0.05$). Plasma total fibrinolytic activity in patients of all groups was significantly lower than the control indicators: in group 1 – by 12.8%, in group 2 – by 14.3% and in group 3 – by 21.7% ($p_{1-3} < 0.05$). The activity of Hageman-factor-dependent fibrinolysis (HFDF) was decreased in all groups: in group 1 – by 1.6 times, in group 2 – by 1.7 times, in group 3 – by 1.8 times ($p_{1-3} < 0.05$) compared with PHI with no significant difference between patient groups ($p > 0.05$). The activity of blood coagulation factor XIII in patients of group 1 was decreased by 24.3%, in group 2 – by 20.1%, in group 3 – by 32.6% ($p_{1-3} < 0.05$). In COPD patients with comorbid CP exacerbation, a significant decrease in plasminogen activity was found: in patients of group 1 – by 21.9%, in group 2 – by 32.2%, and in group 3 – by 42.6%, respectively ($p_{1-3} < 0.05$).**
Conclusions**. The factors that worse the course of CP with hypoxia caused by COPD include a decrease in AT III activity by 29%; a decrease in enzymatic fibrinolytic activity by 21.7% and a decrease in HFDF activity by 1.8 times compared to normal values. Suppression of the anticoagulant potential of blood (decrease in AT III activity and blood coagulation factor XIII), decreased overall fibrinolytic activity due to inhibition HFDF and enzymatic fibrinolysis, a compensatory increase in the activity of non-enzymatic fibrinolysis and an increase in the proteolytic activity of blood plasma indicate the formation of a hypercoagulable syndrome, which is aggravated by dysfunction of external respiration in patients with CP and comorbid COPD. This leads to disorders in microcirculation processes in the pancreas in patients with COPD, which is one of the risk factors for exacerbation of CP.**
Keywords: *chronic obstructive pulmonary disease, chronic pancreatitis, hemocoagulation, fibrinolysis, fibrinogen, prothrombin time, antithrombin III.*

Розлади системи гемостазу на тлі порушення функції зовнішнього дихання при коморбідному перебігу хронічного обструктивного захворювання легень та хронічного панкреатиту

І. В. Дудка

Коморбідний перебіг хронічного обструктивного захворювання легень (ХОЗЛ) і хронічного панкреатиту (ХП) може посилювати клінічну симптоматику обох захворювань і призводити до частих рецидивів патологічного процесу внаслідок змін у системі гемокоагуляції.
Мета дослідження: визначення особливостей функції зовнішнього дихання та стану окремих факторів гемостазу й фібринолітичної активності у хворих на ХОЗЛ із супутнім ХП.
Матеріали та методи. Обстежено 144 хворих на ХОЗЛ та ХП. Досліджували функцію зовнішнього дихання, загальний коагуляційний потенціал плазми крові, стан ферментативного та неферментативного фібринолізу, загальну фібринолітичну активність.
Результати. ХП зумовлює розвиток бронхообструктивного синдрому, при цьому максимальні показники зниження об'єму форсованого видиху за першу секунду порівняно з належними значеннями (в 1,4 раза, $p < 0,05$) та життєвої

ємності легень (в 1,2 раза, $p < 0,05$) спостерігаються у хворих із коморбідним перебігом ХОЗЛ і ХП. Протромбіновий час достовірно знижувався в усіх групах спостереження порівняно з показниками практично здорових осіб (ПЗО): у хворих 1-ї групи – на 20,1%, 2-ї групи – на 26,3%, 3-ї групи – на 38,8% ($p_{1-3} < 0,05$). Вміст фібриногену в крові був достовірно знижений у хворих усіх груп: у 1-й групі – на 12,3%, у 2-й групі – на 18,6%, у 3-й групі – на 29,2% ($p_{1-3} < 0,05$). Встановлено зниження тромбінового часу в усіх групах хворих, при цьому найбільше зниження відмічалося у пацієнтів 3-ї групи – на 36,3% ($p < 0,05$) порівняно з групою ПЗО. Активацію системного протеолізу підтверджували зміни активності антитромбіну III (АТ III), активність якого у хворих 3-ї групи була знижена порівняно з нормативними значеннями на 29% ($p < 0,05$). Сумарна фібринолітична активність плазми крові пацієнтів усіх груп була достовірно нижчою за контрольні показники: у 1-й групі – на 12,8%, у 2-й групі – на 14,3%, у 3-й групі – на 21,7% ($p_{1-3} < 0,05$). Активність Хагеман-залежного фібринолізу (ХЗФ) знижувалася в усіх групах: у 1-й групі – в 1,6 раза, у 2-й групі – в 1,7 раза, у 3-й групі – в 1,8 раза ($p_{1-3} < 0,05$) порівняно з ПЗО, без вірогідної різниці між групами ($p > 0,05$). Активність фактора згортання крові XIII у хворих 1-ї групи знизилася на 24,3%, 2-ї групи – на 20,1%, 3-ї групи – на 32,6% ($p_{1-3} < 0,05$). У хворих на ХОЗЛ із супутнім ХП відзначалося достовірне зниження потенційної активності плазміногену: у 1-й групі – на 21,9%, у 2-й групі – на 32,2%, у 3-й групі – на 42,6% відповідно ($p_{1-3} < 0,05$).
Висновки. До факторів, що погіршують перебіг ХП у пацієнтів із гіпоксією, спричиненою ХОЗЛ, належать зниження активності АТ III на 29%; зниження ферментативної фібринолітичної активності на 21,7% та зниження активності ХЗФ в 1,8 раза відносно норми. Пригнічення антикоагулянтного потенціалу крові (зниження активності АТ III та фактора згортання крові XIII), зниження загальної фібринолітичної активності плазми крові внаслідок пригнічення ХЗФ та ферментативного фібринолізу, компенсаторне підвищення активності неферментативного фібринолізу й зростання протеолітичної активності плазми крові свідчать про формування гіперкоагуляційного синдрому, який посилюється внаслідок дисфункції зовнішнього дихання у пацієнтів із ХП і коморбідним ХОЗЛ. Це призводить до порушень процесів мікроциркуляції в підшлунковій залозі у пацієнтів із ХОЗЛ, що є одним із факторів ризику загострення ХП.
Ключові слова: *хронічне обструктивне захворювання легень, хронічний панкреатит, гемокоагуляція, фібриноліз, фібриноген, протромбіновий час, антитромбін III.*

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung disorder characterized by chronic respiratory symptoms (dyspnea, cough, expectoration), due to airways inflammation (bronchitis and bronchiolitis) and/or alveoli pathology (emphysema) that cause persistent and frequent progressive airflow obstruction. COPD is one of the most important causes of global morbidity and mortality, which leads to significant economic, social, and healthcare burdens, resulted in 3.5 million deaths in 2021, approximately 5% of all global deaths, according to the World Health Organization data [1, 2]. This problem becomes especially important in case of presence of other comorbid chronic diseases in patients with COPD, which are also characterized by progressive course and systemic inflammatory reactions, as, for example, chronic pancreatitis (CP) [3–5].

CP is a progressive inflammatory disease characterized by irreversible damage to the pancreatic tissue, destroying exocrine and endocrine function. Over time pancreatic parenchyma is replaced by fibrotic tissue, leading to severe abdominal pain, malabsorption, and diabetes mellitus [6]. Inflammatory mediators play a leading role in the pathogenesis of exacerbation of chronic diseases. The system of immunoregulation in these patients is characterized by elevated levels of acute phase reactants – C-reactive protein, ceruloplasmin, ferritin, haptoglobin, fibrinogen and others [7, 8]. The increase in these proteins reflects the activation of pathological process inherent in both COPD exacerbation and CP, ultimately leading to tissues and organs damage [3, 9].

Furthermore, the literature data describe quite various disorders of blood coagulation on the background of systemic inflammation and endothelium dysfunction in pancreatic diseases (decrease of antithrombin III (AT III) activity, increase of D-dimer level [10, 11], tendency to vascular thrombosis [12, 13]) as well as in COPD (decrease in prothrombin and AT III activity, a fibrinogen's level increase, an increase in plasma tolerance to heparin, a decrease in blood fibrinolytic activity, an increase activated partial thromboplastin time [14–17]).

It can be expected that the comorbid course of COPD and CP can worsen clinical symptoms of both diseases [18] and lead to frequent exacerbations of the pathological process due to changes in hemocoagulation. In patients with COPD due to hypoxia, accumulation of free radicals, toxic substances that contribute to the release of biologically active substances in the systemic circulation, increase in the total coagulation potential of the blood is observed [19], which is compensated by an increase in the activity of non-enzymatic fibrinolysis. We hypothesized that these disorders will significantly affect the course of concomitant CP and, presumably, can contribute to some mechanisms of progression of comorbid diseases. That is why the aim of our study was to determine the interconnections between computer spirography indicators with hemostasis and fibrinolytic activity parameters.

The objective: to establish the features of the external respiratory function and the state of selected hemostasis factors and fibrinolytic activity in patients with COPD and concomitant CP.

MATERIALS AND METHODS

144 patients were examined, including 50 patients with an isolated course of COPD, GOLD 2, group E in the exacerbation phase (group 1), 49 patients with an isolated course of CP of mixed etiology with moderate severity exacerbation (group 2), 45 patients with COPD, GOLD 2, group E with accompanying CP of mixed etiology in exacerbation phase of moderate severity (group 3). The mean age of the patients was 52.2 ± 4.3 years. The control group consisted of 30 practically healthy individuals (PHI) of the appropriate age and gender.

The diagnosis of CP was made according to the unified clinical protocol approved by the Order of the Ministry of Health (MoH) of Ukraine No. 638 of September 10, 2014 "On the approval and implementation of medical and tech-

nological documents on the standardization of medical treatment for chronic pancreatitis" on the basis of classic clinical, ultrasonographic, biochemical methods, taking into account the Order of the MoH of Ukraine No. 1204 dated July 4, 2023 "On approval of the Unified clinical protocol of primary and specialized medical care "Chronic pancreatitis"" [20, 21]. The degree of pancreatic exocrine insufficiency was studied according to the Pancreatic Exocrine Insufficiency Questionnaire (2018) [22].

Diagnosis and treatment of COPD was prescribed in accordance with the national clinical guidelines (Order of the MoH of Ukraine No. 555 dated 06.27.2013, taking into account the Evidence-Based Adapted Clinical Guidelines for Chronic Obstructive Pulmonary Disease, 2020). Belonging to groups A, B, E of patients with COPD was assessed according to the COPD severity assessment scale according to ABE (GOLD 2023) [23, 24].

The duration of the disease in patients with COPD without concomitant CP was 9.36 ± 0.32 years in average. In patients in the group with concomitant CP, the average duration of COPD was 10.22 ± 0.31 years, which was practically no different from the duration of the disease in the group of patients without concomitant CP ($p > 0.05$). The average duration of CP at the beginning of the study was 5.46 ± 0.28 years. The average smoking history of the examined patients was 12.4 ± 4.6 years.

In accordance with clinical recommendations, combined treatment with inhaled β-adrenomimetics, anticholinergics and glucocorticoids were used in an individually selected dose for COPD control achievement. Patients with CP received analgesics, spasmolytics and pancreatic enzyme replacement therapy in accordance with clinical recommendations.

Inclusion criteria for the study: adult female and male patients, diagnosed with COPD (GOLD 2, 3, group E) in the exacerbation (group 1), CP of mixed etiology in the exacerbation phase of moderate severity (group 2), comorbid COPD and CP with the same characteristics (group 3). All participants were informed about the study plan and signed an informed consent; the study protocol was approved by the Biomedical Ethics Commission of the Bukovinian State Medical University of the MoH of Ukraine (Protocol No. 8).

The exclusion criteria for patients from the study were: acute phase or exacerbation of other chronic diseases, sub- and decompensation of vital organs, including acute myocardial infarction and unstable ischemic heart disease, acute surgical conditions and surgical interventions less than a month ago, abdominal aortic aneurysm, viral hepatitis in the active phase and cirrhosis, renal failure, oncological and hematological diseases, pregnancy, mental disorders.

To study the external respiration function computer spirography was performed on Microlab 3300 spirometer (Sensor-Medics, the Netherlands) and bronchodilator reversibility testing was performed by use of salbutamol and ipratropium bromide inhalations.

The total coagulation potential of blood (prothrombin time (PTT), thrombin time (TT)), plasma total fibrinolytic activity (TFA), enzymatic fibrinolytic activity (EFA) and non-enzymatic fibrinolytic activity (NFA) in blood plasma, the Hageman-factor-dependent fibrinolysis (HFDF), the potential activity of plasminogen (PAP), the level of fibrinogen in blood plasma, the activity of AT III, and the activity of factor XIII (fibrin-stabilizing factor) were carried out using standard methods by sets of reagents from Danysh LTD (Lviv) [25].

Statistical analysis of the obtained results was performed according to the type of types of data that were obtained. The normality of the distribution was checked using the Liliefors, Shapiro–Wilk tests and the method of direct visual assessment of histograms of the distribution of eigenvalues. Quantitative measures that had a normal distribution are presented as mean (M) ± standard deviation (SD). Discrete values are presented in the form of absolute and relative frequencies (percentage of observations to the total number of examinees). Parametric tests with Student's t-test or Fisher's F-test were used to compare data that had a normal distribution. A difference of $p < 0.05$ was considered statistically significant. To assess the degree of dependence between variables, Pearson's correlation analysis was used in the case of a parametric distribution and Spearman's rank correlation coefficient in the case of a distribution of indicators that probably differed from normal. Statistical and graphical analysis of the obtained results was carried out using software packages StatSoft STATISTICA 10.0.1011 Enterprise edition (StatSoft Inc., USA), Microsoft Excel 2007 (Microsoft, USA).

RESULTS AND DISCUSSION

The analysis of our study findings shows that in patients with COPD in the exacerbation phase without comorbid pathology, as well as with comorbid CP, the significant disorders in spirometric indicators are presented (Fig. 1, 2). The obtained data on respiratory function correspond to the stage of COPD in group E: a reduction in forced expiratory volume in the first second (FEV_1) to 50–80% of the predicted value. At the same time, a certain pattern of decreasing FEV_1 was observed. In particular, in patients with COPD the mean post-bronchodilator FEV_1 was 74.2% of the predicted value which was 1.2 times lower than in PHI ($p < 0.05$), in patients with both COPD and CP FEV_1 was 1.4 times lower than in PHI ($p < 0.05$) corresponding to 67.2% of the predicted value. To the contrast in patients with isolated CP the FEV_1 differed from the PHI only by 1.1% ($p < 0.05$) (Fig. 1). The results of the vital capacity (VC) study in patients with a combined course of COPD and CP indicated a significant decrease in patients of group 3 – by 1.2 times ($p < 0.05$), while in patients of groups 1 and 2 the indicator has only a tendency to decrease (Fig. 2).

The analysis of the 2nd phase of coagulation hemostasis showed that PTT was significantly decreased in all patient groups. The maximum decline in the indices was observed in patients of group 3 – by 38.8% compared with PHI ($p < 0.05$); in patients of group 1 PTT decreased by 20.1% compared with PHI ($p < 0.05$); and in patients of group 2 there was a decrease of PTT by 26.3% ($p < 0.05$) (Fig. 3). Evaluation of the 3rd phase of coagulation hemostasis demonstrated a significant decrease of fibrinogen level in the blood of all study patients: in patients of group 1 – by 12.3%, in group 2 – by 18.6%, in group 3 – by 29.2% compared with PHI with significant intergroup differences ($p < 0.05$) (Fig. 4).

FAMILY MEDICINE. EUROPEAN PRACTICES / СІМЕЙНА МЕДИЦИНА. ЄВРОПЕЙСЬКІ ПРАКТИКИ •
ISSN 2786-7218 (Online) | ISSN 2786-720X (Print)
№1 (115)/2026

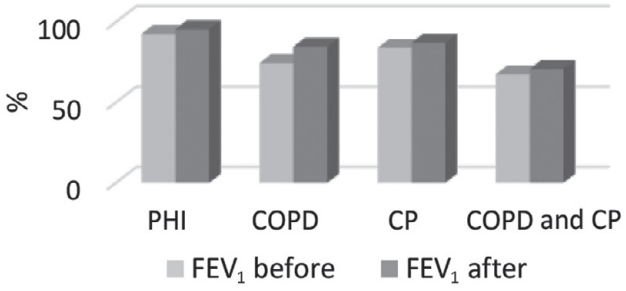

Fig. 1. FEV_1 before and after inhalation of salbutamol
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis; FEV_1 – forced expiratory volume in the first second.

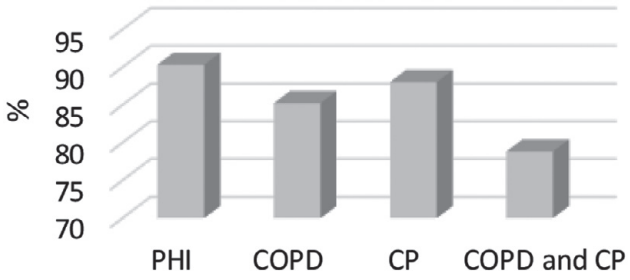

Fig. 2. Vital capacity
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

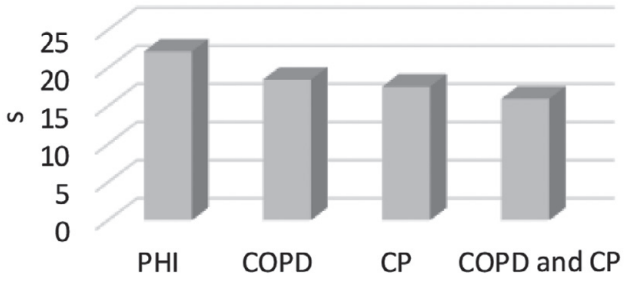

Fig. 3. Prothrombin time
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

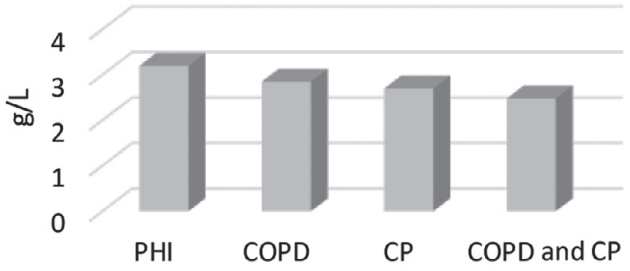

Fig. 4. Fibrinogen level
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

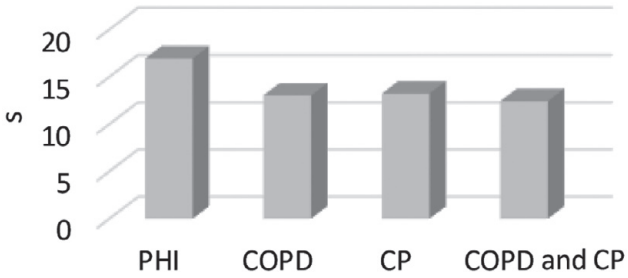

Fig. 5. Thrombin time
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

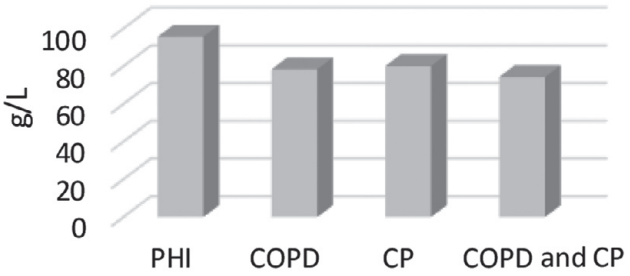

Fig. 6. Antithrombin III
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

Analyzing the blood anticoagulant potential we found a reduction in TT in all groups of patients (Fig. 5) with the highest percentage of decline in the patients of group 3 – by 36.3% ($p < 0.05$) compared with PHI, but in the patients of group 1 TT decreased as well – by 30%, and in group 2 – by 28% with the reliable difference between groups 1, 2 and 3.

Activation of systemic proteolysis in general in patients with CP on the background of COPD was also confirmed by changes in the activity of one of the factors of the proteinase-inhibitory system – AT III (Fig. 6), which activity was reduced in group 3 patients – by 29% (compared to healthy people), which was a most low activity detected in our study, while in patients of group 2, there was a decrease in the activity of AT III by 19%, and in group 1 – by 22%.

The study of the fibrinolytic activity of blood showed that the plasma TFA in patients of all groups was significantly lower than the control indicators: in group 1 – by 12.8%, in group 2 – by 14.3% and in group 3 – 21.7% ($p_{1-3} < 0.05$) (Fig. 7) with a significant intergroup difference ($p < 0.05$). TFA inhibition occurred due to a decrease in EFA: in patients of group 1 the indicator was significantly lower than in controls – by 31.9%, in group 2 – by 26.3%, while in group 3 the maximum suppression of EFA was registered – by 44.6% ($p_{1-3} < 0.05$). At the same time, NFA in patients of all groups was increased – compared to the PHI group by 17, 8 and 20%, respectively ($p_{1-3} < 0.05$), with a significant difference between groups 2 and 3 ($p < 0.05$). In patients of group 3, NFA acquired a compensatory maximum activity ($p < 0.05$).

In addition, there was a significant decrease in the activity of HFDF: in group 1 – by 1.6 times, in group 2 – by 1.7 times, in group 3 – by 1.8 times ($p_{1-3} < 0.05$) in comparison with PHI with no significant difference between

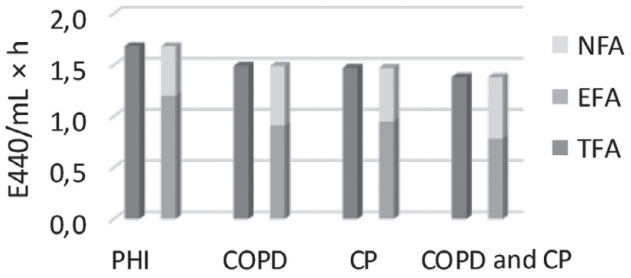

Fig. 7. Fibrinolytic activity
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis; NFA – non-enzymatic fibrinolytic activity; EFA – enzymatic fibrinolytic activity; TFA – total fibrinolytic activity.

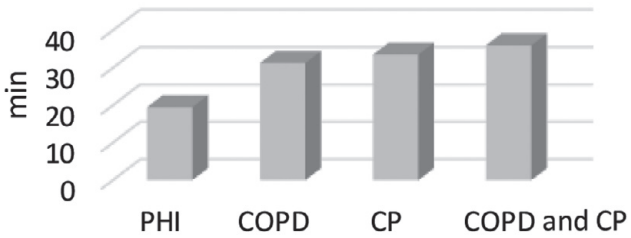

Fig. 8. Hageman-factor-dependent fibrinolysis
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

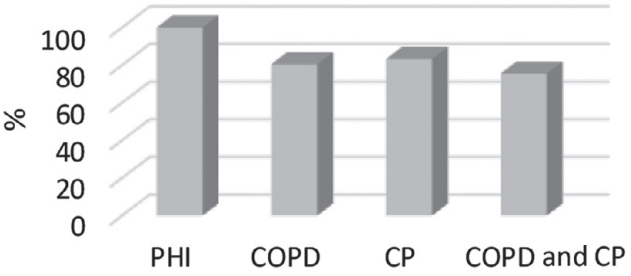

Fig. 9. Factor XIII activity
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

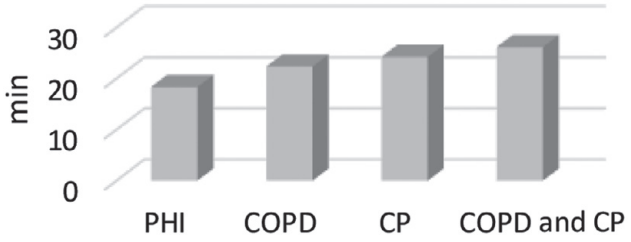

Fig. 10. Potential activity of plasminogen
Notes: PHI – practically healthy individuals; COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis.

groups ($p > 0.05$) (Fig. 8). The activity of factor XIII in patients of group 1 was decreased by 24.3%, in group 2 – by 20.1%, in group 3 – by 32.6% ($p_{1-3} < 0.05$) (Fig. 9) that indicates disturbances in the post-coagulation phase of blood clotting. In COPD patients with accompanying CP, a significant decrease in PAP was found: in group 1 patients – by 21.9%, in group 2 patients – by 32.2%, and in group 3 – by 42.6%, respectively ($p_{1-3} < 0.05$) (Fig. 10).

Investigation of hemostasis and fibrinolysis in the 45 patients with comorbid COPD and CP (group 3), stratified by FEV_1 level into three subgroups – 70–79% (n = 12), 60–69% (n = 17), and 50–59% (n = 16) – showed that blood coagulation activity increases with worsening bronchial obstruction (Table). The analysis included 24 individuals from the PHI with complete data availability.

Indicators of the coagulation hemostasis and fibrinolysis system in patients with COPD with concomitant CP depending on FEV_1, M ± SD

Indexes	PHI (n = 24)	FEV_1 = 70–79% (n = 12)	FEV_1 = 60–69% (n = 17)	FEV_1 = 50–59% (n = 16)
PTT, s	22.10 ± 0.54	16.80 ± 0.26*	15.70 ± 0.15*/**	13.90 ± 0.33*/**/***
Fibrinogen level, g/L	3.190 ± 0.179	2.680 ± 0.019*	2.520 ± 0.031*/**	2.310 ± 0.018*/**/***
TT, s	16.90 ± 0.87	13.20 ± 0.24*	11.90 ± 0.14*/**	10.80 ± 0.20*/**/***
AT III, g/L	95.500 ± 2.014	76.100 ± 2.203*	71.260 ± 3.862*	68.230 ± 2.830*
TFA, E440/mL × h	1.680 ± 0.022	1.480 ± 0.016*	1.400 ± 0.004*/**	1.320 ± 0.002*/**/***
NFA, E440/mL × h	0.480 ± 0.018	0.650 ± 0.026*	0.720 ± 0.003*/**	0.720 ± 0.004*/**
EFA, E440/mL × h	1.200 ± 0.025	0.860 ± 0.004*	0.670 ± 0.005*/**	0.600 ± 0.003*/**/***
HFDF, min	19.40 ± 0.18	34.10 ± 2.13*	35.60 ± 2.03*	37.50 ± 2.39*
Factor XIII activity, %	99.900 ± 3.446	80.760 ± 3.531*	73.160 ± 2.249*	67.390 ± 2.086*
PAP, min	18.30 ± 0.26	23.40 ± 0.60*	25.80 ± 0.28*/**	28.00 ± 0.22*/**

Notes: COPD – chronic obstructive pulmonary disease; CP – chronic pancreatitis; FEV_1 – forced expiratory volume in the first second; PHI – practically healthy individuals; * – the difference is significant compared to the PHI ($p < 0.05$); ** – the difference is significant compared to the COPD patients with FEV_1 = 70–79% ($p < 0.05$); *** – the difference is significant compared to the COPD patients with FEV_1 = 60–69% ($p < 0.05$); PTT – prothrombin time; TT – thrombin time; AT III – antithrombin III; TFA – total fibrinolytic activity; NFA – non-enzymatic fibrinolytic activity; EFA – enzymatic fibrinolytic activity; HFDF – Hageman-factor-dependent fibrinolysis; PAP – potential activity of plasminogen.

FAMILY MEDICINE. EUROPEAN PRACTICES / СІМЕЙНА МЕДИЦИНА. ЄВРОПЕЙСЬКІ ПРАКТИКИ •
ISSN 2786-7218 (Online) | ISSN 2786-720X (Print)
№1 (115)/2026

Thus, we can make a preliminary conclusion that CP contributes to the progression of broncho-obstructive syndrome. The most pronounced reductions in FEV_1, relative to the predicted values were observed in patients with a comorbid course of COPD and CP.

As the VC indicator in the whole cohort ranged between 80–90%, patients with the restrictive type of pulmonary impairment were excluded, however a statistically significant reduction in VC observed in comorbid patients with COPD and CP comparing to mean VC in PHI, can be explained by the phenomenon of maldigestion due to CP with bloating, resulted in unilateral diaphragm elevation and further development of respiratory area restriction in the basal parts of the lungs [12].

Reduction of fibrinogen levels in the blood of patients with COPD indicates either an impaired synthesis of coagulation factor I in the liver (although the functional state of the liver in the examined patients was within normal limits), or activation of the hemostatic system in response to inflammation, which promotes development of the hypercoagulable state, formation of parietal microthrombi and involvement of a significant amount of fibrinogen in this process [16]. A more pronounced decrease in fibrinogen levels in patients suffering from COPD with concomitant CP is suggestive for consumption coagulopathy, that is, increased fibrinogen utilization in the process of intravascular coagulation with simultaneous depletion of the circulating pool of factor I [13].

The intensity of plasma proteolysis in inflammatory conditions generally increases in a variety of internal pathologies and is controlled by multiple tissue and plasma protease inhibitors (α_2-macroglobulin, α_1-proteinase inhibitor, AT III, etc.). An imbalance of these systems can lead to a predominance of protein catabolism processes that perform structural (components of cell membranes, coagulation hemostasis) and transport functions that is also a powerful destabilizing factor [15].

Analysis of hemostasis and fibrinolysis indicators in COPD patients with concomitant CP depending on FEV_1 reduction (%) showed that with increasing bronchial obstruction is associated with increased blood coagulation activity (Table), with the exception of fibrinogen content (most likely due to consumption coagulopathy). In these patients the activity of anticoagulation system factors decreased, the total and enzymatic activity of fibrinolysis declined, while the non-enzymatic activity was compensatorily increased. In COPD conditions hypoxia, activation of anaerobic glycolysis, as well as accumulation of underoxidized products and systemic acidosis are powerful activators of the coagulation system, which contribute to the development of hypercoagulability syndrome in COPD patients. Disturbances in microcirculation processes in the pancreas due to activation of blood coagulation processes with insufficiency in anticoagulant factors and fibrinolytic systems is one of the risk factors for CP exacerbation in patients with COPD and, probably, for pancreatic fibrosis [7].

Reducing the intensity of collagenolysis in patients from groups 1 and 2 contributed to the development of diffuse pulmonary fibrosis as a response to chronic inflammation. At the same time, an imbalanced increase in proteolytic activity due to reduced expression of its inhibitors in COPD patients with CP led to progressive destruction of cell membranes in alveolocytes, acinar epithelium of the pancreas and bronchial mucosa epithelium with further acceleration of their apoptosis and development of desquamation, atrophic changes and metaplasia. Collectively, these factors act as inducers of inflammation, and contribute to the formation of both pulmonary and panctreatic fibrosis [7].

The results of the study of anti-coagulation and fibrinolytic system factors indicate the formation of a hyper-coagulation syndrome in COPD patients with accompanying CP. The consequence of significant hemocoagulation activation on background of TFA suppression is local blood clotting in the small lungs vessels. The main purpose of HFDF is to “cleanse” the vascular bed from fibrin clots formed under these conditions [12, 17]. We found a decrease in the rate of HFDF that is a likely cause of compensatory activation of NFA. Slowing blood circulation in the lungs due to the blood clots formation in the microvessels promotes increased hypoxia and, probably, the formation of reactive oxygen species and free nitrogen radicals with subsequent damage to cell membranes and closure of the “vicious” circle of pathogenesis of COPD and CP progression.

CONCLUSIONS

Factors worsening the course of CP in patients with hypoxia due to COPD are a decrease in AT III activity by 29%; a decrease in enzymatic fibrinolytic activity by 21.7%; a decrease in HFDF activity by 1.8 times from the normal level. The inhibition of anticoagulant potential of the blood (AT III activity, factor XIII), suppression of total fibrinolytic activity of blood plasma due to inhibition of enzymatic, HFDF, compensatory increase in the activity of non-enzymatic fibrinolysis, increased proteolytic activity of blood plasma indicates the formation of hypercoagulable syndrome, which is intensified by respiratory function disorders, in patients with CP with comorbid COPD. As a result, in patients with COPD, microcirculation processes in the pancreas are damaged, which is one of the risk factors for exacerbation of CP.

Information about the author

Dudka Inna V. – Bukovinian State Medical University, Chernivtsi; tel.: (050) 920-07-19. *E-mail: dudka.inna@bsmu.edu.ua*
ORCID: 0000-0001-9941-1878

Відомості про автора

Дудка Інна Володимирівна – Буковинський державний медичний університет, м. Чернівці; тел.: (050) 920-07-19. *E-mail: dudka.inna@bsmu.edu.ua*
ORCID: 0000-0001-9941-1878

REFERENCES

1. Zou W, Ou J, Wu F, Fan H, Hou Y, Li H, et al. Association of mild chronic obstructive pulmonary disease with all-cause mortality: A systematic review and meta-analysis. Pulmonology. 2024;31(1):1-9. doi: 10.1016/j.pulmoe.2023.09.002.
2. Kolsum U, Damera G, Pham T, Southworth T, Mason S, Karur P, et al. Pulmonary inflammation in patients with chronic obstructive pulmonary disease with higher blood eosinophil counts. J Allergy Clin Immunol. 2017;140(4):1181-4. doi: 10.1016/j.jaci.2017.04.027.
3. Zhelezniakova NM, Babak OYa. Routes of implementation and factors of escalation of systemic inflammatory response in comorbidity of chronic obstructive pulmonary disease and chronic pancreatitis. New Armenian Med J. 2017;11(2):27-32.
4. Khorunzhaya V, Dorofeyev A, Chorostowska-Wynimko J, Rozy A, Struniawski R. The prognostic importance of the protease-antiprotease imbalance in development of chronic obstructive pulmonary disease comorbid with chronic pancreatitis. Eur Respirat J. 2015;46(59):PA658. doi: 10.1183/13993003.congress-2015.PA658.
5. Hristich T, Hontsariuk D. Pathogenetic aspects of chronic pancreatitis and chronic obstructive pulmonary disease comorbidity. Gastroenterology. 2021;53(1):54-61. doi: 10.22141/2308-2097.53.1.2019.163459.
6. Goosenberg E, Lappin SL. Chronic Pancreatitis [Internet]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482325/.
7. Dudka I, Khukhlina O, Dudka T, Hryniuk O, Pavliuk V. Features of pancreatic parenchyma fibrosis in the comorbid course of chronic pancreatitis and chronic obstructive pulmonary disease. Med Perspekt. 2024;29(4):101-8. doi: 10.26641/2307-0404.2024.4.319237.
8. Robinson SM, Rasch S, Beer S, Valantiene I, Mickevicius A, Schlaipfer E, et al. Systemic inflammation contributes to impairment of quality of life in chronic pancreatitis. Sci Rep. 2019;9(1):7318. doi: 10.1038/s41598-019-43846-8.
9. Siemiatkowski A, Wereszczynska-Siemiatkowska U, Mroczko B, Galar M, Maziewski T. Circulating endothelial mediators in human pancreatitis-associated lung injury. Eur J Gastroenterol Hepatol. 2015;27(6):728-34. doi: 10.1097/MEG.0000000000000338.
10. Yang N, Hao J, Zhang D. Antithrombin III and D-dimer levels as indicators of disease severity in patients with hyperlipidaemic or biliary acute pancreatitis. J Int Med Res. 2017;45(1):147-58. doi: 10.1177/0300060516677929.
11. Gui M, Zhao B, Huang J, Chen E, Qu H, Mao E. Pathogenesis and Therapy of Coagulation Disorders in Severe Acute Pancreatitis. J Inflamm Res. 2023;16:57-67. doi: 10.2147/JIR.S388216.
12. Walia D, Saraya A, Gunjan D. Vascular complications of chronic pancreatitis and its management. World J Gastrointest Surg. 2023;15(8):1574-90. doi: 10.4240/wjgs.v15.i8.1574.
13. Chung WS, Lin CL. Comorbid risks of deep vein thrombosis and pulmonary thromboembolism in patients with chronic pancreatitis: A nationwide cohort study. J Thromb Haemost. 2016;14(1):98-104. doi: 10.1111/jth.13195.
14. Ibatova ShM, Mamatkulova FKh. Study of the parameters of the blood hemostasis system in patients with chronic obstructive pulmonary disease. Eura Med Res Per. 2023;24:25-30.
15. Zhang S, Li X, Ma H, Zhu M, Zhou Y, Zhang Q, et al. Relationship between antithrombin III activity and mortality in patients with acute exacerbation of chronic obstructive pulmonary disease. COPD. 2022;19(1):353-64. doi: 10.1080/15412555.2022.2106200.
16. Liu M, Hu R, Jiang X, Mei X. Coagulation dysfunction in patients with AECOPD and its relation to infection and hypercapnia. J Clin Lab Anal. 2021;35(4):e23733. doi: 10.1002/jcla.23733.
17. Saienko V, Konopkina L. The systemic inflammation and factors of coagulation in patients with chronic obstructive pulmonary disease (COPD). Eur Respiratory J. 2014;44(58):P4732. doi: 10.1183/13993003/erj.44.Suppl_58.P4732.
18. Babinets LS, Protsyuk RG, Kvasnitska OS. Smoking as a factor of immune deficiency deepening in patients with chronic obstructive pulmonary disease and chronic pancreatitis. Likarska Sprava. 2019;(1-2):17-22. doi: 10.31640/JVD.1-2.2019(3).
19. Yakovlieva VH. Peculiarities of coagulation hemostasis disorders in patients with chronic obstructive pulmonary disease. Med perspekt. 2015;20(3):56-60. doi: 10.26641/2307-0404.2015.3.53133.
20. Ministry of Health of Ukraine. Unified clinical protocol of primary, secondary (specialized) medical care and medical rehabilitation for chronic pancreatitis [Internet]. 2014. Order No. 638; 2014 Sep 10. Available from: https://zakon.rada.gov.ua/rada/show/v0638282-14#Text.
21. Ministry of Health of Ukraine. On the approval of the Unified Clinical Protocol of Primary and Specialized Medical Care "Chronic Pancreatitis" [Internet]. 2023. Order No. 1204; 2023 July 04. Available from: https://zakon.rada.gov.ua/rada/show/v1204282-23#Text.
22. Johnson CD, Williamson N, Janssen-van Solingen G, Arbuckle R, Johnson C, Simpson S, et al. Psychometric evaluation of a patient-reported outcome measure in pancreatic exocrine insufficiency. Pancreatology. 2019;(1):182-90. doi: 10.1016/j.pan.2018.11.013.
23. Global Initiative for Chronic Obstructive Lung Disease. 2022 GOLD Reports. 2022 Global Strategy for Prevention, Diagnosis and Management of COPD [Internet]. 2022. Available from: https://goldcopd.org/2022-gold-reports/.
24. Global Initiative for Chronic Obstructive Lung Disease. GOLD 2022 report. Global strategy for prevention, diagnosis and management of COPD: 2023 Report [Internet]. 2023. Available from: https://goldcopd.org/2023-gold-report-2/.
25. Mahalias VM, Mikheiev AO, Rohovyi Yule, Shcherbinina AV, Turchynets TH, Chipko TM. Modern methods of experimental and clinical research of the central research laboratory of the Bukovinian State Medical Academy. Chernivtsi: BDMA; 2001. 42 p.

Стаття надійшла до редакції 24.04.2025. – Дата першого рішення 29.04.2025. – Стаття подана до друку 06.06.2025