ORIGINAL ARTICLE

PECULIARITIES OF THE COURSE OF PULMONARY EMBOLISM DURING THE COVID-19 PANDEMIC

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ABSTRACT

The aim: A comparative analysis of the course of pulmonary embolism during the COVID-19 pandemic and the era before pandemia

Materials and methods: 294 patients with pulmonary embolism (PE) , 1 group – 188 with PE before the pandemic, 2 group -106 during the pandemic. Two subgroups were distinguished in 2 group : 1- with laboratory-excluded coronavirus (acute and in anamnesis) and 2 – with a history of COVID-19. The diagnosis of PE was confirmed by CT. Echocardiography and ultrasound Doppler imaging of the veins of the lower extremities were performed.

Results: In 1 group there was a more significant increase in pulmonary artery pressure (44.29 ± 17.04 vs 36.91 ± 16.6, p 0.0023) and a decrease in the E/A ratio of the right ventricle (0.80 ± 0,21 vs 1.28 ± 1.42, p 0.0202). In 2 subgroup of patients with COVID-19 had a significantly higher incidence of Diabetes mellitus (73.7% vs 13.3%, p 0.00001) and significantly lower signs of superficial venous thrombosis of the lower extremities (5.3% vs 33,3%, p 0,0175) and signs of proximal deep vein thrombosis (0% vs 56.7%, p 0.00001) and 3 times less often there was a high risk of adverse disease, right ventricular dysfunction were more pronounced (ratio E/A 0.87 ± 0.25 vs 1.13 ± 0.28, p 0.022).

Conclusions: In patients with coronavirus infection, PE was significantly more common in the presence of diabetes mellitus , right ventricular diastole disorders were more common, and superficial and proximal deep vein thrombosis of the lower extremities were less common.

KEY WORDS: risk factors, pulmonary embolism, COVID-19

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INTRODUCTION

Despite advances in the diagnosis and treatment of patients with pulmonary embolism (PE), with the development of scales to determine the risk of venous thromboembolism, stratification of patients with the selection of the group of the negative course of the acute period, widespread introduction of new oral anticoagulants (NOACs), pulmonary embolism remains one of the main causes of cardiovascular death after stroke and myocardial infarction [1, 2]. This is largely due to the increase in the proportion of patients with high risk factors for venous thromboembolism (VTE): prolongation of life expectancy, prevalence of malignant neoplasms, wider joint prosthetics and arthroscopic interventions [3-7]. In addition, the emergence of a coronavirus pandemic, which is able to activate the coagulation system and inhibit fibrinolytic activity by increasing the level of plasminogen activator inhibitor, also affects the risk of developing and the course of VTE [8-11].

Today there are many publications devoted to the study of the frequency, features and treatment of VTE and PE in the period of coronavirus infection [12-18]. Despite reasonable expectations, according to several publications, there is no increase in the incidence of PE, moreover, according to the results of some registers in the pandemic period there is a decrease in the incidence of PE [19, 20]. Perhaps this "paradox" is related to the reduced frequency of patients seeking help due to fear of coronavirus infection. At the same time, the clinical course of PE during the pandemic period was more severe with high hospital mortality, especially of those patients with a combination of active period of infection with thromboembolic complications [21-24].

Given that these publications were foreign, we considered it appropriate to assess the situation with PE during the pandemic on the basis of the register of patients of the MNE "CCH No8" of KCC.

THE AIM

The aim of the study was to conduct a comparative analysis of the course of PE of those patients treated in

Table I. Clinical and anamnestic characteristics of groups of patients with pulmonary embolism before the COVID-19 pandemic and during the pandemic period.

Indicator	Total n=294	1 group (n=188)	2 group (n= 106)	P level
Average age, years (M ± σ)	63.77±13.86	64.51±13.28	62.46±14.81	0.25
Men, n (%)	169 (57,5%)	104 (55,3%)	65(61,3%)	0,32
Females, n (%)	125 (42,5%)	84 (44,7%)	41 (38,7%)	
Risk factors for VTE, n (%)				
Fracture of the femoral neck or lower limb in the previous 3 months, n (%)	11 (3,7%)	7 (3,7%)	4 (3,8%)	0,61
Prosthetics of the hip / knee joint, n (%)	4(1,4%)	2(1,1%)	2(1,9%)	0,46
Major injury in the previous 3 months, n (%)	12(4,1%)	8(4,3%)	4(3,8%)	0,55
Previous venous thrombosis or embolic complications, n (%)	49(16,7%)	31(16,5%)	18(17,0%)	0,91
Previous myocardial infarction, n (%)	4(1,4%)	2(1,1%)	2(1,9%)	0,46
Spinal cord injury, n (%)	2(0,7%)	2(1,1%)	0	0,0001
Arthroscopic knee surgery, n (%)	1(0,3%)	1(0,5%)	0	0,64
Chemotherapy, n (%)	7(2,4%)	5(2,7%)	2(1,9%)	0,51
Chronic respiratory failure, n (%)	16(5,4%)	14(7,4%)	2(1,9%)*	0,03
Congestive heart failure, n(%)	23(7,8%)	12(6,4%)	11(10,4%)	0,22
Malignant tumor, n (%)	49(16,7%)	29(15,4%)	20(18,9%)	0,45
Superficial vein thrombosis, n (%)	86(29,3%)	66(35,1%)	20(18,9%)**	0,0033
Thrombophilia, n (%)	7(2,4%)	2(1,1%)	5(4,7%)	0,22
Obesity, n (%)	42(14,3%)	31(16,5%)	11(0,4%)	0,15
Hypertension, n (%)	181(61,6%)	131(69,7%)	50(47,2%)	0,0001
Diabetes mellitus, n (%)	33(11,2%)	26(13,8%)	7(6,6%)	0,09
Varicose veins, n (%)	27(9,2%)	20(10,6%)	7(6,6%)	0,35
Distribution of patients by stratification of early risk of death from pulmonary embolism, n (%)				
High	146(49,7%)	97(51,6%)	49(46,2%)	0,377
Intermediate high	66(22,4%)	43(22,9%)	23(21,7%)	0,817
Intermediate low	48(16,3%)	30(16,0%)	18(16,9%))	0,820
Low	34(11,6%)	18(9,6%)	16(15,1%)	0,155
Estimation of the patient's prognosis on the PESI[1] scale (except for high-risk patients), n (%)				
	n =148	n=91	n=57	P level
class I	42(28,4%)	27(29,7%)	15(26,3%)	0,660
class II	35((23,6%)	22(24,2%)	13(22,8%)	0,849
class III	31(20,9%)	18(19,8%)	13(22,8%)	0,660
class IV	24(16,2%)	15(16,5%)	9(15,8%)	0,911
class V	16(10,8%)	9((9,9%)	7(12,3%)	0,649
Recurrence of pulmonary embolism, n (%)	3(1,0%)	2(1,1%)	1(0,9%)	0,70
Died, n (%)	34 (11,6%)	25 (13,3%)	9 (8,5%)	0,29

Note. VTE – venous thromboembolism

[1] Original version [8]. Categorical indicators are given as the number of cases and the share, quantitative – in the form of M ± σ.

The difference is statistically significant compared with those in patients of the 1st group: * P <0,05; ** P <0.01; *** P <0.001.

the cardiology departments of the hospital during the year before the pandemic and during the year of the pandemic (provided there is no acute covid infection (COVID-19).

MATERIALS AND METHODS

The total group included 294 patients with PE, among whom there were 169 men (57.5%) and 125 women (42.5%), whose average age was 63.77 years. The diagnosis

Table II. Comparative evaluation of groups based on the results of computed angiography of the pulmonary arteries.

Signs, n (%)	Total group, n = 294	1 group, n=188	2 group, n= 106	P level
Right ventricular lesions (RV)	136 (46,3)	92 (48,9)	44 (41,5)	0,22
Lung trunk thrombus	23 (7,8)	15 (8,0)	8 (7,5)	0,89
TE of both pulmonary arteries (PA) with their partial occlusion	131 (44,6)	86 (45,7)	35 (33,0)	0,03
TE lobular branches of PA	64 (21,8)	43 (22,9)	21 (19,8)	0,54
TE of one lobular branch of PA and segmental branches	38 (12,9)	30 (16,0)	18 (17,0)	0,82

Table III. Indicators of echocardiography and computed angiography of the examined groups of patients with pulmonary embolism.

Indicator	General group (n=294)	1 group (n=188)	2 group (n= 106)	P level
LAD, cm	4,07±0,62	4,08± 0,54	4,05±0,70	0,44
RAD, cm	4,24±0,70	4,31±0,72	4,18±0,71	0,18
LVIDd, cm	4,80±0,58	4,82±0,55	4,75±0,65	0,32
LVIDs, cm	3,31±0,59	3,29±0,53	3,34±0,66	0,43
RVDd, cm	2,97±0,76	3,07±0,76	2,99±0,79	0,19
IVS, cm	1,03±0,17	1,07±0,18	1,00±0,14	0,0009
LVPW, cm	1,02±0,13	1,04±0,13	0,99±0,12	0,0094
LVEF,%	58,23±8,23	58,84±6,59	57,33±10,12	0,91
MPAP, mmHg	40,06±17,25	44,29±17,04	36,91±16,6	0,0023
E/A RV	1,20±1,17	0,80±0,21	1,28±1,42	0,0202
Diameter PT, cm	34,28±14,71	34,76±15,91	33,42±12,16	0,84
Diameter RPA, cm	26,06±6,66	25,50±4,22	27,20±9,74	0,64
Diameter LPA, cm	24,86±3,75	24,61±3,90	25,39±3,43	0,34

Note of Tables III, V. Categorical indicators are given as the number of cases and the share, quantitative – in the form of M ± σ.
LAD – Left atrial diameter , RAD – Right atrium diameter, LVIDd – Left ventricular internal dimension diastole, LVIDs – Left ventricular internal dimension systole, RVDd – Right ventricular dimension at end – diastole, IVS – Interventricular septum , LVPW – Left ventricle posterior wall, LVEF – Left ventricular ejection fraction , MPAP = Mean pulmonary artery pressure, PT – pulmonary trunk, RPA – right pulmonary artery, LPA – left pulmonary artery, E – Peak velocity of early diastolic transtricuspid flow, A- Peak velocity of late transmitral flow, E/A – Ratio of E to A

of PE was confirmed by computed tomography. All these patients had been treated at the MNE "CCH #8" of KCC from March 2019 to March 2021. At hospitalization, all patients underwent risk stratification to determine therapeutic tactics. In total, 146 patients had a high risk in the group (49.7%), intermediate high – 66 (22.4%), intermediate low – 48 (16.3%) and low – 34 patients (11.6%). Low-risk patients had been hospitalized for a variety of reasons, such as comorbiditiesor inability to control INR when warfarin dose adjustment.

The results of the analysis of risk factors for venous thrombosis show that 11 patients had traumatic and orthopedic problems (fracture of the lower extremity, mainly the thigh), 4 – prosthetics of the knee / hip joint, 1 – arthroscopic intervention on the knee joint. In the anamnesis of the disease, 49 patients had already had previous venous embolic complications. Signs of chronic heart failure (HF) occurred in 23 patients (7.8%), malignant neoplasms in 49 (16.7%). At active detailed search of the source of PE in 86 (29.3%) persons with a history of thrombosis of superficial veins of the lower extremities, and in 7 (2.4%) – signs of thrombophilia (Table I).

According to computed angiography performed on Somatom Definition AS 64 (Siemens, Germany) using intravenous contrast Tomohexol-350, 50 ml according to a standard protocol [25]. The presence of PE according to MCT angiography of PA was defined as the detection of contrast enhancement defects that partially and/or completely blocked the lumen of at least one of the branches of the pulmonary artery. A quantitative assessment was made of the size of the pulmonary trunk and pulmonary arteries and the nature of the spread of damage to the branches of the pulmonary arteries. Thus, in 23 (7.8%) patients a massive thrombus of the pulmonary trunk was detected, in 131 (44.6%) TE of both pulmonary arteries (LA) with their partial occlusion, in 64 (21.8%) – lobular branches of the LA and in 38 (12.9%) – TE of one lobular branch of LA and segmental branches.

Table IV. Frequency of detection of limb venous thrombosis in patients with pulmonary embolism.

Indicator n, (%)	General group, n=294	1 group, n=188	2 group n= 106	P level
Thrombosis of the upper extremities	1 (0.3)	1 (0.5)	0	0.64
Thrombosis of the proximal deep veins	85 (28.9)	58 (30.9)	27 (25.5)	0.22
Thrombosis of the distal deep veins	10 (3.4)	4 (2.1)	6 (5.7)	0.1040

Table V. Clinical and anamnestic characteristics of groups of patients with pulmonary embolism with excluded COVID-19 and those having the disease in the past.

Indicator	1 subgroup, n=30	2 subgroup, n= 19	P level
Age, years M ± σ	62,38±14,54	62,79±15,09	0,83
Male , n (%)	19 (63,3)	11 (57,9)	0,70
Female , n (%)	11 (36,7)	8 (42,1)	
Risk factors for VTE, n (%)			
Fracture of the femoral neck or limb, n (%)	0	1 (5,3)	0,39
Prosthetics of the femoral / knee joint, n (%)	2 (6,7)	0	0,37
Major injury in the previous 3 months, n (%), n (%)	1 (3,3)	0	0,61
Previous venous embolic complications, n (%)	7 (23,3)	4 (21,1)	0,57
Previous myocardial infarction, n (%)	7 (23,3)	1 (5,3)	0,10
Spinal cord injury, n (%)	0	0	
Arthroscopic knee surgery, n (%)	0	0	
Chemotherapy, n (%)	0	0	
Chronic respiratory failure, n /%	1 (1,3)	0	0,61
Congestive heart failure, n (%)	5(16,7)	0	0,07
Malignant tumor, n (%)	6(20,0)	3 (15,8)	0,51
Superficial vein thrombosis, n (%)	10 (33,3)	1 (5,3)	0,0175
Thrombophilia, n (%)	1 (1,3)	1(5,3)	0,63
Obesity, n (%)	4 (13,3)	2(10,5)	0,57
Hypertension, n (%)	18(60,0)	9(47,4)	0,57
Diabetes mellitus, n (%)	4(13,3)	14(73,7)	0,00001
Varicose veins, n (%)	5(16,7_	5(26,3)	0,32
Distribution of patients by stratification of early risk of death from pulmonary embolism, n (%)			
High	19 (63,3)	6 (31,6)	0,03
Intermediate high	3 (10,0)	5 (26,3)	0,134
Intermediate low	5 (16,7)	4 (21,1)	0,489
Low	3 (10,0)	4 (21,1)	0,252
Estimation of the patient's prognosis on the PESI1 scale (except for high-risk patients), n (%)			
	n =11	n= 13	
class I	3 (27,3)	3 (23,1)	0,590
class II	3 (27,3)	2 (15,4)	0,415
class III	2(18,2)	2 (15,4)	0,637
class IV	1 (9,1)	3 (23,1)	0,363
class V	2(18,2)	3 (23,1)	0,834
The nature of the prevalence of lesions according to MCT angiography of the LA, n (%)			
Lesion of the right ventricle, n (%)	15 (50,0)	6 (31,6)	0,17
Pulmonary trunk thrombosis, n (%)	4 (13,3)	2(10,5)	0,57
TE of both PA with their partial occlusion, n (%)	11(36,7)	6(31,6)	0,48

Table V. (cont.)

TE lobular branches of PA, n (%)	6 (20,0)	3(15,8)	0,51
TE of one lobular branch of PA and segmental branches, n (%)	9 (30,0)	3 (15,8)	0,22
The frequency of thrombosis of the veins of the extremities n, /% detected during hospital treatment			
Thrombosis of the upper extremities n (%)	0	0	
Proximal deep vein thrombosis, n (%)	17(56,7)	0	0,00001
Distal deep vein thrombosis, n (%)	3 (10,0)	1(5,3)	0,4934
Died, n (%)	13(14,1)	2/ (0,5)	0,0148
Echocardiographic parameters in subgroups of the examined patients			
LA, cm	4,18± 0,68	4,16±0,78	0,77
RA, cm	4,39±0,69	4,38±0,83	0,89
LVIDd, cm	4,79±0,71	4,83±0,59	0,75
LVIDs, cm	3,43±0,76	3,33±0,55	0,86
RV, cm	2,98±0,85	3,00±0,65	0,64
IVS, cm	1,03±0,18	1,02±0,12	1,00
LVPW, cm	1,01±0,12	1,04±0,14	0,67
EF,%	57,43±10,77	59,53±8,03	0,54
MPAP, mmHg	40,27±18,63	34,93±16,55	0,35
E/A RV	1,13±0,28	0,87±0,25	0,022
Diameter PT, cm	31,41±3,99	31,25±4,25	0,75
Diameter RPA, cm	25,79±3,37	26,75±5,50	0,92
Diameter LPA, cm	25,21±3,13	26,75±3,70	0,25

Echocardiographic examination was performed during hospitalization of patients on the device "Acuson X2000" (Siemens, Germany) using a sensor with an ultrasound frequency of 3.0 MHz, according to the standard protocol. Measured the following parameters: Left atrial diameter (LAD), Right atrial diameter (RAD), Left ventricular internal dimension at end –diastole (LVIDd), Left ventricular internal dimension at end –systole (LVIDs), Right ventricular dimension at end – diastole (RVDd), LV ejection fraction (LVEF) according to Simpson. Signs of RV overload were assessed, which were defined as RV diameter greater than 30 mm in the parasternal position or a ratio of RV to LV size greater than 1; and/or presence of systolic flattening of the interventricular septum (IVS); and / or the time of acceleration of blood flow (AT) in the PA trunk, less than 90 ms, or the pressure gradient across the tricuspid valve (TV), more than 30 mm Hg, in the absence of LV hypertrophy; and / or the presence of the sign "60/60" – the time of acceleration of blood flow in the PA trunk is less than 60 ms and the pressure gradient on the TV is less than 60, but more than 30 mm Hg; and / or the presence of McConnell's sign – normo- or hyperkinesia of the apical segment of the RV in the presence of hypo- or akinesia of the middle and basal segments of the RV, and also determined the mean pressure in the PA by the ratio of the time of acceleration (AT) of blood flow in the outflow tract of the RV to the time of expulsion of blood from the RV (ET) [26-29].

Ultrasound Doppler (USD) of the veins of the lower extremities was performed on the device "S20Pro" (SONOSCAPE, China) according to the standard protocol. The presence of thrombotic masses, their level and the nature of placement in the veins of the lower extremities were evaluated [30].

All patients were treated according to the recommendations of ESC 2019 [2]. High-risk and intermediate high-risk patients in the absence of absolute contraindications underwent thrombolysis – 126 high-risk patients. Anticoagulant therapy was prescribed to all patients during hospitalization: patients with thrombolysis began with parenteral anticoagulants. Patients who did not require thrombolytic therapy received parenteral anticoagulants with subsequent administration of dabigatran or apixaban or with warfarin dose adjustment. In the case of rivaroxaban, the drug was prescribed after thrombolysis and parenteral anticoagulants in high-risk patients or from the first day of hospitalization, if thrombolytic therapy was not performed.

In the analysis of the impact of the pandemic, patients were divided into two groups – 1 group (188 patients) before the pandemic, the second (106 patients) – during the pandemic (from March 2020 to March 2021). The divi-

sion of patients into groups was carried out in accordance with the information on the appearance of the first patient with COVID-19 in Ukraine. The uneven distribution of the number of patients reflects the true situation regarding the stay of patients with pulmonary embolism in the hospital during this period.

During the pandemic, our hospital received 82 fewer inpatients than in the same period a year earlier. However, it should be noted that the hospital did not accept patients with COVID-19 or with suspected COVID-19, so the actual number of such patients should be much higher.

Statistical processing of the obtained data was performed using Statistica and Microsoft Office Excel 2013. Categorical variables are given as the number of cases and the share, quantitative – in the form of mean ± standard deviation (M ± σ). In the normal distribution, quantitative characteristics were presented as mean ± standard deviation (M ± σ), and Student's t test was used to compare the mean of the two samples. Intergroup differences in qualitative traits were assessed using Pearson's X2 test. Uni- and multivariate log-regression analyzes were used to determine the predictors of the combined clinical endpoint of clinical and anamnestic indicators.

RESULTS

According to the results of the comparative analysis shown in table I, the groups of patients did not differ significantly in age, sex, the main risk factors for VE. Regarding the revealed reliability of spinal cord injury, in the number of cases 2 in the first group and the absence in the second, to argue about the pattern is not logical.

There were no statistically significant differences between the groups in terms of the size of thrombosis (according to the results of computed angiography) and the results of risk stratification.

We analyzed the results of computed tomography in groups of patients (table II). No differences between the groups were found in the localization of thrombosis, its prevalence and the presence of signs of right ventricular lesions.

It is known that an important factor influencing both the hospital and long-term period after pulmonary embolism is the presence and severity of RV lesions and the presence of pulmonary arterial hypertension (PAH). Table III shows the results of a comparative analysis of echocardiography.

The results of the comparison show no significant difference between the sizes of left chambers of the heart, while it was found that the thickness of the left ventricular myocardium was significantly less in the second group, which may reflect the more frequent proportion of patients with hypertension in the first group.

Regarding the right ventricle (RV), there were significant differences between groups, with more pronounced changes in the first group. Patients in this group had a more significant increase in pulmonary artery pressure and a decrease in E/A RV, which may indicate impaired right ventricular relaxation.

Although polymerase chain reaction (PCR) test was performed to the patients in group 2 to rule out acute coronavirus infection, patients in this group included those who had previously suffered from COVID-19 infection and had relevant medical evidence to support this. In addition, some patients with a history of possible infection were tested for immunoglobulin M and G and tested negative. That is, group 2 was quite heterogeneous. There were patients with COVID-19, patients without COVID-19 confirmed by PCR and with immunoglobulin M and G levels, and patients who could theoretically have an infection but were not adequately screened. We performed a comparative analysis of the first two subgroups – with a history of COVID-19 and laboratory-excluded coronavirus. One subgroup included 30 patients with pulmonary embolism, in whom laboratory tests ruled out COVID -19, both acute and in the anamnesis, the second – included 19 patients who had a previous coronavirus infection. The results of the analysis are shown in table IV. As shown by the results of the subgroup of patients did not differ significantly in age, sex, traumatic and orthopedic risk factors for VTE, malignant neoplasms.

However, in patients with COVID-19 there were significantly less signs of history of superficial venous thrombosis of the lower extremities and signs of deep vein thrombosis (proximal and distal) during examination during hospital stay. In addition, patients with coronavirus infection were 3 times less likely to be a high risk of an unfavorable course of the disease in the hospital period, but right ventricular dysfunction (as assessed by E / A ratio) was more pronounced. The latter fact may be related not only to the development of pulmonary embolism, but also to changes in the heart in COVID- pneumonia [31].

Unfortunately, a total of 34 patients died among the examined patients (11.6%), despite the fact that mortality in the groups differed slightly (in 1 group – 13.3%, in the second – 8.5%), these differences were not significant (Table I).

A seemingly paradoxical fact about the reduction in the number of patients with pulmonary embolism during the pandemic suggested the possibility of an unfavorable course of the disease at the pre-hospital stage. We analyzed data from the Bureau of Forensic Science on cases of pulmonary embolism as a cause of death in periods comparable to clinical analysis. It is noteworthy that according to the results of the Kharkiv Regional Bureau of Forensic Medical Examination during the year before the pandemic with pulmonary embolism, the cause of death was 15 people, while in the pandemic – 32 people. Among those diagnosed with pulmonary embolism there were 30 women (before the pandemic – 9, during the pandemic – 21), men -17 (6

and 11, respectively). At the same time, men were younger – 55.4 ± 4.8 years, against 66.4 ± 4.2, both in total for 2 years and separately for periods. We have not been able to obtain detailed information on these patients who died suddenly from pulmonary embolism, mostly at home (41 people), so it is not possible to conduct an in-depth analysis.

DISCUSSION

The results of our study, which included 294 patients with PE who were treated at the MNE "CCH No8" of KCC in the year before the pandemic and during the first year after the detection of coronavirus infection in Ukraine, show a decrease in the number of hospitalized patients by 43.6%. However, this may not indicate a decrease in the prevalence of pulmonary embolism with the onset of the pandemic, as some patients may have been afraid to go to the hospital for epidemiological reasons, some had COVID-19 and were treated in other hospitals, and some unfortunately, did not managed to go to the hospital. The decrease in the prevalence of VTE has been noted in several foreign publications, including registers, the authors of which also emphasize the careful interpretation of this fact and the possibility of lockdown on the frequency of patients seeking medical help [23, 32].

Comparative analysis of the clinical course of pulmonary embolism in groups of patients depending on the COVID 19 pandemic did not reveal significant differences in terms of computed pulmonary angiography and the results of risk stratification. Moreover, no significant difference in mortality was found. This does not coincide with the results of similar publications by other authors who claim a more severe course and worse prognosis in patients with pulmonary embolism during the pandemic [15, 33, 16, 34, 21, 17]. The difference may be explained by differences in patient structure – we included only patients who were hospitalized in the laboratory who ruled out acute coronavirus infection using laboratory tests, while other authors usually analyzed the general group of patients with pulmonary embolism or patients with acute coronavirus infection.

Many publications and several meta-analyzes have been devoted to the impact of the COVID 19 pandemic on the risk of thromboembolic complications. They can be divided into several groups: the study of the prevalence of venous thrombosis during the pandemic, the study of the disease during this period and venous thromboembolism as a complication of coronavirus infection [18, 32, 35-38].

Interesting results were obtained in one of the first meta-analyzes, which included original articles in English, published from January 1, 2020 to June 15, 2020 in PubMed / MEDLINE, Embase, Web of science and Cochrane. Significant objectively verified VTEs, such as pulmonary embolism and / or proximal deep vein thrombosis (DVT), have been evaluated. The study included 33 studies (n = 4009 patients) who had severe acute coronavirus infection and were hospitalized for this reason. The primary endpoint is the risk of developing these VTE, the secondary – separately the risk of proximal DVT and pulmonary embolism (G. Longchamp et al, Trombosis Journal 19, Art. 15,2021) [18].

The group of patients included in the analysis was quite heterogeneous in terms of thrombotic risk factors, and the incidence of VTE averaged 9% and 21% among patients hospitalized for intensive care unit. The incidence of proximal thrombosis of the lower extremity was 3% and 8%, and the incidence of pulmonary embolism was 8% and 17%, respectively. Proven and predicted risk factor for VTE was the lack of anticoagulants [18].

Other studies have found an even higher incidence of VTE among hospitalized patients with COVID — up to one-third of patients with COVID-19, predominantly pulmonary embolism. It has been shown that VTE is more common in patients with concomitant pathology and severe disease [34].

Our study found significant differences in the frequency of ultrasound examination of deep vein thrombosis of the lower extremities as a possible source of thrombosis in the subgroups comparing patients with pulmonary embolism with excluded and those who had had COVID19 during the pandemic. The "paradox" of the decrease in the proportion of patients with deep vein thrombosis of the lower extremities, among those who have suffered a coronavirus infection, in our opinion, may be due to the fact that there was damage to the endothelium of the pulmonary arteries, which can be observed for a long time. Also, the results of published studies suggest that COVID-19 may be not only thromboembolic impaired blood flow, but also immunothrombosis in situ, initiated by immunopathological response, often hereditary. There is currently uncertainty as to whether COVID19-related thrombotic events are due to routine VTE, immunothrombosis, or a combination thereof, both in the acute and post Covid periods [11].

It is known that SARS-CoV-2 has a predisposition to the respiratory tract, enhances cellular entry through the ACE2 receptor, which is expressed on the surface of epithelial cells of the respiratory tract. Pathological changes in COVID-19 include diffuse alveolar damage, pneumocyte type II activation, hyaline membrane formation, and fibrin deposition, leading to the development of microvascular abnormalities. Pulmonary microvascular abnormalities include intravascular fibrin

deposition, perivascular monocyte infiltration, angiogenesis, and microthrombus formation. The results of autopsy of patients with COVID-19 indicate systemic endothelial dysfunction [39, 11].

If we recall the classic Virchow's triad (chain of events of thrombosis), the impressions of coronavirus can be a classic illustrative material, where there are blood flow disorders and changes in vascular wall with inflammation, and disorders of coagulation and fibrinolysis, as well as platelet and neutrophil function.

An additional activator of thrombosis in COVID 19 is hypoxia, which occurs in moderate to severe COVID-19 and therefore may lead to worsening endothelial dysfunction and hypercoagulation. Activation of endothelial P-selectin and adhesion molecules (eg, intercellular adhesion molecule-1 (ICAM-1)) in hypoxia leads to platelet and leukocyte adhesion. Hypoxia promotes thrombosis by increasing the release of PAI-1 endothelium and inflammatory cytokines (eg, TNF, interleukin (IL) -2), while reducing thrombomodulin regulation. In addition, increased activity of prothrombotic factors may be initiated by immune disorders, activation and local adhesion of macrophages, stimulation of the release of proinflammatory cytokines, including IL-6 and TNF-α [11].

Elevated antiphospholipid antibody (APA) titers have been reported in patients with COVID-19, and it should be noted that the diagnosis of antiphospholipid syndrome in acute infection requires APA to be measured twice a week.

In our opinion, it is reasonable to assume that in some patients with coronavirus infection, PE may be the result of immunotrombosis in situ, as evidenced by significant differences in the incidence of lower extremity thrombosis between subgroups of patients during the pandemic (in a subgroup of patients who had an infection, signs of deep vein thrombosis of the lower extremities were less common).

The results of our study show that despite the lack of significant increase in hospital mortality from pulmonary embolism during the pandemic, the proportion of pulmonary embolism in the structure of overall mortality may increase as the number of pulmonary embolism increased according to forensic examination. A more complete answer to this question could be provided by the results of the national register, which unfortunately does not exist in Ukraine.

CONCLUSIONS

1. In the comparative analysis it was found that in the clinical course of pulmonary embolism in groups of patients treated in the cardiology department of MNE "CCH #8" of KCC, before the pandemic, and during the pandemic COVID -19, but had no signs of acute coronavirus infection, there are no significant differences in age, sex and prevalence of circulatory disorders in the pulmonary arteries according to the results of computed tomography.
2. When comparing subgroups of patients, depending on the presence of a history of COVID-19, it was proved that pulmonary embolism in patients with coronavirus infection is significantly more often observed in the presence of diabetes mellitus and low superficial and proximal vein thrombosis of the lower extremities is less common than in patients with which, according to laboratory tests, there were no signs of coronavirus infection.
3. Subgroups of patients with pulmonary embolism, those who had had COVID-19 and those who had not had COVID-19 did not differ significantly according to the results of ultrasound examination of the heart, except for the presence of signs of right ventricular diastole disorder E/A in a subgroup of patients with a history of coronavirus infection (1 subgroup of patients 1.13 ± 0.28, in the second – 0.87 ± 0.25; $p = 0.022$).
4. We found no differences in mortality among patients with pulmonary embolism before and during the COVID-19 pandemic. However, this statement cannot be definitive, as pre-hospital mortality may have increased.

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