STROKE - CHALLENGE IN PATIENTS WITH COPD, CHRONIC PULMONARY HEART AND COVID-19 INFECTION

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Abstract

Chronic obstructive pulmonary disease (COPD) is the respiratory condition with the highest prevalence, with over 10% of individuals over the age of 40 presenting with this disease[(1)].

The COVID-19 infection has significantly increased morbidity and mortality among COPD patients, as well as the rate of complications within this pathology.

COVID-19 infection is a systemic inflammatory condition, with primary pulmonary involvement, but also with secondary gastrointestinal, cardiovascular, endocrinological, hepatic, renal, and, not least, neurological effects[(2)].

The degree of pulmonary involvement and bacterial superinfection have increased the risk of thromboembolic complications: stroke, atrial fibrillation (FiA), and death.

Keywords: *chronic obstructive pulmonary disease, COVID-19 infection, thromboembolic complications, chronic pulmonary heart.*

Rezumat

Boala pulmonară obstructivă cronică (BPOC) este afecțiunea respiratorie cu cea mai mare prevalență, afectând peste 10% dintre persoanele cu vârsta peste 40 de ani[(1)].

Infecția cu COVID-19 a crescut semnificativ morbiditatea și mortalitatea în rândul pacienților cu BPOC, precum și rata complicațiilor din această patologie.

Infecția cu COVID-19 este o afecțiune inflamatorie sistemică, cu afectare pulmonară primară, dar și cu efecte secundare gastrointestinale, cardiovasculare, endocrinologice, hepatice, renale și, nu în ultimul rând, neurologice[(2)].

Gradul de afectare pulmonară și suprainfecția bacteriană au crescut riscul de complicații tromboembolice: accident vascular cerebral, fibrilație atrială (FiA) și deces.

Cuvinte cheie: *boală pulmonară obstructivă cronică, infecție cu COVID-19, complicații tromboembolice, cord pulmonar cronic.*

Introduction

Chronic obstructive pulmonary disease (COPD) is considered one of the most significant, frequent, and widespread pathologies of the respiratory system. COPD is characterized by airflow limitation due to inflammation in response to inhaling toxins or cigarette smoking

COPD progresses with changes in pulmonary vascularization, with secondary cardiac effects, thereby increasing the incidence of a complex pathology known as Chronic Pulmonary Heart. This complicates diagnosis, medical therapy, and socio-economic costs[3,4].

Chronic pulmonary heart is defined as an alteration in the structure and function of the right ventricle of the heart in response to increased vascular resistance (such as pulmonary stenosis) or pulmonary arterial hypertension[5].

Hypercoagulability in COVID-19 infection is incompletely elucidated. Virchow's triad is present, with the three major categories of risk factors believed to synergistically contribute to thrombosis development. Endothelial injury - namely, endothelial lesions are produced under the action of the severe acute respiratory syndrome coronavirus 2. A complement-mediated endothelial injury has been demonstrated, and an in vitro study found that the SARS-CoV-2 spike protein plays a significant role in the generation of coagulopathy. Microvascular inflammation, endothelial exocytosis, endotheliitis, associated with endothelial lesions, determine the pathogenesis of severe disease[6].

A common in-hospital complication for patients with COPD, chronic pulmonary heart, and COVID-19, is newly developed acute stroke[7].

The purpose of the study

The purpose of this study is to highlight the relationship between COPD, chronic pulmonary heart, COVID-19 infection, and the risk of developing stroke in hospitalized patients.

Material and method

We conducted a retrospective study on a group of 126 patients, selected with the approval of the Management of Dr. Gavril Curteanu Municipal Clinical Hospital in Oradea, who were hospitalized for COVID-19 infection. The study group was selected from patients hospitalized for SARS-CoV-2 infection during the period December 2020 - January 2022.

	Without Stroke (n=89)	With Stroke n=(37)	Statistical Significance (p)
Gender (M/F)	67/22	26/11	0,7181*
Age (years) – median (IQR)	73 (64,75-77,00)	75 (70,00-77,50)	0,0526**
Place of Origin (U/R)	29/60	11/26	0,9177*
BMI (kg/ m^2) - median (IQR)	35 (30,00-37,57)	35 (28,00-37,20)	0,4372**
History of DZ(%)	40,45%	35,14%	0,7213*
History of HTA(%)	70,79%	72,97%	0,9753*
History of CPC (%)	66,29%	97,29%	**0,0006***

Table 1. *Demographic characteristics and pathological histories for the two groups*

AVC = Stroke, M = male, F = female, IQR = interquartil interval , U = urban, R = rural, BMI = Body Mass Index, DZ = Diabetes, HTA = Hypertension, CPC = chronic pulmonary heart
** - Chi-square test with Yates' correction*
*** - Mann-Whitney test*

	Without Stroke (n=89)	With Stroke n=(37)	Statistical Significance (p)
C-reactive protein (mg/dl) - average (DS)	187,54 (56,66)	199,05 (70,34)	0,3360*
Ferritin (mcg/L) – average (DS)	1188,29 (468,49)	1293,56 (507,09)	0,2644*
LDH (U/L) - average (DS)	287,07 (44,32)	310,61 (48,26)	**0,0072***
Procalcitonin (ng/dl) - median (IQR)	0,80 (0,70-0,97)	0,90 (0,80-1,00)	0,0599**
D-dimer (mcg/ml) - median (IQR)	1000 (900-1300)	1350 (1075-1700)	**0,0001****
Percentage of lung involvement (%) - median (IQR)	40 (31,75-55,00)	70 (56,50-78,00)	**<0,0001****

Table 2. *Paraclinical determinations at the time of admission for the two study groups*

AVC = stroke, LDH = Lactate dehydrogenase , DS = standard deviation , IQR = interquartil interval
** - Student's t-test for independent samples*
*** - Mann-Whitney test*

The inclusion criteria were:

- patients with COVID-19 infection
- positive diagnosis of COPD and Chronic Pulmonary Heart
- presence of risk factors: hypertension (HTA), obesity, diabetes (DZ)
- age 57-85 years
- patients fit to give consent and sign the informed consent

Results

Applying the selection criteria, a number of 126 patients with COPD were included in the study. Of these, 29.4% (37 patients) developed acute stroke during hospitalization. Comparing the demographic characteristics and pathological histories of the two groups (with and without stroke), we obtain the following results:

Patients who suffered acute stroke during hospitalization were older (but without reaching statistical significance), and among the pathological antecedents, only the presence of chronic pulmonary heart significantly increases the risk of stroke during hospitalization for SARS-CoV-2-induced pneumonia (relative risk: 11.7474, 95% CI: 1.67-82.17, p=0.0131). Sex, place of origin, body mass index, and history of diabetes mellitus or hypertension do not influence the risk of stroke under these conditions.

Regarding the paraclinical determinations at the time of admission, we obtained the following differences between patients who had a stroke and those who did not during hospitalization (Table 2).

Acute phase proteins showed higher values at admission in patients who developed stroke during hospitalization, but without reaching the threshold of statistical significance. However, LDH and D-dimers were present at much higher levels in the blood of patients in the stroke group. Additionally, the percentage of lung involvement had a negative impact on the outcome, with patients with more extensive lung involvement at increased risk of developing stroke complications.

The evolution of parameters during hospitalization and the occurrence of other complications have also been studied; their involvement in the development of stroke is presented in Table 3.

The negative evolution of acute phase proteins is associated with a higher risk of stroke during hospitalization; both C-reactive protein, ferritin, and procalcitonin were higher at 5 days in patients in the stroke group. The serum level of LDH, as well as D-dimers, were higher in this group. Additionally, the occurrence of a bacterial

	Without Stroke (n=89)	With Stroke n=(37)	Statistical Significance (p)
C-reactive protein at 5 days (mg/dl) – average (DS)	125,21 (65,40)	191,64 (64,00)	**<0,0001***
Ferritin at 5 days (mcg/L) – average (DS)	1159,17 (351,30)	1379,16 (251,62)	**0,0008***
LDH (U/L) at 5 days - average (DS)	297,64	398,38	**<0,0001***
Procalcitonin at 5 days (ng/dl) - median (IQR)	0,70 (0,60-0,90)	1,00 (0,70-1,77)	**0,0035****
D-dimer at 5 days (mcg/ml) - median (IQR)	800 (650-1025)	1800 (1545-2000)	**<0,0001****
Pulmonary bacterial exacerbation (%)	32,58%	75,68%	**<0,0001*****
New-onset atrial fibrillation (%)	55,05%	62,16%	0,5917***

Table 3. *Evolutionary criteria for the study groups*

AVC = Stroke, DS = Standard deviation, IQR = interquartil interval
** - Student's t-test for independent samples*
*** - Mann-Whitney test*
**** - Chi-square test with Yates' correction*

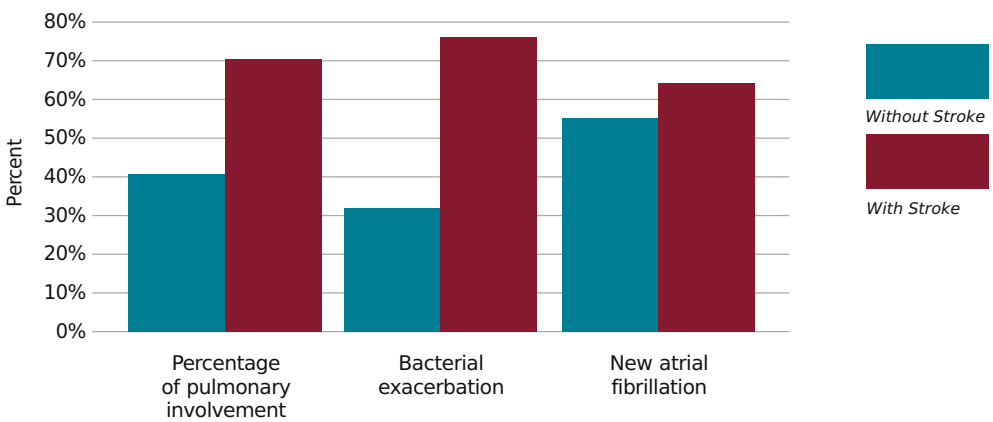

Figure 1. *Percentage of lung involvement (median), frequency of pulmonary bacterial exacerbation, and occurrence of atrial fibrillation for the two study groups*

Fără AVC = Without Stroke, Cu AVC = With Stroke
Procent de afectare pulmonară = Percentage of pulmonary involvement
Exacerbare bacteriana = Bacterial exacerbation
Fibrilație atrială nouă = New atrial fibrillation

exacerbation increases the risk of stroke by 3.7661 times (95% CI: 1.93-7.31), however, surprisingly, newly onset atrial fibrillation does not carry the same risk (Figure 1).

By introducing all variables with significant differences into a logistic regression model with the occurrence of stroke during hospitalization as the target, the percentage of lung involvement (odds ratio = 1.0721; 95% CI: 1.04-1.10, $p < 0.0001$) and serum level of D-dimer at 5 days post-admission (OR = 1.0047; 95% CI: 1.0030-1.0063, $p < 0.0001$) proved to be independent risk factors.

Analyzing the area under the ROC curve for the percentage of lung involvement, we can deduce a threshold value of over 55%, which presents a sensitivity of 75.68% and a specificity of 79.78% in predicting the occurrence of stroke during hospitalization. As for the serum level of D-dimer at 5 days post-admission, the threshold is over 1200 mcg/ml, with a sensitivity of 86.49% and a specificity of 84.27%.

Discussion

According to the conducted study, the presence of chronic pulmonary heart significantly increases the risk of developing a stroke.

Systemic inflammation markers (LDH, D-dimers), the degree of pulmonary impairment, played a major role in the onset of stroke.

Overlapping bacterial infection over viral infection entails risk for stroke.

Conclusions

The COVID-19 pandemic declared by the WHO on March 11, 2020, posed a significant global challenge socially, economically, and especially therapeutically. The major challenge was faced by patients with chronic conditions (COPD, CHF, hypertension, diabetes mellitus, obesity) whose course during SARS-CoV-2 infection was less favorable, resulting in complications (stroke, atrial fibrillation) and very reserved prognoses, including a high percentage of fatalities.

Coronavirus Disease 2019 is associated with a state of hypercoagulability. The degree of hypercoagulability depends on the systemic inflammatory response. Fibrinogen and D-dimers are elevated.

In the progression of cases, it was observed that viral infection often complicated with bacterial superinfection, confirmed by dynamic blood cultures. It should be noted that all these cases resulted in fatalities. The percentage of pulmonary involvement was high in the aforementioned cases and directly proportional to the newly installed complications (stroke, atrial fibrillation).

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