CARDIOVASCULAR PATHOLOGY – RISK AND SEVERITY FACTOR IN SARS-COV2 INFECTION

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Abstract: In the context of the current global pandemic, the COVID-19 pandemic, people and health systems all around the world have been under unprecedented stress. The pandemic has resulted in the dramatic loss of several million lives worldwide and the infection of over 5 hundred million people. According to the World Health Organization, people infected with the SARS-CoV2 virus experience respiratory symptoms, from mild to moderate, and their recovery is done with symptomatic treatment. However, some people may develop a serious form of the disease and require special medical care. Numerous factors help predict the adverse course and development of severe COVID-19 infection, as well as deaths related to this disease. Some of them are demographic in nature, such as age and gender, and others are related to diagnosed conditions, such as cardiovascular disease, diabetes or high blood pressure. It is very important to know the categories of people at risk and it is mandatory for this category of patients to be protected from the virus. This should be done, first of all, through correct information and prophylaxis and then through correct and effective treatment.

INTRODUCTION

In the context of the current global pandemic, the COVID-19 pandemic, people and health systems around the world have been under unprecedented stress. According to the World Health Organization, the pandemic has resulted in the dramatic loss of several million human lives worldwide and poses an unprecedented challenge to public health, food systems and the labour market, and the economic and social effects are devastating: tens of millions people are at risk of falling into extreme poverty, while the number of malnourished people is rising.(1) Since the beginning of the COVID19 pandemic, cardiovascular disease has been associated with higher mortality, and currently, patients with cardiovascular risk factors or heart disease are considered people at risk.(2) It has been shown that there is a causal relationship between cardiovascular diseases and SARS-COV2 virus infection in both directions. Cardiovascular risk factors such as hypertension, diabetes, and chronic cardiovascular disease, including ischemic heart disease and heart failure, are prevalent among hospitalized patients with a moderate to severe form of the new coronavirus 2019 infection (COVID-19).(3)

Although SARS-COV2 virus infection is one that can be treated symptomatically, prevention remains the most important protective factor.(4) Vaccination is the most important method of prophylaxis to prevent the spread of SARS-COV2 virus infection and it has been shown that vaccination stops the spread of the virus, decreases the chances of developing a serious form of the disease and decreases the chances of death of those infected.(5)

AIM

The aim of our study was to establish the role that cardiovascular pathology plays in SARS-CoV2 virus infection.

This paper wanted to verify whether cardiac pathology can be considered a risk factor for infection, as well as the importance of cardiac pathologies in predicting the severity of the infection, within a group of population in Mureș County, Romania. We designed this paper in hope that the findings of this study can be used to guide decisions in the following waves of this pandemic and also in future pandemics.

MATERIALS AND METHODS

A total of 80 patients were included in our observational, retrospective study, that took place between January and April, 2021. The subjects were hospitalized in the COVID-19 sector of the Pneumology Clinic, within the Mureș County Hospital. The selected patients were positively confirmed as being infected with the SARS-CoV2 virus and were chosen according to the history of cardiovascular diseases (hypertension, heart failure, arrhythmias).

When collecting the information needed, we analysed data of the hospitalized patients including: general condition at hospitalization and discharge, treatment, number of days of hospitalization and care in the Intensive Care Unit Department, age, sex, body mass index, comorbidities, symptomatology. Results of laboratory tests (C-reactive protein, fibrinogen, ferritin) and results of imaging examinations (Computer Chest Tomography) were also included in our database.

RESULTS

Of the 80 cases included in the study, 59% (47) were maleS and the remaining 41% (33) females. At hospitalization, depending on the symptoms presented and the general condition, the form of disease associated with SARS-COV2 virus infection was established. Thus, the majority of patients included in the group, namely 66.25% (53) had a moderate form of the disease,

28.75% (23) suffered from a severe form of the disease, and only 5% (4) of hospitalizations had was for a mild form of infection. When comparing the form of COVID disease with the general condition at discharge, we found that there is a significant association (p <0.001) between the severe form of the disease and death (figure no. 1). Thus, 69.6% of those with severe form died, while 86.0% of those with a mild form of infection survived. At the time of hospitalization, the general condition of the patients included in the study was mostly classified as "average" 43.75% (35), and at the opposite end hospitalized patients with severe general condition 17.5% (14).

Figure no. 1. Statistical association between disease form and death
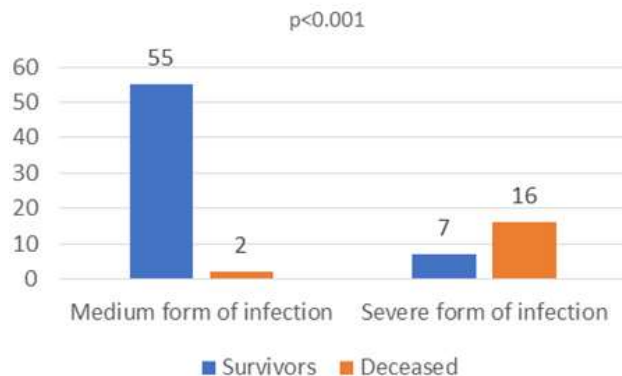
The main symptoms of interest, followed by anamnesis upon arrival at the clinic, were fever (defined by a measured body temperature above 37 degrees Celsius) and cough. It is observed that these symptoms were present in most patients, so 57.5% (46) of the patients have had fever upon arrival and 68.75% (55) of the patients reported coughing. We obtained a statistically significant result regarding fever and as there was a significant association between presence of fever and a severe form of the disease (p <0.05), and 78.3% of those with a severe form of COVID had a fever at hospitalization. (figure no. 2).

Figure no. 2. Statistical association between form of infection and fever
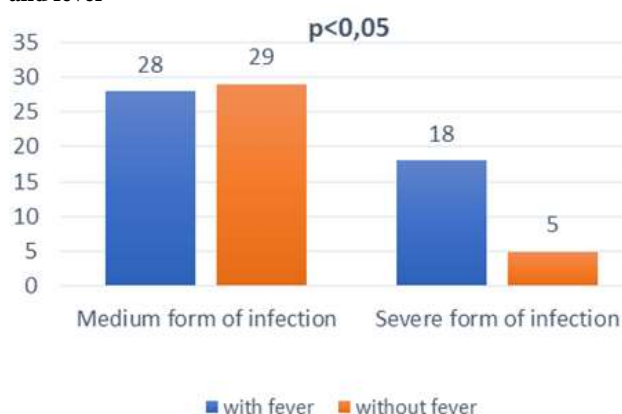
The rate of mortality within the patients included in our study was 22%. This high rate can be attributed to the old age in the group, most of them being aged between 71 and 80 years old (31.25%) (table no. 1), with an average of 71.83 ± 11.32 years. This can be associated with a higher prevalence of comorbidities. About the pre-existing personal pathological history of the patients: 93.75% (75) of the patients presented with hypertension, 62.5% (50) had the diagnosis of heart failure, 35% (28) of them were confirmed as diabetics, respectively 30% (24) with heart rhythm disorders. As for the degree of

hypertension in the group, most, 72% (54), were diagnosed with grade 2 hypertension, and the remaining 16% (12) and 12% (9) of grade hypertension 1 and grade 3, respectively. If in the previously presented ones, we analysed the presence of cardiovascular comorbidities in the studied group, the patients presented at the time of hospitalization and other comorbidities, these being found in a percentage of 78% (62). We calculated the body mass index (BMI) based on the measurements performed at the hospitalization of patients in the clinic, according to the international standard formula (weight / height squared) and the results showed that only one patient in the group (1.25%) was classified as underweight; 21.25% (17) of patients had a normal body mass index between 18.5 and 24.9 at admission; 33.75% (27) were classified as overweight; 27.5% (22) suffered from grade 1 obesity, 7.5% (6) from grade 2 obesity and 8.75% (7) from morbid obesity. As of smoking, the tendency observed in our group of patients was not to smoke. However, 28.75% (23) of the group were smokers or had smoked in the past, of which 64% (16) are men and 36% (7) are women. Diabetus mellitus was another chronic disease present in our group of patients, although in a smaller proportion than hypertension or heart failure, representing only 35% (28), and the distribution by sex was equal and both men as well as women totalling 17.5% (14).

Table no. 1. Age groups – Cardiovascular pathology- Risk and severity factor in SARS-CoV2 infection

| Age group	Number of patients	Percentage of patients
38- 40 years old	1	1,25%
41- 50 years old	3	3,75%
51- 60 years old	7	8,75%
61- 70 years old	24	30%
71- 80 years old	25	31,25%
81- 90 years old	18	22,5%
over 90 years old	2	2,5%

Regarding the treatment followed during the hospitalization, 60% (48) required antibiotic therapy and 13% (10) of the patients needed antiviral treatment. When comparing the group of patients according to the form of the disease and the treatment received during hospitalization, 82.6% of those with severe disease received antibiotic treatment. Thus, there is a significant association (p <0.01) between the form of the disease and antibiotic treatment. A percentage of 97.5% of those included in the group benefited from anti-inflammatory treatment based on corticosteroids. Of these, 10% (8) and 51.25% (41) were treated with dexamethasone 8 milligrams and 16 milligrams per day, respectively and the remaining 18.75% (15) received 250 milligrams of methyl prednisone per day. Anticoagulant treatment benefited all patients included in our study, but in different doses, as 57.5% (46) of the patients received a total of 1.2 milligrams per day of subcutaneous Fraxiparine, 27.5% (22) of them received 0.8 milligrams of Fraxiparine per day, and the remaining 0,4 or 0,6 milligrams per day. During hospitalization, 21% (17) of patients needed care in the Intensive Care Unit. Of these, the majority of 53% (9) spent between 1 and 5 days on this section.

Upon admission in the clinic, patients received a set of tests. D-dimers were analysed and 26% (21) of patients had a positive result, meaning a value greater than 0.5 micrograms / millilitre FEU. In the analysis of C-reactive protein, 86% (69) of the patients in the group obtained pathological results, meaning values higher than 10 milligrams / decilitre. In the analysis of ferritin in the blood, the normal values varying according to sex, all women in the group (33) obtained pathological values higher than 150 nanograms / decilitre, and a percentage of 90% (42) of the total men they obtained pathological values, i.e. values higher than 300 nanograms / decilitre. In the fibrinogen analysis,
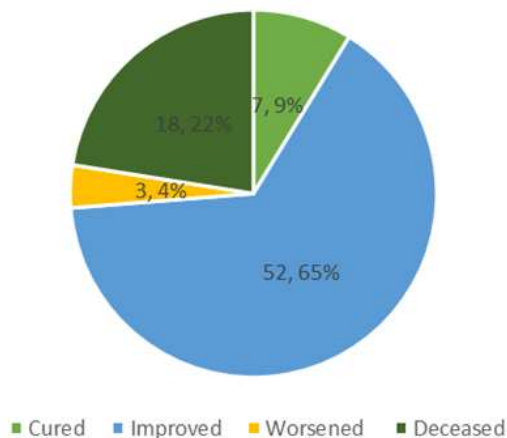
59% (47) of the patients in the group had values higher than 400 mg / dl, being prone to thrombotic events and only one patient had a value below 200 mg / dl, being at risk for bleeding events; the rest having normal values. When analysing the correlations, we compared the number of days of hospitalization and the results of the fibrinogen analysis at hospitalization and we found that there was a statistically significant positive correlation between the 2 data groups, with a p = 0.02, r = -0.25, CI95%: -0.4505 and -0.03862 (figure no. 3). From an imaging point of view, patients were evaluated using computed tomography and 68% (54) of the study participants were found to have the specific appearance of "matte glass" of lung tissue.

Figure no. 3. Statistical correlation between fibrinogen results at admission and number of days spent in the hospital
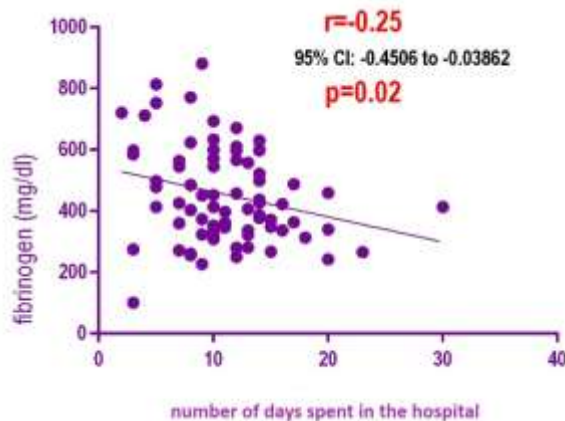
Following the hospitalization period and the care received during hospitalization, 65% (52) of the patients were discharged with an improved general condition, 9% (7) were cured, and unfortunately 22% (18) of the patients died and 4% (3) were discharged in serious general condition, to be readmitted to an intensive care unit (figure no. 4).

Figure no. 4. General condition at discharge

DISCUSSIONS

A mortality rate of 22% is observed in our group of patients included in the study. This high rate can also be attributed to the advanced age of the patients in the group, most of them being included in the age group 71-80 years (31.25%), with an average age of 71.83 ± 11.32 years, but also the higher prevalence of comorbidities associated with old age.(6)

At the same time, the high mortality rate can be explained by the severity of COVID disease in our group of patients. Of these, 28.75% (23) presented with a severe form and 17.5% (14) were hospitalized with a serious general condition, 57.5% (46) of them presenting with fever and 68.75 % (55) accusing cough. We demonstrated statistically the significant association between the general condition at hospitalization and the severity of the disease (p <0.01), respectively the significant association between the severity of the disease and death (p <0.001).

The study, published by Nicholas S. Hendren in the American Heart Association in 2020, which included patients from 88 hospitals in the United States, looked at body mass index and obesity as possible risk factors for SARS-VOC2 infection. It concluded that obese people are more likely to develop a form of illness that requires hospitalization and that the risk of death is higher in these people.(7) In our study, we note that the trend is to have a higher than normal body mass index, with 33.75% (27) being overweight and a total of 43.75% (35) being in one of the following degrees of obesity although statistically the results did not prove statistically significant.

A meta-analysis published in 2021 by Amirhossein Hessami, which studies the results of 56 studies and 198 scientific papers, analysed a total of 159,698 patients worldwide hospitalized with SARS-VOC2 virus infection.(8) It concludes that cardiovascular disease is a factor in the severity of COVID disease and also a factor influencing the mortality of infected patients. She also says that high blood pressure, coronary heart disease, arrhythmias and heart failure can lead to the death of those infected with the SARS-COV2 virus and that close monitoring of these patients is needed.(9) Although they did not exceed the threshold of statistical significance in our study, we consider the conclusions of the applicable meta-analysis and our study given the high incidence of cardiovascular disease in the patient group: 94% (75) with hypertension, 62.5% (50) with heart failure and 30% (24) with heart rhythm disorders.

In a study of patients with COVID-19, it was found that people with severe and very severe forms had elevated serum ferritin levels, this analysis being statistically significantly higher in the more severe group.(10) Although this association was not statistically demonstrated in our study, the pathological values are predominant. Thus, 100% of the women included in the study obtained pathological values, higher than 150 ng / dL, and a percentage of 90% (42) of the total men obtained pathological values higher than 300 ng dL.

A study published in 2021 concludes that an increased level of inpatient C-reactive protein in patients with COVID-19 was associated with increased mortality and indicated the severity of the disease at admission.(11) Although this aspect did not prove to be statistically significant, in our group there is a tendency to have pathological results, respectively 86% (69) of those hospitalized.

Laboratory parameters of patients with COVID-19 showed a prothrombic diathesis with significantly high levels of fibrinogen in critically ill patients, in a study published in 2020, at the beginning of the pandemic.(12) In our study, the correlation between the high level of fibrinogen and the number of days of hospitalization showed significant statistics, p = 0.02, r = -0.25, CI95%: -0.4505 and -0.03862. Most of those included in our study required more than one week of hospitalization (62.5%) with an average hospital stay of 11.03 ± 4.82 days.

In a study of 81 patients in Wuhan, China, the epicentre of the pandemic, it was concluded that COVID-19 pneumonia is manifested by chest CT imaging abnormalities, even in asymptomatic patients, with rapid evolution from focal opacity, unilateral to diffuse, bilateral "frosted glass" opacities.(13) The incidence in our group of patients of the "matte glass" aspect is 68% (54), but no statistical association with other data from the study was found to be significant.

CLINICAL ASPECTS

CONCLUSIONS

Although a direct relationship between the studied cardiovascular pathology and the severity of the SARS-COV2 virus infection has not been proven statistically, the studied group has a high mortality rate. This can be attributed to the advanced age of the patients and the higher incidence of comorbidities with age, as the majority of patients who required hospitalization in the COVID19 ward were in their seventh decade of life and had multiple associated comorbidities, both cardiac and of other nature. The general condition at hospitalization was found to be correlated with the severity of the disease, and the severity of the infection was associated with death.

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