Main Comorbities or Factors that Increase the Risk of Stroke in Patients with COVID-19

Principais Comorbidades ou Fatores que Aumentam o Risco de AVC em Pacientes com COVID-19

Principales Comorbidades o Factores que Aumentan el Riesgo de AVC en Pacientes con COVID-19

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RESUMO

Objetivo: Identificar comorbidades que aumentem a probabilidade do risco do paciente contaminado pela Covid-19 de desenvolver como complicação o quadro de Acidente Vascular Cerebral (AVC). Método: O presente estudo trata-se de uma revisão de literatura, descritiva exploratória, que após a seleção e revisão dos artigos encontrados em bancos de dados virtual, compreendidos nos anos de 2019 a 2021, procedeu-se a análise dos artigos e elaboração da revisão de literatura e discussão sobre o aumento do risco de AVC em paciente com Covid-19. Resultado: A possível relação entre a Covid-19 e o AVC, está no próprio mecanismo de ação do SARS-CoV-2, que ao se ligar no receptor da ECA2 que também está presente no tecido cerebral, o vírus diminui a ação desta enzima, intervindo diretamente no Sistema Renina-Angiotensina-Aldosterona (SRAA), provocando uma lesão tecidual cerebral, gerando um grande fator de risco para ocorrência de AVC. Conclusão: Os principais fatores de risco para complicação da Covid-19, são os cardiovasculares seguidos de pneumopatias, Diabetes Mellitus e idade. Assim, o uso de escore que possa classificar o risco do paciente evoluir com AVC baseado em comorbidades ou fatores de risco, em casos suspeitos ou confirmados de Covid-19, permite a intervenção precoce da equipe e assim a redução de complicações com sequelas ou óbitos.
Descritores: COVID-19, Cuidados da enfermagem; Acidente Vascular Cerebral.

ABSTRACT

Objective: To identify comorbidities that increase the probability of the risk of the patient infected by Covid-19 of developing stroke as a complication. Method: The present study is a literature review, exploratory descriptive, which after the selection and review of articles found in virtual databases, between 2019 and 2021, was carried out the analysis of the articles and preparation of the literature review and discussion on the increased risk of stroke in patients with Covid-19. Result: The possible relationship between Covid-19 and stroke is in the mechanism of action of SARS-CoV-2, which by connecting to the ECA2 receptor that is also present in brain tissue, the virus decreases the action of this enzyme, intervening directly in the Reinnine-Angiotensin-Aldosterone System (AAR), causing a brain tissue injury, generating a great risk factor for stroke occurrence. Conclusion: The main risk factors for complication of Covid-19 are cardiovascular patients followed by pneumopathy, Diabetes Mellitus and age. Thus, the use of a score that can classify the risk of the patient developing stroke based on comorbidities or risk factors, in suspected or confirmed cases of Covid-19, allows the early intervention of the team and thus the reduction of complications with sequelae or deaths.
Descriptors: COVID-19, Nursing care; Stroke.

RESUMEN

Objetivo: Identificar comorbilidades que aumenten la probabilidad de que el paciente infectado por Covid-19 desarrolle ictus como complicación. Método: El presente estudio es una revisión bibliográfica, exploratoria descriptiva, que tras la selección y revisión de artículos encontrados en bases de datos virtuales, entre 2019 y 2021, se llevó a cabo el análisis de los artículos y preparación de la revisión bibliográfica y discusión sobre el mayor riesgo de ictus en pacientes con Covid-19. Resultado: La posible relación entre el Covid-19 y el ictus está en el mecanismo de acción del SARS-CoV-2, que al conectarse al receptor ECA2 que también está presente en el tejido cerebral, el virus disminuye la acción de esta enzima, interviniendo directamente en el Sistema Reinnina-Angiotensina-Aldosterona (AAR), provocando una lesión tisular cerebral, generando un gran factor de riesgo para la ocurrencia de ictus. Conclusión: Los principales factores de riesgo de complicación del Covid-19 son los pacientes cardiovasculares seguidos de neumopatía, Diabetes Mellitus y edad. Así, el uso de una puntuación que puede clasificar el riesgo de que el paciente desarrolle ictus en función de comorbilidades o factores de riesgo, en casos sospechosos o confirmados de Covid-19, permite la intervención precoz del equipo y así la reducción de complicaciones con secuelas o muertes.
Descriptores: COVID-19, Cuidados de enfermería; Accidente Cerebrovascular.

REVIEW

Introduction

The coronavirus had its first case in 1937, and after 28 years, in 1965, another episode was recorded. The World Health Organization (WHO), between 2002 and 2003, recorded 774 deaths as a result of Severe Acute Respiratory Syndrome (SARS); 858 deaths attested in 2012 were caused by Middle East Respiratory Syndrome (Mers-CoV).[1]

On February 7, 2020, Dr. Li Wenliang, an ophthalmologist in Wuhan City, Hubei Province, China, passed away from Covid-19. Months earlier, Dr. Li, in an attempt to notify other professionals, urged physicians to use personal protective equipment during patient care. He is considered as 1 among 8 professionals who tried to warn the world about the disease. For such an action, Dr. Li was considered, in his home country and in the world, a hero due to his constant toil.[2]

We started the year 2020 with the milestone of the pandemic, in the case of pneumonia with the first case confirmed in December 2019 in the city of Wuhan, located in China, caused by SARS-CoV-2, a pathogen with more moderate initial symptoms, on the other hand, its propagation is superior to the others.[1]

Acute Respiratory Syndrome (SARS) is presented as one of the most aggressive symptoms caused by the SARS-CoV-2 virus, however, the risk factors significantly imply the prognosis of patients affected by Covid-19. The most common comorbidities for the disease are age, Diabetes Mellitus, hypertension, smoking and lung diseases. Patients affected by Covid-19 who have any of these risk factors have their mortality rate increased.[3]

On March 11, the WHO officially declares a Public Health Emergency over the pandemic caused by the SARS-CoV-2.4 virus Covid-19 has spread rapidly around the world; such spread is due to acute respiratory syndrome infection caused by SARS-CoV-2 infection. As of July 26, 2020, the virus has reached approximately 15,785,641 confirmed cases, including 640,016 deaths worldwide.[5]

The Health Surveillance System in Brazil recorded in November 2021 the total number of confirmed cases was 252,976,666; while deaths total 5,095,849; Regarding the classification of the 5 countries with the highest incidence of registered cases, the United States led with (47,056,556), India (34,437,307), Brazil (21,953,838), the United Kingdom (9,572,351) and Russia (8,881. 306). As for deaths, there is a differentiation in the classification, in which the United States is first (762,972), followed by Brazil (611,222), followed by India (463,530), Mexico (290,872) and Russia (249,415).[6]

As defined by the World Health Organization (WHO), the signs and symptoms at the beginning of the disease resemble a mild flu. The manifestations vary from individual to individual, and may present as malaise, fever, fatigue, cough, mild dyspnea, anorexia, sore throat, body ache, headache or nasal congestion, and some may also present diarrhea, nausea and vomiting; in the severe form, pneumonia, severe pneumonia and SARS are evident. Elderly people and individuals with preexisting comorbidities have a high probability of accelerated worsening and the emergence of atypical symptoms, causing sequelae or even death.[7]

For the World Health Organization (2020) patients affected by Covid-19 aged over 60 years, with present comorbidity or associated risk factors, tend to have serious complications, not only related to the respiratory system, but also to the neurological, including the stroke.[14]

According to Carmona, Sousa, Miranda (2021), cases of patients with Covid-19 can evolve with ischemic strokes being clinically more serious and with higher mortality, in which the occurrence rate can vary between 1% and 6%; also state that cases of hemorrhagic stroke and cerebral venous thrombosis may be consequences of the effects of Covid-19, where the pathophysiology seems to be associated with the systemic inflammatory response to infection with large cytokine production, post-infection immune-mediated response or by direct effects that the virus generates in the arterial system by inducing angiitis, contributing to thrombogenesis and promoting the instability of existing atheromatous plaques. The authors also report that hypoxia also contributes to the increased incidence of strokes, taking less oxygen to the brain and potentiating the onset of heart and embolic diseases.[8]

For Araújo (2020), patients with positive PCR for SARS-CoV-2, with comorbidities, who are immunosuppressed, hospitalization is recommended regardless of whether the signs and symptoms are mild or not.[9]

Multidisciplinary teams based on technical and scientific knowledge are able to identify signs and symptoms in patients with Covid-19 that can lead to cerebrovascular accidents. Covid-19 is currently the priority. In addition, more research is needed to identify the neurological implications of Covid-19, its systemic manifestations, the possible causal relationship between the occurrence of stroke and SARS-CoV-2 infection and the need for blood components, especially when the pathogenesis of disease contributes to the mechanism of coagulopathy and endothelial dysfunction, as clotting parameters may have prognostic value in Covid-19 infection.

The interpretation of laboratory tests and images are of paramount importance for the identification of possible diseases in patients with Covid-19, D-dimer, a product of fibrin degradation, when elevated, has been associated with a higher mortality rate. Expert opinion, based on clinical experience and analysis of a few descriptive studies, highlights the role of the hypercoagulable state in the pathophysiology of Covid-19, as the level of D-dimer progressively increases with the exacerbation of the infection. The phase of the disease in which ARDS develops and the radiological pattern worsens is marked by a significant increase in D-dimer, with myocardial injury and disseminated intravascular coagulation being observed in the most severe cases.[11]

Although the etiology is not well established, in addition to the difficulties in carrying out some tests in a timely manner, cases of strokes classified as cryptogenic, followed by a cardioembolic condition, are closely related to contamination by SARS-CoV-2, due to their affinity with the receptors for angiotensin 2 converting enzymes which, together with the inflammatory response, causes an increase in blood pressure and may result in the rupture of the arterial wall. Contamination occurs more frequently in a hospital environment and the manifestation of signs of stroke to be diagnosed takes about 10 days from the moment of contamination.8

Cerebrovascular accidents (CVA) are presented in two ways: ischemic and hemorrhagic. Ischemic stroke is the blockage of an artery preventing blood flow and oxygen; hemorrhagic is the rupture of a vessel, causing cerebral hemorrhage.[12]

For Reis, Lima (2020), the use of a table that scores the risk factors helps the team to identify and classify the risk of thrombosis, and with that, start prophylaxis to try to avoid the occurrence that contributes to the worsening of

the condition. of these patients, reducing the number of critically ill patients who reach the stage of hospitalization in the Intensive Care Unit (ICU).[13]

Given the above, knowing the evolution of the disease and risk factors for cardiovascular diseases allows nursing professionals to identify early on the possibility of the patient with the SARS-CoV-2 virus evolving with complications.

Thus, the present study aims to identify comorbidities or risk factors that increase the probability of the patient contaminated by Covid-19 developing as a complication the condition of Cerebral Vascular Accident (CVA).

Method

The present study is an exploratory descriptive literature review, as it is appropriate to describe, discuss and broadly analyze the published literature on the subject, from a theoretical or contextual point of view, on the increased risk of Stroke in a patient with Covid-19, and it is necessary to carry out, seek and gather the contribution of different authors, their professional experiences and differentiated approaches on the subject.

The present study was divided into five stages described below.

First step: Selection and review of articles found in databases such as the Virtual Health Library (VHL), Latin American Literature on Onli Health Sciences (LILACS), Specialized Bibliographies in the Brazilian Nursing Area (BDENF), Bireme, and in the SciELO- Scientific Electronic Library, from 2019 to 2021. A search for articles was carried out in order to prepare a literature review of a descriptive and exploratory nature.

Second stage: The inclusion and exclusion criteria of articles were used, where publications that portray the theme were used: The increased risk of stroke in patients with Covid-19. The following descriptors were used: Covid-19, AVC; nursing care; risk classification, and pre-selection of articles with full text in Portuguese and English was carried out. After the pre-selection of 37 articles, 21 articles were used, which comprised the search text and a systematic review that addressed these descriptors.

Third step: All ethical criteria were followed according to the rules and selection of articles that met the pre-established inclusion criteria. Subsequently, in possession of the potential bibliography, qualitative analysis and analytical reading were carried out. In addition, a careful analysis of the articles was performed because it is a literature review. The importance of preserving the author's idea was also considered.

Fourth stage: After reading and analyzing the articles, a literature review and discussion on the increased risk of stroke in patients with Covid-19 was prepared.

Fifth stage: The present study was developed from September to November 2021 and followed the standards of the NIP (Interdisciplinary Research Center) of the ICESP University Center of Brasília and the Brazilian Association of Technical Standards (ABNT).

Results and Discussion

According to the selected articles and the one described by the World Health Organization, among the main complications associated with Covid-19

are: respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism and clotting disorders, of multiple organs including acute kidney failure, liver failure, heart failure, cardiogenic shock, myocarditis, encephalopathy, stroke, meningoencephalitis, altered sense of smell (anosmia) and taste (ageusia), anxiety, depression, sleep disturbances and Syndrome of Guillain-Barré.[14]

SARS-CoV-2 has neuro-invasive abilities, proliferating from the respiratory system to the central nervous system (CNS), when it reaches the CNS it can cause brain damage by two processes; the virus binds to the receptors for angiotensin-converting enzymes 2 (ACE-2), which are present both in CNS cells and in the endothelium, can also be a consequence of damage to the blood-brain barrier and hypercytokinemia, causing thromboembolic and hemorrhagic episodes , these lesions are intensified by the increase in vascular pressure resulting from the deregulation of the Renin-Angiotensin-Aldosterone System (RAAS), caused by the binding with the angiotensin-2 converting enzyme.[15]

Silva et al., (2020) describes that chronic use of ACE inhibitors (ACEI) and/or angiotensin II receptor blockers (ARB II), causes patients with hypertension to have ACE diffusely expressed by the body; the author reinforces some discussions about the likelihood of involvement of the angiotensin-converting enzyme 2 (ACE2) in the pathophysiological mechanism of cellular incorporation of the virus into host cells, making the patient more susceptible to contamination by the virus SARS-CoV-2.[3]

The possible relationship between Covid-19 and stroke, according to Neto; Oliveira; Vasconcelos (2021), it is in the SARS-CoV-2 mechanism of action that, by binding to the ACE2 receptor, which is also present in brain tissue, the virus reduces the action of this enzyme, directly intervening in the Renin-Angiotensin System. -Aldosterone (RAAS) and causing brain tissue damage, generating a major risk factor for the occurrence of stroke.[16]

For Orsini et al., (2020), the pathophysiology of Covid-19 included an intense activation of the inflammatory process and stimulation of the thrombotic system, generating the clinical complication of disseminated intravascular coagulation, which is associated with most cases of deaths.[17]

It highlights what was described by Bortoluzzi et al., (2017) apud Barbosa et al., (2021), that arterial thrombosis has signs related to tissue hypoperfusion and ischemia of the area, which can be observed depending on its location. Time of vessel occlusion and existence of collateral circulation, intense and progressive pain mainly in distal regions, decreased or absent capillary refill time are coherent signs of the pathology and, in the case of reactive hyperemia, it is proportional to the degree of ischemia, a test that can be used to confirm blood flow. They also state that it is essential to observe the following signs and symptoms: paresis, absence of pulse, pallor, paralysis and hypothermia.[18]

Laboratory tests of blood count, D-dimer, coagulogram paying attention to prothrombin time (PT), C-reactive protein (CRP), activated partial thromboplastin time and Doppler and computed tomography angiography (CT angiography) and observation of the results of changes coagulation-related laboratory tests, are predictors of evolution, increased thrombin synthesis, decreased fibrinolysis, elevated D-dimer values, increased fibrinogen, prolonged prothrombin time, thrombocytopenia, lymphopenia, neutrophilia, leukopenia, changes in erythrogram (decrease in the number of red blood cells and the percentage of hematocrit) are extremely important.[18]

For Nascimento et al., (2020), the decrease in the hypercoagulable state must be balanced with the risk of bleeding, and it is possible that anticoagulant therapy is more beneficial when started in the pre-thrombotic phase than in advanced conditions. When the risk of bleeding is higher, anticoagulation is suggested, and the use of Low Molecular Weight Heparin (LMWH) is recommended, the drug of choice in stable patients with normal creatinine clearance, but in case of shock or creatinine below 50 ml/min/m², intravenous heparin is preferred, targeting an activated partial thromboplastin time between 1.5 and 1.8.[11]

The CHA(2)DS(2)-VASc score was developed to improve stroke risk stratification in patients with atrial fibrillation (AF) by classifying patients according to the factors presented. If the patient has two points or higher, he is classified as a high-risk patient; one point is classified as an intermediate risk; and those that do not score are low risk. However, due to the complications caused by Covid-19, it has been suggested to include 1 point for Covid-19 in the score, and thus, indicate prophylaxis of thromboembolic events before the worsening of the condition, as shown in Figure 1.

Figure 1- Score of CHA (2) DS (2) –VASc. 2022[13]

CHA_2DS_2-VASc	Descrição	Pontos
C	Insuficiência cardíaca	1
H	Hipertensão	1
A_2	Idade (≥ 75 anos)	2
D	Diabetes mellitus	1
S_2	AIT ou AVC prévio	2
V	Doença vascular (IAM prévio, placa aórtica, doença arterial periférica)	1
A	Idade (65-74 anos)	1
C19	Suspeita ou confirmação de COVID-19	1

AIT = ataque isquêmico transitório; AVC = acidente vascular cerebral; IAM = infarto agudo do miocárdio.

Thus, according to Reis and Lima (2020), it would be possible to start prophylaxis to try to avoid the occurrence of what has contributed to the worsening of the clinical picture of these patients by adopting the modified CHA (2) DS (2) -VASc score, facilitating the team in decision making for the initiation of prophylaxis for stroke as shown in Figure 2.[13]

Figure 2- Phase classification according to score score. 2022.[13]

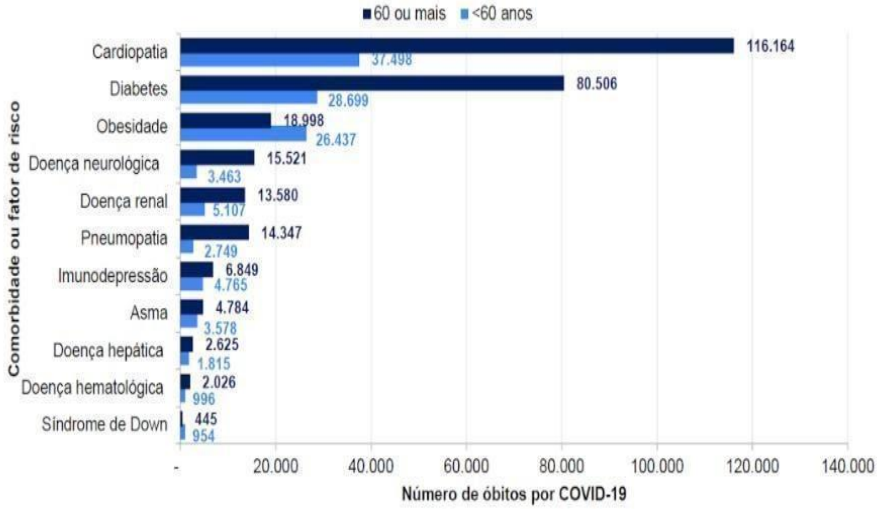
Fases	Clínica	Tratamento
Fase 1	Infecção respiratória gripal	Evitar contágio, diminuir sintomas, diminuir carga viral com as medicações que estão sendo usadas
Fase 2 (verificar Tabela 1)	Alto risco de trombose	Profilaxia, evitar trombose intrapulmonar, anticoagulação profilática
Fase 3	Paciente grave em UTI	Anticoagulação plena terapêutica

UTI = unidade de tratamento intensivo.

According to Filho et al., (2021), histories and vascular risk factors in patients determine the increased chances of developing stroke with the existence of hypotension, heart failure and shock, which collaborate in hypoperfusion, stroke embolic mechanisms and obstruction of great vessels. The author states that about 1.5% of patients progressed with neurological manifestations such as

stroke with a mortality rate of 38%. It also describes a study carried out in China with a group of 4,466 patients, 135 progressed to a stroke, 62.3% of whom were men with a mean age of 63.4 years who had comorbidities such as SAH 64.5%, DM 42.6% and Dyslipidemias 32%.19 The data presented by Filho et al., (2021), are similar to those presented in Brazil, as shown in Figure 3.

Figure 3- Comorbidities and risk factors for deaths from Severe Acute Respiratory Syndrome (SARS) by Covid-19. 2022.[20]



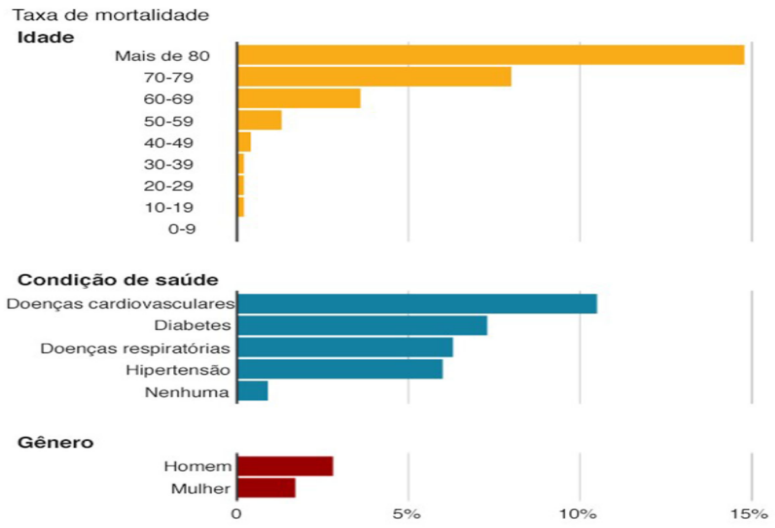
According to Carmona; Sousa and Miranda (2021), the increase in the incidence of ischemic stroke in patients who developed Covid-19 varies between 1 to 6%, with the cases being clinically more severe and disabling, the diagnosis appears late, the author also emphasizes that the most cases settle in older patients and those with cardiovascular risk factors.[8]

For Feitoza et al., (2020), comorbidities are defined as the presence of two or more pathologies in the same period of time in a single patient, for example: heart disease, diabetes and hypertension; among patients with Covid-19, 20% to 51% were identified with the presence of comorbidities.[21]

Rubino (2020) highlights that diabetes is mentioned as one of the most important aggravating factors for the new coronavirus, when he describes that the virus that causes Covid-19, connects to the receptors of the angiotensin-converting enzyme 2 (ACE2), which are expressed in major metabolic organs and tissues, including pancreatic beta cells, adipose tissue, small intestine, and kidneys. Thus, it is plausible that SARS-CoV-2 could cause pleiotropic changes in glucose metabolism, which could exacerbate the pathophysiology of preexisting diabetes or lead to new disease mechanisms.[22]

According to Silva et al., (2020), elderly patients constitute another risk group for the aggravation and mortality of Covid-19 infection, due to the physiological degradation of the immune system, called immunosenescence, which occurs with aging, loss of immunological memory and the body's ability to respond to infections, and it is therefore undeniable that the previous clinical condition in which the patient is already found strongly influences the prognosis of the patient infected with the SARS-CoV-2 virus, as we can see in the Figure 4.[3]

Figure 4- Group of patients who progress poorly from infection with Covid-19. 2022.[13]



The relationship between the SARS-CoV-2 virus and ACE-2 is a consensus among the authors, when they describe that this junction causes an alteration in the Renin-Angiotensin-Aldosterone System, which leads to an increase in blood pressure, causing brain tissue damage and hypercytokinemias, favoring thromboembolic and hemorrhagic factors, and thus, greater risk for the occurrence of stroke.

For Reis and Lima (2020), people with heart diseases, lung diseases, neuropathies, Diabetes Mellitus, obesity, advanced age and being male are more susceptible to developing stroke when infected by SARS-CoV-2. The implementation of the modified CHA(2) DS(2)-VASc Score will be of paramount importance for the early identification of stroke risk and thus outline the appropriate therapeutic action for each phase.[13]

A set of laboratory and imaging tests and the use of scores are essential for monitoring physiological changes, signaling the indication of possible complications, allowing the multidisciplinary team to act in a prophylactic way, reducing the incidence of patients with significant sequelae from stroke or even even the death.

Conclusion

Patients with comorbidities or risk factors are more likely to develop stroke than healthy patients.

The most complex risk factors are cardiovascular, followed by lung disease and Diabetes Mellitus, in addition to age.

Access to diagnostic imaging services and laboratory monitoring are essential for controlling the evolution of the pathology and its complications.

The use of a score that can classify the risk of the patient evolving with stroke based on comorbidity or risk factors, as well as the suspicion or confirmation of Covid-19, associated with test results, allows early intervention by the team and thus the reduction of complications with sequelae or deaths.

Due to the complexity of the pathophysiology and the speed of unfavorable evolution of most patients with various comorbidities or risk factors, further studies are suggested to elucidate the manifestations caused by SARS-CoV-2 for prophylactic action by multidisciplinary teams.

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