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STROKE IN COVID-19 PATIENTS: A SCOPING REVIEW

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ABSTRACT

Objective: to map the scientific production on patients infected by COVID-19 and the occurrence of stroke.
Method: a scoping review, according to the framework proposed by the Joanna Briggs Institute, using the LILACS, MEDLINE, WoS, EMBASE, CINAHL and SCOPUS databases, from April to September 2020. The following keywords were used: coronavirus infections, stroke, nervous system diseases and inpatients, based on the Medical Subject Headings.
Results: 24 studies that evidenced specific clinical symptoms of stroke such as dysarthria, facial paralysis, sensory deficit, headache, hemiparesis and ataxia in patients with COVID-19 were included. The association between stroke and COVID-19 was found by the following exams: C-reactive protein, D-dimer, computed tomography and, magnetic resonance, among others, as well as by care procedures focused on the findings in the exams, associated with three clinical outcomes, based on the brain ischemia zone affected and the time of viral manifestation of each patient.
Conclusion: the specific clinical manifestations of patients who suffered a stroke after COVID-19 were mapped, as well as diagnostic procedures and therapies used, in addition to identifying neurological damage based on the clinical outcome of these patients.

DESCRIPTORS: Coronavirus infections. Stroke. Academic review. Hospital care. Adult's health.

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ACIDENTE VASCULAR CEREBRAL EM PACIENTES COM COVID-19: *SCOPING REVIEW*

RESUMO

Objetivo: mapear a produção científica sobre o acometimento de pacientes pela COVID-19 e a ocorrência do acidente vascular cerebral.
Método: *scoping review*, conforme o referencial proposto pelo Instituto Joanna Briggs, com a utilização das bases de dados LILACS, MEDLINE, WoS, EMBASE, CINAHL e SCOPUS, no período de abril a setembro de 2020. Utilizaram-se dos descritores *coronavirus infections*, *stroke*, *nervous system diseases* e *inpatients,* por meio do *Medical Subject Headings.*
Resultados: incluíram-se 24 estudos que evidenciaram sintomas clínicos específicos do acidente vascular cerebral em pacientes com COVID-19, como disartria, paralisia facial, déficit sensório, cefaleia, hemiparesia e ataxia. O acometimento entre o Acidente Vascular Cerebral e a COVID-19 foi constatado pelos exames de proteína-C reativa, D-dímero, tomografia computadorizada, ressonância magnética, dentre outros, e por condutas assistenciais voltadas para os achados nos exames, associando-se a três desfechos clínicos, tendo por base a zona de isquemia cerebral acometida e o tempo de manifestação viral de cada paciente.
Conclusão: mapearam-se as manifestações clínicas específicas de pacientes que evoluíram para o quadro de Acidente Vascular Cerebral posterior a COVID-19, bem como condutas diagnósticas e terapias utilizadas, além de identificar o dano neurológico a partir do resultado clínico desses pacientes.

DESCRITORES: Infecções por coronavírus. Acidente vascular cerebral. Revisão acadêmica. Assistência hospitalar. Saúde do adulto.

ACCIDENTE CEREBROVASCULAR EN PACIENTES CON COVID-19: *SCOPING REVIEW*

RESUMEN

Objetivo: mapear la producción científica sobre la afectación de pacientes a raíz del COVID-19 y la incidencia de accidente cerebrovascular.
Método: una *scoping review*, conforme al referencial propuesto por el Instituto Joanna Briggs, con uso de las siguientes bases de datos: LILACS, MEDLINE, WoS, EMBASE, CINAHL y SCOPUS, entre abril y septiembre de 2020. Se utilizaron los descriptores *coronavirus infections*, *stroke*, *nervous system diseases* e *inpatients,* por medio de los *Medical Subject Headings.*
Resultados: se incluyeron 24 estudios que pusieron en evidencia síntomas clínicos específicos del accidente cerebrovascular en pacientes con COVID-19, como ser disartria, parálisis facial, déficit sensorial, cefalea, hemiparesia y ataxia. La afectación entre el Accidente cerebrovascular y el COVID-19 fue constatada por medio de los exámenes de proteína-C reactiva, D-dímero, tomografía computada y resonancia magnética, entre otros, y por conductas asistenciales dirigidas a los resultados de los exámenes, asociándose a tres resultados clínicos, y teniendo como base la zona de isquemia cerebral afectada y el tiempo de manifestación viral de cada paciente.
Conclusión: se mapearon las manifestaciones clínicas específicas de pacientes que evolucionaron al cuadro de Accidente cerebrovascular posterior a COVID-19, al igual que conductas diagnósticas y terapias utilizadas, además de identificar el daño neurológico a partir del resultado clínico de estos pacientes.

DESCRIPTORES: Infecciones por coronavirus. Accidente cerebrovascular. Revisión académica. Asistencia hospitalaria. Salud del adulto.

INTRODUCTION

COVID-19 is an infectious disease caused by SARS-CoV-2, a virus with a varied clinical spectrum, which can cause primary effects on the respiratory and cardiac systems, in addition to being associated, at a secondary level, with neurological symptoms that can cause neural complications[1], with headache, dizziness, cerebral hypogenesis and neuralgia as the main signs and symptoms[2].

In brain injury, vasodilation, hypercapnia, hypoxia, accumulation of toxic components, elevation of inflammatory cytokines such as activation of T lymphocytes, endothelial and interleukin cells trigger disseminated intravascular coagulation with implications on the central nervous system, such as acute brain problems, ataxia, epilepsy, encephalitis, encephalopathy with acute hemorrhagic necrosis, myelitis and deficit in the level of consciousness[3]. At the level of the peripheral nervous system, hypogenesis, hyposmia, neuralgia, Guillain-Barré syndrome and musculoskeletal system problems can be noticed[4].

Also with regard to neurological impairment, implications such as the occurrence of stroke were evidenced due to the expression of angiotensin II present in cardiac, intestinal and neural cells, being responsible for the virus blockage in the tissues, with protein dysfunction, promoting viral replication and consequently interfering with the action of angiotensin I and the renin-angiotensin-aldosterone system[5]. The virus attacks the cells that line blood vessels due to their considerable affinity by the receptors on their surface. This infection increases the risk of a coagulopathy, called sepsis-induced coagulopathy, caused by a systemic inflammatory response that generates endothelial dysfunction and microthrombosis, and these microthrombosis can cause blood flow to block in a specific area of the brain, resulting in sudden loss of function, this being classified as ischemic stroke, while hemorrhagic stroke can be attributed to the rupture of some blood vessel or abnormal vascular structure[5].

In this context, a North American consensus pointed to the possible association of the virus with severe cases of hemorrhagic stroke in China. In the guidelines, the neurological system is significantly more affected by the coronavirus, with ischemic or hemorrhagic manifestations of stroke, and this is due to high infectious rates, with rapid clinical deterioration, which contributes to increased mortality[6]. In cases where there is an association with comorbidities, such as systemic arterial hypertension, diabetes mellitus, hyperlipidemia or previous history of stroke, the numbers can be even higher, reaching almost 164 (70%) of 214 total cases, when added up[2]. In this sense, the relationship between COVID-19 and stroke is perceived in the course of the pandemic with a significant increase in both diseases.

According to data from the World Health Organization (WHO), there were 8,993,659 confirmed COVID-19 cases by July 2020, including 469,587 deaths[7]. Stroke, on the other hand, is the second leading cause of death in the world; in addition to that, its association with COVID-19 has considerably increased the number of deaths in European countries[8].

In Brazil, until June 2020,1,106,470 COVID-19 cases were confirmed, in which 51,271 died, with a fatality rate of 4.6%[9]. The Brazilian Society of Cardiology estimated that, in 2020,189,767 deaths from cardiovascular diseases would be recorded in Brazil, with stroke being the second cause of isolated deaths, with a possible significant problem due to COVID-19[10].

There is a need to map the relationship between COVID-19 and stroke in order to direct assistance in the prevention and care of these diseases and health problems by health professionals, including nurses. Thus, until July 2020, systemic arterial hypertension was the only serious finding in the context of SARS-CoV-2 infection, as the ejection fraction contributes to the spread of the virus in the bloodstream, increasing the risk for brain hemorrhages resulting from COVID-19, with thrombocytopenia as a predictive factor for the incidence of stroke[11].

Accurate neurological implications between stroke and COVID-19 constitute a gap in the literature and, in view of this, this work becomes relevant, since the evidence of strokes caused by the SARS-CoV-2 virus is extremely important with respect to the knowledge of the disease spectrum and its implications for the clinic. In this sense, searches for scientific evidence that can elucidate the symptoms and health behaviors in this scenario are necessary in order to present proposals about the theme and to consolidate possible hypotheses raised. Therefore, this study aimed to map the scientific production on patients infected by COVID-19 and the occurrence of stroke.

METHOD

This is a scoping review, based on the recommendations proposed by the Joanna Briggs Institute[12], which is characterized by addressing and reporting on the evidence available on a given topic. To conduct the study, nine stages were listed: title; title and question development; introduction; inclusion criteria; research strategy; selection of the sources of evidence; data extraction; analysis of the evidence; and presentation of the results[13].

To construct the research question, the Population, Concept and Context (PCC) strategy was used, namely: Population: patients hospitalized with COVID-19; Concept: stroke caused by COVID-19; Context: hospital care. Based on these definitions, the guiding question was established: what scientific evidence relates patients infected by COVID-19 and the occurrence of stroke?

The bibliographic survey was carried out from April to September 2020; initially, the "coronavirus infections", "stroke", "nervous system diseases" and "inpatients" descriptors were used in the following databases: Latin American and Caribbean Health Sciences Literature (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*, LILACS); Medical Literature Analysis and Retrieval System Online (MEDLINE) via EBSCO Information Services; Web of Science (WoS), Embase via Elsevier; Cumulative Index to Nursing and Allied Health Literature (CINAHL) and SCOPUS. The Descriptors Health Sciences (*Descritores em Ciências da Saúde*, DeCS) were adopted for Latin American bases, and the Medical Subject Headings (MeSH) for those in English.

Studies published in Portuguese, English and Spanish, with different methodological designs, were included. The selected studies that answered the guiding question of this review were read in full and the references were analyzed in search of additional studies for potential inclusion. Studies that were not related to the objectives of the study were excluded, based on the title and summary, unrelated theme, availability in full after extensive search, analysis of repeated studies, in addition to reading and evaluation of the findings regarding the non-pertinent content. The search strategy conducted in the aforementioned databases is described in Chart 1.

Chart 1 – Database search strategies referring to the research. Crato, Ceará, Brazil, 2020.

Databases	Search strategy
MEDLINE	(*inpatients*) AND ("*coronavirus infections*" AND "*nervous system diseases* e *inpatients*") AND (*stroke*) OR (*inpatients*) AND ("*coronavirus infections*") AND (*stroke*)
Embase	(*inpatients*) AND ("*coronavirus infections*" AND "*nervous system diseases* e *inpatients*") AND (*stroke*) OR (*inpatients*) AND ((("*coronavirus infections*"))) AND ((("*stroke"*)))
SCOPUS and WoS	(TITLE-ABS-KEY (inpatients) AND ("*coronavirus infections*" AND "*nervous system diseases* e *inpatients*") AND (*stroke*) OR TITLE-ABS-KEY (*inpatients*) AND ("*coronavirus infections*") AND (*stroke*)
CINAHL	(*inpatients*) AND ("*coronavirus infections*" AND "*nervous system diseases* e *inpatients*") AND (*stroke*) OR (*inpatients*) AND ("*coronavirus infections*") AND (*stroke*)

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) checklist was used[13], in order to guarantee the methodological quality of this study, contributing with the parts that constitute the review.

Regarding the relevance of the studies, they were reviewed by two independent reviewers and, in case of disagreement, by a third evaluator. These researchers had access to the results of the research obtained in full. The level of evidence of the studies that comprised the sample of this study was not assessed due to the type of review.

In addition to that, the form recommended by the Joanna Briggs Institute[12] was used to guide the synthesis of the information in data collection and in the importance of the recommendations. The results extracted corresponded to the design, the country, the authors, the journals, the conduct and the conclusion; in additions they answered the research guiding question, being presented in tables and discussed in a narrative manner. Simple statistical analysis was performed, with absolute and relative frequency of the findings.

For selection and inclusion of studies, the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA)[14] extension was adopted as a way to assist in the decision and selection process, in Figure 1.

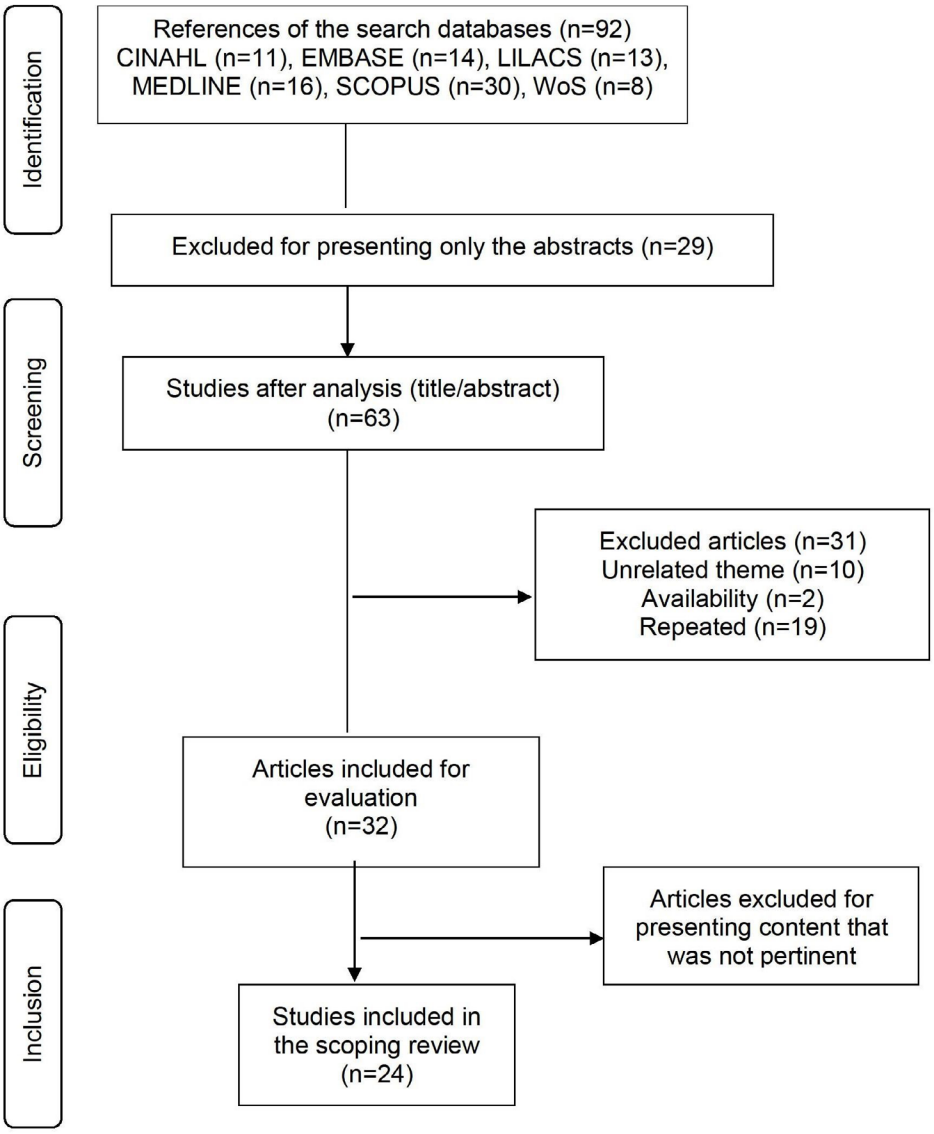

Figure 1 – Flowchart of the search and summary process of the studies found. Crato, CE, Brazil, 2020.

The review studies, based on Resolution No. 510 of 2016, do not need approval by the Research Ethics Committee, guaranteeing the integrity and authorship of the researched documents. However, it is necessary that this type of research be faithful to the data from the primary studies, as well as make reference to the complete texts, applying scientific rigor when exploring the data.

RESULTS

A total of 24 studies were included. With regard to geographic location, there was prevalence of studies from the United States (62%) and with a retrospective design (37%), also obtaining an estimated population of one to 26,175 patients, highlighting the interest of research studies in this study area. Thus, studies in the context of COVID-19 and strokes reveal the importance of the topic and the need to elucidate the assistance mechanisms that corroborate the clinical findings and scientific guidelines. Consequently, the data were extracted and tabulated as shown in Chart 2 below.

Chart 2 – Characterization of the studies included in the scoping review. Crato, CE, Brazil, 2020.

Authors/ Countries	**Titles**	**Journals**	**Designs Samples Stroke cases**
Oxley et al.[15] United States	Large-vessel stroke as a presenting feature of COVID-19 in the young	N Engl J Med	Case report Five patients Age mean: 40 years old Clinical data: 60% COVID-19 and stroke; 40% only stroke Gender: 80% men Evolution: Severe stroke
Co et al.[16] Philippines	Intravenous thrombolysis for stroke in a COVID-19 positive Filipino patient, a case report	J Clin Neurosci	Case report One female patient Age: 62 years old Female gender Clinical data: COVID-19 and stroke Evolution: acute neurological complications
Lodigiani et al.[17] Italy	Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy	Thromb Res	Retrospective Cohort 388 patients Age mean: 66 years old Clinical data: 5.2% stroke Gender: 68% men and 32% women Evolution: thromboembolic complications and DIC*
Moshayedi et al.[18] United States	Triage of Acute ischemic stroke in confirmed COVID-19: large vessel occlusion associated with coronavirus infection	Front Neurol	Case report One male patient Age: 80 years old Male gender Clinical data: COVID-19 and stroke Evolution: intracranial hemorrhage, heart failure, cardiogenic shock and bilateral limb ischemia
Qureshi et al.[19] United States	Management of acute ischemic stroke in patients with COVID-19 infection: report of an international panel	Int J Stroke	Theoretical study

Chart 2 – Cont.

Authors/ Countries	Titles	Journals	Designs Samples Stroke cases
Tunç et al.[20] Peru	Coexistence of COVID-19 and acute ischemic stroke report of four cases	J Clin Neurosci	Case report Four (04) patients Age mean: 65 years old Gender: 50% men and 50% women Clinical data: COVID-19 and stroke 100% Evolution: anterior artery infarction and arrhythmia
Valderrama et al.[21] United States	Severe acute respiratory syndrome coronavirus 2 infection and ischemic stroke	Stroke	Case report One male patient Age: 52 years old Gender: male Clinical data: COVID-19 and stroke Evolution: hemorrhage
Rothstein et al.[22] United States	Acute Cerebrovascular Events in Hospitalized COVID-19 Patients	Stroke	Retrospective and observational 844 patients Age mean: 59 years old Clinical data: 2.4% ischemic stroke, 0.9% hemorrhagic stroke Gender: 52% female Outcome: hemorrhages and DIC*
Lin et al.[23] United States	Racial differences and an increased systemic inflammatory response are seen in patients with COVID-19 and ischemic stroke	Brain, Behav Immun Health	Cross-sectional, observational 60 patients Age mean: 58 years old Gender: 55% female Clinical data: 15% COVID-19 Evolution: increase in mortality and in hospital stay
Avula et al.[24] United States	COVID-19 presenting as stroke	Brain, Behav Immun Health	Retrospective Four patients Age mean: 81 years old Gender: 75% female Clinical data: Stroke Evolution: neuropsychomotor impairment
Benussi et al.[25] Italy	Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy	Neurology	Retrospective Cohort 173 patients Age mean: 72 years old Gender: 53.8% male Clinical data: 34.2% stroke Evolution: high intra-hospital mortality
Hernández-Fernández et al.[26] Spain	Cerebrovascular disease in patients with COVID-19: neuroimaging, histological and clinical description	Brain	Retrospective 1,683 patients Age mean: 67 years old Gender: 78% male Clinical data: 74.2% stroke Evolution: hypercoagulability and systemic complications

Chart 2 – Cont.

Authors/ Countries	Titles	Journals	Designs Samples Stroke cases
Grewal et al.[27] United States	Acute Ischemic Stroke and COVID-19: Experience from a Comprehensive Stroke Center in Midwest US	Frontiers in Neurology	Retrospective and observational 650 patients Age mean: 61 years old Gender: 46% male Clinical data: 2% stroke Evolution: high inflammatory activity and coagulability markers
Hanif et al.[28] United States	Thrombotic complications and anticoagulation in COVID-19 pneumonia: a New York City hospital experience	Ann Hematol Oncol	Retrospective 1,308 patients Age mean: 62 years old Gender: 62.3% male Clinical data: 1.19% stroke Evolution: need for transfusional support and death
Jain et al.[29] United States	COVID-19 related neuroimaging findings: A signal of thromboembolic complications and a strong prognostic marker of poor patient outcome	J Neurol Sci	Retrospective 3,218 patients Age mean: 66 years old Gender: 60.7% male Clinical data: 1.1% stroke Evolution: intracranial hemorrhage and death
Yaghi et al.[30] United States	SARS-CoV-2 and Stroke in a New York Healthcare System	Stroke	Retrospective and observational 3,556 patients Age mean: 63 years old Gender: 71.9% male Clinical data: 0.9% stroke Evolution: elevated D-dimer and high mortality
Shahjouei et al.[31] Spain	Risk of stroke in hospitalized SARS-CoV-2 infected patients: A multinational study	EBioMedicine	Observational, multicentric and multinational 26,175 patients Age mean: 67 years old Gender: 47% female Clinical data: 0.9% stroke Evolution: need for mechanical ventilation and ischemic heart problems
Liu et al.[32] Germany	Clinical outcomes of COVID-19 in Wuhan, China: a large cohort study	Ann Intensive Care	Retrospective Cohort 1,190 patients Age mean: 57 years old Gender: 46.6% female Clinical data: 3.3% stroke Evolution: need for mechanical ventilation and intra-hospital death
Yamakawa et al.[33] United Kingdom	Clinical Characteristics of Stroke with COVID-19: A Systematic Review and Meta-Analysis	Int J Stroke Cerebrovasc. Dis	Theoretical 215 articles 4.6% stroke

Chart 2 – Cont.

Authors/ Countries	Titles	Journals	Designs Samples Stroke cases
Zhang et al.[34] United States	Clinical Course and Mortality of Stroke Patients with Coronavirus Disease 2019 in Wuhan, China	Stroke	A series of unicentric cases 709 patients Age mean: 55 years old Gender: 45% male Clinical data: 8% stroke Evolution: high mortality
Siegler et al.[35] United States	Cerebrovascular events and outcomes in hospitalized patients with COVID-19: The SVIN COVID-19 Multinational Registry	Int I J Stroke	Observational and retrospective cohort study 14,483 patients Age mean: 60 years old Gender: 55.8% female Clinical data: 1.13% stroke Evolution: long-term thrombotic complications
Studart-neto et al.[36] Brazil	Neurological consultations and diagnoses in a large, dedicated COVID-19 university hospital	Arq Neuropsiquiatria	Retrospective study 1,208 patients Age mean: 57 years old Gender: 61.8% male Clinical data: 16.7% stroke Evolution: severe neurological complications, respiratory failure and death
Teo et al.[37] United States	Delays in Stroke Onset to Hospital Arrival Time During COVID-19	Stroke	Retrospective study 386 patients Age mean: 70 years old Gender: 43.8% male Clinical data: 9.1% stroke Evolution: increase in mortality
Nguyen-Huynh et al.[38] United States	Acute Stroke Presentation, Care, and Outcomes in Community Hospitals in Northern California During the COVID-19 Pandemic	Stroke	Cohort study 9,120 patients Age mean: 65 years old Gender: 52.9% female Clinical data: 11.6% stroke Evolution: increase in mortality

Note: *DIC (disseminated intravascular coagulation).

The studies reveal prevalence of black-skinned men aged between 50 and 80 years old who developed a stroke and were infected by COVID-19. Similarly, black-skinned women aged over 50 years old are also more affected by stroke when infected by COVID-19. The main comorbidities evidenced in the studies can be seen in Chart 3. In the initial assessment of stroke patients hospitalized with manifestations of COVID-19, it is important to apply the National Institute of Health Stroke Scale, a scale for neurological assessment that assesses 11 items, whose scores lower than five mean mild clinical levels and scores greater than 14 mean critical levels. In the findings, there is variation in the score of this scale: between 9.5 and 19 points[15–16,20,23,25–26,29,31].

In addition to that, in patients with comorbidities, greater attention must be paid to the respiratory parameters. In this case, it is necessary to consider mechanical ventilation in a maximum time of 14 days[28]. For those without clinical conditions, a high-flow nasal cannula, an oxygen mask, non-invasive mechanical ventilation or invasive mechanical ventilation are indicated[31–32]. The blood alert

Chart 3 – Indication regarding the clinical profile, associated manifestations and laboratory recommendations in people with COVID-19 at high risk of stroke. Crato, CE, Brazil, 2020.

Personal Morbidity History		
Asthma; Transient ischemic attack; Cancer; Type I diabetes mellitus; Type II diabetes mellitus; Dyslipidemia; Ischemic heart disease; Coronary artery disease; Chronic liver disease; Chronic kidney disease; Chronic obstructive pulmonary disease.	Carotid stenosis; Atrial fibrillation; Hypercholesterolemia, Hypertension; Hyperlipidemia; Stroke history; Immunodeficiency; Acute myocardial infarction; Urinary tract infection; Heart failure.	Obesity; Smoking pneumonia; Acute coronary syndrome; Smoking; Pulmonary/venous thromboembolism; Tuberculosis; Substance abuse.
Clinical manifestations		
Specific: Aphasia; Change in the level of consciousness; Ataxia; Coma; Confusion; Sensory deficit; Facial breakdown; Breakdown in speech; Dysarthria; Dysphagia; Altered mental state; Hemianopsia; Hemihypoesthesia; Hemiplegia in upper or lower limbs mainly on the right side; Hemiparesis; Disordered movements; Facial paralysis; Dizziness.		
Nonspecific: Headache; Nasal congestion; Nasal discharges; Seizure; Delirium; Dyspnea; Sore throat; Chest pain; Sneezing; Fatigue; Fever; Hemoptysis; Hypogeusia; Respiratory failure; Myalgia; Nausea; Sialorrhea; Syncope; Gastrointestinal symptoms; Eye symptoms; Tachycardia; Cough; Dizziness; Vomiting.		
Recommendations for biochemical examinations		
Reduced albumin; Recent and increased antiphospholipid (anticardiolipin) antibodies; Increased aspartate; Altered and increased white cell count; Increased creatinine.	Increased glucose; Reduced hematocrit; Decreased hemoglobin; Increased IL-6; Reduced low density lipoprotein; Increased neutrophil; High C-reactive protein; High ferritin; High erythrocyte sedimentation rate.	Increased partial prothrombin action time; Increased partial thromboplastin action time; Increased cardiac troponins; Increased troponin T; Equivalent unit of fibrinogen (D-dimer) elevated at the beginning.
Recommendation for imaging examinations		
Skull **Computed Tomography** with loss of gray-white differentiation in the left occipital and parietal lobes. Internal carotid occlusion and penumbra area. Moderate hypodensity on the right frontal side. On the chest: bilateral ground-glass opacity. **Magnetic Resonance Imaging** (infarction in the middle temporal artery) and vascular infarction in one, two or three areas.		

parameters in the initial assessment are: blood oxygen saturation (SPO2 <76% to 93%); heart rate (HR 90.6 bpm); respiratory rate (RR 22 brpm); mean arterial pressure (MAP 99.6 mmHg)[27,32].

Regarding the medications used in patients with COVID-19 affected by stroke, the literature has pointed out drugs such as hydroxychloroquine, lopinavir, ritonavir, tocilizumab, in addition to antibiotics, antifungals, antivirals and glucocorticoids[22,30,32,34]. The main drugs used in the treatment of acute stroke were the following: enoxaparin, apixaban, rivaroxaban, coumadim, aspirin, clopidogrel and alteplase[27,33]. There was predominance of therapeutic measures implemented to the patients hospitalized due to COVID-19 who were affected by stroke, such as antiplatelet therapy; anticoagulation; mechanical thrombectomy; endovascular treatment; fibrinolysis; bridge therapy; intravenous thrombolysis, mechanical thrombolysis; thrombectomy; anticoagulation therapy[22,25–29,34–38].

As shown in Figure 2, the symptoms of COVID-19 appear after a few days of infection by the causative agent and the studies reveal that, when this infection affects the brain in several parts, it can generate areas of ischemia/infarction and reveal a new associated pathology, in this case stroke, which can evolve to three possible outcomes, namely: non-critical, moderate and critical.

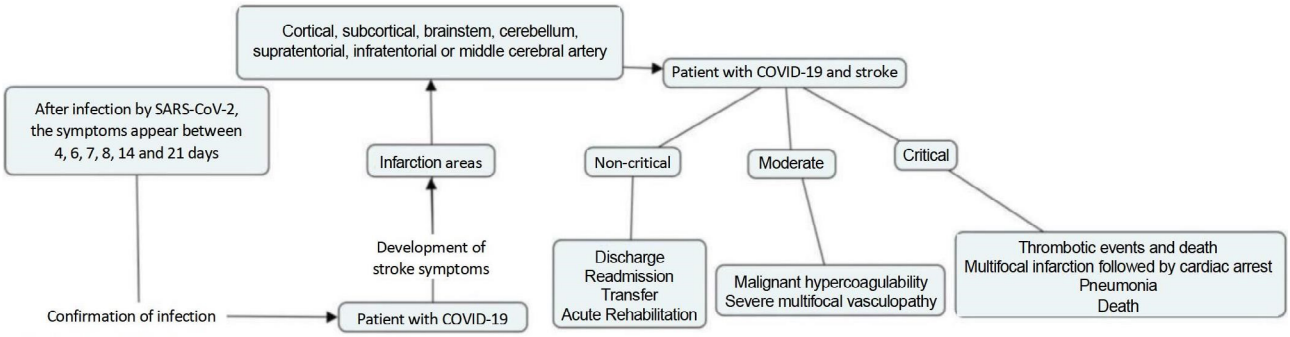

Figure 2 – Flowchart of the disease and clinical outcomes of patients with COVID-19 and stroke. Crato, CE, Brazil, 2020.

DISCUSSION

The evidence found through this study is characterized by being from international journals, predominantly From the United States, with different study methods and varied number of patients, which allowed mapping the scientific production regarding patients with COVID-19 and the occurrence of stroke.

A research study carried out in the United Kingdom, with patients distributed throughout the territory, showed that cerebrovascular events are present in 77 (62%) of the 125 patients who contracted COVID-19, of which stroke is the main complication, associated with 57 (74%) cases[39]. In addition to that, comorbidity is prevalent in women, with a mean age of 71 to 80 years old[39], converging with the results presented in this review, but which requires more robust studies to identify cause and effect, which allows for a better characterization of the sample of patients with COVID-19 and stroke.

In the United States, the prevalence of male patients with a mean age of 52.8 years old was recorded in a research study, which is also in line with the results obtained in this study, emphasizing the importance of proposing greater attention to these age groups, ranging from adults to the aged individuals[40].

The clinical manifestations collaborate to establish the relationship between COVID-19 and stroke, as well as possible consequences. The neurological implications of COVID-19 should be related to the mutations of specific genes and to the interaction between viruses and host, with a direct relation to neurotropism and virulence[4]. The association between suspected COVID-19 cases with severe respiratory complications and occurrence of neurological complications is linked to the important systematic impairment[1].

In turn, the increase in the number of cases, due to the increase in neurological manifestations, points to emergency models with a new neuropathogenic agent and underreported cases of chronic problems with rapid evolution to cardiopulmonary arrest[41].

In addition to these manifestations, the patients' comorbidities are also important factors that contribute to the health status of the individual infected by COVID-19 who can develop stroke, such as systemic arterial hypertension, morbid obesity and diabetes[40]

Nonspecific symptoms such as headache, hypogenesis and hyposmia are frequent findings in the literature for the occurrence of neurological symptoms[4]. The angiotensin II blockade, in the renin-angiotensin system, contributes to difficulties in the expression of angiotensin I and to endothelial dysfunction, damages organs and causes strokes. Therefore, treatments with antagonists of the renin-angiotensin system generate positive impacts in patients with COVID-19 and stroke[5].

For patients who arrive with a stroke at hospital emergencies, the elevation of the D-dimer shows the need for isolation in the ward with a possible association with COVID-19, requiring evaluation by specialists and proof by specific exams[6]. It is also evident that the elevation of this inflammatory

markers and others, such as C-reactive protein and fibrinogen, was associated with greater severity of stroke and also corroborated the possibility of disability in the 30-day period[16], which characterizes a possible outcome.

The high levels of D-dimer and fibrinogen are also observed in a serious condition of COVID-19, which refers to a coagulopathy called sepsis-induced coagulopathy[5]. Thus, there is the collaboration of mechanisms of hypoxia, inflammation and diffuse intravascular coagulation for thromboembolic disease, corroborating the onset of stroke in patients with COVID-19[40].

In turn, for patients with systemic arterial hypertension, it is recommended to pause the use of angiotensin II inhibitors or the renin angiotensin system inhibitors, considering calcium blockers, diuretics and other classes of hypertensive[6]. Patients with atrial fibrillation using antithrombotics can be at increased risk of developing stroke and systemic embolism, when associated with infection by coronavirus[42].

Hypercoagulation, due to the presence or absence of comorbidities in the circulatory system, is an important cerebrovascular mechanism in COVID-19; the main risk factors associated with this dysfunction are shock, arrhythmia-induced cardiomyopathy, embolic mechanisms and major occlusions[43]. The literature[44] also emphasizes the attention focused on the presence of the detectable lupus anticoagulant, suggested as a potential prothrombotic mechanism for stroke in COVID-19.

In this scenario, it is important to understand the occurrence of thrombotic complications in patients with COVID-19 so that decisions can be made regarding the intensity of thromboprophylaxis. Care should be offered to patients admitted to the intensive care unit with a higher thrombotic risk[45].

In stroke patients who do not have COVID-19, classic signs and symptoms are expected, which can be lifted with precise neurological screening. It is possible to find in this evaluation a sudden change in speech, gait, loss of strength on one side of the body or unilateral paresthesia, sudden and unusual headache, sudden vision changes or even the description of other neurological symptoms or signs that may corroborate the clinical suspicion of the nursing and medical team[46].

The symptoms present in patients with COVID-19 can cause unknown information for a rapid diagnosis of stroke, given the difficulty in carrying out complete anamnesis[47]. Consequently, proposing changes in the clinical conduct, being necessary to act quickly, with diagnostic methods such as neuroimaging exams and emergency laboratory exams[46], such as computed tomography, magnetic resonance and biochemical exams evidenced by the literature and organized in the results section, in Chart 3, following the institution's standardized measures with regard to biosafety standards in the care provided to patients with COVID-19.

For a lower impact of stroke, immediate and efficient diagnosis is necessary. However, studies report that the confirmed diagnosis or the suspicion of positive testing for COVID-19 brings with it the difficulty in handling confirmed cases and possible cases of stroke, justified by the team's restriction in carrying out the work, which is associated with extrinsic factors, such as the inappropriate use of personal protective equipment and the high chance of viral proliferation, putting at risk not only the professionals, but also other patients with whom they may have contact[16,19].

The research studies support the creation of scales for assessment of patients with COVID-19 that have strokes, as part of the clinical guidance for these cases. In addition to that, it is necessary to quantify prospective records with differences in the risk classifications, therapeutic response, main manifestations and studies with results that correlate both pathologies. The vulnerability of the affected population and the need for strategies to preserve health status, which are the basis of anticoagulant therapies, are highlighted.

The weaknesses, whether physical or material, must be reconsidered according to the possibilities of the place to which the patients are referred, whether at the secondary and/or tertiary levels. In this sense, the quality of the therapeutic records aligned with the risk classification and the waiting time

must be observed in the treatment of COVID-19 and stroke to collaborate with the progression and outcome of these pathologies. In this scenario, the role of the nurse as a mediator in the interface of care and the management of actions that promote the creation of new technologies with respect to COVID-19 is highlighted[48].

The nurse's work, therefore, goes beyond the direct care of the patient and includes hospital management and organization of the space and the Nursing team in order to meet the demands that have increased substantially with the pandemic and burden these professionals even more. In addition to specific Nursing issues, it is necessary for these professionals to act with the Systematization of Nursing Care (SNC), in addition to the operational flow involved in management[48].

Concerning the study limitations, the reduced search time for articles is highlighted, given the need to move forward with the theme in question. It is emphasized that the sources of evidence are still scarce, the information is not absolute and may undergo new approaches as new scientific discoveries emerge. Furthermore, the results evidenced in this study still follow an exclusively medical approach, with little insertion of other professions, such as Nursing, which constitutes a fundamental part for the management and clinical approach of patient care in hospital units.

CONCLUSION

This paper mapped the scientific production available so far on patients infected with COVID-19 and the occurrence of strokes in individuals hospitalized in the hospital context, demonstrating the main signs and symptoms and the diagnostic tests in the identification of neurological damage, as well as the main therapeutic approaches implemented in patients with COVID-19 who had strokes in the hospital environment. Elevation of serum biomarkers and respiratory dysfunction stand out as important findings, with the possibility of antiplatelet therapy, endovascular thrombectomy and combined anticoagulation as rapid procedures used after confirmation of stroke and COVID-19.

In view of the current scenario experienced by many health professionals during the pandemic, the results of this study offer additional support for studies based on scientific evidence, with an emphasis on the correlation between COVID-19 and stroke, in order to directly collaborate with the practice and actions that should be taken by the professionals, both for quick and accurate diagnosis and for the best treatment proposal to be adopted.

The need to reduce complications and length of hospital stay is a challenge for scientists and health professionals. Therefore, research studies are needed to promote the cause and effect discussion, the relationship between biochemical markers and levels of complexity among the patients, in addition to the clinical manifestations that may arise as a result of the disease.

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CONFLICT OF INTEREST

There is no conflict of interest.

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