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Review Article

Decompressive hemicraniectomy for acute ischemic stroke: A neurosurgical view in a pandemic COVID-19 time highlights of literature

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A R T I C L E I N F O

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A B S T R A C T

Background and purpose: The novel coronavirus, SARS-CoV-2, which was identified after the outbreak in Wuhan, China, in December 2019, has kept the whole world in tenterhooks due to its severe life-threatening nature of the infection. The World Health Organization (WHO) declared coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 a pandemic in 2020, an unprecedented challenge, having a high contagious life-threatening condition with unprecedented impacts for worldwide societies and health care systems. Neurologic symptoms related to SARS-CoV-2 have been described recently in the literature, and acute cerebrovascular disease is one of the most serious complications. The occurrence of large-vessel occlusion in young patients with COVID-19 infection has been exceedingly rare. In this article, we describe the profile of patients undergoing decompressive craniectomy for the treatment of intracranial hypertension by stroke associated with COVID-19 published so far. A narrative review of the central issue in focus was designed: decompressive craniectomy in a pandemic time.

Abbreviations: WHO, World Health Organization; ARDS, acute respiratory distress syndrome; COVID-19, Coronavirus disease 2019; hACE2, angiotensin-converting enzyme 2; MCE, malignant cerebral edema; NIHSS, National Institutes of Health Stroke Scale; GCS, Glasgow coma scale; ICU, intensive unit care; CT, computed tomography; MCA, middle cerebral artery; DHC, decompressive hemicraniectomy; CTA, Computed tomography angiography; MRI, magnetic resonance imaging; DWI, Diffusion-weighted imaging; ECMO, extracorporeal membrane oxygenation; ECCO2R, Extracorporeal carbon dioxide removal.

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1. Introduction

Coronavirus disease (COVID-19) acute respiratory syndrome caused by the virus SARS-CoV-2, appeared in the city of Wuhan, China, in December 2019. It presents a picture of acute respiratory syndrome in humans, characterized by fever, dry cough, dyspnea and hypoxia, with features of interstitial pneumonia on chest X-ray or computed tomography [1]. As of this writing, the pandemic has affected more than 210 countries, with more than 29 million confirmed cases and more than 2 million deaths [2–5] (see Table 1).

The virus has an affinity for human angiotensin-converting enzyme protein 2 (hACE2), and recent reports suggest that it is not just the lung that the virus can target. Cases of patients with COVID-19 with mild to severe neurological manifestations (anosmia and ageusia) have been reported [3–8].

Among a wide range of neurological symptoms, acute cerebrovascular disease is one of the most serious complications and affected 5.7% of patients in the study by Mao et al.

Previous reviews have shown an association between a past history of acute cerebrovascular disease and increased severity and mortality of COVID-19. Other articles have reviewed the spectrum of neurological manifestations in COVID-19. However, it has not yet been established whether COVID-19 can be considered a risk factor for stroke. The occurrence of large-vessel occlusion in young patients with COVID-19 infection has been exceedingly rare. Likewise, little is known about any specific characteristics of stroke associated with COVID-19. There are limited data on patients with coronavirus disease with acute ischemic stroke and malignant cerebral edema (MCE) [4–5]. The purpose of this article is to present a review of published cases on this topic, common characteristics, results and summarize some pertinent issues.

2. Methods

For the identification of stroke and COVID-19, a systematic review article was conducted with patients who underwent decompressive craniectomy due to ischemic stroke and had reported cases of COVID – 19. It was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1). We systematically searched on PubMed database for related published articles from December first, 2019, to February 3rd, 2021. The following combination of MeSH terms: “COVID-19” AND “stroke” AND “decompressive craniectomy”. Moreover, the PubMed tool – “PubMed Advanced Search Builder’’, was used to perform a more specific search, using the term “AND” between all descriptors in the Builder tool. Case reports and correspondences were included. Then, articles with a theme that did not deal with decompressive craniectomy in stroke patients with covid-19 were excluded. The research resulted in

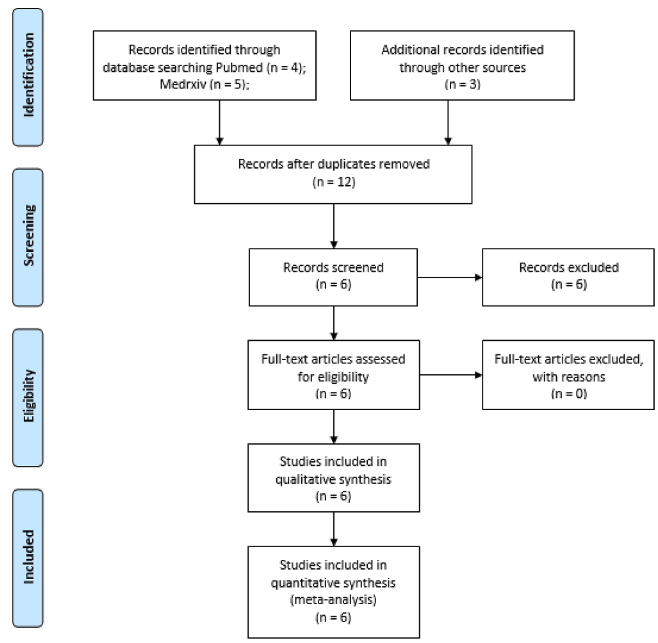

Fig. 1. Methodology used in the search in the database and selection of evaluated articles.

Table 1
Cases of stroke and decompressive craniectomy of patients with covid-19.

Study	Patients	Age	Gender	NIHSS average	Underline disorders	Surgery time after admission	Outcome
Rascón Ramírez et al., 2020	1	51	Male	-	Hypertension and diabetes	3 days	Rankin 4
Alkhaibary et al., 2020	1	31	Female	19	Hypertension and epilepsy	3 days	Intubated
Liang et al., 2020	3	51	Male-66,6% Female – 33,3%	18	Hypertension – 33,3% Diabetes – 100%	4,3 days	Rankin 4 66,6% 33,3% died
Roy, Hollingworth and Kumaria, 2020	1	46	Female	-	Diabetes	9 hours	Intubated and died
Oxley et al., 2020	1	44	Male	23	Diabetes	-	Bad prognosis

seven patients.

As analyzed variables were utilized the following variables: gender, age, comorbidities, National Institutes of Health Stroke Scale (NIHSS), hours after symptom onset the surgery was performed (surgery timing), and patient outcome, including Glasgow Coma Scale (GCS) and Rankin Scale.

3. Results

3.1. Cases of stroke and decompressive craniectomy in patients with COVID-19

From the literature review, it is possible to analyze eight cases of stroke and decompressive craniectomy of patients infected by COVID-19.

In the article published by *Rascón Ramírez et al., 2020* [9], are described two patients with massive stroke and COVID-19, but only one of the patients had decompressive craniectomy, therefore, only one of them met the inclusion criteria.

A 51-year-old-man, with comorbidities (hypertension and diabetes), was admitted to the intensive unit care (ICU) infected by COVID-19, whose tests confirmed. On day 4, he developed acute respiratory failure and left hemiplegia; On day 8, the patient involved with development of ipsilateral hemineglect. Through the study of the computed tomography (CT) angiography was possible to observe M1 segment occlusion of the right middle cerebral artery (MCA), and the non-contrast CT revealed a slight loss of right frontoparietal cortical differentiation and petechial hemorrhage that contraindicated thrombolysis. Was realized a mechanical thrombectomy 2 h after the onset, with complete reperfusion achieved. On day 9, the patient presented signs of intracranial hypertension. CT revealed a malignant infarction of MCA. Was performed an extensive right decompressive hemicraniectomy, observing a severe cerebral infarction. Control CT revealed on post-operative complications and extensive ischemic stroke were confirmed with a significant transcranial herniation. Surgery was indicated as in other patients with this type of stroke. COVID-19 test still positive 48 h before surgery. NIHSS was not informed.

In the study published by Alkhaibary et al., 2020 [10], describe the case of a 31-year-old woman, with comorbidities (arterial systemic hypertension and epilepsy), with a history of right-sided weakness, slurred speech, and decreased vision until 3 days before the admission. The patient progressed with worsening, after a time, become severely dysarthric and unresponsive. On admission has a Glasgow Coma Scale (GCS) of 10 points and NIHSS was 19. Analyzing the brain CT and CT venography was possible to observe an occluded left internal carotid artery and left middle cerebral artery with subacute left MCA territory infarction. Besides that, the CT angiography study revealed a total occlusion of the left common carotid artery. Through that, an emergent decompressive craniectomy was decided to realize; the neurosurgery team performed the procedure and they were successful. The patient was shifted to the intensive care unit and intubated. She was later found to be positive for COVID-19, with tests proving.

In other paper, Liang et al., 2020 [11] did a retrospective single-center study and included all hospitalized adults patients diagnosed with COVID-19 and at risk for ischemia-induced Malignant Cerebral Edema (MCE) during 2 months in 2020. COVID-19 cases with emergent large vessel occlusion (ELVO) who required MCE monitoring, 7 patients, were young patients with an independent baseline functional status. This paper described 3 patients that underwent DHC of whom 1 died. This patient who died experienced a concomitant ST-segment-elevation myocardial infarction with the ELVO stroke. Her follow-up CT scan showed significant midline shift of 10 mm and was required for DHC. Unfortunately, the patient's status worsened postoperatively, and she expired.

The second patient who underwent DHC featured with a right internal carotid artery occlusion and was treated with alteplase and mechanical thrombectomy. Emergent DHC was performed on the first day poststroke due to worsening lethargy and a fixed dilated right pupil. Preoperative CT demonstrated a giant hemorrhagic transformation and uncal herniation with 11 mm of midline shift. Was did a tracheostomy and he was transferred to an artificial ventilator. On discharge, he was awake and able to obey simple commands.

The third patient who underwent DHC in this paper was admitted with a left middle cerebral artery occlusion and was treated with alteplase and mechanical thrombectomy. Emergent DHC was performed on the first poststroke day by the lethargy and 3 mm of midline shift. He had a successfully treatment in intensive care unit (ICU) and was extubated. On the 12th poststroke, he featured a bilateral pulmonary embolism secondary to a deep venous thrombosis. On discharge, he attempts to verbalize and can obey midline commands.

Roy, Hollingworth, and Kumaria, 2020 [12], revealed a 46-year-old woman admitted after suffering a malignant cerebral infarction whilst self-isolating with COVID-19 positive, and with diabetes. On the day of admission, she developed confusion and progressive left-sided weakness and was taken to the stroke unit. CT showed infarction in the right anterior and middle cerebral artery territories and occlusion of the terminal segment of the right internal carotid artery. In view of the changes seen in the CT and the fact that the time of onset of symptoms is not known with greater precision, she was considered ineligible for thrombolytic treatment and mechanical thrombectomy. Nine hours after admission, the patient's GCS reduced to 8 (E1 V2 M5) and she also had dilated and non-reactive right pupil. Repeat imaging demonstrated extensive edema with significant mass effect and midline shift, effacement of the basal cisterns with trans-tentorial herniation, and crowding at the foramen magnum. An emergency DHC was performed. Intra-operatively, the brain was pale and non-pulsatile. Post-operatively, she remained sedated and allocated to the ICU.

At last, Oxley et al., 2020 [13], reported a case of a patient that had treatment for stroke with decompressive hemicraniectomy. A 44 years old man, without diabetes diagnosis, presented reduced a level of consciousness, global dysphasia, hemiplegia on right side, gaze preference, therefore, an NIHSS with 23 points in admission. A CT, CTA, and an MRI were performed and showed that the left MCA was different. In addition to DHC, the patient arrived at the service in reasonable time to undergo thrombolytic therapy with rt-PA. The NIHSS of this patient 24 h after the admission was 19 and the last follow-up NIHSS was 19, on day 12 of hospitalization.

It was observed that the average age was 44.6 years, as the most common comorbidities were hypertension (42.8%) and diabetes (85.7%). The prevalence between genders was 57.1% for males and 42.9% for females.

4. Discussion

4.1. Symptoms and physiopathology – thrombotic events, inflammatory responses

In the study Mao et al. found they showed that the most common neurological symptoms in the patients infected by SARS-CoV-2 are dizziness (about 16%), headache (about 13%) and anosmia (about 5%). Futhermore, anothers neurological symptoms are headache, delirium, epileptic seizure and stroke [15,16].

Significantly high levels of D-dimer and other fibrin degradation products have been increasingly correlated with poor prognosis in patients infected with SARS-CoV-2 [17].

Due to these characteristics, many authors have reported that patients in this phase of disease and with this laboratory profile are in hypercoagulability state, which can also be associated with a worsening in the functioning of noble organs. For Spiezia et al [18], patients who have COVID-19 and are in this state of hypercoagulability due to hyperfibrinogenemia, which results in a greater formation of fibrin and polymerization, which can predispose to the appearance of thrombi.

The cytokine storm consists of one of the main causes of acute respiratory distress syndrome (ARDS) and multiple organ failure, which is an immunological phenomenon, frequently seen in patients infected with SARS-CoV-2. In a study evaluating the outcome of patients with persistent and high levels of inflammatory cytokines, it was concluded that the overproduction of pro-inflammatory cytokines such as tumor necrosis factor (TNF), IL-6 and IL-1B can cause death if high concentrations persist unabated over time [19–21].

Therefore, even though any studies did deaths pathologized, through the careful analysis of the cases described above and the literature review brought by each one of them, it is possible to infer that there are pathophysiological correlations between the occurrence of stroke and the associated inflammation. The inflammation and stroke are completely linked to the hypercoaulability processes promoted by the covid-19 infection.

5. Stroke features in COVID-19 patients compared with non-COVID-19 patients with stroke

What is the difference between characteristics in patients with stroke and COVID-19 infection and without COVID-19? Patients with COVID-19 and stroke were younger than patients with stroke without infection and the onset of neurological symptoms started on average 7 days after the respiratory condition [22–25].

Patients were less likely to have hypertension. There was no significant difference in other cardiovascular risk factors (diabetes mellitus, dyslipidemia, smoking, coronary artery disease and atrial fibrillation). Stroke severity was greater in stroke patients and COVID-19 and had higher mortality.

5.1. Surgical treatment

The DHC is a surgical procedure to reduce increased intracranial pressure and brain tissue displacements that occur in the context of space-occupying lesions such as ischemic stroke [26].

The Inclusion Criteria for Stroke: Age 18 to 60 years, clinical deficits suggestive of infarction in the territory of the MCA with an NIHSS score ≥ 16, Decreased level of consciousness to a score ≥ 1 in NIHSS item 1a ≥ 16, signs in CT brain of a stroke ≥ 50 percent of MCA territory, with or without infarction free additional in the territory of the anterior cerebral artery or ipsilateral posterior, or volume >145 cm^3 the weighted DWI, time from onset of symptoms to the start of surgical decompression < 48 h, written informed consent of the patient or legal representative [26,27].

Regarding neurosurgical management, the guideline states that patients with ≤ 60 years, who neurologically deteriorate, it is reasonable to have DHC with duraplasty in MCA infarction within 48 h of symptoms onset. In older patients, >60 years, the same approach can be considered [28–31].

There are limited data on COVID-19 patients with acute ischemic stroke and MCE [32]. It is unknown whether COVID-19 infection should influence surgical eligibility decision, as these patients can develop severe acute respiratory distress syndrome, acute kidney injury, and, if mechanically ventilated, can have high rates of poor outcome [33].

In the context of the current COVID-19, point for futures studies is the possibility of the coexistence of stroke and refractory hypoxemia, in mechanically ventilated patients. So far too little is known about how to better manage the association of both, especially in large-size strokes under risk of elevated intracranial pressure [34–36].

Clinicians should be mindful of the increased risk for early rapid herniation due to both permissive hypercapnia and hypoxia-induced cerebral vasodilation, particularly among patients with acute respiratory distress syndrome. An early prophylactic DHC strategy in otherwise surgically eligible patients may be appropriate due to the lack of a reliable neurological exam due to sedatives and paralytics usage [26,36].

The ability to deliver timely and efficacious care for the stroke must be balanced with the risk of potential elevated intracranial pressure that happens as a result of “permissive hypercapnia” during the well-established “protective-lung ventilation strategy” [37]. Rescue approaches such as extracorporeal membrane oxygenation (ECMO) coupled with extracorporeal carbon dioxide removal (ECCO2R) may be applied to avoid lung disease worsening and protect the brain from herniation simultaneously [38]. Surgical decompressive craniectomy should also be taking into consideration in selected cases either in combination with ECMO/ECCO2R or alone, especially in low resources centers [26].

Thus, is important and necessary analyze and reinforce care with contamination in the surgical environment, through barrier measures and primary protection methods of the entire neurosurgical team, massive disinfection of the operating room, and encouragement for full team vaccination [39].

The important precautions postulated for the prevention and reduction of the possibility of contagion and dissemination of Covid-19 among the team are the use of personal protective equipment, such as mask and glasses, the recommended mask is N95, instead of the commonly used one in the pre-pandemic period [40], excessive conversation about matters not related to the procedure performed must be avoided, to minimize the escape of aerosols; use of two pairs of gloves, placed one under the other, to ensure that there is no contamination due to glove breakage and contact with the surgical means or materials [40].

Furthermore, there is a recommendation for handwashing after the procedure is performed, even if there has been no contamination or violation of the gloves [40]. The number of individuals in the surgical environment should be minimized as much as possible, prioritizing the professionals strictly necessary to the procedure. Everyone who enter the operating room should be encouraged to use individual protection and complete sanitation equipment [41].

In addition, it is essential to take extra care when performing aerosol dispersing procedures, which increases the chance of contamination. For this reason, it is essential to use a room with negative pressurization and located further away from other operating rooms [41]. In our cases analyzed, there was anything unusual that they did during the surgical procedure, only the artificial respiration and infection control.

5.2. Prognosis

The poor prognosis of patients with COVID-19 and stroke is not fully elucidated. Patients with severe infection are more susceptible to developing acute cerebrovascular events than those with less severe infection. The risk factors for the development of severe COVID-19 are the same as the factors for stroke and cardiovascular disease, and these cardiovascular morbidities are likely to result in worse outcomes [32–33].

The patients with COVID-19 with large territorial infarction can have a good outcome after decompressive craniectomy. This is particularly true in patients who have minimal respiratory involvement or other extracranial organ damage [34]. Although we have limited follow-up data for survivors and neurological recovery, it is reasonable to expect neurological results similar to those shown in previous DHC studies.

Another factor that deserves attention in the analysis of factors that predict the worst outcome of patients with COVID-19 and stroke is hypercapnia caused by mechanical ventilation. Permissive hypercapnia, required during protective mechanical ventilation in patients with severe COVID-19, generates an accumulation of CO2, which can lead to a harmful state of cerebral hyperemia. This permissive hypercapnia is difficult to control in patients with COVID-19, as the patient needs to maintain good pulmonary ventilation, although attention is needed for the possible worsening of the neurological condition through this intervention [28,34].

6. Conclusion

After analyzing the evidence collected, it can be postulated that patients infected with Sars-Cov-2 who were affected with a large stroke could have a relatively good outcome, however, multifactorial analysis is important, also involving the comorbidities of patients and the characteristics of each ischemic event.

7. Limitations

This review has several limitations. Few studies were available for inclusion. More detailed patient data was unavailable in most studies at the time of analyses. Futures studies are necessary to determine protocol management and real prognosis in COVID-19 patients [14].

CRediT authorship contribution statement

Luiz Severo Bem Junior: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Project administration, Supervision. **Otávio da Cunha Ferreira Neto:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Artêmio José Araruna Dias:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Joaquim Fechine de Alencar Neto:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Luís Felipe Gonçalves de Lima:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Nilson Batista Lemos:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Andrey Maia Silva Diniz:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Kaio Moreira Couto:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Jorge Henrique Estrela Gadelha Maia:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Ana Cristina Veiga Silva:** Data curation, Writing – original draft, Investigation, Formal analysis, Resources, Writing – review & editing. **Hildo Rocha Cirne de Azevedo Filho:** Conceptualization, Validation, Formal analysis, Resources, Project administration, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The authors declare that data supporting the findings of this study are available within the article.

Ethical approval

This study is a review, using secondary data, and ethics approval in human research was not required.

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