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Review article

The impact of the COVID-19 pandemic on cerebrovascular disease



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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a systemic disease that affects nearly all organ systems through infection and subsequent dysregulation of the vascular endothelium. One of the most striking phenomena has been a coronavirus disease 2019 (COVID-19)-associated coagulopathy. Given these findings, questions naturally emerged about the prothrombotic impact of COVID-19 on cerebrovascular disease and whether ischemic stroke is a clinical feature specific to COVID-19 pathophysiology. Early reports from China and several sites in the northeastern United States seemed to confirm these suspicions. Since these initial reports, many cohort studies worldwide observed decreased rates of stroke since the start of the pandemic, raising concerns for a broader impact of the pandemic on stroke treatment. In this review, we provide a comprehensive assessment of how the pandemic has affected stroke presentation, epidemiology, treatment, and outcomes to better understand the impact of COVID-19 on cerebrovascular disease. Much evidence suggests that this decline in stroke admissions stems from the global response to the virus, which has made it more difficult for patients to get to the hospital once symptoms start. However, there does not appear to be a demonstrable impact on quality metrics once patients arrive at the hospital. Despite initial concerns, there is insufficient evidence to ascribe a causal relationship specific to the pathogenicity of SARS-CoV-2 on the cerebral vasculature. Nevertheless, when patients infected with SARS-CoV-2 present with stroke, their presentation is likely to be more severe, and they have a markedly higher rate of in-hospital mortality than patients with either acute ischemic stroke or COVID-19 alone.

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1. Introduction

Although the initial understanding of coronavirus disease 2019 (COVID-19) was primarily as a respiratory infection, it quickly became apparent that the virus causes a systemic

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disease that affects nearly all organ systems through multiple mechanisms, including infection and subsequent dysregulation of the vascular endothelium. One of the most striking phenomena observed has been a COVID-19-associated coagulopathy, which appears to be distinct from disseminated intravascular coagulopathy in its viral origins [1,2]. Given these findings, questions naturally emerged regarding the prothrombotic impact of COVID-19 on cerebrovascular disease and whether ischemic stroke is a clinical feature specific to COVID-19 pathophysiology. Early reports from Chinese hospitals found higher rates of ischemic stroke in patients with more severe disease [3], and several sites in the north-eastern United States reported an anecdotal increase in ischemic strokes among young, otherwise healthy patients with COVID-19 [4–6]. These reports stand in stark contrast to multiple cohort studies worldwide that observed decreased rates of stroke since the start of the pandemic, many of which are not easily explained by delaying or avoiding emergency care [7–14]. While geographic and demographic variables may contribute to virulence, the precise pathogenicity of the COVID-19 on cerebral vasculature remains unclear.

An outpouring of research has described the epidemiology and management of strokes throughout the pandemic. In this review, we provide a comprehensive assessment of presentation, epidemiology, treatment, and outcomes to better understand the impact of COVID-19 on cerebrovascular disease.

2. Methods

The field of study on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is rapidly evolving as the pandemic continues and as long-term data begin to emerge. We therefore used Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [15] to help identify articles that would best allow us to evaluate the effect of COVID-19 on cerebrovascular disease. We included only peer-reviewed journal articles, and we focused on stroke, as these studies constitute the bulk of the literature on cerebrovascular disease in the context of the pandemic. All articles were identified via searches on PubMed between December 2020 and February 2021 for terms including COVID-19 or SARS-CoV-2 and *cerebrovascular accident*, *ischemic stroke*, *hemorrhagic stroke*, *venous stroke*, and *aneurysmal rupture*. To minimize bias, single case reports and small case series were generally excluded, with the exception of the initial case series that identified concern for stroke as a presenting symptom of COVID-19 [4]. We specifically sought to assess the impact of COVID-19 on the incidence of stroke, management strategies, quality metrics, and treatment outcomes, with the broader goal of attempting to answer the question regarding whether infection with SARS-CoV-2 causes stroke.

3. Results

3.1. The presentation and epidemiology of stroke during the COVID-19 pandemic

Cerebrovascular injury is one of a plethora of potential mechanisms through which COVID-19 can affect the nervous sys-

tem. The virus has been implicated in encephalitis, Guillain-Barré syndrome, posterior reversible encephalopathy syndrome, and various other neuropathies [16,17]. One of the earliest attempts to characterize these injuries came from a retrospective, observational case series of hospitalized patients collected across three medical centers in Wuhan, China [3]. The rate of acute ischemic or hemorrhagic stroke was found to be 5.7% in patients with severe disease compared to 0.8% in those patients with mild to moderate disease. Subsequently, multiple case reports emerged suggesting COVID-19 could present primarily as large-vessel occlusions in young adult patients without traditional vascular risk factors, further raising concern for acute ischemic stroke as a clinical feature of COVID-19 infection [4–6].

3.1.1. The presentation of stroke in patients with COVID-19

Multiple retrospective observational studies have been performed to better characterize the demographics, laboratory aberrations, and imaging findings in patients with COVID-19 who have acute ischemic stroke. In general, these patients tend to be younger, male, African American or Hispanic, and more likely to have diabetes and obesity [5,18–21]. Interestingly, they are less likely to smoke and to have hypertension and other comorbid risk factors for stroke. The stroke ictus is estimated to follow the onset of more typical COVID-19 symptoms by 7 to 10 days, although in some cases stroke onset is unclear in patients with severe COVID-19 infection who are already in intensive care [8,22]. As measured by the National Institute of Health Stroke Scale, stroke tends to be more severe in patients with COVID-19 than in patients without infection [5,22–24]. Laboratory aberrations that portend a worse prognosis include elevated D-dimer, prothrombin time, C-reactive protein, erythrocyte sedimentation rate, fibrinogen, troponin, lactate dehydrogenase, and interleukin (IL)-6, as well as lymphopenia and thrombocytopenia [3,5,19,22,24–29]. It is important to note that these are nonspecific markers of critical illness and may not be indicative of cerebrovascular insult [16,30].

Diagnostic imaging studies report greater severity of injury from comparable large-vessel occlusions in patients who are infected by the virus compared to those who are not [20]. Furthermore, these occlusions are more likely to be found across multiple territories, both arterial and venous [4,5,20,27,31]. One case series reported that clots in infected patients were particularly fragile and prone to fragmentation [24]. Historically, most ischemic strokes can be attributed to a cardioembolic source or large artery atherosclerosis, but in patients with COVID-19, most ischemic strokes are cryptogenic (51.8%–65.6%), more than double the rate in uninfected patients [5,19,21]. It is unclear to what degree the increase in cryptogenic etiology reflects the interruption of a complete stroke workup due to withdrawal of care or increased early mortality from concomitant COVID-19 manifestations.

3.1.2. The epidemiology of stroke during the COVID-19 pandemic

There has been much debate regarding how the pandemic has impacted the rate of acute ischemic stroke [13]. The incidence in hospitalized patients with COVID-19 is estimated between 0.9% and 6% [17,22]. A study from two centers in New York

City found that patients with COVID-19 were more likely to suffer stroke than patients who contracted influenza during the same time period (odds ratio = 7.6; 95% confidence interval [CI], 2.3–25.2) [25]. However, a multicenter study from a large New York State health care system found no association between COVID-19 and the incidence of stroke in nearly 25,000 hospitalized patients [32], consistent with observations at our own institution [33]. Indeed, many studies around the world have actually reported a decrease ranging from 19.2% to 51% in the rate of diagnosis and hospitalization for acute ischemic stroke [5,7–10,12,19,34]. Furthermore, there has been a decline in transient ischemic attack presentations and referrals [7,34–37]. This decline may disproportionately affect non-White patients, such as African-American patients, and may be related to pre-existing racial disparities in health care delivery [38]. It is possible that stroke assessment in moribund patients may have been overlooked or omitted at the beginning of the pandemic, and most of these studies focused largely on patients admitted in March and April of 2020, comparing these months to the preceding months and to the corresponding months from 2019. Reporting on admission rates for intracranial hemorrhage has been inconsistent, although there is a trend for decreasing rates, as well [7,8,12]. There are multiple case reports and small case series raising concerns for similar trends among aneurysmal rupture, cerebral venous sinus thrombosis, and vasculitis, but there are insufficient data to draw any conclusions regarding the incidence of such cases and COVID-19 [17,22,31,39].

The reason for the global decline in acute ischemic stroke admissions remains unclear and is likely multifactorial. Many theories have been proposed, including the possibility that patients with acute strokes are hesitant to present for medical treatment (either to comply with strict lockdown policies or to avoid the possibility of contracting COVID-19 in the hospital setting) and that stroke symptoms might be identified in a delayed fashion by family members seeking to minimize exposure of SARS-CoV-2 to their elderly parents and grandparents [13,29]. Consistent with these hypotheses, some have reported an increase in the proportion of severe strokes since the start of the pandemic, and others have reported a reduced total number of stroke admissions, but no change in the number of mechanical thrombectomies (MTs) [7,14,34]. The Endovascular Neurosurgery Research Group also reported an average additional delay of 160 minutes from last known normal to presentation that emerged after the start of the pandemic in the United States [40]. However, this group did not find a change in severity of stroke at presentation, and others have reported a decline in the rate of MTs in parallel with the decline in stroke admissions [12,41–43]. A meta-analysis including nine studies and almost 60,000 patients demonstrated that stroke alerts fell 36% in the pandemic period, while intravenous (IV) thrombolysis fell 31% and MTs fell 22%, resulting in a slightly higher number of per-stroke MT interventions [44]. Another explanation for the decrease in stroke admissions is that changes in behavior and air pollution have decreased triggers for ischemic events, but the rate of admissions for acute coronary syndrome has not declined in parallel [8]. More recent evidence suggests this drop in the rate of strokes might be temporary, as a few studies after longer time periods have shown stroke presentations rebound after an initial decrease [45,46].

In summary, there has been an international decline in the rate of hospital admissions for acute ischemic stroke since the start of the pandemic. This drop may stem from the global response to the virus, and the rates of decline may have some geographic variability. Nevertheless, when patients infected with SARS-CoV-2 present with stroke, their presentation is likely to be more severe, and they are found to have multiple laboratory aberrations consistent with severe, systemic inflammatory disease.

3.2. Potential mechanisms for cerebrovascular injury from SARS-CoV-2 infection

Brain imaging [47] and postmortem histology [48,49] from patients with COVID-19 has demonstrated both macrovascular and microvascular thrombosis in both arterial and venous circulations, elevating the concern for direct vascular injury from SARS-CoV-2 infection [50]. Multiple mechanisms contributing to increased ischemic strokes have been proposed, including systemic hypercoagulability, dysregulated immune response, damage to endothelium, direct cytotoxic effect to the central nervous system, angiotensin-converting enzyme-2 (ACE2) receptor uptake of the virus, renin-angiotensin-aldosterone system dysregulation, and hypoxemia from cardiorespiratory distress [26].

3.2.1. Hypercoagulable state

Activation of the innate immune system after infection of the SARS-CoV-2 virus induces a hypercoagulable state leading to so-called “immunothrombosis” [51]. Initial viral infection activates a pro-inflammatory cytokine storm, with elevated IL-1, IL-6, and tumor necrosis factor- α , released by monocytes [26]. IL-1, IL-6, and tumor necrosis factor- α induce neutrophil recruitment and expression of tissue factor (TF). The overexpression of TF on endothelial cells, macrophages, and neutrophils leads to initiation of the extrinsic coagulation pathway via the factor VIIa-TF complex [52]. Recruitment of neutrophils leads to the development of neutrophil extracellular traps, networks of globular proteins, DNA, and histones designed to capture pathogens. Formation of neutrophil extracellular traps activate both the extrinsic and intrinsic coagulation pathways by promoting TF expression and inducing factor XIIIa, factor Xa, and thrombin production [53]. The cytokine storm also promotes expression of plasminogen activator inhibitor-1 from the endothelium, thus impeding fibrinolysis by inhibiting the formation of plasmin [54]. Concurrently, SARS-CoV-2 has a direct cytotoxic effect on endothelial cells and infects the cells themselves. This endotheliopathy results in further TF expression and excess thrombin production [51]. Damaged endothelial cells also release increased von Willebrand factor, with resultant increased factor VIII levels. In turn, this serves to hyperactivate platelets and induce aggregation, further propagating thrombosis [51,54]. It is unclear whether additional treatment beyond typical secondary prevention medication should be prescribed for patients recovering from stroke with concomitant COVID-19 infection.

3.2.2. Route of entry into central nervous system

SARS-CoV-2 initiates infection via attachment of its spike surface glycoprotein (S) to the host cell's ACE2 transmembrane

enzyme. The viral S protein has two functional subunits, S1 and S2 [53]. The S1 subunit binds to the host cell ACE2, and the S2 subunit is responsible for fusion of the membranes to enable viral entry into the host cell's cytoplasm. Host membrane proteases, such as transmembrane protease serine 2 and furin, cleave the S glycoprotein at the S1/S2 site to expose the functional peptides and enable membrane binding and fusion [53]. The susceptibility of the S1/S2 cleavage site to near-ubiquitous membrane proteases enhance SARS-CoV-2 transmissibility to various tissue types, including the central nervous system [55]. ACE2, a homolog to ACE, counteracts the renin-angiotensin-aldosterone system, designed to vasoconstrict and retain sodium, by degrading angiotensin I and II to angiotensin-(1-9) and angiotensin-(1-7), respectively [56]. The ACE2 receptor is expressed by arterial and venous endothelial cells in cerebral capillaries, smooth muscle cells, pericytes, neurons, and microglia. Expression of this receptor across cerebral capillaries, neurons, and microglia may provide a route for SARS-CoV-2 to cross the blood-brain barrier and directly infect the central nervous system. Furthermore, the initial stages of hypoxia in patients with severe pulmonary disease can increase expression of ACE2 via a hypoxia inducible factor (HIF)-1 α -mediated pathway, facilitating uptake of the virus into the central nervous system [52,57].

3.2.3. Cerebrovascular injury

Multiple mechanisms can increase the risk of ischemic stroke in patients with severe COVID-19. The hypercoagulable state induced by the immune response, increased embolic events due to pre-existing and new cardiac arrhythmias, hypoxia-induced ischemia due to cardiopulmonary distress, microangiopathic thrombosis, and endotheliopathy are all thought to be contributing factors to acute ischemic stroke in respiratory infections [26,52]. Direct viral infection of the cerebrovascular endothelium and smooth muscle could cause a viral-induced vasculitis within the brain [52]. Local damage to the cerebrovasculature can induce a focus of thrombotic microangiopathy [55]. Disruption of the ACE2 receptor homeostasis in the cerebrovasculature from infected or apoptotic endothelial cells may alter levels of angiotensin-(1-7) and impair cerebral autoregulation [26]. Hypoxia from severe pulmonary infection and acute respiratory distress syndrome also contribute to increased risk of ischemic stroke. Systemic hypoxia promotes expression of HIF-1 and HIF-2 [57]. The increased HIF promotes activation of the coagulation cascade via extrinsic coagulation pathway activation with increased TF expression and inhibition of fibrinolysis with increased expression of plasminogen activator inhibitor-1. HIF-1 can also induce localized neutrophil extracellular trap formation, perpetuating hypercoagulability in hypoxic regions [54].

In summary, there are multiple mechanisms through which COVID-19 could precipitate acute ischemic stroke but, to date, there is insufficient evidence to ascribe a causal relationship specific to the pathogenicity of SARS-CoV-2 on the cerebral vasculature.

3.3. Impact of COVID-19 on treatment of patients with acute ischemic stroke

The COVID-19 pandemic has influenced the entire stroke treatment pathway, from symptom onset to post-discharge re-

covery. A significant outpouring of research has focused on determining whether hospitals are still able to meet quality metrics despite the increased burden of care imposed by the pandemic, while many others focus on investigating the nuances of treatment of stroke in patients with concurrent COVID-19 infections.

3.3.1. Impact on stroke management quality metrics

Overall, there is minimal consensus in the literature on differences in quality metric trends before and after the onset of the pandemic. Although numerous studies have found delays in stroke onset-to-door time [35,40,43,45,58–60], just as many have shown no difference [7,10,46,61–64]. One study even found improved times [65]. Similarly, there are conflicting reports on delays in door-to-needle time [35,42,43,45,46,58,61,63]. The literature is slightly more supportive of overall stability in door-to-groin time, but again this is not a consistent finding [35,43,45,46,58,61,62,66]. A recent meta-analysis suggests that any delays captured by these quality metrics may reflect a general impact of the pandemic, because concurrent infection with SARS-CoV-2 does not affect the probability of receiving IV tissue plasminogen activator or undergoing MT once patients reach the hospital [21].

3.3.2. Changes in treatment protocols

Several recommendations and guidelines have come out regarding adjustments to stroke care in the COVID-19 era. For example, a hospital in Italy adopted a hotspot model with a mobile computed tomography unit outside the emergency department for stroke code patients with known COVID-19 infection [67]. Other recommendations for adapting to the new patient population include ordering computed tomography of the chest at the same time as head imaging for any patients with suspected COVID-19 infection [68], as well as including laboratory workup for possible organ failure or coagulopathy before administering IV contrast medium or tissue plasminogen activator [69]. Thus far, preliminary data suggest that IV thrombolysis and MT are safe options for treatment of ischemic stroke in patients with COVID-19 [70–72]. Given the additional workup, such as a computed tomography of the chest, there may be a delay to reperfusion treatment in patients with COVID-19 compared to patients with no concurrent infection [70,71].

Another topic of concern has been management of anesthesia for stroke patients with concurrent COVID-19 infection or in patients with unknown infection status. Consensus statements from the Society for Neuroscience in Anesthesiology and Critical Care and the Society of Neurointerventional Surgery recommend all airway procedures be conducted before transferring the patient to the angiography suite and starting with a general anesthetic if there is any concern about the patient's airway [73,74].

3.3.3. Thromboprophylaxis and anticoagulation in patients with COVID-19

Hypercoagulability and thrombosis are known complications of COVID-19, increasing the risk of other thrombotic events, such as deep vein thrombosis and pulmonary embolism [1]. Placing stroke patients on thromboprophylaxis is already

standard of care, and preliminary evidence suggests that prophylaxis is associated with decreased mortality in patients with COVID-19 with sepsis-induced coagulopathy [75]. Therefore, some recommend continued thromboprophylaxis for patients with COVID-19 for some period of time even after resumption of normal activities [76]. However, the risk of intracerebral hemorrhage and unfavorable outcomes is increased in patients receiving tissue plasminogen activator who have elevated D-dimer levels [30]. Given that COVID-19 patients frequently have elevated pro-thrombotic markers, this places them at a theoretically increased risk of bleeding complications. One study found an incidence of spontaneous intracerebral hemorrhage in 8% of patients with COVID-19 and that anticoagulation increased this risk [77]. Another retrospective analysis found that 75% of patients with COVID-19 who developed intracerebral hemorrhage had been on prophylactic or therapeutic doses of anticoagulation [78]. In light of these complications and questionable efficacy, a large multicenter randomized trial (Accelerating COVID-19 Therapeutic Interventions and Vaccines [ACTIV-4]) of prophylactic anticoagulation in patients with severe COVID-19 was recently halted.

3.3.4. Post-stroke treatment and recovery

Skilled nursing facilities and rehabilitation units provide an important role for post-hospitalization recovery for stroke patients, and were also initial hotspots for COVID-19 transmission. Studies have found that patients were discharged home instead of to rehabilitation units more often during the pandemic period [14,45], and a survey of health care practitioners found that most reported a decrease in access to rehabilitation services [59]. The reason for this decrease may be due to the conversion of inpatient rehabilitation units into COVID-19 facilities. Therefore, COVID-19-negative patients needing rehabilitation may lack access to a rehabilitation bed when discharged from hospital. Caregivers have held increased responsibilities with less preparation and support. A qualitative study identified barriers in effective communication, lack of visitation, and lack of updated information on progress and prognosis about loved ones as some of the hardships faced by pandemic-era caregivers [79]. Rehabilitation care should not be put on hold due to the pandemic, however, as telerehabilitation is associated with improved motor strength, cognitive, and speech outcomes, and decreased depression in caregivers [80].

3.3.5. Disparities in access to health care during the COVID-19 pandemic

Decreased stroke care may be affecting some populations disproportionately. Several studies have shown that African-American patients with concurrent stroke and COVID-19 infection received fewer IV thrombolysis and MT, that the largest proportional decrease in stroke consultations to a telenetwork in South Carolina was for African-American patients, and that African-American and Latino/Latina patients reported higher rates of emergency care avoidance because of COVID-19 [81]. A qualitative study examining community readiness for emergency care during the pandemic identified themes of fear of transmission in the hospital and changes in living conditions, such as in employment and childcare, as barriers to access-

ing care. Most of the 15 subjects in the study were African-American women [82].

In summary, the evidence suggests that the pandemic has made it more difficult for patients to get to the hospital once stroke symptoms start. However, despite the need for a more thorough workup before intervention, there does not appear to be a demonstrable impact on quality metrics once patients arrive at the hospital. Additional studies must include subgroup analyses, as minority populations may bear the burden of any decrement in stroke care as a result of the pandemic.

3.4. Outcomes in patients with COVID-19 and stroke

The published outcomes in patients with concomitant COVID-19 and stroke have generally been significantly worse than in patients with either stroke or COVID-19 alone, both with regard to their functional outcomes and their mortality rates [22,23,83,84]. Indeed, one meta-analysis found a five-fold increase of in-hospital mortality rates for acute ischemic stroke patients concurrently infected with SARS-CoV-2 [21]. A national study across 40 states and New York City reported excess cerebrovascular mortality with a high of 7.8% above expected levels in mid-April [85]. They also found that there were 70 to 85 more stroke-related deaths per 1,000 fewer emergency medical services phone calls and that a 10% increase in time spent at home according to Google Community Mobility Reports was associated with a 4.3% increase in stroke deaths. An international study assessed the outcomes of 174 consecutive patients with acute ischemic stroke and COVID-19 compared to outcomes of patients with acute ischemic stroke without COVID-19 taken from the stroke registry of consortium of 28 hospitals in 16 countries. The risk of death for patients with COVID-19 and stroke was higher, with an odds ratio of 4.3 (95% CI, 2.22–8.30); the overall death rate for patients with COVID-19 and acute ischemic stroke was 27.6% [23]. The median modified Rankin score at the longest follow-up point available for patients with COVID-19 and stroke was significantly worse than that for patients with stroke alone (4 and 2, respectively) [23].

Large meta-analyses of the many published series of patients with acute ischemic stroke and COVID-19 have largely corroborated these results. As of February 2021, the most recently published and largest available meta-analysis of cerebrovascular disease in COVID-19 (including 61 individual articles) found that the 1,106 patients with both COVID-19 and cerebrovascular disease had a significantly higher in-hospital mortality rate (OR = 5.21; 95% CI, 3.43–7.90) compared to the 107,465 patients with COVID-19 who did not have cerebrovascular disease [83]. This meta-analysis included patients with COVID-19 and cerebrovascular disease of any type, making the reported mortality rate not directly comparable to the findings of the multicenter consortium above, which was limited to acute ischemic stroke; however, the comparison is still useful and the results are largely mutually supportive, as acute ischemic stroke was overwhelmingly the most common manifestation of cerebrovascular disease (87.4%) [83]. A meta-analysis that was narrowed specifically to patients with COVID-19 and acute ischemic stroke only (39 individual studies, 135 total patients) that was published earlier in the pan-

demic (July 2020) reported an even higher mortality rate (38%) for patients with both of these conditions simultaneously [22].

In summary, concurrent COVID-19 and acute ischemic stroke results in markedly higher rate of in-hospital mortality than either disease alone, approaching nearly 40%. Further research is warranted to define the risk factors and treatment outcomes of COVID-19 patients suffering from stroke. The recently launched Vascular Surgery COVID-19 Collaborative (VASCC), a large international multicentric project that will study the impact of the pandemic on provision of care to patients with vascular diseases, will feature a specific stroke module [86]. This effort, as others that may be under way, might shed further light on the fundamental issues facing cerebrovascular care at the time of COVID-19 pandemic.

4. Conclusions

There has been a critical, negative impact of the COVID-19 pandemic on stroke patients. The presentation of acute ischemic stroke is more severe in patients concomitantly infected with SARS-CoV-2 than in patients who are not infected, a finding that is consistent with other respiratory infections [87,88]. Furthermore, patients with both COVID-19 and acute ischemic stroke have higher mortality rates and worse functional outcomes. The changes in referral patterns and quality metrics argue against healthier lifestyle and fewer actual strokes being responsible for the reduced number of strokes presenting to the health care system during this period. However, there is currently insufficient evidence to support the claim that acute ischemic stroke is a common presenting symptom of infection with SARS-CoV-2, or that patients who contract SARS-CoV-2 are at higher risk for developing an acute ischemic stroke. Further research is warranted to clarify the many questions still unanswered and may provide useful data to improve patient care in the face of predictable resurgences of COVID-19 or future pandemics.

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