

**ASSOCIATION BETWEEN COVID-19 AND ISCHEMIC STROKE:
CLINICAL CHARACTERISTICS, PATHOPHYSIOLOGY, AND
MANAGEMENT**

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Abstract

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, has emerged as a global health challenge affecting multiple organ systems beyond the respiratory tract. One of the most severe neurological complications associated with COVID-19 is ischemic stroke, which contributes significantly to morbidity and mortality. Increasing evidence suggests that COVID-19 promotes a hypercoagulable state through endothelial dysfunction, excessive inflammatory responses, platelet activation, and thrombotic complications. Patients infected with SARS-CoV-2 may experience ischemic stroke even in the absence of traditional vascular risk factors, while individuals with pre-existing cerebrovascular disease are at an increased risk of poor clinical outcomes. This review summarizes the current understanding of the relationship between COVID-19 and ischemic stroke, highlighting epidemiology, underlying pathophysiological mechanisms, clinical manifestations, diagnostic approaches, treatment strategies, and preventive measures. Early recognition of neurological symptoms, rapid neuroimaging, and multidisciplinary management remain essential for improving patient prognosis. Continued research is required to clarify the long-term cerebrovascular consequences of COVID-19 and optimize evidence-based therapeutic approaches.

Keywords: COVID-19, SARS-CoV-2, ischemic stroke, cerebrovascular disease, thrombosis, inflammation, hypercoagulability, neurology, endothelial dysfunction, neurovascular complications.

Introduction

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has affected hundreds of millions of individuals worldwide since its emergence in late 2019. Although initially recognized as a respiratory illness, COVID-19 is now understood to be a multisystem disease capable of affecting the cardiovascular, renal, gastrointestinal, endocrine, and nervous systems. Neurological manifestations occur in a considerable proportion of hospitalized patients and range from headache and anosmia to severe complications such as encephalitis, seizures, and cerebrovascular disease.

Among these complications, ischemic stroke has become one of the most concerning because of its high mortality and long-term disability. Clinical observations during the pandemic demonstrated that patients with COVID-19 had a higher incidence of thrombotic events, including acute ischemic stroke. In some cases, stroke represented the first manifestation of SARS-CoV-2 infection, particularly in younger individuals without significant cardiovascular risk factors. Understanding the relationship between COVID-19 and ischemic stroke is important for neurologists, emergency physicians, and intensive care specialists. Early diagnosis and timely intervention can significantly improve neurological outcomes and reduce disability.

COVID-19 and the Risk of Ischemic Stroke

Ischemic stroke occurs when cerebral blood flow is interrupted due to arterial occlusion, resulting in neuronal ischemia and brain tissue infarction. Traditionally, risk factors include hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, smoking, obesity, and advanced age. However, COVID-19 introduces additional mechanisms that increase stroke risk independently of conventional vascular factors.

Several international cohort studies have reported that approximately 1–3% of hospitalized patients with COVID-19 develop acute ischemic stroke. The incidence is considerably higher among patients admitted to intensive care units,

particularly those requiring mechanical ventilation. Stroke associated with COVID-19 often affects large cerebral vessels and is associated with more severe neurological deficits than non-COVID-related stroke.

Furthermore, patients with previous cerebrovascular disease are more likely to develop severe COVID-19 and experience poorer clinical outcomes, emphasizing the bidirectional relationship between these conditions.

Pathophysiological Mechanisms

The development of ischemic stroke during COVID-19 is multifactorial. One of the primary mechanisms involves **endothelial dysfunction**. SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2) receptors expressed on vascular endothelial cells. Viral invasion damages the vascular lining, promotes inflammation, and disrupts normal anticoagulant functions, increasing the likelihood of thrombus formation.

Another important mechanism is the excessive inflammatory response known as the **cytokine storm**. Elevated concentrations of inflammatory mediators such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and C-reactive protein contribute to vascular injury and activation of the coagulation cascade. COVID-19 also induces a **hypercoagulable state**, characterized by elevated D-dimer, fibrinogen, factor VIII, and von Willebrand factor levels. Platelet activation and impaired fibrinolysis further promote thrombus formation within cerebral arteries.

Cardiac complications including myocarditis, atrial fibrillation, myocardial infarction, and ventricular dysfunction may generate cardiac emboli that subsequently occlude cerebral vessels. In critically ill patients, prolonged immobilization, dehydration, and hypoxia further increase thrombotic risk.

These mechanisms often coexist, explaining why ischemic stroke in COVID-19 patients is frequently severe and associated with multiple vascular territories.

Clinical Manifestations

Patients with COVID-19-associated ischemic stroke generally present with typical neurological symptoms, including sudden unilateral weakness, facial asymmetry, speech disturbances, visual impairment, sensory deficits, dizziness, confusion, and gait instability.

However, several distinguishing features have been reported. Patients tend to be younger than those with conventional ischemic stroke, and many demonstrate elevated inflammatory and coagulation biomarkers. Large vessel occlusions are more common, resulting in higher National Institutes of Health Stroke Scale (NIHSS) scores and greater functional impairment.

In some individuals, neurological symptoms precede respiratory manifestations, making stroke the initial presentation of COVID-19. Therefore, clinicians should maintain a high level of suspicion during infectious outbreaks.

Diagnostic Evaluation

Rapid diagnosis is essential because successful reperfusion therapy depends on early intervention.

Initial assessment includes a detailed neurological examination and evaluation using standardized stroke scales. Brain computed tomography (CT) remains the first-line imaging modality for excluding intracranial hemorrhage, while magnetic resonance imaging (MRI) provides greater sensitivity for early ischemic lesions.

CT angiography or MR angiography should be performed when large vessel occlusion is suspected. Laboratory investigations include complete blood count, coagulation profile, D-dimer, fibrinogen, inflammatory markers, cardiac enzymes, renal function, and liver function tests.

Patients presenting during periods of active viral transmission should also undergo SARS-CoV-2 testing when clinically indicated, especially if respiratory symptoms or epidemiological risk factors are present.

Treatment and Management

Management follows established acute ischemic stroke guidelines while incorporating infection control measures.

Eligible patients should receive **intravenous thrombolysis** within the recommended therapeutic window after exclusion of contraindications. Mechanical thrombectomy remains the preferred treatment for selected patients with large vessel occlusion and has demonstrated favorable outcomes even among COVID-19 patients.

Supportive management includes optimization of oxygenation, blood pressure control, glucose regulation, temperature management, and prevention of complications such as aspiration pneumonia and venous thromboembolism.

Antithrombotic therapy should be individualized according to stroke subtype and bleeding risk. Antiplatelet therapy is generally indicated for non-cardioembolic stroke, whereas anticoagulation is appropriate for cardioembolic etiologies or selected hypercoagulable states.

Early rehabilitation involving neurologists, physiotherapists, speech therapists, occupational therapists, psychologists, and rehabilitation specialists is essential to maximize functional recovery.

Prevention

Preventive strategies focus on reducing both COVID-19 infection and vascular risk factors.

Vaccination remains one of the most effective measures for preventing severe COVID-19 and its thrombotic complications. Appropriate management of hypertension, diabetes mellitus, dyslipidemia, obesity, and atrial fibrillation substantially lowers stroke risk.

Hospitalized patients with moderate to severe COVID-19 should undergo individualized thromboembolism risk assessment, and prophylactic anticoagulation should be administered according to current clinical guidelines when appropriate.

Public education regarding stroke warning signs using the FAST (Face, Arm, Speech, Time) approach remains crucial to encourage immediate medical attention.

Conclusion

COVID-19 has significantly altered the understanding of cerebrovascular disease by demonstrating that viral infection can directly and indirectly promote ischemic stroke through endothelial injury, systemic inflammation, coagulation abnormalities, and cardiac complications. COVID-19-associated ischemic stroke is frequently characterized by large vessel occlusion, severe neurological deficits, and unfavorable outcomes compared with conventional stroke.

Early recognition of neurological symptoms, prompt neuroimaging, evidence-based reperfusion therapy, comprehensive supportive care, and multidisciplinary rehabilitation are fundamental for improving survival and reducing long-term disability. Continued international research is needed to better understand the long-term cerebrovascular consequences of SARS-CoV-2 infection and to refine prevention and treatment strategies for future public health challenges.

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