

Risk of Acute Ischemic Stroke in Patients 65 and Older Is Early After COVID-19 Diagnosis

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Associated acute and long-term medical complications of COVID-19 beyond respiratory illness include acute ischemic stroke (AIS).¹⁻⁵ Hypercoagulability, inflammation, cardiac dysfunction, and endothelial inflammation that occur during the infectious phase can lead to thrombotic events and thus cerebral ischemia.⁶ Reported risks of stroke in COVID-19 have varied substantially across studies.⁷ Most studies have focused on AIS incidence in patients diagnosed during or upon hospitalization. Unlike any other infectious disease in modern times and as a result of the need to trace and monitor for outbreaks to prevent the spread of COVID-19, a very large number of patients have been screened for COVID-19 at the time of hospital admission. This screening has identified both asymptomatic and symptomatic individuals with COVID-19, thus making it more difficult to determine whether and in whom COVID-19 may increase the risk of AIS and whether the association is true or incidental. In this issue of *Neurology*®, Yang et al.⁸ evaluated the estimated incidence rate ratio of AIS after COVID-19 infection in a known high-risk group—patients older than 65—and determined the time frame of highest risk of AIS associated with COVID-19 within this population.⁸

The authors used inpatient and outpatient fee-for-service Medicare claims to identify 37,379 patients with COVID-19 and AIS between January 2019 and February 2021.⁸ A pre-COVID diagnosis phase was used to account for unknown possible inoculation times and the time frame from COVID-19 billing diagnosis to stroke billing diagnosis code of up to 28 days was evaluated.⁸ Applying the self-controlled case series method, the authors found that the incidence rate ratios (IRRs) were highest within 3 days of diagnosis of COVID-19, with an odds ratio of 10.3 (95% confidence interval 9.86–10.8), and that the estimated IRR was higher in those between ages 65 and 74 without a prior history of stroke.⁸ By contrast, the association between stroke and COVID-19 was weaker 15–28 days after the initial diagnosis, suggesting that AIS rarely manifests as a long-term COVID-19 sequela in elderly patients.⁸ Major strengths of the study are the inclusion of COVID-19 cases diagnosed both in outpatient and inpatient settings, the inclusion of a large number of patients from minority groups, and the use of robust statistical methods, such as the self-case-controlled case study, which has the advantage of implicit control for all fixed confounding effects. The authors made a great effort to verify that all assumptions were not violated, albeit with some modifications. They solidified the findings of their study by performing a number of sensitivity analyses.

Interpretation of the study results should consider potential limitations, which were described by Yang et al.⁸ These limitations stem primarily from the retrospective nature of the analysis and the use of administrative claims to identify cases of COVID-19 and AIS. As the Medicare data are updated monthly, cases of COVID-19 and deaths could have been missed. Also, rapid changes in the entire health care system during the COVID-19 pandemic, including access to preventative care, patient presentation to health care facilities for evaluation of stroke-like symptoms, availability of testing and procedures, and acute stroke care, could have affected the results and the applicability of the self-controlled case study.⁹

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The study has important clinical implications. The authors identified both a group of patients (65–74 years without a prior history of stroke) and a critical period (first 3 days) for which the risk of AIS after COVID-19 diagnosis is highest. These raise important questions: Should patients aged 65–74 years be treated more preemptively and aggressively to prevent ischemic stroke? What would be the ideal duration of such specific interventions? Well-designed clinical trials are needed to answer these questions.

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Disclosure

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