

COVID-19 and Risk of Acute Ischemic Stroke Among Medicare Beneficiaries Aged 65 Years or Older

Self-Controlled Case Series Study

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Study Question

Is SARS-CoV-2 infection associated with increased risk of acute ischemic stroke (AIS)?

What Is Known and What This Paper Adds

Findings of association between coronavirus disease 2019 (COVID-19) and stroke remain inconsistent, ranging from significant association to absence of association to less-than-expected ischemic stroke among hospitalized patients with COVID-19. Few studies have focused on the older population (age ≥ 65 years), where most stroke occurred. Differences in study designs, countries, inclusion criteria of patients and comparison groups, sample size, and controlling for confounders may contribute to the inconsistent findings. This study provides Class IV evidence that SARS-CoV-2 infection is associated with increased risk of AIS in first 3 days after diagnosis among Medicare fee-for-service (FFS) beneficiaries ≥ 65 years of age.

Methods

This observational study included data from 37,379 Medicare FFS beneficiaries aged ≥ 65 years diagnosed with COVID-19 from April 1, 2020, through February 28, 2021, and AIS hospitalizations from January 1, 2019, through February 28, 2021. A self-controlled case series design that implicitly controls for all fixed confounding effects was used to examine the association between COVID-19 and AIS. Incident rate ratios (IRRs) were estimated by comparing incidence of AIS in risk period (0–3, 4–7, 8–14, 15–28 days after diagnosis of COVID-19) vs control period.

Results and Study Limitations

Among the 37,379 beneficiaries, the median age at COVID-19 diagnosis was 80.4 years (interquartile range 73.5–87.1), and 56.7% were women. When AIS at day of exposure (day = 0) was included in the risk period, IRRs at 0–3, 4–7, 8–14, and 15–28 days following COVID-19 diagnosis were 10.3 (95% CI, 9.86–10.8), 1.61 (1.44–1.80), 1.44 (1.32–1.57), and 1.09 (1.02–1.18), respectively; when AIS at day 0 was excluded in the risk period, the corresponding IRRs were 1.77 (1.57–2.01; day 1–3), 1.60 (1.43–1.79), 1.43 (1.31–1.56), and 1.09 (1.01–1.17), respectively. The association appeared to be stronger among younger beneficiaries (IRR 14.7 [13.6–15.8; day 0–3] for 65–74 years vs 7.04 [6.46–7.66] for ≥ 85 years) and among beneficiaries without history of stroke (14.6

Table IRRs of AIS Associated With COVID-19

Risk period	Events, n	IRR (95% CI)	Notes
Day 0 cases in the risk period			
–7 to –1 d	789	1.91 (1.78–2.05)	AIS occurred within 7 days before COVID-19 diagnosis
0–3 d	2,173	10.3 (9.86–10.8)	1,924 AIS that occurred at day 0 of COVID-19 diagnosis included in the risk period
4–7 d	322	1.61 (1.44–1.80)	AIS occurred 4–7 days following COVID-19 diagnosis
8–14 d	523	1.44 (1.32–1.57)	AIS occurred 8–14 days following COVID-19 diagnosis
15–28 d	735	1.09 (1.02–1.18)	AIS occurred 15–28 days following COVID-19 diagnosis
Baseline	32,837	1.0	Rest of the period excluding the risk period

Abbreviations: AIS = acute ischemic stroke; CI = confidence interval; IRR = incidence rate ratio.

Baseline included all time from observation start on January 1, 2019, to 7 days before date of COVID-19 diagnosis and after 28 days of diagnosis of COVID-19.

[13.9–15.4] vs 7.92 [7.26–8.63]) but largely consistent across sex and race/ethnicities. This study has several limitations that may affect the accurate timing and exposure to SARS-CoV-2 including potential misclassification from the use of Medicare real-time preliminary claims data and potential errors in the time of COVID-19 diagnosis. The implementation of COVID-19 screening/testing for all patients admitted to hospitals may explain the higher number of AIS and COVID-19 at day 0 and within 7 days before the index date of COVID-19.

Study Funding and Competing Interests

The authors report no competing interests. Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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