

Rising stroke mortality in the wake of COVID-19: unraveling the long-term impact of the pandemic on cerebrovascular health

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ABSTRACT

Evidence indicates that the risk of stroke has increased during the ongoing coronavirus disease 2019 (COVID-19) pandemic. This study aims to analyze recent trends in stroke mortality in the United States from 2018 to 2024. Data from the US Centers for Disease Control and Prevention National Center for Health Statistics (2018-2024) were analyzed using ICD-10 codes I63.X (ischemic stroke) and U07.1 (COVID-19). Age-adjusted death rates and cumulative excess mortality were calculated, with pre-pandemic years (2018-2019) as a baseline. The age-adjusted stroke death rates rose from $8.50 \times 100,000$ in 2018 to $11.76 \times 100,000$ in 2024, with a total of 45,847 excess stroke deaths recorded between 2020-2024 compared to the pre-pandemic period. Among these, COVID-19-associated stroke deaths accounted for 9,143 fatalities, representing 4.7% of total stroke mortality during the same period. Notably, COVID-19-associated stroke deaths contributed to nearly 20% of all excess stroke deaths from 2020 to 2024. However, the proportion of excess stroke deaths attributable to COVID-19 declined over time, starting at 50% in 2020 and decreasing progressively to 3% by 2024. While

early pandemic mortality was driven by prothrombotic effects of COVID-19, the continued increase in stroke deaths indicates long-term impacts, including delayed management of cardiovascular risk factors and possible long-COVID effects. These findings underscore the need for enhanced preventive care and robust stroke management systems to address the ongoing cerebrovascular burden.

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Introduction

Coronavirus disease 2019 (COVID-19) is a strong prothrombotic condition that significantly increases the risk of developing ischemic cerebrovascular events. Moreover, its widespread diffusion has contributed to disrupt the operations of stroke care services globally especially during the early phase of the ongoing pandemic, leading to adverse effects on stroke outcomes.¹ This evidence is supported by a large retrospective cross-sectional study of 171 stroke centers across 49 countries, which found that stroke patients with concurrent COVID-19 experienced higher in-hospital mortality rates during the first year of the pandemic.² An analysis of emergency department stroke admissions in nonfederal US hospitals from 2019 to 2021,³ based on administrative claims data from fee-for-service Medicare enrollees aged 66 years and older, revealed that stroke presentations remained significantly below baseline levels following an initial sharp decline in early 2020. Nonetheless, this reduction in stroke admissions was associated with increased adjusted 30-day mortality rates and higher rates of hospice referrals.

These previous observations prompted us to investigate whether the potentially increased burden of cerebral ischemia directly caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, combined with disruption of stroke care services and risk factor control occurred during the early phase of the pandemic, may have contributed to increase the mortality rates for stroke in the US.

Methods

Our analysis encompassed a digital search of the US Centers for Disease Control and Prevention (CDC) National Center for Health Statistics database using its WONDER (Wide-Ranging Online Data for Epidemiologic Research) “Provisional Multiple Cause of Death Data” interface, which provides comprehensive vital health information for statistical analysis, policy development, and public health improvement.⁴ The data are derived from death certificates of all US residents, each containing detailed demographic information and the underlying causes of death. We queried the database using the 10th revision of the International Classification of Diseases (ICD-10) codes I63.X (cerebral ischemia) with or without the ICD-10 code U07.1 (COVID-19), filtered by year (from 2018 to 2024). Mortality data were extracted as cumulative number and age-adjusted death rates per 100,000 with 95% confidence intervals (95% CI). Excess mortality was calculated with a Poisson regression model using the historical pre-pandemic data (i.e., years 2018 and 2019) to predict the expected number of deaths in the following years while accounting for year-to-year variability. This study complied with the principles outlined in the Declaration of Helsinki. As WONDER provides anonymized, publicly accessible data, this research was exempt from Ethical Committee approval.

Results

The results of our analysis are summarized in Table 1. According to data from the US National Center for Health Statistics, the overall stroke mortality (ICD-10 code I63.X) and the age-adjusted stroke death rate displayed a significant increase over time since the onset of the COVID-19 pandemic. Specifically, the age-adjusted stroke death rate $\times 100,000$ was 8.50 in 2018, 7.53 in 2019, rising to 8.85 in 2020, 10.22 in 2021, 11.58 in 2022, 11.51 in 2023, and 11.76 in 2024 (+38% increase from 2018), respectively. Over the first five years of the pandemic, the cumulative excess stroke deaths also increased, with a total of 45,847 excess deaths recorded between 2020 and 2024 (Table 1).

Stroke deaths (ICD-10 code I63.X) combined with COVID-19-related deaths (ICD-10 code U07.1) were 4,372 in 2020 (age-adjusted death rate of $0.52 \times 100,000$), increasing to 8,473 in 2021

(age-adjusted death rate of $0.69 \times 100,000$), but then declining to 2,635 in 2022 (age-adjusted death rate of $0.63 \times 100,000$), 996 in 2023 (age-adjusted death rate of $0.22 \times 100,000$), and 542 in 2024 (age-adjusted death rate of $0.13 \times 100,000$) (Table 1). Throughout the pandemic, 9,143 stroke deaths were associated with COVID-19 (age-adjusted death rate of $0.44 \times 100,000$). Overall, the crude rate of COVID-19-associated stroke deaths increased from 5.94% of all stroke deaths in 2020 to 6.84% in 2021, before gradually declining to 5.39% in 2022, 2.04% in 2023, and 1.09% in 2024. Over the first five years of the pandemic, COVID-19-associated stroke deaths accounted for 4.70% of all stroke-related mortality.

The crude rate for COVID-19-associated stroke deaths out of the total excess stroke deaths is also summarized in Table 1 and shown in Figure 1.

In the first year of the pandemic, COVID-19-associated stroke deaths accounted for nearly 50% of the excess stroke deaths, decreasing to approximately 33% in 2021, 16% in 2022, 6% in 2023, and 3% in 2024, respectively. Overall, COVID-19-associated stroke deaths accounted for nearly 20% of all excess stroke deaths over the first five years of the pandemic.

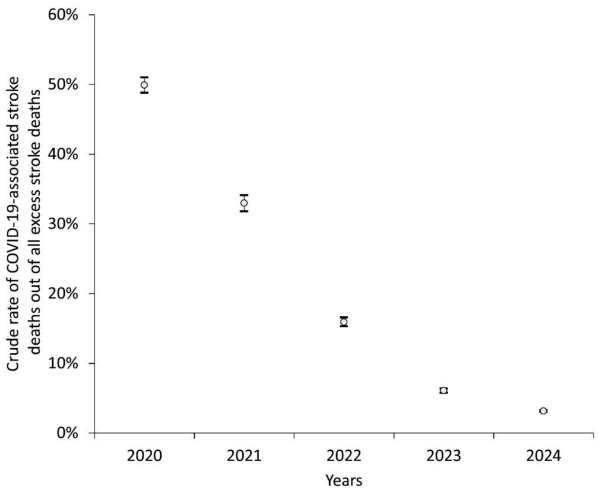


Figure 1. Crude rate for coronavirus disease 2019 (COVID-19)-associated stroke deaths out of the total excess stroke deaths.

Table 1. Stroke mortality in the US between the years 2018 and 2024. Results are shown with their 95% confidence interval (between brackets).

Year	Deaths	Stroke (I63.X) Age-adjusted death rate $\times 100,000$	Excess deaths*	Deaths	Stroke (I63.X)+COVID-19 (U07.1)		
					Age-adjusted death rate $\times 100,000$	Crude rate of COVID-19-associated stroke deaths vs all stroke deaths	Crude rate of COVID-19-associated stroke deaths vs excess stroke deaths
2018	33,958	8.50 (8.41-8.59)	-	-	-	-	-
2019	30,697	7.53 (7.45-7.62)	-	-	-	-	-
2020	36,700	8.85 (8.76-8.95)	4,372	2,181	0.52 (0.49-0.54)	5.94 (5.69-6.19)%	49.90 (48.79-51.01)%
2021	40,801	10.22 (10.12-10.32)	8,473	2,789	0.69 (0.66-0.72)	6.84 (6.58-7.09)%	32.96 (31.81-34.10)%
2022	48,891	11.58 (11.48-11.68)	16,563	2,635	0.63 (0.61-0.66)	5.39 (5.18-5.59)%	15.92 (15.30-16.58)%
2023	48,750	11.51 (11.41-11.62)	16,422	996	0.22 (0.21-0.24)	2.04 (1.92-2.17)%	6.07 (5.76-6.37)%
2024	49,559	11.76 (11.66-11.87)	17,231	542	0.13 (0.18-0.14)	1.09 (1.00-1.19)%	3.15 (3.04-3.25)%
Cumulative [#]	224,701	10.83 (10.78-10.87)	45,847	9,143	0.44 (0.43-0.45)	4.70 (3.99-4.15)%	19.95 (19.04-20.87)%

*Compared to the years 2018-2019; [#]2020-2024.



Discussion

There is now robust evidence that COVID-19, particularly in severe cases, is strongly associated with a hypercoagulable state, which significantly increases the risk of various cardiovascular complications, including stroke.⁶ While numerous studies have aimed to estimate the prevalence of stroke among patients diagnosed with SARS-CoV-2 infection,⁶⁻⁸ our research provides novel insights into the impact of the COVID-19 pandemic on stroke mortality in the US, emphasizing both the direct biological effects of the virus and its indirect consequences.

Our analysis of data from the US National Center for Health Statistics reveals a substantial and sustained increase in stroke-related mortality since the onset of the pandemic. The age-adjusted stroke death rate increased notably, from $8.50 \times 100,000$ in 2018 to $11.76 \times 100,000$ in 2024 (+38%). Over the five-year pandemic period, cumulative excess stroke mortality was estimated at 45,847 deaths. These findings underscore a significant healthcare burden, the causes of which cannot be solely attributed to acute SARS-CoV-2 infection, but suggest that the pandemic has had lasting effects on stroke outcomes or that additional, unaccounted factors have contributed.

Although the concurrent increase in stroke deaths associated with COVID-19 (9,143 deaths over the study period) highlights SARS-CoV-2 as a potent prothrombotic biological agent, the crude rate of COVID-19-associated stroke deaths versus excess stroke deaths has declined over time, from nearly 50% in 2020 to slightly more than 3% in 2024. This indicates that while COVID-19 directly caused a substantial number of stroke deaths during the pandemic's early phase, its impact in subsequent years (2022-2024) has diminished. This raises critical questions about the persistent increase in stroke mortality observed during this period, which cannot be fully explained by direct biological injury or indirect healthcare access disruption related to COVID-19.

One plausible explanation is the worsening of cardiovascular risk factors over the past seven years, potentially due to delayed management of conditions such as hypertension, diabetes, and obesity during the pandemic, both in the US and on a global scale.⁹⁻¹¹ As Jia *et al.*¹⁰ noted, the prevalence of hypertension and diabetes is increasing in the US, likely due to reduced glycemic and blood pressure control after years of improvement. Mohebi *et al.*¹² projected a significant rise in the burden of diabetes (+39.3%) and other cardiovascular risk factors, including hypertension (+27.2%), dyslipidemia (+27.5%), and obesity (1+8.3%), between 2025 and 2060. They also estimated a 34.3% increase in stroke prevalence over the same period. In alignment with our findings, these trends emphasize the critical need to prioritize screening, education, and interventions targeting major cardiovascular risk factors for stroke prevention.

Another potential factor is the long-term biological impact of SARS-CoV-2 infection. Hilser *et al.*¹³ demonstrated that the long-term risk of myocardial infarction and stroke nearly doubles in patients with a history of SARS-CoV-2 infection, persisting up to three years post-diagnosis. Similarly, Knight *et al.*¹⁴ reported a more than two-fold increase in stroke risk 27-49 weeks after recovery from COVID-19. These findings suggest a protracted «long-COVID» effect on human biology, which may not be adequately captured by the association of I63.X and U07.1 ICD-10 codes, as the latter only pertains to acute SARS-CoV-2 infections.

Some limitations should be acknowledged in our study. First, our data were derived from death certificates, which may not comprehensively reflect clinical details such as stroke severity or co-

morbidities that influence mortality. Second, the classification of COVID-19-associated stroke deaths relied on ICD-10 codes, which cannot reliably differentiate between strokes directly caused by COVID-19 and those where SARS-CoV-2 infection was incidental. Finally, coding errors and misclassifications inherent to ICD-10 coding may have impacted the accuracy of data reported in the US National Center for Health Statistics database.

Conclusions

In conclusion, our results indicate that the COVID-19 pandemic has had a profound and potentially enduring impact on stroke mortality in the US. It is hence conceivable that both the direct effects of the virus on cerebrovascular health and indirect factors such as healthcare disruptions and neglected cardiovascular risk factor management have contributed to increase the burden of cerebral ischemia. These findings underscore the importance of maintaining robust stroke care systems and preventive strategies during crises and highlight the need for ongoing research into the long-term consequences of COVID-19 on stroke outcomes.

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