

## BRIEF REPORT

# History of Stroke Is Independently Associated With In-Hospital Death in Patients With COVID-19

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**BACKGROUND AND PURPOSE:** In December 2019, an outbreak of severe acute respiratory syndrome coronavirus causing coronavirus disease 2019 (COVID-19) occurred in China, and evolved into a worldwide pandemic. It remains unclear whether the history of cerebrovascular disease is associated with in-hospital death in patients with COVID-19.

**METHODS:** We conducted a retrospective, multicenter cohort study at Mount Sinai Health System in New York City. Using our institutional data warehouse, we identified all adult patients who were admitted to the hospital between March 1, 2020 and May 1, 2020 and had a positive nasopharyngeal swab polymerase chain reaction test for severe acute respiratory syndrome coronavirus in the emergency department. Using our institutional electronic health record, we extracted clinical characteristics of the cohort, including age, sex, and comorbidities. Using multivariable logistic regression to control for medical comorbidities, we modeled the relationship between history of stroke and all-cause in-hospital death.

**RESULTS:** We identified 3248 patients, of whom 387 (11.9%) had a history of stroke. Compared with patients without history of stroke, patients with a history of stroke were significantly older, and were significantly more likely to have a history of all medical comorbidities except for obesity, which was more prevalent in patients without a history of stroke. Compared with patients without history of stroke, patients with a history of stroke had higher in-hospital death rates during the study period (48.6% versus 31.7%,  $P < 0.001$ ). In the multivariable analysis, history of stroke (adjusted odds ratio, 1.28 [95% CI, 1.01–1.63]) was significantly associated with in-hospital death.

**CONCLUSIONS:** We found that history of stroke was associated with in-hospital death among hospitalized patients with COVID-19. Further studies should confirm these results.

**Key Words:** cerebrovascular disorders ■ COVID-19 ■ hospitalization ■ pandemic ■ stroke

In December 2019, an outbreak of severe acute respiratory syndrome coronavirus 2 causing coronavirus disease 2019 (COVID-19) occurred in Wuhan, China, subsequently evolving into an international pandemic. By late April 2020, >3 million cases have been reported worldwide. Of these, over 1 million cases have been reported in the United States and 170 000 in the New York City area, which has over 30% of US cases.<sup>1,2</sup> Several recent studies have suggested that cerebrovascular disease is associated with a nonsignificant trend toward in-hospital death in patients with COVID-19, but these

results have been limited by small sample sizes.<sup>3,4</sup> Moreover, history of stroke was not reported in several recent large case series.<sup>2,5</sup> We therefore sought to investigate whether history of stroke was associated with in-hospital death among patients hospitalized with COVID-19.

## METHODS

The authors declare that all supporting data are available within the article. We conducted a retrospective multicenter study at the Mount Sinai Health System, an academic health network

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## Nonstandard Abbreviations and Acronyms

**COVID-19** coronavirus disease 2019

in New York City, using patient data from 5 separate hospital campuses serving different geographic populations (Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside, and Mount Sinai West). Using our institutional data warehouse, we identified all adult patients who were hospitalized between March 1, 2020 and May 1, 2020 and defined patients with COVID-19 as any patient who was positive for severe acute respiratory syndrome coronavirus 2 by nasopharyngeal swab polymerase chain reaction test in the emergency department. We excluded all patients who remained hospitalized at the end of the study period.

Using our institutional electronic health record, we then extracted clinical characteristics of the cohort, including patient age, sex, hypertension, coronary heart disease, diabetes mellitus, chronic kidney disease, asthma, chronic obstructive pulmonary disease, congestive heart failure, dyslipidemia, atrial fibrillation, malignancy, obesity, and active smoking. Using our institutional electronic health record, we identified history of stroke, which served as our primary exposure, and in-hospital death, which was our primary outcome. To evaluate the association between history of stroke and in-hospital death, we first used univariable logistic regression to calculate a crude, unadjusted odds ratio. We then used multivariable logistic regression to generate adjusted odds ratios between history of stroke and in-hospital death, while adjusting for the confounding effect of multiple medical comorbidities. We assessed for possible collinearity between medical comorbidities by constructing a correlation matrix of all covariates, which demonstrated a maximum correlation coefficient of 0.35 (data not shown). Because of the mild observed collinearity between covariates, the analysis was not adjusted for collinearity. Alpha was set to 0.05. The Mount Sinai Hospital IRB approved the use of patient data for this study and waived the requirement for informed consent.

## RESULTS

We identified 4460 patients who met initial inclusion criteria. We excluded 1203 (27.0%) patients who were still admitted at the end of the study period and 9 (0.07%) patients who were younger than 18. This resulted in a final cohort size of 3248 patients, of whom 387 (11.9%) had a history of stroke, and 1096 (33.7%) died during their hospitalization. Compared with patients without history of stroke, patients with a history of stroke were significantly older, and were significantly more likely to have a history of all medical comorbidities except for obesity, which was more prevalent in patients without history of stroke. The rate of asthma was not significantly different between both groups. Compared with patients without history of stroke, patients with history of stroke were significantly more likely to die during their hospitalization (48.6% versus 31.7%,  $P<0.001$ ; Table). In the univariable analysis, history of stroke was significantly associated

**Table. Patient Characteristics, Stratified by Presence of Stroke History**

Characteristic	History of Stroke (N=387)	No History of Stroke (N=2861)	P Value
Age, median (IQR), y	75.0 (65.0–83.0)	66.0 (55.0–77.0)	<0.001
Male sex	219 (56.6)	1671 (58.4)	0.53
Comorbidities			
Hypertension	329 (85.0)	1828 (63.9)	<0.001
Coronary artery disease	152 (39.3)	558 (19.5)	<0.001
Diabetes mellitus	231 (59.7)	1283 (44.8)	<0.001
Dyslipidemia	191 (49.4)	958 (33.5)	<0.001
Congestive heart failure	107 (27.6)	357 (12.5)	<0.001
Atrial fibrillation	69 (17.8)	253 (8.8)	<0.001
Chronic kidney disease	127 (32.8)	491 (17.2)	<0.001
Obesity	110 (28.4)	1031 (36.0)	0.004
COPD	55 (14.2)	237 (8.3)	<0.001
Asthma	55 (14.2)	371 (13.0)	0.55
Active smoking	124 (32.0)	604 (21.1)	<0.001
Malignancy	77 (19.9)	447 (15.6)	0.038
Died during hospitalization	188 (48.6)	908 (31.7)	<0.001

Figures are reported as N (%), unless otherwise noted. COPD indicates chronic obstructive pulmonary disease; and IQR, interquartile range.

with in-hospital death (odds ratio, 2.03 [95% CI, 1.64–2.52]). In the multivariable analysis, which adjusted for all medical comorbidities, history of stroke remained significantly associated with in-hospital death (adjusted odds ratio, 1.28 [95% CI, 1.01–1.63]).

## DISCUSSION

In this descriptive, observational study of hospitalized patients with COVID-19, we found that history of stroke was independently associated with in-hospital death. Available data are limited on the relationship between history of stroke and in-hospital death among patients with COVID-19. A recent pooled analysis of 2 studies encompassing a sample of 202 patients with COVID-19 failed to find a significant relationship between cerebrovascular disease and in-hospital death.<sup>3</sup> However, only 19 (9.4%) patients in this population had cerebrovascular disease, thereby limiting the interpretability of these results. Our sample size of nearly 400 patients builds on existing work and may allow a more reliable conclusion regarding the relationship between history of stroke and in-hospital death in patients with COVID-19.

A potential explanation for our findings is that stroke may have served as a proxy for overall frailty, which may have predisposed patients to develop more severe COVID-19, and subsequent in-hospital death. Alternatively, while our analysis lacked information on advance directive status, patients with a history of preexisting stroke may have been more likely to have advance care directives, such as

“do-not-resuscitate” or “do-not-intubate” orders. Based on the independent association with in-hospital death in the multivariable analysis, it is unlikely that stroke served as a surrogate marker for risk factors such as age, diabetes mellitus, hypertension, smoking, or dyslipidemia, which are associated with in-hospital death in COVID-19.<sup>6,7</sup> Importantly, nearly 40% of patients in our study population died during their hospitalization, regardless of history of stroke. Our results suggest that patients hospitalized with COVID-19, and particularly those with history of stroke, have a markedly elevated risk of death that warrants very close monitoring and aggressive treatment measures.

Our study was not without limitations. First, we identified the primary exposure and outcome, as well as confounding factors using data from hospital electronic records, which vary in accuracy and reliability. Second, we did not distinguish between hemorrhagic or ischemic stroke. Third, we did not stratify analyses according to severity of COVID-19 or other factors associated with illness severity, such as D-dimer levels, oxygenation status, intensive care unit admission, intubation, or renal replacement therapy, to determine whether these factors were significant drivers of in-hospital death.<sup>7</sup> Fourth, because our analysis was restricted to in-hospital data, we could not ascertain whether patients who were discharged from the hospital may have died at home or at another facility. Similarly, because of the 2-month study period, our results cannot shed light on longer-term in-hospital death from COVID-19. Finally, our analysis lacked medication data, and we could therefore not adjust for anticoagulation status. This could have mitigated the hypercoagulability associated with COVID-19, which has been linked to poor prognosis.<sup>8,9</sup>

## CONCLUSIONS

In hospitalized patients with COVID-19, we found a significant and independent association between history of stroke and in-hospital death. Further studies should confirm these findings with larger cohort sizes and more granular patient-level data. If confirmatory, further work should investigate the pathophysiological mechanisms underlying the association between the history of stroke and in-hospital death.

## ARTICLE INFORMATION

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