CLINICAL AND POPULATION SCIENCES

Treatment and Outcomes of Patients With Ischemic Stroke During COVID-19
An Analysis From Get With The Guidelines-Stroke

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BACKGROUND AND PURPOSE: The coronavirus disease 2019 (COVID-19) pandemic has created challenges in the delivery of acute stroke care. In this study, we analyze the characteristics, evaluation, treatment, and in-hospital outcomes of patients presenting with acute ischemic stroke (AIS) pre-COVID-19 and during COVID-19.

METHODS: Get With The Guidelines-Stroke is a national registry of adults with stroke in the United States. Using this registry, we identified patients with a diagnosis of AIS before (n=39,113; November 1, 2019–February 3, 2020) and after (n=41,971; February 4, 2020–June 29, 2020) the first reported case of COVID-19 in the registry. Characteristics, treatment patterns, quality metrics, and in-hospital outcomes were compared between the 2 groups.

RESULTS: Stroke presentations decreased by an average of 15.3% per week in the during COVID-19 time period when compared with similar months in 2019. Compared with patients with AIS in the pre-COVID-19 era, patients in the COVID-19 time period had similar rates of intravenous alteplase and endovascular therapy, and similar door to computed tomography, door to needle, and door to endovascular therapy times. In adjusted models, inpatient mortality was similar between those presenting with AIS pre-COVID-19 and during COVID-19 (4.8% versus 5.2%; odds ratio, 1.05 [95% CI, 0.97–1.13]).

CONCLUSIONS: Among hospitals participating in Get With The Guidelines-Stroke, patients presenting with AIS during COVID-19 received, with few exceptions, similar quality care and experienced similar risk-adjusted outcomes when compared with patients with AIS presenting pre-COVID-19. These findings demonstrate that stroke care in the United States remains robust during the COVID-19 pandemic.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: coronavirus • inpatient • ischemic stroke • pandemics • tomography

Stroke serves as a leading cause of disability and the second leading cause of death worldwide. Advances in care, including intravenous thrombolysis and mechanical thrombectomy, have dramatically improved outcomes of patients with stroke, though they require timely presentation and action to be effective. Given the time-sensitive nature of stroke management, there has been growing concern regarding its diagnosis and treatment in the coronavirus disease 2019 (COVID-19) era. While some studies demonstrate no difference in diagnostic and treatment metrics, others show significant delays and even increases in mortality among those presenting with stroke.
Nonstandard Abbreviations and Acronyms

- AIS: acute ischemic stroke
- COVID-19: coronavirus disease 2019
- CT: computed tomography
- GWTG-Stroke: Get With The Guidelines-Stroke

RESULTS

The final cohort consisted of 81,084 patients, with 39,113 patients in the pre-COVID-19 group and 41,971 patients in the during COVID-19 group. In the during COVID-19 group, 1143 (2.7%) patients had a diagnosis of COVID-19. Patient enrollment by week is shown in the Figure and Table II in the Data Supplement. There was a decrease in patients with AIS enrolled following the first COVID-19 registry case, with an average decrease of 15.3% per week during the pandemic when compared with a similar
time period the year prior (Figure). Patient characteristics, stratified by pre-COVID-19 or during COVID-19 time period, are displayed in Table 1. The overall median age (25th–75th percentile) was 71 (61–81) years, with 48.8% and 61.9% of the cohort being female, and White, respectively. There were no significant differences in the general characteristics of the cohort (Table 1).

Treatment patterns of the cohort are shown in Table 2. There were no significant differences between the pre-COVID-19 and during COVID-19 time periods in the proportions of patients who received intravenous alteplase (11.7% versus 11.4%, \( P = 0.26 \)) or endovascular therapy (10.2% versus 10.1%, \( P = 0.90 \)). Door to needle and door to endovascular times were not different between the 2 groups. Door to computed tomography (CT) time was slightly shorter during the COVID-19 time period (median, 35 [14–100] versus 37 [15–111] minutes, \( P < 0.001 \)) and door to endovascular treatment time was slightly longer (median, 95 [58–140] versus 86 [53–129] minutes, \( P = 0.001 \)) in the later during COVID-19 time period compared with pre-COVID-19 (Table VI in the Data Supplement). There were no significant differences in in-hospital mortality, symptomatic intracranial hemorrhage among intravenous alteplase patients, or VTE/PE during hospitalization (Table VII in the Data Supplement).

**DISCUSSION**

In this analysis of 81,084 patients from the GWTG-Stroke registry, we demonstrate an average 15.3% drop in weekly AIS volume in the COVID-19 era when compared with the same time period in 2019. Patients presenting during COVID-19 received high-quality acute evaluation and management, with similar door to CT, door to needle, and door to endovascular times, as well as similar rates of intravenous alteplase therapy and endovascular therapy compared with those presenting pre-COVID-19. Patients had similar adjusted in-hospital mortality in the 2 groups.

Similar to prior studies, we report a decrease in stroke presentations in the months following the onset of the COVID-19 pandemic.\(^6,8,14–18\) From a patient standpoint, fear of contracting the virus in the community or hospital setting is likely playing a significant role. In a national poll of 2201 adults conducted by the American College of Cardiology, the American Stroke Association estimated that 74% of people felt that the pandemic had a major impact on their ability to get medical care for stroke, with younger people being more concerned about getting timely treatment.

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*Figure. Acute ischemic stroke (AIS) presentations in the 458 Get With The Guidelines-Stroke hospitals February to May 2019 vs February to May 2020.*
Table 1. Characteristics of the Cohort Stratified by Pre-COVID-19 and During COVID-19 Time Period

| Time Period                          | Overall | Pre-COVID-19 | During COVID-19 | Absolute standardized difference* |
|--------------------------------------|---------|--------------|-----------------|-----------------------------------|
|                                      | N=81084 | N=39113      | N=41971         |                                   |
|                                      | November 1, 2019–June 29, 2020 | November 1, 2019–February 3, 2020 | February 4, 2020–June 29, 2020 |
| Demographics                         |         |              |                 |                                   |
| Age, y                               | 71 (61–81) | 71 (61–81) | 71 (60–81) | 4.65                              |
| Female, n (%)                        | 39576 (48.8) | 19161 (49.0) | 20406 (48.6) | 0.74                              |
| Race, n (%)                          |         |              |                 |                                   |
| Asian                                | 2703 (3.3) | 1390 (3.6) | 1313 (3.1) | 3.36                              |
| Non-Hispanic Black                   | 17960 (22.2) | 8588 (22.0) | 9372 (22.3) |                       |
| Hispanic                             | 6002 (7.4) | 2776 (7.1) | 3226 (7.7) |                        |
| Non-Hispanic White                   | 50182 (61.9) | 24325 (62.2) | 25857 (61.6) |                     |
| Other                                | 4216 (5.2) | 2033 (5.2) | 2183 (5.2) |                                |
| Insurance, n (%)                     |         |              |                 |                                   |
| Self-pay/no insurance                | 3217 (4.0) | 1485 (3.8) | 1732 (4.1) | 8.46                              |
| Medicare                             | 29864 (36.8) | 14229 (36.4) | 15635 (37.3) |                       |
| Medicaid                             | 10386 (12.8) | 4894 (12.5) | 5492 (13.1) |                       |
| Private/veterans affairs/CHAMPUS/other | 27655 (34.1) | 14065 (36.0) | 13590 (32.4) |                       |
| Not documented                       | 9962 (12.3) | 4440 (11.4) | 5522 (13.2) |                       |
| Medical comorbidities                |         |              |                 |                                   |
| Atrial fibrillation/flutter, n (%)   | 14901 (18.4) | 7445 (19.0) | 7456 (17.8) | 3.28                              |
| Coronary artery disease, n (%)       | 17822 (22.0) | 8672 (22.2) | 9150 (21.8) | 0.9                               |
| Diabetes, n (%)                      | 28871 (35.6) | 13906 (35.6) | 14965 (35.7) | 0.21                              |
| Heart failure, n (%)                 | 8598 (10.6) | 4247 (10.9) | 4351 (10.4) | 1.6                               |
| Hypertension, n (%)                  | 62201 (76.7) | 30325 (77.5) | 31876 (76.0) | 3.75                              |
| Peripheral vascular disease, n (%)   | 3276 (4.0) | 1580 (4.0) | 1696 (4.0) | 0.01                              |
| Previous stroke, n (%)               | 20619 (25.4) | 10072 (25.8) | 10547 (25.1) | 1.43                              |
| Previous transient ischemic attack, n (%) | 6211 (7.7) | 3019 (7.7) | 3192 (7.6) | 0.43                              |
| Serum creatinine >2 mg/dL, n (%)     | 9152 (11.3) | 4385 (11.2) | 4767 (11.4) | 0.46                              |
| NIH Stroke Scale                     | 4 (1–9) | 4 (1–9) | 4 (1–10) | 2.53                              |
| Large vessel occlusion stroke, n (%) | 17119 (23.2) | 8072 (22.6) | 9047 (23.8) | 2.79                              |
| Time from symptom onset to arrival, min† | 319 (102–804) | 315 (101–794) | 322 (103–815) | 1.26                              |
| Medications before admission         |         |              |                 |                                   |
| Prior antiplatelet, n (%)            | 33962 (41.9) | 16514 (42.2) | 17448 (41.6) | 1.32                              |
| Prior anticoagulant, n (%)           | 10781 (13.3) | 5334 (13.8) | 5447 (13.0) | 1.94                              |
| Prior antihypertensive, n (%)        | 47555 (58.7) | 22913 (58.6) | 24642 (58.7) | 0.26                              |
| Prior cholesterol lowering medication, n (%) | 39044 (48.2) | 18988 (48.8) | 20056 (47.8) | 1.52                              |
| Prior diabetic medication, n (%)     | 21381 (26.4) | 10278 (26.3) | 11103 (26.5) | 0.4                               |
| Prior antidepressant medication, n (%) | 10454 (12.9) | 4958 (12.7) | 5496 (13.1) | 1.25                              |
| Labs                                 |         |              |                 |                                   |
| Platelets, ×10^9/L                   | 233 (188–296) | 232 (188–295) | 234 (187–297) | 2.43                              |
| International normalized ratio       | 1.0 (1.0–1.1) | 1.0 (1.0–1.1) | 1.0 (1.0–1.1) | 0.31                              |
| COVID-19 positive, n (%)             | 1143 (1.4) | N/A | 1143 (2.7) |                                |
| Arrival mode                         |         |              |                 |                                   |
| Private transport/taxi/other from home/scene, n (%) | 23813 (29.4) | 11871 (30.4) | 11942 (28.5) | 6.04                              |
| EMS from home/scene, n (%)           | 37112 (45.8) | 17325 (44.3) | 19787 (47.1) |                       |
| Transfer from other hospital, n (%)  | 16141 (19.9) | 7998 (20.5) | 8143 (19.4) |                       |
| Mobile stroke unit, n (%)            | 295 (0.4) | 151 (0.4) | 144 (0.3) |                                |

(Continued)
of Emergency Physicians, 70% of adults reported being concerned about contracting COVID-19 if they were to seek care from their doctor for a condition not related to severe acute respiratory syndrome coronavirus 2, 80% reported concern about contracting COVID-19 from another patient or visitor if they had to go to an emergency room, and 29% of adults reported actively delaying or avoiding seeking medical care due to concerns about contracting COVID-19. 

The initial wave of COVID-19 overwhelmed medical systems around the world, raising the possibility that decreased stroke presentations may partially reflect a lack of capacity in overburdened health systems. While some studies have demonstrated steep increases in calls to EMS, most show that stroke cases have also decreased in medical systems that have not been overwhelmed. In the United States, for example, 911 calls for emergency medical services dropped by almost 26.1% since the start of the pandemic, with many stroke centers reporting adequate resources to effectively manage stroke patients. Conversely, an overburdened health care system in Lombardy, Italy, actually saw increases in the number of ischemic stroke admissions at the height of the pandemic. 

Shelter in place and social distancing orders, while essential to curb the spread of the disease, may also be contributing to decreases in stroke presentation. In a large Northern California cohort, weekly stroke volume and stroke discharges significantly declined after the announcement of shelter in place orders, with volumes increasing again after the initiation of a gradual reopening phase. Social distancing also inherently results in increased social isolation for some, making it more likely for stroke symptoms to be missed or overlooked. Concomitantly, social distancing may be leading to fewer strokes happening to begin with due to factors such as decreases in pollution and work-related stress. While decreases in stroke occurrence may be partly contributing, it is unlikely that they alone account for the significant fall observed. In addition, there was significant heterogeneity across the United States as the virus spread over the Spring and Summer months, and some of the variations in case volume may be less prominent.

| Time Period                      | Overall | Pre-COVID-19 | During COVID-19 | Absolute standardized difference* |
|---------------------------------|---------|--------------|-----------------|-----------------------------------|
| November 1, 2019–June 29, 2020 | N=81084 | N=39113      | N=41971         |                                   |
| Patient location when stroke symptoms discovered |         |              |                 |                                   |
| Not in a health care setting, n (%) | 71659 (88.9) | 34640 (88.7) | 37019 (89.0) | 2.81                             |
| Stroke occurred during hospitalization, n (%) | 2832 (3.5) | 1441 (3.7)  | 1391 (3.3)     |                                   |
| Outpatient health care setting, n (%) | 942 (1.2)   | 483 (1.2)   | 459 (1.1)      |                                   |
| Chronic health care facility, n (%) | 3484 (4.3)  | 1702 (4.4)  | 1782 (4.3)     |                                   |
| Another acute care facility, n (%) | 1366 (1.7)  | 646 (1.7)   | 730 (1.8)      |                                   |
| Cannot be determined, n (%) | 337 (0.4)  | 144 (0.4)   | 193 (0.5)      |                                   |
| Hospital characteristics#       |         |              |                 |                                   |
| Number of beds in hospital      | 434 (290–668) | 439 (292–679) | 425 (287–663) | 4.1                              |
| Hospital type teaching or academic, n (%) | 67547 (84.0) | 32773 (84.5) | 34774 (83.6) | 2.46                             |
| Hospital location rural, n (%)  | 1312 (1.6)  | 570 (1.5)   | 742 (1.8)      | 2.47                             |
| Hospital region, n (%)          |         |              |                 |                                   |
| West                            | 10983 (13.6) | 5125 (13.1)  | 5858 (14.0)    | 3.89                             |
| South                           | 29984 (37.0) | 14291 (36.5) | 15683 (37.4)   |                                   |
| Midwest                         | 14986 (18.5) | 7264 (18.6)  | 7722 (18.4)    |                                   |
| Northeast                       | 25131 (31.0) | 12433 (31.8) | 12698 (30.3)   |                                   |
| Hospital type, n (%)            |         |              |                 |                                   |
| Primary stroke center           | 39533 (48.8) | 18826 (48.1) | 20707 (49.3)   | 2.8                              |
| Comprehensive stroke center     | 19024 (23.5) | 9391 (24.0)  | 9633 (23.0)    |                                   |
| Neither                         | 22527 (27.8) | 10896 (27.9) | 11631 (27.7)   |                                   |

COVID-19 indicates coronavirus disease 2019; EMS, emergency medical services; N/A, not applicable; and NIH, National Institutes of Health.

*Continuous variables presented as median (25th–75th percentile). Missing rates of variables presented in Table I in the Data Supplement. Variables compared between pre-COVID-19 and during COVID-19 time periods using absolute standardized difference. Absolute standardized difference ≥10 indicates a significant difference.

†Symptom onset defined as last known well time.

‡Characteristics are for hospitals to which the cohorts presented.
when analyzing the country as a whole. Last, our findings could be due to lag in AIS entries into the GWTG-Stroke database due to the administrative burden of COVID-19. While this certainly may be playing a role for data from more recent months (eg, June 2020), data entry from earlier months is likely to be more complete. Further, stroke centers around the world have observed similar findings, suggesting that there is likely a real signal of decreased stroke presentations during the pandemic.

For patients who do present to the hospital, rates of intravenous alteplase therapy, endovascular therapy, and door to CT, needle and endovascular treatment times were similar between the pre-COVID-19 and during COVID-19 groups suggesting that those who do present to the hospital do not experience delays in diagnosis or deficiencies in care. Aside from a slightly longer, likely clinically insignificant, time from door to endovascular treatment in the later during COVID-19 group, these findings remained similar when comparing those presenting in the later COVID-19 time period to those presenting pre-COVID-19. Prior studies demonstrate inconsistent findings regarding delayed presentation times, though for the most part show door to CT, needle, and endovascular times remain similar during the pandemic when compared with the pre-COVID-19 era.\textsuperscript{15,26–30} Although we expected delays for thrombolysis and thrombectomy in our during COVID-19 cohort due to the need for additional personal protective equipment, the relatively preserved door to diagnosis and door to intervention times suggest the donning of personal protective equipment did not lead to delayed patient care.

With regards to GWTG-Stroke achievement and quality measures, there was a 1.8% decrease in intravenous alteplase administered within 4.5 hours in those who arrived to the hospital within 3.5 hours of last known well time and around a 1% decrease in dysphagia screen, smoking cessation counseling, stroke education, and rehabilitation consideration in the during COVID-19 group. Though slightly lower in the during COVID-19 cohort, these quality measures remained above the 85% target, further suggesting maintenance of quality care during the pandemic. These results underscore the importance of the creation and maintenance of robust systems of stroke care such as GWTG-Stroke.

From an outcomes perspective, COVID-19 time period did not associate with in-hospital mortality after risk adjustment. The COVID-19 time period was also not associated with increased symptomatic intracranial hemorrhage among intravenous alteplase patients or venous thromboembolism/pulmonary embolism during hospitalization. These results are consistent with prior published studies that demonstrate no increase in in-hospital mortality among stroke patients during COVID-19, further supporting the notion that stroke care has been relatively well preserved during the pandemic.\textsuperscript{15,18,23,31}

In terms of disposition, we demonstrate that similar numbers of patients were discharged to inpatient rehabilitation, more to home and to hospice, and less to skilled nursing facilities during COVID-19 compared with the pre-COVID-19 time period. COVID-19 time period was also associated with decreased odds of length of stay ≥4 days. These trends likely reflect patient and provider hesitancy toward prolonged hospital stays and desire to triage patients away from high-risk environments. They may also reflect competing pressures on beds in both hospital and skilled nursing facilities during the pandemic. Given the limited follow-up available, we are

| Table 2. Treatment Patterns and Process Measures of the Cohort Stratified by Pre-COVID-19 and During COVID-19 Time Period |
|---------------------------------------------------------------|
| **Time period** | **Overall** | **Pre-COVID-19** | **During COVID-19** | **P value*** |
| November 1, 2019–June 29, 2020 | November 1, 2019–February 3, 2020 | February 4, 2020–June 29, 2020 |
| IV alteplase initiated at hospital, n (%) | 9277 (11.5) | 4551 (11.7) | 4726 (11.4) | 0.26 |
| IV alteplase initiated at outside hospital, n (%) | 3903 (7.4) | 1943 (7.7) | 1960 (7.1) | 0.01 |
| Endovascular therapy initiated at hospital, n (%) | 6957 (10.1) | 3347 (10.2) | 3610 (10.1) | 0.90 |
| Endovascular therapy initiated at outside hospital, n (%) | 180 (0.3) | 81 (0.3) | 99 (0.3) | 0.42 |
| Venous thromboembolism prophylaxis, n (%) | 59740 (99.2) | 29340 (99.2) | 30400 (99.2) | 0.51 |
| Telestroke consult, n (%) | 5318 (6.6) | 2344 (6.0) | 2974 (7.1) | <0.0001 |
| **Process measure** | **Door to CT time, min/n** | **Door to needle time, min/n** | **Door to endovascular treatment, min/n** |
| Overall | Pre-COVID-19 | During COVID-19 |
| Door to CT time, min/n | 36 (14–106)/65382 | 37 (15–111)/31407 | 35 (14–100)/33975 | <0.0001 |
| Door to needle time, min/n | 46 (33–64.5)/8732 | 46 (32–65)/4243 | 46 (33–64)/4489 | 0.69 |
| Door to endovascular treatment, min/n | 88 (54–132)/6719 | 86 (53–129)/3231 | 90 (54–134)/3488 | 0.06 |

COVID-19 indicates coronavirus disease 2019; CT, computed tomography; and IV, intravenous.

*Continuous variables presented as median (25th–75th percentile). Differences between continuous and categorical variables compared using Kruskal Wallis and Pearson $\chi^2$ tests, respectively. Significance threshold set to <0.01 to account for multiple comparisons. Treatment pattern total Ns may vary from column headers due to missingness.
This analysis of a cohort of 81,084 patients with AIS from 458 GWTG-Stroke hospitals demonstrates preserved AIS care quality in the pre-COVID-19 and during COVID-19 time periods with similar door to CT, door to needle, and door to endovascular times as well as similar rates of intravenous alteplase therapy, endovascular therapy, and adjusted in-hospital mortality. These findings suggest that stroke management has not deteriorated in the United States during COVID-19, and further validate longstanding private and governmental efforts to establish robust systems of stroke care.

ARTICLE INFORMATION

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Table 3. Association of Time Period (Pre-COVID-19 Versus During COVID-19) With Outcomes Among Patients Presenting With Acute Ischemic Stroke

| Outcome* | Unadjusted | Adjusted |
|----------|------------|----------|
|          | OR (95% CI) | P value  | OR (95% CI) | P value  |
| In-hospital mortality | 1.10 (1.03–1.17) | 0.005 | 1.05 (0.97–1.13) | 0.22 |
| Symptomatic intracranial hemorrhage among IV alteplase patients | 0.85 (0.71–1.02) | 0.08 | 0.84 (0.70–1.02) | 0.08 |
| VTE or PE during hospitalization | 0.93 (0.80–1.08) | 0.34 | 0.95 (0.83–1.10) | 0.51 |
| Discharge modified Rankin Scale score 0–11 | 0.94 (0.90–0.99) | 0.02 | 0.96 (0.91–1.01) | 0.08 |
| Discharge modified Rankin Scale score 0–2 | 0.96 (0.92–1.00) | 0.07 | 0.98 (0.93–1.03) | 0.36 |
| Length of stay ≥4 days | 0.85 (0.82–0.88) | <0.0001 | 0.84 (0.81–0.87) | <0.0001 |
| Discharge to inpatient rehabilitation facility | 1.00 (0.96–1.05) | 0.97 | 1.01 (0.96–1.05) | 0.75 |
| Discharge to skilled nursing facility | 0.77 (0.74–0.81) | <0.0001 | 0.78 (0.74–0.82) | <0.0001 |
| Discharge to hospice | 1.09 (1.03–1.17) | 0.006 | 1.12 (1.03–1.21) | 0.005 |
| Discharge to home | 1.10 (1.06–1.13) | <0.0001 | 1.12 (1.09–1.16) | <0.0001 |

Models are adjusted for patient demographics, clinical characteristics, medical history, and hospital characteristics. COVID-19 indicates coronavirus disease 2019; IV, intravenous; OR, odds ratio; PE, pulmonary embolism; and VTE, venous thromboembolism.

*Regression models compare outcomes of patients admitted during the COVID-19 time period to those admitted in the pre-COVID-19 time period (reference group). Significance threshold set to <0.01 to account for multiple comparisons.

†Discharge modified Rankin Scale population includes both patients who died and survived to discharge.

unable to determine at this time how these disposition changes will ultimately affect stroke long-term outcomes.

Limitations
Our study is limited by its retrospective, observational nature, and therefore, can evaluate associations but not causality. Though the validity and reliability of data collection in GWTG-Stroke have been previously reported, and though data were abstracted by trained hospital personnel, we are unable to validate the accuracy of data collection for the data specifically used in this study. Descriptive statistics performed are hypothesis generating. Not all data were complete, and imputation was used for select variables (described in methods). Though logistic regression models were adjusted for patient and hospital characteristics, the chance for residual unmeasured confounding remains. Postdischarge data from the during COVID-19 cohort are not yet available and so we are unable to report on long-term outcomes of this population. Our findings may not be generalizable to hospitals that differ from GWTG-Stroke and international cohorts given data were derived from 458 hospitals in the United States participating in GWTG-Stroke. Reported COVID-19 prevalence may be underestimated given the availability and extent of COVID-19 testing at the 458 hospitals is not known. As mentioned above, the decline in observed AIS patients during the pandemic may in part be due to lags in data entry during COVID-19.
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Supplemental Materials

Online Tables I–VII
Online Figure I

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Srivastava et al Ischemic Stroke COVID-19

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