BRIEF REPORT

Clinical Characteristics and Outcomes of COVID-19 Patients With a History of Stroke in Wuhan, China

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BACKGROUND AND PURPOSE: Information on stroke survivors infected with coronavirus disease 2019 (COVID-19) is limited. The aim of this study was to describe specific clinical characteristics and outcomes of patients with COVID-19 with a history of stroke.

METHODS: All the confirmed cases of COVID-19 at Tongji Hospital from January 27 to March 5, 2020, were included in our cohort study. Clinical data were analyzed and compared between patients with and without a history of stroke.

RESULTS: Of the included 1875 patients with COVID-19, 50 patients had a history of stroke. The COVID-19 patients with medical history of stroke were older with more comorbidities, had higher neutrophil count, and lower lymphocyte and platelet counts than those without history of stroke. The levels of D-dimers, cardiac troponin I, NT pro-brain natriuretic peptide, and interleukin-6 were also markedly higher in patients with history of stroke. Stroke survivors who underwent COVID-19 developed more acute respiratory distress syndrome and received more noninvasive mechanical ventilation. Data from propensity-matched analysis indicated a higher proportion of patients with COVID-19 with a history of stroke were admitted to the intensive care unit requiring mechanical ventilation and were more likely to be held in the unit or die, compared with non-stroke history COVID-19 patients.

CONCLUSIONS: Patients with COVID-19 with a history of stroke had more severe clinical symptoms and poorer outcomes compared with those without a history of stroke.

Key Words: cardiovascular disease [comorbidity] COVID-19 [platelet count] troponin I

The ongoing novel coronavirus disease 2019 (COVID-19) originally identified in Wuhan is now a pandemic,1 with over 2 million confirmed cases worldwide. Roughly 30% of patients were found to have at least one comorbidity, with hypertension, diabetes mellitus, cardiovascular diseases, and malignant tumors being most often described.2-4 Here, we recruited 1875 cases with confirmed COVID-19 in our cohort study and compared the specific clinical characteristics and outcomes between patients with and without a history of stroke.
Hospital, the largest designated medical center for COVID-19 in the central China, from January 27 to March 5, 2020, were consecutively recruited. Laboratory confirmation of COVID-19 was performed by real-time reverse-transcriptase–polymerase-chain-reaction using method described previously.5 The study was approved by Tongji Hospital Ethics Committee (institutional review board ID: TJ-C20200121). Written informed consent was waived by the Ethics Commission of Tongji hospital for emerging infectious disease.

**Data Collection**

Demographic, clinical, laboratory, management, and outcome data were obtained from patients’ medical records. Clinical outcomes were followed up to March 5, 2020. We defined the clinical end point as severe events comprised of all-cause death, admission to ICU, and mechanical ventilation.

**Statistical Analysis**

Continuous variables were described as mean (SD) if they were normally distributed or medians (interquartile range) if not normally distributed, and compared using Mann-Whitney U test. Categorical variables were delineated as n (%) and compared by χ² test and Fisher exact test. Propensity score matching of patients with and without history of stroke was performed using a 1:4 matching algorithm with a caliper distance of 0.2 of the SD of the logit of the propensity score and controls used only once. Matching was performed using age, sex, smoking history, and comorbidities including hypertension, diabetes mellitus, cardiovascular diseases, and malignant tumor. The matched cohorts were then compared using Pearson χ² test for categorical clinical outcomes and Cox regression test for composite end point. The hazards ratio and the 95% CI are also reported. All the statistical analyses were performed using SPSS version 22.0 software (SPSS Inc). Two-tailed P<0.05 were statistically significant.

**RESULTS**

**Clinical Characteristics of Patients With COVID-19 With a History of Stroke**

Of the 1875 patients with COVID-19 recruited, the median age was 63 years (interquartile range, 51–70) and 945 (52.0%) were men (Table 1). Among them, 50 patients (2.7% [95% CI, 2.0%–3.5%], P<0.001) had a history of stroke. Compared with those cases without stroke, patients with a history of stroke were significantly older (70 [64–80] versus 62 [50–70] years; P<0.001) and had more concomitant hypertension and cardiovascular diseases (76.0% versus 33.0%; P<0.001; 20% versus 9.8%; P=0.029, respectively).

**Laboratory and Radiological Findings of Patients With COVID-19 With a History of Stroke**

Patients with history of stroke had higher leucocyte count (6.3 versus 5.7×10⁹/L; P=0.028), higher neutrophil count (4.9 versus 3.8×10⁹/L; P=0.005), lower lymphocyte (1.0 versus 1.1×10⁹/L; P=0.037), lower platelet (180 versus 221×10⁹/L; P=0.020) counts, and higher neutrophil-to-lymphocyte ratio (4.2 versus 3.2; P=0.005) than those without history of stroke. The levels of D-dimers (1.1 versus 0.7 μg/mL; P=0.042), cardiac troponin I (8.2 versus 4.1 pg/mL; P<0.001), NT pro-Braın natriuretic peptide (292.0 versus 122.0 pg/mL; P=0.005), and interleukin-6 (11.1 versus 5.6 pg/mL; P=0.002) were markedly higher in those patients with a history of stroke. There were no significant differences in chest CT patterns on admission between the 2 groups (Table I in the Data Supplement).

**Treatment, Complications, and Clinical Outcomes of Patients With COVID-19 With a History of Stroke**

There was no significant difference in the time from the onset to hospital admission and the disease severity on admission in those patients with COVID-19, regardless of history of stroke (Table 2). Patients with COVID-19 with a history of stroke were more likely to have acute respiratory distress syndrome and require noninvasive mechanical ventilation compared with those without a history of stroke (32.0% versus 18.9%, P=0.028; 30.0% versus 17.5%, P=0.037, respectively).

As of March 5, 803 patients (42.8%) was discharged and 159 patients (8.5%) died. Patients with history of stroke presented worse outcomes compared with those without a history of stroke, with lower rates of discharge and higher mortality risks (24.0% versus 43.3%, 14.0% versus 8.3%, respectively; P=0.019). The proportion of severe events including all-cause death, admitted to ICU and mechanical ventilation, were higher in those patients with history of stroke than those without (28.0% versus 15.7%; P=0.021). The hazard ratio for severe events after disease onset in the stroke group, as compared to the group without a history of stroke, was 2.110 (95% CI, 1.233–3.610; P=0.026).

Detailed information of patients with a history of stroke are shown in Table II in the Data Supplement. Five (10%) patients had hemorrhagic stroke, and 45 (90%) had ischemic stroke. The types of previous stroke, ischemic or hemorrhagic, were not associated with the severity of COVID-19 (hazards ratio, 24.265 [95% CI, 0.018–32012.887], P=0.384). In addition, the severity of prior stroke before infection, assessed by modified Rankin Scale, was not associated with clinical composite end point of COVID-19, comparing patients with severe stroke disability (modified Rankin Scale, 3–5) to those with mild impairment (modified Rankin Scale, 0–2; hazards ratio, 0.504 [95% CI, 0.113–2.252]; P=0.370).

**Propensity Score Matching and Adjusted Outcomes of Patients With COVID-19 With a History of Stroke**

In the matched cohort of 49 patients with history of stroke and 192 patients without stroke, there were no longer...
any statistically significant differences in baseline characteristics and comorbidities between the 2 groups (Table III in the Data Supplement). After matching, patients with history of stroke still had worse outcomes compared with those without a history of stroke, with lower rates of discharge and higher mortality risks (22.4% versus 42.2%, 14.3% versus 13.0%, respectively; \(P = 0.034\)). A higher percentage of the clinical composite end point was found in those patients with a history of stroke (32.7% versus 19.3%; \(P = 0.037\)). The hazard ratio for severe events after COVID-19 onset in the stroke group, as compared with the group without a history of stroke, was 1.950 (95% CI, 1.081–3.516; \(P = 0.026\); Figure).

**DISCUSSION**

We reported a large cohort of 1875 patients with laboratory confirmed COVID-19 in Wuhan, China. Fifty infected patients had a history of stroke, which was higher than the prevalence of cerebrovascular diseases in the overall population aged >50-year-old in China (1.5% [95% CI, 1.46%–1.52%], according to 2017 stroke epidemiology statistics

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**Table 1. Baseline Characteristics of Patients With COVID-19 With or Without a History of Stroke**

| Characteristics                        | No. (%)                |
|----------------------------------------|------------------------|
|                                         | All Patients (n=1875)  | Patients Without a History of Stroke (n=1825) | Patients With a History of Stroke (n=50) | \(P\) Value |
| Age, median (IQR), y                   | 63 (51–70)             | 62 (50–70)                                   | 70 (64–80)                                   | <0.001*     |
| Sex                                     |                         |                                             |                                             |             |
| Male                                    | 945 (50.4)             | 915 (50.1)                                   | 30 (60.0)                                   | 0.197       |
| Female                                  | 930 (49.6)             | 910 (49.9)                                   | 20 (40.0)                                   |             |
| Smoking                                 | 147 (7.8)              | 139 (7.6)                                    | 8 (16.0)                                    | 0.053       |
| Chronic medical illness                 |                         |                                             |                                             |             |
| Chronic obstructive pulmonary disease   | 28 (1.5)               | 26 (1.4)                                     | 2 (4.0)                                     | 0.170       |
| Hypertension                            | 641 (34.2)             | 603 (33.0)                                   | 38 (76.0)                                   | <0.001*     |
| Cardiovascular disease                  | 189 (10.1)             | 179 (9.8)                                    | 10 (20.0)                                   | 0.029†      |
| Chronic liver disease                   | 24 (1.3)               | 23 (1.3)                                     | 1 (2.0)                                     | 0.479       |
| Diabetes mellitus                       | 295 (15.7)             | 282 (15.5)                                   | 13 (26.0)                                   | 0.050       |
| Tuberculosis                            | 27 (1.4)               | 26 (1.4)                                     | 1 (2.0)                                     | 0.520       |
| Malignant tumor                         | 54 (2.9)               | 54 (3.0)                                     | 0 (0.0)                                     | 0.400       |
| Chronic kidney disease                  | 41 (2.2)               | 39 (2.1)                                     | 2 (4.0)                                     | 0.299       |
| Signs and symptoms                      |                         |                                             |                                             |             |
| Fever                                   | 1469 (78.3)            | 1436 (78.7)                                  | 33 (66.0)                                   | 0.037†      |
| Dry cough                               | 741 (39.5)             | 714 (39.1)                                   | 27 (54.0)                                   | 0.040†      |
| Expectoration                           | 514 (27.4)             | 508 (27.7)                                   | 8 (16.0)                                    | 0.077       |
| Hemoptysis                              | 21 (1.1)               | 21 (1.2)                                     | 0 (0.0)                                     | 1.000       |
| Shortness of breath                     | 834 (44.5)             | 813 (44.4)                                   | 21 (42.0)                                   | 0.774       |
| Myalgia                                 | 259 (13.8)             | 256 (14.0)                                   | 3 (6.0)                                     | 0.143       |
| Confusion                               | 16 (0.9)               | 14 (0.8)                                     | 2 (4.0)                                     | 0.066       |
| Headache                                | 123 (6.6)              | 121 (6.6)                                    | 2 (4.0)                                     | 0.769       |
| Dizziness                               | 87 (4.6)               | 83 (4.5)                                     | 4 (8.0)                                     | 0.289       |
| Fatigue                                 | 477 (25.4)             | 464 (25.4)                                   | 13 (26.0)                                   | 0.871       |
| Rhinorrhea                              | 29 (1.5)               | 29 (1.6)                                     | 0 (0.0)                                     | 1.000       |
| Pharyngalgia                            | 91 (4.9)               | 90 (4.9)                                     | 1 (2.0)                                     | 0.513       |
| Anorexia                                | 449 (23.9)             | 433 (23.7)                                   | 16 (32.0)                                   | 0.181       |
| Nausea and vomiting                     | 139 (7.4)              | 136 (7.5)                                    | 3 (6.0)                                     | 1.000       |
| Diarrhea                                | 311 (16.8)             | 305 (16.7)                                   | 6 (12.0)                                    | 0.446       |
| Abdominal pain                          | 34 (1.8)               | 33 (1.8)                                     | 1 (2.0)                                     | 0.604       |

Data are median (IQR), and n (%). \(P\) values were calculated from the comparison between patients without a history of stroke and patients with a history of stroke using \(\chi^2\) test, Fisher exact test, or Mann-Whitney \(U\) test. Patients without a history of stroke refer to patients who have not been diagnosed with stroke before. Patients with a history of stroke refer to patients who used to be diagnosed with stroke. COVID-19 indicates coronavirus disease 2019; and IQR, interquartile range.

\*\(P<0.001\); †\(P<0.05\).
 Those patients with a history of stroke tended to have more comorbidities, more aggressive inflammatory responses, and more underlying coagulation disorders. Moreover, patients with COVID-19 with a history of stroke were observed to have a higher risk of severe events and poorer outcomes compared with those without stroke.

Elderly people with comorbidities are more likely to be infected and to develop more severe symptoms of COVID-19. Underlying coronary heart disease was found to aggravate the pneumonia in COVID-19 and increase the severity of symptoms. Patients with cancer might have a higher risk of COVID-19 and poorer outcomes than individuals without cancer. However, patients with chronic neurological conditions were usually ignored, presenting challenges to managing patients with a history of stroke during the outbreak of COVID-19. Patients with a history of stroke in our cohort were generally older with more comorbidities, making them at increased risk for complications such as acute respiratory distress syndrome, and consequently underwent more mechanical ventilation.

Anti-inflammatory responses poststroke facilitate infection, which is in itself an important independent contributor to poor outcomes. In this cohort, we noted that most of patients with a history of stroke presented a higher number of neutrophils and elevated levels of IL-6, suggesting that COVID-19 might induce a greater cytokine storm and generate a series of immune responses. Moreover, more severe lymphopenia was found in those patients with a history of stroke, as well as an increased neutrophil-to-lymphocyte ratio, a well-known marker of systemic inflammation and infection. These laboratory changes indicated that inflammatory mechanisms might play a crucial role in the development and progression of COVID-19.

### Table 2. Treatment, Complications and Outcomes of Patients With COVID-19 With or Without a History of Stroke

|                     | No. (%)                     | P Value |
|---------------------|-----------------------------|---------|
|                     | All Patients (n=1875)       |         |
|                     | Patients Without a History of Stroke (n=1825) |         |
|                     | Patients With a History of Stroke (n=50) |         |
| Time from onset to Hospital admission, median (IQR) d | 12 (8–18) | 12 (8–18) | 12 (7–15) | 0.291 |
| Severity on admission Mild | 1414 (75.4) | 1379 (75.6) | 35 (70.0) | 0.405 |
|                     | 461 (24.6) | 446 (24.4) | 15 (30.0) |         |
| Treatment           | Mechanical ventilation      |         |
| Noninvasive (ie, BiPap) | 335 (17.9) | 320 (17.5) | 15 (30.0) | 0.037* |
| Invasive            | 82 (4.4)      | 80 (4.4)   | 2 (4.0)   | 1.000   |
| ECMO                | 11 (0.6)      | 11 (0.6)   | 0 (0.0)   | 1.000   |
| Complications       | ARDS            | 361 (19.3) | 345 (18.9) | 16 (32.0) | 0.028* |
|                     | Shock          | 84 (4.5)   | 81 (4.4)   | 3 (6.0)   | 0.488   |
| Clinical outcomes   | Discharged      | 803 (42.8) | 791 (43.3) | 12 (24.0) | 0.019* |
|                     | Remained in hospital | 913 (48.7) | 882 (48.3) | 31 (62.0) |         |
|                     | Died            | 159 (8.5)  | 152 (8.3)  | 7 (14.0)  |         |
|                     | Composite end point | 301 (16.1) | 287 (15.7) | 14 (28.0) | 0.021* |

Data are median (IQR), and n (%). P values were calculated from the comparison between patients without a history of stroke and patients with a history of stroke using \( \chi^2 \) test, Fisher exact test, or Mann-Whitney U test. ARDS indicates acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; and IQR, interquartile range.

*P <0.05.

![Figure. Risks of developing severe events for patients with or without a history of stroke after propensity score matching.](image-url)
of COVID-19 in stroke survivors. Interestingly, a higher levels of D-dimer and lower platelet counts were also found in those patients with a history of stroke. This phenomenon reminds us of the necessity to adjust the antithrombotic medication regimen according to the platelet counts or coagulation function in those patients with COVID-19 with a history of stroke, in case of hemorrhage caused by thrombocytopenia, or pulmonary embolism with the increase in D-dimer.

It is not surprising that patients with COVID-19 with a history of stroke experienced worse clinical outcomes than those without a history of stroke, given that patients with prior stroke were older and had a higher prevalence of smoking, hypertension, and cardiovascular disease, which were important predictors of poor COVID-19 outcomes. However, after adjusting for differences in available baseline characteristics and comorbidities by propensity-matched analysis, a history of stroke was still independently associated with an increase in severe events and poorer outcomes, which is largely ignored in previous studies. More attention should be paid when stroke survivors are infected with COVID-19, regardless of stroke types and stroke severity.

There are several limitations to our work. First, this is a single-center retrospective study based on extraction of data from medical records. Several unmeasured variables, for example, premorbid level of functioning or nursing-home placement, could not be adjusted in such a retrospective cohort of emerging infectious disease. Second, it is limited by a lack of long-term outcomes, as some patients are still hospitalized at the time of manuscript submission. Thus, continued observations and follow-up of this subpopulation with COVID-19 will be crucial. Nevertheless, these results will hopefully provide guidance for clinicians to understand the whole picture of the disease and are more conducive to the management of patients with a history of stroke who are at a high risk for COVID-19.

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