Stroke

CLINICAL AND POPULATION SCIENCES

Acute Ischemic Stroke and COVID-19

An Analysis of 27 676 Patients

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BACKGROUND AND PURPOSE: Acute ischemic stroke may occur in patients with coronavirus disease 2019 (COVID-19), but risk factors, in-hospital events, and outcomes are not well studied in large cohorts. We identified risk factors, comorbidities, and outcomes in patients with COVID-19 with or without acute ischemic stroke and compared with patients without COVID-19 and acute ischemic stroke.

METHODS: We analyzed the data from 54 health care facilities using the Cerner deidentified COVID-19 dataset. The dataset included patients with an emergency department or inpatient encounter with discharge diagnoses codes that could be associated to suspicion of or exposure to COVID-19 or confirmed COVID-19.

RESULTS: A total of 103 (1.3%) patients developed acute ischemic stroke among 8163 patients with COVID-19. Among all patients with COVID-19, the proportion of patients with hypertension, diabetes, hyperlipidemia, atrial fibrillation, and congestive heart failure was significantly higher among those with acute ischemic stroke. Acute ischemic stroke was associated with discharge to destination other than home or death (relative risk, 2.1 [95% CI, 1.6–2.4]; $P<0.0001$) after adjusting for potential confounders. A total of 199 (1.0%) patients developed acute ischemic stroke among 19 513 patients without COVID-19. Among all ischemic stroke patients, COVID-19 was associated with discharge to destination other than home or death (relative risk, 1.2 [95% CI, 1.0–1.3]; $P=0.03$) after adjusting for potential confounders.

CONCLUSIONS: Acute ischemic stroke was infrequent in patients with COVID-19 and usually occurs in the presence of other cardiovascular risk factors. The risk of discharge to destination other than home or death increased 2-fold with occurrence of acute ischemic stroke in patients with COVID-19.

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

Key Words: coronavirus ■ death ■ electronic health records ■ ischemic stroke ■ morbidity

Coronavirus disease 2019 (COVID-19) may increase the risk of acute ischemic stroke[1] similar to the increased risk of 3.2-fold to 7.8-fold seen within the first 3 days after other respiratory tract infections.[2,3] In a review of literature in April 2020,[4] the proportion of patients with COVID-19 who have acute ischemic stroke was estimated to be 4.9% (95% CI, no continuity correction, 2.8%–8.7%)[5] during initial hospitalization. Using similar assumptions, an estimated 182 485 and 269 383 patients who have COVID-19 will also have ischemic stroke considering 9 988 254 patients had COVID-19 in the world on June 27, 2020,[4] and an estimated 21% to 31% of patients with COVID-19 required hospitalization.[6] Subsequently, several small case series have reported the occurrence of ischemic stroke in patients with COVID-19.[7–12] The increased risk of ischemic stroke is probably multifactorial, with activation of coagulation and inflammatory pathways as reflected in increased fibrin D-dimer levels, erythrocyte sedimentation rate, lactic acid dehydrogenase, and lymphopenia.[8,13–16] An international panel of stroke experts from 18 countries recommended further studies to understand whether

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Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019
ICD-10-CM	*International Classification of Diseases, Tenth Revision, Clinical Modification*
RR	relative risk

there are differences in risk factors, manifestations, response to treatment strategies, and outcomes in acute ischemic stroke patients with COVID-19.[4] We performed this study to identify risk factors, comorbidities, treatment strategies, and outcomes in patients with ischemic stroke derived from a large cohort of COVID-19 patients.

METHODS

We performed this retrospective cohort study with short-term (in hospital) follow-up by analyzing the data from the Cerner deidentified COVID-19 dataset—a subset of Cerner Real-World Data extracted from the electronic medical records of health care facilities that have a data use agreement with Cerner Corporation.[17,18] The methodological aspects of the dataset are available in another publication.[19] The data are based on electronic medical encounters between December 2019 and April 2020. The dataset as part of deidentification procedure does not provide data on regions and hospitals. Institutional review board approval was not required as the data analyzed consisted of deidentified medical encounters. The dataset is available through Cerner Corporation and includes data for patients who qualified for inclusion based on the following criteria:

1. Patient has a minimum of 1 emergency department or inpatient encounter with a discharge diagnosis code that could be associated with exposure to or clinical suspicion of COVID-19 or
2. Patient has a minimum of 1 emergency department or inpatient encounter with a positive laboratory test for COVID-19.

The Cerner Real-World Data-COVID-2020Q2apr version of the data included data from 54 contributing Cerner Real-World Data health systems that had qualifying patients. The dataset included both patients in whom COVID-19 was confirmed and those in whom the diagnosis was suspected but excluded. In general, Cerner Real-World Data comprise >100 clinical and nonclinical variables associated with hospital stays, including primary and secondary diagnoses, primary and secondary procedures, patients' admission and discharge status, and patient demographic information. Race was coded into various categories (White, Black, Asian or Pacific Islander, or American Indian or Alaska Native), and ethnicity was coded as Hispanic or non-Hispanic as recorded in electronic medical records within the US population. The Cerner Corporation has established Health Insurance Portability and Accountability Act–compliant operating policies to establish deidentification for Cerner Real-World Data.

We used the *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*), primary discharge diagnosis codes I63, I65, and I66 to identify the patients admitted with acute ischemic stroke. The *ICD-10-CM* codes were used to identify patients with hypertension (I10, O10.0, O10.9, I16, and I67.4), diabetes (E08, E09, E10, E11, and E13), nicotine dependence (F17), hyperlipidemia (E78), atrial fibrillation (I48), and congestive heart failure (I09.81, I11.0, and I50). The *ICD-10-CM* secondary diagnosis codes were used to identify those with stroke-associated complications such as cerebral edema (G93.5 and G93.6), acute kidney injury (N17), hepatic failure (K72), cardiac arrest (I46), systemic inflammatory response syndrome (R65.1), respiratory failure (J96), pneumonia (J12–J18), urinary tract infection (N30.0, N30.9, N34.1, N34.2, and N39.0), septic shock (A41 and R65.21), deep venous thrombosis (I82), pulmonary embolism (I26), intracerebral (I61 and I62.9) or subarachnoid hemorrhage (I60), and acute myocardial infarction (I21). We also used *ICD-10-CM* procedure codes and current procedural terminology codes to estimate the proportion of acute ischemic stroke patients who underwent thrombolytic treatment identified by *ICD-10* procedure codes 3E03317 and 3E06317 or current procedural terminology codes 37195 and mechanical thrombectomy or intraarterial thrombolytic administration by *ICD-10* procedure codes (03CG3ZZ, 03CG3Z7, 03CH3Z7, 03CJ0ZZ, 03CJ3ZZ, 03CK3Z7, 03CK3ZZ, 03CL3Z7, 03CL3ZZ, 03CL0ZZ, 03CP3ZZ, 03CY3ZZ, 00C73ZZ or 3E03317, and 3E06317) or current procedural terminology codes 61654 or 37195. Intubation and mechanical ventilation were identified by *ICD-10-CM* codes 0BJ17EZ and Z9911 or current procedural terminology codes 31500, 94656, and 94657 (for intubation) or 94002 to 94005 (for mechanical ventilation).

The outcome was based on discharge destination without any postdischarge data. Discharge destination was categorized as home or discharge to destination other than home (acute rehabilitation, intermediate care or skilled nursing facility, or nursing home). Discharge destination to home has been shown to predict none-to-mild disability while discharge to destination other than home predicts moderate-to-severe disability at 3 months post-stroke.[20,21] Our analysis included only patients with medical history to ensure completeness of the records of potential comorbidities that constituted ≈67% of patients within the dataset.

Statistical Analysis

We performed this analysis to identify any significant differences in demographic and clinical characteristics, in-hospital events, and outcomes between (1) COVID-19 patients with and without acute ischemic stroke and (2) acute ischemic stroke patients with and without COVID-19. We compared patients' age, sex, race/ethnicity, cardiovascular risk factors, length of stay, medical complications, procedures performed, and discharge status (categorized into discharge home, discharge to destination other than home, or death) for patients in strata based on the presence or absence of acute ischemic stroke among COVID-19 patients. We also analyzed the data from patients with acute ischemic stroke without COVID-19 to identify differences in abovementioned variables between ischemic stroke patients with or without COVID-19. We used the χ^2 test for categorical data and 2-sample *t* test for continuous data to detect any significant differences in variables among COVID-19 patients with and without ischemic stroke. We adjusted for multiple comparisons using Bonferroni correction. Any $P<0.05$ is considered significant.

We performed stepwise backward logistic regression analysis including all COVID-19 patients to identify the association between the presence of acute ischemic stroke and risk of discharge to destination other than home or death after adjusting for age (age strata, <35, 35–54, 55–70, and >70 years), sex, race/ethnicity, hypertension, diabetes, nicotine dependence, hyperlipidemia, atrial fibrillation, and congestive heart failure. We performed another stepwise backward logistic regression analysis including all ischemic stroke patients to identify the association between the presence of COVID-19 and risk of discharge to destination other than home or death after adjusting for age (age strata), sex, race/ethnicity, hypertension, diabetes, nicotine dependence, hyperlipidemia, atrial fibrillation, and congestive heart failure. All the analyses were done using R, version 3.6.3.

RESULTS

There were a total of 8163 patients with confirmed COVID-19 among 27 676 patients in the Cerner deidentified COVID-19 dataset; 103 (1.3%) patients developed acute ischemic stroke among 8163 patients with COVID-19. One hundred ninety-nine (1.0%) patients developed acute ischemic stroke among 19 513 patents in whom COVID-19 infection was not diagnosed. Of the 103 patients with confirmed COVID-19 and acute ischemic stroke, 94 received their COVID-19 diagnosis during the same encounter that they had acute ischemic stroke.

Comparison Between COVID-19 Patients With and Without Acute Ischemic Stroke

The mean age (years±standard deviation) of COVID-19 patients with acute ischemic stroke was higher compared with those without stroke (68.8±15.1 versus 54.4±20.3; $P<0.0001$). The proportion of Black people (44.7% versus 31.2%; $P=0.003$) was higher and that of Hispanic people (5.8% versus 20.6%; $P=0.0002$) was lower among COVID-19 patients with acute ischemic stroke compared with those without stroke (Table 1). The proportion of patients with hypertension (84.5% versus 48.2%; $P<0.0001$), diabetes (56.3% versus 30.2%; $P<0.0001$), hyperlipidemia (75.7% versus 33.3%; $P<0.0001$), atrial fibrillation (28.2% versus 10.1%; $P<0.0001$), and congestive heart failure (33.0% versus 12.7%; $P<0.0001$) was significantly higher among COVID-19 patients with acute ischemic stroke compared with those without stroke. The proportion of patients who developed cerebral edema (3.9% versus 0.4%; $P<0.0001$; Table 1), intracerebral hemorrhage (1.9% versus 0%), or myocardial infarction (10.7% versus 4.6%; $P=0.003$) was higher among COVID-19 patients with acute ischemic stroke compared with those without stroke. COVID-19 patients with acute ischemic stroke were more likely to develop acute kidney injury (50.5% versus 22.8%; $P<0.0001$), hepatic failure (3.9% versus 1.2%; $P=0.02$), and respiratory failure (52.4% versus 29.6%; $P<0.0001$) compared with those without stroke. There was no difference in the proportion of patients who developed pneumonia, pulmonary embolism, deep venous thrombosis, and cardiac arrest between the two groups.

The in-hospital mortality (19.4% versus 6.2%; $P<0.0001$) and discharge to destination other than home (62.1% versus 29.1%; $P<0.0001$) were significantly higher in COVID-19 patients with acute ischemic stroke compared with those without stroke (Table 2). In the multivariate model including all COVID-19 patients, acute ischemic stroke was associated with discharge to destination other than home or death (relative risk [RR], 2.1 [95% CI, 1.6–2.4]; $P<0.0001$). Other factors associated with discharge to destination other than home or death were age (compared with <35 years) of 35 to 54 years (RR, 1.3 [95% CI, 1.2–1.5]; $P<0.0001$), age of 55 to 70 years (RR, 2.0 [95% CI, 1.8–2.1]; $P<0.0001$), and age >70 years (RR, 2.6 [95% CI, 2.6–2.7]; $P<0.0001$), men (RR, 1.1 [95% CI, 1.1–1.2]; $P=0.0003$), Black race (RR, 1.1 [95% CI, 1.0–1.2]; $P=0.005$), Hispanic ethnicity (RR, 0.7 [95% CI, 0.6–0.8]; $P<0.0001$), diabetes (RR, 1.3 [95% CI, 1.2–1.4]; $P<0.0001$), atrial fibrillation (RR, 1.4 [95% CI, 1.2–1.5]; $P<0.0001$), and congestive heart failure (RR, 1.4 [95% CI, 1.3–1.5]; $P<0.0001$).

Comparison Between Acute Ischemic Stroke Patients With and Without COVID-19

The mean age (±standard deviation) of acute ischemic stroke patients with COVID-19 was similar compared with those without COVID-19 (68.8±15.1 versus 71.0±14.9; $P=0.24$). The proportion of Black people (44.7% versus 19.6%; $P<0.0001$) was higher and that of White people (35.9% versus 56.3%; $P=0.0007$) was lower among acute ischemic stroke patients with COVID-19 compared with those without COVID-19 (Table 1). The proportions of patients with hypertension, diabetes, hyperlipidemia, atrial fibrillation, myocardial infarction, and congestive heart failure among acute ischemic stroke patients with COVID-19 were similar compared with those without COVID-19. The proportions of patients who developed cerebral edema, intracerebral hemorrhage, pulmonary embolism, deep venous thrombosis, and cardiac arrest were similar between acute ischemic stroke patients with and without COVID-19 (Table 1). There was no difference in the proportions of patients who developed acute kidney injury, hepatic failure, respiratory failure, or pneumonia between the two groups. The proportions of patients who received intravenous thrombolysis (1.0% versus 1.0%; $P=0.98$) or mechanical thrombectomy (1.0% versus 1.0%; $P=0.98$) among acute ischemic stroke patients with COVID-19 were similar compared with those without COVID-19.

The in-hospital mortality among acute ischemic stroke patients with COVID-19 was similar compared with those without COVID-19 (19.4% versus 21.6%;

Table 1. Demographic and Clinical Characteristics of Patients

Items	Patients with COVID-19 and acute ischemic stroke (n=103)	Patients with COVID-19 but without any stroke (n=7606)	Patients with acute ischemic stroke without COVID-19 (n=199)
Baseline characteristics			
Mean age (±SD), y*	68.8±15.1	54.4±20.3	71.0±14.9
Age <35 y*	2 (1.9%)	1488 (19.6%)	6 (3.0%)
Age 35–54 y*†	17 (16.5%)	2105 (27.7%)	17 (8.5%)
Age 55–70 y	32 (31.1%)	2188 (28.8%)	57 (28.6%)
Age >70 y*	52 (50.5%)	1825 (24.0%)	119 (59.8%)
Men	46 (44.7%)	3575 (47.0%)	110 (55.3%)
White, non-Hispanic†	37 (35.9%)	2290 (30.1%)	112 (56.3%)
Black*†	46 (44.7%)	2374 (31.2%)	39 (19.6%)
Asian or Pacific Islander	2 (1.9%)	199 (2.6%)	3 (1.5%)
American Indian or Alaska Native	1 (1.0%)	99 (1.3%)	2 (1.0%)
Hispanics*	6 (5.8%)	1570 (20.6%)	23 (11.6%)
Hypertension*	87 (84.5%)	3662 (48.2%)	165 (82.9%)
Diabetes*	58 (56.3%)	2295 (30.2%)	103 (51.8%)
Nicotine dependence	11 (10.7%)	650 (8.6%)	39 (19.6%)
Hyperlipidemia*	78 (75.7%)	2535 (33.3%)	142 (71.4%)
Atrial fibrillation*	29 (28.2%)	768 (10.1%)	72 (36.2%)
Congestive heart failure*	34 (33.0%)	969 (12.7%)	72 (36.2%)
In-hospital events			
Mean length of hospitalization (±SD), d	10±8	7±6	9±7
Cerebral edema*	4 (3.9%)	27 (0.4%)	5 (2.5%)
Pneumonia	58 (56.3%)	3424 (45.0%)	109 (54.8%)
Deep venous thrombosis	7 (6.8%)	284 (3.7%)	22 (11.1%)
Pulmonary embolism	4 (3.9%)	173 (2.3%)	5 (2.5%)
Intubation/mechanical ventilation	7 (6.8%)	265 (3.5%)	25 (12.6%)
Urinary tract infection	29 (28.2%)	1349 (17.7%)	59 (29.7%)
Acute kidney injury*	52 (50.5%)	1737 (22.8%)	95 (47.7%)
Hepatic failure*	4 (3.9%)	94 (1.2%)	6 (3.0%)
Cardiac arrest	4 (3.9%)	117 (1.5%)	10 (5.0%)
Acute myocardial infarction*	11 (10.7%)	347 (4.6%)	36 (18.1%)
Intracerebral hemorrhage*	2 (1.9%)	0 (0%)	6 (3.0%)
Systemic inflammatory response syndrome	2 (1.9%)	113 (1.5%)	4 (2.0%)
Septic shock	37 (35.9%)	1338 (17.6%)	81 (40.7%)
Respiratory failure*	54 (52.4%)	2249 (29.6%)	99 (49.8%)

COVID-19 indicates coronavirus disease 2019; and SD, standard deviation.
*Significant difference between COVID-19 patients with acute ischemic stroke compared with those without any stroke.
†Significant difference between acute ischemic patients with COVID-19 compared with those without COVID-19.

P=0.66). There was a significantly higher rate of discharge to destination other than home among acute ischemic stroke patients with COVID-19 compared with those without COVID-19 (62.1% versus 48.2%; *P*=0.02; Table 2). In the multivariate model, COVID-19 (RR, 1.2 [95% CI, 1.0–1.3]; *P*=0.03) was associated with discharge to destination other than home or death in patients with acute ischemic stroke. Another factor associated with discharge to destination other than home or death was atrial fibrillation (RR, 1.2 [95% CI, 1.0–1.3]; *P*=0.014).

DISCUSSION

Salient Findings

We identified several findings from the study of 103 acute ischemic stroke patients among 8163 patients with COVID-19. Patients with COVID-19 (compared with those without COVID-19) who developed acute ischemic stroke were older, more likely to be Black, and had a higher frequency of hypertension, diabetes, hyperlipidemia, atrial fibrillation, and congestive heart

Table 2. Outcomes of Patients

Outcome	Patients with COVID-19 and acute ischemic stroke (n=103)	Patients with COVID-19 but without any stroke (n=7606)	Patients with acute ischemic stroke without COVID-19 (n=199)
Discharge home*	19 (18.5%)	4939 (64.9%)	60 (30.2%)
Discharge to destination other than home*†	64 (62.1%)	2215 (29.1%)	96 (48.2%)
In-hospital death*†	20 (19.4%)	474 (6.2%)	43 (21.6%)

COVID-19 indicates coronavirus disease 2019.
*Significant difference between patients with COVID-19 and acute ischemic stroke compared with those without any stroke.
†Significant difference between acute ischemic patients with COVID-19 compared with those without COVID-19.

failure. Patients with COVID-19 who developed acute ischemic stroke compared with those without acute ischemic stroke had higher cardiovascular events during hospitalization including cerebral edema, intracerebral hemorrhage, and myocardial infarction. Patients with COVID-19 and acute ischemic stroke compared with those without acute ischemic stroke were more likely to have multisystem involvement with acute kidney injury, hepatic failure, and respiratory failure. The in-hospital mortality and discharge to destination other than home were significantly higher in patients with COVID-19 and acute ischemic stroke compared with those without stroke. Patients with acute ischemic stroke had 2-fold higher risk of discharge to destination other than home or death compared with those without acute ischemic stroke among all patients with COVID-19 after adjustment for potential confounders. However, when acute ischemic stroke patients with COVID-19 were compared with those without COVID-19, there were minimal differences in baseline and clinical characteristics. There was a higher proportion of Black people among patients who had acute ischemic stroke and COVID-19 and compared with those with acute ischemic stroke without COVID-19. There was a higher rate of discharge to destination other than home or death in ischemic stroke patients with COVID-19 compared with those without COVID-19. Occurrence of COVID-19 was associated with a 1.2× higher risk of discharge to destination other than home or death among ischemic stroke patients after adjustment for potential confounders.

COVID-19 and Risk of Acute Ischemic Stroke

We found a low occurrence (1.3%) of acute ischemic stroke among COVID-19 patients. A similar prevalence (1%) of ischemic stroke was seen among patients without COVID-19 in our analysis. The initial estimates had suggested a higher proportion (≈5%) of patients with acute ischemic stroke among those hospitalized with COVID-19.[8] Other studies have suggested that the proportion of patients with acute ischemic stroke may range between 1% and 3% among those hospitalized with COVID-19 receiving standard thromboprophylaxis.[9–11] One study[16] reported that 0.9% of 3556 hospitalized patients with COVID-19 had acute ischemic stroke. Another recent study[1] reported that 1.6% of 1916 patients with emergency department visit or hospitalization related to COVID-19 experienced an acute ischemic stroke. Our findings suggest that most of the COVID-19 patients who develop acute ischemic stroke have preexisting cardiovascular risk factors for large vessel atherosclerosis, small vessel disease, and cardioembolism similar to acute ischemic stroke patients without COVID-19. Our findings may be somewhat different from the earlier observations from smaller case series that suggested that patients with COVID-19 who developed acute ischemic stroke were younger and without preexisting cardiovascular risk factors.[16,22,23] Other studies have reported findings similar to our findings[7,13,15] suggesting that even if COVID-19 was a predisposing factor, the risk was mainly seen in those who were already at risk for acute ischemic stroke due to other cardiovascular risk factors. Merkler et al[1] also reported that patients with COVID-19 had higher rates of hypertension, diabetes, coronary artery disease, chronic kidney disease, or atrial fibrillation compared with those with influenza.

COVID-19 and Outcome of Acute Ischemic Stroke

The higher risk of discharge to destination other than home or death among COVID-19 patients who also develop acute ischemic stroke may be multifactorial. Patients with COVID-19 and acute ischemic stroke have a much higher occurrence of multisystem involvement including acute kidney injury, hepatic failure, and respiratory failure. Our findings of higher in-hospital mortality and discharge to destination other than home in COVID-19 patients with ischemic stroke compared with those without stroke have been identified in other studies.[7,12,16,23] The rate of discharge to destination other than home was higher in acute ischemic stroke patients with COVID-19 compared with those without COVID-19, supporting the contribution of COVID-19 in determining the outcome in acute ischemic stroke patients. Patients with COVID-19 have multisystem involvement as mentioned previously[7,8,23] and elevation in serum markers of inflammation and fibrin activation,[7,13,16] all of which are shown to increase the rate

of death or disability in patients with acute ischemic stroke. There is some evidence that the severity of neurological deficits may be greater[13,23] and response to mechanical thrombectomy more limited[24] in acute ischemic stroke patients with COVID-19. There was no difference between the rates of utilization of thrombolysis and mechanical thrombectomy among ischemic stroke patients with COVID-19 compared with those without COVID-19 in our analysis.

Implications for Practice

COVID-19 was diagnosed in most acute ischemic stroke patients at the same encounter as ischemic stroke. Therefore, acute ischemic stroke patients may present without a diagnosis of COVID-19 and not always occur in those with advanced stages of COVID-19.[2] COVID-19 is unlikely to be confirmed or excluded using laboratory assessment during the time frame for initial evaluation and decision-making in acute stroke patients. Therefore, an acute ischemic stroke patient with suspected COVID-19 has to be evaluated under the assumption that the patient has COVID-19. The high rate of discharge to destination other than home or death in acute ischemic stroke with COVID-19 may be related to multiple organ dysfunction/failure and is unlikely to be influenced from acute treatment of ischemic stroke. An assessment of the magnitude of multiple organ dysfunction maybe helpful in delineating the overall care paradigm in acute ischemic stroke patients considering the effect of COVID-19–related factors independent of stroke. Relatively low rates of intravenous thrombolysis and mechanical thrombectomy were seen in acute ischemic stroke patients with or without COVID-19. New challenges and delays in existing triage protocols for facilitating rapid transfers from emergency department to angiographic suite and between facilities may be partly responsible because of new protocols to ensure early detection of COVID-19 and reduction in transmission.[25,26]

Limitations

Certain aspects of the analysis may have direct implications for interpretation. Our analyses used Cerner deidentified COVID-19 dataset derived from large number of health care facilities. However, the dataset provides minimal details on the severity of neurological deficits and diagnostic study results (neuroimaging and laboratory tests), and, therefore, the exact reasons for differences in outcomes between patients with COVID-19 who developed acute ischemic stroke and those who did not could not be determined. The dataset also depends on the accuracy of diagnosis and procedures listed in the data collection system. *ICD-10* diagnosis codes have a high positive predictive value to identify acute ischemic stroke from the principle discharge diagnosis.[27] The discharge functional outcome cannot be measured with the available data, and the closest index was using the destination of discharge as done in previous studies using Nationwide Inpatient Sample data.[20,28] Discharge to home has a high negative predictive value (ability to exclude) for patients with a modified Rankin Scale score of 2 to 6 at 3 months. The positive predictive value of discharge to nursing home or skilled nursing facility is high (ability to include) for patients with a modified Rankin Scale score of 2 to 6 at 3 months.[21] Therefore, discharge destination may allow differentiation of patients with different functional outcomes with reasonable level of accuracy. The acute ischemic stroke patients without COVID-19 in the dataset were those who were screened for COVID-19 due to either history of exposure or respiratory symptoms. These patients may have clinical presentation suggestive of respiratory tract infections, which could mean that they may have other respiratory tract infections or even a small minority have undetected COVID-19 depending upon the screening tests undertaken.[29–31] Therefore, these patients may not be completely reflective of acute ischemic stroke patients in the general population. The high proportion of patients with a history of cigarette smoking and pneumonia among acute ischemic stroke patients without COVID-19 is presumably explained by this bias. Furthermore, the proportion of patients who have COVID-19 among all patients who were admitted with ischemic stroke during the same time period cannot be deduced. Since our analysis only includes patients who were hospitalized, those with transient ischemic attack and minor ischemic stroke maybe underrepresented. This underrepresentation is particularly prominent during the COVID-19 pandemic because patients with mild diseases are avoiding hospitalization in an effort to reduce exposure.[32] We estimated the proportion of patients with acute ischemic stroke (using same *ICD-10-CM* diagnosis codes or *International Classification of Diseases, Ninth Revision, Clinical Modification* equivalent) in the CERNER Health Facts database with similar design to provide data for qualitative comparisons. Patients with acute ischemic stroke constituted 0.72% of all hospitalized patients between January 1, 2000, and July 1, 2018 (A.I. Qureshi, W. Huang, I. Lobanova, unpublished data, 2020).

Conclusions

Acute ischemic stroke was infrequent in patients with COVID-19 and usually in the presence of other cardiovascular risk factors. The risk of discharge to destination other than home or death increased 2-fold with the occurrence of acute ischemic stroke in patients with COVID-19. Among all acute ischemic stroke patients, COVID-19 was associated with increased risk of

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discharge to destination other than home or death for reasons that need to be determined.

ARTICLE INFORMATION

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Disclosures

None.

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