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Impact of COVID-19 on Outcomes in Ischemic Stroke Patients in the United States

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Background: Studies have shown worse outcomes in patients with comorbid ischemic stroke (IS) and coronavirus disease 2019 (COVID-19), but have had small sample sizes. *Methods:* We retrospectively identified patients in the Vizient Clinical Data Base® with IS as a discharge diagnosis. The study outcomes were in-hospital death and favorable discharge (home or acute rehabilitation). In the primary analysis, we compared IS patients with laboratory-confirmed COVID-19 (IS-COVID) discharged April 1-July 31, 2020 to pre-COVID IS patients discharged in 2019 (IS controls). In a secondary analysis, we compared a matched cohort of IS-COVID patients to patients within the IS controls who had pneumonia (IS-PNA), created with inverse-probability-weighting (IPW). *Results:* In the primary analysis, we included 166,586 IS controls and 2086 IS-COVID from 312 hospitals in 46 states. Compared to IS controls, IS-COVID were less likely to have hypertension, dyslipidemia, or be smokers, but more likely to be male, younger, have diabetes, obesity, acute renal failure, acute coronary syndrome, venous thromboembolism, intubation, and comorbid intracerebral or subarachnoid hemorrhage (all $p < 0.05$). Black and Hispanic patients accounted for 21.7% and 7.4% of IS controls, respectively, but 33.7% and 18.5% of IS-COVID ($p < 0.001$). IS-COVID, versus IS controls, were less likely to receive alteplase (1.8% vs 5.6%, $p < 0.001$), mechanical thrombectomy (4.4% vs. 6.7%, $p < 0.001$), to have favorable discharge (33.9% vs. 66.4%, $p < 0.001$), but more likely to die (30.4% vs. 6.5%, $p < 0.001$). In the matched cohort of patients with IS-COVID and IS-PNA, IS-COVID had a higher risk of death (IPW-weighted OR 1.56, 95% CI 1.33-1.82) and lower odds of favorable discharge (IPW-weighted OR 0.63, 95% CI 0.54-0.73). *Conclusions:* Ischemic stroke patients with COVID-19 are more likely to be male, younger, and Black or Hispanic, with significant increases in morbidity and mortality compared to both ischemic stroke controls from 2019 and to patients with ischemic stroke and pneumonia.

Key Words: COVID-19—Ischemic stroke—Outcome—Neurology/cerebrovascular disease—Epidemiology

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Received October 8, 2020; revision received December 3, 2020; accepted December 4, 2020.

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1052-3057/\$ - see front matter

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<https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105535>

Introduction

Following the rise of coronavirus disease 2019 (COVID-19) infections, studies have reported a decrease in hospital encounters for ischemic stroke (IS).^{1–5} This is contrary to the expectation that IS hospitalization rates would remain stable or increase because viral infections are a risk factor for thromboembolic events.^{6,7} Preliminary data also suggest that interventions for IS may have declined. In China, data from 280 hospitals showed that the number of intravenous alteplase (tPA) administrations and mechanical thrombectomies (MT) for IS dropped 26.7% and 25.3%, respectively, during the peak of their COVID-19 outbreak.⁸

The clinical outcomes of IS patients with COVID-19 are not fully known, because only small cohorts of patients with IS and comorbid COVID-19 have been published to date.^{9–12} To inform clinical care and public health during this and future pandemics, it is important to provide reliable data on IS patients with comorbid COVID-19 infection, which cannot be accomplished with small cohorts in geographically limited samples. Using a dataset of hospitals throughout the United States, our study examines the clinical characteristics and outcomes of over two thousand IS patients with COVID-19, in comparison to historical IS controls and patients with IS and pneumonia.

Methods

Population and outcomes

We performed a retrospective analysis using the Vizient Clinical Data Base® (CDB), a healthcare analytics platform employed by 568 participating US hospitals for purposes of benchmarking clinical performance, costs, and outcomes.¹³ Requests from qualified researchers trained in human subject confidentiality protocols to access the dataset used in this study may be sent to Vizient at vizientsupport@vizientinc.com. IRB approval was not required for this retrospective analysis of deidentified data per the University of Utah Institutional Review Board Guidelines. We identified patients with ICD-10 codes for IS (I63 and H34.1)¹⁴ in any position amongst the discharge diagnoses. We excluded elective hospital admissions and patients on hospice prior to admission. We identified cases with comorbid COVID-19 during the same hospitalization using the ICD code U07.1, which is reserved for laboratory testing confirmed cases.¹⁵

The primary outcome is in-hospital death and the secondary outcome is favorable discharge, defined as discharge to home or acute rehabilitation. We compared IS patients with laboratory-confirmed COVID-19 (IS-COVID) discharged from April 1–July 31, 2020 to a pre-COVID control group of IS patients discharged in all months of 2019 (IS controls). We further stratified patients by the following hospital characteristics: total volume of patients with COVID-19, monthly IS volume in 2019, hospital bed size, teaching status, and United States Census

region. We also created a matched cohort of the IS-COVID patients and patients from IS controls who had pneumonia (IS-PNA) as their principal discharge diagnosis (J09-99), to model the effect of IS-COVID on our outcomes in comparison to patients with IS and PNA, which has been previously shown to have a negative impact on stroke outcome and mortality.¹⁶

Statistical approach

We report descriptive statistics and test for differences between the cohorts with Student's t-test for interval variables and the chi-squared test for binary variables. Due to data restrictions in the Vizient CDB, the actual patient age cannot be reported, so we used age categories (<18, 18-50, 51-64, 65-74, 75-79, and ≥80 years). The race categories described as White, Black, Asian, and other/unreported are non-Hispanic.

To create the matched cohort, inverse-probability-weighting (IPW) was used to balance the distributions of age, sex, race/ethnicity, and Elixhauser comorbidity score.^{17–19} These weights are calculated by calculating the propensity score with respect to being in a certain exposure group and taking the inverse of those weights. The IPW weights are applied to both exposed (COVID present) and unexposed individuals (PNA present) to create a pseudopopulation where the two groups have better balance in their baseline covariate distributions.^{3,4} Standardized differences in the baseline characteristics after application of IPW weights were used to assess for proper balance (Supplemental Table 1), which is defined as a standardized difference <0.10. Sufficient balance was also assessed by Rubin's R and Rubin's B.²⁰ Values of Rubin's R between 0.5-2 and of Rubin's B below 25.0 are considered to be balanced.²⁰ For each outcome, we fit an unadjusted and IPW-weighted model. Outcome estimates were reported in terms of odds ratios with the IS-COVID patients considered the exposure group.

In a sensitivity analysis, we repeated our primary analysis using patients with IS as their primary discharge diagnosis, which is less sensitive for identifying patients with comorbid COVID-19, but informative because it improves the classification of IS and its importance as a primary case of hospitalization. All analyses were performed using Stata 16.0 (StataCorp, College Park, TX) and significance was set at $p \leq 0.05$.

Results

We included 166,586 IS controls and 2,086 IS-COVID patients from 312 non-federal hospitals in 46 states, with 97 hospitals in the Northeast Census region, 85 in the Midwest region, 85 in the South region, and 45 in the West region. There were 98 hospitals with ≤150 beds, 40 with 151-250 beds, 71 with 251-500 beds, and 103 with ≥500 beds; and 256/312 hospitals were designated as teaching hospitals. In April-July 2020, comorbid COVID-

19 infection was present in 2,086/43,582 (4.8%) of IS patients. At these same hospitals, we identified 70,085 patients discharged with confirmed COVID-19, of which IS was present in 3.0%.

Demographics and outcomes are shown in Table 1. IS-COVID patients were more likely to be aged <75, obese, diabetic, and have congestive heart failure, and less likely to have hypertension, dyslipidemia, or be smokers. In IS controls, Black and Hispanic patients accounted for 21.7% and 7.4%, respectively, while in IS-COVID they accounted for 32.1% and 18.5% respectively ($p < 0.001$). IS-COVID, versus IS controls, developed more acute complications, including respiratory failure requiring mechanical ventilation (43.5% vs. 11.8%, $p < 0.001$), acute coronary syndrome (18.3% vs. 8.5%, $p < 0.001$), pulmonary embolus (7.4% vs. 2.0%, $p < 0.001$), and comorbid intracerebral hemorrhage (9.6% vs. 6.6%, $p < 0.001$). IS-COVID patients were less likely to receive tPA (1.8% vs. 5.6%, $p < 0.001$) or mechanical thrombectomy (4.4% vs. 6.7%, $p < 0.001$). The hospital length of stay was longer for IS-COVID compared to IS controls (17.7 vs. 7.5 days, $p < 0.001$), as was their intensive care unit length of stay in patients requiring over 24 hours in an intensive care unit (15.7 vs. 5.7 days, $p < 0.001$).

IS-COVID patients were more than four times as likely to die in-hospital compared to IS controls (30.4% vs. 6.5%, $p < 0.001$) and approximately half as likely to have a favorable discharge (33.9% vs. 66.4%, $p < 0.001$). After stratification of the hospitals by total volume of patients with COVID-19, monthly IS volume in 2019, bed size, teaching status, and Census region, we did not observe heterogeneity of these associations with respect to hospital characteristics (Table 2).

We show the robustness of the matching procedure for IS-COVID and IS-PNA patients in Fig. 1. We included 2,068 patients with IS-PNA for matching to the 2,086 IS-COVID patients. Prior to matching, Rubin's R and Rubin's B were 1.39 and 70.0, respectively, and after matching they were within the acceptable ranges with values of 1.05 and 5.5, confirming a well-matched cohort. We found that IS-COVID remained associated with higher risk of death and unfavorable discharge (Supplemental Table 2). For IS-COVID patients, compared to IS-PNA patients, the IPW odds ratio for death was 1.56 (95% CI, 1.33–1.82) and the IPW odds ratio for favorable discharge was 0.63 (95% CI, 0.54–0.73).

In the sensitivity analysis of patients with IS as the primary discharge diagnosis, we included 81,735 IS controls from 2019 and 526 IS-COVID patients. The demographic and medical complication differences we observed in the principal analysis were also seen in the sensitivity analysis (Table 3). The rate of death in the sensitivity analysis remained higher for IS-COVID compared to IS controls (13.3% vs. 4.6%, $p < 0.001$), although it approached a three-fold increase instead of the over fourfold increase in the primary analysis. In this sensitivity analysis, we did not see difference in the rate of alteplase (IS-COVID vs. IS control, 7.0% vs. 7.7%, $p = 0.778$), but observed a higher rate of

mechanical thrombectomy in IS-COVID patients (13.7% vs. 10.3%, $p < 0.001$).

Discussion

In patients discharged with IS from April 1 to July 31, 2020, comorbid COVID-19 infection was relatively common, comprising 4.8% of all discharges. Amongst all patients discharged with COVID-19, IS was observed in 3.0%. A disproportionate burden of stroke with COVID-19 is borne by Black and Hispanic patients. According to the Centers for Disease Control (CDC) Black and Hispanic patients have had higher rates of COVID-19 and hospitalization for COVID-19 than whites,²¹ consistent with our findings. The impact of the increase in absolute number of minority patients with ischemic stroke and COVID-19 is more cumulative morbidity and mortality, exacerbating pre-existing racial and ethnic healthcare disparities.²²

IS-COVID patients were younger than historical IS controls, consistent with prior reports.^{9,23} The reasons for this finding remain unknown. Despite fewer traditional cardiovascular risk factors such as smoking, hypertension, and dyslipidemia, IS-COVID patients were more likely to be obese or diabetic. The CDC has identified both as risk factors for severe illness from COVID-19 and we confirm them as risk factors for cerebrovascular disease in COVID-19.²⁴ It remains unclear if the increased risk of IS in COVID-19 patients with obesity and diabetes is due to those risk factors predisposing to more severe COVID-19 infection or if the risk factors exert independent or synergistic pro-thrombotic effects in COVID-19.

Compared to historical IS controls, IS-COVID patients had over a fourfold increase in mortality and were approximately half as likely to have a favorable discharge. This finding is not surprising since we also found that IS-COVID patients had dramatically higher rates of systemic complications, such as acute respiratory failure requiring intubation, acute renal failure, comorbid intracerebral hemorrhage, cerebral venous sinus or deep vein thrombosis, and pulmonary emboli, which likely contributed to increased morbidity and mortality, as did other factors we were not able to capture including degrees of pulmonary morbidity, co-infections, and multiorgan failure.^{10,11,25} However, in the cohort of matched IS-COVID and IS-PNA patients, the IS-COVID patients still had worse outcomes and were less likely to have favorable discharge.

Because COVID-19 is thought to be pro-thrombotic²⁶ and could theoretically increase the incidence or severity of IS,^{9,27} the decrease in mechanical thrombectomy and alteplase in IS patients with COVID-19 was surprising. However, in our sensitivity analysis of patients who had IS as their primary discharge diagnosis, we saw an increase in the rate of mechanical thrombectomy. These divergent findings suggest that a subset of IS patients with COVID-19 may be particularly susceptible to large vessel occlusive stroke, as prior reports have suggested.²³ Regardless, why IS-COVID

Table 1. Baseline demographics and outcomes in patients discharged with ischemic stroke.

Variable	IS Controls (2019) (n=166,586)	IS-COVID (April-July 2020) (n=2,086)	p value
Age category			<0.001
<18 [n (%)]	643 (0.4)	suppressed*	
18-50	18,926 (11.4)	242 (11.6)	
51-64	42,904 (25.8)	608 (29.2)	
65-74	41,248 (24.8)	604 (29.0)	
75-79	19,616 (11.8)	229 (11.0)	
≥80	43,249 (26.0)	400 (19.2)	
Age <75	103,721 (62.3)	1457 (69.9)	<0.001
Male sex	84,963 (51.0)	1209 (58.0)	<0.001
Race/Ethnicity*			<0.001
White	103,376 (62.1)	703 (33.7)	
Black	36,167 (21.7)	669 (32.1)	
Hispanic	12,392 (7.4)	385 (18.5)	
Asian	4660 (2.8)	94 (4.5)	
Other/Unknown	9991 (6.0)	235 (11.3)	
Elixhauser comorbidity score			
Median, IQR	3, 2–5	4, 3–6	<0.001
Mean±SD	3.4 ± 2.0	4.3 ± 2.1	<0.001
Congestive heart failure	38,979 (23.4)	530 (25.4)	0.031
Obese	27,991 (16.8)	517 (24.8)	<0.001
Smoker	26,037 (15.6)	112 (5.4)	<0.001
Atrial fibrillation	45,810 (27.5)	569 (27.3)	0.821
Hypertension	121,762 (73.1)	1402 (67.2)	<0.001
Diabetes	66,408 (39.9)	1147 (55.0)	<0.001
Dyslipidemia	102,137 (61.3)	1156 (55.4)	<0.001
Interfacility transfer	43,022 (25.8)	586 (28.1)	0.019
Seen in emergency department (n=166,134)	133,073 (81.1)	1539 (78.0)	<0.001
Intubated	19,703 (11.8)	284 (43.5)	<0.001
Acute coronary syndrome	14,142 (8.5)	382 (18.3)	<0.001
Percutaneous coronary intervention	754 (0.5)	suppressed*	0.149
Intracerebral hemorrhage	11,069 (6.6)	200 (9.6)	<0.001
Subarachnoid hemorrhage	3344 (2.0)	58 (2.8)	0.013
Acute renal failure	34,026 (20.4)	1102 (52.8)	<0.001
Pulmonary embolus	3276 (2.0)	154 (7.4)	<0.001
Cerebral venous sinus or deep vein thrombosis	890 (0.5)	23 (1.1)	<0.001
Length of hospital stay [days, mean±SD]	7.5 ± 12.2	17.7 ± 17.5	<0.001
Length of intensive care unit stay [days, mean±SD]*	5.7 ± 9.8	15.7 ± 15.3	<0.001
Mechanical thrombectomy	11,202 (6.7)	92 (4.4)	<0.001
Treated with alteplase	9304 (5.6)	38 (1.8)	<0.001
Favorable discharge	110,546 (66.4)	707 (33.9)	<0.001
In-hospital death	10,865 (6.5)	634 (30.4)	<0.001

*Binary variables presented as n, %; ordinal variables as median, IQR; interval variables as mean (SD). P values calculated with the chi-squared test for binary variables, the Wilcoxon ranksum test for ordinal variables, and Student's t-test for interval variables. Length of intensive care unit stay restricted to patients with >24 hours spent in intensive care. White, Black, Asian and other/unreported race/ethnicity categories are non-Hispanic. Some cells suppressed for counts <10, in compliance with Vizient regulations.

patients with IS in any discharge position (our primary analysis) received less mechanical thrombectomy is not clear. It could be that COVID-19 patients who have stroke in any discharge position generally present with respiratory symptoms which could mask stroke symptoms, slow patient evaluation, and result in delayed diagnosis, pushing patients beyond the time window for efficacious interventions.^{28,29}

Providers may also have felt that alteplase for IS was contraindicated given the possibility of an infectious stroke mechanism or patients with COVID-19 were anticoagulated at the time of their stroke, which is a firm contraindication for alteplase.^{29,30} In addition, we observed that more IS-COVID patients were intubated, had acute renal failure, acute coronary syndrome, and pulmonary emboli, introducing the

Table 2. Primary and secondary outcomes of IS-COVID patients in stratifications based off hospital characteristics.

Hospital Stratification	In-hospital Death n (%)	p value	Favorable Discharge n (%)	p value
Total COVID-19 discharges		0.703		0.979
<50	243 (31.3)		265 (34.2)	
50-300	192 (29.3)		222 (33.8)	
≥300	199 (30.4)		220 (33.6)	
Monthly stroke count in 2019		0.105		0.716
<30	190 (27.5)		190 (27.5)	
30-60	280 (32.4)		280 (32.4)	
≥60	164 (30.8)		164 (30.8)	
Hospital bed size				0.858
≤250	141 (27.7)	0.292	178 (34.9)	
251-499	122 (31.8)		129 (33.6)	
≥500	371 (31.3)		400 (33.6)	
Hospital type				0.581
Teaching	604 (30.6)	0.361	666 (33.8)	
Non-teaching	30 (26.6)		41 (36.3)	
Census region				0.117
Northeast	343 (32.0)	0.280	349 (32.5)	
Midwest	130 (30.1)		140 (32.4)	
South	118 (26.9)		170 (38.7)	
West	43 (30.3)		48 (33.8)	

possibility that they were too medically unstable for acute stroke intervention.

Our study has several important limitations, including that the Vizient CDB is not designed to be fully representative of inpatient discharges in the United States and that case identification with administrative and billing codes has bias. However, the data sampling methods, hospitals included, and data extraction were consistent across the time points, lending it validity. We cannot fully capture the nuances of COVID-19 infection severity or stroke severity in patients, which limits our ability to make definitive associations. We do not know when stroke happened during the hospital

admission, which prevents us from knowing if stroke was the reason for hospital admission or happened later during an admission for COVID-19. Finally, patients under investigation may have had COVID-19, but were not documented as such. Longitudinal data should be evaluated over subsequent time frames to confirm these findings.

Conclusion

In April-July 2020, COVID-19 comorbidity was relatively common in patients discharged with ischemic stroke, particularly in Black and Hispanic patients. Ischemic stroke

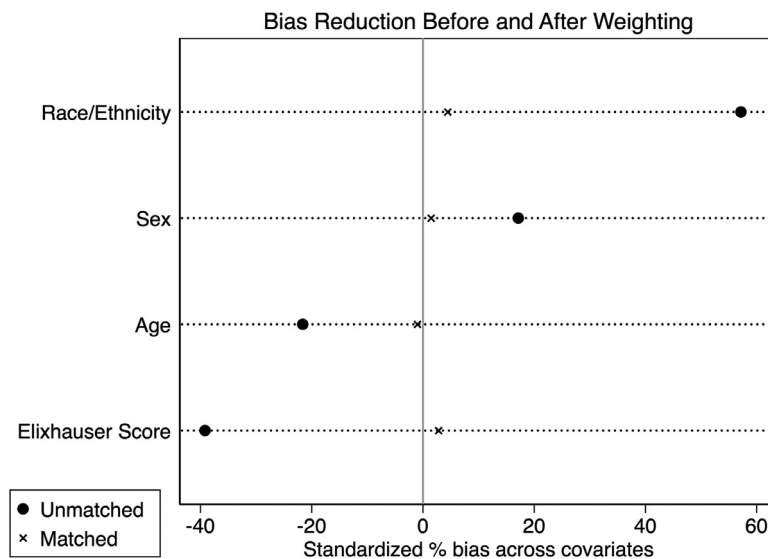


Fig. 1. Bias reduction in our matched cohort of IS-COVID and IS-PNA patients.

Table 3. Baseline demographics and outcomes of patients with ischemic stroke as the primary discharge diagnosis.

Variable	IS Controls (2019) (n=81,735)	IS-COVID (April-July 2020) (n=526)	p value
Age category			<0.001
<18 [n (%)]	140 (0.2)	0	
18–50	8669 (10.6)	88 (16.7)	
51–64	21,391 (26.2)	163 (31.0)	
65–74	20,128 (24.6)	119 (22.6)	
75–79	9553 (11.7)	59 (11.2)	
≥80	21,854 (26.7)	97 (18.4)	
Age <75	50,328 (61.6)	370 (70.3)	<0.001
Male sex	41,944 (51.3)	295 (56.1)	0.034
Race/Ethnicity*			<0.001
White	49,054 (60.0)	193 (36.7)	
Black	19,331 (23.7)	172 (32.7)	
Hispanic	5489 (6.7)	99 (18.8)	
Asian	2541 (3.1)	17 (3.2)	
Other/Unknown	5320 (6.5)	45 (8.6)	
Elixhauser score			
Median, IQR	3, 2–4	3, 2–5	<0.001
Mean±SD	3.3 ± 1.8	4.3 ± 2.1	<0.001
Congestive heart failure	16,617 (20.3)	130 (24.7)	0.013
Obese	13,750 (16.8)	96 (18.3)	0.383
Smoker	13,150 (16.1)	33 (6.3)	<0.001
Atrial fibrillation	22,271 (27.3)	128 (24.3)	0.135
Hypertension	61,744 (75.5)	396 (75.3)	0.891
Diabetes	32,722 (40.0)	284 (54.0)	<0.001
Dyslipidemia	52,418 (64.1)	313 (59.5)	0.027
Interfacility transfer	22,196 (27.2)	163 (31.0)	0.049
Seen in emergency department (n=81,317)	65,888 (81.5)	413 (82.1)	0.740
Intubated	6312 (7.7)	93 (17.7)	<0.001
Acute coronary syndrome	4681 (5.7)	51 (9.7)	<0.001
Percutaneous coronary intervention	63 (0.1)	0	0.524
Intracerebral hemorrhage	6127 (7.5)	62 (11.8)	<0.001
Subarachnoid hemorrhage	1264 (1.6)	12 (2.3)	0.174
Acute renal failure	12,420 (15.2)	128 (24.3)	<0.001
Pulmonary embolus	1066 (1.3)	22 (4.2)	<0.001
Cerebral venous sinus or deep vein thrombosis	287 (0.4)	suppressed*	0.021
Length of hospital stay [days, mean±SD]	6.1 ± 8.3	9.3 ± 10.9	<0.001
Length of intensive care unit stay [days, mean±SD]*	3.8 ± 5.3	5.4 ± 7.1	<0.001
Mechanical thrombectomy	8420 (10.3)	72 (13.7)	0.011
Treated with alteplase	6013 (7.4)	37 (7.0)	0.778
Favorable discharge	57,011 (69.8)	277 (52.7)	<0.001
In-hospital death	3769 (4.6)	70 (13.3)	<0.001

*Binary variables presented as n, %; ordinal variables as median, IQR; interval variables as mean (SD). P values calculated with the chi-squared test for binary variables, the Wilcoxon ranksum test for ordinal variables, and Student's t-test for interval variables. Length of intensive care unit stay restricted to patients with >24 h spent in intensive care. White, Black, Asian and other/unreported race/ethnicity categories are non-Hispanic. Some cells suppressed for counts <10, in compliance with Vizient regulations.

patients with comorbid COVID-19 had worse clinical outcomes than expected and worse outcomes than patients with ischemic stroke and pneumonia. This warrants additional study to determine if there are potential interventions to improve outcomes for these high-risk patients and to further address the disproportionate burden borne by minority patients.

Sources of Funding

Dr. de Havenon is supported by NIH-NINDS [K23NS105924](#). The research reported in this publication was supported (in part or in full) by the Utah Stimulating Access to Research in Residency Transition Scholar (StARRTS) under Award Number [1R38HL143605-01](#). The content is solely the

responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Disclosures

Dr. de Havenon has received investigator-initiated funding from AMAG and Regeneron pharmaceuticals. Dr. Callaghan consults for DynaMed, and performs medical legal consultations including consultations for the Vaccine Injury Compensation Program. Dr. Majersik reports NIH/NINDS funding U24NS107228, Associate Editor for *Stroke*, consulting fees for Foldax scientific advisory board, and Editorial Board member of *Neurology*. The remaining authors report no potential conflicts of interest.

Acknowledgements

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2020.105535.

References

- Morelli N, Rota E, Terracciano C, Immovilli P, Spallazzi M, Colombi D, Zaino D, Michieletti E, Guidetti D. The baffling case of ischemic stroke disappearance from the casualty department in the COVID-19 Era. *Eur Neurol* 2020;83(2):213-215.
- Kansagra AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of covid-19 on stroke evaluation in the United States. *N Engl J Med* 2020;383:400-401.
- Uchino Ken, Kolikonda Murali K., Brown Dena, Kovi Shivakrishna, Collins Dana, Khawaja Zeshawn, Buletko A. Blake, Russman Andrew N., Hussain M. Shazam. Decline in stroke presentations during COVID-19 surge. *Stroke*. 2020;51:2544-2547.
- Lange SJ. Potential indirect effects of the COVID-19 pandemic on use of emergency departments for acute life-threatening conditions — United States, January–May 2020. *MMWR Morb Mortal Wkly Rep* 2020. [cited 2020 Jun 30];69. Available from: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6925e2.htm>.
- Nguyen-Huynh Mai N., Tang Xian Nan, Vinson David R., Flint Alexander C., Alexander Janet G., Meighan Melissa, Burnett Molly, Sidney Stephen, Klingman Jeffrey G. Acute stroke presentation, care, and outcomes in community hospitals in northern California during the COVID-19 pandemic. *Stroke*. 2020;51:2918-2924.
- Cowan Logan T, Lutsey Pamela L, Pankow James S, Kunihiro Matsushita, Junichi Ishigami, Kamakshi Lakshminarayan. Inpatient and outpatient infection as a trigger of cardiovascular disease: the ARIC study. *J Am Heart Assoc* 2018;7:e009683.
- Boehme AK, Luna J, Kulick ER, Kamel H, Elkind MSV. Influenza-like illness as a trigger for ischemic stroke. *Ann Clin Transl Neurol* 2018;5:456-463.
- Zhao Jing, Li Hang, Kung David, Fisher Marc, Shen Ying, Liu Renyu. Impact of the COVID-19 epidemic on stroke care and potential solutions. *Stroke*. 2020;51:1996-2001.
- Yaghi Shadi, Ishida Koto, Torres Jose, Mac Grory Brian, Raz Eytan, Humbert Kelley, Henninger Nils, Trivedi Tushar, Lillemoe Kaitlyn, Alam Shazia, et al. SARS2-CoV-2 and stroke in a New York healthcare system. *Stroke*. 2020;51:2002-2011.
- Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA Cardiol* 2020;5(7):831-840.
- Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, Barnaby DP, Becker LB, Chelico JD, Cohen SL, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;323(20):2052-2059.
- Merkler AE, Parikh NS, Mir S, Gupta A, Kamel H, Lin E, Lantos J, Schenck EJ, Goyal P, Bruce SS, et al. Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. *JAMA Neurol* 2020;77(11):1366-1372.
- CDB|healthcare analytics platform for clinical benchmarking [Internet]. [cited 2020 Apr 24];Available from: <https://www.vizientinc.com/our-solutions/clinical-solutions/clinical-data-base>
- Chang TE, Tong X, George MG, Coleman King SM, Yin X, O'Brien S, Ibrahim G, Liskay A, Paul Coverdell National Acute Stroke Program team, Wiltz JL. Trends and factors associated with concordance between international classification of diseases, ninth and tenth revision, clinical modification codes and stroke clinical diagnoses. *Stroke* 2019;50:1959-1967.
- WHO | Emergency use ICD codes for COVID-19 disease outbreak [Internet]. WHO. [cited 2020 Jun 29];Available from: <http://www.who.int/classifications/icd/covid19/en/>
- Finlayson O, Kapral M, Hall R, Asllani E, Selchen D, Saposnik G. Canadian stroke network, stroke outcome research Canada (SORCan) working group. Risk factors, inpatient care, and outcomes of pneumonia after ischemic stroke. *Neurology* 2011;77:1338-1345.
- Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009;28:3083-3107.
- Austin PC. Variance estimation when using inverse probability of treatment weighting (IPTW) with survival analysis. *Stat Med* 2016;35:5642-5655.
- Chang H-J, Chen P-C, Yang C-C, Su Y-C, Lee C-C. Comparison of Elixhauser and Charlson methods for predicting oral cancer survival. *Medicine (Baltimore)* 2016;95:e2861.
- Rubin DB. Using propensity scores to help design observational studies: application to the tobacco litigation. *Health Serv Outcomes Res Methodol* 2001;2:169-188.
- CDC. Coronavirus disease 2019 (COVID-19). *Cent Dis Control Prev* 2020. [cited 2020 Jul 2];Available from: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/racial-ethnic-minorities.html>.
- McClure ES, Vasudevan P, Bailey Z, Patel S, Robinson WR. Racial capitalism within public health: how occupational settings drive COVID-19 disparities. *Am J Epidemiol* 2020;189(11):1244-1253.
- Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, De Leacy RA, Shigematsu T, Ladner TR, Yaeger KA, et al. Large-vessel stroke as a presenting feature of covid-19 in the young. *N Engl J Med* 2020;382:e60.
- CDC. Coronavirus disease 2019 (COVID-19) [Internet]. *Cent Dis Control Prev* 2020. [cited 2020 Jun 30];Available from: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>.

25. Coronavirus disease 2019 (COVID-19): complications [Internet]. Available from: <https://bestpractice.bmj.com/topics/en-us/3000168/complications>
26. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, Chen H, Ding X, Zhao H, Zhang H, et al. Coagulopathy and antiphospholipid antibodies in patients with covid-19. *N Engl J Med* 2020;382:e38.
27. Cardiac arrest deaths at home in New York CITY have increased by a startling 800% [Internet]. [cited 2020 May 20]; Available from: http://www.ptca.org/news/2020/0408_INCREASED_DEATHS_NYC.html
28. Patel MR, Calhoun JH, Dehmer GJ, Grantham JA, Maddox TM, Maron DJ, Smith PK. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2016 appropriate use criteria for coronary revascularization in patients with acute coronary syndromes: a report of the American college of cardiology appropriate use criteria task force, American association for thoracic surgery, American heart association, American society of echocardiography, American society of nuclear cardiology, society for cardiovascular angiography and interventions, society of cardiovascular computed tomography, and the society of thoracic surgeons. *J Am Coll Cardiol* 2017;69:570-591.
29. Powers William J, Rabinstein Alejandro A, Teri Ackerson, Adeoye Opeolu M, Bambakidis Nicholas C, Kyra Becker, José Biller, Michael Brown, Demaerschalk Bart M, Brian Hoh, Guidelines for the Early Management of Patients With Acute Ischemic Stroke, et al. Update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American heart association/American stroke association. *Stroke* 2019;50:e344-e418.
30. Rico-Mesa JS, Rosas D, Ahmadian-Tehrani A, White A, Anderson AS, Chilton R. The role of anticoagulation in COVID-19-induced hypercoagulability. *Curr Cardiol Rep* 2020;22:53.