

Original research

# Endovascular thrombectomy in acute ischemic stroke patients with COVID-19: prevalence, demographics, and outcomes

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/neurintsurg-2020-016777>).

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Received 19 August 2020  
Revised 8 September 2020  
Accepted 10 September 2020  
Published Online First  
27 September 2020



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**To cite:** de Havenon A, Yaghi S, Mistry EA, et al. *J NeuroIntervent Surg* 2020;**12**:1045–1048.

## ABSTRACT

**Background** We aimed to compare the outcome of acute ischemic stroke (AIS) patients who received endovascular thrombectomy (EVT) with confirmed COVID-19 to those without.

**Methods** We performed a retrospective analysis using the Vizient Clinical Data Base and included hospital discharges from April 1 to July 31 2020 with ICD-10 codes for AIS and EVT. The primary outcome was in-hospital death and the secondary outcome was favorable discharge, defined as discharge home or to acute rehabilitation. We compared patients with laboratory-confirmed COVID-19 to those without. As a sensitivity analysis, we compared COVID-19 AIS patients who did not undergo EVT to those who did, to balance potential adverse events inherent to COVID-19 infection.

**Results** We identified 3165 AIS patients who received EVT during April to July 2020, in which COVID-19 was confirmed in 104 (3.3%). Comorbid COVID-19 infection was associated with younger age, male sex, diabetes, black race, Hispanic ethnicity, intubation, acute coronary syndrome, acute renal failure, and longer hospital and intensive care unit length of stay. The rate of in-hospital death was 12.4% without COVID-19 vs 29.8% with COVID-19 ( $P<0.001$ ). In mixed-effects logistic regression that accounted for patient clustering by hospital, comorbid COVID-19 increased the odds of in-hospital death over four-fold (OR 4.48, 95% CI 3.02 to 6.165). Comorbid COVID-19 was also associated with lower odds of a favorable discharge (OR 0.43, 95% CI 0.30 to 0.61). In the sensitivity analysis, comparing AIS patients with COVID-19 who did not undergo EVT ( $n=2139$ ) to the AIS EVT patients with COVID-19, there was no difference in the rate of in-hospital death (30.6% vs 29.8%,  $P=0.868$ ), and AIS EVT patients had a higher rate of favorable discharge (32.4% vs 47.1%,  $P=0.002$ ).

**Conclusion** In AIS patients treated with EVT, comorbid COVID-19 infection was associated with in-hospital death and a lower odds of favorable discharge compared with patients without COVID-19, but not compared with AIS patients with COVID-19 who did not undergo EVT. AIS EVT patients with COVID-19 were younger, more likely to be male, have systemic complications, and almost twice as likely to be black and over three times as likely to be Hispanic.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19), a viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in a pandemic affecting different aspects of acute ischemic stroke (AIS) care.<sup>1</sup> In addition to a delay in AIS care, such as endovascular thrombectomy (EVT), there has been a significant decline in AIS hospitalizations and procedures.<sup>2–5</sup> Previous studies demonstrated an association between COVID-19 and poor outcome in patients presenting with AIS.<sup>6,7</sup>

The effect of COVID-19 on the clinical outcomes of EVT-treated patients has not been adequately assessed in a diverse sample of United States' hospitals. Furthermore, it is unclear if the outcome of EVT-treated AIS patients with comorbid COVID-19 is different than AIS patients with COVID-19 who do not undergo EVT, such as lacunar stroke or non-occlusive atherosclerotic stroke. In this study of AIS patients treated with EVT from April to July 2020, we compared the outcome of patients with confirmed COVID-19 to those without COVID-19.

## METHODS

We performed a retrospective analysis using the Vizient Clinical Data Base (CDB), a healthcare analytics platform employed by participating US hospitals.<sup>8</sup> Data is entered into the CDB using a combination of the electronic medical record and administrative claim data for purposes of benchmarking clinical performance, costs, and outcomes. The Vizient CDB is a validated administrative database used to answer diverse research questions.<sup>9–10</sup> We identified patients whose date of hospital discharge was from April 1 to July 31 2020 and included those with ICD-10 codes for EVT and ischemic stroke (online supplemental table 1).<sup>11–12</sup> The concordance between the clinical diagnosis of ischemic stroke and the used ICD-10 codes has previously been shown to be >95%<sup>11</sup> and the codes for mechanical thrombectomy are specific to a procedure, making the use of the code without performing the procedure unlikely. Patients <18 years of age and those who were in a hospice at the time of admission were excluded. We stratified the cohort by the presence of comorbid COVID-19, determined by the ICD code U07.1, which is reserved for laboratory-confirmed SARS-CoV-2.<sup>13</sup>

IRB approval was not required for this retrospective study of deidentified data per University of Utah Institutional Review Board Guidelines.

The primary outcome was in-hospital death. Favorable discharge, defined as a discharge to home or acute rehabilitation, was the secondary outcome. We report descriptive statistics stratified by COVID-19 status, and test for significant differences using the chi-squared test, student's *t*-test, or Wilcoxon rank-sum tests, as appropriate. We also stratified hospitals by their monthly volume of AIS EVT cases with low volume (<5 cases/month), medium volume (5–10 cases/month), and high volume (>10 cases/month) stratum, and report the primary and secondary outcomes in the stratifications. Consistent with Vizient regulations for deidentification, we have suppressed values for cell counts that are <10, which occurs after stratification.

To account for patient clustering by hospital and different patient volumes at individual hospitals, we fit mixed-effects (random intercept) logistic regression models to our outcomes with the hospital identifier as a random effect. To assess the stability of the results, standard errors and bias-confidence intervals were estimated with 1000 cluster bootstrap replications.<sup>14–16</sup> The mixed-effects model estimates a separate intercept for each hospital to account for between-hospital differences, such as hospital EVT volume. The models were adjusted for: Model 1: patient age, sex, race, ethnicity, and Elixhauser comorbidity score; and Model 2: patient age, sex, race, ethnicity, Elixhauser comorbidity score, acute respiratory failure requiring intubation, acute coronary syndrome, acute renal failure, pulmonary embolism, and hospital length of stay.

As a sensitivity analysis, we created a cohort of AIS patients who did not undergo EVT but had laboratory-confirmed COVID-19. We compared this cohort to the AIS EVT patients with COVID-19 and fitted our mixed effects' model adjusted for the covariates in Models 1 and 2. All analysis was conducted in Stata 16.1 (StataCorp, College Station, TX) and we defined statistical significance as  $P < 0.05$ .

**RESULTS**

We included data from 190 non-federal hospitals in 45 states who, from April 1 to July 31 2020, discharged 3165 AIS patients who underwent EVT. The hospitals' bed sizes were ≤150 beds (34/190), 151–250 beds (9/190), 251–500 beds (44/190), and >500 beds (103/190). 184/190 hospitals were teaching facilities and 189/190 were in urban locations. Comorbid SARS-CoV-2 infection was detected in 104/3,165 (3.3%) patients from 49/190 (25.8%) of included hospitals in 17/45 (37.8%) states. The mean (SD) and median (IQR) number of EVTs performed each month at the hospitals were 5.9 (4.0) and 5 (3.3–7.8). Because the number of hospitals in the dataset fluctuates by month, to compare the volume of AIS EVT patients we can focus on monthly data. In June, for example, the mean (SD) volume of AIS EVT patients was 6.0 (4.6) in hospitals without COVID-19 cases vs 6.1 (3.6) ( $P = 0.943$ ) in hospitals with COVID-19 cases. We also did not find significant differences in the months of April, May, or July (all  $P > 0.05$ , data not shown).

The baseline demographics are shown in table 1. Patients with COVID-19 were younger, more likely to be male, black, or Hispanic, had higher rates of diabetes, but were less likely to be smokers or have atrial fibrillation. The proportion of non-Hispanic black patients increased from 16.9% to 26.0%, and Hispanic patients increased from 5.6% to 19.2%, while non-Hispanic whites decreased from 65.4% to 26.0% ( $P < 0.001$ ). Patients with COVID-19 were also more likely to have acute respiratory failure requiring intubation, acute coronary

**Table 1** Baseline demographics and outcomes of patients discharged with acute ischemic stroke who had endovascular thrombectomy, with and without COVID-19.

| Variable                                   | COVID - (n=3061) | COVID + (n=104) | P-value* |
|--|------------------|-----------------|----------|
| <b>Age category (years)</b>                |                  |                 |          |
| 18–50 (n, %)                               | 388 (12.7%)      | 25 (24.0%)      |          |
| 51–64                                      | 770 (25.1%)      | 38 (36.5%)      | <0.001   |
| 65–74                                      | 771 (25.2%)      | 19 (18.3%)      |          |
| ≥75  | 1132 (37.10%)    | 22 (21.2%)      |          |
| Male sex                                   | 1571 (51.3%)     | 71 (68.3%)      | 0.001    |
| <b>Race</b>                                |                  |                 |          |
| White                                      | 2003 (65.4%)     | 27 (26.0%)      |          |
| Black                                      | 517 (16.9%)      | 27 (26.0%)      | <0.001   |
| Hispanic                                   | 172 (5.6%)       | 20 (19.2%)      |          |
| Asian                                      | 86 (2.8%)        | suppressed      |          |
| Other/unknown                              | 283 (9.3%)       | 26 (25.0%)      |          |
| <b>Elixhauser comorbidity score</b>        |                  |                 |          |
| Median (IQR)                               | 4, 3–5           | 4, 3–5          | 0.672    |
| Congestive heart failure                   | 883 (28.9%)      | 32 (30.8%)      | 0.671    |
| Obese                                      | 620 (20.3%)      | 26 (25.0%)      | 0.238    |
| Smoker                                     | 490 (16.0%)      | suppressed      | 0.011    |
| Atrial fibrillation                        | 1301 (42.5%)     | 30 (28.9%)      | 0.006    |
| Diabetes                                   | 1038 (33.9%)     | 49 (47.1%)      | 0.005    |
| Dyslipidemia                               | 1961 (64.1%)     | 58 (55.8%)      | 0.083    |
| Hypertension                               | 2327 (76.0%)     | 74 (71.2%)      | 0.254    |
| Interfacility transfer                     | 1280 (41.8%)     | 34 (32.7%)      | 0.063    |
| Mechanical ventilation                     | 923 (30.2%)      | 56 (53.9%)      | <0.001   |
| Acute renal failure                        | 639 (20.9%)      | 36 (34.6%)      | 0.001    |
| Acute coronary syndrome                    | 274 (9.0%)       | 18 (17.3%)      | 0.004    |
| Pulmonary embolism                         | 87 (2.8%)        | suppressed      | 0.241    |
| Length of hospital stay (days)             | 9.1 (10.6)       | 14.2 (15.4)     | <0.001   |
| Length of intensive care unit stay (days)* | 4.1 (6.0)        | 6.2 (8.0)       | 0.002    |
| Favorable discharge                        | 1893 (61.8%)     | 49 (47.1%)      | 0.002    |
| In-hospital death                          | 378 (12.4%)      | 31 (29.8%)      | <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 rank-sum 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. Some values are suppressed for low count. White and black racial categories are non-Hispanic.

syndrome, and acute renal failure, but not pulmonary embolism. The mean hospital length of stay was longer in patients with COVID-19 vs without (14.2 vs 9.1 days,  $P < 0.001$ ).

There were 409/3,165 (12.9%) patients who died in hospital and 1,942/3,165 (61.4%) who had a favorable discharge. Compared with EVT-treated patients without COVID-19, those with COVID-19 were more likely to die in hospital (29.8% vs 12.4%,  $P < 0.001$ ) and less likely to have favorable discharge (47.1% vs 61.8%,  $P = 0.002$ ). In the mixed-effects adjusted logistic regression models, comorbid COVID-19 remained highly associated with in-hospital death (table 2). The OR for death related to comorbid COVID-19 in Model 1 was 4.48 (95% CI, 3.02 to 6.165) and in Model 2 was 3.37 (95% CI, 1.77 to 6.943). Comorbid COVID-19 was associated with lower odds

**Table 2** Mixed-effects logistic regression fit to in-hospital death and favorable discharge, showing ORs for patients with comorbid COVID-19

|          | OR for death | 95% CI*      | SE*  | P-value | OR for favorable discharge | 95% CI*      | SE*  | P-value |
|----------|--------------|--------------|------|---------|----------------------------|--------------|------|---------|
| Model 1† | 4.48         | 3.02 to 6.65 | 0.90 | <0.001  | 0.43                       | 0.30 to 0.61 | 0.08 | <0.001  |
| Model 2† | 3.37         | 1.77 to 6.43 | 1.11 | <0.001  | 0.58                       | 0.36 to 0.91 | 0.14 | 0.019   |

\*CI: confidence interval, SE: standard error, calculated with 1000 cluster bootstrap replications.

†Model 1 adjusted for patient age, sex, race, ethnicity, and Elixhauser comorbidity score. Model 2 adjusted for patient age, sex, race, ethnicity, Elixhauser comorbidity score, acute respiratory failure requiring intubation, acute coronary syndrome, acute renal failure, pulmonary embolus, and hospital length of stay.

of a favorable discharge in Model 1 (OR 0.43, 95% CI 0.30 to 0.61) and Model 2 (OR 0.58, 95% CI 0.36 to 0.91).

The primary and secondary outcomes for patients with and without COVID-19 are shown after age stratification in online supplemental table 2. The largest increase in the rate of death was seen in patients aged 51–64 and the lowest increase in patients aged 18–50. We also stratified hospitals by <5, 5–10, and >10 EVT cases a month and saw a significantly higher rate of death and lower rate of favorable discharge across the EVT volume stratifications (online supplemental table 3).

In the sensitivity analysis, comparing AIS patients with COVID-19 who did not undergo EVT (n=2139) to AIS EVT patients with COVID-19, there was no difference in the rate of in-hospital death (30.6% vs 29.8%, P=0.868), and AIS EVT patients had a higher rate of favorable discharge (32.4% vs 47.1%, P=0.002). In the mixed-effects logistic regression models there was not a significant difference in death, but the AIS patients with COVID-19 who did not undergo EVT had a significantly lower odds of a favorable discharge in Model 2 (OR 0.55, 95% CI 0.34 to 0.89) (table 3).

## DISCUSSION

In this study of 3165 hospitalized AIS patients treated with EVT and discharged from April to July 2020, 3.3% of patients had comorbid COVID-19. Despite adjusting for comorbidities, including respiratory failure requiring intubation, acute renal failure, and hospital length of stay, COVID-19 remained a significant predictor of mortality. We also found that COVID-19 was negatively associated with favorable discharge after EVT. However, AIS EVT patients with COVID-19 had a near identical rate of death as 2139 AIS patients who did not undergo EVT but had COVID-19, suggesting the higher rate of adverse outcomes was inherent to COVID-19 infection. These results argue that eligible AIS patients with COVID-19 should receive EVT, given the overwhelming benefit of that intervention.<sup>17</sup>

Since the beginning of the COVID-19 outbreak, there has been accumulating evidence of an association between COVID-19, stroke, and worse outcomes after stroke, including large-vessel occlusion stroke.<sup>5 6 18–20</sup> Unlike prior studies, we provide data on AIS EVT patients from a broad sample of 190 United States' hospitals in 45 states. However, because this sample is not generalizable to the United States, we cannot provide reliable data on the incidence and prevalence of COVID-19 in AIS patients undergoing EVT.

The higher rate of mortality in patients with COVID-19 is not surprising since COVID-19 has been associated with other complications including acute respiratory failure, acute renal failure, and coagulopathy.<sup>21</sup> The most likely explanation for our findings is that patients with COVID-19 were sicker and had more systemic complications than patients without COVID-19, which, in turn, led to worse outcome. In addition, COVID-19 may have delayed diagnosis and intervention<sup>22</sup> due to the high rates of respiratory illness, sedation, and intubation in this group. Although we do not have access to stroke-specific variables such as baseline severity and EVT procedural metrics, the rate of baseline medical comorbidities, as reflected in the Elixhauser comorbidity score, was not different between AIS EVT patient with or without COVID-19. However, it is possible that the AIS EVT patients with COVID-19 presented with more severe stroke and we were not able to capture that, which is a limitation of our analysis.<sup>18 20</sup>

Other notable findings of our study are the differences in baseline characteristics for the patients with COVID-19, who were younger than those without COVID-19, with 24.0% of the COVID-19 patients being under the age of 50 compared with 12.7% of patients without COVID-19. This finding could be due to the pro-thrombotic effects of COVID-19<sup>19,23</sup> or because elderly patients with COVID-19 may have been deemed too unstable or unlikely to benefit from EVT. The proportion of Hispanic ethnicity among the the COVID-19 patients more than tripled (from 5.6% to 19.2%) and the proportion of black patients almost doubled (from 16.9% to 26.0%), consistent with the health disparities that are well documented for COVID-19.<sup>24 25</sup>

Our study has several limitations, mostly related to the use of administrative data, which introduces the possibility of classification bias from improper coding of exposures or outcomes. We do not know the location of vessel occlusion, stroke severity, time from stroke onset to EVT, or disease severity. Therefore, the differences in outcomes between the studied groups could be related to factors that were not accounted for in this study. Second, we identified COVID-19 patients with laboratory-confirmed SARS-CoV-2 infection: therefore, it is possible that asymptomatic patients with COVID-19 were included in the COVID-19 negative group. The conclusions of our study should also be interpreted in light of the limited sample size and are not generalizable to the United States, representing instead a selection of patients from hospitals with available data. Finally, with

**Table 3** Mixed-effects logistic regression fit to in-hospital death and favorable discharge, showing ORs for AIS patients with COVID-19 who did not undergo EVT compared with those had EVT

|          | OR for death | 95% CI       | SE   | P-value | OR for favorable discharge | 95% CI       | SE   | P-value |
|----------|--------------|--------------|------|---------|----------------------------|--------------|------|---------|
| Model 1* | 1.14         | 0.73 to 1.79 | 0.24 | 0.564   | 0.68                       | 0.44 to 1.06 | 0.15 | 0.091   |
| Model 2* | 1.52         | 0.87 to 2.66 | 0.44 | 0.140   | 0.55                       | 0.34 to 0.89 | 0.14 | 0.015   |

\*Model 1 adjusted for patient age, sex, race, ethnicity, and Elixhauser comorbidity score. Model 2 adjusted for patient age, sex, race, ethnicity, Elixhauser comorbidity score, acute respiratory failure requiring intubation, acute coronary syndrome, acute renal failure, pulmonary embolus, and hospital length of stay.

the current data we are not able to evaluate the 90-day modified Rankin Scale score, which is a more informative measure of functional outcome after ischemic stroke.<sup>26</sup> Despite these limitations, we provide important data on AIS patients treated with EVT in the context of laboratory-confirmed COVID-19 infection.

**CONCLUSION**

In AIS patients treated with EVT, comorbid COVID-19 infection was associated with in-hospital death and a lower odds of favorable discharge compared with patients without COVID-19, but not compared with AIS patients with COVID-19 who did not undergo EVT. AIS EVT patients with COVID-19 were younger, more likely to be male, black, or Hispanic, and have systemic complications.

**Correction notice** Since this article was first published online first changes have been made to table 1. The use of ‘to’ has been changed to the % symbol in both covid columns.

**Acknowledgements** Dr. de Havenon has received investigator-initiated funding from AMAG and Regeneron pharmaceuticals.

**Contributors** AdH and MA conceived of the study and drafted/edited the manuscript, AD helped with statistical analysis, ESh and SH helped conceive of the study and provided the data, SY, EM, Est, DT, NP, and JS provided critical revisions and feedback.

**Funding** Dr. de Havenon is supported by NIH-NINDS K23NS105924. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**Competing interests** Dr. de Havenon has received investigator-initiated funding from AMAG and Regeneron pharmaceuticals. The remaining authors report no potential conflicts of interest.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article or uploaded as supplementary information.

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