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Original research

Endovascular thrombectomy time metrics in the era of COVID-19: observations from the Society of Vascular and Interventional Neurology Multicenter Collaboration

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ABSTRACT

Background Unprecedented workflow shifts during the coronavirus disease 2019 (COVID-19) pandemic have contributed to delays in acute care delivery, but whether it adversely affected endovascular thrombectomy metrics in acute large vessel occlusion (LVO) is unknown.

Methods We performed a retrospective review of observational data from 14 comprehensive stroke centers in nine US states with acute LVO. EVT metrics were compared between March to July 2019 against March to July 2020 (primary analysis), and between state-specific pre-peak and peak COVID-19 months (secondary analysis), with multivariable adjustment.

Results Of the 1364 patients included in the primary analysis (51% female, median NIHSS 14 [IQR 7–21], and 74% of whom underwent EVT), there was no difference in the primary outcome of door-to-puncture (DTP) time between the 2019 control period and the COVID-19 period (median 71 vs 67 min, $P=0.10$). After adjustment for variables associated with faster DTP, and clustering by site, there remained a trend toward shorter DTP during the pandemic ($\beta_{\text{adj}}=-73.2$, 95% CI $-153.8-7.4$, $P=0.07$). There was no difference in DTP times according to local COVID-19 peaks vs pre-peak months in unadjusted or adjusted multivariable regression ($\beta_{\text{adj}}=-3.85$, 95% CI $-36.9-29.2$, $P=0.80$). In this final multivariable model (secondary analysis), faster DTP times were significantly associated with transfer from an outside institution ($\beta_{\text{adj}}=-46.44$, 95% CI -62.8 to -30.0 , $P<0.01$) and higher NIHSS ($\beta_{\text{adj}}=-2.15$, 95% CI -4.20 to -0.1 , $P=0.05$).

Conclusions In this multi-center study, there was no delay in EVT among patients treated for intracranial occlusion during the COVID-19 era compared with the pre-COVID era.

BACKGROUND

Coronavirus disease 2019 (COVID-19) has placed unprecedented stress on the US healthcare system. Delays in the evaluation of acute stroke and treatment with intravenous thrombolytics during the COVID-19 pandemic have been previously demonstrated.^{1–3} However, little has been reported in regard to patients harboring intracranial occlusions who undergo endovascular thrombectomy (EVT).^{4–5} Guidelines during the COVID-19 pandemic have called for streamlined and efficient processes,^{6–11} however, there remain considerable variations in management paradigms with ongoing debates, including recommendations for pre-thrombectomy airway management, intravenous thrombolysis, and antithrombotics.¹² Due to the enforcement of contact precautions, the use of personal protective equipment, and decontamination procedures for imaging and treatment facilities, it stands to reason that the COVID-19 pandemic may result in delays of acute interventions for stroke. Furthermore, delays in acute care may also be affected by local surges in COVID-19 cases as healthcare systems become overrun and resources exhausted.^{13–14}

The aim of the present study was to evaluate the impact of COVID-19 on the emergent management of acute intracranial occlusions. We hypothesized that the COVID-19 pandemic would lead to a delay in EVT time metrics, similar to the delay we have shown among patients treated with intravenous thrombolysis.¹

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request, after clearance by the local ethics committee.

Study population

We conducted a retrospective review of our prospectively maintained observational registry data to identify all consecutive patients with acute ischemic stroke and intracranial occlusion who underwent emergent angiography and/or thrombectomy at 14 Comprehensive Stroke Centers (CSCs) across nine US states between January 1, 2019 and July 31, 2020. At the time of data consolidation, these states accounted for 47% of all reported US cases of COVID-19 and 37% of COVID-19-associated deaths.¹⁵ Participating registry centers were recruited based on their affiliation with the Society of Vascular and Interventional Neurology.

Patients were eligible for inclusion if they experienced an acute intracranial occlusion of the internal carotid artery (ICA), middle cerebral artery (inclusive of M1, M2, or M3 segments), or vertebral and/or basilar arteries. Occlusion location was determined by CT angiography or by digital subtraction angiography. Patients were excluded if they were triaged by a mobile stroke unit (with these data being reported separately), if the stroke occurred while hospitalized (in-hospital stroke) given unique triage protocols associated with patient populations, and if they were admitted outside the study periods as outlined below.

Study periods

To maximize sensitivity for detecting differences in treatment times based on the differential burden and delayed spread of the novel coronavirus among the included sites, two analyses were performed. In the primary analysis, patients admitted between March 1, 2019 and July 31, 2019 (seasonal control period) were compared against patients admitted between March 1, 2020 and July 21, 2020 (COVID-19 period) across all sites. A secondary analysis was conducted based on relative COVID-19 surges affecting sites on the state level, according to data published by the New York Times.¹⁶ In this analysis, patients were compared between two contemporaneous months around the time of the first local COVID-19 “peak”. Months were selected for state-specific COVID-19 peak comparisons using a modified Delphi consensus between first, second, and senior authors (ALC, AMZ, JES) using qualitative visualization of new daily COVID-19 diagnoses and total COVID-19 hospitalizations in that state.¹⁶ In this analysis, the month of the first clinically significant increase in daily COVID-19 diagnoses and/or hospitalizations was categorized as the COVID-19 peak. To maximize sensitivity of the state-specific COVID-19 peak comparisons, the pre-peak (referent) period preceded the COVID-19 peak period by 1 month. For example, if the COVID-19 peak occurred in May 2020, the referent month would be March 2020 for that state. In this analysis, only the time of the first peak was used and only months through July 2020 could be selected as COVID-19 peak months due to the recent nature of multicenter data consolidation. For states in which new daily COVID-19 diagnoses did not have a clear peak (eg, Iowa), the peak of COVID-19 hospitalizations was used as the primary indicator of COVID-19 peak.

Variables and outcomes

Baseline demographic data including age (which was binned by decade to protect personal health information), sex, race, and ethnicity, as well as key vascular risk factors were collected from participating sites. Patient arrival method (use of emergency medical services (EMS) vs walk-in/private vehicle vs transfer from outside hospital), baseline stroke severity according to the National Institutes of Health Stroke Scale (NIHSS), occlusion location, and treatment with intravenous thrombolysis and/or EVT are also reported. To account for site EVT volume as a

confounder, we included a variable recognizing sites as ‘high-volume’ if the 2019 EVT volume exceeded 50, in accordance with previously published data indicating faster treatment times.¹⁷

The primary outcome was door-to-puncture time, assessed as a continuous variable. We further explored the time windows from last known well (LKW) to arrival at the CSC, door to initial imaging, puncture to first pass, puncture to recanalization (or completion of angiography if recanalization unsuccessful), and overall LKW to recanalization. Additional endpoints included successful recanalization (defined as a thrombolysis in cerebral infarction (TICI) score of 2b/3) and discharge disposition (stratified by home, acute inpatient rehabilitation, other facility, or hospice/death which was consolidated). Due to the incompleteness of data regarding discharge mRS scores (48% completion rate) and lack of available 90-day mRS scores for recently discharged patients from the COVID-19 pandemic, functional and long-term outcomes are not reported.

Statistical analysis

Categorical variables are reported using absolute counts and proportions, while non-normally distributed continuous variables are reported using medians and interquartile ranges (IQRs). Baseline characteristics between pre-COVID-19 and COVID-19 groups were compared using the Chi-square test or Fisher’s exact test for categorical variables, when appropriate, and the Wilcoxon rank-sum test for continuous variables. Unadjusted logistic and linear regression models were generated to estimate the effect of the COVID-19 period on the primary and secondary outcomes of interest. An adjusted linear regression model was used to estimate the impact of the COVID-19 period on any potential delay in the primary outcome of door-to-puncture time, with adjustment for all variables significant to $P \leq 0.1$ in univariate regression. Each adjusted regression model was clustered by site.

All statistical tests were 2-sided and conventional levels of significance ($\alpha = 0.05$) were used for interpretation, with P-values reported for conventional purposes only. Odds ratios and beta coefficients were reported with 95% confidence intervals (OR or β [95% CI]). No adjustments were made for multiple comparisons as analyses were exploratory and hypothesis-generating. Missing data were not imputed. STATA 15.0 (StataCorp, LLC) software was used for data analysis.

Ethics statement

The local institutional review board (Committee for the Protection of Human Subjects) at each participating center reviewed and approved the study with waiver of consent and HIPAA authorization was granted. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.

RESULTS

Primary analysis

Of 12 187 patients screened from the multicenter registry, 6277 patients were admitted within the study window for the primary analysis. Of these, 4868 were excluded due to lack of intracranial occlusion, 26 for experiencing an in-hospital stroke, and 18 due to initial evaluation in a mobile stroke unit, leaving 1364 included in the primary analysis (online supplemental figure 1). More than half (51%) were ≥ 70 years of age, 48% were female, and 61% were White (table 1). The median NIHSS was 14 (IQR 7–21), and 74% had an occlusion of the internal carotid,

Table 1 Demographics and clinical characteristics by seasonal period

Baseline characteristics	Total (n=1364)	March–July 2019 (n=794)	March–July 2020 (n=570)	P-value
Age group, no. (%)				0.47
<50	151 (11%)	93 (12%)	58 (10%)	
50–69	524 (38%)	310 (39%)	214 (38%)	
≥70	689 (51%)	391 (49%)	298 (52%)	
Female, no. (%)	649 (48%)	382 (48%)	267 (47%)	0.64
Hispanic, no. (%)	199/1,349 (15%)	102/786 (13%)	97/563 (17%)	0.03
Race, no. (%)				0.07
White	827 (61%)	460 (58%)	367 (64%)	
Black	329 (24%)	198 (25%)	131 (23%)	
Asian	29 (2%)	19 (2%)	10 (2%)	
Other/unknown	179 (13%)	117 (15%)	62 (11%)	
Medical history, no. (%)				
Hypertension	1021 (75%)	600 (76%)	421 (74%)	0.47
Dyslipidemia	637 (47%)	359 (45%)	278 (49%)	0.19
Diabetes	437 (32%)	245 (31%)	192 (34%)	0.27
Atrial fibrillation	297 (22%)	174 (22%)	123 (22%)	0.88
Tobacco use	256 (19%)	153 (19%)	103 (18%)	0.58
Prior ischemic stroke	248 (18%)	135 (17%)	113 (20%)	0.18
Coronary artery disease	204 (15%)	91 (11%)	113 (20%)	<0.01
Arrival method, no. (%)				0.42
EMS	416/1,245 (33%)	222/696 (32%)	194/549 (35%)	
Walk-in/private vehicle	85/1,245 (7%)	50/696 (7%)	35/549 (6%)	
Transfer	744/1,245 (60%)	424/696 (61%)	320/549 (58%)	
NIHSS on arrival, median (IQR)	14 (7–21) (n=1035)	14 (6–20) (n=596)	15 (7–21) (n=439)	0.16
Intravenous thrombolysis, no. (%)	180/1,124 (16%)	93/655 (14%)	87 (19%)	0.05
Site of occlusion, no. (%)				
ICA	327 (24%)	189 (24%)	138 (24%)	0.86
MCA–M1	659 (48%)	381 (48%)	278 (49%)	0.77
MCA–M2	317 (23%)	190 (24%)	127 (22%)	0.48
MCA–M3	68 (5%)	44 (6%)	24 (4%)	0.27
Basilar artery	86 (6%)	42 (5%)	44 (8%)	0.07
Vertebral artery	55 (4%)	34 (4%)	21 (4%)	0.58
Thrombectomy, no. (%)	1003 (74%)	563 (71%)	440 (77%)	<0.01
Thrombectomy for ICA, M1, or basilar occlusions, no. (%)	789/1,003 (79%)	430/569 (76%)	359/434 (83%)	<0.01

EMS, emergency medical services; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale score.

proximal middle cerebral (M1), or basilar artery. There was a 28% decrease in the total number of patients with any intracranial occlusion during the COVID-19 period when compared with the 2019 seasonal control period (570 vs 794 patients). Compared with patients who presented in the seasonal control period, patients who presented in the COVID-19 period were more frequently Hispanic (OR 1.40, 95% CI 1.03 to 1.89, $P=0.03$), had coronary artery disease (OR 1.91, 95% CI 1.41 to

2.58, $P<0.01$), and had a higher probability of undergoing EVT (OR 1.39, 95% CI 1.08 to 1.78, $P=0.01$).

For the primary outcome of door-to-puncture time, there was no significant difference in door-to-puncture times among patients admitted during the COVID-19 period vs the seasonal control period ($\beta=-41.9$, 95% CI $-93.0-9.1$, $P=0.11$; see [table 2](#) for absolute time differences). After adjustment for all candidate variables associated with door-to-puncture ($P<0.1$: history of hypertension, diabetes, dyslipidemia, transfer from outside institution, and baseline NIHSS) and clustering by site, there was a trend toward faster door-to-puncture times during the COVID-19 period ($\beta_{\text{adj}}=-73.2$, 95% CI $-153.8-7.4$, $P=0.07$; [table 3](#)). While transfer from an outside institution was significantly associated with faster door-to-puncture time in univariate regression ($P=0.04$), it was no longer associated with faster treatment in multivariable regression ($p_{\text{adj}}=0.30$). Only a history of hypertension was independently associated with delayed EVT during the COVID-19 period ($\beta_{\text{adj}}=57.1$, 95% CI $-1.3-115.5$, $P=0.05$). A greater proportion of patients were discharged home over acute inpatient rehabilitation during the COVID-19 period when compared with the control period (38% vs 33%, $P<0.01$; [table 2](#)).

Secondary analysis

For the secondary analysis of state-specific COVID-19 peaks, there was 100% agreement among the three raters regarding each state's first COVID-19 peak ([figure 1](#)). In this analysis, 123 patients were admitted in the state-specific pre-peak month and 84 patients were admitted during the state-specific COVID-19 peak (32% decline during local COVID-19 peak). Compared with the pre-peak month, patients admitted during the local COVID-19 peak more frequently had atrial fibrillation (OR 2.18, 95% CI 1.12 to 4.26, $P=0.02$) with a trend toward lower odds of prior stroke (OR 0.43, 95% CI 0.18 to 1.02, $P=0.06$). There was a higher prevalence of basilar occlusion during the COVID-19 peak (OR 5.41, 95% CI 1.44 to 20.28, $P=0.01$), but no other differences with respect to age, sex, or comorbidities (online supplemental table 1).

For the primary outcome of door-to-puncture, there was no significant difference in treatment times among patients admitted during the local COVID-19 peak vs the pre-peak month ($\beta=2.29$, 95% CI $-23.9-28.5$, $P=0.86$) and there remained no significant difference after adjustment for all candidate variables included in the multivariable regression model ($P<0.1$: White race, transfer from an outside institution, NIHSS, and occlusion of the ICA/M1/basilar artery), and after clustering by site ($\beta_{\text{adj}}=-3.85$, 95% CI $-29.9-22.2$, $P=0.77$; online supplemental table 2). In this final multivariable model, faster door-to-puncture times were significantly associated with transfer from an outside institution ($\beta_{\text{adj}}=-46.44$, 95% CI -62.8 to -30.0 , $P<0.01$) and higher NIHSS ($\beta_{\text{adj}}=-2.15$, 95% CI -4.2 to -0.1 , $P=0.05$).

CONCLUSIONS

In this multicenter investigation evaluating treatment times of 1364 patients with an acute intracranial occlusion across nine US states, we observed no significant delay in thrombectomy treatment time during the COVID-19 pandemic. Our findings of a nearly one-third reduction in LVO incidence may be in part due to a reduction in patients seeking care during the pandemic,¹⁸ rather than a reduction in LVO stroke incidence. The increased likelihood of EVT is not fully explained in the present analysis, and it may be related to patient-level factors and imaging findings (eg, estimated infarct volume, collateral status, perfusion findings) which were not collected as part of this observational

Table 2 Procedural and clinical outcomes of EVT by seasonal period

Outcomes	Total (n=1364)	March–July 2019 (n=794)	March–July 2020 (n=570)	P-value
Door-to-puncture, median min (IQR)				
Overall	70 (37–103) (n=982)	71 (41–104) (n=556)	67 (33–102) (n=426)	0.10
Transfers	45 (24–80) (n=579)	47 (28–81) (n=309)	43 (22–80) (n=270)	0.25
EMS	94 (73–123) (n=305)	94 (73–127) (n=167)	95 (73–118) (n=138)	0.56
Private vehicle/walk-in	117 (84–209) (n=28)	106 (82–128) (n=19)	265 (168–319) (n=9)	0.04
LKW to CSC arrival, median min (IQR)				
Overall	335 (165–807) (n=1257)	345 (162–794) (n=736)	325 (170–839) (n=521)	0.81
Transfers	406 (237–857) (n=707)	400 (227–837) (n=401)	412 (247–862) (n=306)	0.47
EMS	146 (66–606) (n=385)	159 (68–642) (n=208)	138 (60–482) (n=177)	0.16
Private vehicle/walk-in	683 (156–1622) (n=63)	589 (40–1280) (n=40)	813 (23–736) (n=23)	0.27
Door to imaging, median min (IQR)				
Overall	17 (10–33) (n=660)	17 (10–34) (n=357)	17 (11–33) (n=303)	0.87
Transfers	18 (11–52) (n=143)	21 (12–97) (n=61)	16 (10–45) (n=82)	0.13
EMS	15 (9–24) (n=375)	14 (9–24) (n=191)	17 (10–25) (n=184)	0.21
Private vehicle/walk-in	32 (19–77) (n=64)	34 (18–71) (n=37)	30 (23–83) (n=27)	0.72
Puncture to first pass, median min (IQR)				
Overall	18 (12–29) (n=947)	19 (12–32) (n=529)	18 (12–26) (n=418)	0.04
Transfers	19 (13–28) (n=560)	19 (13–31) (n=294)	18 (13–26) (n=266)	0.22
EMS	18 (10–30) (n=289)	20 (10–35) (n=155)	17 (10–27) (n=134)	0.10
Private vehicle/walk-in	23 (13–33) (n=25)	19 (12–33) (n=19)	29 (16–41) (n=6)	0.36
Puncture to recanalization, median min (IQR)				
Overall	33 (21–56) (n=882)	34 (21–57) (n=497)	32 (20–53) (n=385)	0.33
Transfers	33 (21–53) (n=527)	33 (22–57) (n=282)	32 (20–49) (n=245)	0.31
EMS	34 (21–57) (n=275)	37 (23–60) (n=151)	32 (20–55) (n=124)	0.24
Private vehicle/walk-in	43 (25–84) (n=21)	37 (23–75) (n=14)	91 (38–103) (n=7)	0.07
LKW to recanalization, median min (IQR)				
Overall	431 (260–832) (n=844)	434 (255–816) (n=475)	425 (265–854) (n=369)	0.93
Transfers	499 (313–906) (n=510)	455 (297–841) (n=274)	525 (327–923) (n=236)	0.26
EMS	284 (193–711) (n=267)	331 (206–783) (n=145)	264 (188–592) (n=122)	0.04
Private vehicle/walk-in	748 (494–1187) (n=20)	624 (339–856) (n=14)	1169 (744–1918) (n=6)	0.08
TICI 2b/3 recanalization, no. (%)	917/979 (94%)	509/551 (92%)	408/428 (95%)	0.06
Discharge disposition, no. (%)				<0.01
Home	479/1,361 (35%)	262/794 (33%)	217/567 (38%)	
Acute rehabilitation	227/1,361 (17%)	158/794 (20%)	69/567 (12%)	
Skilled nursing facility/LTAC/unspecified facility	401/1,361 (29%)	241/794 (30%)	160/567 (28%)	
Hospice/death	254/1,361 (19%)	133/794 (17%)	121/567 (21%)	

CSC, Comprehensive Stroke Center; EMS, emergency medical services; IQR, interquartile range; LKW, last known well; LTAC, long-term acute care facility; TICI, thrombolysis in cerebral infarction.

study. Declines in LVO rate during the COVID-19 period (and in the state-specific COVID-19 peaks) were not driven by any one particular center, as 11 sites observed the same effect (three sites had similar or higher case rates during COVID-19; data not otherwise shown). Furthermore, we observed a trend toward shorter door-to-puncture times during the COVID-19 period when compared with the 2019 seasonal control period. This may be related, at least in part, to the lower volume of elective angiographic and neurointerventional cases as part of the health-care response to the pandemic,^{19 20} as well as the lower volume of emergent endovascular cases.²¹ The shorter time between arrival and angiography may also be related to the manner in which patients arrived to CSCs included in this analysis. More

than half of patients were transferred from an outside institution (60% of cohort), and these individuals were generally treated with greater expediency when compared with non-transferred patients. Longer door-to-puncture delays during the COVID-19 period were observed among included patients who arrived at the CSC using private transportation, which is unsurprising given prior experiences.^{22 23} Pre-hospital evaluation and notification by EMS and external providers can expedite the preparedness of the CSC interventional team and shorten delays from CSC arrival to skin puncture.^{24 25} While only a small proportion of patients included in this analysis presented by private vehicle/walk-in (7% of cohort), the effect of private transport on EVT throughput is likely a significant underestimation of the national

Table 3 Candidate variables associated with door-to-puncture time in the primary analysis

Candidate variable	β (95% CI)	P-value	β_{adj} (95% CI)	P-value
Admission during COVID-19 period	-41.9 (-93.0 to 9.1)	0.11	-73.2 (-153.8 to 7.4)	0.07
Age (per tertile)	-3.0 (-39.7 to 33.8)	0.88		
Female	9.0 (-41.7 to 59.7)	0.73		
Hispanic	59.5 (-19.3 to 138.4)	0.14		
White	17.3 (-34.5 to 69.2)	0.51		
Hypertension	52.6 (-4.8 to 110.0)	0.07	57.1 (-1.3 to 115.5)	0.05
Dyslipidemia	53.2 (2.1 to 104.3)	0.04	22.8 (-39.2 to 84.7)	0.44
Diabetes	47.2 (-8.0 to 102.5)	0.09	32.3 (-36.6 to 101.1)	0.33
Atrial fibrillation	9.8 (-51.4 to 70.9)	0.75		
Tobacco use	49.3 (-14.8 to 113.3)	0.13		
Prior ischemic stroke	26.0 (-39.4 to 91.4)	0.44		
Coronary artery disease	32.7 (-43.7 to 109.2)	0.40		
Transfer vs direct CSC arrival	-55.1 (-107.6 to -2.6)	0.04	-40.4 (-122.2 to 41.3)	0.30
High-volume center*	13.5 (-40.3 to 67.4)	0.62		
NIHSS (per point)	-7.2 (-11.6 to -2.8)	<0.01	-5.9 (-13.9 to 2.1)	0.13
Intravenous thrombolysis	24.0 (-170.6 to 122.5)	0.75		
ICA, M1, or basilar occlusion	-26.0 (-87.6 to 35.7)	0.41		

Variables were included in the final multivariable model if they were significant to $P < 0.1$ in unadjusted regression. The final multivariable model was clustered by site.

*A high-volume stroke center was defined as having performed 50 or more thrombectomies during 2019, as this volume threshold has been shown to improve treatment times. CI, confidence interval; COVID-19, coronavirus disease 2019; EMS, emergency medical services; ICA, internal carotid artery; NIHSS, National Institutes of Health Stroke Scale.

(and international) experience. This study was limited to the experience of CSCs which are vastly outnumbered by Primary Stroke Centers, urgent care facilities, and community hospitals where these patients may initially present. Therefore, we would continue to encourage patients to call for emergency services in the event of a sudden, significant neurologic symptom. Earlier symptom recognition in the field and at non-CSCs can expedite reperfusion therapies.

Regarding other time metrics in the acute care of patients with intracranial occlusion, we found no significant delay in arrival to first head imaging at participating CSCs. Presumably, any delay in the acute care of patients treated in the emergency department during the COVID-19 pandemic would relate to initial triage as providers are committing more time and attention to contact precautions, hygiene, and decontamination. However, there appeared to be no difference in time from CSC arrival to first head imaging between patients admitted during COVID-19 vs the 2019 seasonal control period (or among patients admitted during local COVID-19 peaks vs the preceding period). In a related study, we found a small but significant 8-min decrease in arrival to first head imaging among patients evaluated during the COVID-19 pandemic, including patients without an intracranial occlusion (median 29 vs 37 min, $P < 0.01$).¹ It is possible that faster imaging times may not have been observed in this cohort due to its smaller sample size or more restrictive inclusion criteria.

Unsurprisingly, patients who were transferred from an outside hospital with an acute ischemic stroke had faster treatment times. In the primary analysis, shorter door-to-puncture times among patients transferred vs those who arrived initially at the CSC was no longer significant after adjustment for measurable confounders. However, when state-specific COVID-19 peaks were evaluated, there remained a strong and independent relationship between transfer status and shorter door-to-puncture times.

Of note, there was a significant difference in discharge disposition among hospitalized patients during COVID-19 when compared with the seasonal control. This is likely mediated by several indirect effects of the pandemic. First, patients admitted during COVID-19 typically have more severe disease and more comorbidities, as we have shown in an overlapping cohort.²⁶ Therefore, the in-hospital mortality risk would be expectedly higher in this population. Second, unprecedented depletion of acute care beds to manage patients with COVID-19 has been met with a commensurate decrease in available inpatient rehabilitation and nursing beds for discharge-eligible patients.²⁷ In order to safely and efficiently discharge patients with stroke and other medical diseases, many patients have been (and are being) discharged to home with home or outpatient services, and close neuro-medical follow-up. It is possible that a small proportion of these patients would have otherwise benefited from more aggressive inpatient rehabilitation, however constraints on medical infrastructure have demanded creative, patient-level responses during this pandemic.^{28 29}

Our investigation is unique in that we conducted an analysis that accounted for the first local COVID-19 peak in each state. As shown in figure 1, several states (notably California, Florida, Georgia, Ohio, and Texas) experienced delayed surges in COVID-19 cases. Therefore, an analysis limited to the first few months of the pandemic in the US might have been too early to detect any impact of COVID-19 surges on treatment times in these regions. In this secondary analysis—while the sample size was lower than that of the primary analysis—there was still no statistically or clinically significant difference in treatment times between pre-peak and peak periods.

Limitations

While this study is the largest pooled data set reflecting multiple unique regions in the US affected by the COVID-19

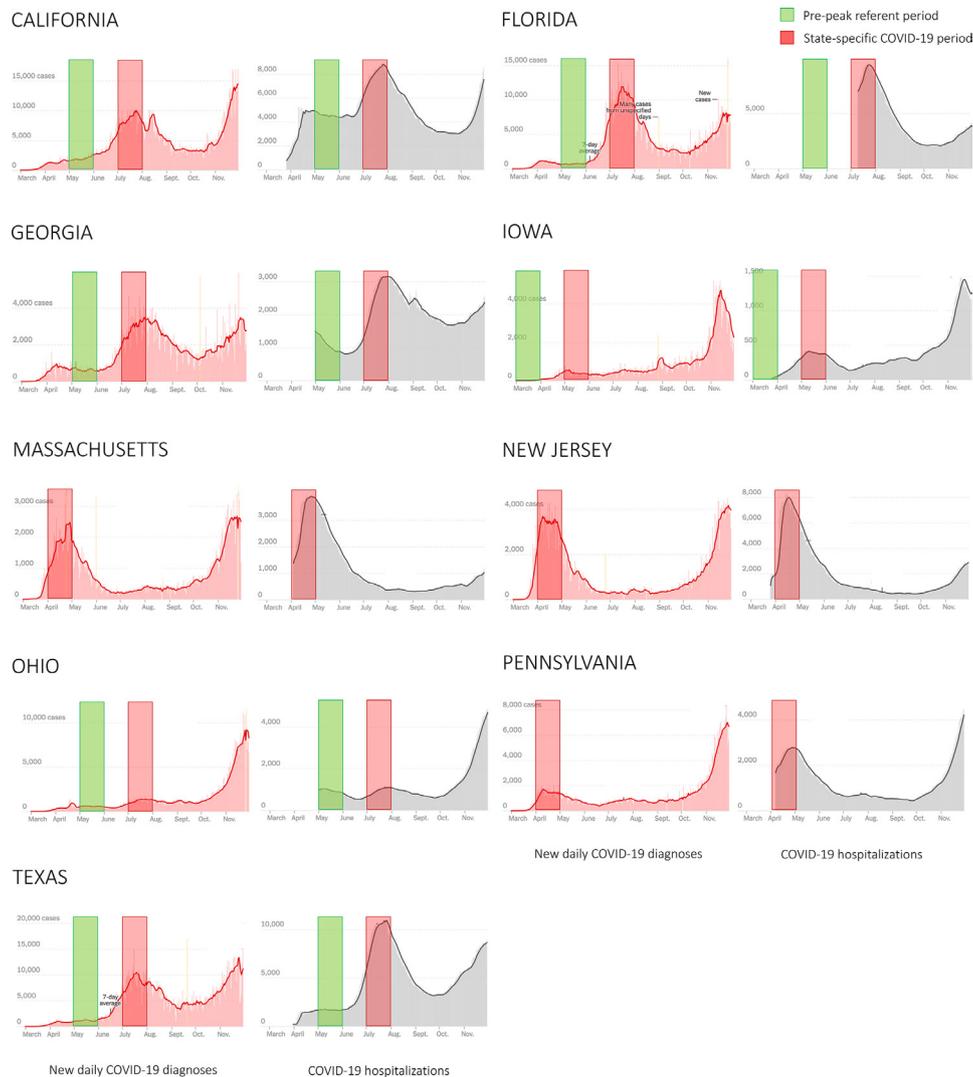


Figure 1 State-specific COVID-19 peak and pre-peak periods for secondary analysis. April 2020 was selected as the month of the first COVID-19 peak for New Jersey (n=2 sites), Pennsylvania (n=2 sites), and Massachusetts (n=1 site); May 2020 as the first COVID-19 peak for Iowa (n=1 site); and July 2020 the first COVID-19 peak for Texas (n=2 sites), Ohio (n=2 sites), Georgia (n=2 sites), Florida (n=1 site), and California (n=1 site). COVID-19 denotes coronavirus disease 2019.

pandemic, it is limited by its retrospective and exploratory nature. The brief study periods and small sample size included in the primary and secondary analyses may have contributed to a type II error. Certain data elements, such as vital signs on admission and variables related to social history or emergency department volume, may have also contributed to delays in endovascular treatment times, but these data were not available from the consolidated prospective registries. In spite of these limitations, we still believe there to be no clinically significant delay in EVT as a consequence of the pandemic. If anything, there appeared to be a trend toward shorter arrival to EVT times during the COVID-19 pandemic when compared with identical months in the preceding year ($p_{adj}=0.07$).

The lack of available long-term outcome data in the present analysis, and lack of adjustment for COVID-19 infection status among included patients are other shortcomings of this study. However, as we have previously shown using data that overlaps with this registry,³⁰ the prevalence of ischemic stroke in patients with COVID-19 was 1.1%–1.4% with approximately half of these patients harboring

an intracranial occlusion. Although COVID-19-associated stroke is typically more severe, this low prevalence is unlikely to significantly confound the results of this investigation. Due to the recency of data consolidation for this analysis, long-term follow-up data remain unavailable. That said, the impact of delays in door-to-puncture have been extensively described in relation to long-term functional outcomes.³¹

In this multi-center observational registry representing the experience at 14 CSCs in nine US states, which accounted for nearly half of all reported COVID-19 cases during the early wave of the pandemic, we found no significant delay in thrombectomy among patients with acute intracranial occlusion. While the number of new LVO cases fell considerably, the proportion of thrombectomies increased among all intracranial occlusions, and among patients with proximal occlusions. While patients with mild strokes may be avoidant of the hospital,²⁶ further research is called upon to explore potential reasons for the decline in new LVOs. The majority of patients in this analysis were transferred from an outside institution to the CSC, and in general, treatment times were quicker for these patients when compared with

patients who presented via EMS or private vehicle. Treatment times remained significantly and independently shorter among patients who were transferred in the secondary analysis evaluating local COVID-19 peaks. Slower treatment among patients who present directly to CSC emergency departments remains a potential gap for the improvement in the care of patients with acute stroke. Centers are encouraged to evaluate their local paradigms for opportunities to facilitate the throughput of patients who arrive directly to their emergency department with stroke due to intracranial occlusion.

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REFERENCES

- 1 Siegler JE, Zha AM, Czap AL, *et al.* Influence of the COVID-19 pandemic on treatment times for acute ischemic stroke: the Society of Vascular and Interventional Neurology Multicenter collaboration. *Stroke* 2021;52:40–7.
- 2 Zhao J, Li H, Kung D, *et al.* Impact of the COVID-19 epidemic on stroke care and potential solutions. *Stroke* 2020;51:1996–2001.
- 3 Pop R, Quenardelle V, Hasiu A, *et al.* Impact of the COVID-19 outbreak on acute stroke pathways – insights from the Alsace region in France. *Eur J Neurol* 2020;27:1783–7.
- 4 Wang A, Mandigo GK, Yim PD, *et al.* Stroke and mechanical thrombectomy in patients with COVID-19: technical observations and patient characteristics. *J Neurointerv Surg* 2020;12:648–53.
- 5 Mansour OY, Malik AM, Linfante I. Mechanical thrombectomy of COVID-19 positive acute ischemic stroke patient: a case report and call for preparedness. *BMC Neurol* 2020;20:358.
- 6 Nguyen TN, Abdalkader M, Jovin TG, *et al.* Mechanical thrombectomy in the era of the COVID-19 pandemic: emergency preparedness for neuroscience teams: a guidance statement from the Society of Vascular and Interventional Neurology. *Stroke* 2020;51:1896–901.
- 7 Fraser JF, Arthur AS, Chen M, *et al.* Society of NeuroInterventional Surgery recommendations for the care of emergent neurointerventional patients in the setting of COVID-19. *J Neurointerv Surg* 2020;12:539–41.
- 8 Qureshi AI, Abd-Allah F, Al-Senani F, *et al.* Management of acute ischemic stroke in patients with COVID-19 infection: report of an international panel. *Int J Stroke* 2020;15:540–54.
- 9 Stroke Council Leadership A. Temporary emergency guidance to US stroke centers during the coronavirus disease 2019 (COVID-19) pandemic: on behalf of the American Heart Association. *Stroke* 2020;51:1910–2.
- 10 Aggour M, White P, Kulcsar Z, *et al.* European Society of Minimally Invasive Neurological Therapy (ESMINT) recommendations for optimal interventional neurovascular management in the COVID-19 era. *J Neurointerv Surg* 2020;12:542–4.
- 11 He Y, Hong T, Wang M, *et al.* Prevention and control of COVID-19 in neurointerventional surgery: expert consensus from the Chinese Federation of Interventional and Therapeutic Neuroradiology (CFITN) and the International Society for Neurovascular Disease (ISNVD). *J Neurointerv Surg* 2020;12:658–63.
- 12 Siegler JE, Jovin TG. Thrombolysis before thrombectomy in acute large vessel occlusion: a risk/benefit assessment and review of the evidence. *Curr Treat Options Neurol* 2020 https://doi.org/10.1007/s11940-020-00633-5&casa_token=FvMxT3upRH8AAAAA:Rjd8wzZlHiuQmsK2F7RFxyVmwXJS0QOepvFNzl-scgRS3TPA4cPmWSTIW4mAHd3oE5XM3DMGoZlyfNEA
- 13 Schull MJ, Vermeulen M, Slaughter G, *et al.* Emergency department crowding and thrombolysis delays in acute myocardial infarction. *Ann Emerg Med* 2004;44:577–85.
- 14 Jaffe TA, Goldstein JN, Yun BJ, *et al.* Impact of emergency department crowding on delays in acute stroke care. *West J Emerg Med* 2020;21:892–9.
- 15 Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020;20:533–4.
- 16 Coronavirus in the U S: latest map and case count. New York Times, 2020. Available: <https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html> [Accessed 1 Dec 2020].
- 17 Gupta R, Horev A, Nguyen T, *et al.* Higher volume endovascular stroke centers have faster times to treatment, higher reperfusion rates and higher rates of good clinical outcomes. *J Neurointerv Surg* 2013;5:294–7.
- 18 Desai SM, Guyette FX, Martin-Gill C, *et al.* Collateral damage – impact of a pandemic on stroke emergency services. *J Stroke Cerebrovasc Dis* 2020;29:104988.
- 19 Fontanella MM, De Maria L, Zanin L, *et al.* Neurosurgical practice during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic: a worldwide survey. *World Neurosurg* 2020;139:e818–26.

- 20 Jean WC, Ironside NT, Sack KD, *et al.* The impact of COVID-19 on neurosurgeons and the strategy for triaging non-emergent operations: a global neurosurgery study. *Acta Neurochir* 2020;162:1229–40.
- 21 Fiehler J, Brouwer P, Diaz C, *et al.* COVID-19 and neurointerventional service worldwide: a survey of the European Society of Minimally Invasive Neurological Therapy (ESMINT), the Society of NeuroInterventional Surgery (SNIS), the Sociedad IberoLatinoamericana de Neuroradiologia Diagnostica Y Terapeutica (SILAN), the Society of Vascular and Interventional Neurology (SVIN), and the World Federation of Interventional and Therapeutic Neuroradiology (WFITN). *J Neurointerv Surg* 2020;12:726–30.
- 22 Lacy CR, Suh DC, Bueno M, *et al.* Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology (S.T.R.O.K.E.). *Stroke* 2001;32:63–9.
- 23 Asif KS, Lazzaro MA, Zaidat O. Identifying delays to mechanical thrombectomy for acute stroke: onset to door and door to clot times. *J Neurointerv Surg* 2014;6:505–10.
- 24 Patel MD, Rose KM, O'Brien EC, *et al.* Prehospital notification by emergency medical services reduces delays in stroke evaluation: findings from the North Carolina Stroke Care Collaborative. *Stroke* 2011;42:2263–8.
- 25 Meretoja A, Strbian D, Mustanoja S, *et al.* Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology* 2012;79:306–13.
- 26 Ortega-Gutierrez S, Farooqui M, Zha A. Decline in mild stroke presentations and intravenous thrombolysis during the COVID-19 pandemic: SVIN multicenter collaboration. *Clin Neurol Neurosurg* 2020 <https://www.sciencedirect.com/science/article/pii/S0303846720307794?via%3Dihub>
- 27 Dohle C, Oh-Park M, Gitkind A, *et al.* The vital role of inpatient rehabilitation facilities in a large health system: the COVID-19 pandemic. *J Int Soc Phys Rehabil Med* 2020;3:75–9.
- 28 McNeary L, Maltser S, Verduzco-Gutierrez M. Covid-19 in psychiatry: a can report for inpatient rehabilitation facilities. *PM&R* 2019;2020:512–5.
- 29 Simpson R, Robinson L. Rehabilitation after critical illness in people with COVID-19 infection. *Am J Phys Med Rehabil* 2020;99:470–4.
- 30 Siegler JE, Cardona P, Arenillas JF. Cerebrovascular events and outcomes in hospitalized patients with COVID-19: the SVIN COVID-19 multinational registry. *Int J Stroke* 2020 https://journals.sagepub.com/doi/10.1177/1747493020959216?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20pubmed
- 31 Saver JL, Goyal M, van der Lugt A, *et al.* Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA* 2016;316:1279–88.