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Adaptive Approach to Endovascular Management of Large Vessel Occlusion During the COVID-19 Pandemic

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Introduction: The COVID-19 pandemic has resulted in unprecedented strain on the health care system. An adaptive strategy for the handling of thrombectomy for patients with large vessel occlusion has evolved at our center to optimize patient care while also minimizing risk of virus transmission. The purpose of this study was to evaluate the effects of the new thrombectomy protocol by comparing thrombectomy times and patient outcomes during the pandemic and pre pandemic period. *Methods:* A retrospective cohort study was conducted on patients who underwent emergent thrombectomy from April 4th, 2020 to August 25th, 2020 (pandemic period) and between December 2nd, 2019 to April 3rd, 2020 (pre-pandemic period). The new protocol centered on a standardized approach to airway management in patients considered 'high-risk' for infection. An array of patient-specific factors and outcomes were compared between the two groups. *Results:* A total of 126 patients were included in the study. There was no significant difference in door-to-recanalization or other time parameters between the two groups (138 minutes during the pandemic vs. 129 minutes pre-pandemic; p=0.37). However, outcomes measured as discharge modified Rankin Scale (mRS) were worse for patients during the pandemic (mRS $\leq$ 2, 10/58; 17.2% during pandemic vs. 24/68; 35.3% pre-pandemic, $p = 0.02$). No neurointerventional providers have been found to contract COVID-19. *Conclusion:* Our approach to mechanical thrombectomy during the COVID-19 era was associated with similar recanalization rates but worse clinical outcomes compared to pre pandemic period. Further studies are necessary to identify factors contributing to worse outcomes during this ongoing pandemic.

Key Words: Mechanical thrombectomy—Large vessel occlusion—ischemic—stroke—COVID-19—outcomes—management

Introduction

The COVID-19 pandemic has increased the complexity of endovascular treatment of large vessel occlusion (LVO) in acute ischemic stroke. In response to the pandemic, stroke centers have undergone substantial reorganization and alterations to mechanical thrombectomy protocols.[1,2] Recent studies suggest trends in increased time from hospital arrival to puncture and hospital arrival to reperfusion, despite reported reductions in acute stroke cases.[3] The additional time required to screen patients and protect hospital staff against COVID-19 exposure are potential explanations for these delays.[4,8,9] However, patient transport, evaluation, and preparations for intervention during the era of a pandemic have also added to patient management complexity, which have a negative influence on clinical outcomes.

Many institutions have proposed guidelines to streamline the interventional process for thrombectomy candidates.[5] Additionally, mandated staff simulation training has also been used to incorporate these newly established protocols with the goal of improving efficiency.[6] Despite unprecedented demands on the emergency healthcare services, early multidisciplinary efforts to adapt the acute stroke treatment process have resulted in maintaining stroke quality time metrics close to pre-pandemic levels.[7]

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The purpose of this study was to evaluate how changes in thrombectomy management have influenced outcomes at a single comprehensive stroke center.

Methods

This is a single-center retrospective review of patients who underwent thrombectomy for acute ischemic stroke from April 4th, 2020 to August 25th, 2020 (pandemic period) and between December 2nd, 2019 to April 3rd, 2020 (pre-pandemic period). These dates were chosen because they represented a similar overall time interval, yielding a nearly equivalent sample size. Additionally, April 4th signified the date in which an adjusted code stroke protocol was in effect.

Patients who presented to the emergency department, either by emergency medical services or outside hospital transfer, were included in the study. Additionally, all patients underwent emergent thrombectomy for large vessel occlusion (limited to occlusion of the internal carotid artery, M1 segment of the middle cerebral artery, or basilar artery). All large vessel occlusions were confirmed by computed tomography (CT) angiography of the head. Appropriate candidates for thrombectomy were determined by a stroke neurologist and a neuro-interventionalist based on time of symptom onset, baseline functional status, admission National Institutes of Health Stroke Scale (NIHSS) score, favorable pre-procedural imaging studies (CT Head without contrast and CT Perfusion), and clinical judgement.

The following patient specific variables and stroke timing metrics were collected via the electronic medical record: age, gender, method of arrival, time of symptom onset, intravenous alteplase administration, admission NIHSS, site of large vessel occlusion, time from arrival to code-stroke activation, time from arrival to imaging obtained, time from arrival to femoral artery puncture, time from arrival to first attempt at thrombectomy (first pass), time from arrival to vessel recanalization, time from puncture to vessel recanalization, time from last-known-well (LKW) to recanalization, procedure performed with the use of general anesthesia or conscious sedation, modified thrombolysis in cerebral ischemia (TICI) score, modified Rankin Scale (mRS) at the time of discharge, and discharge disposition. The TICI score was further stratified into 'favorable' and 'unfavorable' groups; TICI score $\geq$ 2b was considered a favorable result. The mRS at the time of discharge was divided into favorable and unfavorable outcomes; mRS $\leq$ 2 was considered favorable and mRS $\geq$ 3 was considered an unfavorable outcome. Discharge disposition was also divided into two categories: 1) patients discharged home or to an inpatient rehabilitation facility; 2) patients discharged to a nursing home, long-term acute care hospital, hospice or expired. Institutional Review Board (IRB) approval was obtained based on institutional protocol.

Statistical analysis

The difference in means of the two cohorts were compared utilizing a Mann-Whitney U test and categorical variables were compared using chi-square testing. A p -value of < 0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to determine independent predictors of outcome. Statistical analysis was performed with *IBM SPSS Statistics 26* software.

Pre-pandemic protocol

Prior to the pandemic, the decision to perform thrombectomy with the use of general anesthesia versus conscious sedation was determined based on the patient's hemodynamic and airway stability, neurologic exam, and ability to safely cooperate during the procedure. Historically, approximately half of the thrombectomies performed at our institution are done under conscious sedation rather than general anesthesia, with no apparent implications on discharge disposition or mortality rates.[16] When GA is employed, our pre-pandemic protocol involves intubation in the angiography suite by the anesthesia team, rather than in the emergency department by an emergency medicine physician.

Adaptive code stroke protocol

Effective on April 4, 2020, an institutional code stroke protocol was implemented for the evaluation of patients presenting to the emergency department with symptoms of an acute ischemic stroke which accounted for a recent rise in COVID-19 cases in the state of Alabama. The protocol was formulated based on a 'Guidance Summary for Large Vessel Occlusion in the era of COVID-19.[5] The protocol was intended to protect healthcare workers from possible COVID-19 exposure while efficiently preparing and executing MT. There were no changes made in the selection criteria or pre-procedural imaging process in determining appropriate candidates for thrombectomy. All patients who presented with signs or symptoms of acute ischemic stroke were treated as 'high risk,' or 'person-under-investigation' (PUI), regardless of any symptoms concerning for a concomitant COVID-19 infection. A nasal swab COVID-19 test was obtained immediately upon arrival. A negative pressure isolation room was prepared prior to patient arrival to the emergency department. All patients who were determined to be candidates for thrombectomy were intubated in the emergency department in a negative pressure isolation room. Intubation was performed by an emergency medicine physician. The subsequent procedures were conducted under general anesthesia (GA) with involvement of the anesthesia team. Post-intubation chest radiographs were deferred, and appropriate endotracheal tube placement was confirmed via live fluoroscopy during the procedure.

Results

A total of 126 patients were included in the study (58 in the pandemic group vs. 68 in the pre-pandemic group). Two patients tested positive for COVID-19 in the pandemic group (3.4%). Patient-specific variables and admission characteristics are presented in Table 1. There was no statistically significant difference in patient demographics and pre-procedural characteristics.

Fewer patients were discharged with mRS $\leq$ 2 in the pandemic cohort when compared to the pre-pandemic cohort (17.2% vs. 35.3% respectively, p = 0.023). There was a non-significant trend toward longer door to puncture and door to first pass times ($p = 0.07$) in the pandemic group, but no significant difference in door to recanalization time ($p = 0.37$). There was no statistically significant difference in mortality ($p = 0.576$), successful recanalization (TICI $\geq$2b, $p = 0.728$), or discharge disposition ($p = 0.204$) between the two cohorts (Table 2). On multivariate logistic regression analysis, admission NIHSS $\geq$ 15 was an independent predictor of poor outcome defined by mRS > 2 (OR 3.31, [95% CI 1.44−7.58], $p = .005$).

To our knowledge, no neurointerventional or stroke neurology personnel have contracted COVID-19 during the interval of this study.

Discussion

This study demonstrates that through an adaptive code stroke protocol which standardizes airway management, our institution has experienced stroke care timing metrics similar to before the pandemic. Despite this, patient functional outcomes have been worse.

One variable that may account for the decline in our functional outcomes at discharge is the elective intubation and routine use of general anesthesia for all patients undergoing thrombectomy during the pandemic. This aspect of our protocol is in accordance with recent recommendations to treat all patients with unknown COVID-19 infection status as 'high risk', and to have a low threshold for elective intubation.[10] Recent reports of increasing incidence of asymptomatic COVID-19 carriers have made the reliability of screening for symptoms, rather than nasal swab testing, of pre-thrombectomy patients uncertain.[11] In response to this, our center has classified all patients undergoing thrombectomy as 'high infection-risk,' or persons under investigation (PUI). Endotracheal intubation provides a theoretically reduced risk of infection transmission to healthcare personnel due to ventilation within a closed circuit. Similar results are suggested by a recent multi-institutional prospective study in which patients who underwent thrombectomy under general anesthesia (GA) had a higher probability of in-hospital mortality and lower probability of functional independence at discharge.[12] However, unlike in the present study, door-to-puncture and door-to-reperfusion times were significantly increased in the GA group.

The standardization of airway management has streamlined pre-procedural preparations. This process has contributed to a pre-pandemic level of efficiency. Although there have been national trends toward more liberal use of GA for mechanical thrombectomy (MT) in response to the pandemic, our center's policy of intubating all-comers is unlike any other currently documented protocols in the literature. The threshold for which to incorporate GA for patients undergoing thrombectomy during the pandemic remains a subject of debate. More specifically, Nguyen et al. recommend conscious sedation as first line for thrombectomy in candidates with unknown COVID-19 status, as it may minimize delays to treatment, optimize patient outcomes, conserve ventilator and critical care bed resources, and conserve anesthesiologist and staff exposure to the aerosolizing events of intubation and extubation.[17] Recent randomized control trials suggest that there is no significant difference in outcomes based on the use of general anesthesia versus conscious sedation during MT.[13-15] However, anesthetic induction and maintenance were highly controlled in these studies. During the pandemic, these variables were not consistently regulated. A recent study reports comparable stroke outcome data to the present study with regard to door-to-recanalization times and discharge outcomes.[7] The similarity in results despite differences in institutional protocols suggests that further studies are necessary to determine sources for poor outcomes during an ongoing pandemic.

Limitations of this study include the single-institution retrospective study design, lack of long-term follow up and a small sample size which precludes the ability to

Table 1. *Patient demographics and admission characteristics*

	Pre-Pandemic (n = 68)	Pandemic (n = 58)	p value
Mean age (years), ± SD	65 ± 12.6	67 ± 13.2	0.66
Gender, male, N (%)	43 (63.2%)	39 (67.2%)	0.71
Mean Admission NIHSS (IQR)	16.6 (9−22)	15.2 (10−20)	0.46
Anterior circulation stroke, N (%)	61 (89.7%)	52 (89.6%)	0.41
Presented directly to the emergency department, N (%)	20 (29.4%)	17 (29.3%)	0.96
Transferred from other centers, N (%)	48 (70.6%)	41 (70.7%)	0.96
Received intravenous alteplase, N (%)	29 (42.6%)	27(40.3%)	0.78

Table 2. *Comparison of stroke management time intervals and outcomes*

	Pre-pandemic (n = 68)	Pandemic (n = 58)	*p* value
Door to code stroke interval*	12 (10−14)	7 (5−14)	0.3
Door to imaging interval*	15 (4−26)	12 (5−16)	0.38
Door to puncture interval*	79 (53−86)	90 (61−101)	0.07
Door to first pass interval*	104 (89−120)	129 (87−140)	0.07
Door to recanalization interval*	129 (99−157)	138 (123−147)	0.37
Puncture to recanalization interval*	40 (25−67)	44 (23−65)	0.91
LKW to Recanalization interval*	487 (311−577)	481 (367−756)	0.93
Number of patients who underwent thrombectomy under GA	54 (79.4%)	58 (100%)	0.01
Number of patients with TICI score ≥ 2b	57 (83.8%)	50 (86.2%)	0.73
Number of patients with discharge mRS score ≤ 2	24 (35.3%)	10 (17.2%)	0.02
Number of patients with favorable disposition**	40 (58.8%)	35 (60.3%)	0.6
Mortality	10 (14.7%)	10 (17.2%)	0.57

*mean values reported in minutes (interquartile range);
**defined as discharge to home or inpatient rehabilitation, SD: standard deviation, IQR: interquartile range, LKW: last known well, GA: General anesthesia, TICI: thrombolysis in cerebral infarction, mRS: modified Rankin scale, NIHSS: National Institutes of Health Stroke Scale.

match for patient specific comorbidities. It is unclear how many patients had 'false-negative' COVID-19 screening tests, and if this ultimately played a role in the decline in outcomes. This distinction is important since patients with COVID-19 and LVO who undergo successful recanalization have notably poor outcomes despite optimal medical care.[18]

Conclusion

Through an adaptive code stroke protocol that standardizes airway management, our institution has experienced door-to-recanalization times similar to pre-pandemic metrics while minimizing risk of transmission of the virus to neuro-interventional staff. Despite this, functional outcomes have been worse, possibly due to the routine use of GA for all patients undergoing thrombectomy during the pandemic. With no obvious end in sight for an ongoing pandemic, additional studies are required to determine predictors of poor outcomes under these unique circumstances.

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