Impact of the COVID-19 pandemic on the process and outcome of thrombectomy for acute ischemic stroke

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ABSTRACT
Background The novel coronavirus disease 2019 (COVID-19) pandemic is still spreading across the world. Although the pandemic has an all-round impact on medical work, the degree of its impact on endovascular thrombectomy (EVT) for patients with acute ischemic stroke (AIS) is unclear.

Methods We continuously included AIS patients with large artery occlusion who underwent EVT in a comprehensive stroke center before and during the Wuhan shutdown. The protected code stroke (PCS) for screening and treating AIS patients was established during the pandemic. The efficacy and safety outcomes including the rate of successful reperfusion (defined as modified Thrombolysis In Cerebral Infarction [mTICI] graded 2b or 3) and time intervals for reperfusion were compared between two groups: pre-pandemic and pandemic.

Results A total of 55 AIS patients who received EVT were included. The baseline characteristics were comparable between the two groups. The time from hospital arrival to puncture (174 vs 125.5 min; p=0.002) and time from hospital arrival to reperfusion (213 vs 172 min; p=0.047) were significantly prolonged in the pandemic group compared with the pre-pandemic group. The rate of successful reperfusion was not significantly different between the two groups (85.7% [n=18] vs 88.2% [n=30]; OR 0.971, 95% CI 0.785 to 1.203; p=1.000).

Conclusion The results of this study suggest a proper PCS algorithm which combines the COVID-19 screening and protection measures could decrease the impact of the disease on the clinical outcomes of EVT for AIS patients to the lowest extent possible during the pandemic.

INTRODUCTION
Although the pandemic of the novel coronavirus disease 2019 (COVID-19) in China has been brought under control to some extent, as indicated by the end of the Wuhan shutdown on April 8, 2020, the virus is still spreading rapidly around the rest of the world and it is too early for us to ease off. Official data from the website of the World Health Organization (WHO) showed that up to April 14, more than 1840000 patients were diagnosed as confirmed cases all over the world, including 117021 deaths.1

During the pandemic, almost all elective operations have been deferred or even stopped because of the need for SARS-CoV-2 infection prevention and relocation of limited medical resources.2 Emergency surgeries such as endovascular thrombectomy (EVT) for acute ischemic stroke (AIS) must be performed without any delay even during the pandemic, in order to rescue important functions and save lives.1,3 However, the impact of the pandemic may be inevitable, because the hospitals have to take the necessary measures to prevent further spread of SARS-CoV-2 among medical personnel and patients.2 It can be expected that, given the current situation of the pandemic, strict prevention and control measures will remain and be implemented across the world for at least the next few months. It is still unclear whether the evaluation and treatment process and clinical outcomes of AIS patients who need EVT have been affected, and what we can do to ensure the quality of treatment of AIS patients as well as avoid the spread of SARS-CoV-2 during the pandemic.

Therefore, based on the data from a comprehensive stroke center, we compared the evaluation and treatment process as well as clinical outcomes of AIS patients who underwent EVT before and during the pandemic, with the aim of evaluating the impact of the pandemic on the process and outcome of EVT implementation for AIS patients.

METHODS
Patient selection and data collection
We continuously included all AIS patients treated with EVT in a comprehensive stroke center between January 23 and March 7, 2020 (44 days in total from the date of the Wuhan shutdown to the date of no newly confirmed cases locally) as the pandemic group. Similar patients with the same time span (44 days) between December 1, 2019 and January 14, 2020 were included as the pre-pandemic group. The Stroke Code team in our center was composed of seven attending physicians, five residents, eight nurses, five technicians and three anesthetists. All confirmed and suspected COVID-19 patients were transferred to designated hospitals in accordance with the guidelines of the National Health Commission2 and thus excluded from this study. The following data were obtained from our prospective database: patient demographics, past medical history, presenting National Institutes of Health Stroke Scale (NIHSS), Alberta Stroke Program Early CT Score (ASPECTS), site of thrombus, side of thrombus, therapeutic interventions, preintervention and postintervention modified Thrombolysis In Cerebral Infarction (mTICI)
The screening and interventional process for acute ischemic stroke patients during the COVID-19 pandemic. CTA, CT angiography; CTP, CT perfusion.

Protected code stroke

The regular code stroke algorithm was used to prioritize the hyperacute assessment and care of a patient presenting with clinical manifestations for stroke. However, during the pandemic, the algorithm needed to be modified to the protected designation to provide an additional layer of protection for patients and medical personnel who were engaged in triage, rapid assessment, and treatment of patients. Herein, we established a protected code stroke (PCS) for AIS patients who need EVT during the pandemic based on expert consensus from the Chinese Federation of Interventional and Therapeutic Neuroradiology and the Chinese Society of Cardiology (figure 1).

On arrival at the emergency department (ED), each patient was screened and evaluated for AIS by a stroke team. The personnel at the ED were equipped with adequate personal protective equipment (PPE). Additional screening for COVID-19, including travel history, body temperature measurement, complete blood count and chest CT, were performed simultaneously. The patient triage was done by multidisciplinary consultation based on the above screening results, as shown in figure 1. In short, COVID-19 clinically negative patients who needed EVT were treated in a routine angio-suite with standard surgical protection. COVID-19 clinically positive or suspected patients were treated in a dedicated angio-suite with the highest level of protection and transferred to a dedicated COVID-19 ward (for positive cases) or COVID-19 casualty ward (for suspected cases) after the procedure. The involved personnel were pre-alerted for adopting adequate PPE. A real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay for COVID-19 nucleic acid was not a routine test for AIS patients because of the limited access at the early stage of the pandemic and the urgent nature of evaluation and treatment for AIS. Only clinically confirmed and suspected cases diagnosed by multidisciplinary consultation according to the guidelines of the National Health Commission received further nucleic acid testing. The regular angio-suites in our center do not contain a negative-pressure system, so were unsuitable for the treatment for patients with an infectious disease like COVID-19. We therefore converted one of the regular angio-suites into a dedicated angio-suite with a negative-pressure system immediately after the outbreak of the pandemic, in order to meet the necessary requirements.

Procedure

Local anesthesia was recommended during the procedure, but general anesthesia was chosen if the patient was irritable and uncooperative. Intravenous heparin would be administered if thrombolysis was not performed. Any mechanical stent retriever (Solitaire, Medtronic and Trevo, Stryker; Irvine, CA, and Freemont, CA, respectively) or aspiration catheter (Penumbra System, Penumbra, Alameda, CA) and distal access catheter (Navien, Medtronic, Sofia Plus, MicroVention and Catalyst, Stryker; Irvine, CA, Tustin, CA and Freemont, CA, respectively) were approved for use. Any procedure such as a direct aspiration first-pass technique (ADAPT), stent retrieval, or stent retriever combined with aspiration (Solumbra technique) was permitted to be performed. The decisions as to whether to use a rescue therapy and which technique to use were left at the discretion of the surgeon. Permitted rescue techniques were intra-arterial tirofiban and angioplasty with or without stenting. Angiographic success was defined as achieving thrombolysis in mTICI grade 2b or 3.

Outcomes

The primary outcome was the rate of successful reperfusion defined as an mTICI grade 2b or 3 assessed on angiography. Secondary outcomes included the change in the NIHSS score from baseline to 3 days after the procedure, and the safety outcome which was defined as a composite of all-cause mortality at 3 days after the procedure, intracerebral hemorrhage (ICH) on brain imaging at 24±12 hours after the procedure, and procedure-related serious adverse events (arterial perforation, arterial dissection, and subarachnoid hemorrhage (SAH)).

Statistical analysis

Categorical variables are reported as frequencies and percentages. Quantitative variables are reported as mean±SD or median (IQR) for non-normal distribution. Differences in continuous variables were assessed with the Mann-Whitney U test with non-normal distribution. Differences between proportions were assessed with the χ² test or Fisher’s exact test. Differences were considered statistically significant at p<0.05. Data were analyzed using SPSS version 22.0 software package (IBM Corp, Armonk, NY).
RESULTS
Baseline characteristics
A total of 167 AIS patients were screened in the ED; 112 of them were declined for EVT due to low NIHSS scores, high modified Rankin Scale (mRS) scores, no obvious mismatch on multimodal CT scan, no evidence of large artery occlusion or refusal to undergo EVT. Fifty-five patients (mean±SD age, 65.1±13.1 years; 37 men (67.3%)) with AIS caused by intracranial large artery occlusion were finally included (table 1): 34 (61.8%) in the pre-pandemic group and 21 (38.2%) in the pandemic group, treated before and during the Wuhan shutdown, respectively. No statistically significant differences in all baseline characteristics were found between the two groups. All 21 patients in the pandemic group went through additional screening for COVID-19, including chest CT scans and multidisciplinary consultations during the evaluation process. One patient was screened as a clinically suspected case of COVID-19 and PCS was launched throughout the procedure until the diagnosis of COVID-19 was ruled out by further examinations. The median (IQR) preoperative NIHSS score was 13 (11–17) in the pre-pandemic group and 12 (11–18) in the pandemic group (p=0.537). The median baseline ASPECTS and time from symptom onset to hospital arrival in both groups were similar. None of our team members has been infected by SARS CoV-2.

Outcomes
The primary outcome, the rate of successful reperfusion, was not significantly different in the pre-pandemic group versus the pandemic group (88.2% (n=30) vs 85.7% (n=18); OR 0.971, 95%CI 0.785 to 1.203; p=1.000) (table 2, figure 2).

Compared with the pre-pandemic group, hospital arrival to puncture time (174 vs 125.5 min, p=0.002) and hospital arrival to reperfusion time (213 vs 172 min, p=0.047) in the pandemic group was prolonged significantly. No difference in anesthesia approaches (67.6% vs 85.7%; OR 1.267, 95%CI 0.947 to 1.695; p=0.240), puncture to reperfusion time (32 vs 40.5 min, p=0.231), and the first-line choice of thrombectomy technique and rescue treatment after first-line strategy (29.4% vs 23.8%; OR 0.810, 95%CI 0.321 to 2.043; p=0.650) was revealed between the two groups. Early improvement in neurological outcomes was not significantly different between the two groups, with no obvious change in NIHSS score at 24 hours in both groups (table 2).

DISCUSSION
In this retrospective study during the COVID-19 pandemic, we evaluated the impact of the PCS algorithm (figure 1) on EVT for AIS patients by comparing its process and clinical outcomes between the pre-pandemic period and the pandemic period. The results showed: (1) hospital arrival to puncture time and hospital arrival to reperfusion time were significantly prolonged during the pandemic compared with the pre-pandemic period (table 2); (2) puncture to reperfusion time decreased by an average of 10 min but without statistical significance (table 2); (3) rate of successful reperfusion and other clinical outcomes were all comparable between the two groups (table 2 and figure 2).

Table 1 Baseline characteristics of AIS patients treated with EVT in the pre-pandemic and pandemic groups

| Gender, male, n (%) | Pre-pandemic group | Pandemic group | OR (95% CI) | P value |
|---------------------|---------------------|----------------|-------------|---------|
| Age, meansD, years  | 65.2±13.1           | 62.3±12.8      | NA          | 0.431   |
| Hypertension, n (%) | 20 (58.8%)          | 16 (76.2%)     | 1.295 (0.895 to 1.874) | 0.188   |
| Diabetes mellitus, n (%) | 12 (35.3%) | 6 (28.6%) | 0.810 (0.358 to 1.829) | 0.606   |
| Hyperlipidemia, n (%) | 2 (5.9%) | 0 | NA | 0.519   |
| Coronary heart disease, n (%) | 9 (26.5%) | 3 (14.3%) | 0.540 (0.165 to 1.770) | 0.476   |
| Myocardial infarction, n (%) | 2 (5.9%) | 0 | NA | 0.519   |
| Atrial fibrillation, n (%) | 9 (26.5%) | 6 (28.6%) | 1.079 (0.449 to 2.597) | 0.865   |
| Cerebral infarction, n (%) | 2 (5.9%) | 3 (14.3%) | 2.429 (0.442 to 13.354) | 0.359   |
| Anticoagulation, n (%) | 5 (14.7%) | 0 | NA | 0.174   |
| Antiplatelet, n (%) | 1 (2.9%) | 0 | NA | 1.000   |
| Pulmonary inflammation on chest CT, n (%) | NA | 6 (28.6%) | NA | NA   |
| Pre-NIHSS score, median (IQR) | 13 (11–17) | 12 (11–18) | NA | 0.537   |
| ASPECTS, median (IQR) | 9 (8–10) | 9 (8–10) | NA | 0.727   |
| Anterior circulation, n (%) | 28 (82.4%) | 13 (61.9%) | 0.752 (0.519 to 1.088) | 0.091   |

**Stroke etiology**

- Cardioembolic, n (%) | 15 (44.1%) | 9 (42.9%) | 0.971 (0.521 to 1.810) | 0.249   |
- Large vessel atherosclerosis, n (%) | 13 (38.2%) | 11 (52.4%) | 1.370 (0.759 to 2.473) | 0.359   |
- Tandem lesion, n (%) | 5 (14.7%) | 0 | NA | 0.174   |
- Dissection, n (%) | 1 (2.9%) | 1 (4.8%) | 1.619 (0.107 to 24.526) | 0.212   |
- Use of rt-PA | 12 (35.3%) | 11 (52.4%) | 1.484 (0.806 to 2.734) | 0.212   |
- Onset to hospital arrival, median (IQR), min | 322 (166–420) | 253 (191–441) | NA | 0.315   |

AIS, acute ischemic stroke; ASPECTS, Alberta Stroke Program Early CT score; EVT, endovascular thrombectomy; IQR, interquartile range (25–75%); NA, not applicable; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator.
Table 2  Procedural details and clinical outcomes of EVT for AIS patients in pre-pandemic and pandemic groups

|                              | Pre-pandemic group | Pandemic group | OR (95% CI) | P value |
|------------------------------|--------------------|----------------|-------------|---------|
| mTICI 2b–3, n (%)            | 30 (88.2)          | 18 (85.7)      | 0.971 (0.785 to 1.203) | 1.000   |
| Local anesthesia, n (%)      | 23 (67.6)          | 18 (85.7)      | 1.267 (0.947 to 1.695) | 0.240   |
| ADAPT as the first choice, n (%) | 10 (29.4)         | 9 (42.9)       | 1.457 (0.711 to 2.987) | 0.308   |
| Solumbra as the first choice, n (%) | 18 (52.9)         | 10 (47.6)      | 0.899 (0.519 to 1.558) | 0.701   |
| Stent retriever as the first choice, n (%) | 3 (8.8)            | 0              | NA          | 0.279   |
| Rescue treatment, n (%)      | 10 (29.4)          | 5 (23.8)       | 0.810 (0.321 to 2.043) | 0.650   |
| Balloon angioplasty, n (%)   | 4 (11.8)           | 4 (19.0)       | 1.619 (0.453 to 5.792) | 0.464   |
| Stent placement, n (%)       | 8 (23.5)           | 1 (4.8)        | 0.202 (0.027 to 1.505) | 0.146   |
| Hospital arrival to puncture time, median (IQR), min | 125.5 (113–153) | 174 (139–204) | NA | 0.002 |
| Puncture to reperfusion time, median (IQR), min | 40.5 (28.5–55.5) | 32 (28–43) | NA | 0.231 |
| Hospital arrival to reperfusion time, median (IQR), min | 172 (148–218.5) | 213 (177–256) | NA | 0.047 |
| Onset to reperfusion time, median ±SD, min | 478.28±160.6 | 511.68±213.54 | NA | 0.529 |
| 24 hours NIHSS score, median (IQR) | 14 (6–40)          | 10 (6–40)      | NA | 0.380 |
| 72 hours NIHSS score, median (IQR) | 8 (5–14)           | 8 (4–21)       | NA | 0.675 |
| Overall adverse events, n (%) | 12 (35.3)          | 6 (28.6)       | 0.810 (0.358 to 1.829) | 0.606   |
| Subarachnoid hemorrhage, n (%) | 3 (8.8)            | 4 (19.0)       | 2.159 (0.535 to 8.707) | 0.408   |
| All intracranial hemorrhage, n (%) | 9 (26.5)          | 3 (14.3)       | 0.540 (0.165 to 1.770) | 0.467   |
| Hemorrhagic transformation, n (%) | 7 (20.6)           | 2 (9.5)        | 0.463 (0.106 to 2.021) | 0.482   |

ADAPT, a direct aspiration first pass technique; AIS, acute ischemic stroke; EVT, endovascular thrombectomy; IQR, interquartile range (25–75%); mTICI, modified Thrombolysis In Cerebral Infarction; NA, not applicable.

Figure 2  (A) The mTICI grade distribution. No significant difference was revealed between the pre-pandemic and pandemic groups. (B) The time intervals from onset to successful reperfusion. Compared with the pre-pandemic group, the time from hospital arrival to puncture time (174 vs 125.5 min, p=0.002) and hospital arrival to reperfusion time (213 vs 172 min, p=0.047) in the pandemic group was prolonged significantly. HTP, hospital arrival to puncture; mTICI, modified Thrombolysis In Cerebral Infarction; OTH, onset to hospital arrival; PTR, puncture to reperfusion.

Yang B, et al. J NeuroIntervent Surg 2020;12:664–668. doi:10.1136/neurintsurg-2020-016177 667
The prolonged hospital arrival to puncture time (by 48.5 min, p=0.002) and hospital arrival to reperfusion time (by 41 min, p=0.047) mainly reflected the delay caused by the COVID-19 screening process. In accordance with guidelines of the National Health Commission, all hospitals need to conduct strict COVID-19 screening for all newly admitted patients, including emergency cases. The screening included taking a travel history, chest CT scanning, complete blood count test, body temperature measurement and the ensuing multidisciplinary consultation. Although this screening was started simultaneously with the screening for AIS, and patient transfer among different departments within the hospital was facilitated, it still delayed the subsequent treatment. Another reason was perhaps the launch of PCS. A middle-aged patient was diagnosed as a clinically suspected case of COVID-19 by the multidisciplinary consultation based on fever, abnormal lymphocyte count and signs of inflammation in the chest CT; thus PCS was triggered and EVT was performed under the highest level of protection. Postoperative mTICI 2b recanalization was achieved. Hospital arrival to puncture time was 287 min, 46 min longer than the average hospital arrival to reperfusion time (241 min). On the other hand, our results showed the lengthy increases of hospital arrival to puncture time and hospital arrival to reperfusion time did not impact the short-term outcomes. The currently available data in this study were not enough to explain the above situation. Although there was no significant difference in relation to short-term outcomes, we did not have the long-term follow-ups (eg, 90 day mRS scores) to evaluate the long-term efficacy. Whether the delayed window size for treatment had an impact on the long-term outcomes is thus still unclear. Both situations need further studies.

In conclusion, the PCS algorithm which combines COVID-19 screening and protection measures could decrease the impact of the disease on the clinical outcome of EVT for AIS patients to the lowest extent possible during the pandemic. This needs to be confirmed by future well-designed studies.

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REFERENCES
1 World Health Organization. Coronavirus disease (COVID-19). Available: https:// covid19.who.int/ [Accessed 15 Apr 2020].
2 Gagliano A, Villani PG, Co’ FM, et al. COVID-19 epidemic in the middle province of Northern Italy: impact, logistics, and strategy in the first line hospital. Disaster Med Public Health Prep 2020;24:1–5.
3 Zangrillo A, Beretta L, Silvani P, et al. Fast reshaping of intensive care unit facilities in a large metropolitan hospital in Milan, Italy: facing the COVID-19 pandemic emergency. Crit Care Resusc 2020.
4 Powers Wu, Rabinstein AA, Ackersten T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 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:e344–418.
5 National Health Commission of the People’s Republic of China. Protocol for diagnosis and treatment of COVID-19. 7th edn, 2020. http://www.gov.cn/zhengce/202003/06/content_5481772.htm
6 Khosravani H, Rajendram P, Notario L, et al. Protected code stroke: hyperacute stroke management during the coronavirus disease 2019 (COVID-19) pandemic. Stroke 2020;STROKEAHA120029838.
7 Hong T, Yi M, Chen F, et al. Expert consensus on prevention and control for the 2019-novel coronavirus infection in neurointervention (first edition). Chin J Cerebrovasc Dis 2020;17:107–12.
8 Han Y, Zeng H, Jiang H, et al. CSC expert consensus on principles of clinical management of COVID-19 patients with severe emergent cardiovascular diseases during the COVID-19 epidemic. Circulation 2020. doi:10.1161/CIRCULATIONAHA.120.047011. [Epub ahead of print: 27 Mar 2020].
9 Turk AS, Spriotta A, Frei D, et al. Initial clinical experience with the ADAPT technique: a direct aspiration first pass technique for stroke thrombectomy. J NeuroInterv Surg 2014;6:231–7.
10 Delgado Almendros JF, Kayan Y, Young ML, et al. Comparison of clinical outcomes in patients with acute ischemic strokes treated with mechanical thrombectomy using either Solantra or ADAPT techniques. J NeuroInterv Surg 2016;8:1123–8.
11 Mehta T, Male S, Quinn C, et al. Institutional and provider variations for mechanical thrombectomy in the treatment of acute ischemic stroke: a survey analysis. J NeuroInterv Surg 2019;11:884–90.