Influence of coronavirus disease 2019 (COVID-19) on working flow, safety and efficacy outcome of mechanical thrombectomy for acute ischemic stroke with large vessel occlusion

Xiaochuan Huo⁴, Raynald¹, Xuan Sun¹, Dapeng Mo³, Feng Gao¹, Ning Ma¹, Yilong Wang²,³,⁴, Yongjun Wang²,³,⁴ and Zhongrong Miao¹

Abstract
Aim: The epidemic of COVID-19 has greatly affect the world health care system, particular measures have been taken not only to provide safety for health care providers but also to maintain the treatment quality. We evaluate the effect of COVID-19 epidemic to acute ischemic stroke (AIS) patients with large vessel occlusion (LVO) received endovascular treatment (EVT) in our institution.

Methods: AIS patients with LVO who underwent EVT in the period of January 1st to April 30th between 2015 and 2020 from our stroke center. The baseline characteristics, working flow time, safety and efficacy outcome and the hospitalization status were retrospectively reviewed, compared and analyzed.

Results: There is significant decline in the number of AIS patients with LVO treated compared with the previous year (36 Vs 72 patients) during the epidemic period. The door to puncture time was significantly prolong (225 minutes versus 115 minutes) as well as the length of hospital stay with increase of the hospitalization costs ($P < 0.05$ for all). There is no significant difference on the safety and efficacy outcome, such recanalization rate, incidence of intracranial hemorrhage, functional independence and mortality during the epidemic ($P > 0.05$ for all).

Conclusions: Prolongation of the working time flow during the COVID-19 epidemic did not influence the safety and efficacy of EVT in AIS patients with LVO. However, special policy and particular measures in this circumstances is still need to evolve to improve the treatment quality.

Keywords
COVID-19, epidemic, acute ischemic stroke, large vessel occlusion, endovascular treatment

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Background
The incidence of global pandemic of coronavirus disease 2019 (COVID-19), has become a great challenge to the world health care system.¹ ² During the outbreak of COVID-19, many extreme and strict measures have been taken by the health care institute to control the spread of the disease,³ ⁴ such providing special quarantine wards for patients who contracted the disease, suspending all the routine outpatient clinics and elective procedures, and performed treatment only for very highly selective cases. Although stroke is a common disease with high prevalence, morbidity, mortality and recurrence rate,⁶ ⁷ many stroke centers, have greatly reduced functioning due to the fear of in-hospital cross infection and lack of experienced stroke care physicians.

To address this issue, the Society of NeuroInterventional Surgery has given recommendations for the care of emergent neurointerventional patients in the setting of COVID-19². An emphasis on safety measures for health care providers were highlighted in this recommendation, suggesting that elective and non-urgent
cerebrovascular cases can be postponed until the pandemic’s peak decline. Subsequently, our institution has developed a treatment policy and designed a specific protocol for treating patients with acute stroke to provide quality and uninterrupted care to all who seek for health service in our hospital during the epidemic period. Here, we retrospectively review our experience treating AIS patients with LVO during the epidemic of COVID-19.

Method

Population

AIS patients with LVO who underwent EVT in the period of January 1st to April 30th between 2015 and 2020 from our comprehensive stroke center were retrospectively reviewed. Data were included in the data analysis. Patients enrolled in the data analysis were fulfilled the following criteria: (1) Age more than 18 years; (2) Clinical diagnosis of ischemic stroke in which the stroke symptoms last for more than 30 min and no improvement prior to treatment; (3) Patient had large vessel occlusion including the internal carotid artery, middle cerebral artery (M1/2/3 segment), anterior cerebral artery, basilar artery or dominant vertebral artery, posterior cerebral artery which is confirmed by CTA, MRA or DSA. (4) All the patients were given EVT treatment.

Patient characteristics

Patient baseline characteristics were collected, including demographic (age and sex), systolic blood pressure (SBP), vascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, previous stroke, smoking and drinking history), National Institutes of Health Stroke Scale (NIHSS) score on admission, Alberta Stroke Program Early CT (ASPECTS) score from pre-treatment non-contrast CT. The time points of working flow including onset-to-door (OTD), door to puncture (DTP) and puncture to recanalization (PTR) time.

Endovascular treatment and periprocedural anti-thrombotic agent

Intravenous thrombolysis (IVT) was introduced to AIS patients who were admitted within 4.5 hours from stroke onset. While, if IVT was contraindicated, EVT was performed directly. Stent retriever (Solitaire AB/FR, Coudien/ev3, Irvine, CA; Trevo Proview, Stryker, CA) or aspiration device (Penumbra, Alameda, CA) was introduced as the first recanalization attempt. Additional thrombectomy and alternative rescue therapies, (administration of tirofiban, balloon angioplasty, thrombolysis and rescuing stent) were adopted at the discretion of the operator.

Comparison and outcome analysis

The time period (January 1st to April 30th) were chosen as this time period was the beginning of the COVID-19 outbreak to the pandemic’s peak. The time points of working flow including OTD, DTP and PTR time in the period of January 1st to April 30th between 2015 and 2020 were compared. Successful recanalization defined as modified Tissue Thrombolysis in Cerebral Ischemia (mTICI) 2b/3 and complete recanalization defined as mTICI 3 on the final angiogram were compared in this time period as well as the incidence of symptomatic intracranial hemorrhage (sICH) within 24 hours post-EVT which was defined according to ECASS-III, while, asymptomatic ICH (aICH) detected was considered as the secondary safety outcome. For the functional outcome, excellent outcome (mRS 0–1), functional independence (mRS 0–2) and mortality (mRS 6) at 3-month follow-up in this time period were also analyzed. At last, we also compared the inhospitalization status such as the length of hospital stay and hospitalization costs.

Statistical analysis

The demographic, clinical and procedural characteristics of the stroke patients in each time period were compared using the ANOVA test for categorical variables and continuous variables. The data were analyzed with SPSS version 20.0 statistical software. All reported P values were 2 sided with P < 0.05 considered significant.

Results

Baseline characteristics and working flow time

As shown in Table 1 and, a total of 258 AIS patients with LVO were included from the time period of January 1st to April 30th between 2015 and 2020. There is a significant increase in the number of AIS patients with LVO who received EVT in our hospital from 2017 to 2019 (36, 62, 70 patients, respectively), however, in the year 2020 this number was significantly reduced almost half (36 patients) (Figure 1). Between these period, there is no significant difference in the baseline characteristics of the patients (P > 0.05 for all). Regarding the working flow time as it is shown in Figure 2, the DTP time were gradually shorten from 2015 to 2019 (146 minutes to 115 minutes). During the outbreak the DTP time prolong significantly (225 minutes) (P < 0.0001). As well as the PTR (100 minutes) in which a year before was only 70 minutes (P = 0.014). The number of drip and ship was also significantly reduced in during the epidemic period (13.9%) compared with the previous year (37.1%) (P = 0.014).
| Variables                  | Total (Jan–Apr) | 2015 (Jan–Apr) | 2016 (Jan–Apr) | 2017 (Jan–Apr) | 2018 (Jan–Apr) | 2019 (Jan–Apr) | 2020 (Jan–Apr) | P value |
|----------------------------|-----------------|----------------|----------------|----------------|----------------|----------------|----------------|---------|
| Number of cases            | 258             | 32             | 22             | 36             | 62             | 70             | 36             |         |
| Age, mean ± SD             | 61.8 ± 12.5     | 61.4 ± 11.8    | 56 ± 13.5      | 63.6 ± 16.0    | 60.8 ± 12.2    | 63.3 ± 11.1    | 62.7 ± 11.2    | 0.992   |
| Male, n (%)                | 188 (72.9)      | 26 (75)        | 20 (90.9)      | 24 (66.7)      | 49 (79)        | 47 (67.1)      | 24 (66.7)      | 1       |
| SBP, mean ± SD             | 152 (140–170)   | 150 (136–171)  | 160 (138–178)  | 158 (160–180)  | 150 (140–161)  | 156 (140–170)  | 150 (141–168)  | 0.119   |
| Admission NIHSS, median (IQR) | 14 (11–17)     | 14 (11–16)     | 15 (12–17)     | 15 (12–18)     | 15 (11–16)     | 13 (10–17)     | 12 (11–15)     | 0.738   |
| Anterior circulation       | 165 (64)        | 20 (62.5)      | 5 (22.7)       | 23 (63.9)      | 44 (71)        | 47 (67.1)      | 26 (72.2)      | 0.662   |
| ASPECTS (anterior circulation only) | 9 (8–9)        | 8.5 (8–10)     | 8 (7–9)        | 9 (8–9)        | 9 (8–9)        | 9 (8–9)        | 0.704   |
| IV tPA                     | 45 (17.4)       | 4 (12.5)       | 3 (13.6)       | 11 (30.6)      | 20 (32.3)      | 25 (35.7)      | 11 (30.6)      | 0.668   |
| Vascular risk factors      |                 |                |                |                |                |                |                |         |
| Hypertension               | 168 (65)        | 20 (62.5)      | 11 (50)        | 22 (61.1)      | 41 (66.1)      | 50 (71.4)      | 24 (66.7)      | 0.658   |
| Diabetes mellitus          | 75 (29.1)       | 7 (21.9)       | 8 (36.4)       | 11 (30.6)      | 15 (24.2)      | 22 (31.4)      | 12 (33.3)      | 0.83    |
| Hyperlipidemia             | 45 (17.4)       | 10 (31.3)      | 4 (18.2)       | 5 (13.9)       | 7 (19.4)       | 10 (16.1)      | 9 (12.9)       | 0.171   |
| Atrial fibrillation        | 45 (17.4)       | 7 (21.9)       | 3 (13.6)       | 7 (19.4)       | 10 (16.1)      | 9 (12.9)       | 9 (25)         | 0.171   |
| Previous stroke            | 73 (28.3)       | 5 (15.6)       | 7 (31.8)       | 12 (33.3)      | 15 (24.2)      | 28 (40)        | 6 (16.7)       | 0.016   |
| Smoking                    | 117 (45.3)      | 16 (50)        | 13 (59.1)      | 10 (27.8)      | 32 (51.6)      | 32 (45.7)      | 14 (38.9)      | 0.541   |
| Drinking                   | 116 (45.0)      | 15 (46.9)      | 13 (59.1)      | 12 (33.3)      | 32 (51.6)      | 32 (45.7)      | 16 (44.4)      | 0.682   |
| Working flow time          |                 |                |                |                |                |                |                |         |
| OTD time, median (IQR), min | 215 (120–332)  | 142 (39–303)   | 205 (108–241)  | 269 (130–474)  | 220 (151–382)  | 234 (131–353)  | 220 (120–368)  | 0.852   |
| DTP time, median (IQR), min | 142 (100–180)  | 146 (113–167)  | 143 (118–180)  | 139 (93–177)   | 137 (92–161)   | 115 (92–180)   | 225 (140–299)  | <0.0001 |
| PRT time, median (IQR), min | 89 (60–122)    | 92 (63–133)    | 82 (60–123)    | 92 (60–121)    | 99 (64–122)    | 70 (58–122)    | 100 (61–146)   | 0.044   |
| Drip and ship              | 74 (28.7)       | 7 (21.9)       | 5 (22.7)       | 11 (30.6)      | 20 (32.3)      | 26 (37.1)      | 5 (13.9)       | 0.014   |
| Outcome evaluation         |                 |                |                |                |                |                |                |         |
| mTICI 2b/3                 | (51.2)          | 25 (78.1)      | 17 (77.3)      | 30 (83.3)      | 54 (87.1)      | 61 (87.1)      | 29 (80.6)      | 0.737   |
| sICH                       | 14 (5.4)        | 2 (6.3)        | 3 (8.3)        | 3 (8.3)        | 3 (4.3)        | 1 (4.2)        | 2 (5.6)        | 1       |
| Any ICH                    | 42 (16.3)       | 6 (18.8)       | 5 (22.7)       | 7 (19.4)       | 8 (12.9)       | 8 (11.4)       | 8 (22.2)       | 0.16    |
| 90d mortality              | 39 (15.1)       | 3 (9.4)        | 3 (13.6)       | 12 (33.3)      | 9 (14.5)       | 10 (16.3)      | 1 (8.3)        | 0.215   |
| 7d mRS 0–2                 | 75 (29.1)       | 7 (21.9)       | 9 (40.9)       | 7 (19.4)       | 21 (33.9)      | 23 (32.9)      | 8 (22.2)       | 0.367   |
| 90d mRS 0–2                | 100 (38.8)      | 14 (43.8)      | 11 (50)        | 9 (25)         | 28 (45.2)      | 33 (47.1)      | 5 (40.1)       | 0.765   |
| Inhospitalization          |                 |                |                |                |                |                |                |         |
| Hospital stay              | 11 (7–16)       | 12 (8–15)      | 12 (8.6–16.4)  | 13.9 (8.1–16.5)| 12.1 (8.2–15.9)| 6.8 (4.8–12.3)| 13.5 (8–24.3)  | <0.0001 |
| Hospitalization costs      | 99545           | 82161          | 104780         | 107242         | 119529         | 85449          | 122259        | <0.0001 |
| (69066–125789)             | (62463–102584)  | (68537–112724) | (78076–132882) | (87807–131595) | (51802–116964) | (75681–163010) |             |         |

Abbreviation: SD, standard deviation; SBP, systolic blood pressure; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale score; ASPECTS, Alberta Stroke Program Early CT score; TOAST, trial of ORG 10172 in acute stroke treatment; OTD, onset-to-door; DTP, door-to-puncture; PRT, puncture-to-recanalization; IV, intravenous; mTICI, modified treatment in cerebral infarction; sICH, symptomatic intracranial hemorrhage; mRS, modified rankin score.
Outcome evaluation and hospitalization status

During the epidemic period, there is no difference regarding the safety and efficacy outcome of endovascular treatment, including recanalization rate, postoperative hemorrhage, functional independence at 7 days and 3 months as well as the mortality rate in our institution in compared with the time period before the outbreak ($P > 0.05$ for all). Nevertheless, the length of hospital stay were significantly prolong (13.5 days) in compared with previous year (6.8 days) ($P < 0.0001$), in line with that, the hospitalization cost were also increase during the pandemic (122259 CNY) compared with a year before (85449 CNY) ($P < 0.0001$).

Discussion

During the epidemic period of COVID-19, the working flow time was significantly prolong as well as the length of hospital stay and hospitalization cost. Nevertheless, the quality of the treatment was maintained well in our hospital as there is no significant change of the safety and efficacy outcome of EVT in compared with the period before the outbreak.

During the pandemic of COVID-19, recorded from January to April 2020, the number of patients who received MT decreased significantly compared with the same period in the past 5 years, with the rate of patients meeting the highest level of evidence recommendation increased significantly. However, the number of patient referred to our hospital was significantly reduced almost half compared with the previous year during the epidemic period as well as the drip and ship number. This phenomena also occur in other region and countries. During the epidemic, strict selection of patients not only lead to more ratio of patient with highest level of evidence who eligible for the endovascular procedure, but also the number of patients who seek for treatment from other provinces. Meanwhile, the ratio of patient with mild stroke symptoms, lower ASPECT score, stroke onset more than 6 hours and patient with posterior circulation stroke were significantly declined. Subsequently, patient with older age, more underlying diseases and higher risk of complications were preferred to take conservative treatment. All these were attributed to the significant decline in the EVT number. On the other hand, most of the Neurointervention center in the city of Wuhan were suspended during the outbreak and some of them were converted into isolated ward to treat the COVID-19 patients. As a consequence, the majority of AIS patients with large vessel occlusion were only taken drug therapy for the treatment. Nevertheless, similar with recently reported meta-analysis study, the number of patients receiving mechanical thrombectomy per stroke increased although not as significant compared with the past years.

Since the AHA recommended a high level of evidence for thrombectomy to treat AIS in 2015, the number of MT procedure for AIS has been increase steadily (Figure 3). A robust statistic data recorded a raise of 10 fold. However, after the outbreak of COVID-19, on February 2020, the National health commission of stroke committee and the Chinese Federation of Interventional and Therapeutic Neuroradiology (CFITN) published “The neurointervention recommendation guidelines for COVID-19 prevention (trial version).” Subsequently, on
Figure 2. The working flow time in the period of January to April from year 2015 to year 2020.

Figure 3. Cumulative number of AIS patients received mechanical thrombectomy in China during 2015–2020 period.
April 2020, the Society of Neurointerventional surgery (SNIS) provided neurointerventionalists with rapid and up-to-date information by publishing a recommendations on the management of stroke thrombectomy in this setting with an emphasis on safety measures for health care providers as well as to maintain the safety and efficacy of the EVT.\(^2\)

Recent study reported that despite the pandemic cause a delay in patients arriving at hospital, in-hospital evaluation and treatment times remain unchanged.\(^12\) From 2015 to 2018, the number of patients received mechanical thrombectomy (MT) increased gradually in our institution, and working flow times were improved significantly. However, after the emergence of COVID-19, strict screening have been taken on AIS patients who received MT to contain the spread of the disease and to improve the efficacy of epidemic prevention. As a consequence strict screening of the patients has greatly affect the time working flow of endovascular treatment (EVT) which is different with previous report,\(^12\) particularly the door to puncture time prolong approximately 110 minutes compared with previous year. As a high level of national stroke center, despite the strict screening for COVID-19, which affect the time workflow for stroke screening, the regular stroke diagnosis and treatment flow should be remained standard to maintained the efficacy of the treatment. If the patient was suspected with large vessel occlusion either the stroke onset was less or more than 6 hours, multiple pre-operative imaging evaluations were performed to confirm the diagnosis. During this outbreak, there were some special precautions were adopted to prevent and reducing the risk of cross-infection among healthcare workers, such as keep the social distance and strengthen the protection devices. If there is a need for specialist consultation, the doctor in charge should wear personal protective equipment. Patients who need to be admitted to the hospital for inpatient and patients who were eligible for the surgery need to take the swab test and nucleic acid screening test. These patient were not only had the head CT evaluation but also pulmonary CT. Moreover, the catheter lab has a strict management and the neuroanesthesist will rigorously make pre-surgical evaluation, more strict protection was applied for intubation. All these measures may influence the time workflow, especially the door to puncture time.

Despite a significant prolong in the working time flow, the safety and efficacy outcome of EVT treatment in our institution were remain the same with the previous year before the outbreak. This might be attributed due to the patient who received during pandemic were younger and had less ischemic area, thus they may still have higher chance to get benefit from mechanical thrombectomy even the door to puncture time time were prolong during pandemic. This result may also suggest that the treatment policy and protocol which is adopted in our institution\(^8\) during the epidemic is well effective, not only this protocol provide a safety for the health care member in our hospital, but also can maintain the treatment quality. We would like to share this experience as it might be helpful in facing worldwide disaster such as this COVID-19 epidemic. Although, we also face another important problem which need to further adjustment policy in which the hospital stay and hospitalization costs were significantly increases during this epidemic. The costs increase were mainly due to more COVID-19 screening and preventive measures such as pulmonary CT examination. As the largest stroke center in this country, the patient were immediately transfer to local hospital after the condition was stable post-mechanical thrombectomy. However, during the pandemic, immediate transfer was impeded due to lack of COVID-19 screening and preventive measures in the local hospital, thus significantly increase the hospital length of stay in our institution. Another possibility might because of the patient who received during pandemic were younger and had less ischemic area, thus they may still have higher chance to get benefit from mechanical thrombectomy even the door to puncture time were prolong during pandemic. The limitation in our study is that this is a single institution experience and limited to one country, in which different country faced different situation with different policy. Unfortunately, the present study couldn’t provide further information regarding stroke management in patients with COVID-19 due to no stroke patients with positive COVID-19 admitted to our hospital. Nevertheless, the stroke management should be more concerned as it has a high prevalency, morbidity and mortality and recurrence rate.

Conclusions

During the COVID-19 epidemic, the working time flow may prolong, however strict management and protocol may provide safety measures for health care providers as well as maintain the safety and efficacy of the EVT in AIS patients with LVO.

Ethical approval

This study was approved by Institutional Review Board of Beijing Tiantan Hospital, Capital Medical University.

Declaration of conflicting interests

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ORCID ID
Zhongrong Miao https://orcid.org/0000-0003-1970-1221

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