

Intravenous Thrombolysis for Acute Ischemic Stroke during COVID-19 Pandemic in Srinagarind Hospital

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Background: Stroke is the leading cause of death and disability worldwide. In COVID-19 pandemic, stroke remains to be a medical emergency. To treat patients with acute ischemic stroke (AIS), early intravenous thrombolysis is highly time sensitive. This research investigated the impact of regionally imposed social and healthcare restrictions of COVID-19 on the time metrics in the management of AIS patients admitted at the stroke unit center in Srinagarind Hospital.

Objective: Comparison of door to needle time for intravenous thrombolysis for AIS patients before and after the COVID-19 outbreak.

Materials and Methods: The present study is a retrospective analysis of patients with AIS who received intravenous tissue plasminogen activator (tPA) from 1 January 2019 to 31 December 2020 in Srinagarind Hospital, Khon Kaen. The patients admitted before and after the COVID-19 outbreak (January 13, 2020, as officially announced by the World Health Organization) were screened to collect sociodemographic data, medical history information, and symptom onset status from clinical medical records and to compared door-to-needle time (DNT) for intravenous thrombolysis before and after the outbreak.

Results: A total of 239 patients were included, of which 113 were enrolled before and 126 after the COVID-19 outbreak. According to the findings, DNT is 35.3 minutes before the pandemic and 35.8 minutes after the epidemic.

Conclusion: COVID-19 has remarkable impacts on the management of AIS. However, DNT for before and after COVID-19 outbreak is nearly identical. It was established that administering intravenous thrombolysis to patients in the emergency room rather than the stroke unit allowed for speedier access. Therefore, a policy which provides quick AIS treatments in COVID-19 situations should be implemented.

Keywords: Acute stroke; COVID-19; Intravenous thrombolysis; Door-to-needle time

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The severe acute respiratory syndrome coronavirus 2 (SARSCoV-2), has quickly spread worldwide and coronavirus disease 2019 (COVID-19) was declared as a pandemic outbreak on January 13, 2020⁽¹⁾. Reports have emerged globally on the impact of the COVID-19 pandemic on the management of stroke patients. Stroke experts and international organizations have highlighted the need to preserve the best standards and comprehensiveness of care at all stages during the COVID-19 pandemic outbreak⁽²⁾.

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Reports of declining stroke admission volumes and delays in hospital presentation, which have resulted in decreased systematic and endovascular reperfusion treatments, due to presumed patient fears, as well as the social and logistical barriers imposed by community and healthcare preventive measures, are accumulating⁽³⁾.

Recently developed treatments, such as intravenous thrombolysis can significantly improve the outcomes of acute ischemic stroke (AIS). However, the effects of these treatments were highly time-dependent. For selected patients with onset-to-needle time (ONT) shorter than 4.5 h, intravenous thrombolysis could be applied. Significant difference for changes in ambulation status⁽⁴⁾ when applying intravenous thrombolysis in AIS patients, the shorter the treatment delays, the better the functional outcomes.

In COVID-19 pandemic, stroke remains to be a medical emergency. To treat patients with acute ischemic stroke (AIS), early intravenous thrombolysis is highly time sensitive. This research investigated the impact of regionally imposed social and healthcare restrictions of COVID-19 on the time metrics in the management of AIS

patients admitted at the stroke unit center in Srinagarind Hospital.

Objective

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Materials and Methods

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Demographic and clinical data were collected after hospitalization

Onset-to-door time (ODT) was defined as the duration from stroke symptom onset or time last known well to hospital arrival, which included awareness time, decision time, and transporting time. Decision time is defined as the duration from symptom onset to the decision being made to go to hospital. Door-to-needle time (DNT) was defined as the time from hospital arrival to the start of intravenous thrombolysis from hospital arrival to the start of intravenous thrombolysis.

Etiology was classified using the Trial of ORG 10172 in Acute Stroke Treatment categories (TOAST). The severity of stroke was measured with the National Institutes of Health Stroke Scale (NIHSS). In the present study, the authors choose 4.5 h as the cut point for defining delayed treatment because 4.5 h is the accepted deadline for rt-PA intravenous thrombolysis at present⁽⁵⁾.

The present study was approved by the Human Ethics Committee, Faculty of Medicine, Khon Kaen University (HE631574).

Statistical analysis

Continuous variables were expressed as mean, standard deviation or median and interquartile range (IQR) as appropriate. Categorical variables were presented as number and percentages.

Results

A total of 239 patients were included, of which 113 were enrolled before and 126 after the COVID-19 outbreak.

The mean age of the included patients was 65.8 years and 66.2 years, respectively. The NIHSS score at admission was 10.9 in the pre-COVID-19 group and 10.5 in the post-COVID-19 group, however, no significant differences concerning age, sex, residence, onset time and comorbidities were detected between patients who arrived before and after the COVID-19 pandemic were showed as Table 1.

DNT is 35.3 minutes before the pandemic and 35.8 minutes after the epidemic were showed as Table 2 and Figure 1.

Discussion

During COVID-19, patients may be reluctant to seek medical help for fear of being infected. Patients with mild symptoms may stay at home and manage stroke by themselves or by their relatives. The similar pattern of delay in seeking medical care due to fear of being infected within the hospitals was observed in the Ebola epidemic in West Africa⁽⁶⁾.

Regarding stroke, previous studies⁽⁷⁾ indicated that the major factors for prehospital delay included unawareness of stroke symptoms, lack of understanding on importance of early response, and lack of knowledge on early management.

In terms of posthospital management of stroke patients, guidelines recommended that the green channel be equipped with personal protective equipment (PPE) and continue to promote intravenous thrombolysis and endovascular therapy in accordance with the regular procedures⁽⁸⁾.

In Jiangsu province, the study revealed that both pre- and posthospital delays were prolonged significantly, and the proportion of patients arrived within the 4.5-h time window for intravenous thrombolysis treatment was decreased⁽⁴⁾. Similarly, Hamilton General Hospital–Hamilton Health Sciences reported an increase in institutional time to treatment metrics for acute ischemic stroke patients receiving tPA and/or endovascular reperfusion therapies, which was linked to delays from hospital admission to cranial CT imaging for both tPA and endovascular thrombectomy (EVT)-treated patients, as well as an additional delay to tPA treatment⁽⁹⁾.

In Srinagarind Hospital, giving fibrinolytic drugs for the treatment of acute ischemic stroke within 4.5 hours is urgent. The procedures before COVID-19 consist of, firstly, emergency physician staff screen patients or are coordinated that there are patients with sudden onset of a stroke. Then the personnel notify doctors for the evaluation as soon as the patients arrives at the hospital. In the meantime, they also need to collect and send blood for tests as well as prepare blood clot dissolving drugs. After that, if the patients qualify for AIS, the staff will immediately inform the computerized tomography room to perform CT scan on the patients' brains. At the same time, neurological doctors will be

Table 1. Characteristics and treatment of stroke patients before and after COVID-19 pandemic

Characteristics	1 January 2019 to 31 December 2019	1 January 2020 to 31 December 2020
Stroke fast tack, (n)	113	126
Age, year, mean (year)	65.8	66.2
Male gender, n (%)	55 (48.7)	66 (52.4)
Female gender, n (%)	58 (51.3)	60 (47.6)
Residence, n (%)		
Urban	32 (28.3)	52 (41.3)
Rural	81 (71.7)	74 (58.7)
No underlying disease, n (%)	42 (37.2)	45 (35.7)
Underlying disease, n (%)	71 (62.8)	81 (64.3)
Diabetes, n (%)	26 (23.0)	35 (27.8)
Hypertension, n (%)	50 (44.3)	66 (52.4)
Hyperlipidemia, n (%)	7 (6.2)	15 (11.9)
Atrial fibrillation, n (%)	24 (21.2)	18 (14.3)
Old CVA, n (%)	9 (8.0)	15 (11.9)
Smoking, n (%)	22 (19.5)	9 (7.1)
Alcohol drinking, n (%)	23 (20.4)	7 (5.6)
NIHSS Score, median (IQR)	10 (6.0 to 16.0)	10 (5.0 to 15.0)
Door to Electrocardiogram (min, median, IQR)	5 (2.5 to 9.5)	6 (3.0 to 10.0)
Door to Laboratory (min, median, IQR)	5 (3.0 to 9.5)	6 (3.0 to 10.0)
Door to CT brain NC (min, median, IQR)	8 (6.0 to 12.0)	9 (6.0 to 13.0)
Onset to Door, median (min, median, IQR)	122 (82.0 to 180.0)	120 (75.0 to 165.5)
Door to Needle (min, median, IQR)	31 (25.0 to 38.0)	29 (22.0 to 39.0)
Complication rt-PA: ICH, n (%)	11 (9.7)	4 (3.2)
In-hospital mortality, n (%)	5 (4.4)	3 (2.4)
Against advice discharge, n (%)	5 (4.4)	2 (1.6)

Table 2. Comparison between before and after Covid 19 outbreak

Months	1 January 2019 to 31 December 2019		1 January 2020 to 31 December 2020	
	n=113	Door to needle time, min, mean (SD)	n=126	Door to needle time, min, mean (SD)
January	7	38.3 (12.0)	9	37.4 (14.9)
February	6	40.8 (16.7)	11	28.5 (9.4)
March	8	30.5 (14.9)	3	37.7 (15.2)
April	8	30.4 (6.2)	3	29.7 (4.7)
May	10	37.4 (9.2)	13	31.5 (14.9)
June	3	29.3 (3.2)	12	29.3 (7.0)
July	12	31.7 (6.1)	7	32.3 (16.5)
August	7	42.3 (49.7)	17	29.5 (10.2)
September	15	30.4 (9.3)	8	32.4 (13.4)
October	17	39.7 (21.5)	20	45.0 (41.3)
November	8	42.6 (18.2)	11	48.5 (41.1)
December	12	30.5 (9.3)	12	47.7 (40.5)
Average		35.3 (5.3)		35.8 (7.4)

consulted to check for indications and contraindications for the administration of fibrinolytic drugs. If indicated for thrombolysis, the patients will be immediately transported to the stroke unit a distance of approximately 100 meters and administered fibrinolytics in accordance with the standards

of drug administration.

However, due to COVID-19, the original stroke unit in Srinagarind Hospital has been converted to COVID-19 ward, resulting in the stroke unit to move with the distance of 400 meters away from the emergency room. Consequently,

Table 3. Comparison Between Before and After Covid 19 Outbreak, time for evaluation and intravenous thrombolysis for acute ischemic stroke

	1 January 2019 to 31 December 2019	1 January 2020 to 31 December 2020	p-value
Door to electrocardiogram (min, median, IQR)	5 (2.5 to 9.5)	6 (3.0 to 10.0)	0.102
Door to laboratory (min, median, IQR)	5 (3.0 to 9.5)	6 (3.0 to 10.0)	0.226
Door to CT brain NC (min, median, IQR)	8 (6.0 to 12.0)	9 (6.0 to 13.0)	0.414
Onset to door, median (min, median, IQR)	122 (82.0 to 180.0)	120 (75.0 to 165.5)	0.454
Door to needle (min, median, IQR)	35.3 (25.0 to 38.0)	35.8 (22.0 to 39.0)	0.154

CT brain NC=computerized tomography brain non-contrast

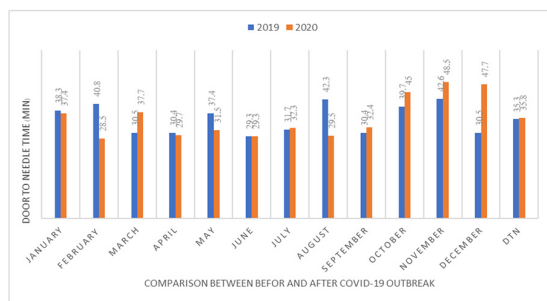


Figure 1. Door to needle time comparison between before and after Covid 19 outbreak.

the measures to care for patients with acute ischemic stroke were implemented to prevent infection risks among hospital personnel and reduce the time to administer fibrinolytic drugs in the patients who have been diagnosed with acute ischemic stroke. All patients must be tested for COVID-19 using Antigen Test Kit (ATK). That is, after completing cranial CT scan, the patients will be transferred back to the emergency room and given thrombolytic medication immediately in case of an indication, as Figure 2.

According to the aforementioned policy initiated by Srinagarind Hospital, DNT for before and after COVID-19 outbreak in this study is nearly identical. This is due to the fact that the policy provides for speedier thrombolytic medication delivery in the treatment of patients with acute ischemic stroke since patients would receive intravenous thrombolysis in the emergency room rather than the stroke unit which is a long distance away.

Concerning the research limitation, the further studies should more examine the potential influencing factors for delayed treatment (ONT >4.5 h) in patients before and after COVID-19. Additionally, there should be the inclusion of various types of patients, such as patients with advanced educations and patients who live in the urban areas.

Conclusion

COVID-19 has remarkable impacts on the management of AIS. However, DNT for before and after COVID-19 outbreak is nearly identical. It was established that

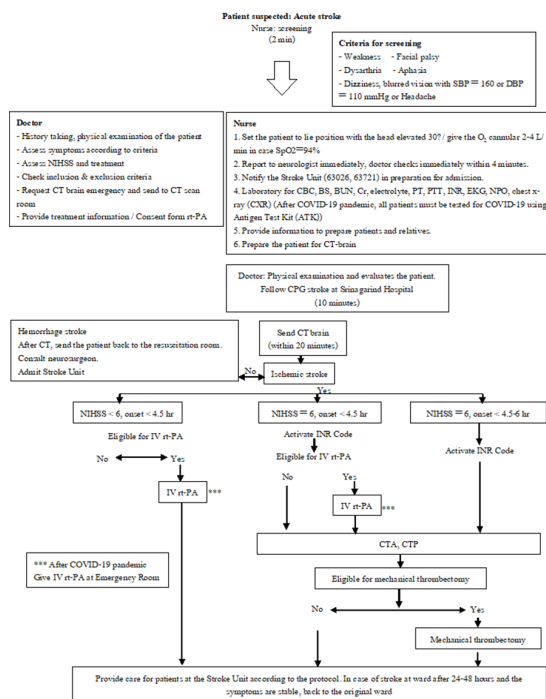


Figure 2. Stroke Fast Track Workflow after COVID-19 Pandemic.

CTA=CT-angiogram; CTP=CT-perfusion; SBP=systolic blood pressure; DBP=diastolic blood pressure; CPG=clinical practice guideline

administering intravenous thrombolysis to patients in the emergency room rather than the neuro ward allowed for speedier access. Therefore, a policy which provides quick AIS treatments in COVID-19 situations should be implemented.

What is already known on this topic?

COVID-19 has remarkable impacts on the management of acute ischemic stroke.

What this study adds?

Door to needle time for before and after COVID-19 outbreak is nearly identical.

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Conflicts of interest

The authors declare no conflict of interest.

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