

The First 10 Thrombolysis for Acute Ischemic Stroke in Lao People's Democratic Republic under Teleconsultation from Thailand

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Background: Acute ischemic stroke patients in Lao People's Democratic Republic (Lao PDR) are unable to access the intravenous thrombolytic therapy using recombinant tissue plasminogen activator (rtPA) due to various reasons. *Aims:* This study aimed to evaluate the feasibility and safety of thrombolytic therapy administration at Mittaphab Hospital, Lao PDR under the international telestroke consultation system from King Chulalongkorn Memorial Hospital, Thailand. *Methods:* Acute ischemic stroke patients who presented at Mittaphab Hospital within 4.5 hours after the onset and received thrombolytic therapy between December 2016 and June 2017 were studied. An immediate real time teleconsultation with 24 hours availability between neurologists at Mittaphab hospital and the Chulalongkorn stroke team was performed in all cases for patient evaluation and decision for thrombolytic treatment. *Results:* There were 205 patients with acute stroke, 28 patients (14%) arrived at the hospital within 4.5 hours after the onset. Ten patients (5%) were eligible for intravenous rtPA. The mean duration from onset to hospital arrival was 122.50 minutes and the mean door to needle time was 108 minutes. The mean National Institute of Health stroke scale (NIHSS) before thrombolysis was 10. At 90 days, the mean NIHSS was 3 and the mean mRS was 2. Seventy percent of patients had good outcome (mRS \leq 2). Only one patient developed massive cerebral infarction. None of the patient developed symptomatic intracerebral hemorrhage or major bleedings. *Conclusions:* Telestroke consultation from Thailand can facilitate the thrombolytic therapy for acute ischemic stroke patients in Lao PDR.

Key Words: Laos—acute ischemic stroke—thrombolytic—telestroke
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Received April 21, 2019; revision received July 21, 2019; accepted July 28, 2019.

This study is funded by Chula Unisearch/Chulalongkorn University.

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1052-3057/\$ - see front matter

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<https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104327>

Introduction

Stroke is the third leading cause of death in Lao People's Democratic Republic (Lao PDR) after respiratory tract infection and coronary heart disease. According to the World Health Organization (WHO) statistics, the age-standardized death rate of stroke in Lao PDR is 123.84 per 100,000 population and ranks 49th in the world.¹ Intravenous thrombolysis has been established as the standard treatment for acute ischemic stroke for more than 20 years but it is still not available in some countries especially low-to-middle income including Lao PDR.^{2,3} Patients with acute ischemic stroke in Lao PDR have never received intravenous recombinant tissue plasminogen activator (rtPA). The major reasons were the lack of knowledgeable personnel and the availability of the drug.

Thailand is a neighboring country of Lao PDR and shares the same time zone and cultures including language. In Thailand, the stroke fast track program at emergency rooms for identifying candidates for thrombolytic therapy has been established countrywide.^{4,5} The treatment is widely available because 3 major healthcare programs cover medical expenses for all Thais. The data from the universal coverage health care scheme (2014) showed that 3.8% of ischemic stroke patients in Thailand received thrombolysis.⁶ King Chulalongkorn Memorial Hospital (KCMH), Bangkok, Thailand is the pioneer in the stroke fast track program which has been using the rtPA in ischemic stroke patients for more than 20 years.⁵

During the past 3 years, the KCMH has been using the telestroke to advise other hospitals, mainly in Thailand on the stroke treatment including the decision of thrombolysis. With no limitation on distance, the international telestroke consultation system was developed after addressing countries' medical and legal issues. To overcome the 2 major barriers for thrombolytic therapy in Lao PDR (the lack of knowledgeable personnel and the unavailability of the drug), the KCMH provided the advice on thrombolytic treatment and 10 initial doses of rtPA to Lao patients.

Aims

This study aimed to assess the characteristic of stroke patients who were eligible for thrombolysis and the outcome of treatment under telestroke consultation as well as to facilitate the use of rtPA in Lao PDR.

Methods

Between December 2016 and June 2017, consecutive patients with acute ischemic stroke who presented at the emergency room of Mittaphab hospital, Vientiane, Lao PDR within 4.5 hours of the symptom onset were screened for eligibility of thrombolytic treatment.

The international telestroke system was organized and consisted of (1) the KCMH stroke team of 5 neurologists in

Thailand and (2) the neurologists and nurses at Mittaphab Hospital in Lao PDR. The teleconsulting team at KCMH was available 24 hours a day and 7 days a week. On-site trainings at Mittaphab hospital were performed to provide the knowledge about acute ischemic stroke, stroke fast track system, thrombolytic treatment, and post-thrombolytic care to physicians, nurses, and health care workers.

The video telecommunication consisted of the existing telecommunication devices (smartphones, tablets or personal computers) using the LINE application (Naver Corporation, Japan), a freeware app, via 3G, 4G, or Wi-Fi for immediate communications. Real time communications were made in all acute stroke cases using the "chat" mode and the group video calls were used during the physical examinations.

When a patient with suspicious history of acute stroke arrived at the emergency room of Mittaphab hospital within 4.5 hours after onset, the stroke fast track was activated and a neurologist at Mittaphab hospital was notified. A computerized tomography (CT) scan of the brain was performed as quickly as possible. An immediate teleconsultation by telestroke system was performed. A real-time video streaming on patient evaluation was done in every patient. The CT imagings were sent by the telestroke system. The patients were assessed for the inclusion and exclusion criteria of thrombolytic therapy according to the American Heart Association/American Stroke Association guideline for the early management of patients with acute ischemic stroke.³ The benefit and risk of thrombolytic management was discussed with the patient and family by the neurologist at Mittaphab hospital in the emergency room. A written informed consent from each participant was obtained.

Baseline data, stroke risk factors, and medical history were obtained from each patient and recorded in the case record form. The data included age, sex, weight, the presence of hypertension, diabetes mellitus, coronary heart disease, dyslipidemia, atrial fibrillation, cigarette smoking, alcohol drinking, history of transient ischemic attack/stroke, the onset of stroke and the hospital arrival time. Physical and neurological examinations including National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), and Barthel index (BI) were performed before and after thrombolytic treatment. Blood samples were collected for random blood glucose by glucometer, complete blood count, fasting plasma glucose, total cholesterol, triglyceride, high-density lipoprotein, and low-density lipoprotein. After thrombolytic therapy, the patient was close monitored with general post-thrombolytic care. A CT scan was performed at 24 hours after thrombolysis or if the patient had clinical deterioration. Stroke physicians at the KCMH were available for teleconsultation at all times and a scheduled teleconsultation was performed again at 24 hours after the treatment. Clinical assessment by NIHSS, mRS, and BI were done at 7 days and 90 days after thrombolysis. Good or favorable outcome was defined by mRS 0-2 at day 90.

Stroke subtypes were classified by Trial of ORG 10172 in Acute Stroke Treatment (TOAST) and the Oxfordshire Community Stroke Project criteria.^{7,8}

This study was approved by the local Ethics Committee from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (COA no. 797/2016; IRB no. 387/59) and the Institutional Review Board of Mittaphab hospital (IRB no. 366).

Results

Between December 2016 and June 2017, 205 patients presented with acute ischemic stroke at Mittaphab hospital. Twenty eight patients (14%) arrived within 4.5 hours after stroke onset. Ten patients received intravenous thrombolysis via the telestroke consultation system which was 5% of all acute ischemic stroke patients. The other 18 patients did not receive the treatment due to the inability to administer thrombolytic treatment within 4.5 hours in 14 cases and 4 cases had contraindication for the thrombolytic treatment.

The baseline characteristics of 10 patients who received rtPA are shown in Table 1. Among these rtPA treated patients, 90% were self-pay and 10% were under the government insurance system. Eighty percent of the patients came to the hospital by a private car and only 20% by an ambulance. Dyslipidemia and hypertension were the most common stroke risk factors which were found in 80% and 60% of patients, respectively. As per Oxfordshire Community Stroke Project stroke subtypes classification, 60% had anterior circulation infarction (TACI and PACI). Cardioembolism was the most common pathophysiology of stroke. The mean (\pm SD) time from stroke onset to hospital arrival was 122 (\pm 74) minutes. The mean (\pm SD) time from stroke onset to thrombolytic treatment was 225 (\pm 39) minutes. The average door-to-needle time was 108 minutes; the fastest was 55 minutes and the longest was 185 minutes. Three patients (30%) received thrombolysis with the door-to-needle time less than 60 minutes. The mean (\pm SD) door to CT and door to teleconsultation was 38 (\pm 23) minutes and 68.8 (\pm 35) minutes, respectively. All patients received the standard dose of intravenous thrombolysis (.9 mg/kg).

Clinical Outcome and Complications

Significant improvements of NIHSS, mRS, and BI were observed at 90 days after thrombolysis (Table 2). Good functional outcome (mRS 0-2) on day 90 was found in 70% of the patients (Fig 1). Eighty percent of patients were almost back to normal (Fig 2). There were no significant differences in baseline characteristics between patients with favorable (mRS 0-2) and nonfavorable outcome. Patients with favorable outcome had lower mean NIHSS before thrombolysis, lower mean blood glucose at presentation, and shorter mean stroke onset to thrombolytic treatment time (Table 3). One patient developed hemorrhagic infarction type 2 (HI2) by ECASS II criteria and can be classified

Table 1. Baseline characteristics of patients receiving thrombolysis in Lao PDR

Baseline characteristics	Patients (N = 10)
Age (years, mean \pm SD)	59.90 \pm 15
Asian race (%)	100
Female (%)	50
Weight (kg, mean \pm SD)	60.70 \pm 9
Risk factors	
Dyslipidemia (%)	80
Hypertension (%)	60
Diabetes mellitus (%)	10
Atrial fibrillation (%)	50
Valvular heart disease (%)	30
Previous TIA/Stroke (%)	20
Smoking (%)	50
Alcohol drinking (%)	40
Timing	
Duration from onset to hospital (min, mean \pm SD)	122.50 \pm 74
Duration from onset to rtPA time (min, mean \pm SD)	225.00 \pm 39
Door to needle time (min, mean \pm SD)	108.00 \pm 47
Stroke severity	
NIHSS before rtPA (median [range])	10 (3-20)
NIHSS before rtPA (mean \pm SD)	10 \pm 6
mRS before rtPA (mean \pm SD)	4.20 \pm 1
Stroke subtype by TOAST classification	
Cardioembolic (%)	50
Small vessel disease (%)	40
Undetermined (%)	10
Stroke subtype by OCSF criteria	
TACI (%)	30
PACI (%)	30
LACI (%)	40
POCI (%)	0
SBP (mm Hg, mean \pm SD)	161.60 \pm 17
DBP (mm Hg, mean \pm SD)	86.70 \pm 10
Initial plasma glucose (mg/dL, mean \pm SD)	148 \pm 129

Abbreviations: DBP, Diastolic Blood Pressure; LACI, Lacunar Infarcts; mRS, modified Rankin Scale; NIHSS, National Institute of Health stroke scale; OCSF, Oxfordshire Community Stroke Project; PACI, Partial Anterior Circulation Infarcts; POCI, Posterior Circulation Infarcts; rtPA, recombinant tissue plasminogen activator; SBP, Systolic Blood Pressure; TACI, Total Anterior Circulation Infarcts; TIA, Transient Ischemic Attack; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

as asymptomatic intracerebral hemorrhage by ECSS III study criteria.^{9,10} Unfortunately, this patient developed malignant cerebral edema due to a large vessel occlusion and was discharged in terminal condition. One patient had urinary tract infection during hospitalization.

Discussion

Lao PDR is one of the developing countries in Southeast Asia. This paper reports on the first 10 thrombolytic cases

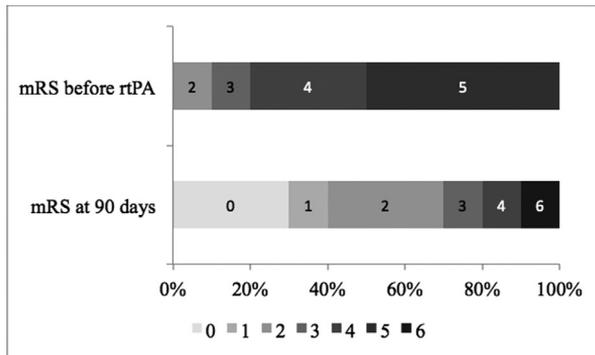
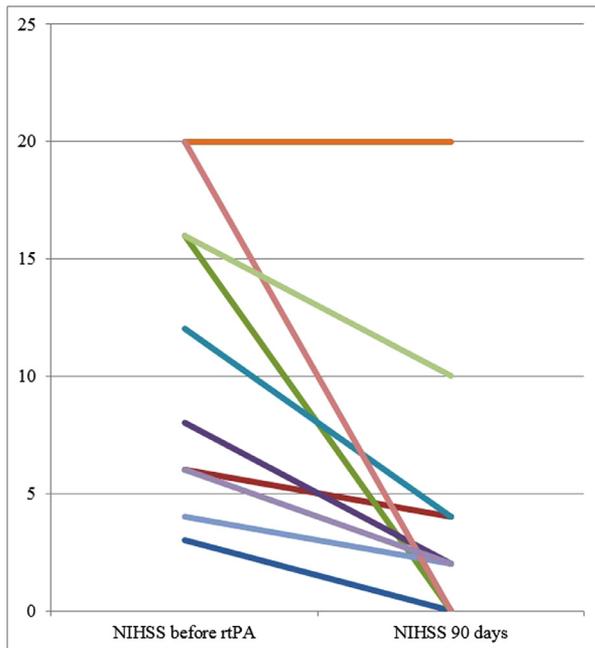
Table 2. NIHSS, mRS and BI of all patients before thrombolytic treatment, day of discharge or day 7 (whatever comes first) and day 90 after stroke

	Before rtPA	Discharge or 7 days	P-value	90 days	P-value
NIHSS (mean \pm SD)	10 \pm 6	5 \pm 4	.072	3 \pm 3	.008**
mRS (mean \pm SD)	4.20 \pm 1	2.80 \pm 2	.050*	2.00 \pm 2	.003**
Barthel index (mean \pm SD)	38.89 \pm 17	70 \pm 28	.030*	87.78 \pm 18	.000**

Abbreviations: BI, Barthel index; mRS, modified Rankin Scale; NIHSS, National Institute of Health stroke scale.

*Statistically significant.

** $P < .05$.

**Figure 1.** Functional outcome (mRS) of patients before thrombolytic treatment and day 90 after stroke.**Figure 2.** NIHSS of patients before thrombolytic treatment and day 90 after stroke. Abbreviation: NIHSS, National Institute of Health stroke scale.

stroke treatment in Lao PDR. The treatment was made possible because of the collaboration between the 2 countries and the telestroke system. The international telestroke consultation between 2 countries have rarely been reported. One study of international telestroke between New Zealand and Scotland demonstrated that the advantage of different

time zones and the telestroke can improve the access to stroke thrombolysis. They included 5 patients including 2 who received thrombolysis.¹¹

Prior to this study, the on-duty physician screened patients who had suspicion of stroke at the emergency room. Basic labs and electrocardiogram were obtained, however prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR) were not available within 24 hours. It also took several hours to wait for CT scan of the brain. If the condition of the patients was unstable, the physician on duty would then call the consultant and send the patient to the intensive care unit. Other patients were admitted to the internal medicine ward or surgery ward depending on the result of the CT scan. The severity of stroke in patients (NIHSS, mRS, and BI) was not regularly assessed during admission. Prior to this system, patients and physicians were either unaware or did not adhere to the 4.5 hours period to receive treatment because it was not available.

After the international telestroke system was organized however, the physician at the emergency room immediately informed the neurologist if patients with acute ischemic stroke presented at the emergency room at Mittaphab Hospital within 4.5 hours of symptom onset. History, physical examination and basic labs including PT, aPTT, INR were obtained. The international line group was notified to prepare for consultation. CT scans of the brain were performed as soon as possible. Then, an immediate teleconsultation by telestroke system was performed. Neurological examination and stroke severity could be assessed on site and the eligibility of thrombolytic management was then discussed. As a result of the introduction of telestroke system, more patients presented to the emergency room to receive proper evaluation of stroke symptoms. Once the system became fully functional, hundreds of patients and medical personnel gained more confidence to seek out stroke care at Mittaphab Hospital.

This study demonstrated that there were at least 13% of patients in Lao PDR who arrived at Mittaphab hospital within the thrombolytic time window. However, there were 14 patients (7%) who arrived close to 4.5 hours thus it was too late for thrombolysis due to the prolonged hospital process. Among patients who received the thrombolytic treatment, the mean hospital arrival time after stroke onset was 123 minutes, which doubles the time of a previous study

Table 3. Comparison of the baseline characteristics and risk factors between patients with favorable and unfavorable outcomes

	Unfavorable outcome mRS >2 (N = 3)	Favorable outcome mRS 0-2 (N = 7)	P-value (95% CI)
Age (years)	54.00 ± 6	62.43 ± 18	.46
Mean NIHSS pre-rtPA	14 ± 7	10 ± 6	.39
Mean NIHSS at 90 days	6 ± 6	2 ± 2	.90
Systolic BP (mm Hg)	149 ± 9	167.00 ± 18	.14
Diastolic BP (mm Hg)	88.67 ± 2	85.86 ± 12	.71
INR	1.15 ± 0	1.28 ± 0	.65
Platelet count (× 103/mm ³)	209.33 ± 47	246.00 ± 51	.32
Blood glucose at presentation (mg/dl)	238.00 ± 197	95.20 ± 16	.14
Onset-to-needle time (min)	238.33 ± 33	219.29 ± 42	.58
Female N (%)	20	30	.50
Hypertension N (%)	30	30	.17
Diabetes mellitus N (%)	10	0	.30
Hyperlipidemia N (%)	20	10	.18
Atrial fibrillation N (%)	10	40	.50
Smoking N (%)	10	40	.50
Alcohol N (%)	10	30	.67

Abbreviations: CI, confidence interval; INR, international normalized ratio; NIHSS, National Institute of Health stroke scale; rtPA, recombinant tissue plasminogen activator.

from Thailand (65 minutes).⁵ Almost all patients came to the hospital by a private car. The late arrival of patients may be due to many prehospital barriers such as the lack of knowledge of stroke signs among patients, relatives and coworkers, the distance from the hospital, and poor transportation system. Improvements of public awareness about stroke, emergency medical services, and improved quality of road infrastructure may help shorten the hospital arrival time.

The median NIHSS score at baseline in the patients who received intravenous thrombolytic in this study was 10 which was less than other previous Asians, NINDS and SITS-MOST studies.^{2, 5, 12-14} In the original study among the first thrombolytic cases in Thailand the median NIHSS was as high as 20 (9-32).⁵

Cardiogenic embolism was the cause of stroke in 50% of the cases. This is higher than the previous studies from the NINDS, SITS-MOST and other studies from Asia. However, previous studies from Thailand showed a high percentage (71%) of cardioembolic stroke.^{2,5,13-15} The sudden onset of cardioembolic stroke may contribute to the decision for coming to the hospital.

In this study, the stroke fast track program was successfully launched at the Mittaphab hospital in Lao PDR. The system was successfully activated by the triage nurses. However, the average door to needle time in this study was quite long when compared to previous studies in SITS-NEW, SITS-MOST, Thailand and Vietnam where the mean door to needle time ranged from 66 to 75 minutes.^{5, 13-15} In this study, there were only 30% of patients who received the treatment within 60 minutes. The main reason for prolonged door-to-needle time was the delayed decision by patients and relative for thrombolytic treatment which may be related to the lack of general knowledge about stroke. One patient had high blood pressure which required antihypertensive treatment before

thrombolytic therapy. Fast emergency department evaluation, quick stroke team activation, and prompt brain imaging process are needed to shorten the door to needle time.

The outcome of the treatment was compatible with previous studies.^{2,13} Seven patients returned to normal or had minimal deficits (mRS 0-2) at day 90. The independent functional outcome (mRS 0-1) was also comparable to other studies in developed countries.^{12,15} The complication rate related to thrombolysis was low. However, the number of patients in this study was small.

This study confirmed that thrombolytic treatment was beneficial for acute stroke patients who presented to the hospital in Lao PDR and had similar outcome with other studies. More importantly, this study demonstrated the feasibility to give thrombolysis with the assistance of teleconsultation from Thailand. Despite many obstacles, many patients in Lao PDR managed to arrive at the hospital within the rtPA time window. The authors hope that this study would be the beginning of thrombolysis in Lao PDR. In the future, more trainings to increase the number of knowledgeable neurologists and nurses as well as making the rtPA available should be advocated. Further steps should be the generalization of the treatment and the policy of coverage for thrombolysis cost.

Lastly, the authors would like to emphasize the World Stroke Organization (WSO) campaign on "Stroke is treatable" by awareness, access, and action. This study started with the action using a model of stroke fast track and teleconsultation for intravenous rtPA. Future action should be taken on the direction for stroke care especially the establishment of stroke unit and later, thrombectomy. However, the awareness and access are still lacking in the country which should be endorsed by the policy makers.

Conclusions

Telestroke consultation from Thailand can facilitate the thrombolytic therapy for acute ischemic stroke patients at Mittaphab Hospital. The outcome was good and the complication rate was low. This was the first case series of acute ischemic stroke who received thrombolytic treatment in Lao PDR. This study should be the initiating point to raise awareness among patients, physicians, and policy makers to make thrombolytic treatment available in Lao PDR.

Acknowledgment: The authors gratefully acknowledge the support of the Chula Unisearch/Chulalongkorn University, Thailand

Declaration of Competing Interest

None.

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