ORIGINAL RESEARCH



Impact of Hospital Level on Stroke Outcomes in the Thrombolytic Therapy Era in Northeast Thailand: A Retrospective Study

Nisa Vorasoot \cdot Narongrit Kasemsap \cdot Kannikar Kongbunkiat \cdot

Udomlack Peansukwech · Somsak Tiamkao · Kittisak Sawanyawisuth 🝺

Received: February 2, 2021 / Accepted: May 1, 2021 / Published online: May 18, 2021 \odot The Author(s) 2021

ABSTRACT

Introduction: Stroke is a common neurological disease. Thrombolytic therapy has been shown to be beneficial in acute ischemic stroke. This treatment can be given in various hospital levels. This study aimed to evaluate the quality of acute ischemic stroke care among various hospital levels. *Methods*: Data were randomly selected from the medical records that were sent to the National Health Security Office (NHSO) for reimbursement purposes between October 2015 and August 2016. Patient demographics, risk factors, stroke subtypes, stroke severity, quality of care indicators, and complications were

Division of Neurology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand e-mail: naroka@kku.ac.th

N. Vorasoot \cdot N. Kasemsap \cdot K. Kongbunkiat \cdot S. Tiamkao North-Eastern Stroke Research Group, Khon Kaen University, Khon Kaen 40002, Thailand

U. Peansukwech CKDnet, Khon Kaen University, Khon Kaen 40002, Thailand

K. Sawanyawisuth (⊠) Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand e-mail: kittisak@kku.ac.th recorded. Paired comparisons between two groups were carried out using the Bonferroni correction.

Results: A total of 947 patients, including 169 patients from community hospitals (CHs), 629 from regional hospitals (RHs), and 149 from tertiary hospitals (THs), were included in the final analysis. The CH group had a higher median age but lower median initial National Institutes of Health Stroke Scale (NIHSS) score than the RH and TH groups (median age = 70, 66, and 67 years, respectively, and initial NIHSS = 6, 8, and 9, respectively). The CH group had shorter onset-to-needle times for intravenous recombinant tissue plasminogen activator (rt-PA) treatment than the other two groups (147 vs. 178.5 and 180 min). After adjustment for baseline characteristics, stroke type, and stroke severity, the CH group was significantly associated with lower mortality and presence of complications. The adjusted odds ratios (95% confidence intervals) for the two factors were 0.13 (0.03, 0.67) and 0.59 (0.35, 0.99). None of the patients received endovascular therapy or non-thrombolytic interventional therapy.

Conclusion: CHs may have the potential for acute ischemic stroke care in the same way as RHs or THs, with faster rt-PA treatment, in northeast Thailand. However, further studies should be performed to evaluate appropriate patient characteristics for CHs.

N. Vorasoot \cdot N. Kasemsap (\boxtimes) \cdot K. Kongbunkiat \cdot S. Tiamkao

Keywords: Acute ischemic stroke; Community hospitals; Quality of care; Thrombolysis

Key Summary Points

Why carry out this study?

Acute ischemic stroke is a common neurological disease. Patients with acute ischemic stroke can be significantly improved with thrombolytic therapy if indicated.

In northeast Thailand, the Stroke Fast Track Network has been established for years in three hospital levels: community hospitals, regional hospitals, and tertiary hospitals.

This study aimed to evaluate the quality of acute ischemic stroke care in the various hospital levels. We hypothesized that stroke care should be comparable among hospital levels under the Stroke Fast Track Network.

What was learned from the study?

Patients with acute ischemic stroke treated at community hospitals had significantly lower mortality rates and presence of complications compared with the other two hospital levels. However, there were some clinical differences at baseline among the three hospital levels.

Community hospitals may have the potential for acute ischemic stroke care in the same way as regional or tertiary hospitals, with faster intravenous recombinant tissue plasminogen activator (rt-PA) treatment, in northeast Thailand.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/ m9.figshare.14510853.

INTRODUCTION

Stroke is a leading cause of death and disability throughout the world. In Thailand, the prevalence of stroke is estimated to be 1880/100,000 among adults aged 45 years and older [1]. The most common type of stroke in Thailand is ischemic stroke, which accounts for 80% of cases [2]. Intravenous recombinant tissue plasminogen activator (rt-PA) treatment within 4.5 h of stroke onset [3, 4] is one part of a multidisciplinary approach for treatment of acute ischemic stroke that may improve stroke outcomes. This treatment has been shown to lead to significantly better outcomes than placebo (52.4% vs. 45.2%) [4].

Hospitals in Thailand are divided into three levels, similar to hospitals in other Asian countries. These are community hospitals (CHs), regional hospitals (RHs), and tertiary hospitals (THs). Referrals travel up stepwise from CHs to RHs to THs. In Thailand, rt-PA therapy began to be implemented in 1996 [2]. A previous study conducted an evaluation of acute ischemic stroke care from 2008 to 2010 among the three levels of hospitals in Thailand. For rt-PA treatment, the CHs had the lowest rates, followed by RHs and THs, at 0.4% vs. 1.8% and 9.1%, respectively, while aspirin therapy within 48 h was also lowest at the CHs (33.6% vs. 87.5% vs. 72.6%) [5]. The Thai Stroke Society and Khon Kaen University have established the Stroke Fast Track Network, which has been in practice for more than 10 years, in order to improve stroke care, particularly in CHs. This study, therefore, aimed to evaluate the quality of acute ischemic stroke care in the various hospital levels.

METHODS

Study Design

This was a cross-sectional retrospective study of patients with acute ischemic stroke who were enrolled from 30 hospitals in northeast

Thailand: CHs, RHs, and THs under the National Health Security Office (NHSO). The NHSO covers 98.26% of the Thai population. The study period was from October 2015 to August 2016. The study protocol was approved by the ethics committees for human research of all hospitals. The protocol was reviewed and approved by the ethics committee in human research, Khon Kaen University, Thailand (HE591294). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Permission was obtained to access and use the data from the National Health Security Office database.

Subjects

All patients aged 15 years or older admitted with acute ischemic stroke to hospitals in northeast Thailand were included in this study. Stroke was defined according to the World Health Organization (WHO) criteria [6] and was confirmed by neuroimaging studies. Patients diagnosed with hemorrhagic stroke or misdiagnosis of stroke or those with incomplete data were excluded from this study.

Subject Enrollment

Nine CHs, 16 RHs, and five THs participated in the study. All eligible patients were randomly selected from the NHSO list, stratified by level of hospital. We included 20 patients from each CH and 40 patients from each RH and TH. A total of 1020 patients, including 180, 640, and 200 patients from CHs, RHs, and THs, were eligible for the study. Of those, patients were randomly selected by treatment with intravenous rt-PA versus non-rt-PA treatment to meet a ratio of 1:1. The randomization process was performed using a random number generator.

Data Collection

Data were collected from electronic medical records submitted to the NHSO. The medical records included history, physical signs, laboratory results, treatment, and outcomes. Patient demographics, stroke risk factors, ischemic stroke subtypes classified according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) [7], initial stroke severity as measured by the National Institutes of Health Stroke Scale (NIHSS) [8], time of hospital arrival, and onset of stroke were collected from the medical admission records. Quality of acute stroke care indicators were recorded as follows: stroke unit admission; NIHSS evaluation; electrocardiogram (EKG) study; EKG monitoring; brain imaging study before and after rt-PA; vascular study; onset-to-needle time of rt-PA; door-toneedle time of rt-PA; aspirin used within 48 h; prescription of antihypertensives at discharge; lipid-lowering drugs and anticoagulants for patients with atrial fibrillation (AF); and assessment for stroke rehabilitation services, complications, hospital costs, length of hospital stay, and discharge status. If the admission NIHSS values were missing from the medical record, we estimated them on the basis of the history and physical examinations recorded. If there were no data of stroke subtype by TOAST classification, we evaluated stroke subtypes using clinical factors including risk factors, history, physical examination, and brain imaging including vascular study (if available) for classified cause of stroke. The stroke subtypes were reviewed by two board-certified neurologists.

The CHs are located in the district level. In this study, the CHs that can accommodate thrombolysis patient have a CT scanner and capacity of 90-120 beds. These CHs are the referral centers for the other CHs. The RHs are located in the province level, and have a capacity of 120-500 beds. The THs have a capacity of more than 500 beds. The physicians who treat patients at the CH and the RH levels are non-neurologists and include internists and emergency physicians. There are few neurologists at the RH level. In the THs, the physicians who treat patients are neurologists. Thailand has three major health insurance schemes, namely the Universal Coverage Scheme (UCS), the Social Security Scheme (SSS), and the Civil Servant Medical Benefit Scheme (CSMBS). The UCS, which is operated by the NHSO, is the largest scheme, covering 73.71% of the population and available to anyone who is not

eligible for SSS or CSMBS. The SSS is a compulsory health insurance program for private sector employees, which covers 17.18% of the population. The CSMBS provides health insurance to government sector employees, their dependents (parents, spouses, and children), and retirees, and covers 7.37% of the population. The UCS and the CSMBS are funded primarily through the general tax; the SSS receives a tripartite contribution of 1.5% of salary, divided equally by employer, employee, and government. In fiscal year 2015, the total Thai population was 65.580 million, and 65.530 million people (99.92%) were insured by a health insurance scheme, so there was a very low financial barrier to stroke care [9].

Statistical Analysis

Baseline characteristics were analyzed using mean and standard deviation or median and interquartile range for continuous variables. Categorical variables were presented as percentages and frequencies. A chi-square or Fisher's exact test (as appropriate) was applied to compare categorical variables, and the Scheffé test was used for comparisons between two groups. Analysis of variance (ANOVA) or the Kruskal-Wallis test (as appropriate) was applied to compare continuous variables. Paired comparisons between two groups were carried out using the Bonferroni correction. Statistical significance was set at a two-sided p value < 0.05. Association between hospital level and stroke outcome was calculated and adjusted for age, sex, stroke risk factors, stroke subtype, initial NIHSS, stroke onset, thrombolysis treatment, plasma glucose, and complications. Analyses were performed using STATA version 10.1 software (StataCorp, College Station, TX, USA).

RESULTS

One thousand patients with acute ischemic stroke were randomly sampled from the reimbursement data, 73 of whom were excluded due to misdiagnosis of stroke (53 patients) or incomplete data (20 patients). Thus, a total of 947 patients (169 patients from CHs, 629 from

스 Adis

RHs, and 149 from THs) were included in the final analysis. There were five factors that differed significantly among the three study populations in terms of baseline characteristics (Table 1). The CH group had a higher median age and lower median initial NIHSS than the RH and TH groups (median age = 70, 66, and 67 years, respectively, and initial NIHSS = 6, 8, and 9, respectively). The CH group also had a higher proportion of patients with dyslipidemia than the RH group (33.1% vs. 21.9), while the TH group had a higher median body weight than the RH group (60 vs. 56 kg).

In terms of stroke care, the TH group had the highest proportion of admissions to the stroke unit, NIHSS evaluations, brain imaging post-rt-PA, vascular study, and speech rehabilitation among the three groups (Table 2). The CH group had shorter onset-to-needle times for rt-PA than the other two groups (147 vs. 178.5 and 180 min). The TH group had longer door-to-needle rt-PA times and lower proportions of antiplatelet therapy within 48 h and administration of lipid-lowering drugs than the other two groups (Table 2).

The groups were comparable in terms of stroke outcomes and complications, with the exceptions of being asymptomatic intracerebral hemorrhage, hospital cost, and discharge status (Table 3). The CH group had a lower proportion of asymptomatic intracerebral hemorrhage (0.6%), lower hospital costs (24,400 Baht), and lower mortality rate (1.2%) than either the RH or TH group. With regard to complication rates, the CH group had a significantly lower rate than the RH and TH groups (29.59% vs. 41.02% vs. 40.94%; *p* value 0.022).

After adjustment for baseline characteristics, stroke type, and stroke severity, the CH group was significantly associated with lower mortality and complications (Table 4). The adjusted odds ratios (95% confidence interval: CI) for the two factors were 0.13 (0.03, 0.67) and 0.59 (0.35, 0.99). Hospital level was not associated with asymptomatic or symptomatic intracerebral hemorrhage, length of stay, or cost.

Characteristics	Hospital levels				
	CHs $(n = 169)$	RHs $(n = 629)$	THs $(n = 149)$	Total $(n = 947)$	
Male sex	95 (56.2)	311 (49.4)	71 (47.7)	477 (50.4)	0.23
Age (years)	70 (61–76)	66 (56–75)	67 (58–74)	67 (58–75)	< 0.01 ^{a,b}
Body weight (kg)	58 (50-66)	56 (50-65)	60 (54–67)	57 (50-65)	< 0.01 ^c
Risk factors					
Diabetes mellitus	49 (29.0)	161 (25.6)	41 (27.5)	251 (26.5)	0.64
Hypertension	82 (48.5)	307 (48.8)	74 (49.7)	463 (48.9)	0.97
Dyslipidemia	56 (33.1)	138 (21.9)	47 (31.5)	241 (25.4)	< 0.01 ^a
Chronic kidney disease	2 (1.2)	32 (5.1)	8 (5.4)	42 (4.4)	0.08
Atrial fibrillation	39 (23.1)	144 (22.9)	44 (29.5)	227 (24.0)	0.38
Coronary artery disease	5 (3.0)	39 (6.2)	8 (5.4)	52 (5.5)	0.26
Previous TIA/stroke	22 (13.0)	84 (13.4)	17 (11.4)	123 (13.0)	0.82
Smoking	12 (7.1)	82 (13)	21 (14.1)	115 (12.1)	0.08
Stroke subtype					
LAA	52 (30.8)	235 (37.4)	45 (30.2)	332 (35.1)	0.11
CE	42 (24.9)	164 (26.1)	50 (33.6)	256 (27.0)	0.14
SVD	74 (43.8)	224 (35.6)	47 (31.5)	345 (36.4)	0.06
Others	0 (0.0)	1 (0.2)	1 (0.7)	2 (0.2)	0.32
Undetermined	1 (0.6)	3 (0.5)	4 (2.7)	8 (0.8)	0.04 ^c
Initial NIHSS	6 (3–10)	8 (5–13)	9 (6–15)	8 (4–14)	< 0.01 ^{a,b}
Arrival					< 0.01 ^{a,b}
Self	44 (26.0)	108 (17.2)	19 (12.8)	171 (18.1)	
EMS	18 (10.7)	42 (6.7)	12 (8.1)	72 (7.6)	
Refer	53 (31.4)	382 (60.7)	109 (73.2)	544 (57.4)	
Others	0 (0.0)	2 (0.3)	0 (0.0)	2 (0.2)	
No data	54 (32.0)	95 (15.1)	9 (6.0)	158 (16.7)	
Onset more than 24 h	36 (34.3)	110 (33.1)	14 (20.0)	160 (31.6)	0.08

Table 1 Demographic and baseline characteristics of acute ischemic stroke patients treated at various hospital levels

Data presented as number (%) or median (1st-3rd IQR)

CHs community hospitals, RHs regional hospitals, THs tertiary hospitals, TLA transient ischemic attack, NIHSS National Institutes of Health Stroke Scale, LAA large artery atherosclerosis, CE cardioembolic, SVD small vessel disease, IQR interquartile range

^a CHs vs. RHs (p < 0.05)

^b CHs vs. THs (p < 0.05)

^c RHs vs. THs (p < 0.05)

Acute stroke care indicators	Hospital levels				
	CHs $(n = 169)$	RHs $(n = 629)$	THs $(n = 149)$	Total $(n = 947)$	
Admission stroke unit	92 (54.4)	378 (60.1)	117 (78.5)	587 (62.0)	$< 0.01^{b,c}$
NIHSS evaluation	97 (57.4)	328 (52.1)	104 (69.8)	529 (55.9)	< 0.01 ^c
Plasma glucose (mg/dL)	122 (98–168)	117 (98–150)	125 (101–161)	118 (98–158)	0.09
EKG	161 (95.3)	597 (94.9)	144 (96.6)	902 (95.2)	0.67
EKG monitoring	74 (43.8)	257 (40.9)	72 (48.3)	403 (42.6)	0.24
Brain imaging	169 (100.0)	628 (99.8)	146 (98.6)	943 (99.7)	0.09
Imaging pre-rt-PA	64 (100.0)	287 (96.6)	79 (100.0)	430 (97.7)	0.12
Imaging post-rt-PA	61 (95.3)	265 (89.2)	79 (100.0)	405 (92.1)	< 0.01 ^c
Vascular study	1 (0.7)	17 (2.9)	27 (18.4)	45 (5.0)	$< 0.01^{b,c}$
Carotid Doppler ultrasound	1 (0.6)	6 (1.0)	5 (3.4)	12 (1.3)	0.06
CTA	0 (0.0)	2 (0.3)	0 (0.0)	2 (0.2)	1.00
MRA	0 (0.0)	9 (1.4)	7 (4.7)	16 (1.7)	$< 0.01^{b,c}$
Thrombolysis (rt-PA)					
Onset to needle (min)	147 (120–194)	178.5 (135–210)	180 (143–225)	174.5 (135–210)	0.01 ^{a,b}
Door to needle (min)	55 (40-69)	60 (45-80)	73 (55–94)	60 (48-82)	$< 0.01^{b,c}$
Antiplatelet within 48 h	142 (84.0)	463 (73.6)	94 (63.1)	699 (73.8)	< 0.01 ^{a,b,c}
Antihypertensive	35 (20.7)	141 (22.4)	27 (18.1)	203 (21.4)	0.50
Lipid-lowering drugs	152 (89.9)	543 (86.3)	117 (78.5)	812 (85.7)	0.01 ^{b,c}
Anticoagulant if AF	10 (25.6)	49 (31.4)	15 (34.1)	74 (31.0)	0.70
Rehabilitation	125 (74.0)	490 (77.9)	113 (75.8)	728 (76.9)	0.53
Motor	126 (74.6)	466 (74.1)	107 (71.8)	699 (73.8)	0.83
Swallow	3 (1.8)	16 (2.5)	7 (4.7)	26 (2.7)	0.26
Speech	0 (0.0)	36 (5.7)	12 (8.1)	48 (5.1)	< 0.01 ^{a,b}

Table 2 Laboratory investigations and treatments for patients with acute ischemic stroke treated at various hospital levels

Data presented as number (%) or median (1st-3rd IQR)

CHs community hospitals, RHs regional hospitals, THs tertiary hospitals, NIHSS National Institutes of Health Stroke Scale, CTA computed tomography angiography, MRA magnetic resonance angiography, AF atrial fibrillation, IQR interquartile range

^a CHs vs. RHs (p < 0.05)

^b CHs vs. THs (p < 0.05)

^c RHs vs. THs (p < 0.05)

733

Outcomes	Hospital level				
	CHs (n = 169)	RHs $(n = 629)$	THs $(n = 149)$	Total $(n = 947)$	
Complications					
Pneumonia	30 (17.8)	155 (24.6)	38 (25.5)	223 (23.5)	0.14
Urinary tract infection	4 (2.4)	38 (6.0)	6 (4.0)	48 (5.1)	0.14
Sepsis	7 (4.1)	34 (5.4)	11 (7.4)	52 (5.5)	0.44
Gastrointestinal bleeding	3 (1.8)	21 (3.3)	1 (0.7)	25 (2.6)	0.18
Acute kidney injury	5 (3.0)	27 (4.3)	5 (3.4)	37 (3.9)	0.80
Myocardial infarction	0 (0.0)	1 (0.2)	1 (0.7)	2 (0.2)	0.32
Heart failure	6 (3.6)	14 (2.2)	2 (1.3)	22 (2.3)	0.44
Brain herniation	4 (2.4)	33 (5.2)	12 (8.1)	49 (5.2)	0.07
Asymptomatic ICH	1 (0.6)	31 (4.9)	5 (3.4)	37 (3.9)	0.01 ^a
Symptomatic ICH	5 (3.0)	27 (4.3)	4 (2.7)	36 (3.8)	0.62
Cost (baht)	24,400 (2654–50,376)	39,506 (17,051–64,315)	53,649 (8798–79,320)	39,656 (6689–64,805)	< 0.01 ^{a,b,c}
LOS, days	5 (4-6)	5 (4-7)	5 (4-8)	5 (4–7)	0.19
Discharge status					$< 0.01^{b,c}$
Complete recovery	1 (0.6)	2 (0.3)	4 (2.7)	7 (0.7)	
Improved	145 (85.8)	515 (81.9)	118 (79.2)	778 (82.2)	
Not improved	21 (12.4)	80 (12.7)	12 (8.1)	113 (11.9)	
Death	2 (1.2)	32 (5.1)	15 (10.1)	49 (5.2)	

Table 3 Stroke outcomes and complications of acute ischemic stroke patients treated at various hospital levels

Data presented as number (%) or median (1st-3rd IQR)

CHs community hospitals, *RHs* regional hospitals, *THs* tertiary hospitals, *ICH* intracerebral hemorrhage; *LOS* length of stay ^a CHs vs. RHs (p < 0.05)

^b CHs vs. THs (p < 0.05)

^c RHs vs. THs (p < 0.05)

DISCUSSION

The results of this study suggest that CHs may be able to treat acute ischemic stroke in the thrombolytic era in terms of fast rt-PA treatment, stroke awareness, fewer complications, and lower mortality rates compared with the two higher hospital levels. However, proper patient selection for CHs may be needed.

The CHs had significantly better acute ischemic stroke care and outcomes than the higher hospital levels. The times of rt-PA treatment at the CHs were shorter than at the RHs and THs in terms of onset to needle (147 min) and door to needle (55 min), as shown in

Hospital level	Mortality ^a	Asymptomatic ICH ^a	Symptomatic ICH ^a	LOS ^b	Cost ^c	Complications ^a
CHs	0.13 (0.03, 0.67)	0.25 (0.03, 2.36)	1.23 (0.30, 4.96)	0.72 (0.42, 1.21)	-337.56 (p 0.97)	0.59 (0.35, 0.99)
RHs	0.45 (0.19, 1.04)	2.06 (0.68, 6.25)	1.76 (0.58, 5.32)	0.89 (0.60, 1.32)	8667.64 (p 0.23)	1.03 (0.69, 1.55)
THs	1	1	1	1	1	1

 Table 4 Hospital levels and various outcomes in acute ischemic stroke patients

CHs community hospitals, *RHs* regional hospitals, *THs* tertiary hospitals, *ICH* intracerebral hemorrhage, *LOS* length of stay; models adjusted for age, sex, stroke risk factors, stroke subtype, initial NIHSS, stroke onset, thrombolysis treatment, plasma glucose, and complications

^a Adjusted odds ratio (95% confidence interval)

^b Incidence risk ratio (95% confidence interval)

^c Coefficient (*p* value)

Table 2. These data indicate that CHs may provide stroke care more promptly than the larger hospitals.

Regarding stroke awareness and knowledge, the CH group had a higher but comparable proportion of late presentations to the hospital relative to the other two hospital levels. In this group, 65.7% of stroke patients came to the hospital within 24 h, while 66.9% and 80.0% did so in the RH and TH groups (*p* value 0.08), respectively. A previous study showed that the average proportion of stroke awareness was 41%, which was somewhat higher than that of the CH group in this study [9]. These data may indicate good knowledge and awareness of stroke at the community level in northeast Thailand.

There was no statistical difference in the various complications among the three hospital levels, with the exception of asymptomatic intracerebral hemorrhage (Table 3). The rate of symptomatic intracerebral hemorrhage in this study was higher than that of a previous landmark study of rt-PA (3.8% vs. 2.4%) [4]. However, the symptomatic intracerebral hemorrhage rate was not higher than the rates of 5-7% that have been found in general reports [10, 11]. The CH group had a significantly lower rate of asymptomatic intracerebral hemorrhage, than did the THs. These findings may be explained by the higher proportion of patients with small vessel disease in CHs than in the other two hospital levels, 43.8% vs. 35.6% vs. 31.5%, as shown in Table 1. As a result, the CH group had lower initial NIHSS than the others, leading to higher odds of intracerebral hemorrhage [12]. Patients with acute ischemic stroke with higher initial NIHSS had higher odds of symptomatic intracerebral hemorrhage than those with lower NIHSS (16.53 vs. 10.19; p < 0.001). Additionally, faster rt-PA treatment may reduce symptomatic intracerebral hemorrhage by as much as 4% (p < 0.001). [13].

Overall, the favorable discharge rate in cases of acute ischemic stroke was 82.9% (Table 3). The mortality rate was lowest in the CHs (1.2%), which is comparable to that found in another previous study (1.9%) [5]. However, the mortality rate in this study was somewhat higher than in the aforementioned previous study (5.2% vs. 3.2%). These higher mortality rates may be due to the inclusion of more severe cases in this study, as the median NIHSS was higher than that of the previous study (8 vs. 6.5). [5] After adjustment for stroke severity, the CH group was still significantly associated with lower mortality, by 87% compared with the TH group, regardless of stroke severity. There are two possible reasons for these results: more complex patients treated at higher hospital levels, and faster thrombolytic therapy in CHs than the other two hospital levels. Faster time

to rt-PA treatment reduced mortality by 4% (*p* value < 0.001) [13].

The main strength of this study is that stroke outcomes in CHs or RHs were comparable to or even better than those at THs when the rt-PA treatment was equal to non-rt-PA treatment in all groups. Note that rt-PA treatment in both CHs and RHs was prescribed by non-neurologists. The internists or emergency physicians at both hospital levels prescribed rt-PA. Therefore, this may imply that rt-PA may be prescribed by non-neurologists at CHs and RHs. The length of stay in our study was shorter than that in other studies [14, 15], because in Thailand, patients with acute ischemic stroke are transferred from the TH or the RH to a CH or discharged home after stroke stabilization. After discharge, further home rehabilitation is undertaken by village health volunteers and nurses.

This study had some limitations. First, the study population was drawn only from northeast Thailand, where the stroke network mentioned above has been active. The stroke network consists of academic conferences. consultation with the experienced neurologists, nursing care, and stroke unit management. Second, there were no long-term data after discharge. Third, no details were investigated with regard to rt-PA doses or other medications, or with home rehabilitation or endovascular therapy. Clinical comparison was not performed between those treated with and without rt-PA. The CH group had lower stroke severity, which may be explained by the higher rate of small vessel disease. Additionally, CHs may have less complex patients than RHs or THs. The actual rt-PA treatment rate in each hospital level was not studied or compared. Fourth, there was some discharge bias in our study because we report only the deaths during the admission (inhospital mortality), and do not include early post-discharge mortality combined with short in length of stay [16]. Finally, there were no private hospitals included in the study, nor were other factors related to stroke investigated [17–19].

In conclusion, the CHs showed higher-quality care for acute ischemic stroke than they had in the past. The acute ischemic stroke outcomes and quality of care were comparable among the three hospital levels in northeast Thailand. These results may be applicable in other countries with similar hospital level systems if a stroke network is established.

CONCLUSIONS

Ease of access to CHs and good referral systems were able to improve the quality of acute ischemic stroke care in Thailand, meaning that development of a "hub-and-spoke" model is the key to success. Moreover, CHs may have the potential for acute ischemic stroke care in the same way as RHs or THs, with faster rt-PA treatment, in northeast Thailand. However, further studies should be performed to evaluate appropriate patient characteristics for CHs. Therefore, the development of stroke services in CHs may help increase access to stroke treatment in rural areas.

ACKNOWLEDGEMENTS

We would like to thank Dr. Dylan Southard for English proofreading which was funded by the Faculty of Medicine, Khon Kaen University, Thailand, via the Publication Clinic Project. The authors also would like to thank the Thailand Research Fund (TRF), National Health Security Office (NHSO) for their kind assistance in providing the database, and the Neurological Society of Thailand for their kind support.

Funding. This study was supported by the Faculty of Medicine, Khon Kaen University (Grant Number IN59314). The journal's Rapid Service Fee was funded by the authors.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. NV conceived and designed the study, gathered data, interpreted data, and wrote the draft. NK conceived and

designed the study, gathered data, analyzed data, interpreted data, and contributed to the draft. KK gathered data and interpreted data. UP analyzed data. ST gathered data and interpreted data. KS interpreted data and reviewed the final draft. All authors critically revised the manuscript for important intellectual content.

Prior Presentation. A portion of this study was presented in abstract form at the 4th European Stroke Organization Conference, Gothenburg, Sweden, on May 16–18, 2018. The authors would like to thank the participants of the study.

Disclosures. Nisa Vorasoot, Narongrit Kasemsap, Kannikar Kongbunkiat, Udomlack Peansukwech, Somsak Tiamkao, and Kittisak Sawanyawisuth have nothing to disclose.

Compliance with Ethics Guidelines. The protocol was reviewed and approved by the ethics committee in human research, Khon Kaen University, Thailand (HE591294). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Informed consent was not obtained, as the study is a retrospective study of data from a database. Permission was obtained to access and use the data from the National Health Security Office database.

Data Availability. The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/bync/4.0/.

REFERENCES

- 1. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol. 2007;6(2):182–7.
- 2. Suwanwela NC. Stroke epidemiology in Thailand. J Stroke. 2014;16(1):1–7.
- 3. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995; 333:1581–7.
- 4. Hacke W, Kaste M, Bluhmki E, Brozman M, Davalos A, Guidetti D, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359(13):1317–29.
- Nilanont Y, Nidhinandana S, Suwanwela NC, Hanchaiphiboolkul S, Pimpak T, Tatsanavivat P, et al. Quality of acute ischemic stroke care in Thailand: a prospective multicenter countrywide cohort study. J Stroke Cerebrovasc Dis. 2014;23(2):213–9.
- 6. Hatano S. Experience from a multicentre stroke register: a preliminary report. Bull World Health Organ. 1976;54(5):541–53.
- Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1): 35–41.
- Kasner SE, Chalela JA, Luciano JM, Cucchiara BL, Raps EC, McGarvey ML, et al. Reliability and validity of estimating the NIH stroke scale score from medical records. Stroke. 1999;30(8):1534–7.
- 9. National Health Security Office annual report fiscal year 2015 [Internet]. Bangkok; 2015. www.nhso.go.th.
- 10. LaBresh KA, Reeves MJ, Frankel MR, Albright D, Schwamm LH. Hospital treatment of patients with ischemic stroke or transient ischemic attack using the "Get With The Guidelines" program. Arch Intern Med. 2008;168(4):411–7.

- 11. Hsieh FI, Jeng JS, Chern CM, Lee TH, Tang SC, Tsai LK, et al. Quality improvement in acute ischemic stroke care in Taiwan: the breakthrough collaborative in stroke. PLoS ONE. 2016;11(8):1–12.
- 12. Chenna V, Kaul S, Tandra S, Yareeda S, Mathukumalli N, Kohat AK, et al. Predictors of intracerebral hemorrhage in acute stroke patients receiving intravenous recombinant tissue plasminogen activator. Ann Indian Acad Neurol. 2018;21(3):214–9.
- 13. Saver JL, Fonarow GC, Smith EE, Reeves MJ, Grau-Sepulveda MV, Pan W, et al. Time to treatment with intravenous tissue plasminogen activator and outcome from acute ischemic stroke. JAMA. 2013;309(23):2480–8.
- 14. Hillmann S, Wiedmann S, Rücker V, Berger K, Nabavi D, Bruder I, et al. Stroke unit care in Germany: the German stroke registers study group (ADSR). BMC Neurol. 2017;17(1):1–8.
- 15. Huang YC, Hu CJ, Lee TH, Yang JT, Weng HH, Lin LC, et al. The impact factors on the cost and length

of stay among acute ischemic stroke. J Stroke Cerebrovasc Dis. 2013;22(7):E152–8.

- Pouw ME, Peelen LM, Moons KGM, Kalkman CJ, Lingsma HF. Including post-discharge mortality in calculation of hospital standardised mortality ratios: retrospective analysis of hospital episode statistics. BMJ. 2013;347:f5913–f5913.
- 17. Sawunyavisuth B. What are predictors for a continuous positive airway pressure machine purchasing in obstructive sleep apnea patients? Asia Pac J Sci Technol. 2018;23:APST-23-03-10.
- Kingkaew N, Antadech T. Cardiovascular risk factors and 10-year CV risk scores in adults aged 30–70 years old in Amnat Charoen Province, Thailand. Asia Pac J Sci Technol. 2019;24:APST-24-04-04.
- 19. Jingmark S, Kuhirunyaratn P, Theeranut A, Nonjui P. Subjective well-being and related factors among community-dwelling elderly in Udon Thani Province, Thailand. Asia Pac J Sci Technol. 2020;25: APST-25-01-09.