Ineligibility of Intravenous Thrombolysis among Activated Stroke Fast Track Patients of Khon Kaen Hospital

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Abstract

Background and objective: The primary objective was to identify factors responsible for thrombolytic ineligibility. The secondary one was to determine the ratio of stroke type and stroke–mimic conditions, and to evaluate achievement of stroke fast track.

Materials and Methods: We collected all recruited stroke fast track patient data including age, gender, occupation, comorbidity, current medication, symptom onset or last–seen–normal time, vital signs, National Institutes of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), hospital arrival time, time of neurologist consultation, arrival time of neurologist, time of laboratory register and result, time of brain computed tomography (CT) request, performance and interpretation, alteplase administration and its contraindication. Statistical analysis was done appropriately.

Results: There were 181 stroke fast track candidates. One patient was referred to another tertiary hospital because of unavailable brain CT, then 180 patients were enrolled. There were 9 (5.0%) patients of stroke–mimic condition, 39 (19.44%) patients of hemorrhagic stroke, and 136 (75.56%) patients of acute ischemic stroke. Of these 136 patients, 50 (36.76%) cases received thrombolytic therapy and there were 17 (34.0%) cases had got alteplase within target (60 minutes). The avoidable ineligible factors were 2 (2.33%) delayed laboratory report, 1 (1.16%) missed neurologist consultation, delayed Door–to–Neurologist time and no decision making relative. The other unavoidable factors were 74 (86.05%) protocol exclusion, 5 (5.81%) inaccurate onset, 1 (1.16%) denial and 1 (1.16%) high risk brain CT.

Conclusion: The highlights were that most of stroke fast track patients were thrombolytic candidates. One third of them were excluded because of both avoidable and unavoidable reasons that could be resolved by further systemic development.

Keywords: avoidable factor, ineligibility, intravenous thrombolysis, stroke fast track, unavoidable factor (J Thai Stroke Soc. 2019;18(2):15–28)

การศึกษาคุณสมบัติของผู้ป่วยโรคหลอดเลือดสมองที่เข้าสู่ระบบบริการ Stroke Fast Track แต่ไม่เข้าเกณฑ์การรับยาละลายลิ่มเลือด ณ โรงพยาบาลขอนแก่น

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บทคัดย่อ

ความเป็นมาและวัตถุประสงค์: วัตถุประสงค์หลักคือศึกษาสาเหตุ และ/หรือข้อห้ามที่มีผลให้แพทย์ตัดสินใจไม่ให้ยาละลายลิ่มเลือดแก่ผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน วัตถุประสงค์รอง ได้แก่ ศึกษาสัดส่วนของผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน โรคหลอดเลือดสมองแตก และผู้ป่วยที่มีอาการเหมือนโรคหลอดเลือดสมอง แต่ไม่ได้มีสาเหตุจากโรคหลอดเลือดสมอง (stroke-mimic) รวมทั้งศึกษาผลการดำเนินการ Stroke fast track

วัสดุและวิธีการ: รวบรวมข้อมูลของผู้ป่วยโรคหลอดเลือดสมองที่เข้าสู่ระบบบริการ Stroke fast track ในช่วงเวลาที่กำหนด โดยเก็บข้อมูลอายุ เพศ อาชีพ โรคประจำตัว ยาที่ใช้ประจำ เวลาที่เริ่มมีอาการ หรือล่าสุดที่ผู้ป่วยยังมีอาการเป็นปกติ สัญญาณชีพ ความรุนแรงของอาการโดยประเมินด้วย National Institutes of Health Stroke Scale (NIHSS) และ modified Rankin scale (mRS) เวลาที่มาถึงโรงพยาบาล เวลาปรึกษา และเวลาที่อายุรแพทย์ประสาทวิทยามาถึง เวลาที่ส่งตรวจ เวลาที่รายงานผลตรวจ และผลตรวจทางห้องปฏิบัติการ เวลาที่ขอและทำเอกซเรย์คอมพิวเตอร์สมอง ผลตรวจทางรังสีวินิจฉัย เวลาที่เริ่มให้ยาละลายลิ่มเลือด และข้อห้ามของการให้ยาดังกล่าว แล้วนำข้อมูลเหล่านี้มาวิเคราะห์โดยวิธีทางสถิติ

ผลการศึกษา: ผู้ป่วย 181 รายที่เข้าเกณฑ์ Stroke fast track มีผู้ป่วย 1 ราย ไม่ได้เข้าระบบบริการ เนื่องจากทางโรงพยาบาลปิดให้บริการเอกซเรย์คอมพิวเตอร์ และได้ส่งตัวไปโรงพยาบาลแห่งอื่น จึงเหลือผู้ป่วยที่ทำการศึกษาจำนวน 180 ราย มีผู้ป่วย 9 ราย (ร้อยละ 5) มีอาการเหมือนผู้ป่วยที่มีอาการเหมือนโรคหลอดเลือดสมอง แต่ไม่ได้มีสาเหตุจากโรคหลอดเลือดสมอง ผู้ป่วย 39 ราย (ร้อยละ 19.44) เป็นโรคหลอดเลือดสมองแตก และอีก 136 ราย (ร้อยละ 75.56) มีภาวะสมองขาดเลือดเฉียบพลัน โดยในผู้ป่วยเหล่านี้มี 50 ราย (ร้อยละ 36.76) ได้รับยาละลายลิ่มเลือด และพบว่ามีผู้ป่วยจำนวน 17 ราย (ร้อยละ 34) ได้รับยาตามเป้าหมาย คือภายใน 60 นาที สาเหตุที่สามารถหลีกเลี่ยงได้ซึ่งทำให้ผู้ป่วยไม่ได้รับยาละลายลิ่มเลือดได้แก่ ความล่าช้าในการรายงานผลตรวจทางห้องปฏิบัติการจำนวน 2 ราย (ร้อยละ 2.33) ไม่ได้ปรึกษาอายุรแพทย์ประสาทวิทยาจำนวน 1 ราย (ร้อยละ 1.16) ความล่าช้าของอายุรแพทย์ประสาทวิทยาจำนวน 1 ราย (ร้อยละ 1.16) และไม่มีญาติที่ตัดสินใจการรักษาจำนวน 1 ราย (ร้อยละ 1.16) นอกจากนี้สาเหตุที่ไม่อาจหลีกเลี่ยงได้ ได้แก่ มีเกณฑ์คัดออกของ Stroke fast track จำนวน 74 ราย (ร้อยละ 86.05) ความคลาดเคลื่อนของเวลาที่เริ่มมีอาการจำนวน 5 ราย (ร้อยละ 5.81) ญาติปฏิเสธการให้ยาละลายลิ่มเลือดจำนวน 1 ราย (ร้อยละ 1.16) และเอกซเรย์คอมพิวเตอร์สมองมีลักษณะที่มีความเสี่ยงสูงจำนวน 1 ราย (ร้อยละ 1.16)

สรุป: การศึกษานี้พบว่าผู้ป่วยที่เข้าสู่ระบบบริการ Stroke fast track ส่วนใหญ่เป็นผู้ป่วยที่มีโอกาสได้รับยาละลายลิ่มเลือด แต่มีจำนวนถึง 1 ใน 3 ที่ไม่ได้รับยาดังกล่าว โดยมีเหตุผลทั้งที่หลีกเลี่ยงได้และไม่ได้ ซึ่งหากนำไปทบทวนปรับปรุงระบบ จะสามารถพัฒนาแก้ไขสาเหตุดังกล่าวได้

คำสำคัญ: สาเหตุที่สามารถหลีกเลี่ยงได้, การขาดคุณสมบัติ, ยาละลายลิ่มเลือด, stroke fast track, สาเหตุที่ไม่อาจหลีกเลี่ยงได้ (J Thai Stroke Soc. 2019;18(2):15-28)

Introduction

Acute stroke is one of the common neurological disorders. In Thailand, the incidence was 690–1,880 per 100,000 population.[1,2] According to The National Institute of Neurological Disorders and Stroke study (NINDS study), recombinant tissue plasminogen activator (rt-PA; alteplase) administration improved neurological outcome of acute ischemic stroke patients whose onset was within 3 hours.[3] The latter one, The European Cooperative Acute Stroke Study III (ECASS III), demonstrated the benefit of alteplase treatment among acute ischemic stroke patients with extended onset to 4.5 hours.[4] As The American Heart Association/American Stroke Association[5] and Thai clinical practice guideline of ischemic stroke[6] recommended thrombolytic administration for eligible ischemic stroke patients (Class I; Level of Evidence A). The stroke fast track and clinical practice guideline of Khon Kaen hospital, the tertiary care hospitals of 7th health area of Thailand, has been established since 2011. The symptom onset of enrolled patients must not exceed 4.5 hours.

After stroke fast track activation, there were various reasons why some patients did not receive thrombolytic. These causes might be associated with individual medical conditions, their relatives' judgement, the medical service system and medical personnel. Some prior studies reported that 25–94% of acute ischemic stroke patients arrived in time but did not receive thrombolytic therapy because of low National Institutes of Health Stroke Scale (NIHSS), rapidly clinical improvement, massive infarction, intracranial hemorrhage, perceived protocol exclusion (e.g., gastrointestinal bleeding, prolonged International normalised ratio (INR), recent surgery, etc.), interhospital or intrahospital referral delay, individual comorbidity and patient denial.[7-13]

The primary objective of this study was to identify the reason why some patients were ineligible for IV thrombolytic therapy despite they were transferred in golden period time. The secondary objectives were to determine the ratio of acute ischemic stroke, hemorrhagic stroke, stroke-mimic conditions (e.g., hypoglycemia, hyperglycemia, encephalopathy, primary headache disorder, tumor, abscess, seizure, peripheral vestibular disorder, polyneuropathy, delirium and psychiatric disorders)[14-19] and to evaluate achievement of stroke fast track protocol.

Materials and Methods

All activated stroke fast track patients in Khon Kaen hospital between August 2017 and February 2018 were recruited into this study. The collected data were age, gender, occupation, comorbidity (hypertension, diabetic mellitus, dyslipidemia, heart disease, previous cerebrovascular disease), current medication, symptom onset or last-seen-normal time, vital signs, neurodeficit determined by NIHSS, physical disability measured by modified Rankin scale (mRS), emergency department arrival time, time of brain computed tomography (CT) request, time of brain CT performance, time of brain CT interpretation, time of neurologist consultation, arrival time of neurologist, time of laboratory register, time of laboratory report, time of thrombolytic administration, contraindication of thrombolytic, complete blood count with platelet count, initial capillary blood glucose, coagulogram, brain CT result and diagnosis.

These are definitions for the present study. Door-to-CT time (DTC) was defined as duration from arrival time to completely performed brain CT time and classified to be late if it was more than 30 minutes. Door-to-Lab time (DTL) was the

duration from arrival time to result report time and defined to be late if it was more than 30 minutes. According to Thai Stroke Service Plan, both DTC and DTL were indicated to be less than 30 minutes. The definition of Door-to-Neurologist time (DTNe) was period from arrival time to neurologist or medicine resident visiting time and that should not be more than 30 minutes. Door-to-Needle time (DTN) was time from arrival to thrombolytic administration. According to Thai Stroke Service Plan, it was indicated to be less than 60 minutes. Thrombocytopenia was defined as platelet count less than 100,000/mm$^{3.6,20}$ Coagulopathy meant prothrombin time (PT) was more than 15 seconds or INR was more than 1.7[6,20] or partial thromboplastin time (PTT) was more than 30 seconds. The large infarction on brain CT was early ischemic change of one third or more of the MCA territory.[21-23]

Statistical analysis

The data were presented as mean and standard deviation (SD) for continuous variables with normal distribution (according to Kolmogorov-Smirnov test) and as median and interquartile range (IQR) for the other. The categorical data were reported as frequency and percentage.

Chi-square, Fischer-exact test or McNemar's test was used as appropriates for proportion comparison. T-test or Wilcoxon-Mann Whitney test was used for continuous variables comparison properly. The level of statistical significance was defined when *P*-value was less than 0.05.

Results

From August 2017 to February 2018, there were 181 patients compatible with stroke fast track candidates. There was one patient referred to another tertiary hospital, Srinagarind Hospital of Khon Kaen university, because of unavailable brain CT at that time. One hundred and eighty patients got stroke fast track activation and were enrolled to the present study. As shown in Figure 1, among stroke fast track activation patients, there were 9 (5.0%) patients of stroke-mimic condition, i.e., 3 (33.33%) epilepsy and transient ischemic attack, 1 (11.11%) Guillain-Barre syndrome, 1 (11.11%) hyponatremia and 1 (11.11%) encephalitis patients. Thirty-five (19.44%) patients had hemorrhagic stroke, and the remaining 136 (75.56%) had got acute ischemic stroke. From 136 patients, 50 (36.76%) cases received thrombolytic therapy while the other 86 (63.24%) cases did not.

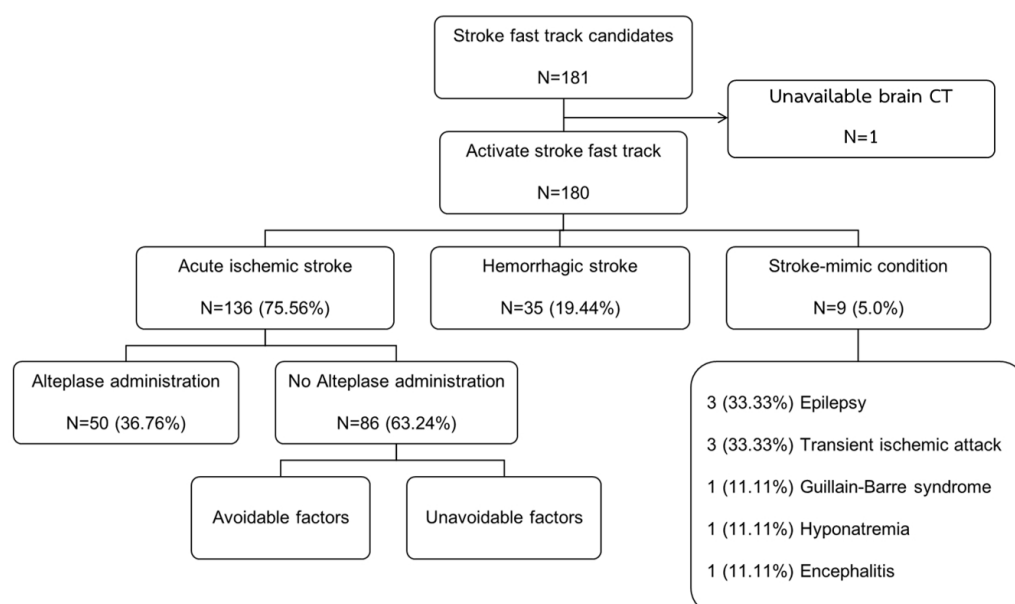*Figure 1. Diagnoses among activated stroke fast track patients*

Table 1. *Baseline characteristics of activated stroke fast track patients (N=180)*

Baseline characteristics	Mean ± SD or N (%)	Median (IQR)
Age	65.32 ± 12.67	
Male	95 (52.78)	
Onset duration (minute)	144.21 ± 89.85	141 (95.5–182)
Comorbidities	149 (82.78)	
Hypertension	106 (58.89)	
Diabetes mellitus	58 (32.22)	
Dyslipidemia	44 (24.44)	
Atrial fibrillation	42 (23.33)	
Previous cerebrovascular disease	23 (12.78)	
Valvular heart disease	11 (6.11)	
Cardiomyopathy	6 (3.33)	
Sick sinus syndrome	4 (2.22)	
Congestive heart failure	4 (2.22)	
Anticoagulant usage	8 (4.88)	
Systolic blood pressure (mmHg)	164.07 ± 33.90	
Diastolic blood pressure (mmHg)	94.74 ± 22.88	
NIHSS	10.79 ± 8.39	9 (3–16.5)
mRS on admission	4.41 ± 0.96	
Capillary blood glucose (mg/dL)	141.19 ± 66.56	
Thrombocytopenia (Platelet < 100,000/mm3)	2 (1.11)	
Coagulopathy*	16 (8.89)	
Large infarction on brain CT	16 (8.89)	
Door–to–CT time (minute)	31.84 ± 14.99	
Door–to–Lab time (minute)	35.16 ± 14.90	
Door–to–Neurologist time (minute)	49.27 ± 37.19	40 (33–58)
Door–to–Needle time (minute)	73.7 ± 22.39	

**PT > 15 seconds or INR ≥ 1.7 or PTT > 30 seconds

CT, computed tomography; INR, international normalised ratio; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PT, prothrombin time; PTT, partial thromboplastin time; SD, standard deviation;

From Table 1, age of stroke fast track activation patients was 65.32 ± 12.67 years old. Ninety–five (52.78%) of them were male patients. The median with IQR of onset duration was 141 (95.5–182) minutes. There were 149 (82.78%) patients who had comorbidities that were 106 (58.89%) with hypertension, 58 (32.22%) with diabetes mellitus, 44 (24.44%) with dyslipidemia, 42 (23.33%) with atrial fibrillation, 23 (12.78%) with previous cerebrovascular disease (CVD), 11 (6.11%) with valvular heart disease, 6 (3.33%) with cardiomyopathy, 4 (2.22%) with sick sinus syndrome and 4 (2.22%) congestive heart failure. Multiple comorbidities had been found in 102 (56.67%) patients. Anticoagulant was used in 8 (4.88%) cases. The mean ± SD of systolic and

diastolic blood pressure was 164.07 ± 33.90 and 94.74 ± 22.88 mmHg, respectively. Their NIHSS was 9 (3–16.5) and mRS was 4.41 ± 0.96. According to protocol laboratory investigation, there were 2 (1.11%) patients who had platelet less than 100,000/mm^3. The mean and SD of capillary blood glucose was 141.19 ± 66.56 mg/dL. There were 2 (1.11%) hypoglycemic[24] patients whose neurodeficit persisted despite of out of hypoglycemia, one was ischemic and the other was hemorrhagic stroke.

From the brain CT results, there were 16 (8.89%) patients who had large infarction. The mean of DTC time was 31.84 ± 14.99 minutes and DTL time was 35.16 ± 14.90 minutes. The DTNe time of 104 (76.47%) acute ischemic stroke patients was 40 (33–58) minutes. (The rest was managed by emergency physician collaborating with on–call neurologist (via phone)). The mean of DTN time was 73.7 ± 22.39 minutes.

Table 2. Principal factors responsible for thrombolysis ineligibility of each acute ischemic stroke patient (N=86)

Factors	N (%)
Avoidable factors	
– Delayed Laboratory report	2 (2.33)
– Miss neurologist consultation	1 (1.16)
– delayed Door-to-Neurologist time	1 (1.16)
– No decision making relative	1 (1.16)
Unavoidable factors: Protocol exclusion	
– NIHSS < 4	42 (48.84)
– Rapid neurodeficit recovery	10 (11.63)
– Large infarction on brain CT	7 (8.14)
– Hypodensity on brain CT	3 (3.49)
– Onset > 180 minutes with diabetes mellitus and old cerebrovascular disease	3 (3.49)
– Onset > 180 minutes and age > 80 years	2 (2.33)
– Onset > 180 minutes and NIHSS > 25	2 (2.33)
– Onset > 180 minutes and anticoagulant usage	2 (2.33)
– Recent stroke	1 (1.16)
– Uncontrollable blood pressure	1 (1.16)
– Coagulopathy*	1 (1.16)
Unavoidable factors: Others	
– Inaccurate onset	5 (5.81)
– Thrombolytic denial	1 (1.16)
– Severe small vessel disease on brain CT	1 (1.16)

*PT > 15 seconds or INR ≥ 1.7 or PTT > 30 seconds

CT, Computed tomography; NIHSS, National Institutes of Health Stroke Scale

Table 2 demonstrated the principal reasons why each acute ischemic stroke patient was ineligible for thrombolytic therapy. The avoidable factors are 2 (2.33%) patients with delayed laboratory report, 1 (1.16%) patient with miss neurologist consultation, 1 (1.16%) delayed DTNe time and 1 (1.16%) without decision making relative. And other unavoidable factors, according to protocol exclusion, were 42 (48.84%) patients with minor stroke (NIHSS < 4), 10 (11.63%) patients with rapid neurodeficit recovery, 7 (8.14%) with large infarction on brain CT, 3 (3.49%) patients with seen hypodensity on their brain CT and onset > 180 minutes with diabetes mellitus and old cerebrovascular disease. Two (2.33%) patients with onset > 180 minutes who had age > 80 years, NIHSS > 25 and anticoagulant usage were not eligible. There was 1 (1.16%) ineligible case with recent stroke, uncontrolled blood pressure despite appropriate medication and coagulopathy (prolonged PT/INR). The others of unavoidable factors were 5 (5.81%) patients with inaccurate onset and 1 (1.16%) case of severe small vessel disease on brain CT. There was 1 (1.16%) case whose relative denied the treatment.

Table 3. *Achievement of stroke fast track protocol between alteplase and no alteplase administration (N=86)*

Indicators	Alteplase (N=50)	No alteplase (N=86)	*P*–value
Door–to–CT time (minute)	36.32 ± 16.51	29.23 ± 13.46	0.01
Delayed Door–to–CT time	31 (62.0)	35 (40.70)	0.02
Door–to–Lab time (minute)	40.98 ± 20.03	34.28 ± 11.69	0.02
Delayed Door–to–Lab time	34 (68.0)	56 (65.12)	0.73
Door–to–Neurologist time (minute)	41.5 (36 – 59)	37.5 (33 – 51)	0.14
Delayed Door–to–neurologist	37 (80.43)	45 (77.59)	0.81

CT, Computed tomography

Table 3 revealed the achievement of stroke fast track for acute ischemic stroke patients and compared the indicators between thrombolytic and non-thrombolytic groups. The median of DTC time of thrombolytic treatment group was 36.32 ± 16.51 minutes while the other was 29.23 ± 13.46 minutes (*P*-value = 0.01). Thirty-one (62.0%) cases with delayed DTC time was found in thrombolytic and 35 (40.70%) in the other group (*P*-value = 0.02). The mean of DTL time was 40.98 ± 20.03 minutes and the other one was 34.28 ± 11.69 minutes (*P*-value = 0.02). In the first group, there were 34 (68.0%) delayed DTL time cases, and 56 (65.12%) in the latter (*P*-value = 0.73). The DTNe time of thrombolytic and non-thrombolytic groups were 41.5 (36–59) and 37.5 (33–51) minutes respectively (*P*-value = 0.14). The number of delayed DTNe time was 37 (80.43%) of thrombolytic and 45 (77.59%) of non-thrombolytic group (*P*-value = 0.81).

Table 4. *Achievement of stroke fast track protocol between early and late thrombolytic (N=50)*
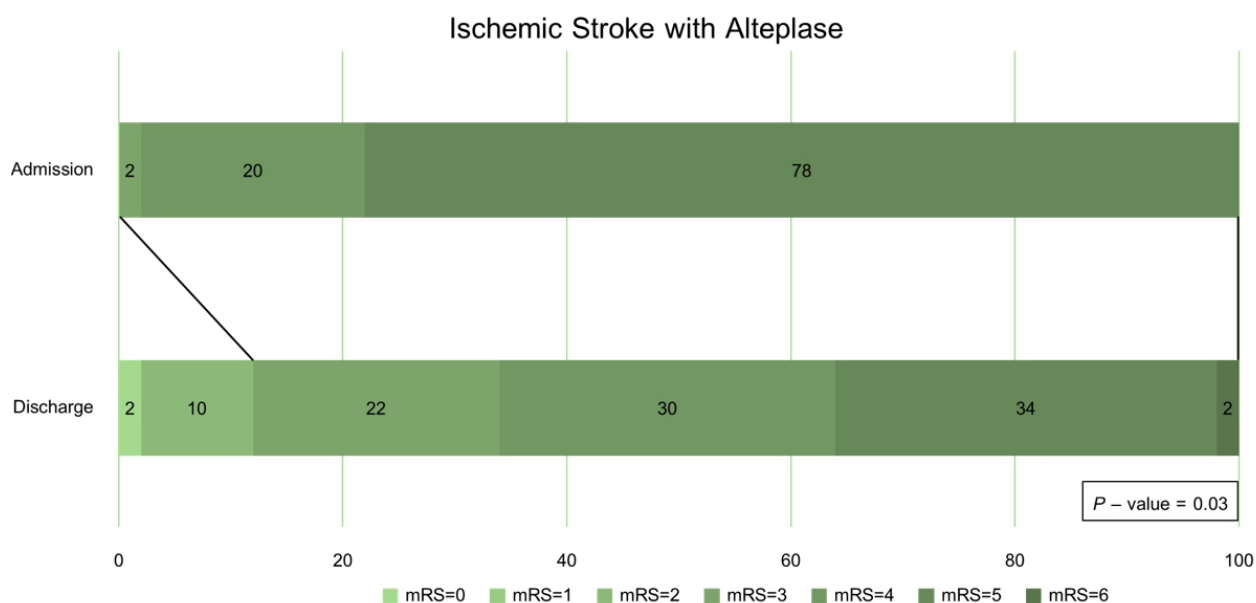
Indicators	Early thrombolytic (N=17)	Late thrombolytic (N=33)	P–value
Door-to-CT time (minute)	29.35 ± 11.01	39.91 ± 17.82	0.01
Delayed Door-to-CT time	7 (41.18)	24 (72.73)	0.03
Door-to-Lab time (minute)	40.47 ± 14.67	41.24 ± 20.03	0.44
Delayed Door-to-Lab time	11 (64.71)	23 (69.70)	0.72
Door–to–Neurologist time (minute)	40 (31 – 44)	47 (37 – 71)	0.05
Delayed Door–to–neurologist time	12 (80.0)	25 (80.65)	1.00

CT, Computed tomography

Table 4 showed indicator comparison between 2 groups of the patients who received alteplase within 60 minutes and the others got after 60 minutes since arrival. The DTC time of the early thrombolytic group was 29.35 ± 11.01 while the late group was 39.91 ± 17.82 minutes (*P*-value = 0.01). Seven cases (41.18%) of early group got delayed DTC time and 24 (72.73%) were found in the other (*P*-value = 0.03). The early group had DTL time of 40.47 ± 14.67 and the other had 41.24 ± 20.03 minutes (*P*-value = 0.44). Delayed DTL time were 11 (64.71%) and 23 (69.70%) in early and late groups, respectively (*P*-value = 0.72). The DTNe time of the early group was 40 (31–44) while of the other was 47 (37–71) minutes (*P*-value = 0.05). There were 12 (80.0%) patient in the early group had delayed DTNe time, and 25 (80.65%) in the other (*P*-value = 1.00).

Figure 2. *On admission and discharge modified Rankin scale (mRS) of each stroke type*

Ischemic Stroke without Alteplase
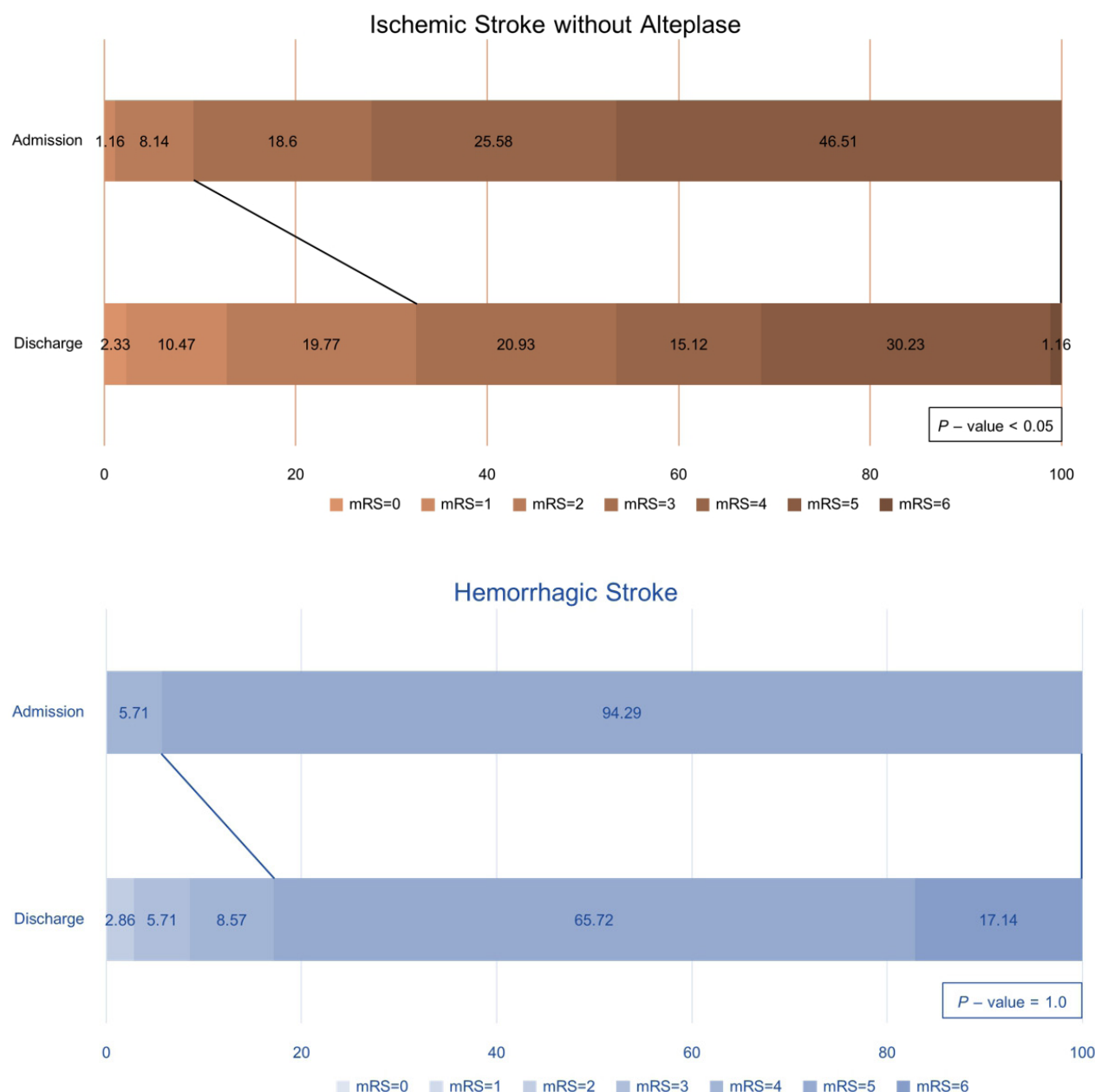

Hemorrhagic Stroke

Figure 2 demonstrated physical disability among stroke fast track activation. The first group, acute ischemic stroke with thrombolytic therapy, severe disability (mRS > 2) decreased from 100% on admission to 88.0% on discharge (P-value = 0.03). The second, acute ischemic stroke without thrombolytic decreased from 90.7% to 67.43% (P-value < 0.05). And the last, hemorrhagic stroke decreased from 100% to 97.14% (P-value = 1.0).

Discussion

This is the first report of Khon Kaen hospital stroke fast track activation analysis for the reasons while some cases did not receive thrombolytic therapy. It will be baseline information before revised guideline evaluation.

In the present study, the number of stroke fast track candidates was 181 patients, but there was 1 case that cannot be activated because that time was turn-off time for the only one CT machine of Khon Kaen hospital. Among 180 activations, most cases (75.56%) were still acute

ischemic stroke as prevalence of 75–80% from other studies[1,25]. Most stroke-mimic conditions were found similarly to previous reports[14–19] except a case of hyponatremia who presented alike brainstem stroke. If these stroke-mimic conditions were carefully excluded prior to stroke fast track activation, this might be relieved the burden at the emergency department. Furthermore, there was a case who received thrombolytic therapy and diagnosed of infective endocarditis later. He got post-thrombolytic intracerebral hemorrhage and mRS of 5.

The average age of these patients was not different from Thai Epidemiological Stroke (TES) study which report of 65.0 ± 13 years old.[1,26] Their median of onset was within first 180 minute. One hundred and twenty-six patients (70.0%) arrived within 180 minutes leading to less relatively contraindications than late arrivals. The comorbidities were mostly atherosclerotic risks and heart diseases which increased risks of embolic stroke.[27,28] Nevertheless, the patients who should have anticoagulant usage, 8 (4.88%) cases, were still suboptimal. The mean of initial blood pressure was 164.07 ± 33.90/94.74 ± 22.88 mmHg that was not thrombolytic contraindication. The median of NIHSS was 9 (3–16.5) which was not high probability of death or severe disability (less than 15).[29,30] The mean of mRS was 4.41 ± 0.96 that classified to be severe (more than 2).[31] There were 2 case of thrombocytopenia, 1 had encephalitis and the other had minor acute ischemic stroke. Sixteen cases had coagulopathy, 12 of these was acute ischemic stroke, 3 hemorrhagic stroke and 1 epilepsy. There were 2 cases with high PTT (30.4 and 34 seconds) received thrombolytic but there was no post-thrombolytic intracerebral hemorrhage.

According to some clinical practice guidelines[6,30,32] including of Khon Kaen hospital, large infarction on brain CT was one of contraindication for thrombolytic whereas it was not in another guideline[20] nor increased symptomatic intracerebral hemorrhage[33], here were 2 patients considered to receive thrombolytic therapy. Their follow-up brain CT had no intracerebral hemorrhage. The means of both DTC and DTL time exceeded the service plan limits (< 30 minutes). The DTNe time was various, depending on regular or off hours (regular hours meant duration in Monday through Friday from 08:00 to 16:00, off hours meant duration in Monday through Friday from 16:01 to 07:59 and Friday at 16:01 through Monday at 07:59, or any time during a holiday)[34], its median was 40 (33–58) minutes. The mean of DTN time was more than the desired goal (< 60 minutes).

The main factors associated with thrombolytic ineligibility were identified in Table 2. The first, avoidable factors, 2 (2.33%) cases got laboratory result after their onset had passed 270 minutes. One case (1.16%) was not evaluated by neurologist whereas he had no contraindication and was in time. Another one, although he arrived within 180 minutes, the neurologist assessed him at the time passing 270 minutes. And the last one, the medical personnel was not able to look for his relative who could make treatment decision.

The unavoidable factors, most were minor stroke (NIHSS < 4), the second were rapid recovery of neurodeficit (10 (11.63%)). Seven (8.14%) patients' brain CT showed large infarction which thrombolytic protocol, i.e., onset > 180 minutes coexisting with diabetes mellitus and old cerebrovascular disease, age > 80 years, NIHSS > 25 and anticoagulant usage.

The small number of exclusions was recent stroke, failed medical control of blood pressure in time and prolong PT/INR.

There were 5 (5.81%) cases with inaccurate onset or last-seen-normal time. And small amount of cases denied the treatment due to hemorrhagic risk unacceptance. There was 1 (1.16%) case that the neurologist decided not to give him thrombolytic because his brain CT showed severe small vessel disease, proposed risk factor of thrombolytic-related ICH[35], although this was not thrombolytic contraindication.[6,20,36,37] The other contraindication, thrombocytopenia, was found in 1 patient whom neurologist excluded from thrombolytic candidates because of minor stroke.

Among 86 acute ischemic stroke patients, there were 50 (36.76% or 62.50% of all stroke fast track activations) received thrombolytic. Of these 50 cases, 17 (34.0%) had got thrombolytics within target time (60 minutes). The mean of DTC time and the proportion of patients with delayed DTC time (> 30 minutes) of non-thrombolytic were significantly lower than thrombolytic group. It might be caused by more severity, transfer difficulty and required resuscitation of patients in thrombolytic group. Contrast with early and late thrombolytic group comparison, the early group had significantly shorter DTC time and less proportion of patients with delayed DTC time as shown in table 4. This was considered that delayed DCT time had impact in DTN but it was not the main factor causing thrombolytic ineligibility.

The thrombolytic group had significantly higher mean of DTL time with statistical significance. This had to be further analyzed how to get faster. There was insignificant difference of delayed DTL ratio between thrombolytic vs non-thrombolytic and early vs late thrombolytic groups. The delayed DTL time was also not the main impact in ineligible thrombolysis. DTNe time was not significantly different between thrombolytic-nonthrombolytic and early-late thrombolytic groups. However, these parameters could be improved to be faster. The further amelioration is analysis of laboratory and brain CT algorithm to make them lean. Prereferral blood test for CBC and PT/INR at the primary care hospital and sending report via LINE application may shorten laboratory awaiting time. Early stroke fast tract activation prior to emergency department arrival can make better coordination.

Severe disability ratio of acute ischemic stroke both thrombolytic and non-thrombolytic patients was decreased after discharge with statistical significance (P-value = 0.03 and < 0.05, respectively) while of hemorrhagic stroke was not significantly different from initial. This was according with the natural history of hemorrhagic stroke.[38-40]

In this study, there was not enough follow-up patients' information. In the next evaluation, follow-up data and regular indicator monitoring could be the important resource for stroke fast track and stoke service plan development.

Conclusion

The highlights of this present study were that most of stroke fast track activation patients were thrombolytic candidates. One third of them were excluded from stroke fast track protocol because of both avoidable and unavoidable reasons. Some identified factors could be improved according to the new guideline and systemic development in the future.

Originality and body of knowledge

These analyses would be the intrahospital benchmark of stroke fast track quality. For other resource-limited hospitals, these study results might be useful to develop their stroke fast track protocols.

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Conflicts of interest

There is no conflict of interest.

References

1. Suwanwela NC. Stroke epidemiology in Thailand. J Stroke. 2014; 16(1): 1-7.

2. Hanchaiphiboolkul S, Poungvarin N, Nidhinandana S, Suwanwela NC, Puthkhao P, Towanabut S, et al. Prevalence of stroke and stroke risk factors in Thailand: Thai Epidemiologic Stroke (TES) Study. J Med Assoc Thai. 2011; 94(4): 427-36.

3. National Institute of Neurological D, Stroke rt PASSG. Tissue plasminogen activator for acute ischemic stroke. The New England journal of medicine. 1995;333(24):1581-7.

4. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos 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.

5. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association.Stroke. 2018; 49(3): e46-e110.

6. ทัศนีย์ ตันติฤทธิศักดิ์, บรรณาธิการ. แนวทางการรักษาโรคหลอดเลือดสมองตีบหรืออุดตันสำหรับแพทย์. พิมพ์ครั้งที่ 2. กรุงเทพฯ: หจก. จีซัตเซส พริ้นติ้ง; 2555.

7. Pidaparthi L, Kotha A, Aleti VR, Kohat AK, Kandadai MR, Turaga S, et al. Factors influencing nonadministration of thrombolytic therapy in early arrival strokes in a university hospital in Hyderabad, India. Ann Indian Acad Neurol. 2016; 19(3): 351-5.

8. Koennecke HC, Nohr R, Leistner S, Marx P. Intravenous tPA for ischemic stroke team performance over time, safety, and efficacy in a single-center, 2-year experience. Stroke. 2001; 32(5): 1074-8.

9. Katzan IL, Furlan AJ, Lloyd LE, Frank JI, Harper DL, Hinchey JA, et al. Use of tissue-type plasminogen activator for acute ischemic stroke: the Cleveland area experience. JAMA. 2000; 283(9): 1151-8.

10. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. Neurology. 2001; 56(8): 1015-20.

11. Van den Berg JS, de Jong G. Why ischemic stroke patients do not receive thrombolytic treatment: results from a general hospital. Acta Neurol Scand. 2009; 120(3): 157-60.

12. Cocho D, Belvís R, Martí-Fàbregas J, Molina-Porcel L, Díaz-Manera J, Aleu A, et al. Reasons for exclusion from thrombolytic therapy following acute ischemic stroke. Neurology. 2005; 64(4): 719–20.

13. O'Connor RE, McGraw P, Edelsohn L. Thrombolytic therapy for acute ischemic stroke: why the majority of patients remain ineligible for treatment. Ann Emerg Med. 1999; 33(1): 9–14.

14. Hosseininezhad M, Sohrabnejad R. Stroke mimics in patients with clinical signs of stroke. Caspian J Intern Med. 2017; 8(3): 213–6.

15. Dupre CM, Libman R, Dupre SI, Katz JM, Rybinnik I, Kwiatkowski T. Stroke chameleons. J Stroke Cerebrovasc Dis. 2014; 23(2): 374–8.

16. Hand PJ, Kwan J, Lindley RI, Dennis MS, Wardlaw JM. Distinguishing between stroke and mimic at the bedside: the brain attack study. Stroke. 2006; 37(3): 769–75.

17. Kose A, Inal T, Armagan E, Kıyak R, Demir AB. Conditions that mimic stroke in elderly patients admitted to the emergency department. J Stroke Cerebrovasc Dis. 2013; 22(8): e522–7.

18. Vilela P. Acute stroke differential diagnosis: Stroke mimics. Eur J Radiol. 2017; 96: 133–44.

19. Fernandes PM, Whiteley WN, Hart SR, Al-Shahi Salman R. Strokes: mimics and chameleons. Pract Neurol. 2013; 13(1): 21–8.

20. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013; 44(3): 870–947.

21. Wijdicks EF, Sheth KN, Carter BS, Greer DM, Kasner SE, Kimberly WT, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014; 45(4): 1222–38.

22. Patel SC, Levine SR, Tilley BC, Grotta JC, Lu M, Frankel M, et al. Lack of clinical significance of early ischemic changes on computed tomography in acute stroke. JAMA. 2001; 286(22): 2830–8.

23. Hacke W, Kaste M, Fieschi C, Toni D, Lesaffre E, von Kummer R, et al. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). JAMA. 1995; 274(13): 1017–25.

24. C RM, George B, Lawrence B, J.M. BA, David DA, Mary d, et al. Standards of medical care in diabetes 2018. Diabetes Care. 2018; 41: S61.

25. Sridharan SE, Unnikrishnan JP, Sukumaran S, Sylaja PN, Nayak SD, Sarma PS, et al. Incidence, types, risk factors, and outcome of stroke in a developing country: the Trivandrum Stroke Registry. Stroke. 2009; 40(4): 1212–8.

26. 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.

27. Kistler JP. The risk of embolic stroke. Another piece of the puzzle. N Engl J Med. 1994; 331: 1517–9.

28. Arboix A, Alió J. Cardioembolic stroke: clinical features, specific cardiac disorders and prognosis. Curr Cardiol Rev. 2010; 6(3): 150–61.

29. Adams HP, Davis PH, Leira EC, Chang KC, Bendixen BH, Clarke WR, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology. 1999; 53(1): 126–31.

30. Dharmasaroja PA, Muengtaweepongsa S, Pattaraarchachai J, Dharmasaroja P. Intracerebral hemorrhage following intravenous thrombolysis in Thai patients with acute ischemic stroke. J Clin Neurosci. 2012; 19(6): 799–803.

31. Weisscher N, Vermeulen M, Roos YB, de Haan RJ. What should be defined as good outcome in stroke trials; a modified Rankin score of 0–1 or 0–2? J Neurol. 2008; 255(6): 867–74.

32. Committee ESOEE, Committee EW. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis. 2008; 25(5): 457–507.

33. Salintip K, Pawut M. Factors Associated with Symptomatic Intracerebral Hemorrhage after Thrombolytic Therapy in Acute Ischemic Stroke. Thai Journal of Neurology. 2014; 30: 16–23.

34. Rodríguez-Rivera IV, Santiago F, Estapé ES, González-Sepúlveda L, Brau R. Impact of Day of the Week and Time of Arrival on Ischemic Stroke Management. P R Health Sci J. 2015; 34(3): 164–9.

35. Palumbo V, Boulanger JM, Hill MD, Inzitari D, Buchan AM, Investigators C. Leukoaraiosis and intracerebral hemorrhage after thrombolysis in acute stroke. Neurology. 2007; 68(13): 1020–4.

36. Pantoni L, Fierini F, Poggesi A. Thrombolysis in acute stroke patients with cerebral small vessel disease. Cerebrovasc Dis. 2014; 37(1): 5–13.

37. Charidimou A, Pasi M, Fiorelli M, Shams S, von Kummer R, Pantoni L, et al. Leukoaraiosis, Cerebral Hemorrhage, and Outcome After Intravenous Thrombolysis for Acute Ischemic Stroke: A Meta-Analysis (v1). Stroke. 2016; 47(9): 2364–72.

38. Saulle MF, Schambra HM. Recovery and Rehabilitation after Intracerebral Hemorrhage. Semin Neurol. 2016; 36(3): 306–12.

39. Fogelholm R, Murros K, Rissanen A, Avikainen S. Long term survival after primary intracerebral haemorrhage: a retrospective population based study. J Neurol Neurosurg Psychiatry. 2005; 76(11): 1534–8.

40. Paolucci S, Antonucci G, Grasso MG, Bragoni M, Coiro P, De Angelis D, et al. Functional outcome of ischemic and hemorrhagic stroke patients after inpatient rehabilitation: a matched comparison. Stroke. 2003; 34(12): 2861–5.