

**FACTORS INFLUENCING EARLY NEUROLOGICAL  
RECOVERY IN PATIENTS WITH ACUTE  
ISCHEMIC STROKE**



**ORAPEN SUKHAVULLI**

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Thesis  
entitled  
**FACTORS INFLUENCING EARLY NEUROLOGICAL  
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ISCHEMIC STROKE**

*Orapen Sukhavulli*

.....  
Miss Orapen Sukhavulli  
Candidate

*Siriorn Sindhu*

.....  
Assoc. Prof. Siriorn Sindhu,  
Ph.D. (Nursing)  
Major advisor

*Wanpen Pinyopassakul*

.....  
Assoc. Prof. Wanpen Pinyopassakul,  
Ph.D. (Nursing)  
Co-advisor

*Chukiat Viwatwongkasem*

.....  
Assoc. Prof. Chukiat Viwatwongkasem,  
Ph.D. (Statistics)  
Co-advisor

*Patcharee Lertrit*

.....  
Prof. Patcharee Lertrit,  
M.D., Ph.D. (Biochemistry)  
Dean  
Faculty of Graduate Studies  
Mahidol University

*Fongcum Tilokskulchai*

.....  
Assoc. Prof. Fongcum Tilokskulchai,  
Ph.D. (Nursing)  
Program Director  
Doctor of Philosophy Program in Nursing  
Faculty of Nursing  
Mahidol University

Thesis  
entitled  
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on  
July 26, 2016

*Orapan Sukhavulli*

Miss Orapan Sukhavulli  
Candidate

*Orapan Thosingha*

Assist. Prof. Orapan Thosingha,  
DNS.  
Chair

*Chukiatt Viwatwongkasem*

Assoc. Prof. Chukiatt Viwatwongkasem,  
Ph.D. (Statistics)  
Member

*Siriorn Sindhu*

Assoc. Prof. Siriorn Sindhu,  
Ph.D. (Nursing)  
Member

*Sombat Mueng*

Assoc. Prof. Sombat Muengtaweepongsa,  
M.D. (Neurology)  
Member

*Piyamitr Sritara*

Prof. Piyamitr Sritara,  
M.D., FRCPT, FACP, FRCP  
Dean  
Faculty of Medicine, Ramathibodi Hospital  
Mahidol University

*Patcharee Lertrit*

Prof. Patcharee Lertrit,  
M.D., PhD. (Biochemistry)  
Dean  
Faculty of Graduate Studies  
Mahidol University

*Yajai Sitthimongkol*

Assoc. Prof. Yajai Sitthimongkol,  
Ph.D. (Nursing)  
Dean  
Faculty of Nursing  
Mahidol University

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**FACTORS INFLUENCING EARLY NEUROLOGICAL RECOVERY IN  
PATIENTS WITH ACUTE ISCHEMIC STROKE**

**ORAPEN SUKHAVULLI 5237814 NRNS/D**

**Ph.D. (NURSING)**

**THESIS ADVISORY COMMITTEE: SIRIORN SINDHU, Ph.D. (NURSING),  
WANPEN PINYOPASSAKUL, Ph.D. (NURSING),  
CHUKIAT VIWATWONGKASEM, Ph.D. (STATISTICS)**

**ABSTRACT**

Ischemic stroke is a significant worldwide cause of morbidity and mortality. The goal of therapy for acute ischemic stroke (AIS) is early neurological recovery in the brain. The purposes of this cross-sectional descriptive study were to describe the early neurological recovery in patients with acute ischemic stroke and to identify the statistical predictors of early neurological recovery at 24 hours and 3 days after admission of patients with acute ischemic stroke. A purposive random sampling was employed to recruit 220 AIS patients from 8 hospitals in the southern region of Thailand starting from January to May 2016, and analyzed using multivariate logistic regression analysis.

The result revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR =.095,  $p < .001$  and OR =.126,  $p < .01$ , respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=22.22,  $P < .001$  and OR =17.28,  $P < .01$ , respectively), compared with those who did not receive rt-PA treatment. Lastly, age  $>80$  years decreased neurological recovery at 24 hours after admission (OR=.361,  $P < .05$ ).

For the neurological recovery at 3 days, showed that moderate and severe stroke severity decreased the neurological recovery (OR=.10,  $p < .001$  and OR =.09,  $p < .001$ , respectively), compared with mild stroke severity. The stroke patients who had onset time to rt-PA within 3 hours and within 3.0-4.5 hours increased the neurological recovery at 3 days (OR=16.95,  $P < .05$  and OR =14.43,  $P < .01$ , respectively) compared with those who did not receive rt-PA treatment.

The study showed that stroke severity and onset time to rt-PA influence early neurological recovery in AIS patients. Information about early recognition of stroke signs and symptoms should be developed to enable patients gain early access to the hospital for intravenous rt-PA treatment.

**KEY WORDS: EARLY NEUROLOGICAL RECOVERY/ ACUTE ISCHEMIC  
STROKE/ STROKE SEVERITY/ ONSET-TIME-TO rt-PA**

219 pages

ปัจจัยที่มีผลต่อการฟื้นตัวของสมองระยะแรกในผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน

FACTORS INFLUENCING EARLY NEUROLOGICAL RECOVERY IN PATIENTS WITH ACUTE ISCHEMIC STROKE

อรเพ็ญ สุชะวัลดี 5237814 NRNS/D

ปร.ด. (การพยาบาล)

คณะกรรมการที่ปรึกษาวิทยานิพนธ์: ศิริอร สิ้นธุ, Ph.D. (การพยาบาล),

วันเพ็ญ ภิญญโณภาสกุศล, Ph.D. (การพยาบาล), ชูเกียรติ วิวัฒนวงศ์เกษม, Ph.D. (ชีวสถิติ)

#### บทคัดย่อ

โรคหลอดเลือดสมองเป็นสาเหตุสำคัญของความพิการและชีวิต เป้าหมายของการรักษาเพื่อให้มีการฟื้นตัวของสมองให้เร็วที่สุด การศึกษาครั้งนี้เป็นการศึกษาเชิงบรรยายภาคตัดขวาง มีวัตถุประสงค์เพื่อศึกษาปัจจัยที่มีผลต่อการฟื้นตัวของสมองระยะแรกในผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน สุ่มตัวอย่างผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน 220 ราย จาก 8 โรงพยาบาลในเขตภาคใต้ของประเทศไทย ระหว่างเดือนมกราคม ถึง เดือนพฤษภาคม 2559 และวิเคราะห์ข้อมูลโดยใช้การวิเคราะห์ถดถอยโลจิสติกแบบหลายตัวแปร

ผลการศึกษาพบว่า ปัจจัยที่มีผลต่อการฟื้นตัวของสมอง ในระยะ 24 ชั่วโมงหลังเข้ารับการรักษา ได้แก่ ผู้ป่วยที่มีความรุนแรงปานกลาง (OR =.095, p <.001) ผู้ป่วยที่มีความรุนแรงมาก (OR =.126, p <.01) เปรียบเทียบกับกลุ่มที่มีความรุนแรงน้อย ระยะเวลาตั้งแต่เกิดอาการถึงได้รับยา rt-PA ภายใน 3 ชั่วโมง (OR = 22.22, P <.001) ได้รับยา rt-PA 3-4.5 ชั่วโมง (OR = 17.282, P <.01) เปรียบเทียบกับกลุ่มที่ไม่ได้รับยา และ อายุมากกว่า 80 ปี (OR =.361, P <.05) เปรียบเทียบกับกลุ่มที่อายุน้อยกว่า 60 ปี ในขณะที่ปัจจัยที่มีผลต่อการฟื้นตัวของสมอง ในระยะ 3 วันหลังเข้ารับการรักษา ได้แก่ ผู้ป่วยที่มีความรุนแรงปานกลาง (OR =.10, p <.001) ผู้ป่วยที่มีความรุนแรงมาก (OR =.09, p<.001) ระยะเวลาตั้งแต่เกิดอาการถึงได้รับยา rt-PA ภายใน 3 ชั่วโมง (OR = 16.95, P <.05) และได้รับยา rt-PA 3-4.5 ชั่วโมง (OR = 14.43, P <.01)

ผลการวิจัยชี้ให้เห็นว่าความรุนแรงและระยะเวลาในการเข้ารับการรักษาด้วยยา rt-PA มีผลต่อการฟื้นตัวของสมอง ระยะแรกในผู้ป่วยภาวะสมองขาดเลือดเฉียบพลัน ดังนั้นการให้ข้อมูลแก่ผู้ป่วยเกี่ยวกับอาการสำคัญของโรคหลอดเลือดสมอง และการเข้าถึงการรักษาให้ทันเวลา จะช่วยให้สมองฟื้นตัวได้เร็ว

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## **CHAPTER I**

### **INTRODUCTION**

#### **1.1 The significance of the problem**

Ischemic stroke is a significant cause of morbidity and mortality in worldwide. It accounts for approximately 5.5 million deaths annually, with 44 million disability-adjusted life-years lost. In the absence of any meaningful clinical or public health interventions, it is expected that this number will increase to an estimated 23 million first-ever strokes, with an associated 7.8 million deaths, by 2030 (Strong, Mathers, & Bonita, 2007). Stroke is pervasive and rapidly expanding, affecting the poor and disadvantaged disproportionately, furthering health gaps within and between countries. The vast majority (>85%) of these deaths occur in low and middle income countries with one third under the age of 70.

In Thailand, the stroke prevalence in people aged 45-80 years conducted in 2004 to 2006 found that the prevalence was reported as 1,880 per 100,000 populations. It differed among five geographic regions of the country including Bangkok 3.34%, Central region 2.41%, Southern 2.29%, Northern 1.46% and Northeastern 1.09% (Hanchaiphiboolkul et al., 2011). Each year 40,000 people suffer a new recurrent stroke, and stroke remains the fourth leading cause of death (Health Information Unit, Bureau of Policy and Strategy, 2003). The mortality rate tended to be higher constantly from 20.6 per hundred thousand people in 2006 to 27.5 per hundred thousand people in 2010 (Bureau of Policy and Strategy, 2010). One study found that 1 death due to stroke every 12 minutes (Channaroung, 2009).

Stroke can be subdivided into 2 categories, ischemic and hemorrhagic stroke (Deba, Sharma, & Hassan, 2010). Ischemic stroke is account for approximately 80% of all strokes (Zerwic, Hwang, & Tucco, 2007; Channaroung, 2009). Among patients with ischemic stroke, lacunar infarction is the most common subtype followed by large artery atherosclerosis, and cardioembolism. Similar to the findings among other East Asian and Southeast Asian countries, significant carotid atherosclerosis was

found in only 11% of patients. In contrast, intracranial atherosclerosis was found more frequently, accounting for 23% of the cases. Furthermore, the number of patients with intracranial atherosclerosis is likely to be even higher since some of them may present clinically as lacunar infarction where sometimes CT scan is the only diagnostic imaging modality. The subtypes of stroke in Thailand from Chulalongkorn stroke database are lacunar stroke 37%, large vessel atherosclerosis 31%, cardiac embolism 22% and others 10% (Suwanwela, Eusattasak, Phanthumchinda, Piravej, & Locharoenkul, 2014). The penumbra is the region of the brain surrounding the infarct area where the blood supply is significantly reduced, but viability is maintained owing to collateral flow. With acute vascular occlusion, threatened penumbral tissue is lost at all too brisk a pace (Saver, 2006). In a typical infarct in the middle cerebral large artery, 20 million additional neurons die every 10 min if reperfusion is not achieved (Hossmann, 2009).

The goal of therapy for acute ischemic stroke is early neurological recovery because “time is brain.” It has been clearly shown, however, that while the therapeutic efficacy of rt-PA in ischemic stroke persists beyond 90 minutes, and possibly beyond 3 hours, its efficacy is significantly greater in the first 90 minutes. The adjusted odds ratio (OR) (95% CI) for a favorable 3-month outcome associated with rt-PA in the NINDS study was 2.11 in the 0 to 90 minute stratum and 1.69 in the 91 to 180 minute stratum (Marler et al., 2000). The patients with early neurological recovery have lower 30 day mortality and are far more likely to have a favorable functional outcome (modified Rankin et al., 2002; Khiaocharoen, Pannarunothai, Riewpaiboon, Ingrisawang, & Teerawattananon, 2012). Muresan et al. (2010) demonstrated that 68% of patients who show evidence of such early recovery experience a favorable 3 months outcome in comparison to 29% of those without early recovery (Muresan et al., 2010)

Current treatment options include noninvasive intravenous thrombolysis or invasive catheter-based reperfusion therapies that include intra-arterial thrombolysis, mechanical thrombectomy, or balloon angioplasty with or without stent placement. Intravenous tissue plasminogen has vastly improved outcomes for stroke patients. In 1996, the U.S. Food and Drug Administration (FDA) approved the use of IV recombinant tissue plasminogen activator (rt-PA), based largely on the results of

the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study. In 2008, the European Cooperative Acute Stroke Study III trial (Hacke et al., 2008) demonstrated a statistically significant benefit of IV rt-PA administered within the 3 to 4.5 hour treatment window. The drug rt-PA essential works by dissolving blood clots that interrupt blood flow to the brain, thereby reducing damage and disability. The drug is highly fibrin specific and when bound to fibrin, the lytic activity of the drug is increased exponentially (Brott et al., 1997). The recommended dose of alteplase for the treatment of acute ischemic stroke is 0.9 mg alteplase/kg body weight (maximum of 90 mg) infused intravenously during 60 minutes period, with 10% of the total dose administered as an initial intravenous bolus (NICE, 2012).

Intravenous rt-PA is now the standard treatment for patients with acute ischemic stroke and is recommended by the Thai Stroke Guidelines. The stroke fast track program is a hospital system designed to allow medical triage personnel at the hospital to identify patients with stroke early on in order to take proactive measures for prompt investigation and management with the stroke team. Leading to a higher number of acute stroke patients receiving intravenous thrombolysis within the critical window of time, the stroke fast track system has proven successful. At present, the fast track system has been adopted by many other university hospitals as well as regional, provincial, and some community hospitals (Muengtaweepongsa, Dharmasaroja, Kummark, 2012). According to the Ministry of Public Health (2013), the proportion of patients receiving intravenous thrombolysis among those with acute ischemic stroke or acute stroke in Thailand has increased from 0.38% in 2008 to 1.95% in 2012. In addition, National registries from the USA (2001-2004), Sweden (2003-2008) and Korea (2006) reported percentage of patients receive rt-PA about 8.5%, 3.2% and 2.1% respectively (Kim et al., 2011).

Although it is already known that quicker treatment leads to better neurological recovery, the study determined that the rt-PA still showed benefits if used within 4.5 hours of a stroke onset. After this time, however, the risks of side effects may outweigh the benefits. Numerous factors could explain the limited use of rt-PA, but the most important is pre-hospital delay, that is, late presentation at the emergency department after symptom onset. In a comprehensive review of studies examining delay in acute stroke published since 2000, median pre-hospital delay was

between 3 and 4 hours (Evenson, Foraker, Morris, & Rosamond, 2009). A proportion of the pre-hospital delay consists of the time interval from symptom onset to seeking medical assistance, often referred to as decision delay or patient delay. Several factors are related to decision delay, including failure to recognize stroke symptoms, not regarding symptoms as serious because of a lack of knowledge, a wait-and-see attitude, a hope that symptoms will resolve, and hesitation to contact emergency medical services (Jarrell, Tadros, Whiteman, Crocco & Davis, 2007). With regard to the in-hospital delay, the critical time is divided into two parts: 1) The time between arriving at hospital and CT scan and 2) The time between CT scan and the start of thrombolysis (Herlitz et al., 2010).

For the resource of stroke care, the Stroke Unit is a critical component towards the betterment of stroke care in the country. Current data show that there are more than 110 stroke units across Thailand, mostly in regional and provincial hospitals (Suwanwela et al., 2007). However, according to the Thai Stroke Registry, only one-fourth of patients were admitted to a specialized acute stroke care unit. The proportion of stroke unit admission was higher in university hospitals (50%) compared to 17.1% and 3.4% in regional and community hospitals, respectively. With develop care stroke systems, many facilities have organized special Stroke Teams, composed of representatives from various disciplines and departments, who can collaboratively diagnose stroke and initiate rapid treatment. Stroke teams commonly consist of an ED physician, an emergency nurse, a neurologist, a pharmacist, a radiologist, laboratory personnel, and a nursing supervisor. Several studies have shown that implementing a stroke team approach to the care of this population greatly increases the number of patients who receive thrombolytic therapy within the 3-hour window, resulting in improved patient outcomes (Magid, Navlaux, & Wears, 2005). Currently, Thailand has about 300 active neurologists. However, more than two-thirds of this specialized group resides in the greater Bangkok metropolitan area and other neighboring provinces. Therefore, the concentrated grouping of neurologists in Bangkok reveals that there is a shortage of neurologists across the country, especially in rural areas including the North eastern and Southern parts of Thailand (Suwanwela, 2014).

In term of cost after stroke, it found that the total cost of stroke was approximately 19,451 bath/month. It included direct medical costs, indirect cost and

informal care cost (Youngkong, 2001; Ponsoongern, 2007). In addition, disabled person receive an allowance 500 bath/month from government. It indicated that the social welfare was much less than that supposed to pay. Based on reports of the Bureau of Empowerment for Persons with Disabilities, there were 446,614 registered disabled people in 2005, the country would lose 2,005,734,474 bath/month (two billion bath/month) or annual cost was 24,068,921,688 bath/month (twenty-four billion bath/month). The estimation was from the opportunity cost using GDP per capita (4,491bath/month) (Ponsoongern, 2007). The American Heart Association predicts that by 2030, the direct cost of caring for stroke patients will triple from \$61.55 to \$183.13 billion, due in large part to increasing life expectancy, declining stroke-related mortality, and aging population (Go et al., 2014).

There are various variable related to early neurological recovery in patient with acute ischemic stroke. This study focuses on the variables which base on a behavioral model of access to health services including contextual characteristics, individual characteristics and health behaviors of patient.

### **1.1.1 Contextual characteristics**

#### **1.1.1.1 The Distance from the place of symptom attack to the hospital**

The distance travelled by the patients to hospital was categorized as 10 km or less and more than 10 km. The distance was arbitrarily considered because people living within a 10-km radius from the hospital, logically, would be able to arrive within the 3-hour window period. Moreover, this distance also approximately coincided with the border between urban and rural areas (Pandian et al., 2006). Previous study indicated that patients living in close proximity to the hospital are more likely to receive thrombolytic therapy for stroke compared with those living farther away (Acharya et al., 2011).

#### **1.1.1.2 The level of first hospital visits**

Referral from other hospitals is one of the primary causes of delayed thrombolysis therapy after acute ischemic stroke (AIS). Even when rt-PA is administered within 3-4.5 hours after stroke onset, the onset-to-rt-PA time is subsequently prolonged in AIS patients arriving at an emergency department late after

onset compared with those with shorter onset-to-door time. This is because the time of hospital admission is prolonged (Saver et al., 2010). One study found that a total of 48.7% of AIS patients treated with intravenous thrombolytic therapy were transferred from other hospitals. Patients who were directly admitted to stroke center had a shorter onset-to-door time (61 versus 120 minutes,  $p < 0.001$ ) and onset-to-rtPA time 103 versus 155 minutes,  $p < 0.001$ ) than those referred from other hospitals. Direct admission was associated with a good outcome with an odds ratio of 2.03 (95% confidence interval 1.051–3.917,  $p = 0.035$ ), after adjusting for baseline variables. Thrombolysis after direct admission to a hospital offering intravenous thrombolysis therapy could shorten onset-to-rtPA time and improve stroke outcome in patients with AIS (Kim et al., 2014).

#### **1.1.1.3 Specialty of Physician**

Patients in many hospital settings have limited access to specialists with stroke expertise. Although evidence supporting the utility of acute “code stroke” teams and telestroke systems is plentiful, their availability is dependent on local resources. The evidence on the safety of thrombolytic delivery without a neurologist stroke specialist present in person or by telemedicine is less robust. Although emergency physicians exhibit high sensitivity and positive predictive value in identifying patients with stroke (Morgenstern et al., 2004). Some studies have identified instances of thrombolytic delivery in the setting of acute stroke by an emergency or primary care physician (either alone or in telephone consultation with a neurologist) (Wang, Rose, Honings, Garwacki, & Milbrandt, 2000; Rymer, Thurtchley, & Summers, 2003; Akins et al., 2005). The patients were treated by general neurologists, stroke neurologists, and emergency physicians reported mean times to rt-PA infusion were 44, 86, and 141 minutes, respectively. In-hospital mortality rate was 10% (4 intracerebral hemorrhages, 1 cardiogenic shock). Complications were more frequent among patients with protocol violations compared with those without all hemorrhages (75% versus 10%,  $P=0.001$ ), symptomatic ICH (38% versus 5%,  $P=0.02$ ), and ICH attributable to rt-PA, occurring within 36 hours (38% versus 2.4%,  $P=0.01$ ), respectively. One study noted an increase in intracerebral hemorrhage in patients treated by community neurologists (Katzan et al., 2000) and

found increased in hospital mortality among intravenous rt-PA treated stroke patients (Katzan et al., 2000; Bravata, Kim, Concato, Krumholz, & Brass, 2002).

#### **1.1.1.4 Years experience of triage nurse**

Nurses play a pivotal role in all phases of care of the stroke patient:(1) The emergency or hyperacute care phase (Bader & Palmer, 2006) which includes the prehospital setting and the emergency department, and (2) the acute care phase, which includes critical care units, intermediate care units, stroke units, and general medical units. Stroke is a complex disease that requires the efforts and skills of all members of the multidisciplinary team. Triage nurses are key members of the stroke team and provide a vital role that is imperative to treatment of persons who are experiencing an acute stroke. Knowing that “time is brain,” nurses who can quickly and accurately triage patients with stroke symptoms can help save lives and improve the chances of a meaningful recovery. Assessment of patients presenting with stroke-like symptoms, including a thorough medical history, onset and description of initial symptoms, assessment of current symptoms, and evaluation for the possibility of acute stroke treatments, are critical skills for ED nurses (Bergman, Kindler, & Pfau, 2012). Knowing that stroke treatment options are highly dependent on the time of the onset of symptoms, nurses and the stroke team must work diligently and have processes in place to quickly triage, assess, and perform diagnostic tests in order to provide treatment for patients who have had a stroke, when providing treatment is possible.

In addition, the National Institute of Neurological Disorders recommends a ‘door to physician’ time of less than 10 minutes. Fonarow et al. (2011) provide multivariable analyses demonstrating that a reduction in door-to-needle time by 15 minutes is associated with 5% lower odds of in-hospital death. This study describes five domains associated with early use of IV rt-PA. Each of the five domains that emerged from staff interviews at hospitals that have achieved higher-than-average percentages of IV rt-PA administration within 60 minutes of patient arrival provides insight for hospitals seeking to improve their process of thrombolytic therapy for acute ischemic stroke.

#### **1.1.1.5 Triage rating score**

A triage system should define how quickly patients need care based on the acuity of their condition, and should also contribute to emergency

department efficiency and effectiveness (Wuerz, Milne, Eitel, Travers, & Gilboy, 2000). The American Heart Association/American Stroke Association recommends that patients with suspected acute stroke should be triaged with the same priority as patients with acute myocardial infarction regardless of the severity of deficits (Adams, et al., 2007). Further, the National Institute of Neurological Disorders and Stroke (NINDS) recommends that stroke patients who present to an Emergency Department should be seen by a medical practitioner within 10 min from arrival (Marler et al., 2000). These recommendations align to the allocation of a triage priority category of 1 or 2 on the Emergency Severity Index (ESI).

Previous study found that among stroke patients, who presented within two hours, 94% were identified as stroke at triage and 71% were allocated an urgent triage category. Virtually all acute stroke patients were identified at triage, however over 30% were not allocated an emergent triage category (Morphet, Innes, Braitberg, & Mosley, 2011). Patients presenting with facial weakness or speech problems were more likely to be given an emergent triage category while patients with resolving symptoms or loss of coordination were less likely to be allocated a category 1 or 2 of ESI (Mosley, Morphet, Innes, & Braitberg, 2013).

Emergency care providers are at the front line of stroke treatment. Therefore, it is paramount that emergency nurses be able to identify stroke symptoms, swiftly and accurately assess a patient's neurologic status, and implement current stroke care standards. To assist with rapid stroke identification and assessment, the NIH created the National Institute of Health Stroke Scale (NIHSS) (Krock, &Massaro, 2008).

#### **1.1.1.6 Compliance to clinical practice guideline**

Clinical practice guidelines, defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances,” have been expected to optimize patient care through organized and standardized approaches while reducing health care costs. Health providers and health policy makers in Thailand and overseas have formulated guidelines designed to improve treatment for stroke patients (Australian National Stroke Foundation, 2007; Canadian Heart & Stroke Foundation, 2006; Prasat Neurological Institute, 2009) and have developed an arsenal of innovative stroke cares

and treatments, such as dedicated stroke care units (Geoffrey, Marc, Malcolm, & Stephen, 2008), intravenous rt-PA (Adams et al., 2003; Foell et al., 2003; Ducrocq et al., 2005), care protocols and guidelines and specialized stroke teams (Katzan, Hammer, Furlan, Hixson, Nadzam, 2003). Many prospective and retrospective studies in the sample from 140 to 439 participants demonstrated that the clinical practice guideline can shorten time to treatment and investigations, and also increase the numbers of patients receiving timely treatments such as intravenous thrombolysis (Katzan et al., 2003; Mehdiratta & Caplan, 2006) and aspirin (Grotta et al., 2001). In another study, the use of clinical practice guideline in acute stroke patients from 257 to 439 participants was able to decrease post-stroke complication occurrence such as urinary tract infection (0.097 VS 0.05), pressure sore (0.0259 VS 0.0253), pneumonia, and fall (Kwan, Hand, & Sandercock et al., 2004; Widjaja et al., 2002). Importantly, providing care following clinical practice guideline was able to improve early recovery in patients with acute ischemic stroke.

#### **1.1.1.7 Onset-to- rt-PA time**

Onset-to- rt-PA time is important factor associated with patient outcomes (Saver, 2006). The National Institutes of Neurological Disorders and Stroke (NINDS) rt-PA stroke study (Marler et al., 2000) reported that patients treated using rt-PA within 0-90 min after stroke onset showed an increased likelihood of improvement at 24 hours and a favorable 3-month outcome compared to patients treated > 90 min. In other words, early rt-PA treatment should improve patient outcomes. Furthermore, we have already reported that early recanalization depended on onset-to- rt-PA time (Kimura et al., 2010).

In an updated pooled analysis of the Alteplase Thrombolysis for Acute Non interventional Therapy in Ischemic Stroke, European Cooperative Acute Stroke Study (ECASS), and NINDS studies of rt-PA in ischemic stroke found that odds of a favourable 3-month outcome increased as onset-to- rt-PA time decreased ( $p=0.0269$ ) and no benefit of alteplase treatment was seen after around 270 min. Adjusted odds of a favourable 3-month outcome were 2.55 (95% CI 1.44-4.52) for 0-90 min, 1.64 (1.12-2.40) for 91-180 min, 1.34 (1.06-1.68) for 181-270 min, and 1.22 (0.92-1.61) for 271-360 min in favour of the alteplase group. Adjusted odds of mortality increased with onset-to- rt-PA time ( $p=0.04$  and were 0.78 (0.41-1.48) for

0-90 min, 1.13 (0.70-1.82) for 91-180 min, 1.22 (0.87-1.71) for 181-270 min, and 1.49 (1.00-2.21) for 271-360 min (Lees et al., 2010).

Although a number of studies have investigated recovery after stroke, most of them have focused on functional outcome on intermediate and long time. There is a need for more accurate and quantitative information about the natural history of recovery of general neurological dysfunctioning after stroke, as well as for more insight into factors that might influence this recovery. Such information and insight not only will enrich our theoretical understanding of recovery processes, but will also provide us with clinically relevant information. Indeed, knowing the factors in which early recovery is more pronounced may help clinicians formulate more adequate treatment strategies. Furthermore, successful reintegration into the physical, vocational, and social roles in which patients were previously engaged often depends on factors other than the degree of motor or sensory deficit.

### **1.1.2 Individual Characteristics**

#### **1.1.2.1 Age**

Aging is the most important non-modifiable risk factor for stroke. As life expectancy increases, the very old are expected to become a growing proportion of stroke victims (Feigin et al., 2003; Rothwell et al., 2005; Mayo, Nadean, Daskalopoulou, & Cote, 2007). At present, more than half of all strokes already occur in people over 75 years of age (Feigin et al., 2003). The case-fatality rates are higher in the very old, and, among the survivors, the post stroke functional status is worse, both in short and long term (Dennis et al., 1993; Pohjasvaara et al., 1997; Di Carlo et al., 1999; Arboix et al., 2001; Kammersgaard et al., 2004; Rojas, Zurru, Romano, Patrucco, & Cristiano, 2007). Mean age of 206 acute ischemic stroke patients treated with IV tPA was 71.0 years (range: 24-92 years), of whom 141/206 (68.5%) were aged  $\leq$  80 years (Costello et al., 2012). Patients  $>$ 80 years have less favourable outcomes (modified Rankin Scale score, mRS: 0-1) and higher mortality than younger populations post thrombolysis for acute ischemic stroke (Berrouschot et al., 2005; Engelter, Bonati, & Lyrer, 2006).

Age can predict functional recovery in ADL when measured by the BI (Konig et al., 2008). When coordinated with an admission NIHSS, age was

able to correctly predict functional recovery after 3 months more than 70% of all 5,419 ischemic stroke patients (Weimar et al., 2003). Additionally, age together with stroke severity can be used to predict functional recovery in ADL (by the BI) at any time up to 1 year after stroke (Tilling et al., 2001).

### **1.1.2.2 Admission blood pressure**

The majority of patients will demonstrate increased blood pressure in response to acute ischemic stroke (Qureshi, 2008). Blood pressure typically decreases spontaneously during the acute phase of ischemic stroke, starting within 90 minutes after onset of stroke symptoms (Ahmed, Nasman, & Wahlgren, 2000). Previous study found that high baseline, maximum, and mean level of systolic BP profiles were each inversely associated with favorable outcome (OR=0.84, 95% CI: 0.74 to 0.94; OR=0.82, 95% CI: 0.73 to 0.91; OR=0.81, 95% CI: 0.71 to 0.93, respectively) and associated with an increased risk of parenchymal hemorrhage within the first 7 days (OR=1.27, 95% CI: 1.07 to 1.51; OR=1.49, 95% CI: 1.27 to 1.75; OR=1.52, 95% CI: 1.23 to 1.87; respectively) in recombinant tissue plasminogen activator-treated patients (Yong & Kaste, 2008). Willmot, Leonardi-Bee, Bath (2004) revealed that high admission systolic blood pressure (SBP) is associated with poorer outcome in patients who are not treated with rt-PA.

High blood pressure on admission in patients with impaired consciousness was associated with increased mortality while lower systolic blood pressure on admission was reported in patients deteriorating within 36 h of stroke onset (Christensen, Meden, Overgaard, & Boysen, 2002). In one observational study, the systolic blood pressure was >139 mmHg in 77% and >184 mmHg in 15% of patients on arrival at the ED (Qureshi et al., 2007). The blood pressure is often higher in acute stroke patients with a history of hypertension than in those without premonitory hypertension. Blood pressure typically decreases spontaneously during the acute phase of ischemic stroke, starting within 90 minutes after onset of stroke symptoms (Ahmed, Nasman, & Wahlgren, 2000). Multiple studies investigated various blood pressure parameters during the admission for acute ischemic stroke and clinical outcomes. Some studies found a U-shaped relation between the admission blood pressure and favorable clinical outcomes, with an optimal systolic blood pressure ranging from 121 to 200 mmHg and diastolic blood pressure ranging from 81 to 110 mm Hg (Castillo

et al., 2004; Vemmos et al., 2004) among these studies. However, elevated in-hospital blood pressure during acute ischemic stroke has been associated with worse clinical outcomes in a more linear fashion. A logistic regression model confirmed that elevated mean pulse pressure was independently associated with poor outcome at discharge and 30-day mortality (Grabska et al., 2009).

### **1.1.2.3 Admission stroke severity**

Stroke severity on admission, measured by the National Institute Health stroke scale (NIHSS), has been showed to be a predictor for clinical outcomes; severe stroke is associated with an increased risk of death, disability and length of hospital stay (Jorgensen, Nakayama, Reith, Raaschou, & Olsen, 1995). Patient's neurological deficits were evaluated with the NIHSS and categorized, according to admission score, as mild (0–6), moderate (7–15), or severe  $\geq 16$  (Adams et al., 1999; Tseng & Chang, 2006). NIHSS Baseline severity is the strongest predictor of outcome, with recovery occurring early in mild stroke and later, if at all, in severe stroke. However, in patients with severe stroke, early recovery is also a predictor of a good outcome (Baird et al., 2001). The prospective study collected from 360 first-ever ischemic stroke patients found that the NIHSS score at admission was strongly associated with outcomes of acute hospitalization after multivariate adjustment. The odds ratio (OR) for moderate (versus mild) stroke patients to achieve excellent status was 0.04 (95% CI, 0.02-0.10), and for severe stroke the OR was less than 0.01 (95% CI, 0-0.05). The OR (95% CI) for moderate stroke patients to have good or improved outcome was 0.19 (0.10-0.36), for severe stroke 0.04 (0.01-0.13). The ORs for moderate and severe (versus mild) stroke patients to have better subsequent change in neurologic impairments were 5.18 (1.94–13.85) and 4.12 (1.38-12.30); to remain stationary 0.43 (0.19–0.96) and 0.15 (0.06-0.36), respectively (Tseng & Chang, 2006).

## **1.1.3 Health behaviors of patient**

### **1.1.3.1 Smoking status**

Cigarette smoking is a well-established risk factor for initial and recurrent stroke. Weng, et al. (2011) found that smoking was associated with higher scores on the National Institutes of Health Stroke Scale for smoking patients with small-vessel occlusions than nonsmoking patients. However, it was associated

with a lower NIHSS score in the cardioembolic stroke (Weng et al., 2011). Similar, cohort study reported long-time smoking was associated with an increased risk of poor functional outcome at discharge, in ischemic stroke patients, associated with an increase of mortality risk at 1 year and associated with an increased LOS in hospital (Edjoc, Reid, Sharma, & Fang, 2013).

In summary, acute ischemic stroke is a complex condition that requires early recognition and management at both patient and health service delivery to promote early neurological recovery. By limiting rt-PA to urban centers, the added burden of reaching a hospital with an established rt-PA protocol within 4.5 hour of an onset of symptom is placed on either the patient or the emergency response in teams in rural communities. The number 1 contraindication for rt-PA administration of symptom onset > 4.5 hours, the problem is meeting time guidelines may be compounded if rt-PA is limited to urban centers. Many studies about stroke in Thailand were conducted in university hospital or Prasat neurological institute have fully resources of stroke care systems. In addition, provincial or community hospitals, ability to administer intravenous rt-PA, have limit resources such as neurosurgical expertise, nurse specialized stroke care, or stroke unit. The research focus on recovery in acute ischemic stroke patient is still limited. Therefore, this study aims to investigate the predictive ability of influencing factors on early recovery of patients with acute ischemic stroke in provincial or community hospitals at the first 24 hours and 3 days.

## **1.2 Research framework**

A Behavioral Model of Access to Health Services that define the basic concepts “access” as actual use of personal health services and everything that facilitates or impedes patient use of health care services. Access means not only visiting a medical care provider but also getting to the right services at the right time to promote improved health outcomes (Andersen & Davidson, 2007).

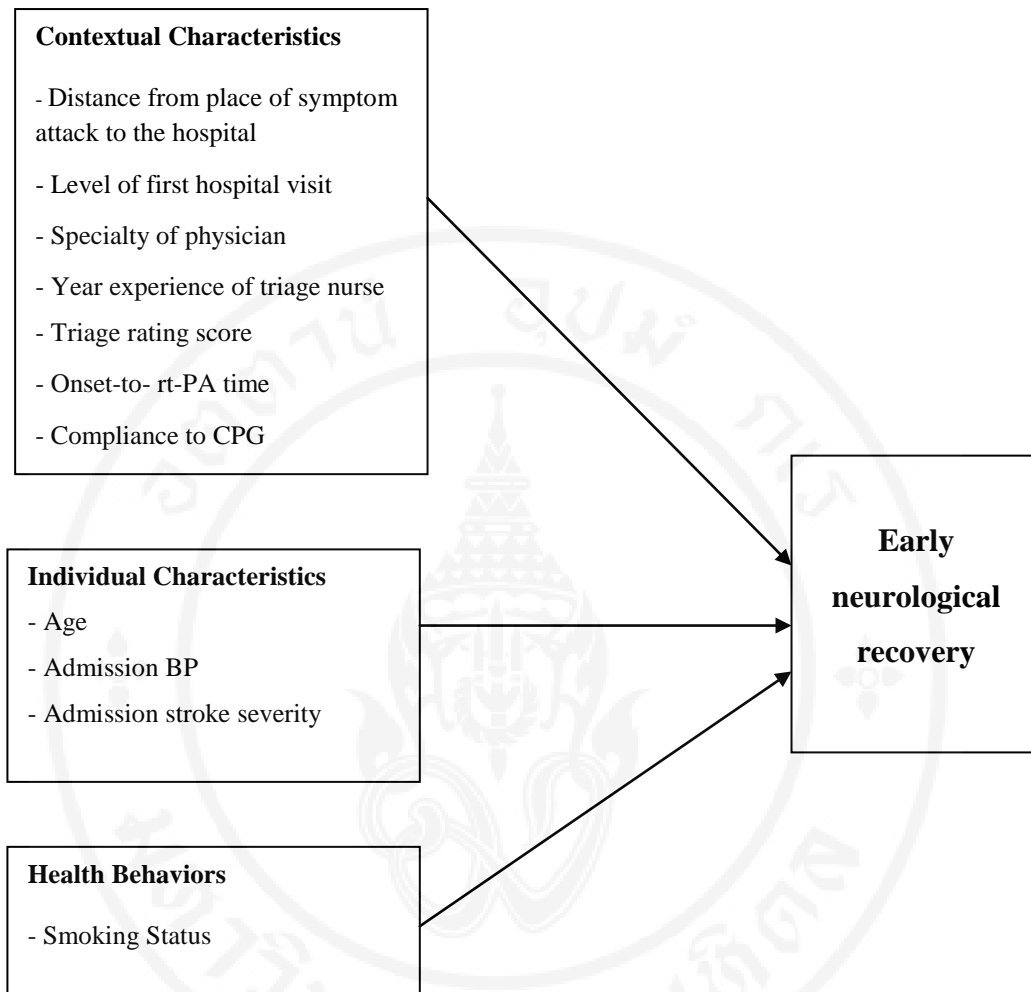
This framework focuses on contextual, the circumstances and environment of health care access and individual determinants of access to medical care. The model suggests that the major components of contextual characteristics are divided in the

same way as individual characteristics determining access: (1) existing conditions that predispose people to use or not use services even though these conditions are not directly responsible for use, (2) enabling conditions that facilitate and impede use of services, and (3) need or conditions that lay people or health providers recognize as requiring medical treatment (Andersen & Davidson, 2007).

The researcher consider that the framework in line with the nature of the service system for the patients with acute ischemic stroke, that need to maintain the speedy and effective services, especially when the good results of health service is receive treatment in target time. Concept of health service access from Anderson's views is consistent with the health system for the patients with acute ischemic stroke. It contains the relation of four major components, a system of health service effect on characteristics of the patients who access to health services lead to the healthcare utilization behavior that result in the health outcomes. In the system of health services held by the development of the stroke center policy, which in this project the university hospital and provincial hospital has the potential to treat acute ischemic stroke patients with thrombolytic therapy, so it must prepare the element of health service to have enough resources to organize service in the particular environment. The organizing system of stroke health service must be early performed and compliance with the standard practice guidelines for the patients with acute ischemic stroke in both pre-hospital and in-hospital management. It is required to maintain the contextual characteristic that supports the performance of service including the distance from the place of symptom attack to the hospital, the level of first hospital visit, specialty of physician, year experience of triage nurse, triage rating score, onset-to-rt-PA time and compliance to CPG.

The individual characteristics of patients who access to the health services are a feature of pathological conditions, social, and environment that affect patients' access to health service. For the patient with acute ischemic stroke, age, admission blood pressure, and stroke severity, are an important characteristic because it effect on blood vessel that interrupt blood flow to the brain.

Health Behaviors of patients, smoking status is an important factor that effect on early neurological recovery.



**Figure 1.1** Framework of the study

### 1.3 Research Question

What is the effectiveness factor associated with early neurological recovery acute ischemic stroke patient?

## **1.4 Research Purpose**

The purposes of this study are to:

1. To describe the early neurological recovery in patients with acute ischemic stroke.
2. To identify the statistical predictors of early neurological recovery at 24 hours and 3 days after admission in patients with acute ischemic stroke.

## **1.5 Research Hypotheses**

The distance from place of symptom attack to the hospital, the level of first hospital visits, specialty of physician, years experience of triage nurse, triage rating score, onset-to-rt-PA time, compliance to clinical practice guideline, age, admission blood pressure, admission stroke severity, and smoking status can predict the early neurological recovery at 24 hours and 3 days after admission in patients with acute ischemic stroke.

## **1.6 Scope of the Study**

This study aim to examine the factors influencing early neurological recovery in patient with acute ischemic stroke conducts at the hospitals in southern part of Thailand.

## **1.7 Expected Outcomes and Benefits**

1. Provide the knowledge concerning the individual characteristic that effect on early neurological recovery in patient with acute ischemic stroke.
2. Provide the knowledge concerning the effective aspect of in-hospital service systems for early neurological recovery in patient with acute ischemic stroke.

## 1.8 Definition of Terms

**Early neurological recovery** was defined as a NIHSS score of 0 to 3 or a decrease of  $\geq 4$  points in the NIHSS score at 24 hours and confirmation at 3 days (Stolz et al., 2008; Mazighi et al., 2012).

**Severity of stroke** defined as the NIH stroke scale (NIHSS) score on admission and categorized as mild (0-6), moderate (7-15), or severe ( $\geq 16$ ) (Tseng & Chang, 2006).

**The level of first hospital visit** defined as the community, general or excellent center hospital that acute ischemic stroke patients were first visits after symptom onset.

**Triage rating score** defined as triage acuity levels were assigned by the presenting complaint, clinical signs and vital signs. The conditions evaluates patient and states rationale for assignment of triage category including *critical*: threat to life or limb requiring immediate aggressive intervention, *emergent*: Potential threat to life, limb, or function requiring rapid medical intervention, *urgent*: could potentially progress to a serious problem requiring emergency intervention; may be associated with significant discomfort or affect ability to function at work or perform activities of daily living, *less urgent*: conditions related to patient age, distress, or potential for deterioration or complications that would benefit from intervention or reassurance within 1 to 2 hours, and *non-urgent*: conditions that may be acute or part of a chronic problem with or without evidence of deterioration; could be referred to other areas of the hospital or healthcare system (Rankin, Then, & Attack, 2013). This triage rating score was performed by emergency nurse.

**Smoking** defined as three the smoking status including 1) Current smokers (patients who have been smoking within the last 5 years or longer and been smoking 6 months before their cerebrovascular event, 2) Ex-smokers (patients who have quit smoking in the past and have not been a smoker within the last 6 months before their cerebrovascular event) , and 3) Non smokers (Edjoc et al.,2013).

**Admission blood pressures** are measured with a calibrated sphygmomanometer and with patients in the supine position. The systolic blood pressure (SBP) first value recorded at the emergency department is declared as "admission SBP".

**The Distance from the hospital** defined as direct distance from place of symptom onset to the rt-PA hospital measured by kilometers.

**Physician specialty** defined as health care personal who provide treatment in acute ischemic patient divided neurologist, medical physician, emergency physician, and general physician.

**Year experience of triage nurse** defined as numbers of year experience of triage nurse at emergency department who triage patients with stroke symptoms with stroke-like symptoms, including a thorough medical history, onset and description of initial symptoms, assessment of current symptoms and assign accurate triage rating score.

**Onset-to-rt-PA time** defined as the time (minute) from onset of symptom to receive intravenous rt-PA in hospital.

## **CHAPTER II**

### **LITERATURE REVIEW**

A review of literature associated to the study of factors influencing early neurological recovery in patients with acute ischemic stroke in regional hospital enhances the understanding of situations and factors access to definite care in patient with ischemic stroke in health service system as the following issues

- 2.1 Situations of patient with ischemic stroke in global and Thailand
- 2.2 Characteristics of patients with acute ischemic stroke who presented in Emergency department
  - 2.2.1 Stroke types and subtypes
  - 2.2.2 Pathophysiology of ischemic stroke
  - 2.2.3 Signs and symptoms
- 2.3 Health Service Systems for patient with acute ischemic stroke
  - 2.3.1 Pre-hospital service
  - 2.3.2 In-hospital service access to intravenous rt-PA in patient with ischemic stroke
- 2.4 Recovery in patient with acute ischemic stroke
- 2.5 Models and framework related to recovery in patient with ischemic stroke
- 2.6 Factor influencing early recovery in patient with ischemic stroke

## **2.1. Situations of patient with ischemic stroke in global and Thailand**

Stroke remains one of the most devastating of all neurological conditions. Worldwide it accounts for approximately 5.5 million deaths annually, with 44 million disability-adjusted life-years lost. In the absence of any meaningful clinical or public health interventions, it is expected that this number will increase to an estimated 23 million first-ever strokes, with an associated 7.8 million deaths, by 2030 (Strong et al., 2007). As a disease of aging, the prevalence of stroke is expected to increase significantly around the world in the years ahead as the global population older than 65 years of age continues to increase by approximately 9 million people per year (World Health Organization, 2004). In high-income countries such as the United States of America, one person died from stroke every four minutes, and stroke ranks fourth among leading causes of deaths in the country after heart disease, cancer, and chronic lower respiratory syndrome (Go et al., 2013). By 2025, the global population of people older than age of 65 years is estimated to be approximately 800 million people, of whom two-thirds are expected to live in still-developing countries, particularly in Latin America and Asia (Weng et al., 2013). In 2002, stroke-related disability was judged to be the sixth most common cause of reduced disability-adjusted life-years (DALYs-the sum of life-years lost as a result of premature death and years lived with disability adjusted for severity). However, because of the burgeoning elderly population in western societies, the estimation is that by 2030 stroke-related disability in western societies will be ranked as the fourth most important cause of DALYs (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006).

In Thailand, the stroke prevalence in people aged 45-80 years conducted in 2004 to 2006 found that the prevalence was reported as 1,880 per 100,000 populations (Suwanwela, 2014). Men had a higher prevalence of stroke than did women in all age groups. Stroke prevalence differed among the five geographic regions of the country with the highest prevalence in the capital city, Bangkok (3.34%) followed by central (2.41%), southern (2.29%), northern (1.46%), and north-eastern regions (1.09%) (Hanchaiphibookkul et al., 2011). Hypertension, diabetes, dyslipidemia, metabolic syndrome, and atrial fibrillation are major risk factors of stroke in the Thai population. The Bureau of Policy and Strategy, Ministry of Public Health (2003) reported the morbidity rate of stroke during 2002-2003 increased from 138.3 to 151.5 per 100,000.

Each year 40,000 people suffer a new recurrent stroke, and stroke remains the fourth leading cause of death (Health Information Unit, Bureau of Policy and Strategy, 2003). According to the data from the Ministry of Public Health, the mortality rate of stroke in Thailand is increasing during the past 5 years. The mortality increased from 20.8 in the year 2008 to 30.7 per 100,000 populations in the year 2012 (Thailand Health Statistics, 2013).

## **2.2. Characteristics of patients with acute ischemic stroke who presented in Emergency department**

### **2.2.1 Stroke types and subtypes**

Stroke can be subdivided into 2 categories, ischemic and hemorrhagic.

2.2.1.1 Ischemic Stroke account for approximately 87% of all strokes (Channaroung, 2009; Go et al., 2013). Ischemic strokes occur as a result of an obstruction within a blood vessel supplying blood to the brain. The underlying condition for this type of obstruction is the development of fatty deposits lining the vessel walls. These fatty deposits can cause two types of obstruction:

- Cerebral thrombosis refers to a thrombus (blood clot) that develops at the clogged part of the vessel. A major cause of ischemic stroke is atherosclerosis, which is a time-consuming process that results in narrowing or blockage of the blood vessels (Deba et al., 2010). Ischemic stroke can be further divided into different sub-groups. Thrombotic stroke is caused by a thrombus or blood clot that develops in the arteries supplying blood to brain, resulting in the plaque that eventually clogs the arteries, thus depriving the brain of blood supply. Ischemic stroke can occur with large arteries and small arteries. If the thrombus occurs in small arteries deep inside the brain, it is called lacunar stroke. Lacunar stroke is generally caused by hypertension and lipohyalinosis. The other type of stroke is embolic stroke. It is caused when an embolus or a blood clot that forms elsewhere in the body travels through the bloodstream to the brain, hence blocking the brain's blood supply.

- Cerebral embolism refers generally to a blood clot that forms at another location in the circulatory system, usually the heart and large arteries of the upper chest and neck. A portion of the blood clot breaks loose, enters the bloodstream and travels through the brain's blood vessels until it reaches vessels too small to let it pass. A second important cause of embolism is an irregular heartbeat, known as atrial fibrillation. It creates conditions where clots can form in the heart, dislodge and travel to the brain (Toni, Sacco, Brainin, & Mohr, 2011; Hickey & Todd, 2009).

Among patients with ischemic stroke, lacunar infarction is the most common subtype followed by large artery atherosclerosis, and cardioembolism. Similar to the findings among other East Asian and Southeast Asian countries, significant carotid atherosclerosis was found in only 11% of patients. In contrast, intracranial atherosclerosis was found more frequently, accounting for 23% of the cases. Furthermore, the number of patients with intracranial atherosclerosis is likely to be even higher since some of them may present clinically as lacunar infarction where sometimes CT scan is the only diagnostic imaging modality. The subtypes of stroke in Thailand from Chulalongkorn stroke database are Lacunar stroke 37%, Large vessel atherosclerosis 31%, Cardiac embolism 22% and Others 10% (Suwanwela, 2014).

2.1.1.2 Hemorrhagic stroke accounts for about 13 percent of stroke cases. It results from a weakened vessel that ruptures and bleeds into the surrounding brain. The blood accumulates and compresses the surrounding brain tissue. The two types of hemorrhagic strokes are intracerebral (within the brain) hemorrhage, which is found in about 10% of all patients with stroke and subarachnoid hemorrhage, which is found in approximately 3% of all patients with stroke. Hemorrhagic stroke occurs when a weakened blood vessel ruptures. Two types of weakened blood vessels usually cause hemorrhagic stroke: aneurysms and arteriovenous malformations (AVMs). Intracerebral hemorrhage is commonly found at the basal ganglia and adjacent internal capsule, accounting for 50% of the total cases. This is followed by thalamus, cerebellum, and pons, making up 30%, 10%, and another 10%, respectively. On the other hand, subarachnoid hemorrhage is mostly caused by aneurysms, 85% of which is found in front of the circle of Willis (Go et al., 2013; Hickey & Todd, 2009).

## **2.2.2 Pathophysiology of Ischemic stroke**

Ischemic stroke may manifest in the form of thrombotic stroke (large vessel and small vessel types); embolic stroke (with/without known cardiac and/or arterial factor); systemic hypoperfusion (Watershed or Border Zone stroke); or venous thrombosis. Irrespective of the cause, compromised vascular supply to the brain is the primary event in majority (85-90%) of acute strokes. Low respiratory reserve and complete dependence on aerobic metabolism make brain tissue particularly vulnerable to effects of ischemia. A spectrum of severity is generally observed in the affected region of the brain, owing to the presence of collateral circulation. Thus, part of the brain parenchyma (core) undergoes immediate death, while others may only be partially injured with potential to recover (penumbra) (Deba et al., 2010).

### **2.2.2.1 Effects of ischemia at cellular level**

Ischemia causes brain damage by activating the ischemic cascade, which progresses to local depletion of oxygen or glucose, causing failure of production of high energy phosphate compounds, like adenine triphosphate (ATP). This adversely affects energy-dependent processes necessary for tissue cell survival, and sets off a series of inter related events culminating in cellular injury and death. The extent of damage usually depends on duration, severity, and location of ischemia. Neuron, owing to its role in impulse transmission, requires constant supply of glucose and oxygen, in order to maintain the ionic gradients across its membrane, and is most susceptible to hypoxic changes.

### **2.2.2.2 Concept of ischemic penumbra**

Cerebrovascular tissue undergoing ischemia has two layers: (a) inner core of severe ischemia with blood flow below 10-25%, displaying necrosis of both neuronal as well as supporting glial elements; and (b) outer layer of less severe ischemia (*penumbra*), supplied by collaterals, and contain cells which can be retrieved by timely therapeutic intervention. Following an ischemic event, the centre of the core is perfused at 10-12 ml/100 g/min or less, while the ischemic area around it (surrounded by the penumbra) is critically hypoperfused at less than 18-20 ml/100 g/min and is at risk of dying within hours. In contrast, the penumbra is perfused at less likely at approximately 60 ml/100 g/min and is less likely to die (Heuschmann et al., 2003).

### **2.2.2.3 Cerebral edema and its effects**

This is of primary concern since it accounts for much of the death and disability. An understanding of the underlying mechanism, is important since management over the years have primarily addressed the effect without targeting the cause, which probably is attributable to the effects of neurogenic inflammation, mediated via neuropeptides. Klatzo specified two categories of cerebral edema - cytotoxic and vasogenic edema as follow.

- Cytotoxic/cellular edema: Evolves within minutes to hours and are potentially reversible. It is characterized by swelling of all the cellular elements of the brain, including neurons, glia, and endothelial cells, due to failure of ATP-dependent ion (sodium and calcium) transport, as well as release of oxygen-derived free radicals (Deba et al., 2010).

- Vasogenic edema: Occurs over hours and days and are irreversible. It causes increased permeability of brain capillary endothelial cells to macromolecular serum proteins (e.g., albumin), resulting in increase in extracellular fluid volume along with increased intracranial pressure (ICP). This may displace the brain hemisphere; or shift one compartment of the brain, thereby compressing neurons, nerve tracts, and cerebral arteries. A sustained increase in pressure causes persistent ischemia; irreversible damage to brain cells; and, when severe may lead to cerebral herniation and potentially death (Deba et al., 2010).

### **2.2.2.4 Effects of ischemia on structural integrity of brain**

Apart from the deleterious effect on brain cells, hypoxia also causes loss of structural integrity of brain tissue and blood vessels, partly through the release of proteases like matrix metal loproteases (MMP). Loss of vascular structural integrity results in breakdown of the protective blood brain barrier, manifesting as cerebral edema, along with secondary progression of brain injury (Adibhatla, & Hatcher, 2008). Studies have shown alterations of vascular endothelin receptor expression in ischemic stroke. Enhanced expression of vascular endothelin receptors is possibly mediated by both protein kinase C (PKC) and mitogen activatingprotein kinase (MAPK) which is the basis of treatment with PKC and MAPK inhibitors to limit the infarct volume (Edvinsson, 2009).

Angiogenesis: Extent of angiogenesis within penumbra of ischemic stroke correlated with patient's survival time. This is mediated by either: (a) hypoxia inhibiting degradation of hypoxia-inducible factor-1 (HIF-1), which stimulates VEGF, which is essential for angiogenesis; (b) angiogenic growth factor secreted by inflammation-associated infiltrates (leucocyte, macrophages, damaged blood platelets) (Deba et al., 2010).

Brain ischemia also tends to activate the immunemechanism, which in some cases may be the cause for the exacerbation of damage and clinical deterioration of the patient. Experimental studies have shown that inhibition of the inflammatory process has led to control of the extent of injury, an aspect which has gained paramount importance in understanding stroke and management of cases thereof (Adibhatla & Hatcher, 2008; Tanasescu et al., 2008).

This study focuses on acute ischemic stroke because it account for 87% of all strokes. Early recognition and administration of treatment can improves outcome. However, many factors associated early neurological recovery that is limit study in patient with acute ischemic stroke.

### **2.2.3 Signs and symptoms of stroke**

Stroke should be considered in any patient presenting with an acute neurologic deficit (focal or global) or altered level of consciousness. Signs and symptoms of stroke vary, depending on individual patients, as well as the location and size of dangers to the brain. Commonly found symptoms in stroke patients include weakness of arm and leg, abnormal speech, weakness of facial muscles, numbness, confusion, loss of vision, difficulty walking, dizziness, loss of balance, paresthesia, headache, other forms of pain besides headache, decreased consciousness, fainting, falls, shortness of breath, and seizure (Gargano, Wehner, & Reeves, 2009; Jerath, Reddy, Freeman, Jerath, & Brown, 2011). According to the American Heart and Stroke Association, symptoms of stroke can be divided into five groups of symptoms based on warning signs of stroke as follows (American Heart Association, 2013):

1) Weakness of limb or facial muscles and numbness is most frequently found in stroke patients, accounting for 79 %. There was significant difference between men and women in symptoms of arm, leg, or face weakness.

Female were present with arm, leg, or face weakness by 81.8% and male 76.3% (Jerath, Reddy, Freeman, Jerath, & Brown, 2011).

2) Confusion and abnormal speech include difficulty speaking, inability to speak, or speaking unintelligibly, making up 43.3% of the cases, second only to muscle weakness. Difficulty speaking is found in 48%, while the incidence rate of confusion is lower (Gargano et al., 2011). Generally, female patients suffer more communication difficulty than male patients (OR 1.47, 95% CI 1.17 – 1.85;  $p = 0.001$ ) (Roquer, Campello, & Gomis, 2003).

3) Abnormal vision such as blurred vision, seeing composite images, or delayed vision is found in only about 22% of the cases (Gargano et al., 2011), with abnormality of visual field and seeing composite images accounting for 14.6% and 5.5%, respectively (Rathore et al., 2002).

4) Difficulty walking, lack of muscle coordination, loss of balance, and dizziness can be found in about 30% of the cases. The incidence rates of difficulty walking and dizziness are rather similar, making up about 28% to 31% (Bray, Mosley, Bailey, Barger, & Bladin, 2011; Gargano et al., 2011).

5) Acute headache with no apparent cause is found in about 40% of the cases (Gargano et al., 2011). It is mostly found in patients with hemorrhagic stroke rather than ischemic stroke, and 80% of patients with hemorrhagic stroke tend to suffer from severe headache (Rathore et al., 2002).

In addition to the aforementioned symptoms, other important symptoms of stroke include a decrease in level of consciousness or loss of consciousness, which is found in 38.4% and seizure which is found in approximately 4.4%, and they are more common in hemorrhagic stroke than in ischemic stroke (Gargano et al., 2011; Rathore et al., 2002).

It can be seen that weakness of facial muscles, weakness of limb muscles, and abnormal speech are common symptoms of stroke. Thus, “The FAST” (Face, Arm, Speech, Time to Call) campaign has been developed, as well as “The 5 Suddens” (Sudden muscle weakness, sudden abnormal speech, sudden abnormal vision, sudden loss of balance or dizziness, and sudden severe headache), to create awareness and disseminate knowledge of stroke among the public to ensure appropriate response of calling the emergency number as fast as possible (Jauch et al.,

2013). It has been found that the median of hospital arrival time of stroke patients in England after the FAST campaign had been established reduced from those in the previous years, from 4.22 hours (2007-2008) to 3.87 hours (2009-2010) (Addo et al., 2012).

### **2.3 Health Service Systems for patient with acute ischemic stroke**

The Stroke Chain of Survival guidelines are published by the AHA/ASA (2013) to promote prompt recognition and treatment of acute ischemic stroke. The guidelines emphasize the eight Ds including (1) Detection: patient or bystander recognition of stroke signs and symptoms (2) Dispatch: immediate activation of call and priority EMS dispatch (3) Delivery: prompt triage and transport to most appropriate stroke hospital and pre-hospital notification (4) Door Immediate ED triage to high-acuity area (5) Data: prompt ED evaluation, stroke team activation, laboratory studies, and brain imaging (6) Decision: diagnosis and determination of most appropriate therapy; discussion with patient and family (7) Drug: administration of appropriate drugs or other interventions (8) Disposition: timely admission to stroke unit, intensive care unit, or transfer.

The early management of patients with acute ischemic stroke is to stabilize the patient and to complete initial evaluation and assessment, including imaging and laboratory studies, within a definitive time period of patient arrival to the hospital (Jauch et al., 2013). Critical decisions focus on the need for intubation, blood pressure control, and determination of risk/benefit for thrombolytic intervention. The National Institute of Neurological Disorders and Stroke (NINDS) guidelines suggested that patients who were candidates for acute thrombolytic therapy should be evaluated by a physician with general assessment within 10 minutes of arrival at the ED, 15 minutes from the ED to stroke team or expert physician notification, CT scanning within 25 minutes, CT interpretation within 45 minutes, and that they should undergo drug within 60 minutes (Jauch et al., 2013).

The assessment and treatment of a stroke patient can be managed in many emergency departments with advanced planning. However, this streamlined process is facilitated at designated stroke centers (Schwamm et al., 2005) which have rapid

response protocols, integrated systems, and increased experience in completing an efficient evaluation of the possible stroke patient. History and physical examination provide the basis for diagnosis of acute stroke. CT scan is usually normal or age-appropriate in acute ischemic stroke, and is used to exclude other diagnoses that may preclude intervention. Careful attention must be paid to the many stroke mimics. The decision to treat must consider important contraindications to thrombolytic. For these reasons, physicians at stroke centers are often more comfortable administering thrombolytic than the average community emergency medicine physician. Moreover, comprehensive stroke centers also have the ability to do endovascular interventions for patients who fall outside of thrombolytic guidelines.

### **2.3.1 Pre-hospital Management**

Emergency Medical Service (EMS) refers to the full scope of pre-hospital stroke care, including call activation and dispatch, emergency medical response, triage and stabilization in the field, and ground or air ambulance transport. Emergency Medical Service System (EMSS) refers to the system that involves the organization of public and private resources and includes the community, emergency healthcare personnel, public safety agencies, emergency facilities, and critical care units. Issues related to communication, transportation, access to care, patient transfer, mutual aid, and system review and evaluation are addressed in EMSS. To reach full potential, stroke systems of care must incorporate EMSS into the process (Jauch et al., 2013). The way of patients with ischemic stroke access to hospital is divided into Dispatcher Call, Emergency Medical Service and Ambulance transport.

#### **2.3.1.1 Call activation and dispatch**

The role of the dispatch system is to ensure immediate triage and dispatch of appropriate EMS providers when acute stroke is suspected by either the caller or the dispatcher. Data from 2 systems indicate that dispatchers correctly suspected or identified 52% of patients ultimately proven to have had a stroke on initial telephone evaluation (Handschu, Poppe, Rauss, Neundorfer, & Erbguth, 2003). These data imply that educational programs should be aimed at dispatchers to increase their awareness of stroke symptoms. Stroke should be given a priority dispatch similar to that for acute myocardial infarction or trauma (American Heart Association

Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, 2005).

### **2.3.1.2 Emergency Medical Response**

EMS activation appears to be a function primarily of individuals other than the patient, with one report indicating that a family member, paid caregiver, coworker, or other bystander accounted for 62% to 95% of 9-1-1 activation calls. In addition to bystander recognition of a problem, other reported predictors of EMS use by stroke patients include stroke severity, presence of intracranial hemorrhage, age, sense of urgency, unemployment, and race (black). The benefits of EMS activation by patients with stroke symptoms appear to occur in both the pre-hospital and in-hospital settings. Hospital arrival is faster for patients who use EMS as their initial medical contact than for those who contact their primary physician or hospital directly<sup>18</sup> or a primary care site.

### **2.3.1.3 Ambulance transport**

After ambulance arrival on the scene, EMS providers should obtain a focused history and patient assessment, provide necessary stabilization and treatment, and transport immediately to the closest, most appropriate facility such as manage ABCs, cardiac monitoring, intravenous access, oxygen, assess for hypoglycemia, and alert receiving ED (Adam et al., 2007). An ambulance may bypass a hospital that does not have the resources or institutional commitment to treat patients with stroke if a more appropriate hospital is available within a reasonable transport interval. Advance notice to the receiving emergency department (ED) of the impending arrival of a potential stroke patient, along with information on comorbid conditions and estimated time of symptom onset, will speed the subsequent ED assessment.

Critical elements of the patient's history must include information on time of symptom onset such as onset of symptoms, recent events, comorbid diseases, and use of medications. This may require obtaining information from bystanders or, preferably, transporting witnesses with the patient. Similarly, next of kin, if available, may be needed for information or consent and should travel to the receiving hospital concurrently.

### **2.3.2 In-hospital management**

A systems approach is necessary to improve how stroke is treated so that patients have access to the most appropriate treatment in centers that are best equipped to deal with their critical. The time-sensitive nature of stroke care is central to establishment of successful stroke systems. Rapid access to a specialist service can reduce the risk of death and disability following stroke as early assessment enables accurate diagnosis, provision of acute treatment, early detection and response to complications, and provision of care by a multi-disciplinary team with expertise in stroke (Swain, Turner, Tyrrell, & Rudd, 2008). Building effective and efficient stroke care systems is a critical step in improving patient outcomes in the prevention, treatment, and rehabilitation of stroke. There are four proven acute interventions supported by evidence from randomized controlled trials: Stroke Care Units; thrombolysis treatment with rt-PA agent; aspirin; and decompressive surgery for ischemic stroke (American Heart Association, 2010).

#### **2.3.2.1 Emergency Triage and Initial Evaluation**

ED patients with suspected acute stroke should be triaged with the same priority as patients with major trauma or acute myocardial infarction, regardless of the severity of neurological deficits. Although specific data on the efficacy of stroke screening tools and scoring systems are lacking for ED triage, the demonstrated utility of such tools in the pre-hospital environment supports their use in this setting (Harbison et al., 2003; Ramanujam et al., 2009). The initial evaluation of a potential stroke patient is similar to that of other critically ill patients: immediate stabilization of the airway, breathing, and circulation (ABCs). This is quickly followed by an assessment of neurological deficits and possible comorbidities. The overall goal is not only to identify patients with possible stroke but also to exclude stroke mimics (conditions with stroke like symptoms), identify other conditions that require immediate intervention, and determine potential causes of the stroke for early secondary prevention. Importantly, early implementation of stroke pathways and/or stroke team notification should occur at this point.

Given that time is an absolutely crucial factor in successful evaluation and treatment of this type of patient, time-frames must be established to

guide an institutional response (National Institute of Neurological Disorders and Stroke, 2011)

- Door to physician evaluation: A candidate for acute intervention should have initial physician evaluation within 10 minutes of arrival at the ED.

- Door to stroke team notification: Members of the stroke team should be notified within 15 minutes of arrival.

- Door to CT scan initiation: The CT scan should be initiated within 25 minutes of arrival.

- Door to CT scan interpretation: The CT scan should be interpreted by a capable individual within 45 minutes of arrival.

- Door to drug (needle) time: If indicated, the patient should be receiving thrombolysis within 60 minutes of arrival. A threshold of 80% is indicated for this parameter.

- Door to monitored bed: The patient should be transferred to the appropriate inpatient setting within 3 hours of arrival.

#### **2.3.2.2 Supplemental Oxygen**

Stroke is a primary failure of focal tissue oxygenation and energy supply. Thus, it is intuitive that systemic hypoxemia and hypotension be avoided and, if present, corrected to limit further cellular damage. Initial assessment of the airway, breathing, and circulation occurs in the pre-hospital setting and again on arrival in the emergency department.

Hypoxia appears frequently after stroke. Previous study of hemiparetic patients, 63% developed hypoxia (defined as oxygen saturation <96% for a period >5 minutes) within 48 hours of stroke onset (Roffe et al., 2003). Common causes of hypoxia include partial airway obstruction, hypoventilation, aspiration, atelectasis, and pneumonia. Patients with decreased consciousness or brain stem dysfunction are at increased risk of airway compromise because of impaired oropharyngeal mobility and loss of protective reflexes (Milhaud, Popp, Thouvenot, Heroum, & Bonafe, 2004). AHA guidelines for emergency cardiovascular care for stroke and resuscitated cardiac arrest patients recommend administration of oxygen to hypoxemic patients to maintain oxygen saturation >94% (Jauch et al., 2013).

### **2.3.2.3 Fluid repletion and maintenance therapy**

Intravascular volume depletion is frequent with acute stroke, particularly in the elderly, and may worsen cerebral blood flow. For most patients with acute stroke and volume depletion, isotonic saline without dextrose is the agent of choice for intravascular fluid repletion and maintenance therapy (Rodriguez et al., 2009). In general, it is best to avoid excess free water because hypotonic fluids may exacerbate cerebral edema in acute stroke. In addition, it is best to avoid fluids containing glucose, which may exacerbate hyperglycemia.

### **2.3.2.4 Hypoglycemia evaluation**

Focal deficits and neuronal injury, mimicking stroke, can be caused by hypoglycemia. Rapid evaluation and correction of a low blood glucose level (<60 mg/dL or 3.3 mmol/L) is essential - with normoglycemia being the desired goal (Bruno et al., 2002).

### **2.3.2.5 Hyperglycemia control**

Elevated glucose (glucose level >126 mg/dL or >7.0 mmol/L) is associated with poor outcomes in stroke. The AHA/ASA and European Stroke Initiative guidelines recommend treatment for glucose >180 mg/dL (>10 mmol/L) while aiming for concentrations in the range of 140-180 mg/dL (7.8–10 mmol/L) (Dave et al., 2010; Bejot et al., 2012).

### **2.3.2.6 Intravenous thrombolysis**

Thrombolysis is the process of using thrombolytic therapy that restores cerebral blood flow in some patients with acute ischemic stroke and may lead to improvement or resolution of neurologic deficits. Thrombolysis with rt-PA is one of the most biologically effective treatments for acute ischemic stroke.

### **The treatment with intravenous thrombolysis 0 to 3 hours after acute ischemic stroke**

The landmark National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study reported the benefits of IV rt-PA in December 1995, and subsequently, the US Food and Drug Administration (FDA) approved the drug in 1996. IV rt-PA usage rates, however, remain relatively low. Overall, the NINDS study showed an absolute increase in favorable 90-day outcomes of 11% to 13% for IV rt-PA treatment within 3 hours of ischemic stroke onset

compared with placebo, even when the 5.8% absolute increase in the difference in symptomatic intracranial bleeding was taken into account (The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995). A post hoc analysis of the NINDS data showed that the IV rt-PA treated subjects had a 4-fold higher chance of having no measurable neurological deficit (NIHSS score =0) at 24 hours than controls (11.5% vs 2.6%;  $P = 0.001$ ) (Lyden et al., 2001). Furthermore, the NINDS data clearly demonstrated diminishing benefits with increasing onset-to-treatment times (Marler et al., 2000). Eligibility criteria for administration of intravenous rt-PA are listed as follow:

**Inclusion criteria for rt-PA**

- Age 18 years or older
- Clinical diagnosis of ischemic stroke causing a measurable neurologic deficit
- Time of symptom onset well established to be <270 minute before treatment

**Exclusion criteria for rt-PA (0-3 hours)**

- Imaging evidence of intracranial hemorrhage, mass effect, or hypodensity more than one-third of hemisphere
- Minor or rapidly resolving symptoms likely to result in minimal or no residual deficit
- Clinical presentation suggestive of subarachnoid hemorrhage
- Active bleeding
- Known bleeding diathesis, including but not limited to:
  - : Platelet count < 100,000
  - : Heparin use within 48 hours and prolonged a PTT
  - : INR>1.7, or anticoagulant use with residual biologic activity
- Major surgery or serious trauma excluding head trauma within 14 days
- Intracranial surgery, serious head trauma, or previous stroke within 3 months
- Gastrointestinal or urinary tract hemorrhage within 21 days
- Non compressible arterial puncture within 7 days

- Lumbar puncture within 7 days
  - Pretreatment SBP >185 mmHg or DBP > 110 mmHg and uncontrollable
  - Known history of intracranial hemorrhage
  - Blood glucose < 50 mg/dL
  - Myocardial infarction within 3 months, suspected endocarditis, or pericarditis
  - Seizure with residual deficits thought to be postictal and not likely due to stroke
  - Severe underlying disease with short-term life expectancy
- Intravenous thrombolysis extended 3 to 4.5 hours after acute ischemic stroke

As per recommendations made by American Academy of Neurology, thrombolytics were not shown to be effective beyond 3 hours after onset of stroke. A pooled analysis of 2,775 subjects from IV rt-PA trials for ischemic stroke who were treated up to 6 hours, showed a possible benefit of IV rt-PA therapy up to 4.5 hours from symptom onset (The ATLANTIS, ECASS, and NINDS rt-PA Study Group Investigators, 2004). The European Cooperative Acute Stroke Study investigators tested this hypothesis in a randomized placebo controlled trial (ECASS III) of IV rt-PA (0.9 mg/kg dose with 10% bolus) in 821 subjects presenting with ischemic stroke from 3 to 4.5 hours from symptom onset (Hacke et al., 2008). ECASS III showed a favorable outcome, defined as a modified Rankin scale (MRS) score of 0 or 1 (minimal or no deficit) at 90 days, in 52.4% of treated subjects versus 45.2% in controls (odds ratio 1.34; 95% CI=1.02-1.76; P= 0.04). Symptomatic intracranial hemorrhage was reported in 2.4% of the IV rt-PA treated group compared with 0.2% of controls (P= 0.008). The inclusion and exclusion criteria for ECASS III were comparable to the original NINDS study except that those with NIHSS > 25, oral anticoagulant use, the presence of both diabetes mellitus and a previous stroke, and age >80 years were excluded.

A Cochrane systematic review of the 11 completed trials of thrombolysis (including 3,977 patients) with intravenous rt-PA for acute ischemic stroke showed that treatment was associated with a significant increase in survival free

of disability, despite an early 3% excess of fatal intracranial hemorrhage. The review also suggested that treatment might be beneficial up to 6 hours (Wardlaw, Murray, Berge, & Del Zoppo, 2010). On putting all these together; thrombolytic therapy within 3 hours of onset of stroke has advantage in terms of mortality and functional outcome. Its use between 3 to 4.5 hours does not reduce the mortality but increases functional outcome at discharge and at 3 months (Hacke et al., 2008).

### **The benefit of rt-PA in patient with ischemic stroke**

The time-sensitive nature of stroke care is central to establishment of successful stroke systems. The treatment within 4.5 hours of symptom onset is the largest benefits to improve neurological outcome. Recombinant tissue plasminogen activator (rt-PA) has improved the management of acute ischemic strokes (AIS) over the last ten years. However, intravenous rt-PA is only administered to a small percentage of patients; national registries from the USA (2001-2004), Sweden (2003-2008) and Korea (2006) report rates of about 8.5%, 3.2% and 2.1% respectively (Kim et al., 2011). Suwanwela, Phanthumchinda, & Likitjaroen (2006) found that thirty-four patients of 1,619 acute ischemic stroke patients or 2.1% of patients with acute ischemic stroke received intravenous thrombolysis in Bangkok, Thailand.

There is now evidence of benefit of rt-PA for up to 4.5 hours with most stroke centers using this time window as a standard clinical practice. Because of the short therapeutic time window, the number of patients who might receive treatment and therefore potentially benefit remains small; prevention of disability is seen in only six patients per 1000 ischemic strokes. Most stroke centers use rt-PA in only about 5% of stroke patients. Even in developed countries, many hospitals treating acute stroke do not offer thrombolysis, largely because of a worldwide shortage of physicians who are experts in acute stroke management. The major adverse effect of thrombolysis is symptomatic intracerebral hemorrhage, seen in about 6%-7% of cases (Lloyd-Jones et al., 2010).

Apart from Stroke Care Units and thrombolysis, evidence from about 40,000 randomized patients show that the administration of oral aspirin within 48 hour of onset of ischemic stroke reduces 14 days morbidity and mortality, however, the magnitude of the benefit is quite small. Decompressive surgery (the removal of

part of the skull to relieve pressure on the swollen brain) proved beneficial for some patient groups with ischemic stroke.

### **2.3.2.7 Antiplatelet drugs**

Platelet activation is a crucial mechanism in the pathophysiology of ischemic stroke. Activated platelets release various mediators and chemokines to recruit more activated platelets and leukocytes, which, in turn, accentuate local thrombogenesis and inflammatory responses (McColl, Allan, & Rothwell, 2009; Angiolillo, Ueno, & Goto, 2010). Propagation of thrombosis and inflammation might cause more injury to the ischemic brain tissue and lead to poor outcomes. Several markers of platelet activation were linked to poor outcomes of acute ischemic stroke (Yip, Liou, Chang, Lan, Liu, & Chen, 2005; Tsai et al., 2009). Inhibition of platelet function is an important therapeutic strategy in ischemic vascular diseases. Aspirin is an important and effective therapeutic strategy in secondary prevention of other thrombotic events in acute ischemic stroke (Baigent et al., 2009).

The initiation of oral antiplatelet therapy after acute ischemic stroke is recommended to prevent the recurrence and progression of stroke as well as other serious vascular events because of the elevated risk of recurrence during the acute stage and a possible intense procoagulant state (Gentile et al., 2007). In the Chinese Acute Stroke Trial (1997) demonstrated that 21,106 patients received aspirin treatment (160 mg/day) that was started within 48 hours of the onset of suspected acute ischemic stroke and was continued in hospital for up to 4 weeks reduced mortality to 3.3%, compared with 3.9% with placebo. The risk of a recurrent stroke is highest early after an ischemic stroke or transient ischemic attack (TIA) about 1% at 6 hours, 2% at 12 hours, 3% at 2 days, 5% at 7 days, and 10% at 14 days (Chandratheva et al., 2009; Wang et al., 2013). Therefore, ischemic stroke or TIA is a medical emergency that demands immediate diagnosis and treatment.

As a single antiplatelet therapy, aspirin 160-300 mg. daily, started within 48 hours of onset of ischemic stroke in 40,000 patients, and continued for 2-4 weeks, reduced the odds of recurrent ischemic stroke by 23% (2.4% aspirin vs 3.1% control; odds ratio 0.77, 95% CI: 0.69-0.87), increased the odds of symptomatic intracranial hemorrhage by 22% (1.0% vs 0.8%; OR 1.22, 95% CI: 1.00-1.50), and reduced the odds of any recurrent stroke by 12% (3.4% vs 3.9%; OR 0.88, 95% CI:

0.79-0.97) compared with control (Sandercock, Counsell, Gubitz, & Tseng, 2008). In addition, a meta-analysis of 14 randomized controlled trials comparing dual antiplatelet therapy with antiplatelet monotherapy, both started within 3 days of onset of ischemic stroke or TIA in 9,102 adults showed that dual antiplatelet therapy significantly reduced early recurrent stroke by a third (6.21% dual therapy vs 8.95% monotherapy; risk ratio 0.69 (95% CI: 0.60-0.80) absolute risk reduction 2.74%) at about 3 month's follow up, compared with monotherapy, and non-significantly increased the risk of major bleeding (0.52% dual therapy vs 0.36% monotherapy; RR 1.35, 95% CI= 0.70-2.59, absolute risk increase 0.16%)(Wong et al., 2013).

On the other hand, hemorrhagic complications associated with antiplatelet might pose a serious challenge, especially during the acute stage of stroke, as severe critical illness or elevated intracranial pressure might increase the risk of hemorrhagic complications (Roden-Jullig, Britton, Malmkvist, Leijd, 2003).

### **2.3.2.8 Clinical practice guidelines**

Clinical practice guidelines, defined as “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances,” have been expected to optimize patient care. Health providers and health policy makers in Thailand and overseas have formulated guidelines designed to improve treatment for stroke patients (Australian National Stroke Foundation, 2007; Canadian Heart & Stroke Foundation, 2006; Prasat Neurological Institute, 2009) and have developed an arsenal of innovative stroke cares and treatments, such as dedicated stroke care units (Geoffrey, Marc, Malcolm, & Stephen, 2008), intravenous rt-PA (Adams et al., 2003; Foell et al., 2003; Ducrocq et al., 2005), care protocols and guidelines and specialized stroke teams (Katzan, Hammer, Furlan, Hixson, Nadzam, 2003). Many prospective and retrospective studies in the sample from 140 to 439 participants demonstrated that the clinical practice guideline can shorten time to treatment and investigations, and also increase the numbers of patients receiving timely treatments such as intravenous thrombolysis (Katzan et al., 2003; Mehdiratta & Caplan, 2006) and aspirin (Grotta et al., 2001). In another study, the use of clinical practice guideline in acute stroke patients from 257 to 439 participants was able to decrease post-stroke complication occurrence such as urinary tract infection (0.097 vs 0.05), pressure sore (0.0259 vs 0.0253),

pneumonia, and fall (Widjaja et al., 2002; Kwan et al., 2004). Importantly, providing care following clinical practice guideline was able to improve early recovery in patients with acute ischemic stroke.

## **2.4 Recovery in patient with acute ischemic stroke**

### **2.4.1 Definition of recovery**

Defining “recovery” is difficult, as health professionals and users understand it in a variety of ways. As Jacobson & Greenley (2001) have noted,

“Recovery is variously described as something that individuals experience, that services promote, and that systems facilitate, yet the specifics of exactly what is to be experienced, promoted, or facilitated – and how – are often not well understood either by the consumers who are expected to recover or by the professionals and policy makers who are expected to help them.”

Diverse definitions may be related to the difference between someone “having recovered” and “being in recovery”. The former accords with the conventional definition of ‘a cure or restoration to former health and stability’ (Shorter Oxford Dictionary) or ‘regaining something lost’ (Wikipedia). The latter, used by the recovery movement and particularly by people with longer-term conditions, expands the definition to a ‘personal process, way of life or attitude, involving the growth of new meaning and purpose beyond the effects of mental illness (Deegan, 2003).

A review of the entry for recovery suggests another potential source of the confusions concerning the term, given that Webster Dictionary offers the following four different definitions: 1) A return to a normal condition; 2) An act, instance, process, or period of recovering; 3) Something gained or restored in recovering; and 4) The act of obtaining useable substances from unusable sources, as with waste material. In addition, recovery can also be divided into four categories of: 1) acute physical conditions; 2) trauma, its sequel, and related post-traumatic stress disorders; 3) substance use disorders; and 4) severe psychiatric disorders (Davidson, Lawless, & Leary, 2006).

The physical recovery is most appropriate to return to a normal condition. This definition of recovery represents by far the most common use of the term, and a use of the term that is perfectly appropriate when referring to the resolution of acute physical illnesses and conditions such as a cold, the flu, or a broken bone. In all of these cases, recovery is taken to mean that the person has been restored, through whatever means, to the same presumably normal condition she or he had prior to the onset of the illness or the precipitating event that led to the condition. In all of these cases, there also is an assumption that a healthy, normal state existed prior to the onset of disease and/or dysfunction; i.e., that people are “naturally” healthy until something happens to deprive them of their health, “recovery” then being restoration of the person to this prior state.

Recovery takes on a different meaning, however, even within physical medicine when applied to chronic physical health conditions such as asthma, diabetes, or cancer. In these cases, the person is not expected to be restored to a previous, pre-morbid, condition of health. To the degree that the term recovery is used at all in relation to these more prolonged conditions (e.g., partial recovery from a stroke, being in recovery from cancer), it ordinarily is taken to mean a partial return to normal functioning or no longer refers to restoration to a previous condition of normality (Davidson et al., 2006).

For the mental recovery, this term means gaining and retaining hope, understanding of one’s abilities and disabilities, engagement in an active life, personal autonomy, social identity, meaning and purpose in life, and a positive sense of self. It refers both to internal conditions-the attitudes, experiences, and processes of change of individuals who are recovering-and external conditions-the circumstances, events, policies, and practices that may facilitate recovery (Jacobson & Greenley, 2001).

#### **2.4.2 Stroke recovery**

The primary goals of stroke management are to reduce brain injury and promote maximum patient recovery. Rapid detection and appropriate emergency medical care are essential for optimizing health outcomes (Jauch et al., 2010). Recovery may be measured by assessing impairments, disabilities or quality of life. Impairments are the neurological signs and symptoms of stroke, disabilities are the

functional consequences of the neurological deficits, and handicap or quality of life reflects limitations in role performance (WHO, 1980). Recovery of the neurological signs and symptoms of stroke probably reflect some resolution of the pathology of stroke. Changes in the functional consequences (physical and psychosocial) may be associated with improvements in neurological function, but they may also reflect behavioral compensation. Finally, reintegration into prior physical and social roles is often modified by factors other than the degrees of neurological recovery (Duncan et al., 1999).

The patients with early recovery more frequently had an excellent outcome (modified Rankin Scale 0-1) than patients without early recovery (67.6% versus 9.0%;  $P < 0.0001$ ). After adjustment for admission NIHSS, the OR for excellent outcome associated with early recovery was 23.83 (95% CI: 10.85-52.35,  $P < 0.001$ ) in all patients and 19.95 (95% CI: 8.56-46.50;  $P < 0.001$ ) in patients eligible for IV rt-PA treatment and less frequently had hemorrhage (17.3% versus 33.9%,  $P = 0.024$ ) (Mazighi et al., 2012).

### **2.4.3 Measures of stroke recovery**

#### **2.4.3.1 Measures of early neurological recovery**

Early neurological recovery was defined as a NIHSS score of 0 to 3 at 24 hours or a decrease of  $\geq 4$  points in the NIHSS score at 24 hours by the end of infusion (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995; Stolz et al., 2008; Mazighi et al., 2012). In addition, a study evaluates very early neurologic improvement (VENI) after intravenous rt-PA perfusion in patients with acute ischemic stroke (AIS). The VENI was defined 1 hour after the start of IV rt-PA by a NIHSS score of 0 or an improvement of 5 points or more compared with the baseline NIHSS score, so VENI was determined at the end of rt-PA infusion (Muresan et al., 2010). Previous study defined early recovery as improvement of 50% within 24 hours as measured by the National Institutes of Health Stroke Scale (NIHSS) score predicted a favorable outcome (Machumpurath, Davis, & Yan, 2011). Furthermore, one study defined acute recovery as an improvement of greater than or equal to 75% on National Institutes of Health Stroke Scale (NIHSS) between baseline and 24 hours (Johnston, Leira, Hansen, & Adams, 2003).

The NIHSS is used for both initial assessments of stroke severity and monitoring changes in a patient's condition. The percent NIHSS score change also appears to be a sensitive measure of early improvement in acute stroke. In the NINDS rt-PA Acute Stroke Trial measured a significantly greater percent improvement at 24 hours after stroke onset with rt-PA than with placebo (29% vs 15%,  $P = .001$ ), whereas there was only a trend toward greater improvement with rt-PA (47% vs 39%,  $P = 5.06$ ) according to the original dichotomized definition (complete resolution of neurologic deficits or a decrease on the NIHSS score by  $\geq 4$  points) (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995).

The National Institutes of Health Stroke Scale (NIHSS) is often used as a standard measurement instrument by physicians (Lyden et al., 2005) and nurses (Summers et al., 2009) to evaluate the severity of a patient's neurological deficit in emergency departments and at stroke units. The NIHSS contains parameters for observing changes in the patient's neurological status and measuring stroke severity. The NIHSS is a stroke specific quantitative scale that examines the level of consciousness, language function, neglect, visual fields, eye movements, facial symmetry, motor strength, sensation, and coordination (Kasner et al., 1999). The examination can be performed quickly, and the NIHSS score can be assessed by neurologists and non-neurologists after appropriate training. The scale shows excellent clinimetric properties in terms of reliability and validity (Lyden et al., 2005). The NIHSS has been repeatedly validated as a tool for assessing stroke severity and as an excellent predictor for patient outcomes (Muir, Weir, Murray, Povey, & Lees, 1996; Frankel et al., 2000). Recently, the American Heart Association (AHA) recommended bedside NIHSS assessment as a valuable tool for nursing and inter disciplinary care of the acute ischemic stroke patient (Summer et al., 2009). The NIHSS shows significant association with lesion volume (Lyden et al., 2005) as well as with final outcome after a stroke in terms of survival, discharge destination (Muir et al., 1996), length of stay (LOS) (Appelros, 2007), activities of daily living (ADL) (Appelros & Terent, 2004; Celik, Aksel, & Karaoglan, 2006). The NINDS trial showed that a lower baseline NIHSS score during the first 24 hours post stroke was independently associated with a favorable outcome in terms of the Barthel Index (BI) and the modified Rankin Scale

(mRS) measured one year post stroke (Kwiatkowski et al., 1999). Furthermore, a longitudinal study investigating changes in impairments in a repeated measurement design showed that progress of time is an independent covariate related to improvements of body functions and activities in the first weeks post stroke, reflecting spontaneous neurological recovery (Kwakkel, Kollen, & Twisk, 2006).

NIHSS consists of 11 items that assess the severity of impairments. The total score ranges from 0 (no deficit) to 42 (significant deficit). Eleven items are evaluated:

1) Level of consciousness (LOC) testing is divided into three sections: LOC Responsiveness (0-3), LOC Questions (0-2), and LOC Commands (0-2). The final LOC sub-section is based on the patient's ability to follow verbal commands to perform simple task. Although this item is broken into three parts, each sub-section is added to the final score as if it is its own item.

2) Horizontal Eye Movement assesses ability for patient to track a pen or finger from side to side only using his or her eyes. This is designed to assess motor ability to gaze towards the hemisphere opposite of injury. The score is 0 (Normal) to 2 (Total gaze paresis; gaze is fixed to one side).

3) Visual fields test assesses the patient's vision in each visual fields. The score is 0 (No vision loss) to 2 (Bilateral Blindness).

4) Facial Palsy assesses partial or complete paralysis of portions of the face. The score is 0 (Normal and symmetrical movement) to 3 (Complete facial Hemi-paresis).

5) Motor Arm assesses the arm movement. The score is 0 (No arm drift) to 4 (No movement).

6) Motor Leg assesses the leg movement. The score is 0 (No leg drift) to 4 (No movement).

7) Limb Ataxia assesses coordination, smooth and accurate movement. This item is aimed at finding evidence of a unilateral cerebella lesion. The score is 0 (Normal coordination, smooth and accurate movement) to 2 (Ataxia present in 2 or more limbs: rigid and inaccurate movement in both limbs on one side).

8) Sensory testing is performed via pinpricks in the proximal portion of all four limbs. The score is 0 (No evidence of sensory loss) to 2 (Severe to total sensory loss on one side).

9) Language measures the patient's language skills. The score is 0 (Normal; no obvious speech deficit) to 3 (global aphasia; Unable to speak or understand speech).

10) Speech assesses dysarthria which is the lack of motor skills required to produce understandable speech. The score is 0 (Normal; clear and smooth speech) to 2 (Severe dysarthria; speech is so slurred that he or she cannot be understood, or patients that cannot produce any speech).

11) Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. The score is 0 (No abnormality) to 2 (Profound hemi-inattention or extinction to more than one modality; does not recognize own hand or orients to only one side of space).

#### **2.4.3.2 Measures of long-term recovery**

For the measurement of long-term recovery, there are many methods for measuring recovery following: the Fugl-Meyer Assessment of Motor Recovery (Fugl-Meyer et al., 1975), the Barthel Index of Activities of Daily Living (Mahoney and Barthel, 1965), the Physical Function Index (PFI) of the SF-36 (Ware and Sherbourne, 1992), and the Modified Rankin Stroke Outcome Scale (Van Swieten, Koudstaal, Visser, Schouten, & Van Gijn, 1988). Each of the measures has established reliability and validity.

1) The National Institutes of Health Stroke Scale (NIHSS) can also measure long-term favorable outcome that was defined as an NIHSS score of  $\leq 4$  at 90 days, and a poor outcome as an NIHSS score of  $> 4$  at 90 days (Kumagai et al., 2013).

2) The Fugl-Meyer is a measure of motor impairments. Scoring is based on direct observation of performance. Scale items are scored on the basis of ability to complete the item using a 3-point ordinal scale where 0=cannot perform, 1 = performs partially and 2 = performs fully. The total possible scale score is 100. This score is divided into 66 points for upper extremity and 34 points for the lower extremity. The FM has been shown to have high test-retest reliability (Duncan,

Propst, & Nelson, 1983), inter rater reliability (Duncan et al., 1983), and construct validity (Di Fabio, & Badke, 1990).

3) The Barthel Index is a reliable disability scale. It includes 10 items that can be divided into self care (feeding, grooming, bathing, dressing, bowel and bladder care, and toileting) and mobility (ambulation, transfers and stair climbing). The max score is 100 and lowest score is 0, patient is bed ridden. The cut-off scores for defining recovery used by Barthel ADL > 90. The activities of daily living (ADL) outcome measured in various time such as 3, 6, or 12 months post stroke (Kwakkel et al., 2010).

The Modified Barthel Index (MBI) was translated into Thai and the interrater reliability was assessed by 2 psychiatrists, 2 physical therapists and 2 occupational therapists, under supervision of English specialist. The MBI (Thai Version) was applied in the assessment of 30 stroke patients referred for comprehensive rehabilitation in Buddhachinaraj Phitsanulok Hospital during January-March 2007 by 2 physical therapists and 2 occupational therapists in the same visit.

The MBI (Thai Version) had high interrater reliability (ICC=0.96) and substantial interrater agreement between therapists for bowel and bladder control ( $k = 0.90$  and  $0.87$ , 95% CI: 0.61-0.80). The most of other subscales had fair agreement ( $k = 0.46-0.58$ , 95% CI: 0.21-0.40).

4) The SF-36 physical function index includes 10 question about limitations in physical activities (vigorous activities such as running, lifting heavy objects, moderate activities such as moving a table, pushing a vacuum, lifting or carrying groceries, climbing several flights of stairs, climbing one flight of stairs, bending, kneeling or stooping, walking more than a mile, walking several blocks, walking one block, bathing or dressing yourself). The maximum score is 100. Scores on the physical function index of the SF-36 have been normalized for age and gender. The average score for 70 year old women on the SF-36 PFI is 66 and for 70 year old men the average score is 75 (Ware, Snow, Kosinski, & Gandek, 1993). The cut-off scores for defining recovery used by SF-36 > 66 for women and >75 for men.

5) The modified Rankin Scale (mRS) is a global outcomes rating scale for stroke patients. The scale includes 6 grades, from 0 to 5, with 0 corresponding to no symptoms and 5 to severe disability, bedridden. Scores to define

stroke recovery on the various measures are highly variable (Sulter et al., 1999; Duncan et al., manuscript in preparation). The cut-off scores for defining recovery used by mRS score 0 to 1 at 3 months (Labiche et al., 2003; Zhao et al., 2014). The mRS usually measured clinical outcomes in patients with acute ischemic stroke in 3 Or 6 months after stroke (Aoki et al., 2013).

Score	Description
0	No symptoms
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance
3	Moderate disability; requiring some help but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

In this study, the researcher selects the NIHSS because this instrument appears to be a sensitive measure of early improvement in acute ischemic stroke.

## **2.5 Models and framework related access to rt-PA in patient with acute ischemic stroke**

In order to systematically examine factors influencing access to rt-PA in patient with acute ischemic stroke, an appropriated framework are required. There are 2 different models that were considered congruent with the present study: the International Classification of Impairments, Disabilities, and Handicaps (ICIDH-2) model and A Behavioral Model of Access to Health Services. These models were explained and discussed as follows.

### 2.5.1 The International Classification of Impairments, Disabilities, and Handicaps (ICIDH-2) Model

Specific aims of the ICIDH-2 were to provide a scientific basis for understanding and studying the functional states associated with health conditions; to establish a common language for description and discussion of functional states associated with health conditions; to permit comparison of data across countries, health care disciplines, services and time; and, to provide a systematic coding scheme for health information systems (WHO, 1999). Applications of the document include: 1) use as a statistical tool in collection and recording of data; 2) use as a research tool in measurement of outcomes, quality of life, or environmental factors; 3) use as a clinical tool in needs assessment, vocational assessment, rehabilitation, and outcome evaluation; 4) use as a social policy tool for use in social security planning, compensation systems, policy design, and implementation; and 5) use as an educational tool for curriculum design (WHO, 1999).

The ICIDH-2 is designed to encompass all aspects of human health and relevant aspects of well-being. As illustrated in Figure 2, the structure of the ICIDH-2 is hierarchical. First, the ICIDH-2 is organized in two general parts: Part I Functioning and disability; and, Part II Contextual factors.

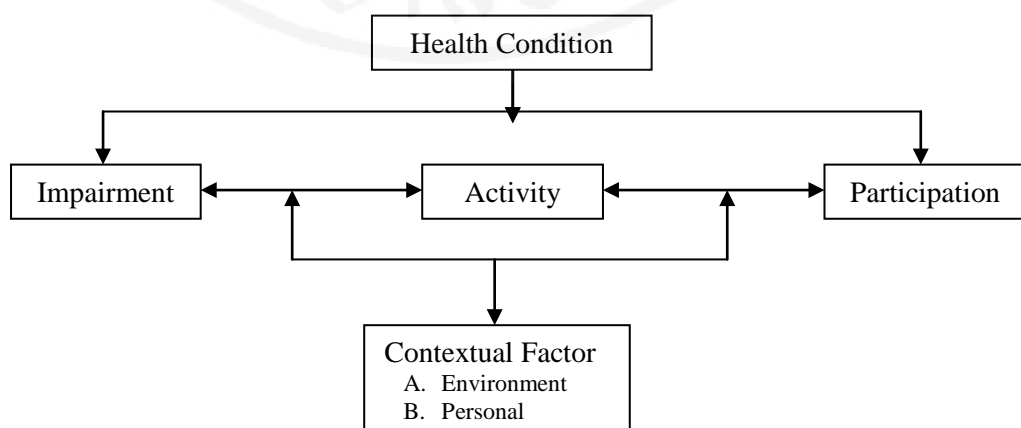
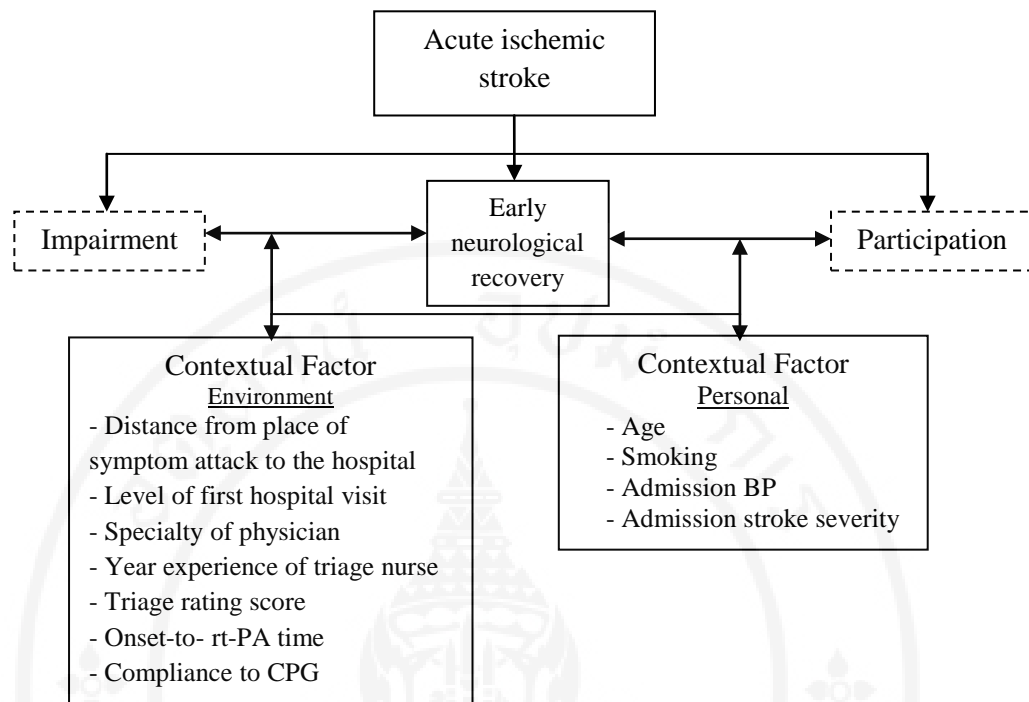


Figure 2.1 ICIDH-2 (WHO, 1998)

This model was considered in the description of the consequences of acute ischemic stroke. According to the ICIDH-2, information is organized into three dimensions: (1) body level; (2) individual level; (3) societal level. These dimensions are named: (1) body functions and structure; (2) activities; and (3) participation. In addition, contextual factors are recognized which include both personal and environmental factors. More specifically, the model distinguishes disease from disease consequences and influencing contextual factors; the model links its dimensions with double sided arrows, symbolising room for bidirectional influences and interactions; and disease consequences can be named in positive terms, emphasizing that abilities as well as disabilities are regarded as important factors.

Assessment of recovery in patient with acute ischemic stroke able to give an entire picture should measure at the body function, activity, and participation levels which allows the determination of the impact of changes in impairments on changes in activity and perceived quality of life. For example, many ADLs can be performed despite the presence of significant impairments. If only the level of activity is monitored, the patterns of neurological recovery, particularly in cognition, may be deviated. Therefore, the ICIDH-2 provides a comprehensive and standard conceptual framework that is useful for describing patterns of recovery in patient with acute ischemic stroke.

However, rather than describe each potential neurological deficit that may result from stroke, it may be more beneficial to identify associations between body functions, structures, and activity and participation as they are affected by stroke, thereby providing evidence to guide functional assessment practices. Additionally, the ICIDH-2 model also provides the definition of each category of components.



**Figure 2.2** Application of the ICIDH-2 model for factors influencing early neurological recovery in patients with acute ischemic stroke

### 2.5.2 A Behavioral Model of Access to Health Services

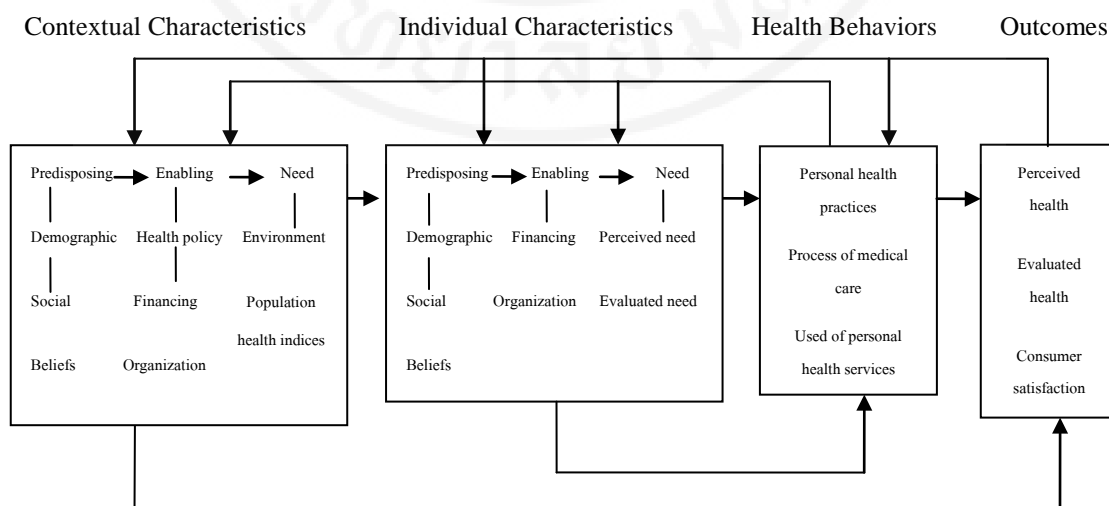
The key thing that access model by Andersen and his colleagues noted was this concept of use of health care focused on 2 major alternative dimensions: the characteristics of the population and the characteristics of the delivery system. Andersen also noted that it was the use of service and outcomes of the use process that could be used to measure access.

The framework presented in figure 4 stresses that improving access to care is best accomplished by focusing on contextual as well as individual determinants. By contextual, they point to the circumstances and environment of health care access. Context includes health organization and provider-related factors as well as community characteristics. Contextual factors are measured at some aggregate rather than individual level. These aggregate levels range from units as small as the family to those as large as a national health care system. In between are workgroups and teams, provider organizations, health plans, neighborhoods, local communities, and metropolitan statistical areas. Individuals are related to the segregated units through

membership (family, workgroup, provider institutions, health plan) or residence (neighborhood, community, metropolitan area, national health system). Lastly, the model indicates that health behaviors (personal health practices, process of medical care, used of personal health services) are the direct cause of health outcomes.

According to the model, usage of health services is determined by three dynamics: predisposing factors, enabling factors, and need. Predisposing factors include the socio-cultural characteristics that exist prior to their illness such as demographic, social structure, and health beliefs. Enabling factors include family characteristics such as income, insurance coverage, access to services (transportation and distance to care), and community characteristics such as availability of resources and region of the country. Need Factors compost of perceived need and evaluated need. Perceived need will better help to understand care-seeking and adherence to a medical regimen, while evaluated need will be more closely related to the kind and amount of treatment that will be provided after a patient has presented to a medical care provider (Andersen, 1995).

The outcome measures of access model focused on patient’s perceived health status, evaluated health status, and consumer satisfaction (Anderson, 2007).



**Figure 2.3** A Behavioral Model of Access to Medical Care (Andersen, 2007)

## 2.6 Factor influencing early recovery in patient with ischemic stroke

### 2.6.1 Contextual Characteristics

#### 2.6.1.1 Predisposing

1) **Demographic characteristics** include the age, gender, and marital status composition of a community. Thus a community populated primarily by older persons might well have a different mix of available health services and facilities from one in which the majority are younger parents and children.

In Thailand, life expectancy at birth increased from 55.2 years to 69.9 years for men and 61.8 years to 74.9 years for women. The proportion of the population in their elderly years (aged 60 and over) is anticipated to increase from 8.7% in 2000 to 10.8 % in the year 2010, 15.2 % in the year 2020, and 30 % in the year 2050. The number of older persons will continue to rise, from approximately 5.3 million at present to 7.2 million in 2010 and will reach 11 million by 2020. Aging is the most important non-modifiable risk factor for stroke. As life expectancy increases, the very old are expected to become a growing proportion of stroke victims (Feigin et al., 2003; Rothwell et al., 2005; Mayo et al., 2007). At present, more than half of all strokes already occur in people over 75 years of age (Feigin et al., 2003). The case-fatality rates are higher in the very old, and, among the survivors, the post stroke functional status is worse, both in short and long-term (Dennis et al., 1993; Pohjasvaara et al., 1997; Di Carlo et al., 1999; Arboix et al., 2001; Kammersgaard et al., 2004; Rojas et al., 2007).

Sex ratio of total population in Thailand is 0.98 male(s)/female. The total population, 75% were Ethnic Thai, 14% were Thai Chinese, and 3% were ethnically Malay.

2) **Social characteristics** at the contextual level describe how supportive or detrimental the communities where people live and work might be to effect to their health and access to health services. Relevant measures include educational level, ethnic and racial composition, proportion of recent immigrants, employment level, and crime rate.

At present 98 % of the Thai older persons live with their families while only 2 percent live in institutions. Almost 50 % of older persons in

Thailand live in the three-generation households. One-third of older persons live in two-generation households. One-fifth of them lived in one generation households (mostly with their spouses). One study in USA analysis of patient pre-stroke living situation demonstrated found that 21.4% lived alone, 4.3% lived alone while receiving services, 21.9% lived at home with family or friends, and 52.3% lived with their spouse. Patients living alone had less severe strokes on admission and better recovery at 3 months compared with the other cohorts. Patients living alone or those who lived with a spouse had less severe strokes on presentation and better recovery at both 3 and 12 months after stroke compared with the other cohorts (Aron, Staff, Fortunato, & McCullough, 2015).

For education level, approximately thirty-one percent of Thai older persons have never attended school. Thai older women have much less opportunity to formal education compared with Thai older men. Among older men and women, 71 percent and 48 percent have finished grade 4 or higher level.

Thai food is generally quite healthy but if the cook likes things salty so adds lots of fish sauce the dishes will contain a lot of sodium, just like adding table salt to western dishes.

**3) Beliefs** refer to underlying community or organizational values and cultural norms and prevailing political perspectives regarding how health services should be organized, financed, and made accessible to the population.

For the Religion of Thai population, Buddhism is the official religion of Thailand and is officially the religion of about 94.6% of its people. Muslims are some 4.6% and 0.7% other religions including Christianity, and others including population with no religion (0.1 percent). In considering by region, it was found that most population in every region were Buddhist (more than 90 per cent), except the Southern region, where there were mostly Muslim with higher proportion than other regions (24.5 per cent).

Although scientific reality has become the major belief system in Thai society that determines our current perception, Buddhist reality, which is deeply infused into Thai culture, has an important impact on the perception as well. An investigation of Buddhist principles and perspectives on health and healing offers an alternative perception for understanding health and illness that may lead to other

approaches form an aging or solving health problems. Another Buddhist concept that explains human life is Kamma. It is one part of the natural law that refers to the working of intention, or the process of mental proliferation and its consequences. In essence, this is summarized in the words, 'gooddeeds bring good results, bad deeds bring bad results' (Bhikkhu & Payutto, 1993: 1-2).

Health problem solving when faced with illness, most people in the neighborhoods in rural city would attempt to address the problem on the basis of available knowledge in the family or immediate community, using medicines from the drugstore or herbal treatment. It was especially common for the elderly in this community to first turn to what has been described as a therapy management group (Janzen, 1987). This local, non professional group comprised of lay people who played an important role in the interpretation of abnormal symptoms and decisions regarding treatment and disease management. Some of the management strategies suggested by this group included staying in bed, buying medicine from a grocery or drug store, praying or seeing health professionals at a medical clinic, primary care unit or hospital. Also, elderly people preferred to go to their usual drugstore. For what was perceived as more serious or persistent illness, people would seek professional healthcare providers (Seeberg et al., 2014).

#### **2.6.2.2 Enabling**

**1) Health policies** are authoritative decisions made pertaining to health or influencing the pursuit of health. They can be public policies made in the legislative, executive, or judicial branch of government, at all levels from local to national. They can also be policies made in the private sector by such decision makers as executives of managed care organizations concerning product lines, pricing, or marketing, or by accrediting agencies.

The ASA task force on the development of stroke systems has defined key components of a regional stroke system of care and recommended methods for the implementation of stroke systems (Schwamm et al., 2005). Stroke systems of care integrate regional stroke facilities, including acute stroke-ready hospitals (ASRHs) that often have telemedicine and teleradiology capability, primary and comprehensive stroke centers, EMSS, and public and governmental agencies and resources. The goals of creating stroke systems of care include stroke prevention,

community stroke education, optimal use of EMS, effective acute and subacute stroke care, rehabilitation, and performance review of stroke care delivery. Essential to effective stroke systems of care are hospitals with the capacity and commitment to deliver acute stroke care, both in the ED and on the stroke unit. In regions with effective stroke systems, the majority of patients are now being transported to these stroke centers, which optimizes their chances for timely appropriate therapy and admission to stroke units, both of which decrease the morbidity and mortality associated with stroke (Meretoja et al., 2010; Smith et al., 2010).

### **Stroke Care Resource**

#### **i) Hospital Stroke Capabilities**

- **Comprehensive Stroke Center**

The recommendations to establish Comprehensive Stroke Center (CSCs) were published in 2005 (Alberts et al., 2005). In 2011, the ASA published the scientific statement, “Metrics for Measuring Quality of Care in Comprehensive Stroke Centers,” which delineates the set of metrics and related data that CSCs should track to ensure optimal stroke outcome and adherence to current recommendations (Leifer et al., 2011). According to these recommendations, a CSC should be able to offer 24/7(24 hours per day, 7 days per week) state-of-the-art care on the full spectrum of cerebrovascular diseases.

The data highlighting the patient-centered benefits of integrating CSCs into regional stroke systems of care are emerging. Recently, Orange County, California, organized regional stroke care around CSCs in a hub-and-spoke model, serving just over 3 million people (Cramer et al., 2012). Among patients taken directly to the CSCs in this model, 25.1% received acute reperfusion therapies (intravenous rt-PA, endovascular therapies, or both). A recent analysis of 134,441 stroke patients in New Jersey hospitals showed that CSCs had no gap in mortality rate between weekday and weekend admissions, whereas mortality was higher when patients were admitted on weekends at other stroke centers (McKinney, Deng, Kasner, & Kostis, 2011). In Finland, where stroke systems of care are organized on a national level, a 7-year study of all stroke patients in the country demonstrated a clear association between the level of acute stroke care and patient outcomes, with the lowest rates of mortality and severe disability seen in CSCs (Meretoja et al., 2010).

Neurocritical care units are essential elements of CSCs. Improvements in clinical outcome attributable to focused critical care have been documented (Suarez, 2006), as have a reduction in and an earlier recognition of complications and reduced days of hospitalization (Suarez et al., 2004). In patients with acute ischemic stroke, admission to neurocritical care units should be considered for those with severe deficits, large-volume infarcts with the potential for significant cerebral edema, significant comorbidities, blood pressure that is difficult to control, or prior intravenous and intra-arterial recanalization interventions.

- **Primary Stroke Center**

The definition of a primary stroke center (PSC) was first published in 2000 (Alberts et al., 2000). This article defined the critical pre-hospital and hospital elements to deliver effective and efficient stroke care. Since The Joint Commission (TJC) began providing PSC certification in 2004, more than 800 certified PSCs have been established in the United States (The Joint Commission, 2011). Regardless of certifying agent (TJC or state health department), it is mandatory for all PSCs to closely track their performance on key quality stroke care measurements. In cluster controlled clinical trials comparing patient outcomes in PSCs with those in community hospitals without specialized stroke care, patients with ischemic stroke treated in centers with dedicated stroke resources had better clinical outcomes (Audebert, Schenkel, Heuschmann, Bogdahn, & Haberl, 2006) and increased rates of intravenous rt-PA administration (Morgenstern et al., 2002). In addition, numerous observational studies have demonstrated that PSC certification improves stroke care in many ways, for instance, by shortening door to physician contact time, door to CT time, and door to intravenous rt-PA time, as well as by increasing rates of intravenous rt-PA use (Sung, Ong, Wu, Hsu, & Su, 2010; Xian et al., 2011).

- **Acute Stroke-Ready Hospital**

Acute Stroke-Ready Hospital (ASRHs), previously called stroke-capable hospitals, are hospitals that have made an institutional commitment to effectively and efficiently evaluate, diagnose, and treat most ED stroke patients but that do not have fully organized inpatient stroke systems of care. ASRHs have many of the same elements as a PSC:

- Written emergency stroke care protocols
- Written transfer agreement with a hospital with neurosurgical expertise
- Director of stroke care to oversee hospital stroke policies and procedures (this may be a clinical staff member or the designee of the hospital administrator)
- Ability to administer intravenous rt-PA
- Ability to perform emergency brain imaging (eg. CT scan) at all times
- Ability to conduct emergency laboratory testing at all times
- Maintenance of a stroke patient log

Additionally, ASRHs have well-developed relationships with regional PSCs and CSCs for additional support. Stroke expertise and neuroimaging interpretation in ASRHs are often in the forms of telemedicine and teleradiology, which require close collaboration within the regional stroke system of care. Many ASRHs do not have sufficient resources to establish and maintain a stroke unit; thus, in some circumstances, once patients are diagnosed and initial treatments delivered, patients are transported to a PSC or CSC. ASRHs are also responsible for EMS stroke education and integration into the stroke system of care. The development of ASRHs has the potential to greatly extend the reach of stroke systems of care into underserved regions.

## **ii) Telemedicine or “Telestroke”**

Telemedicine is a resource that lets doctors remotely evaluate patients, thereby promoting access to thrombolysis for patients whose treatment options are geographically limited (Heninger, Chowdhury, Fisher & Moonis, 2009). Telemedicine (also called *telestroke*) may help solve the shortage of neurologists and radiologists, allowing hospitals to become acute stroke ready (Schwamm et al., 2009). Many uses of telemedicine for stroke involve a hub-and-spoke model, in which the hub hospital, often a tertiary stroke center, provides specialty services to spoke hospitals. Telemedicine is integrated audio and visual remote assessment. Telemedicine can provide 24 hours and 7 days acute stroke expertise to hospitals

without full-time neurological or radiological services at the spoke hospital (Ickenstein et al., 2005).

Although the technological sophistication and prices of the systems can vary, it is essential that the system have the capability to provide 2-way real-time audiovisual conferencing and share the images. The benefits of telestroke are several: Telestroke optimizes the use of intravenous rt-PA to treat patients in hospitals without an on-site neurologist (Switzer & Hess, 2008) decreases time to initiate intravenous rt-PA, and provides treatment with similar safety as primary stroke center (Switzer et al., 2009; Sairanen et al., 2011). These benefits include immediate access to specialty consultations, reliable neurological examinations, and National Institutes of Health Stroke Scale (NIHSS) scores; high rates of intravenous thrombolysis with low rates of hemorrhage; and mortality rates and functional outcomes of intravenous thrombolysis comparable to those in randomized trials (Demaerschalk et al., 2010). Therefore, when the physical presence of a stroke team physician at the bedside is not possible, telestroke should be established so that additional hospitals can potentially meet the criteria to become Acute Stroke-Ready Hospital and a primary stroke center (Smith et al., 2008).

### **iii) Stroke unit**

The stroke unit defined as a hospital ward with dedicated beds (at least 80% stroke admission) and with a dedicated stroke staffs (at least one physician and one nurse) who work exclusively in the care of stroke patients. Regular communications and coordinated care are also key aspects of the stroke unit. Standardized stroke orders or integrated stroke pathways improve adherence to best practices for treatment of patients with stroke (Read & Levy, 2006). The benefits from treatment in a stroke unit are comparable to the effects achieved with intravenous administration of rt-PA (Gilligan et al., 2005). Thus, recommendations are based on customary care and the findings from multiple randomized trials that efficient delivery of the combination of these treatments in a stroke unit yields better outcomes than does less organized delivery of these therapies in general medical wards (Jauchet et al., 2013).

#### **iv) Specialty of physician**

Patients in many hospital settings have limited access to specialists with stroke expertise. Although evidence supporting the utility of acute “code stroke” teams and telestroke systems is plentiful, their availability is dependent on local resources. The evidence on the safety of thrombolytic delivery without a neurologist stroke specialist present in person or by telemedicine is less robust. Although emergency physicians exhibit high sensitivity and positive predictive value in identifying patients with stroke (Morgenstern et al., 2004). Some studies have identified instances of thrombolytic delivery in the setting of acute stroke by an emergency or primary care physician (either alone or in telephone consultation with a neurologist) (Wang et al., 2000; Rymer et al., 2003; Akins et al., 2005). The patients were treated by general neurologists, stroke neurologists, and emergency physicians reported mean times to rt-PA infusion were 44, 86, and 141 minutes, respectively. In-hospital mortality rate was 10% (4 intracerebral hemorrhage, 1 cardiogenic shock). Complications were more frequent among patients with protocol violations compared with those without all hemorrhages (75% versus 10%,  $P=0.001$ ), symptomatic ICH (38% versus 5%,  $P=0.02$ ), and ICH attributable to rt-PA, occurring within 36 hours (38% versus 2.4%,  $P=0.01$ ), respectively. One study noted an increase in intracerebral hemorrhage in patients treated by community neurologists (Katzan et al., 2000) and found increased in hospital mortality among intravenous rt-PA treated stroke patients (Katzan et al., 2000; Bravata et al., 2002).

In the case of the Cleveland, Ohio, experience, these poor outcomes led to quality improvement initiatives that decreased overall rates of symptomatic hemorrhage from 15.7% to 6.4% (Katzan et al., 2003). The studies found no evidence of increased risk for mortality, intracerebral hemorrhage (ICH), or reduced functional recovery with a variety of acute response arrangements in a US series of 273 consecutive stroke patients treated with thrombolytics. These patients were treated by 95 emergency physicians from 4 hospitals without an acute fibrinolytic stroke team over a 9-year period (Meurer et al., 2010). One third of the cases were treated without a neurological consultation, with a telephone consultation only, or with an in-person consultation, respectively. An ongoing National Institutes of Health-supported study is expected to accrue >500 intravenous rt-PA-treated patients in a

randomly selected cohort of 24 Michigan hospitals and will provide a comprehensive assessment of the safety of intravenous rt-PA use in the community ED setting (Scott et al., 2010). Thus, current data support multiple approaches to obtaining specialist consultation when needed in the setting of acute stroke. These range from using committed local physicians to using telephones and telemedicine (integrated audio and visual remote assessment) to access local or regional specialists or activating an acute stroke team. Development of local stroke processes to maximize available local and regional resources and to clearly identify access to neurological expertise optimizes opportunities for acute treatment.

#### **v) Year experience of triage Nurse**

Nurses play a pivotal role in all phases of care of the stroke patient: (1) The emergency or hyperacute care phase (Bader & Palmer, 2006) which includes the pre-hospital setting and the emergency department (ED), and (2) the acute care phase, which includes critical care units, intermediate care units, stroke units, and general medical units. Stroke is a complex disease that requires the efforts and skills of all members of the multidisciplinary team. Nurses are often responsible for the coordination of care throughout the continuum (Jahnke et al., 2003; Birbeck et al., 2006). Coordinated care of the acute ischemic stroke patient's results improved outcomes, decreased lengths of stay, and decreased costs (Alberts et al., 2000).

Triage nurses are often the first clinicians in the emergency department that play a vital role to assess and recognize patients who present with acute stroke symptoms and timely activation of rapid acute stroke protocols. Among stroke patients who presented within two hours, 94% were identified as stroke at triage and 71% were allocated an urgent triage category. Virtually all acute stroke patients were identified at triage, however over 30% were not allocated an emergent or urgent triage category. Patients presenting with facial weakness or speech problems were more likely to be given an emergent or urgent triage category (category 1 or 2) while patients with resolving symptoms or loss of coordination were less likely to be allocated a category 1 or 2 (Mosley et al., 2013).

#### **vi) Health insurance**

The health system in Thailand, the results of the survey showed that the population receiving health insurance increased continuously from

96.0 percent in 2006 to 98.3 per cent in 2013 (The National Statistical Office, 2014). The health insurance system comprises 4 main categories in Thailand: 1) the universal coverage scheme (UC) intended for the poor and uninsured people funded by the government (74.4%); 2) the civil servants medical benefits scheme (CSMBS) for civil servants, state enterprise employees, and family members (8.6%); 3) the Social Security Scheme (SSS) / Worker men Compensation Fund (WCF) (15.4%); and 4) the private health insurance scheme for those who can pay the premiums (2%). For the private health insurance increased by 2.3 times from 2.3 per cent in 2006 to 5.3 per cent in 2013 (Bureau of Policy and Strategy MoPH, 2010; The National Statistical Office, 2014).

In urban areas, large public and private hospitals were the main curative service providers. There were a few small hospitals at sub-district level and a municipality clinic providing basic primary care to a fraction of the urban population. People living in provincial tended to prefer private clinics, drug stores and practitioners of complementary medicine, and this pattern has not changed drastically after the introduction of the UC scheme (Pannarunothai & Mills, 1997; Limwattananon, Tangcharoensathien, Tisayaticom, Boonyapaisarncharoen & Prakongsai, 2012).

**2) Financing characteristics** are described by an array of contextual measures that suggest resources potentially available to pay for health services, including per capita community income, and wealth. Other financial characteristics are incentives to purchase or provide services, such as rate of health insurance coverage, relative price of medical care and services, and method of compensating providers. Also included here are per capita expenditures for health services.

Thailand is an upper middle income country with a gross national income (GNI) of USD 4,440 in 2011 (USD 2,460 in 2004) (World Bank, 2013). It has undergone significant economic and health transitions and gradually changed from a traditional agricultural base to that of a flourishing industrialized system.

**3) Organization at the contextual level** includes the amount and distribution of health services facilities and personnel as well as how they are

structured to offer services. Structure includes supply of services in the community, such as the ratios of physicians and hospital beds to population. Structure also includes how medical care is organized in a particular institution or delivery system where people receive care, as with office hours and location of service, provider mix, utilization and quality control oversight, and outreach and education programs.

- **Mode of transportation**

Mode of transportation influences to hospital arrival time of the acute stroke patients (Bray, 2011). It found that mode in transporting the patients to the hospital by Emergency medical services (EMS) spends time less than others ( $B = -0.385$ ;  $p = 0.002$ ) (Maestroni et al., 2008). Meanwhile, transporting the patients by a private car or public transportation causes the delay of hospital arrival (Hong, Kim, Kim, Ahn, & Hong, 2011; Iosif, Papathanasiou, Staboulis, & Gouliamos, 2012).

Prospective study in a Brazilian population found that 29 (17.6%) arrived by EMS and 136 (82.4%) arrived by their own means. The patients who arrived by EMS had a higher median NIHSS score (12 [3-18] vs 1 [0-4];  $P < .01$ ), greater frequency of atrial fibrillation (37.9% vs 7.4%;  $P < .01$ ), higher frequency of the Alberta Stroke Program Early CT Score (ASPECTS) method  $\leq 7$  (11.1% vs 1.0%;  $P < .01$ ), a trend toward lower door-to-CT time (38 minutes [24-59 minutes] vs 46.5 minutes [27-97 minutes];  $P = .10$ ), and a trend toward a higher frequency of treatment with thrombolysis (13% vs 5%;  $P = .10$ ) (Kuster et al., 2012).

Although use of ambulance service is the fastest transportation, rate of using this service is different in each area depending on medical advancements in each area, local values, and personal knowledge and beliefs. Approximately 65% of patients with signs or symptoms of stroke access their initial medical evaluation via local EMS in the United States (Rossnagel et al., 2004). Western and European countries mostly chose EMS in transporting the patients to the hospital (Gargano et al., 2011; Tong et al., 2012). In Japan, more than 70% of the patients used EMS vehicles (Inatomi, Yonehara, Hashimoto, Hirano, & Uchino, 2008) and other countries, such as South Korea, the rates are approximately 36% (Kim et al., 2011), and 30% in China (Chen et al., 2007). On the contrary, EMS in India was used only 12% and most of the patients came to the hospital by private cars that spending time less than other modes ( $p = 0.006$ ) (Pandian et al., 2006). In Thailand, the patients with acute stroke come to

the hospital by public transportation highly 55%, but the patients who use ambulance service have only 14.17% (Pinyosree, 2008).

### 2.6.1.3 Need

Environment of characteristics include health related measures of the physical environment, among them the quality of housing, water, and air (for example, residing in a county that met national ambient air quality standards throughout the year). Other measures suggesting how healthy the environment might be are illness or death rate.

Thailand is a country located in South-east Asia with an approximate current population of 67 million people. The total area of the country covers around 514,000 square kilometers. Thailand's tropical climate is generally hot and humid from March to November and very mild during the cooler seasons. The Thai Ministry of Public Health has divided Thailand into 13 geographical areas. Each area covers a population of approximately 5 million with about 5,000 hospital beds.

The distance travelled by the patients to hospital was categorized as 10 km or less and more than 10 km. This distance was arbitrarily considered because people living within a 10-km radius from the hospital, logically, would be able to arrive within the 3-hour window period. Moreover, this distance also approximately coincided with the border between urban and rural areas (Pandian et al., 2006).

- **Population health indices** are more general indicators of community health that may or may not be associated with the physical environment. These indices include general and condition-specific rates of mortality (for example, infant mortality; age-adjusted mortality; and mortality rates for heart disease, cancer, stroke, HIV); morbidity (incidence of preventable childhood communicable diseases and AIDS, and prevalence of cancer, hypertension, and untreated dental caries); and disability (disability days due to acute conditions and limitation of activity due to chronic conditions).

The arrows in Figure 2 leading from the contextual characteristics indicate that they can influence health behaviors and outcomes in multiple ways. They can work through individual characteristics, as when increased generosity of a state

Medicaid program leads to previously uninsured low-income children being covered by health insurance and subsequent increase in their use of health services. Contextual characteristics can also influence health behaviors and outcomes directly, over and above their influence through individual characteristics, as when presence of community health clinics in a metropolitan statistical area leads to increased use of primary care services by low-income persons independent of personal income or other individual characteristics. Understanding the nature of contextual influences on access to care presents many analytic challenges, but it may permit important new insights into how to improve access to care.

## 2.6.2 Individual Characteristics

### 2.6.2.1 Predisposing

1) **Demographic factors** such as age and gender of the individual represent biological imperatives suggesting the likelihood that people will need health services.

- **Age:** The demographic characteristics of patient with acute ischemic stroke presented that ischemic is mostly a disease of the elderly. The overall average age of stroke onset in United Kingdom, Newzeland, US, and Chiana were 73.6 , 73, 72.1, and 70.2 years, respectively (Morikawa et al., 2000; Bejotet al., 2008; Jianget al., 2006).According to the Thai Stroke Registry, the mean age of patients at the onset of ischemic stroke in Thailand is approximately 65 years (Nilanont et al., 2014). This age is similar to findings from previous reports from developing countries.

The acute ischemic stroke patients are elderly patients whose decision-making ability is deteriorated (Isella et al., 2008). Furthermore, an increase in age is negatively related to short-term member which is important for development of a complete perception process( $r = -0.33$ ;  $p < 0.05$ ) (Ganzer, Insel, & Ritter, 2012). Kim et al. (2011) have reported that older patients had longer hospital arrival time than younger patients (OR 1.06, 95% CI: 1.024 - 1.089;  $p < 0.01$ ). Chang, Tseng, and Tan (2004) also found that patients who were younger than 65 years of age had longer hospital arrival time than those who were 65 years old or older ( $p = 0.05$ ). In contrast, contradictory findings have been reported by a number of studies. For instance, Chen et al. (2007) investigated delay in hospital arrival time of 129 acute ischemic stroke

patients and factors associated with such a delay in both the pre-hospital care phase and the hospital care phase. They found that acute stroke patients who were younger than 65 years old had longer hospital arrival times than those who were equal to or older than 65 years old (OR 4.31, 95% CI: 1.26 - 16.8;  $p = 0.0253$ ). This is because most of them thought that the symptoms may disappear on their own and chose to take the medication instead of going to the hospital. When they saw that the symptoms did not improve, they then went to the hospital. Such findings yielded support to the findings of Jin et al. (2012) who found that patients who were younger than 65 years of age had longer hospital arrival time than those who were 65 years old and older ( $p = 0.01$ ). In Thailand, the relationship between age and hospital arrival time has been explored in patients with acute stroke and patients with ischemic stroke, but such a relationship has not been identified (Pinyosree, 2008; Klungman & Sangsuwan, 2012).

- **Gender:** Stroke is more prevalent in male than female (Addo et al., 2012; Iosif et al., 2012; Jin et al., 2012). Overall, men also have higher age-specific stroke incidence rates than women. Exceptions are in 35 to 44 year-olds and in those over 85 years of age in whom women have slightly greater age-specific incidence than men. Circumstances such as oral contraceptive use and pregnancy uniquely contribute to the risk of stroke in women.

A review of literature has revealed that gender is related to hospital arrival time. According to previous studies, females have later hospital arrival time than males (Gargano et al., 2009; Tong et al., 2012). Mandelzweig et al. (2006) found that female patients were three times more likely to have late hospital arrival time than males. Likewise, Smith et al. (2010) conducted a study with 1,134 ischemic stroke patients in the United States and found that more male patients arrived at the hospital within three hours than female patients (OR= 0.7, 95% CI: 0.5 - 0.9;  $p = 0.0103$ ). However, an inconsistent finding was reported by Derex, Adeleine, Nighoghossian, Honnorat, & Trouillas (2002) who carried out a study with 166 acute stroke patients in France and found that the male gender was a factor that could predict delay in hospital arrival time in admission into the stroke unit ( $B = -0.075$ ,  $SE = 0.036$ ;  $p = 0.05$ ).

**2) Social factors** determine the status of a person in the community as well as his or her ability to cope with presenting problems and

command resources to deal with those problems. Traditional measures include an individual's education, occupation, and ethnicity. Expanded measures might include people's social network and social interactions that can facilitate or impede access to services.

- **Educational:** There is a positive relationship between educational background and ability to memorize stroke symptoms ( $r = 0.36$ ;  $p < 0.01$ ) (Ganzer et al., 2012). If patients are highly educated, they have means to seek timely medical help after stroke onset. A study conducted by Iosif et al. (2012) indicated that patients who were highly educated, particularly those with a college degree, had the shortest hospital arrival time after stroke onset (OR= 2.8540, 95% CI: 1.8452 - 4.4142;  $p < 0.0001$ ), while those who had only basic compulsory education had the longest hospital arrival time (OR= 0.3643, 95% CI: 0.2692 - 0.4930;  $p < 0.0001$ ). A consistent finding was reported by Chen et al. (2007) who found that uneducated patients were 16.25 times more likely to arrive at hospital later than those who were educated ( $p = 0.0141$ ). However, in Thailand, the relationship between educational background and hospital arrival time has not yet been documented (Klungman & Sangsuwan, 2012).

- **Knowledge of stroke:** The chain of events favoring good functional outcome from an acute ischemic stroke begins with the recognition of stroke when it occurs. Data show that the public's knowledge of stroke warning signs remains poor (Jurkowski, Maniccia, Dennison, Samuels, & Spicer, 2008). Fewer than half of 9-1-1 calls for stroke events were made within 1 hour of symptom onset, and fewer than half of those callers thought stroke was the cause of their symptoms (Mosley, Nicol, Donnan, Patrick, & Dewey, 2007). Many studies have demonstrated that intense and ongoing public education about the signs and symptoms of stroke improves stroke recognition (Chiti, Fanucchi, Sonnoli, Barni, & Orlandi, 2007). The California Acute Stroke Pilot Registry (CASPR) reported that the expected overall rate of thrombolysis treatment within 3 hours could be increased from 4.3% to 28.6% if all patients arrived early after onset, which indicates a need to conduct campaigns that educate patients to seek treatment sooner (California Acute Stroke Pilot Registry (CASPR) Investigators, 2005).

However, factors of socioeconomic status, occupation, and rights to medical reimbursements were not found to be related to hospital arrival time

in this group of patients (Ellis et al., 2012; Gargano, Wehner, & Reeves, 2011; Jin et al., 2012; Memis et al., 2008).

**3) Health beliefs** are attitudes, values, and knowledge people have about health and health services that can influence their subsequent perception of need and use of health services.

When individuals develop symptoms of stroke, their perception varies depending on their knowledge, attitude, and belief. Some patients believe that the symptoms they have are normal symptoms that may result from stiff tendon or Karma, and others may realize that they have abnormal symptoms but they do not know what they are. For these reasons, they may delay seeking for medical help (Chuenjairuang & Srithanyarat, 2012).

#### **2.6.2.2 Enabling**

**1) Financing of health services** for the individual involves the income and wealth available to the individual to pay for services. Financing also includes the effective price of health care to the patient, determined by having insurance and cost-sharing requirements.

For all Thai citizens, treatment costs (70,000 baths) can be reimbursed from the Universal Coverage Program provided by the National Health Security Office. Other costs involving patients and relatives were direct nonmedical costs and indirect costs. Direct nonmedical costs included cost of living during the stroke episode such as transport and food costs. Indirect costs included opportunity costs such as loss of income of patients and relatives for the whole illness episode (Khiaocharoen et al., 2012).

- **Income:** A study was carried out to explore perceived income in 50 first responders to symptoms, which could be patients or bystanders. It was found that those with comfortable income took a longer time to make decision to send the patients to the hospital when compared to those with sufficient and insufficient income. This may have been because they wanted to observe the symptoms until they were sure or wanted to make telephone calls to consult a doctor or healthcare workers before going to the hospital (Maze & Bakas, 2004).

However, the rights to medical reimbursements were not found to be related to hospital arrival time in this group of patients (Ellis et al., 2012; Gargano et al., 2011; Jin et al., 2012; Memis et al., 2008).

**2) Organization of health services for the individual** describes whether or not the individual has a regular source of care and the nature of that source (private doctor, community clinic, and emergency room). It also includes means of transportation and reported travel time to and waiting time for care.

The first patient ever treated with intravenous thrombolysis was in 1996 and later on, the stroke fast track program was developed. In Thailand, since 2008, the Stroke Fast Track System has been developed to enable stroke patients to allow medical triage personnel at the hospital to identify patients with stroke early on in order to take proactive measures for prompt investigation and management with the stroke team. The system is supported by the National Health Security Office in three main areas including development of hospitals' potential, development of service provision systems of hospitals and networks, and development of access to healthcare provision of patients. At present, the fast track system has been adopted by many other university hospitals as well as regional, provincial, and some community hospitals. Intravenous thrombolysis with recombinant tissue plasminogen activator is now the standard treatment for patients with acute ischemic stroke and is recommended by the Thai Stroke Guidelines. For this reason, these patients have more access to treatment and the duration of treatment with administration of anticoagulants has been reduced (Tiamkao et al., 2012).

Stroke committee has been set which included stroke neurologist, neurosurgeon, rehabilitation doctor, radiologist, stroke nurse (case manager), nurses from each internal medicine ward, observe ward and emergency department, physical therapist, nutritionist, social worker and laboratory personnel (Dharmasaroja, 2008). Currently, Thailand has about 300 active neurologists. However, more than two-thirds of this specialized group resides in the greater Bangkok metropolitan area and other neighboring provinces.

### 2.6.2.3 Need

**1) Perceived need** is how people view their own general health and functional state. Also included here is how they experience and emotionally

respond to symptoms of illness, pain, and worry about their health condition. Perceptions about the importance and magnitude of a health problem or symptom lead to a decision to seek medical care (or not to do so).

Stroke patients reported presence of one or more of the following symptoms as follow: talking (44%), moving (40%), other (40%), facial (22%), breathing (9%), and behavior (7%). Other symptoms involved: weakness, seizure, paralysis, off balance, passing out, falling, numbness, nauseous, dizziness, blurred vision, and so forth. Symptoms were reported as occurring all of a sudden 62%-85% of the time, depending on the symptom. Most of the time (72%) patients (rather than someone with them) were the first to notice the symptoms (Maleket al., 2014).

The study was conducted in French, stroke symptoms were recognized by the patient in 43% of cases and by bystanders in 44%. Ninety-three percent of the patients considered stroke a medical emergency. Fifty-eight percent of the patients could identify a single sign or symptom of stroke. Nine percent of the patients had a prior stroke, and 15% had a prior TIA. Univariate analysis of this study showed that the recognition of symptoms by bystanders significantly shortened the admission delay (Derex et al., 2002). Conversely, in the studies conducted in the UK, recognition of symptoms as stroke did not reduce delay or increase the proportion of patients who attended an emergency department (Lasserson, Chandratheva, Giles, Mant, & Rothwell, 2008). Despite the results of previous studies that showed that early arrival is not associated with patients' knowledge about stroke, it is still believed that awareness of stroke as a severe symptom may lead to shorter delay times and increased thrombolysis rates (Barr, McKinley, O'Brien, & Herkes, 2006). In Korea study, stroke awareness and knowledge about thrombolysis were independently associated with lower pre-hospital delay. Interestingly, awareness of the patient/bystander that the initial symptom was stroke-related was the factor most strongly associated with early arrival (Kim et al., 2011).

- **Patient and bystander recognize symptoms of stroke**

Early recognition and rapid response to the symptoms of stroke by patients and bystander are important dimensions of improving access to rt-PA and improving outcome following stroke. National Institute of Clinical Excellence

recommends thrombolysis as an effective treatment for acute ischemic stroke. When given to carefully selected patients within three hours of the onset of symptoms intravenous rt-PA reduces the risk of death or dependency (odds ratio 0.64, 95% confidence intervals 0.5-0.83) (Wardlaw et al., 2009). The study in UK reported that only 41% of the patients correctly assessed their symptoms to be stroke; 44% perceived their symptoms to be mild; and 59% would wait to see whether their symptoms would improve spontaneously. About 61% of the patients and 80% of the bystanders worried about troubling other people with their problem. The bystander was a relative in 68% of cases. Of the bystanders, 65% correctly assessed the symptoms as stroke; only 42% perceived the patient's symptoms as severe. About 25% of the bystanders took a passive approach and would wait and see whether symptoms improved spontaneously; 93% did not find it difficult to ask for assistance (Shah, Makinde & Thomas, 2007).

**2) Evaluated need** represents professional judgment and objective measurement about a patient's physical status and need for medical care (blood pressure, temperature, respiratory rate, pulse, or blood examination, as well as diagnoses and prognoses for particular conditions the patient experiences). Of course, evaluated need is not simply, or even primarily, a valid and reliable measure from biological science. It also has a social component and varies with the changing state of the art and science of medicine, clinical guidelines and protocols, and prevailing practice patterns, as well as the training and competency of the professional expert doing the assessment.

- **Admission Blood Pressure**

High blood pressure levels are commonly observed during the first 24-48 hour after an ischemic stroke (Aslanyan et al., 2003; Semplicini et al., 2003; Castillo et al., 2004). The International Stroke Trial (IST, 1997) and the Chinese Acute Stroke Trial (CAST, 1997) reported, respectively, 82% and 75% of patients having systolic blood pressure (SBP) levels > 140 mmHg within the first 48 hours following the acute stroke. These trials identified also that 28% and 25% of patients had markedly raised SBP levels > 180 mmHg.

Observational data suggest that elevated BP levels in the acute stroke period are associated with poor prognosis, in terms of mortality and disability

(Jorgensen et al., 1995; Paradiso, Ohkubo, & Robinson, 1997; Castillo et al., 2004; Lawes, Bennett, Feigin, & Rodgers, 2004; Willmot, Leonardi-Bee, & Bath, 2004). Poor outcome has been found to be related both to low (Allen, 1984; Osaki et al., 1998) and high BP levels in the acute stroke period (Robinson et al., 1997; Ahmed and Wahlgren, 2000; Castillo et al., 2004). In contrast, other studies have found no relationship between BP levels and prognosis (Carlberg et al., 1993).

- **Severity of stroke**

Severity of stroke depends on the location and size of the blocked, clogged, or ruptured arteries. Like symptoms of patients, levels of severity of stroke are associated with hospital arrival time. A study conducted by Faiz, Sundseth, Thommessen, & Ronning (2013) assessed the levels of severity of stroke using the National Institute of Health Stroke Scale (NIHSS) and found that higher NIHSS scores or more severe stroke resulted in shorter hospital arrival time than lower NIHSS scores or less severe stroke (OR=0.92, 95% CI: 0.88 - 0.97,  $p < 0.001$ ). Likewise, Inatomi et al. (2008) found that patients with higher NIHSS scores had shorter hospital arrival time than those with lower NIHSS scores (OR=0.98, 95% CI: 0.95 - 1.01,  $p < 0.05$ ). Furthermore, Derex et al. (2002) have reported that levels of severity of stroke were associated with hospital arrival time of patients ( $\rho = -0.261$ ;  $p = 0.001$ ). In Italy, a similar finding was reported by Maestroni et al. (2008) that NIHSS scores of acute stroke patients could be used to predict hospital arrival time ( $B = -0.031$ ,  $p = 0.003$ ).

The NIHSS score at admission was strongly associated with outcomes of acute hospitalization after multivariate adjustment. The odds ratio (OR) for moderate (versus mild) stroke patients to achieve excellent status was 0.04 (95% CI: 0.02–0.10), and for severe stroke the OR was less than 0.01 (95% CI: 0–0.05). The odds ratio for moderate stroke patients had good or improved outcome reached by 0.19 (95% CI, 0.10–0.36), for severe stroke 0.04 (95% CI: 0.01–0.13). The ORs for moderate and severe versus mild) stroke patients to have better subsequent change in neurologic impairments were 5.18 (1.94–13.85) and 4.12 (1.38–12.30); to remain stationary 0.43 (0.19–0.96) and 0.15 (0.06–0.36), respectively (Tseng & Chang, 2006).

### 2.6.3 Health Behaviors

**2.6.3.1 Personal health practices** are behaviors on the part of the individual that influence health status. They include diet and nutrition, exercise, stress reduction, alcohol and tobacco use, self-care, and adherence to medical regimens.

- **Smoking**

Cigarette smoking is a well-established risk factor for initial and recurrent stroke. Weng, et al. (2011) found that smoking was associated with higher scores on the National Institutes of Health Stroke Scale for smoking patients with small-vessel occlusions than non smoking patients. However, it was associated with a lower NIHSS score in the cardioembolic stroke (Weng et al., 2011). Similar, cohort study reported long-time smoking was associated with an increased risk of poor functional outcome at discharge, in ischemic stroke patients, associated with an increase of mortality risk at 1 year and associated with an increased LOS in hospital (Edjoc et al., 2013).

**2.6.3.2 The process of medical care** is the behavior of providers interacting with patients in the process of care delivery. General process measures might relate to patient counseling and education, test ordering, prescribing patterns, and quality of provider-patient communication. Process measures might also describe the specifics of caregiving for particular conditions, such as whether a provider check plasma glucose in a person with diabetes or reviews the patient's record of home blood pressure monitoring in a hypertension.

**2.6.3.3 Use of personal health services** is the essential component of health behaviors in a comprehensive model of access to care. The purpose of the original behavioral model was to predict health services use, measured rather broadly as units of physician ambulatory care, and hospital inpatient services. They hypothesized that predisposing, enabling, and need factors would have differential ability to explain use depending on what type of service was examined. Hospital services used in response to more serious problems and conditions would be primarily explained by need and demographic characteristics.

## 2.6.4 Outcomes

**2.6.4.1 Perceived health status** is one kind of result or outcome of health behavior. This depends on many factors in addition to use of personal health services, including all of the contextual factors as well as an individual's demographic and social characteristics, health beliefs, and personal health practices. Perceived health status indicates the extent to which a person can live a functional, comfortable, and pain-free existence. *Measures* include reports of general perceived health status, activities of daily living, and disability.

**2.6.4.2 Evaluated health status** is dependent on the judgment of the professional, on the basis of established clinical standards and state-of-the-art practices. Measures include tests of patient physiology and function as well as diagnosis and prognosis regarding their condition. Outcome measures of perceived and evaluated health may appear suspiciously like perceived and evaluated need measures. Indeed, they are. The ultimate outcome validation of improved access is to reduce individual needs previously measured and evaluated.

**2.6.4.3 Consumer satisfaction** is how individuals feel about the health care they receive. It can be judged by patient ratings of waiting time, travel time, communication with providers, and technical care received.

This framework focuses on contextual, the circumstances and environment of health care access and individual determinants of access to medical care. The model suggests that the major components of contextual characteristics are divided in the same way as individual characteristics determining access: (1) existing conditions that predispose people to use or not use services even though these conditions are not directly responsible for use, (2) enabling conditions that facilitate and impede use of services, and (3) need or conditions that laypeople or health providers recognize as requiring medical treatment (Andersen & Davidson, 2007).

The researcher consider that the framework in line with the nature of the service system for the patients with acute ischemic stroke, that need to maintain the speedy and effective services, especially when the gold results of health service is receive treatment in target time and successful stroke recovery. Concept of health service access from Anderson's views is consistent with the health system for the patients with acute ischemic stroke. It contains the relation of four major components,

a system of health service effect on characteristics of the patients who access to health services lead to the healthcare utilization behavior that result in the health outcomes. In the system of health services held by the development of the Stroke Center policy, which in this project the provincial hospital has the potential to treat acute ischemic stroke patients with thrombolytic therapy, so it must prepare the element of health service to have enough resources to organize service in the particular environment. The organizing system of stroke health service must be early performed and compliance with the standard practice guidelines for the patients with acute ischemic stroke in both pre-hospital and emergency department management. It is required to maintain the external environment that support the performance of service including the crowding level of emergency department, while the distance between health service and location where patients experience symptom must be consider in the remote service.

The characteristics of patients who access to the health services are a feature of pathological conditions, social, and environment that affect patients' access to health service. For the patient with acute ischemic stroke, the decision to seek treatment is an important characteristic because the symptoms occurred immediately if the patient and witness are fast decision making they would transport to receive the treatment timely. Moreover, the severity of illness is the major factor of the treatment needs and the successful of stroke recovery.

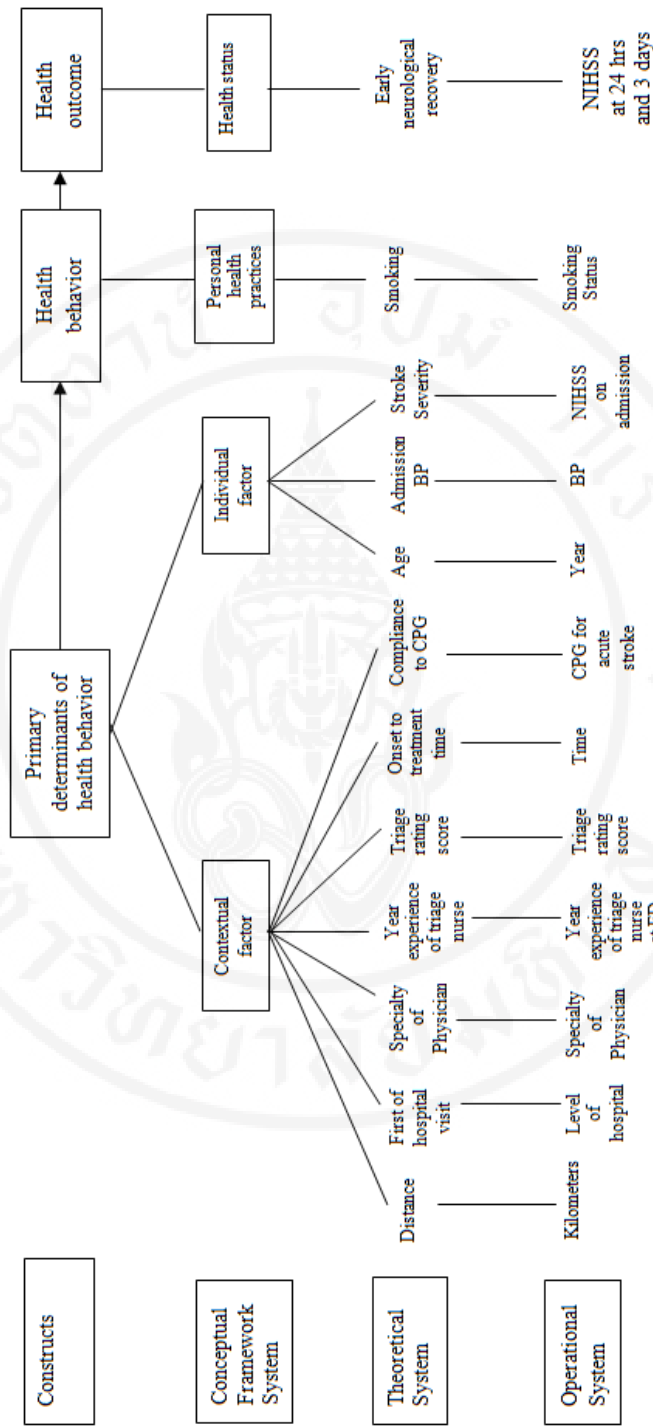


Figure 2.4 Theoretical substruction

## **CHAPTER III**

### **METHODOLOGY**

This study was to explore the factors influencing early neurological recovery in patients with acute ischemic stroke. The factors in this study are from the contextual characteristics, individual characteristics, and health behavior. This chapter provided a description of the research methodology used in this study including research design, population and sample size, sampling method, instrumentation, and data collection, protection of human participants, data management and analysis.

#### **3.1 Research Design**

A cross-sectional descriptive correlation design was used to examine the effect of factors on early neurological recovery in patients with acute ischemic stroke including the contextual characteristics, individual characteristics, and health behavior. The data was obtained from interview and observational questionnaires completed by the acute ischemic stroke patients or witnesses and by the researcher.

1.1 Contextual characteristic was including seven independent variables: distance from place of symptom attack to the hospital, level of first hospital visit, specialty of physician, triage nurse, onset-to-rt-PA time, triage rating score, and compliance to clinical practice guideline.

1.2 Individual characteristic was including three independent variables: age, admission blood pressure, and stroke severity.

1.3 The health behavior was including one independent variable: smoking status.

### 3.2 Population and Sample

The population in this study was acute ischemic stroke patients being admitted into hospitals which able to provide thrombolytic drug in patient with acute ischemic stroke.

The inclusion criteria for eligible patients are the following characteristics:

- 1) Being age greater than 18 years old
- 2) Being diagnosed by the doctor or the neurologist as first-ever acute ischemic stroke

The exclusion criteria are the patients who:

- 1) received other diagnosis after confirming by CT scan or MRI such as of head injuries, tumors, and central nervous system infections
- 2) had underlying psychotic disorders and mental disorders

### 3.3 Sample size

The sample size was estimated through several methods based on power analysis or parameters. The logistic regression requires a large sample size same as the other statistics.

The formula by Cohen (1988) was used determine sample size given an effect size index, which he call L. For this study, the sample size was calculated as a function of relevant effect size in regression analysis. The effect size in regression analysis was indicated by the  $R^2$  and L. L was defined by Cohen as a function of power and number of independent variables at a given level of alpha. Conventionally, in a power analysis, the value of alpha was set 0.05. Using Cohen's advocated 0.80 as the level of power, Cohen defines as a small effect as an  $R^2$  of 0.02, a moderate effect as an  $R^2$  of 0.13, and a large effect as an  $R^2$  of 0.30. Cohen & Cohen (1983) provided a formula for determining sample size as follows:

$$N = \frac{L(1-R^2) + K+1}{R^2}$$

n = total sample size

L = effect size index

K = number of independent variables

This study selected a power of 0.80; an alpha of 0.05; of 11 independent variables (distance from place of symptom attack to the hospital, level of first hospital visit, specialty of physician, year experience of triage nurse, onset-to-rt-PA time, triage rating score, compliance to clinical practice guideline, age, admission blood pressure, stroke severity, and smoking status). The value of L was 18.2 (Cohen, 1988, p.453) to determine appropriate sample size. A moderate effect size was recommended for the study of alpha of 0.05 (Polit & Beck, 2006, p.483) and for a descriptive study (Thato, 2008, p.43). The calculation was as follows.

$$n = \frac{18.2(1 - 0.13) + 411 + 1}{0.13}$$
$$= 214.107 \text{ or } 214 \text{ persons}$$

Therefore, the sample size of this study was 214. Additionally, approximately 5% of the total number of samples was needed as over-estimation to account for incomplete questionnaires, which was equal to 11 cases. Therefore, about 225 acute ischemic stroke patients were estimated for the sample size of this study. However, during the process of collecting data, there were five of them were excluded with the reasons of discharge before 3 days. Therefore, two hundred and twenty ischemic stroke patients were qualified in the study.

### 3.4 Settings

The samples in this study were the acute ischemic stroke patients who admitted in the hospital located in southern region of Thailand. These hospitals have a capacity for providing care for acute ischemic stroke patients. The certified hospitals for acute stroke care management in this study have to be able to approach acute stroke management with the following criteria that can be the guarantee of acute stroke care qualification including 1) able to provide acute stroke care with stroke fast track approach 2) have a CT 3) have the physician to provide thrombolytic drug in patient with acute ischemic stroke.

### 3.5 Sampling Procedure

**3.5.1 Hospital Sampling:** The hospitals are simple random sampling by selected four provinces from Health Service Area 11 and 12 in southern region of Thailand and then select all hospitals in the selected provinces that able to provide thrombolytic drug in patient with acute ischemic stroke. There are total 14 provinces in southern region following the Royal Institute. It consists of 6 tertiary hospitals and 16 general hospitals (the Royal Institute, 2014).

#### 3.5.2 Patient Sampling:

The participants who meet the inclusion criteria are conveniently recruited in each setting. The number of participants in each hospital is various depending on the number of patient's admission in each hospital during the time of data collection until reaching the goal of 220 cases.

**Table 3.1** Random sampling of hospital setting

Region of Thailand	Health Service Area	Provinces	Hospital	n
southern region of Thailand	Health Service Area 11	Province 1	Hospital 1	29
			Hospital 2	28
			Hospital 3	28
			Hospital 4	28
		Province 2	Hospital 1	28
	Health Service Area 12	Province 1	Hospital 1	28
			Hospital 2	28
Province 2		Hospital 1	28	
<b>Total</b>	2 health service areas	4 provinces	8 hospitals	n=225

### 3.6 Research instruments

The instruments in this study included: 1) the Patient's Personal information questionnaire, 2) Clinical characteristics questionnaire, 3) Time form record, 4) The National Institutes of Health Stroke Scale (NIHSS), 5) Clinical practice guideline for patients with acute ischemic stroke and details of each instrument were described as below.

#### 1. The Patient's Personal Information Questionnaire

The personal data questionnaire is developed by the researcher was divided into three parts as follows.

**Part 1** Demographic characteristics questionnaire include age, gender, education level, occupation, income, income sufficiency, welfare, mode of transportation, first hospital admission and distance from the hospital.

**Part 2** Clinical characteristics questionnaire include chief complain, presenting clinical symptoms in emergency department, vital sign, stroke subtype diagnosis, CT/ MRI and the results of lesion site, co-morbid diseases, and complication

**Part 3** Time form record include onset time of symptom, time to register in emergency department, time to start triage by nurse, time to finish triage, time to start assessment by physician, time to lab, time to CT, time to neurologist assessment, time to rt-PA treatment or start treatment and discharge time from emergency department.

**Part 4** The National Institutes of Health Stroke Scale (NIHSS), this instrument measure stroke severity on admission and measure early neurological recovery at 24 hours and day 3 after treatment.

The NIHSS consists of 11 items that assess the severity of impairments (loss of consciousness, ability to respond to questions and to obey simple commands, deviation of gaze, hemianopsia, facial palsy, limb movements of paretic limb, limb ataxia, sensory loss, neglect, dysarthria, and aphasia). Each item is rated on a 3-4 point ordinal scale, with lower scores reflecting less impairment. The total score ranges from 0 (no deficit) to 42 (significant deficit). It has validity and reliability at the excellent level and easy to administration by 5-10 minutes (Barak & Duncan, 2006).

The early neurological recovery was measure neurological improvement at 24 hours after admission. The total score was interpreted early neurological recovery as a NIHSS score of 0 to 3 or a decrease of  $\geq 4$  points in the NIHSS score (Felberg et al., 2002; Mazighi et al., 2012).

Validity: the National Institutes of Health Stroke Scale (NIHSS) is a standard instrument that is recommended by the National Institute of Neurological Disorders and Stroke for using stroke assessment and measurement. The NIHSS is currently used to determine treatment options, anticipate discharge planning, and measure patient outcomes (Adams et al., 1999; Schlegel et al., 2003; Weimar, Konig, Kraywinkel, Ziegler, & Diener, 2004 ).

The content validity index (CVI) was used to quantify the extent of agreement between the experts. This interrater agreement will be perfect if the value of CVI of 1.00 is outlined (Waltz, Strickland, & Lenz, 2005). Polit and Beck (2008) recommended the value of CVI to determine an excellent content validity as at .78 or higher. The content validity of studied instruments was calculated from the proportion of rating by three experts. The results were quite or very relevant (4). The CVI value of the National Institutes of Health Stroke Scale (NIHSS) was 1.0. The CVI of these instruments were at acceptable level.

The stroke rating scales each predicted 3-month outcome with an accuracy of 0.79 or greater. The NIHSS provided the most prognostic information: sensitivity to poor outcome, 0.71 (95% confidence interval [CI], .64 to .79); specificity, 0.90 (95% CI, .86 to .94); and overall accuracy, 0.83 (95% CI, .79 to .87). One measure of validity of the NIHSS scale is its correlation with infarct volumes (concurrent validity). This measure has been reported in several studies, using both CT and MRI, yielding correlation coefficients of 0.4-0.8, which suggests a high degree of validity (Schiemanck, Post, Witkamp, Kappelle, & Prevo, 2005). The clinical predictive validity of the NIHSS has been shown in several investigations (Adams et al., 1999; Lyden et al., 2001; Schlegel et al., 2004). In a post-hoc analysis by stroke subtype of 1,268 patients enrolled in an acute stroke trial, baseline NIHSS scores strongly predicted outcome at 7 days and at 3 months. An excellent outcome was achieved by almost two-thirds of patients with a score of three or less at day 7; however, very few

patients with baseline scores of more than 15 had excellent outcomes after 3 months (Adams et al., 1999).

#### **Part 5 Clinical Practice Guideline for acute ischemic stroke,**

The measurement of compliance to Clinical Practice Guideline (CPG) for acute ischemic stroke was developed by the researcher based on the related literature which contained 12 items for onset time < 4.5 hr and 9 items for onset time 4.5-72 hr. It comes from the obligate procedures provided in timeline of the standard stroke CPG of collaboration of Prasat Neurological Institute and other educational institutes (2005) that is congruent with the Helsingborg Declaration 2006 on Stroke Strategies (World Health Organization, 2006) and the Canadian Best Practice (2006). It is based on the good practice indicators for ischemic stroke by Toward Clinical Excellence' Network of Thailand (2005). The items include care in stroke unit, computed tomography scan (CT scan) or magnetic resonance imaging (MRI), blood sugar examination, diagnosis, early antiplatelet therapy (ASA), control blood pressure, control blood pressure, oxygen supplement, early stroke rehabilitation, and swallowing test within 24 hr. or before giving any food. If the stroke service follows each item, it means one point score. In contrast, if the service does not follow the item, the score of zero will obtain.

The total score ranges from 0 to 12 for onset time < 4.5 hr. and 0 to 9 for onset time 4.5-72 hr. The higher score of received care service indicate the higher quality of access of acute stroke care. The total score was divided into 2 levels. The score of 0-9 for onset time < 4.5 hr. and 0-6 for onset time 4.5-72 hr. indicate not compliance to CPG. The score of 10-12 for onset time < 4.5 hr. and 7-9 for onset time 4.5-72 hr. indicate compliance to CPG.

#### **Reliability test**

Although the NIHSS indicate that do not special training requirement for using, the training is need to improve the reliability of data collection. The training process of interpret the NIHSS criteria as described below.

1. Enhance the skill of the NIHSS interpretation with the neurologist instructor or qualifiedly trained nurses in stroke unit. Then the researcher has successfully completed NIHSS certificate from National Stroke Association.

2. Test interrater of measurement reliability by comparing with a neurologist or medical physician in assessing 20 stroke patients of pilot study group who have the same characteristics as the eligible samples. The neurologist or medical physician employs the NIHSS to assess the early neurological recovery with their interpretation in those patients. Then the researcher's self-assessment and interpretation compared with the result from the neurologist, medical physician, or qualifiedly trained nurses in stroke unit. The Kappa statistics was employed to evaluate the interrater reliability. The Kappa coefficient of the NIHSS was at 0.87. The results of interrater reliability were at the accepted level of 0.80 and the best of 0.90 or higher (Burns & Grove, 2005).

### **3.7 Data Collection**

In data collection, the researcher will begin to collect data after receiving permission from Mahidol University Institution Review Board. The processes of data collecting are:

1. The permission letter was send to the director of the hospitals and the director of nursing for data collection in emergency department, stroke unit, medical ward and intensive care unit.
2. The researcher approached head nurse of emergency department, stroke unit, medical ward and intensive care unit, and inform about the objective of study and details of the data collection.
3. Prepare the research assistants (RA) who provided stroke nursing care in each setting before the data collection procedure. This study requires experience of the RA including 1) have experience in emergency department or stroke unit or medical ward more ten years 2) can correctly assess the NIHSS score.

The RA responsible for three procedures as follow

Firstly, assess the NIHSS score at admission before acute ischemic patients receive treatment.

Secondly, record real time to treatment in emergency department that the researcher cannot approach in real time.

Thirdly, contact the researcher when the acute ischemic stroke patients admitted in their hospital.

Therefore, the nurses who volunteers to be RA were trained for clearly understanding the study and the data collection procedure.

4. Participants were recruited from the stroke patients who had been admitted to the selected hospitals during the data collection period. The researcher informed the potential participants or their families in case that the potential participants were unable to communicate by themselves, and then asked for participation in the research. Formal written consent form was subsequently processed.

5. The participants or their families or witnesses who took the participants to the hospital were asked to complete demographic data and some clinical data of presenting clinical symptoms, activities done after symptom onset, time of stroke onset, and transportation to the hospital that were not available in the patient files.

6. The researcher or research assistants measure the NIHSS on admission for assessing stroke severity which is categorized as mild (0-6), moderate (7-15), or severe ( $\geq 16$ ). In addition, the NIHSS is performed at 24 hour and day 3 after treatment to assess the early neurological recovery in stroke's patients by researcher or research assistants.

7. The researcher completed the items of personal information questionnaire by deriving the data from patients' files and professionals who provided care for each patient.

### **3.8 Protection of human rights:**

Approval for human participant protection was sought and obtained from committees for the protection of human participants, including the Committee on Human Rights Related to Human Experimentation at Mahidol University and the Ethic Committee of the selected hospitals. The written permission to collect data from the setting was obtained before data collections begin. All participants were informed and consented to participate in this study. The findings were also guaranteed confidentiality and an anonymous presentation. The participants have the opportunity to ask questions if they have any doubts, and they will be ensured that they have right to agree to

participate in the study and to withdraw their participation any time if they wish. Also, they will be ensured that their withdrawal from participant will not affect the treatment they received at the hospital in any way. The patients who had progressive stroke or complications that needed advance treatment to rescue were terminated from the sample.

### **3.9 Data Analysis**

Data are doubly entered into the Statistical Package of the Social Sciences for Personal Computer (SPSS/PC+) and analyze as follow:

1. The demographic characteristics of the samples and the variables of the study were analyzed by using frequency, percentage, means, and standard deviations.
2. Multivariate logistic regression analysis used to predictability among early neurological recovery in patients with acute ischemic stroke and independent variables that are distance from place of symptom attack to the hospital, level of first hospital register, specialty of physician, triage nurse, triage rating score, onset-to-rt-PA time, age, admission BP, admission stroke severity, and smoking. The statistically significant prediction of the early neurological recovery will be at interval 95%.

## **CHAPTER IV**

### **RESULTS**

The main purpose of this study of this cross-sectional study was to explore factors influencing early neurological recovery in patients with acute ischemic stroke. The results of this study were presented in four sections. The first section demonstrated the background of the sample and descriptive statistics of the sample. The second section displayed the descriptive analysis of study variables. Then, the assumption testing was displayed. Lastly, the results of the research hypotheses testing were also explained.

#### **4.1 Characteristics of patients with acute ischemic stroke**

There were 8 hospitals randomly recruited into the study. Two hundred and twenty ischemic stroke patients, ranging 26-28 per hospital, were recruited. The gender proportion of participants was male more than female (55.9% and 44.1% respectively) (Table 4.1).

**Table 4.1** Ischemic stroke patients participating from each of 8 hospitals

Hospital ID	Total		Male		Female	
	Number	Percent <sup>1</sup>	Number	Percent <sup>2</sup>	Number	Percent <sup>2</sup>
1	28	12.7	9	32.1	19	67.9
2	28	12.7	14	50.0	14	50.0
3	28	12.7	14	50.0	14	50.0
4	28	12.7	17	60.7	11	29.3
5	28	12.7	16	57.1	12	42.9
6	27	12.3	20	74.1	7	25.9
7	27	12.3	14	51.9	13	48.1
8	26	11.8	19	73.1	7	26.9
<b>Total Participants</b>	<b>220</b>	<b>100.0</b>	<b>123</b>	<b>55.9</b>	<b>97</b>	<b>44.1</b>

<sup>1</sup> Percent from total of 220 participants

<sup>2</sup>Percent of each gender within hospital

#### 4.1.1 General Characteristics of Patients

Patient characteristics are shown in table 4.2. Patients had a mean of age 64.35 (SD 14.08) years (range, 20 to 98 years). The majority (55.9%) was male and was married (75.0%) and had a primary school level education (71.4%). The occupations were farmer or gardener (38.6%), housework (28.6%), Employee (17.3%) and Merchant (9.1%). Half of the participants had income 5,000-15,000 Bath per month (49.5%) and most (76.8%) used Universal Coverage as their health care service payment.

**Table 4.2** General characteristics of acute ischemic stroke patients

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Gender</b>						
Male	123	55.9	18	62.1	105	55.0
Female	97	44.1	19	37.9	86	45.0
<b>Age (Year)</b>						
≤ 30	1	.50	-	-	1	0.5
31-40	7	3.2	2	6.9	5	2.6
41-50	34	15.5	7	24.1	27	14.1
51-60	48	21.8	6	20.7	42	22.0
61-70	49	22.3	4	13.8	45	23.6
71-80	54	24.5	9	31.0	45	23.6
≥ 81	27	12.3	1	3.4	26	13.6
Mean ±SD, Range	64.35 ±14.08	20 - 98	60.41 ±14.16	32-83	64.95 ±14.0	20 - 98
<b>Marital status</b>						
Single	14	6.4	4	13.8	10	5.2
Married	165	75.0	22	75.9	143	74.9
Widowed/Divorced/ Separated	41	18.6	3	10.3	38	19.9
<b>Level of education</b>						
None	15	6.8	2	6.9	13	6.8
Primary school	157	71.4	17	58.6	140	73.3
Secondary school	29	13.2	5	17.2	24	12.6
Diploma	7	3.2	2	6.9	5	2.6
Bachelor & Higher degree	12	5.5	3	10.3	9	4.7

**Table 4.2** General characteristics of acute ischemic stroke patients (cont.)

Characteristics	Total		Receiving rt-PA		Non receiving rt-PA	
	(N=220)		(N=29)		(N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Monthly Income</b>						
<b>(bath)</b>						
<5,000	87	39.5	9	31.1	78	40.8
5,000-15,000	109	49.5	13	44.8	96	50.3
15,001-30,000	21	9.5	6	20.7	16	7.9
>30,000	3	1.4	1	3.4	2	1.0
<b>Occupation</b>						
Farmer/Gardener	85	38.6	11	37.9	74	38.7
Housework	63	28.6	9	31.0	54	28.3
Employee	38	13.7	6	20.7	32	16.8
Merchant	20	9.1	-	-	20	10.5
Government officer	8	3.6	3	10.3	5	2.6
Business	3	1.4	-	-	3	1.6
Others	3	1.4	-	-	3	1.5
<b>Health Service</b>						
<b>Payment</b>						
Universal coverage	169	76.8	22	75.9	147	77.0
Government welfare	37	16.8	3	10.3	34	17.8
Social security insurance	14	6.4	4	13.8	10	5.2

#### 4.1.2 Clinical Characteristics of Patients

Clinical characteristics of participants are shown in table 4.3. Most of the patients (99.5%) were diagnosed ischemic stroke at emergency room. More than half were non smokers and one-third of them were current smokers (32.7%). The participants had underlying disease, i.e. Hypertension (73.2%), Dyslipidemia (36.4%), Diabetes Mellitus (26.8%) and TIA (12.7%). Most of patient (56.8%) in this study had systolic blood pressure between 141 and 180 mmHg. (mean 166.6, SD 27.98).

**Table 4.3** Clinical characteristics of acute ischemic stroke patients

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Diagnosed at emergency room</b>						
Ischemic stroke	219	99.5	29	100.0	190	99.5
TIA	1	0.5	-	-	1	0.5
<b>Smoking status</b>						
Non smokers	119	54.1	11	37.9	108	56.5
Ex-smokers	29	13.2	5	17.2	24	12.6
Current smokers	72	32.7	13	44.8	59	30.9
<b>Underlying disease</b>						
Yes	173	78.6	22	75.2	151	79.1
No	5	2.3	2	6.9	3	1.6
Never check up	42	19.1	5	17.2	37	19.4

**Table 4.3** Clinical characteristics of acute ischemic stroke patients (cont.)

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Underlying disease (each item n=220)</b>						
Hypertension	161	73.2	19	65.5	142	74.3
Dyslipidemia	80	36.4	13	44.8	67	35.1
Diabetes Mellitus	59	26.8	3	10.3	56	29.3
TIA	27	12.7	2	6.9	25	13.1
CAD	7	3.2	-	-	7	3.7
Atrial Fibrillation	6	2.7	1	3.4	5	2.6
<b>Systolic blood Pressure on admission at rt-PA hospital</b>						
SBP ≤ 140 mmHg.	34	15.5	7	24.1	27	14.1
SBP 141-180 mmHg.	125	56.8	18	62.1	107	56.0
SBP 181-220 mmHg.	54	24.5	2	6.9	52	27.2
SBP > 220 mmHg.	7	3.2	2	6.9	5	2.6
Mean ± SD, Range (minutes)	166.6 ± 27.98	92-240	155.2 ± 30.85	92-229	168.3 ±27.19	104-240
<b>Admission stroke severity</b>						
Mild (NIHSS = 0-6)	114	51.8	5	17.2	109	57.1
Moderate (NIHSS = 7-15)	85	38.6	17	58.6	68	35.6
Severe (NIHSS = ≥ 16)	21	9.5	7	24.1	14	7.3

The situations of symptom onset revealed by this study are illustrated in Table 4.4. The participants had symptoms occurring at scene including weakness of limb (94.5%), abnormal speech (73.2%), weakness of facial muscle (29.2%), loss of balance/dizziness (26.4%) and abnormal vision (1.4%). Seventy-five percent of participants decided access to the hospital by weakness of limb. The witness was family member (82.2%) while five percent (5%) were alone when symptom occurred. Most patients (36.8%) had symptom onset during 6:01-12:00 am.

**Table 4.4** Symptom onset situation

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Symptom occurring at home</b>						
- Weakness of limb	208 (n=220)	94.5	29 (n=29)	100.0	178 (n=191)	93.2
- Abnormal speech	161 (n=220)	73.2	22 (n=29)	75.9	139 (n=191)	72.8
- Weakness of facial muscles	65 (n=220)	29.5	11 (n=29)	37.9	56 (n=191)	29.3
- Loss of balance/ dizziness	58 (n=220)	26.4	9 (n=29)	31.0	49 (n=191)	25.7
- Abnormal vision	3 (n=220)	1.4	-	-	3 (n=191)	1.6

**Table 4.4** Symptom onset situation (cont.)

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Major symptom</b>						
<b>determined to hospital</b>						
- Weakness of limb	165	75.0	22	75.9	142	74.3
- Abnormal speech	31	14.1	5	17.2	26	13.6
- Loss of balance/ dizziness	16	7.3	1	3.4	16	8.4
- Weakness of facial muscles	5	2.3	-	-	5	2.6
- Abnormal vision	2	0.9	-	-	2	1.0
- Alteration of consciousness	1	0.5	1	3.4	-	-
<b>Witness</b>						
None	11	5.0	-	-	11	5.8
Family member	194	88.2	25	86.2	169	88.5
Colleague	9	4.1	3	10.3	6	3.1
Neighbor	4	1.8	-	-	4	2.1
Other (Nurse)	2	1.0	1	3.4	1	0.5
<b>Time of symptom onset</b>						
0:01 – 6:00 am	47	21.4	6	20.7	41	21.5
6:01 – 12:00 am	81	36.8	9	31.0	72	37.7
12:01 – 6:00 pm	58	26.4	8	27.6	50	26.2
6:01 – 12:00pm	34	15.5	6	20.7	28	14.7

Transportation and Health service access of acute ischemic stroke patients are shown in Table 4.5. The mean of distance from place of symptom onset to the hospital that can provide rt-PA was 24.58 (SD 22.03) kilometers (range 0-130 kilometers) and nearly half of all patients (42.7%) had the distance 10 kilometers from hospital. Most of patients (96.8%) went to hospital by Self-transportation. Only 0.9% of participants used emergency medical service. In two-third of participants (65.4%) went to the hospital with could perform intravenous rt-PA treatment consist of General hospital (44.5%) and Excellent hospital (20.9%), while nearly thirty five percents (34.5%) went to health care service with could not perform intravenous rt-PA including Community hospital (28.6%), Primary care unit (3.2%) and Private clinic (2.7%). The mean time of onset time to hospital was 477.55 minutes (SD 620.17) with a range of 1 - 3,470 minutes. Interestingly, approximate 41% access to hospital within 3 hours. For referring time, the mean time of referral system was 107.47 minutes (SD 91.55) with a range of 25-555 minutes. Only 32.1% of participants had been referred within 60 minutes recommended guideline of referral system.

**Table 4.5** Transportation and Health service access of acute ischemic stroke patients

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Distance from place of symptom onset to the hospital (able to provide rt-PA treatment)</b>						
≤ 10 kilometers	94	42.7	11	37.9	83	43.5
11-25 kilometers	46	20.9	7	24.1	39	20.4
26-50 kilometers	55	25.0	9	31.0	46	24.1
51-80 kilometers	20	9.1	2	6.9	18	9.4
> 80 kilometers	5	2.3	-	-	5	2.6
Mean±SD, Range (kilometers)	24.58± 22.03	0-130	23.66± 19.92	0-78	24.72±2 2.38	1-130

**Table 4.5** Transportation and Health service access of acute ischemic stroke patients (cont.)

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
	<b>Transportation to first hospital</b>					
- Self-transportation	203	96.8	28	96.6	185	97.0
- Volunteer car service	2	0.9	-	-	2	1.0
- Local government emergency service	2	0.9	-	-	2	1.0
- Emergency medical service (1669)	2	0.9	-	-	2	1.0
- Other (symptom occurred during admission)	1	0.5	1	3.4	-	-
<b>First hospital visit</b>						
Private hospital/ clinic	6	2.7	-	-	6	3.1
Primary care unit	7	3.2	-	-	7	3.7
Community hospital	63	28.6	12	41.4	51	26.7
General hospital	98	44.5	10	34.5	88	46.1
Excellent hospital	46	20.9	7	24.1	39	20.4

**Table 4.5** Transportation and Health service access of acute ischemic stroke patients (cont.)

Characteristics	Total		Receiving rt-PA		Non receiving rt-PA	
	(N=220)		(N=29)		(N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Onset time to rt-PA hospital</b>						
< 180 minute	92	41.8	29	100.0	63	33.0
- Direct to rt-PA hospital	53	57.60	17	58.62	36	57.14
- Refer from other hospital	39	42.40	12	41.38	27	42.86
181-270 minute	27	12.3	-	-	27	14.1
- Direct to rt-PA hospital	19	70.37			19	70.37
- Refer from other hospital	8	29.63			8	29.63
>270 minute	101	45.9	-	-	101	52.9
- Direct to rt-PA hospital	69	68.32			69	68.32
- Refer from other hospital	32	32.68			32	32.68
Mean±SD, Range	477.5± 620.17	1 - 3,470	107± 56.07	1-180	534± 686.81	20 - 3,470
<b>Refer time between first hospital and rt-PA hospital</b>						
0-60 minute	25	32.1	6	50.0	19	28.8
> 60 minute	53	67.9	6	50.0	47	71.2
Mean±SD, Range	107.5± 91.55	25-555	85.67± 42.82	35-150	106.4± 86.15	25-555

In-hospital services of acute ischemic stroke patients are shown in Table 4.6. On triage levels of acute ischemic stroke patients presented at the emergency department in this study were emergency, urgency, semi-urgency, non-urgency, and critical (70.5%, 24.5%, 2.5%, 1.8% and 0.9%), respectively. Approximately forty five percents of participant (45.5%) were assigned to stroke fast track system where as more than a half (54.5%) were not assigned because they went to hospital with delay time > 4.5 hours. In this study, Intravenous rt-PA therapy was performed in 29 cases (13.18%). The mean onset to needle (rt-PA) time was 185.83 minutes (SD 46.51), ranging 62-240 minutes. Only 2 participants received intravenous rt-PA within 90 minutes. Most of patients (68.7%) were compliance to clinical practice guideline for acute ischemic stroke including complied to CPG for arrival time to hospital > 4.5 hours (51.4%) and 17.31% complied to CPG for arrival time to hospital  $\leq$  4.5 hours.

For overall triage nurse experience, the averages years of emergency nursing experience was 7.1 (SD 5.50), ranging from 1 to 30 years. A half of triage nurses (49.1%) had experience of emergency care less than five years. For characteristics of physician who treated acute ischemic stroke patients were internal medicine 68.2%, neurologist 22.7%, general physician 8.2%, and emergency physician 0.9%.

**Table 4.6** In-hospital care service of acute ischemic stroke patients

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Allocated to Stroke</b>						
<b>Fast track</b>						
Yes	100	45.5	29	100.0	70	36.6
No	120	54.4	-	-	121	63.4
<b>Emergency triage level</b>						
Critical	2	0.9	1	3.4	1	0.5
Emergency	155	70.5	28	96.6	127	66.5
Urgency	54	24.5	-	-	54	28.3
Semi-urgency	5	1.8	-	-	5	2.6
Non-urgency	4	0.9	-	-	4	2.1
<b>Door to physician first seen</b>						
≤ 10 minutes	78	35.5	19	65.5	59	30.9
11-20 minutes	90	40.9	7	24.1	83	43.5
21-30 minutes	26	11.8	2	6.9	24	12.6
> 30 minutes	26	11.8	1	3.4	25	13.1
Mean±SD, Range	17.58± 12.02	4-70	12.10± 7.41	4-33	18.41± 12.38	4-70

**Table 4.6** In-hospital care service of acute ischemic stroke patients (cont.)

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Time from completed triage to physician first seen</b>						
≤ 5 minutes	74	33.6	19	65.5	55	28.8
6-10 minutes	64	29.1	7	24.1	57	29.8
11-15 minutes	42	19.1	2	6.9	40	20.9
16-20 minutes	12	5.5	1	3.4	11	5.8
21-25 minutes	8	3.6	-	-	8	4.2
26-30 minutes	5	2.3	-	-	5	2.6
> 30 minutes	16	6.8	-	-	15	7.9
Mean±SD, Range	11.47± 9.85	2-58	5.76± 3.77	2-18	12.34± 10.20	2-58
<b>Door to CT interpretation</b>						
≤ 45 minutes	91	41.4	16	55.2	75	
45-60 minutes	55	25.0	7	24.1	48	
> 60 minutes	74	33.6	6	20.7	68	
Mean±SD, Range						
<b>Onset to needle (rt-PA) time (n=29)</b>						
0-90 min			2	6.9		
91-180 min			8	27.6		
181-270 min			19	65.5		
Mean±SD, Range			185.83 ±46.51	62-240		

**Table 4.6** In-hospital care service of acute ischemic stroke patients (Cont.)

Characteristics	Total (N=220)		Receiving rt-PA (N=29)		Non receiving rt-PA (N=191)	
	Number	Percent	Number	Percent	Number	Percent
<b>Compliance to CPG of stroke care</b>						
- Compliance to CPG for arrival time to hospital ≤4.5 hours	69	17.3	10	34.5	50	26.2
- Compliance to CPG for arrival time to hospital >4.5 hours	113	51.4	19	65.5	113	59.2
- Non Compliance to CPG	38	31.4	-	-	28	14.7
<b>Years of triage nurse experience</b>						
≤ 2 years	19	8.8	2	6.9	17	8.9
3-5 years	91	41.4	7	24.1	84	44.0
6-10 years	85	38.6	14	48.8	71	37.2
11-20 years	16	7.3	4	13.8	12	6.3
> 20 years	9	4.1	2	6.9	7	3.7
Mean±SD, Range	7.10± 5.50	1-30	8.62± 6.37	2-29	6.83± 5.35	1-30
<b>Physician who treated stroke patients emergency department</b>						
Neurologist	50	22.7	16	55.2	34	17.8
Internal Medicine	150	68.2	13	44.8	137	71.1
Emergency Physician	2	0.9	-	-	2	1.0
General Physician	18	8.2	-	-	18	9.4

The result demonstrated the baseline characteristics differences in patients with non receiving rt-PA therapy (Table 4.7). A total of 191 who had recovery group had younger than the non recovery group ( $61.06 \pm 13.55$  versus  $67.94 \pm 13.67$ ,  $p = .001$ ) and had mean score of NIHSS less than non recovery group ( $4.83 \pm 4.88$  versus  $8.66 \pm 4.42$ ,  $p = .000$ ). The 2 groups did not differ between male and female (recovery group, 44:39; non recovery group, 61:47,  $P = .635$ ). Similarly, all risk factors including hypertension, diabetes, dyslipemia, and smoking are no difference ( $P = .368$ ,  $.457$ ,  $.567$  and  $.855$ , respectively). For Onset-to-door time, there are no significant differences between the recovery group and the non recovery group ( $583.05 \pm 645.79$  versus  $495.91 \pm 648.57$ ,  $P = .358$ )

**Table 4.7** Baseline characteristics differences between the early neurological recovery and non early neurological recovery in non receiving rt-PA therapy Groups

Characteristics	Early neurological recovery		p-value
	Yes (n=83)	No(n=108)	
Gender (male : female)	44:39	61:47	.635
Age (mean $\pm$ SD)	$61.06 \pm 13.55$	$67.94 \pm 13.67$	.001
Risk factors			
Hypertension	59 (71.08)	83(76.85)	.368
Diabetes	22 (26.50)	34 (31.48)	.457
Dyslipemia	31 (37.35)	36 (33.33)	.567
Smoking	38 (45.78)	48 (44.44)	.855
Initial NIHSS score (mean $\pm$ SD)	$4.83 \pm 4.88$	$8.66 \pm 4.42$	.000
Onset-to-door time	$583.05 \pm 645.79$	$495.91 \pm 648.57$	.358

The change of NIHSS at 24 hours, the difference between NIHSS on admission and NIHSS at 24 hours, varied among groups. All participants (n=220) showed both improved and worsened NIHSS, most of participants (49.1%) improved 1-3 points. On participants who received rt-PA treatment (n=29) showed only improved NIHSS, most of participants (51.7%) improved NIHSS 4-7 points. For participants who non received rt-PA treatment (n=191) showed improved NIHSS 1-3 points (55%), improved NIHSS 4-7 points (6.3%), improved NIHSS >8 points (2.1%), NIHSS non change 31.4%, worsened NIHSS 1-3 points (2.1%), worsened NIHSS 4-7 points (2.7%), and worsened NIHSS >8 points (0.5%).

The change of NIHSS at 3 days, the difference between NIHSS on admission and NIHSS at 3 days, demonstrated the improvement 1-3 points (57.3%) of all participants. On participants who received rt-PA treatment (n=29) showed only improved NIHSS, most of participants (48.3%) improved NIHSS > 8 points. For participants who non received rt-PA treatment (n=191) showed improved NIHSS 1-3 points (64.9%), improved NIHSS 4-7 points (15.2%), improved NIHSS >8 points (4.7%), NIHSS non change (10.5%), worsened NIHSS 1-3 points (1.6%), worsened NIHSS 4-7 points (2.6%), and worsened NIHSS >8 points (0.5%).

**Table 4.8** The change of NIHSS at 24 hours and 3 days after admission

NIHSS	24 hours after admission		3 day after admission	
	Number	Percent	Number	Percent
<b>All participants (n=220)</b>				
- NIHSS improved $\geq$ 8 points	15	6.8	23	10.5
- NIHSS improved 4-7 points	27	12.3	42	19.1
- NIHSS improved 1-3 points	108	49.1	126	57.3
- NIHSS non change	60	27.3	20	9.1
- NIHSS worsened 1-3 points	4	1.8	3	1.4
- NIHSS worsened 4-7 points	5	2.3	5	2.3
- NIHSS worsened $\geq$ 8 points	1	0.5	1	0.5
<b>Participants who received rt-PA treatment (n=29)</b>				
- NIHSS improved $\geq$ 8 points	11	37.9	14	48.3
- NIHSS improved 4-7 points	15	51.7	13	44.8
- NIHSS improved 1-3 points	3	10.3	2	6.9
<b>Participants who non received rt-PA treatment (n=191)</b>				
- NIHSS improved $\geq$ 8 points	4	2.1	9	4.7
- NIHSS improved 4-7 points	12	6.3	29	15.2
- NIHSS improved 1-3 points	105	55.0	124	64.9
- NIHSS non change	60	31.4	20	10.5
- NIHSS worsened 1-3 points	4	2.1	3	1.6
- NIHSS worsened 4-7 points	5	2.7	5	2.6
- NIHSS worsened $\geq$ 8 points	1	0.5	1	0.5

## 4.2 Characteristic of participants who non received rt-PA treatment and change of NIHSS

Characteristics of acute ischemic stroke patients with non receiving rt-PA are shown in table 4.9. The characteristics of stroke patients who change the NIHSS by improved 1-3 points were male 57.1%, range of 61-80 years 48.6%, HT 77.1%, mild stroke 58.1%, distance from rtPA hospital  $\leq$  10 kilometers 39% and onset time to rtPA hospital  $>$  270 minutes 42.2%.

**Table 4.9** Characteristic of participants who non received rt-PA treatment and change of NIHSS at 24 hours (n=191)

Characteristic	NIHSS non change (n=60)		NIHSS improved 1-3 points(n=105)		NIHSS improved 4-7 points(n=12)		NIHSS improved $\geq$ 8 points(n=4)	
	N	Percent	N	Percent	N	Percent	N	Percent
	<b>Gender</b>							
Male	29	48.3	60	57.1	8	66.7	1	25.0
Female	31	51.7	45	42.9	4	33.3	3	75.0
<b>Age (years)</b>								
< 30	1	1.7						
31-40	2	3.3	3	2.9	-	-	-	-
41-50	6	10.0	17	16.2	1	8.3	-	-
51-60	14	23.3	20	19.0	4	33.3	-	-
61-70	16	26.7	24	22.9	3	25.0	2	50.0
71-80	12	20.0	27	25.7	4	33.3	-	-
$\geq$ 81	9	15.0	14	13.3	-	-	2	50.0
<b>Underlying disease</b>								
Hypertension	41	68.3	81	77.1	11	91.7	3	75.0
Dyslipidemia	20	33.3	37	35.2	6	50.0	3	75.0
DM	15	25.0	32	30.5	6	50.0	2	50.0
TIA	7	11.7	11	10.47	2	16.7	1	25.0
CAD	1	1.7	5	4.8	-	-	-	-

**Table 4.9** Characteristic of participants who non received rt-PA treatment and change NIHSS (n=191) (cont.)

Characteristic	NIHSS non change (n=60)		NIHSS improved 1-3 points (n=105)		NIHSS improved 4-7 points (n=12)		NIHSS improved ≥8 points (n=4)	
	N	Percent	N	Percent	N	Percent	N	Percent
	<b>Admission stroke severity</b>							
Mild (NIHSS = 0-6)	36	60.0	61	58.1	6	50.0	-	-
Moderate (NIHSS = 7-15)	21	35.5	37	35.2	6	50.0	-	-
Severe (NIHSS = ≥ 16)	3	5.0	7	6.7	-	-	4	100.0
<b>Distance from place of symptom onset to the rt-PA hospital</b>								
≤ 10 kilometers	30	50.0	41	39.0	7	58.3	3	75.0
11-25 kilometers	7	11.7	26	24.8	4	33.3	1	25.0
26-50 kilometers	14	23.3	24	22.9	1	8.3	-	-
51-80 kilometers	6	10.0	12	11.4	-	-	-	-
> 80 kilometers	3	5.0	2	1.9	-	-	-	-
Mean±SD, Range (km.)								
<b>Onset time to rt-PA hospital</b>								
≤180 min	14	23.3	37	35.2	5	41.7	2	50.0
181-270 min	8	13.3	16	15.2	7	58.3	1	25.0
>270 min	38	63.3	52	49.2	-	-	1	25.0

### 4.3 Simple Logistic Regression Analysis

For interpretation of the influencing factors, multivariate Logistic regression was used to answer the predictive factors influencing early neurological recovery in patients with acute ischemic stroke at 24 hours and day 3 after admission. The eleven theoretical related factors composed of the distance from place of symptom attack to the hospital, the level of first hospital registers, specialty of physician, triage nurse, triage rating score, onset-to-rt-PA time, compliance to clinical practice guideline, age, admission blood pressure, admission stroke severity, and smoking.

Simple logistic regression analysis was first investigated variable for its associations with neurological recovery as well as each outcome of interest. For screening steps, variables whose respective associations had p-value  $\leq 0.15$  were considered for potential factors. The results revealed that four variables had p-value  $< 0.15$  including admission stroke severity (p-value = .000), onset-to-rt-PA time (p-value = .003), age, (p-value = .005), and specialty of physician (p-value = .069) (Table 4.10) and then analyze by multiple logistic regression analysis.

Therefore, four variables, admission stroke severity, onset-to-rt-PA time, age, and specialty of physician, had potential to predict early neurological recovery outcome.

**Table 4.10** Simple Logistic Regression Analysis

Variable	$\beta$	Wald	OR	95%CI	P-value
<b>Stroke severity</b>					
Stroke severity(mild) ( <i>ref</i> )					
Stroke severity(moderate)	-1.685	28.648	.185	.100-.344	.000
Stroke severity(severe)	-1.179	5.755	.308	.117-.806	.016
<b>Onset-to-rtPA time</b>					
No received rt-PA ( <i>ref</i> )					
Onset time to rt-PA (within 3 hours)	1.650	4.210	5.205	1.077-25.160	.040
Onset time to rt-PA (3.0-4.5 hours)	1.937	8.997	6.940	1.957-24.610	.003

**Table 4.10** Simple Logistic Regression Analysis (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<b>Age</b>					
< 60 years ( <i>ref</i> )					
60-80 years	-.792	7.221	.453	.254-.807	.007
>80 years	-1.549	9.990	.213	.081-.555	.005
<b>Specialty of Physician</b>					
Non neurologist ( <i>ref</i> )					
Neurologist	.594	3.298	1.812	.954-3.440	.069
<b>Compliance CPG</b>					
Non compliance to CPG( <i>ref</i> )					
Compliance to CPG1	.507	1.552	1.660	.748-3.684	.213
Compliance to CPG2	-.303	.662	.738	.356-1.533	.416
<b>Triage nurse experience</b>					
< 5years ( <i>ref</i> )					
5-10 years	.263	.833	1.301	.739-2.292	.361
>10 years	-.093	.043	.911	.380-2.188	.836
<b>First hospital visit</b>					
Not able rt-PA treatment( <i>ref</i> )					
Able rt-PA treatment	-.164	.333	.849	.487-1.480	.564
<b>Smoking status</b>					
Smoking ( <i>ref</i> )					
Non smoking	-.211	.606	.810	.476	1.377
<b>Triage rating score</b>					
Non emergency ( <i>ref</i> )					
Emergency	.017	.003	1.017	.562-1.841	.956
<b>Admission SBP</b>					
<180 mmHg. ( <i>ref</i> )					
180-220 mmHg.	-.211	.443	.810	.436-1.506	.506
>220 mmHg.	.300	.148	1.350	.293-6.229	.700

**Table 4.10** Simple Logistic Regression Analysis (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<b>Distance from hospital</b>					
< 30 km. ( <i>ref</i> )					
31-50 km.	-.079	.055	.924	.476-1.791	.814
>50 km.	-21.191	.000	.000	.000	.999

#### 4.4 Multiple Logistic Regression Analysis

A binary logistic regression was applied to determine the power of prediction. The early neurological recovery of 24 hours and 3 days were regressed. The four variables, admission stroke severity, onset-to-rt-PA time, age, and specialty of physician, had potential to analyze by multiple logistic regression analysis. Those entered one, two, three and four factors into the model respectively. The findings were displayed in Table 4.11 to Table 4.32.

##### 4.4.1 Multiple logistic regression analysis of related factors associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients

###### 4.3.1.1 M<sub>1</sub> model

This model showed one factor influences the neurological recovery at 24 hours after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR=.308, 95%CI: .117-.806,  $p < .05$  and OR=.185, 95%CI: .100-.344,  $p < .001$ , respectively), compared with mild stroke severity.

The log likelihood ratio was 272.289 (Chi-square 32.532,  $df = 2$ ,  $p = .000$ ). Overall prediction rate was 68.6%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\chi^2 = .000$   $p = 1.000$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .183 or 18.3% of the variance. The detail of binary logistic regression is presented in table 4.11.

**Table 4.11** Logistic regression of one factor associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	.693	12.171	2.000		
Stroke severity(mild)					
Stroke severity(moderate)	-1.179	5.755	.308	.117-.806	.016
Stroke severity(severe)	-1.685	28.648	.185	.100-.344	.000
Method = Enter					
Model Chi-square 32.532 (df = 2, sig = .000, p <.05)					
Hosmer and Lemeshow goodness of fit test .000 (df = 0, sig = 1.000, p >.05)					
-2 Log likelihood = 272.289, AIC= 274.289					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .183					
Overall rate of correct classification = 68.6%					

#### 4.3.1.2 M<sub>2</sub> model

This model showed two factors influences the neurological recovery at 24 hours after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR=.106, 95%CI: .030-.375, p<.001 and OR=.087, 95%CI: .041-.188, p<.01, respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=21.175, 95%CI: 6.481-103.746, P<.001 and OR=14.288, 95%CI: 3.233-97.795, P<.01, respectively), compared with those who did not receive rt-PA treatment.

The log likelihood ratio was 233.828 (Chi-square 37.624, df = 4, p = .000). Overall prediction rate was 75.9%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 2.302$ , p = .319) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .368 or 36.8% of the variance. The detail of binary logistic regression is presented in table 4.12.

**Table 4.12** Logistic regression of two factors associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	.630	9.850	1.877		
Stroke severity(mild)					
Stroke severity (moderate)	-2.249	12.095	.106	.030-.375	.000
Stroke severity (severe)	-2.445	38.982	.087	.041-.188	.001
No received rt-PA					
Onset time to rt-PA (within 3 hours)	3.255	21.175	21.175	6.481-103.746	.000
Onset time to rt-PA (3.0-4.5 hours)	2.878	10.949	14.288	3.233-97.795	.001
Method = Enter					
Model Chi-square 70.993 (df = 4, sig = .000, p <.05)					
Hosmer and Lemeshow goodness of fit test 2.302 (df = 2, sig = .316, p >.05)					
-2 Log likelihood = 233.828, AIC=237.828					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .368					
Overall rate of correct classification = 75.9%					

#### 4.3.1.3 M<sub>3</sub> model

This model showed three factors influences the neurological recovery at 24 hours after admission. The finding revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR=.095, 95%CI: .044-.205, p<.001 and OR=.126, 95%CI: .034-.465, p<.01, respectively), compared with mild stroke severity. Onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=22.22, 95%CI: 5.454-90.527, P<.001 and OR=17.28, 95%CI: 3.079-97.001, P<.01, respectively), compared with those who did not receive rt-PA treatment. Lastly, age >80 years decreased neurological recovery at 24 hours after admission (OR=.361, 95%CI: .120-1.085 P<.05).

The log likelihood ratio was 229.163 (Chi-square 75.658, df = 6, p = .000). Overall prediction rate was 76.8%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of

observed and predicted dependence values ( $\lambda^2 = 3.415, p = .755$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .388 or 38.8% of the variance in the neurological recovery at 24 hours. The detail of binary logistic regression is presented in table 4.13.

**Table 4.13** Logistic regression of three factors associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	.992	12.697	2.696		
Stroke severity (mild)					
Stroke severity (moderate)	-2.355	35.751	.095	.044-.205	.000
Stroke severity (severe)	-2.068	9.702	.126	.034-.465	.002
No received rt-PA					
Onset time to rt-PA (within 3 hours)	3.101	18.723	22.220	5.454-90.527	.000
Onset time to rt-PA (3.0-4.5 hours)	2.850	10.483	17.282	3.079-97.001	.001
Age(<60 years)					
Age(60-80 years)	-.582	2.829	.559	.283-1.101	.093
Age(>80 years)	-1.019	3.295	.361	.120-1.085	.049
Method = Enter					
Model Chi-square 75.658 (df = 6, sig = .000, p <.05)					
Hosmer and Lemeshow goodness of fit test 3.415 (df = 6, sig = .755, p >.05)					
-2 Log likelihood = 229.163, AIC=235.163					
Nagelkerke R Square (Pseudo $R^2$ ) = .388					
Overall rate of correct classification = 76.8%					

#### 4.3.1.4 M<sub>4</sub> model

This model showed three factors influences the neurological recovery at 24 hours after admission. The finding revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR=.126, 95%CI: .035-.457, p<.01 and OR=.095, 95%CI: .044-.205, p<.001, respectively), compared with mild stroke severity. Onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=19.730, 95%CI: 4.692-82.960,

P<.001 and OR=16.383, 95%CI: 2.877-93.303, P<.01, respectively), compared with those who did not receive rt-PA treatment. Age and specialty of physician are not significant (P>.05)

The log likelihood ratio was 228.623 (Chi square = 79.918, df = 7, p <.001). Overall prediction rate was 76.8%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\chi^2 = 1.712$ , p = .974) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .390 or 39.0% of the variance in the neurological recovery at 24 hours. The detail of binary logistic regression is presented in table 4.14.

**Table 4.14** Logistic regression of four factors associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odds ratio	95%CI	P-value
(Constant)	.941	10.715	2.563		
Stroke severity (mild)					
Stroke severity (moderate)	-2.072	9.924	.126	.035-.457	.002
Stroke severity (severe)	-2.359	35.605	.095	.044-.205	.000
No received rt-PA					
Onset time to rt-PA (within 3 hours)	2.982	16.562	19.730	4.692-82.960	.000
Onset time to rtPA (3.0-4.5 hours)	2.796	9.925	16.383	2.877-93.303	.002
Age(<60 years)					
Age(60-80 years)	-.579	2.778	.560	.283-1.107	.096
Age(>80 years)	-1.008	3.281	.365	.123-1.086	.070
Non Neurologist					
Neurologist	.309	.537	1.363	.596-3.116	.464

Method = Enter

Model Chi-square = 79.918 (df = 7, sig = .000, p <.001)

Hosmer and Lemeshow goodness of fit test = 1.712 (df = 7, sig = .974, p >.05)

-2 Log likelihood = 228.623, AIC= 236.623

Nagelkerke R Square (Pseudo R<sup>2</sup>) = .390

Overall rate of correct classification = 76.8%

#### 4.3.1.5 M<sub>5</sub> model

This model aimed to evaluate interaction effect, the effect of one variable changes when another variable changes. Because there is more than one way in which can define an effect in a nonlinear model, there must also be more than one way in which can define an interaction effect. The following statements use the logistic procedure to fit a two-way logit with four factors and one interaction effect. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and one interaction effect included age\*stroke severity.

The finding revealed that moderate severity decreased the neurological recovery at 24 hours (OR=.063, 95%CI: .018-.216,  $p < .001$ ), compared with mild stroke severity. Onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=27.290, 95%CI: 3.933-189.369,  $P < .01$  and OR=24.635, 95%CI: 5.396-112.481,  $P < .001$ , respectively), compared with those who did not receive rt-PA treatment. Age  $> 80$  years decreased neurological recovery at 24 hours after admission (OR=.234, 95%CI: .057-.971,  $P < .05$ ), compared with age  $< 60$  years. Specialty of physician and age\* stroke severity are not significance ( $p > .05$ ).

The log likelihood ratio was 221.80 (Chi square = 83.021, df = 11,  $p < .001$ ). Overall prediction rate was 77.3%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was not significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 4.590$ ,  $p = .710$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .419 or 41.9% of the variance. The detail of binary logistic regression is presented in table 4.15.

**Table 4.15** Logistic regression of four factors and one interaction effect associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.045	9.975	2.845		
Stroke severity (mild)					
Stroke severity (moderate)	-2.770	19.238	.063	.018-.216	.000
Stroke severity (severe)	-2.469	3.462	.085	.006-1.141	.063
No received rt-PA					
Onset time to rt-PA (within 3 hours)	3.307	11.192	27.290	3.933-189.369	.001
Onset time to rtPA (3.0-4.5 hours)	3.204	17.102	24.635	5.396-112.481	.000
Age(<60 years)					
Age(60-80 years)	-.704	2.592	.495	.210-1.165	.107
Age(>80 years)	-1.451	4.000	.234	.057-.971	.045
Non Neurologist					
Neurologist	.290	.424	1.336	.559-3.193	.515
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	.675	.716	1.964	.411-9.381	.397
Stroke severity (moderate)					
Age(60-80yrs)*	-.691	.194	.501	.023-10.895	.660
Stroke severity (severe)					
Age(>80yrs)*	-.120	.006	.887	.046-17.025	.936
Stroke severity (moderate)					
Age(>80yrs)*	2.802	2.445	16.480	.491-552.683	.118
Stroke severity (severe)					

Method = Enter

Model Chi-square 83.021 (df = 11, sig = .000, p <.001)

Hosmer and Lemeshow goodness of fit test 4.590 (df = 7, sig = .710, p >.05)

-2 Log likelihood = 221.800

Nagelkerke R Square (Pseudo R<sup>2</sup>) = .419

Overall rate of correct classification = 77.3%

### 4.3.1.6 M<sub>6</sub> model

This model aimed to evaluate four factors and two interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and two interaction effects included age\*stroke severity and age\*onset time to rt-PA. The finding revealed that moderate severity decreased the neurological recovery at 24 hours (OR=.036, 95%CI: .007-.177, p<.001), compared with mild stroke severity. Age >80 years decreased neurological recovery at 24 hours after admission (OR=.238, 95%CI: .057-.985, P<.05), compared with age< 60 years. Onset time to rt-PA, specialty of physician, age\*stroke severity and age\*onset time to rt-PA are not significance (p>.05).

The log likelihood ratio was 210.876 (Chi square = 93.545, df =11, p <.001). Overall prediction rate was 77.7%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was not significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 2.141$ , p = .906) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .464 or 46.4% of the variance. The detail of binary logistic regression is presented in table 4.16.

**Table 4.16** Logistic regression of four factors and two interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.031	9.684	2.805		
Stroke severity (mild)					
Stroke severity (moderate)	-3.319	19.773	.036	.007-.177	.000
Stroke severity (severe)	-19.777	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.162	.000	3.745	.000	.998
Onset time to rtPA (3.0-4.5 hours)	37.585	.000	2.103	.000	.998

**Table 4.16** Logistic regression of four factors and two interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Age(<60 years)					
Age(60-80 years)	-.692	2.507	.500	.212-1.179	.113
Age(>80 years)	-1.437	3.921	.238	.057-.985	.048
Non Neurologist					
Neurologist	.341	.558	1.406	.575-3.440	.455
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.531	2.566	4.621	.710-30.066	.109
Stroke severity (moderate)					
Age(60-80yrs)*	17.455	.000	3.809	.000	.998
Stroke severity (severe)					
Age(>80yrs)*	-17.695	.000	.000	.000	.999
Stroke severity (moderate)					
Age(>80yrs)*	20.097	.000	5.348	.000	1.000
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-36.443	.000	.000	.000	.998
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-35.694	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	4.425	.000	83.500	.000	1.000
Onset time to rt-PA (within 3 hours)					
Method = Enter					
Model Chi-square 93.945 (df = 14, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 2.141 (df = 6, sig = .906, p >.05)					
-2 Log likelihood = 210.876					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .464					
Overall rate of correct classification = 77.7%					

### 4.3.1.7 M<sub>7</sub> model

This model aimed to evaluate four factors and three interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and three interaction effects included age\*stroke severity, age\*onset time to rt-PA, and age\*specialty of physician. At 24 hours after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.034, 95%CI: .007-.169, p<.001), compared with mild stroke severity. Age >80 years decreased neurological recovery (OR=.211, 95%CI: .049-.899, P<.05), compared with age< 60 years. Onset time to rt-PA, specialty of physician, age\*stroke severity, age\*onset time to rt-PA, and age\*specialty of physician are not significance (p>.05).

The log likelihood ratio was 208.734 (Chi square = 96.078, df =16, p <.001). Overall prediction rate was 77.7%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was not significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 12.903$ , p = .045) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .472 or 47.2% of the variance. The detail of binary logistic regression is presented in table 4.17.

**Table 4.17** Logistic regression of four factors and three interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.152	10.095	3.165		
Stroke severity (mild)					
Stroke severity (moderate)	-3.382	17.127	.034	.007-.169	.000
Stroke severity (severe)	-18.898	.000		.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.100	.000	.000	.000	.998
Onset time to rtPA (3.0-4.5 hours)	37.896	.000	.000	.000	.998
Age(<60 years)					
Age(60-80 years)	-.845	3.125	.430	.168-1.096	.077
Age(>80 years)	-1.558	4.426	.211	.049-.899	.035

**Table 4.17** Logistic regression of four factors and three interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Non Neurologist					
Neurologist	-.242	.109	.785	.187-3.303	.742
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.597	2.754	4.940	.749-32.589	.097
Stroke severity (moderate)					
Age(60-80yrs)*	17.567	.000	.000	.000	.998
Stroke severity (severe)					
Age(>80yrs)*	-36.050	.000	.000	.000	.998
Stroke severity (moderate)					
Age(>80yrs)*	19.611	.000	.000	.000	.998
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-36.404	.000	.000	.000	.998
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-36.094	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	22.941	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
<i>Age*Specialty of physician</i>					
Age(60-80yrs)*	.781	.696	.000	.000	.404
Neurologist					
Age(>80yrs)*	19.789	.000	.000	.000	.999
Neurologist					
Method = Enter					
Model Chi-square 96.078 (df = 16, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 12.903 (df = 6, sig = .045, p <.05)					
-2 Log likelihood = 208.734					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .472					
Overall rate of correct classification = 77.7%					

### 4.3.1.8 M<sub>8</sub> model

This model aimed to evaluate four factors and four interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and four interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, and physician\*stroke severity. At 24 hours after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.024, 95%CI: .004-.130, p<.001), compared with mild stroke severity. Age, onset time to rt-PA, specialty of physician, age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, and specialty of physician\*stroke severity are not significance (p>.05).

The log likelihood ratio was 202.478 (Chi square = 102.344, df =18, p <.001). Overall prediction rate was 77.7%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = .900$ , p = .996) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .496 or 49.6% of the variance. The detail of binary logistic regression is presented in table 4.18.

**Table 4.18** Logistic regression of four factors and four interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.212	10.927	3.359		
Stroke severity (mild)					
Stroke severity (moderate)	-3.739	18.628	.024	.004-.130	.000
Stroke severity (severe)	-20.004	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.243	.000	.000	.000	.998
Onset time to rtPA (3.0-4.5 hours)	37.152	.000	.000	.000	.998
Age(<60 years)					
Age(60-80 years)	-.698	2.063	.498	.192-1.290	.151
Age(>80 years)	-1.617	4.746	.198	.046-.850	.029

**Table 4.18** Logistic regression of four factors and four interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Non Neurologist					
Neurologist	-.489	.484	.613	.155-2.430	.486
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.551	2.490	4.716	.687-32.379	.115
Stroke severity (moderate)					
Age(60-80yrs)*	16.438	.000	.000	.000	.998
Stroke severity (severe)					
Age(>80yrs)*	-34.560	.000	.000	.000	.998
Stroke severity (moderate)					
Age(>80yrs)*	19.716	.000	.000	.000	.998
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-36.038	.000	.000	.000	.998
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-35.656	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	21.665	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
<i>Age*Specialty of physician</i>					
Age(60-80yrs)*	-.172	.033	.842	.132-5.394	.856
Neurologist					
Age(>80yrs)*	16.710	.000	.000	.000	.999
Neurologist					
<i>Specialty of physician *</i>					
<i>Stroke severity</i>					
Neurologist*	2.156	4.237	8.636	1.109-67.282	.053
Stroke severity (moderate)					
Neurologist*	3.363	3.243	28.889	.743-1123.59	.072
Stroke severity (severe)					
Method = Enter					
Model Chi-square 102.344 (df = 18, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test .900 (df = 7, sig = .996, p >.05)					
-2 Log likelihood = 202.478					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .496					
Overall rate of correct classification = 77.7%					

**4.3.1.9 M<sub>9</sub> model**

This model aimed to evaluate four factors and five interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and five interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, physician\*stroke severity, and onset time to rt-PA\*stroke severity. At 24 hours after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.027, 95%CI: .005-.144, p<.001), compared with mild stroke severity. Age >80 years decreased neurological recovery (OR=.203, 95%CI: .047-.868, P<.05), compared with age< 60 years. Onset time to rt-PA, specialty of physician, age\* stroke severity, age\*onset time to rt-PA, age\*specialty of physician, specialty of physician\*stroke severity, and onset time to rt-PA\*stroke severity are not significance (P>.05).

The log likelihood ratio was 190.447 (Chi square = 114.374, df = 22, p <.001). Overall prediction rate was 79.1%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = .748, p = .998$ ) reflecting that the full model appeared to fit the data. The Nagelkerke’s R<sup>2</sup> was shown at .541 or 54.1% of the variance. The detail of binary logistic regression is presented in table 4.19.

**Table 4.19** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.190	10.662	3.288		
Stroke severity (mild)					
Stroke severity (moderate)	-3.602	18.018	.027	.005-.144	.000
Stroke severity (severe)	-20.588	.000	.000	.000	.999
No received rt-PA					
Onset time to rt-PA (within 3 hours)	18.174	.000	.000	.000	.999
Onset time to rtPA (3.0-4.5 hours)	20.414	.000	.000	.000	.999

**Table 4.19** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Age(<60 years)					
Age(60-80 years)	-.659	1.835	.518	.200-1.342	.176
Age(>80 years)	-1.596	4.629	.203	.047-.868	.031
Non Neurologist					
Neurologist	-.402	.317	.669	.165-2.707	.573
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.129	1.275	3.092	.436-21.936	.259
Stroke severity (moderate)					
Age(60-80yrs)*	-.731	.000	.482	.000	1.000
Stroke severity (severe)					
Age(>80yrs)*	-17.509	.000	.000	.000	.999
Stroke severity (moderate)					
Age(>80yrs)*	20.301	.000	.000	.000	.999
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-37.757	.000	.000	.000	.999
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-57.205	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	-16.721	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
<i>Age*Specialty of physician</i>					
Age(60-80yrs)*	.090	.008	1.094	.162-7.389	.927
Neurologist					
Age(>80yrs)*	-.570	.000	.566	.000	1.000
Neurologist					
<i>Specialty of physician *</i>					
<i>Stroke severity</i>					
Neurologist*	1.540	1.789	4.666	.488-44.596	.181
Stroke severity (moderate)					
Neurologist*	21.793	.000	.000	.000	.999
Stroke severity (severe)					

**Table 4.19** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Onset time to rt-PA*</i>					
<i>Stroke severity</i>					
Onset time to rt-PA* (within 3 hours)	41.267	.000	.000	.000	.999
Stroke severity (moderate)					
Onset time to rt-PA* (within 3 hours)	40.371	.000	.000	.000	.998
Stroke severity (severe)					
Onset time to rt-PA* (3.0-4.5 hours)	39.637	.000	.000	.000	.998
Stroke severity (moderate)					
Onset time to rt-PA* (3.0-4.5 hours)	17.533	.000	.000	.000	1.000
Stroke severity (severe)					
Method = Enter					
Model Chi-square 114.374 (df = 22, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test .748 (df = 7, sig = .998, p >.05)					
-2 Log likelihood = 190.447					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .541					
Overall rate of correct classification = 79.1%					

#### 4.3.1.10 M<sub>10</sub> model

This model aimed to evaluate four factors and six interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and six interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, physician\*stroke severity, onset time to rt-PA\*stroke severity, and onset time to rt-PA\*specialty of physician. At 24 hours after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.030, 95%CI: .006-.156, p<.001), compared with mild stroke severity. Age >80 years decreased neurological recovery (OR=.206, 95%CI: .048-.881, P<.05), compared with age< 60 years. Onset time to rt-PA, specialty of physician, age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, specialty of

physician\*stroke severity, onset time to rt-PA\*stroke severity, and onset time to rt-PA\*specialty of physician are not significance ( $P>.05$ ).

The log likelihood ratio was 188.909 (Chi square = 115.912, df = 24,  $p <.001$ ). Overall prediction rate was 79.1%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = .206$ ,  $p = 1.000$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .546 or 54.6% of the variance. The detail of binary logistic regression is presented in table 4.20.

**Table 4.20** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.174	10.378	3.236		
Stroke severity (mild)					
Stroke severity (moderate)	-3.508	17.381	.030	.006-.156	.000
Stroke severity (severe)	-20.238	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	19.121	.000	2.014	.000	.999
Onset time to rtPA (3.0-4.5 hours)	1.745	.000	5.726	.000	1.000
Age(<60 years)					
Age(60-80 years)	-.630	1.669	.533	.205-1.385	.196
Age(>80 years)	-1.580	4.541	.206	.048-.881	.033
Non Neurologist					
Neurologist	-.336	.215	.715	.173-2.957	.643
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.106	1.236	3.022	.430-21.248	.266
Stroke severity (moderate)					
Age(60-80yrs)*	-1.223	.000	.294	.000	1.000
Stroke severity (severe)					

**Table 4.20** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Age(>80yrs)*	-17.396	.000	.000	.000	.999
Stroke severity (moderate)					
Age(>80yrs)*	19.951	.000	4.618	.000	.998
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-18.506	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-75.270	.000	.000	.000	.997
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	-17.807	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
<i>Age*Specialty of physician</i>					
Age(60-80yrs)*	-.048	.002	.953	.134-6.766	.962
Neurologist					
Age(>80yrs)*	-.450	.000	.638	.000	1.000
Neurologist					
<i>Specialty of physician *</i>					
<i>Stroke severity</i>					
Neurologist*	1.013	.576	2.753	.201-37.624	.999
Stroke severity (moderate)					
Neurologist*	21.994	.000	3.563	.000	1.000
Stroke severity (severe)					
<i>Onset time to rt-PA*</i>					
<i>Stroke severity</i>					
Onset time to rt-PA* (within 3 hours)	41.198	.000	7.800	.000	.999
Stroke severity (moderate)					
Onset time to rt-PA* (within 3 hours)	20.303	.000	6.566	.000	1.000
Stroke severity (severe)					
Onset time to rt-PA* (3.0-4.5 hours)	75.319	.000	5.137	.000	.998
Stroke severity (moderate)					
Onset time to rt-PA* (3.0-4.5 hours)	35.723	.000	3.269	.000	.999
Stroke severity (severe)					

**Table 4.20** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 24 hours after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Onset time to rt-PA*</i>					
<i>Specialty of physician</i>					
Onset time to rt-PA* (within 3 hours) Neurologist	-21.070	.000	.000	.000	1.000
Onset time to rt-PA* (3.0-4.5 hours) Neurologist	18.619	.000	1.220	.000	.998
Method = Enter					
Model Chi-square 115.912 (df = 24, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test .206 (df = 7, sig = 1.000, p >.05)					
-2 Log likelihood = 188.909					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .546					
Overall rate of correct classification = 79.1%					

#### 4.3.1.11 Interpretation of selected model for the early neurological recovery at 24 hours

This section aims to compare two logit models that are demonstrated through the analysis of factors influencing neurological recovery under several goodness-of-fit statistics such that Wald, AIC (Akaike's Information Criterion), SC (Schwarz Criterion), likelihood ratio statistics ( $G^2$ ,  $-2\log L$ ) and that the use of ROC (Receiver Operating Characteristic) curve. In this study, the dichotomous logit model gives better fits due to AIC and Likelihood ratio estimates compared to those of proportional odds model.

Akaike's Information Criterion (AIC) is a way of selecting a model from a set of models. Calculate AIC value for each model with the same data set, and the best model is the one with minimum AIC value.

$$AIC = -2\log L + 2k$$

k= number of estimated parameters (including the variance)

**Table 4.21** Comparison the goodness-of-fit model for the factors influencing a neurological recovery at 24 hours with -2 Log L and AIC statistic

Model	-2 Log L	AIC
M <sub>1</sub> : Stroke severity	272.289	274.289
M <sub>2</sub> : Stroke severity, Onset time to rt-PA	233.828	237.828
M <sub>3</sub> : Stroke severity, Onset time to rt-PA, Age	229.163	235.163
M <sub>4</sub> : Stroke severity, Onset time to rt-PA, Age, Physician	228.623	236.623
M <sub>5</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity	221.800	231.800
M <sub>6</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA	210.876	222.876
M <sub>7</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician	208.734	222.734
M <sub>8</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician, Specialty of physician * Stroke severity	202.478	218.478
M <sub>9</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician, Specialty of physician*Stroke severity Onset time to rt-PA* Stroke severity	190.447	208.447
M <sub>10</sub> = Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age*Onset time to rt-PA, Age*Specialty of physician, Specialty of physician* Stroke severity, Onset time to rt-PA*Stroke severity, Onset time to rt-PA*Specialty of physician	188.909	208.909

Compared the goodness-of-fit model for the factors influencing a neurological recovery at 24 hours with -2 Log L and AIC statistic (Table 4.21) shown that M<sub>9</sub> Model is minimum AIC value (AIC = 208.447), but model M<sub>5</sub> to M<sub>10</sub> of interaction effects model are not significance at p=.05. Therefore, M<sub>3</sub> Model is seem to appropriate model because there are three significant factors and minimum AIC value (AIC = 235.163). The effect coefficients for each factors are summarize in Table 4.13. The result provides three predictor's contribution to the early neurological recovery at 24 hours.

The odds ratio significantly demonstrated that three independent variables effect on early neurological recovery at 24 hours after admission including stroke severity, onset time to rt-PA and age. The finding revealed that moderate and severe stroke severity decreased the neurological recovery at 24 hours (OR=.095, 95%CI: .044-.205, p<.001 and OR=.126, 95%CI: .034-.465, p<.01, respectively), compared with mild stroke severity. Onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=22.22, 95%CI: 5.454-90.527, P<.001 and OR=17.28, 95%CI: 3.079-97.001, P<.01, respectively), compared with those who did not receive rt-PA treatment. Lastly, age >80 years decreased neurological recovery at 24 hours after admission (OR=.361, 95%CI: .120-1.085 P<.05). Therefore, the final model could be represented as;

Log odds of early neurological recovery at 24 hours = .992 - 2.355stroke severity (moderate) - 2.068stroke severity(severe) + 3.101 time to rt-PA(within 3 hours) + 2.850 time to rt-PA(3.0-4.5 hours) - .582age(60-80 years) - 1.019 Age(>80 years)

**4.3.2 Multiple logistic regression analysis of related factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients**

**4.3.2.1 M1 Model**

This model showed one factor influences the neurological recovery at 3 days after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.193, 95%CI: .072 - .517,  $p < .01$  and OR=.156, 95%CI: .082 - .298,  $p < .001$ , respectively), compared with mild stroke severity.

The log likelihood ratio was 250.788 (Chi-square 37.624,  $df = 2$ ,  $p = .000$ ). Overall prediction rate was 70.0%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\chi^2 = .000$   $p = 1.000$ ) reflecting that the full model appeared to fit the data. The Nagelkerke’s  $R^2$  was shown at .215 or 21.5% of the variance. The detail of binary logistic regression is presented in table 4.22.

**Table 4.22** Logistic regression of one factor associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	1.548	39.496	4.70		
Stroke severity (mild)					
Stroke severity (moderate)	-1.643	10.730	.193	.072 - .517	.001
Stroke severity (severe)	-1.856	31.649	.156	.082 - .298	.000

Method = Enter

Model Chi-square 37.624 (df = 2, sig = .000,  $p < .05$ )

Hosmer and Lemeshow goodness of fit test .000 (df = 0, sig = 1.000,  $p > .05$ )

-2 Log likelihood = 250.788, AIC= 252.778

Nagelkerke R Square (Pseudo  $R^2$ ) = .215

Overall rate of correct classification = 70.0%

#### 4.3.2.2 M<sub>2</sub> model

This model showed two factors influences the neurological recovery at 3 day after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.100, 95%CI: .050 - .201,  $p < .001$  and OR=.087, 95%CI: .027 - .282,  $p < .001$ , respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours (OR=17.012, 95%CI: 1.974- 146.627,  $P < .05$  and OR=16.602, 95%CI: 3.516-78.401,  $P < .001$ , respectively), compared with those who did not receive rt-PA treatment.

The log likelihood ratio was 222.925 (Chi-square 65.487,  $df = 4$ ,  $p = .000$ ). Overall prediction rate was 78.2%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 1.797$ ,  $p = .426$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .352 or 35.2% of the variance. The detail of binary logistic regression is presented in table 4.23.

**Table 4.23** Logistic regression of two factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	1.497	36.641	4.468		
Stroke severity(mild)					
Stroke severity(moderate)	-2.302	41.595	.100	.050 - .201	.000
Stroke severity(severe)	-2.439	16.602	.087	.027 - .282	.000
No received rt-PA					
Onset time to rt-PA (within 3 hours)	2.834	6.650	17.012	1.974- 146.627	.010
Onset time to rt-PA (3.0-4.5 hours)	2.810	12.584	16.602	3.516-78.401	.000
Method = Enter					
Model Chi-square			65.487 (df = 4, sig = .000, p < .05)		
Hosmer and Lemeshow goodness of fit test			1.797 (df = 2, sig = .426, p > .05)		
-2 Log likelihood = 222.925, AIC=226.925					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .352					
Overall rate of correct classification = 78.2%					

### 4.3.2.3 M<sub>3</sub> model

This model showed three factors influences the neurological recovery at 3 day after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.102, 95%CI: .050-.209, p<.001 and OR=.093, 95%CI: .028-.312, p<.001, respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 3 days (OR=16.591, 95%CI: 1.939-148.185, P<.05 and OR=14.429, 95%CI: 3.018-68.982, P<.01, respectively), compared with those who did not receive rt-PA treatment. In addition age is not significance at p=.05.

The log likelihood ratio was 219.200 (Chi-square 69.212, df = 7, p = .000). Overall prediction rate was 78.2%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 6.805$ , p = .414) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .370 or 37.0% of the variance. The detail of binary logistic regression is presented in table 4.24.

**Table 4.24** Logistic regression of three factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	1.557	24.913	4.746		
Stroke severity (mild)					
Stroke severity (moderate)	-2.283	39.134	.102	.050-.209	.000
Stroke severity (severe)	-2.377	14.782	.093	.028-.312	.000
No received rt-PA					
Onset time to rtPA (within 3 hours)	2.830	6.546	16.951	1.939-148.185	.011
Onset time to rtPA (3.0-4.5 hours)	2.669	11.181	14.429	3.018-68.982	.001
Age(<60 years)					
Age(60-80 years)	.104	.079	1.109	.538-2.287	.778
Age(>80 years)	-.886	2.663	.412	.142-1.195	.103

**Table 4.24** Logistic regression of three factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (conts.)

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Method = Enter	
Model Chi-square	69.212 (df = 7, sig = .000, p <.05)
Hosmer and Lemeshow goodness of fit test	6.805 (df = 7, sig = .414, p >.05)
-2 Log likelihood =	219.200, AIC=225.200
Nagelkerke R Square (Pseudo R <sup>2</sup> ) =	.370
Overall rate of correct classification =	78.2%

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#### 4.3.2.4 M<sub>4</sub> model

This model showed four factors influences the neurological recovery at 3 day after admission. The result revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.101, 95%CI: .049-.207, p<.001 and OR=.087, 95%CI: .026-.296, p<.001, respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 3 days (OR=16.131, 95%CI: 1.797-144.782, P<.05 and OR=11.897, 95%CI: 2.412-58.679, P<.01, respectively), compared with those who did not receive rt-PA treatment. In addition age and specialty of physician are not significance (p>.05).

The log likelihood ratio was 217.620 (Chi-square 70.792, df = 7, p = .000). Overall prediction rate was 78.2%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 5.236$ , p = .514) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .377 or 37.7% of the variance. The detail of binary logistic regression is presented in table 4.25.

**Table 4.25** Logistic regression of four factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	Odd ratio	95%CI	P-value
(Constance)	1.479	21.522	4.390		
Stroke severity (mild)					
Stroke severity (moderate)	-2.295	39.124	.101	.049-.207	.000
Stroke severity (severe)	-2.440	15.330	.087	.026-.296	.000
No received rt-PA					
Onset time to rt-PA (within 3 hours)	2.781	6.618	16.131	1.797-144.782	.013
Onset time to rt-PA (3.0-4.5 hours)	2.476	9.250	11.897	2.412-58.679	.002
Age(<60 years)					
Age(60-80 years)	.111	.089	1.118	.539-2.320	.765
Age(>80 years)	-.927	2.990	.396	.138-1.132	.084
Non Neurologist					
Neurologist	.568	1.534	1.765	.718-4.335	.215
Method = Enter					
Model Chi-square		70.792 (df = 7, sig = .000, p <.05)			
Hosmer and Lemeshow goodness of fit test		5.236 (df = 6, sig = .514, p >.05)			
-2 Log likelihood = 217.620, AIC=255.620					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .377					
Overall rate of correct classification = 78.2%					

#### 4.3.2.5 M<sub>5</sub> model

This model aimed to evaluate four factors and one interaction effect influencing neurological recovery at 3 days. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and one interaction effect included age\*stroke severity. The finding revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.050, 95%CI: .014-.175,  $p < .001$  and OR=.047, 95%CI: .003-.640,  $p < .05$ ), compared with mild stroke severity. Onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 3 days (OR=36.682, 95%CI: 2.669-495.929,  $P < .01$  and OR=14.020, 95%CI: 2.580-76.188,  $P < .01$ , respectively), compared with those who did not receive rt-PA treatment. In addition, age, specialty of physician, and age\*stroke severity are not significance ( $p > .05$ ).

The log likelihood ratio was 206.889 (Chi square = 81.523, df = 11,  $p < .001$ ). Overall prediction rate was 77.7%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\chi^2 = 6.228$ ,  $p = .513$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .424 or 42.4% of the variance. The detail of binary logistic regression is presented in table 4.26.

**Table 4.26** Logistic regression of four factors and one interaction factor associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.728	17.491	5.629		
Stroke severity (mild)					
Stroke severity (moderate)	-2.989	22.042	.050	.014-.175	.000
Stroke severity (severe)	-3.067	5.258	.047	.003-.640	.022
No received rt-PA					
Onset time to rt-PA (within 3 hours)	3.594	7.271	36.382	2.669-495.929	.007
Onset time to rtPA (3.0-4.5 hours)	2.640	9.347	14.020	2.580-76.188	.002

**Table 4.26** Logistic regression of four factors and one interaction effect associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
Age(<60 years)					
Age(60-80 years)	-.533	.962	.587	.202-1.702	.327
Age(>80 years)	-.881	1.199	.415	.086-2.005	.274
Non Neurologist					
Neurologist	.827	2.492	2.286	.819-6.383	.274
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.481	3.443	4.395	.918-21.045	.064
Stroke severity (moderate)					
Age(60-80yrs)*	.189	.015	1.209	.059-24.799	.902
Stroke severity (severe)					
Age(>80yrs)*	-1.473	.871	.229	.010-5.055	.351
Stroke severity (moderate)					
Age(>80yrs)*	2.017	1.227	7.519	.212-266.991	.268
Stroke severity (severe)					
Method = Enter					
Model Chi-square 81.523 (df = 11, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 6.228 (df = 7, sig = .513, p >.05)					
-2 Log likelihood = 206.889					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .424					
Overall rate of correct classification = 77.7%					

#### 4.3.2.6 M<sub>6</sub> model

This model aimed to evaluate four factors and two interaction effects influencing neurological recovery at 3 days. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and one interaction effect included age\*stroke severity and age\*onset time to rt-PA. The finding revealed that moderate stroke severity decreased the neurological recovery at 3 days (OR=.038, 95%CI: .010-.148, p<.001), compared with mild stroke severity. In addition, onset time to rt-PA, age, specialty of physician, age\*stroke severity, and age\*onset time to rt-PA are not significance (P>.05).

The log likelihood ratio was 196.506 (Chi square = 91.906, df = 14,  $p < .001$ ). Overall prediction rate was 78.6%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 1.150$ ,  $p = .992$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .467 or 46.7% of the variance. The detail of binary logistic regression is presented in table 4.27.

**Table 4.27** Logistic regression of four factors and two interaction factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.717	17.272	5.570		
Stroke severity (mild)					
Stroke severity (moderate)	-3.259	22.245	.038	.010-.148	.000
Stroke severity (severe)	-20.432	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.124	.000	.000	.000	.998
Onset time to rtPA (3.0-4.5 hours)	37.315	.000	.000	.000	.998
Age(<60 years)					
Age(60-80 years)	-.526	.936	.591	.204-1.716	.333
Age(>80 years)	-.870	1.170	.419	.087-2.027	.279
Non Neurologist					
Neurologist	.884	2.686	2.420	.841-6.961	.101
<i>Age* Stroke severity</i>					
Age(60-80yrs)* Stroke severity (moderate)	1.882	4.919	6.569	1.245-34.671	.057
Age(60-80yrs)* Stroke severity (severe)	18.110	.000	.000	.000	.998
Age(>80yrs)* Stroke severity (moderate)	-19.292	.000	.000	.000	.999
Age(>80yrs)* Stroke severity (severe)	19.369	.000	.000	.000	.998

**Table 4.27** Logistic regression of four factors and two interaction factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-36.409	.000	.000	.000	.998
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-36.248	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	4.793	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					
Method = Enter					
Model Chi-square 91.906 (df = 14, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 1.150 (df = 7, sig = .992, p >.05)					
-2 Log likelihood = 196.506					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .467					
Overall rate of correct classification = 78.6%					

#### 4.3.2.7 M<sub>7</sub> model

This model aimed to evaluate four factors and three interaction effects influencing neurological recovery at 3 days. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and three interaction effects included age\*stroke severity, age\*onset time to rt-PA, and age\*specialty of physician. The finding revealed that moderate stroke severity decreased the neurological recovery at 3 days (OR=.038, 95%CI: .010-.148, p<.001), compared with mild stroke severity. In addition, onset time to rt-PA, age, specialty of physician, age\*stroke severity, age\*onset time to rt-PA, and age\*specialty of physician are not significance (P>.05).

The log likelihood ratio was 195.436 (Chi square = 92.976, df = 16, p <.001). Overall prediction rate was 78.2%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 2.724, p = .950$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown

at .472 or 47.2% of the variance. The detail of binary logistic regression is presented in table 4.28.

**Table 4.28** Logistic regression of four factors and three interaction factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.708	16.255	5.518		
Stroke severity (mild)					
Stroke severity (moderate)	-3.271	22.170	.038	.010-.148	.000
Stroke severity (severe)	-20.420	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.098	.000	.000	.000	.998
Onset time to rtPA (3.0-4.5 hours)	37.293	.000	.000	.000	.998
Age(<60 years)					
Age(60-80 years)	-.496	.786	.609	.203-1.824	.375
Age(>80 years)	-.861	1.130	.423	.086-2.067	.288
Non Neurologist					
Neurologist	.966	.916	2.627	.364-18.980	.338
<i>Age* Stroke severity</i>					
Age(60-80yrs)*	1.883	4.913	6.571	1.243-34.722	.056
Stroke severity (moderate)					
Age(60-80yrs)*	18.136	.000	.000	.000	.998
Stroke severity (severe)					
Age(>80yrs)*	-37.414	.000	.000	.000	.998
Stroke severity (moderate)					
Age(>80yrs)*	18.880	.000	.000	.000	.998
Stroke severity (severe)					
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)*	-36.400	.000	.000	.000	.998
Onset time to rt-PA (within 3 hours)					
Age(60-80yrs)*	-36.161	.000	.000	.000	.998
Onset time to rt-PA (3.0-4.5 hours)					
Age(>80yrs)*	22.943	.000	.000	.000	1.000
Onset time to rt-PA (within 3 hours)					

**Table 4.28** Logistic regression of four factors and three interaction factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Age*Specialty of physician</i>					
Age(60-80yrs)* Neurologist	-.263	.048	.768	.073-8.053	.826
Age(>80yrs)* Neurologist	18.582	.000	.000	.000	.999
Method = Enter					
Model Chi-square 92.976 (df = 16, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 2.724 (df = 6, sig = .950, p >.05)					
-2 Log likelihood = 195.436					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .472					
Overall rate of correct classification = 78.2%					

#### 4.3.2.8 M<sub>8</sub> model

This model aimed to evaluate four factors and four interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and four interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, and specialty of physician\*stroke severity. At 3 days after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.040, 95%CI: .010-.160, p<.001), compared with mild stroke severity. Age, onset time to rt-PA, specialty of physician, age\* stroke severity, age\*onset time to rt-PA, age\*specialty of physician, and specialty of physician\*stroke severity are not significance (P>.05).

The log likelihood ratio was 192.282 (Chi square = 96.130, df = 18, p <.001). Overall prediction rate was 80.5%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = 1.284, p = .973$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .485 or 48.5% of the variance. The detail of binary logistic regression is presented in table 4.29.

**Table 4.29** Logistic regression of four factors and four interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.690	15.842	5.149		
Stroke severity (mild)					
Stroke severity (moderate)	-3.218	20.711	.040	.010-.160	.000
Stroke severity (severe)	-20.407	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	38.133	.000	.000	.000	.998
Onset time to rtPA (3.0-4.5 hours)	36.974	.000	.000	.000	.998
Age(<60 years)					
Age(60-80 years)	-.429	.580	.651	.216-1.965	.446
Age(>80 years)	-.843	1.082	.431	.088-2.107	.298
Non Neurologist					
Neurologist	1.140	.954	3.127	.318-30.788	.329
<i>Age* Stroke severity</i>					
Age(60-80yrs)* Stroke severity (moderate)	1.842	4.711	6.312	1.196-33.318	.060
Age(60-80yrs)* Stroke severity (severe)	16.922	.000	.000	.000	.998
Age(>80yrs)* Stroke severity (moderate)	-34.423	.000	.000	.000	.998
Age(>80yrs)* Stroke severity (severe)	18.867	.000	.000	.000	.998
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)* Onset time to rt-PA (within 3 hours)	-35.545	.000	.000	.000	.998
Age(60-80yrs)* Onset time to rt-PA (3.0-4.5 hours)	-35.443	.000	.000	.000	.998
Age(>80yrs)* Onset time to rt-PA (within 3 hours)	19.863	.000	.000	.000	1.000

**Table 4.29** Logistic regression of four factors and four interaction factors associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Age*Specialty of physician</i>					
Age(60-80yrs)* Neurologist	-.826	.416	.438	.036-5.387	.519
Age(>80yrs)* Neurologist	15.733	.000	.000	.000	.999
<i>Specialty of physician *</i>					
<i>Stroke severity</i>					
Neurologist*	-.429	.131	.651	.064-6.635	.717
<i>Stroke severity (moderate)</i>					
Neurologist*	2.737	2.049	15.435	.364-654.134	.152
<i>Stroke severity (severe)</i>					
Method = Enter					
Model Chi-square 96.130 (df = 18, sig = .000, p <.001)					
Hosmer and Lemeshow goodness of fit test 1.284 (df = 6, sig = .973, p >.05)					
-2 Log likelihood = 192.282					
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .485					
Overall rate of correct classification = 80.5%					

#### 4.3.2.9 M<sub>9</sub> model

This model aimed to evaluate four factors and five interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and five interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, physician\*stroke severity, and onset time to rt-PA\*stroke severity. At 3 days after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.044, 95%CI: .011-.176, p<.001), compared with mild stroke severity. Age, onset time to rt-PA, specialty of physician, age\* stroke severity, age\*onset time to rt-PA, age\*specialty of physician, specialty of physician\*stroke severity, and onset time to rt-PA\*stroke severity are not significance (p>.05).

The log likelihood ratio was 179.580 (Chi square = 108.832, df = 22,  $p < .001$ ). Overall prediction rate was 79.1%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = .991$ ,  $p = .998$ ) reflecting that the full model appeared to fit the data. The Nagelkerke's  $R^2$  was shown at .534 or 53.4% of the variance. The detail of binary logistic regression is presented in table 4.30.

**Table 4.30** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.656	15.444	5.241		
Stroke severity (mild)					
Stroke severity (moderate)	-3.120	19.633	.044	.011-.176	.000
Stroke severity (severe)	-20.444	.000	.000	.000	.998
No received rt-PA					
Onset time to rt-PA (within 3 hours)	55.488	.000	.000	.000	.999
Onset time to rtPA (3.0-4.5 hours)	18.001	.000	.000	.000	.999
Age(<60 years)					
Age(60-80 years)	-.368	.423	.692	.228-2.099	.515
Age(>80 years)	-.809	1.001	.445	.091-2.172	.317
Non Neurologist					
Neurologist	1.545	1.283	4.688	.323-67.936	.257
<i>Age* Stroke severity</i>					
Age(60-80yrs)* Stroke severity (moderate)	1.635	3.648	5.131	.958-27.478	.056
Age(60-80yrs)* Stroke severity (severe)	17.770	.000	.000	.000	.998
Age(>80yrs)* Stroke severity (moderate)	-18.925	.000	.000	.000	.999
Age(>80yrs)* Stroke severity (severe)	18.904	.000	.000	.000	.999

**Table 4.30** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)* Onset time to rt-PA (within 3 hours)	-36.644	.000	.000	.000	.999
Age(60-80yrs)* Onset time to rt-PA (3.0-4.5 hours)	-74.960	.000	.000	.000	.997
Age(>80yrs)* Onset time to rt-PA (within 3 hours)	-15.315	.000	.000	.000	1.000
<i>Age*Specialty of physician</i>					
Age(60-80yrs)* Neurologist	-1.423	.933	.241	.013-4.325	.334
Age(>80yrs)* Neurologist	-.177	.000	.000	.000	1.000
<i>Specialty of physician *</i>					
Stroke severity Neurologist*	-1.376	.905	.253	.015-4.300	.341
Stroke severity (moderate) Neurologist*	20.531	.000	.000	.000	.998
<i>Onset time to rt-PA*</i>					
Stroke severity Onset time to rt-PA* (within 3 hours)	2.228	.000	.000	.000	1.000
Stroke severity (moderate) Onset time to rt-PA* (within 3 hours)	-17.457	.000	.000	.000	.999
Stroke severity (severe) Onset time to rt-PA* (3.0-4.5 hours)	78.131	.000	.000	.000	.998
Stroke severity (moderate) Onset time to rt-PA* (3.0-4.5 hours)	19.248	.000	.000	.000	.999
Stroke severity (severe)					

**Table 4.30** Logistic regression of four factors and five interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

---

Method = Enter
Model Chi-square 108.832 (df = 22, sig = .000, p <.001)
Hosmer and Lemeshow goodness of fit test .991 (df = 8, sig = .998, p >.05)
-2 Log likelihood = 179.580
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .534
Overall rate of correct classification = 80.5%

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#### 4.3.2.10 M<sub>10</sub> model

This model aimed to evaluate four factors and six interaction effects. Four factors included stroke severity, onset time to rt-PA, age, and specialty of physician, and six interaction effects included age\*stroke severity, age\*onset time to rt-PA, age\*specialty of physician, physician\*stroke severity, onset time to rt-PA\*stroke severity, and onset time to rt-PA\*specialty of physician. At 3 days after admission, the finding revealed that moderate severity decreased the neurological recovery (OR=.044, 95%CI: .011-.176, p<.001), compared with mild stroke severity. In addition, age, onset time to rt-PA, specialty of physician, age\* stroke severity, age\*onset time to rt-PA, age\*specialty of physician, specialty of physician\*stroke severity, onset time to rt-PA\*stroke severity, and onset time to rt-PA\*specialty of physician are not significance (P>.05).

The log likelihood ratio was 179.850 (Chi square = 108.832, df = 24, p <.001). Overall prediction rate was 80.9%. The Hosmer and Lemeshow goodness of fit test of a full model presented that there was no significance in the distribution of observed and predicted dependence values ( $\lambda^2 = .991$ , p = .998) reflecting that the full model appeared to fit the data. The Nagelkerke's R<sup>2</sup> was shown at .543 or 54.3% of the variance. The detail of binary logistic regression is presented in table 4.31.

**Table 4.31** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220)

Variable	$\beta$	Wald	OR	95%CI	P-value
(Constance)	1.656	15.444	5.241		
Stroke severity (mild)					
Stroke severity (moderate)	-3.120	19.633	.044	.011-.176	.000
Stroke severity (severe)	-20.483	.000	.000	.000	.998
Not received rt-PA					
Onset time to rt-PA (within 3 hours)	54.458	.000	4.474	.000	.999
Onset time to rt-PA (3.0-4.5 hours)	38.132	.000	3.634	.000	.999
Age (<60 years)					
Age (60-80 years)	-.368	.423	.692	.228-2.099	.228
Age (>80 years)	-.809	1.001	.445	.091-2.172	.091
Non Neurologist					
Neurologist	1.545	1.283	4.688	.323-67.936	.257
<i>Age* Stroke severity</i>					
Age(60-80yrs)* Stroke severity (moderate)	1.635	.000	5.131	.958-27.478	.056
Age(60-80yrs)* Stroke severity (severe)	17.808	.000	5.422	.000	.998
Age(>80yrs)* Stroke severity (moderate)	-18.881	.000	.000	.000	.999
Age(>80yrs)* Stroke severity (severe)	18.943	.000	1.685	.000	.998
<i>Age* Onset time to rt-PA</i>					
Age(60-80yrs)* Onset time to rt-PA (within 3 hours)	-36.713	.000	.000	.000	1.000
Age(60-80yrs)* Onset time to rtPA (3.0-4.5 hours)	-55.792	.000	.000	.000	.998
Age(>80yrs)* Onset time to rt-PA (within 3 hours)	-14.782	.000	.000	.000	.998

**Table 4.31** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

Variable	$\beta$	Wald	OR	95%CI	P-value
<i>Age* Physician specialty</i>					
Age(60-80yrs)* Neurologist	-1.423	.933	.241	.013-4.325	.334
Age(>80yrs)* Neurologist	-.270	.000	.763	.000	1.000
<i>Physician specialty*</i>					
<i>Stroke severity</i>					
Neurologist*	-1.376	.905	.253	.015-4.300	.341
Stroke severity (moderate) Neurologist*	20.964	.000	1.272	.000	.998
Stroke severity (severe)					
<i>Onset time to rt-PA*</i>					
<i>Stroke severity</i>					
Onset time to rt-PA* (within 3 hours) Stroke severity (moderate)	2.681	.000	14.956	.000	1.000
Onset time to rt-PA* (within 3 hours) Stroke severity (severe)	-16.358	.000	.000	.000	1.000
Onset time to rt-PA* (3.0-4.5 hours) Stroke severity (moderate)	58.762	.000	3.311	.000	.999
Onset time to rt-PA* (3.0-4.5 hours) Stroke severity (severe)	-.708	.000	.493	.000	1.000
<i>Onset time to rt-PA*</i>					
<i>Physician specialty</i>					
Onset time to rt-PA* (within 3 hours) Neurologist	1.074	.000	2.926	.000	1.000
Onset time to rt-PA* (3.0-4.5 hours) Neurologist	-20.130	.000	.000	.000	.999

**Table 4.31** Logistic regression of four factors and six interaction effects associated with the early neurological recovery at 3 days after admission in acute ischemic stroke patients (n = 220) (cont.)

---

Method = Enter
Model Chi-square 108.832 (df = 24, sig = .000, p <.001)
Hosmer and Lemeshow goodness of fit test .991 (df = 8, sig = .998, p >.05)
-2 Log likelihood = 179.850
Nagelkerke R Square (Pseudo R <sup>2</sup> ) = .543
Overall rate of correct classification = 80.9%

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#### 4.3.2.11 Interpretation of selected model for the factors influencing a neurological recovery at 3 days

Compared the goodness-of-fit model for the factors influencing a neurological recovery at 3 days with -2 Log L and AIC statistic (Table 4.32) shown that M<sub>9</sub> Model is minimum AIC value (AIC = 197.580), but the factors in M<sub>3</sub> to M<sub>4</sub> model and model M<sub>5</sub> to M<sub>10</sub> of interaction effect models are not significance at p=.05. Therefore, M<sub>2</sub> Model is seem to appropriate model because there are three significant factors and minimum AIC value (AIC = 226.925). The effect coefficients for each factors are summarize in Table 4.23.

The odds ratio significantly demonstrated that two independent variables effect on early neurological recovery at 3 days after admission including stroke severity and onset time to rt-PA. The finding revealed that moderate and severe stroke severity decreased the neurological recovery at 3 days (OR=.100, 95%CI: .050 - .201, p<.001 and OR=.087, 95%CI: .027 - .282, p<.001, respectively), compared with mild stroke severity. In addition, onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 3 days (OR=17.012, 95%CI: 1.974- 146.627, P<.05 and OR=16.602, 95%CI: 3.516-78.401, P<.001, respectively), compared with those who did not receive rt-PA treatment. Therefore, the final model could be represented as;

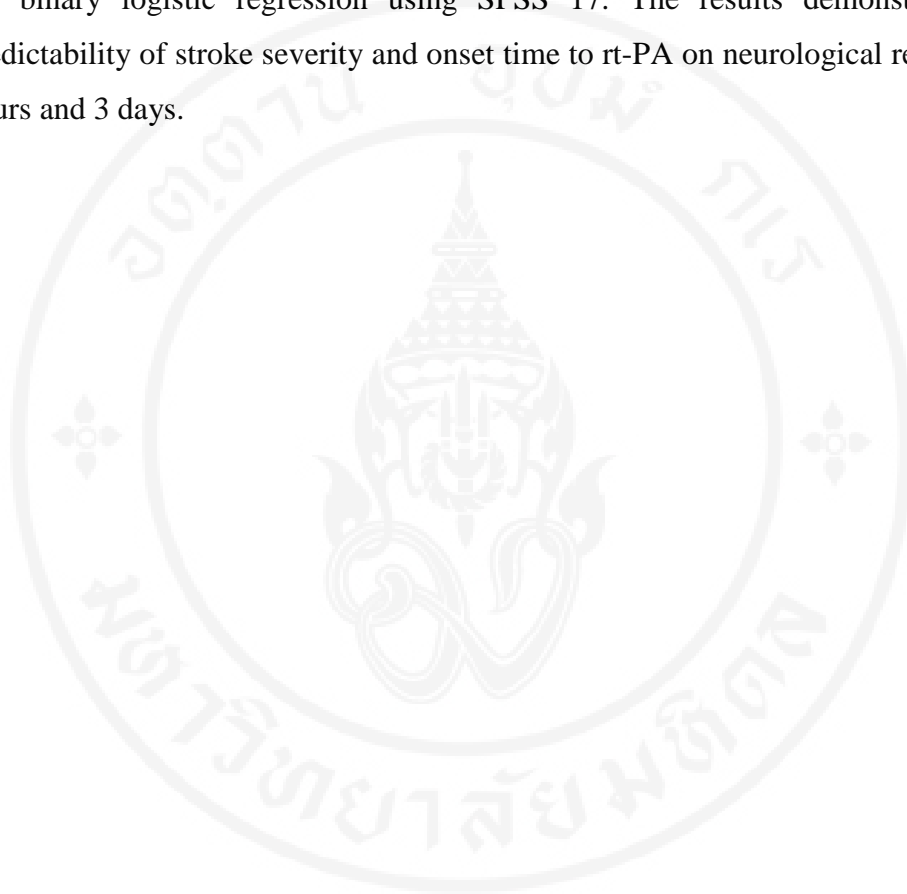
Log odds of early neurological recovery at 3 days = 1.557 - 2.283stroke severity (moderate) - 2.377stroke severity(severe) + 2.830time to rt-PA(within 3 hours) + 2.669time to rt-PA(3.0-4.5 hours)

**Table 4.32** Comparison the goodness-of-fit model influencing a neurological recovery at 3 days with -2 Log L and AIC statistic

Model	-2 Log L	AIC
M <sub>1</sub> : Stroke severity	250.788	252.788
M <sub>2</sub> : Stroke severity, Onset time to rt-PA	222.925	226.925
M <sub>3</sub> : Stroke severity, Onset time to rt-PA, Age	219.200	225.200
M <sub>4</sub> : Stroke severity, Onset time to rt-PA, Age, Physician	217.620	255.620
M <sub>5</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity	206.889	216.889
M <sub>6</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA	196.506	208.506
M <sub>7</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician	195.436	209.436
M <sub>8</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician, Specialty of physician * Stroke severity	192.282	208.282
M <sub>9</sub> : Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age* Onset time to rt-PA, Age*Specialty of physician, Specialty of physician*Stroke severity Onset time to rt-PA* Stroke severity	179.580	197.580
M <sub>10</sub> = Stroke severity, Onset time to rt-PA, Age, Physician, Age* Stroke severity, Age*Onset time to rt-PA, Age*Specialty of physician, Specialty of physician* Stroke severity, Onset time to rt-PA*Stroke severity, Onset time to rt-PA*Specialty of physician	179.580	199.580

## 4.5 Summary

This chapter illustrated the characteristics of acute ischemic stroke patients. Descriptive statistics of the variables were proposed. The statistic program SPSS 17 was used to analyze preliminary results. The hypotheses were analyzed by the binary logistic regression using SPSS 17. The results demonstrated strong predictability of stroke severity and onset time to rt-PA on neurological recovery at 24 hours and 3 days.



## **CHAPTER V**

### **DISCUSSION**

The research findings were based on the purpose of this study which was to explore factors influencing early neurological recovery in patients with acute ischemic stroke through a multivariate logistic regression. The discussion will present the characteristics of acute ischemic stroke and independent variables first. The second discussed on hypotheses testing. The last discussed strengths and limitation of this study. The detailed of which were as follows.

#### **5.1 Characteristics of the Sample and Independent Variables**

##### **Characteristics of the Sample**

The mean age of the participants was 64.35 years. This age is similar to findings from the Thai Stroke Registry, the mean age of patients at the onset of ischemic stroke in Thailand is approximately 65 years (Nilanont et al., 2014) and similar to findings from previous reports from developing countries (Venketasubramanian et al., 2009; Sridharan et al., 2009). However, this mean age of patients with stroke is lower than the report in other international studies such as German 65.9 years (Grau et al., 2001) Norway 70.1 years (Altmann et al., 2015), and New York 70.6 years (Sharma et al., 2016).

The major of the participants (55.9%) were male. Consistently, the Medical Bureau, Ministry of Public health (2007) reported 58.2% of hospitalized stroke patients around the country were male, while 44.1% were female. Congruently, male were the major proportion (59%) in an epidemiologic study of the Thai stroke rehabilitation study (Kuptniratsaikul et al., 2008). Several surveys supported this incidence such as Korea being 56.4%, China being 56.52-60%, and Canada being 50.75% (Lee & Roh, 2006; Liu et al., 2007; Silver, Kapsal, Lindsay, Tu, & Richards, 2006). Those may be due to more risk behavior found in male than female, but less

awareness such as in blood pressure and blood sugar check-up, and sweet diet consumption (Petchareoun et al., 2008). Furthermore, prevalence of cigarette smoking and alcohol consumption were found in male more than female (Liu, et al., 2007; Petchareoun, et al., 2008).

In regards occupation and resource, the occupations of participant's were farmer/gardener 38.6% and house work 28.6%, Employee 17.3%. They got the health care expense support from the universal health care coverage (76.8%) and government welfare (16.8%) and national health insurance (6.4%). The reason why most of them got the health care expense support from those resources because every people who do not have any health care welfare are eligible for getting the support from the universal health care coverage. Especially in the case of emergency as stroke, they got this right even though they accessed to unregistered hospital.

Most of the patients had ischemic stroke as their risk factors including hypertension (73.2%), dyslipidemia (36.4%) diabetes mellitus (26.8%), and stroke/TIA (12.3%). The study by the INTERSTROKE demonstrated that a large international case-control study of risk factors for incidence of stroke in 22 countries including low- and middle-income countries (LMICs), found evidence of 10 significant modifiable risk factors, including history of hypertension, current smoking, diabetes mellitus, waist-to-hip ratio, diet risk score, physical inactivity, alcohol intake, psychosocial stress and depression, cardiac causes, and ratio of apolipoproteins B to A1. Non-modifiable risk factors related to hereditary or natural processes include age, sex/gender, and race/ethnicity (O'Donnell et al., 2010).

For hypertension, similar findings were reported the risk factor in Thai population that the factors associated with higher stroke prevalence were history of hypertension, diabetes mellitus, and hypercholesterolemia (Hanchaiphiboolkul et al., 2011). Congruently, previous study found that stroke risk factors focusing on hypertension were studied in a multicenter observational at 24 selected stroke hospitals (8 academic hospitals, 9 regional referral center hospitals, and 7 provincial and other hospitals) in 6 geographical regions across Thailand. Self-reported hypertension prior to stroke was found in 62.5% of the patients (Nidhinandana, Ratanakorn, Charnnarong, Muengtawepongsa, Towanabut, 2013).

This study finding revealed that dyslipidemia was found in 36.4% of stroke patients. Similar to the finding of Thai Stroke Registry demonstrated that hypercholesterolemia was found in 30% stroke cases (Nilanont, 2014). However, the prevalence of dyslipidemia was much higher in a single center hospital based study at our King Chulalongkorn Memorial Hospital where 80% of patients with ischemic stroke had a high LDL-C level of more than 100 mg/dL (Suwanwela, 2014).

In addition, the study findings revealed that diabetes mellitus was found in 26.8% of stroke patients. In a cross-sectional, multi-center hospital-based diabetes registry among 9,037 diabetic patients in Thailand, the Thailand Diabetes Registry Project, stroke was found in 3.5% of diabetic patients (Plengvidhya et al., 2006). According to the Thai Stroke Registry, diabetes was found in 26% of stroke patients (Nilanont, 2014). In a meta-analysis of prospective studies (including 530 083 participants), the reported hazard ratio for ischemic stroke was 2.3 (95% CI 2.0–2.7) in people with versus those without diabetes (The Emerging Risk Factors Collaboration, 2010). Assuming a population-wide prevalence of diabetes of around 10%, these findings indicate a diabetes-attributable risk of stroke of around 12% (ie, one in eight or nine cases of stroke is attributable to diabetes).

## **5.2 Early neurological recovery in patients with acute ischemic stroke**

Early neurological recovery was defined as a decrease of greater than or equal to 4 points on National Institutes of Health Stroke Scale (NIHSS) between baseline and 24 hours or an NIHSS score of 0 to 3 points. A total of 220 stroke patients who met the inclusion criteria were recruited. The finding demonstrated that the patients with acute ischemic stroke had the neurological recovery account for 48.8% at 24 hours after admission.

For patients receiving rt-PA treatment, the recovery occurs 82.75% and the NIHSS change at admission and 24 hours from worse 3 point to improve 21 points (mean 6.97, median 6, SD 5.04). The rate of the recovery in this study higher than the other two previous studies found that the overall re-canalization rate in thrombolytic therapy 46.2% during the first 24 hours after treatment (Pandian, 2009). The other one study found that among 216 patients with acute stroke who were treated with alteplase,

48.6% had improvement at 24 hours and the median change in the NIHSS score was 7 in the group with improvement and 1 in the group with lack of improvement (Saposnik et al., 2004).

The neurological recovery in the ischemic stroke patients who had not received the rt-PA treatment was seen in 43.45%. The changes of the NIHSS were worse 14 point to improve 12 points (mean 1.33, median 1, SD 2.38). In addition, a study conducted in Taiwan aim to explore outcomes of acute hospitalization in patients with first-ever ischemic stroke who had not received acute thrombolytic therapy indicated that the better outcome (decreased on the NIHSS  $\geq 4$  points) at discharge was seen in 78 (22%) patients, stationary outcome (change of the NIHSS within  $\pm 3$  points) was reached by 221 (61%) patients, and 61(17%) patients achieved a worse outcome (increase on the NIHSS  $\geq 4$  points or died) (Tseng & Chang, 2006).

### **5.3 Factors influencing early neurological recovery in patients with acute ischemic stroke**

The present study explored the multivariate factors influencing early neurological recovery in patients with acute ischemic stroke. Therefore, logistic regression analysis was employed to test the correlation between the eleven dependents variables including the distance from place of symptom attack to the hospital, the level of first hospital registers, specialty of physician, triage nurse, triage rating score, onset-to- rt-PA time, compliance to clinical practice guideline for acute ischemic stroke, age, admission blood pressure, admission stroke severity, and smoking. The hypothesis of this study is those variables can predict the early neurological recovery at 24 hours and day 3 after admission in patients with acute ischemic stroke.

The discussion followed by the framework of the study including the contextual characteristics, individual characteristics, and health behavior.

#### **5.3.1 Contextual Characteristics**

##### **5.3.1.1 Onset-to- rt-PA time**

Of 220 acute ischemic patients in this study, 29 (13.18%) received intravenous rt-PA within the time window; a mean age was 60 years (range

32-83), with 62.1% being men, a mean NIHSS score of 12.7 points (range 4-28), and a mean onset-to-treatment time of 185.8 minutes (range 62-240). The finding demonstrated the participants who received the rt-PA treatment in 0-90 minutes were 6.9% (2 cases), in 91-180 minutes were 21.8% (8 cases), in 181-270 minutes were 65.5% (19 cases).

The finding partially supported this hypothesis in that time to rt-PA could predict early neurological recovery at 24 hours and 3 days. On binary logistic regression analysis, the odds ratio for receiving rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours 22.22 times (95%CI=5.454-90.527,  $P<.001$ ) and 17.282 times (95%CI=3.079-97.001,  $P<.01$ ). For 3 days after admission, the neurological recovery were 16.95 times (95%CI=5.454-90.527,  $P<.05$ ) and 14.43 (95%CI=3.018-68.982,  $P<.01$ ) compared with not received rt-PA treatment. The previous suggested that after rt-PA therapy within 3 hours in 41 acute ischemic stroke patients that early recanalization within 1 hour after rt-PA infusion improved neurological recovery. They presented of whom with early recanalization had significant NIHSS lower score since after 24 hour rt-PA infusion (mean score at the following 24 hours=8.2, and at day 7 =6.8,  $p=0.043$ , 0.023). This reflected the recovery of NIHSS could be seen since 24 hour rt-PA infusion (Kimura et al., 2008).

Consistently, the National Institutes of Neurological Disorders and Stroke (NINDS) rt-PA stroke study reported that patients treated using rt-PA within 0-90 min after stroke onset showed an increased likelihood of improvement at 24 hours and a favorable 3-month outcome compared to patients treated > 90 min (Marler et al., 2000). The study in long term outcome demonstrated that adjusted odds of a favourable 3 month outcome were 2.55 (95% CI 1.44-4.52) for 0-90 min, 1.64 (1.12-2.40) for 91-180 min, and 1.34 (1.06-1.68) for 181-270 min in favour of the alteplase group (Lees et al., 2010).

### **5.3.1.2 Specialty of physician**

For characteristics of physician who treated acute ischemic stroke patients were internal medicine 68.2%, neurologist 22.7%, general physician 8.2%, and emergency physician 0.9%. The previous study in Indianapolis of the United States found that fifty patients were treated by general neurologists (70%), stroke neurologists (24%), or emergency physicians (6%). Mean times to hospital

arrival, brain CT, and start of rt-PA infusion were 44, 86, and 141 minutes, respectively (Lopez-Yunez et al, 2001).

This finding revealed that there are not difference of door-to-needle time between treated by neurologist and the other physician (82.7 and 87.5 minutes,  $p=.696$ ). In contrast, the study in USA report that average door-to-needle time of 35 minutes in the neurologic emergency department (ED) is statistically significant when compared to the main emergency department physicians using specialty consultation with average door-to-needle times of 83 minutes. It is also important to note that there was no significant difference in cases of symptomatic intracranial hemorrhage with rapid administration of rt-PA by the neuro ED physicians (Greenberg et al., 2015).

Interestingly, this study showed that specialty of physician was not associated with the neurological recovery in logistic model both 24 hours and 3 days. This result disagree with previous study reported that discharge NIHSS score was significantly lower, and more patients were discharged to home in the neuro ED group compared to the main ED group (Greenberg et al., 2015).

### **5.3.1.3 The distance from place of symptom attack to the hospital**

The mean of distance from place of symptom onset to the hospital that can provide rt-PA was 24.58 (SD 22.03) kilometers (range 0-130 kilometers). Nearly half of all patients (42.7%) had the distance 10 kilometers from hospital and the median and mean time to arrival at the hospital were 4.6 and 9.2 hours. In addition, the median and mean time of stroke patients who lived relatively farther away from the hospital were 4.3 and 7.4 hours respectively.

The result from univariate logistic analysis revealed that the distance from place of symptom onset to the hospital was not found to affect the early neurological recovery both 24 hours and 3 days. This finding is consistent with previous study in two countries. The study in St Louis City/County, USA reported that there was no difference between those living close to the hospital (< 4.2 kilometers) and those living farther away in terms of arrival within 1, 2, or 3 hours after onset of stroke symptoms (Acharya et al., 2011). The study in Japan showed that

distance did not show a significant association with rt-PA administration (Kunisawa et al., 2014).

The data suggest that even those living within close proximity to a hospital was not related to arrive within period time of rt-PA administration. Many factors play a role in timely arrival at the ED after stroke onset, including recognition of stroke symptoms, time taken to transport the subject to the ED, activation of the emergency medical system, geography, and traffic networks. However, a previous study in the Kumamoto region of Japan showed that the direct distance was significantly correlated with the transportation time by ambulance (Tanaka, Nakajima, Hirano, & Uchino, 2009).

Patients who were directly admitted to stroke center had a shorter onset-to-door time (61 versus 120 minutes,  $p < 0.001$ ) and onset-to-rtPA time 103 versus 155 minutes,  $p < 0.001$ ) than those referred from other hospitals.

#### **5.3.1.4 The level of first hospital registers**

In two-third of participants (65.4%) went to the hospital with could perform intravenous rt-PA treatment consist of general hospital (44.5%) and excellent hospital (20.9%), while nearly thirty five percents (34.5%) went to health care service with could not perform intravenous rt-PA including community hospital (28.6%), primary care unit (3.2%) and private clinic (2.7%). The level of first hospital register and arrival time within 3 hours to the hospital that can provide rt-PA and rtPA receiving were excellent hospital (34.78% vs 15.22%), general hospital (38.77% vs 12.20%), community hospital (53.98% vs 19.04%), primary care unit (14.28%), and private clinic (16.66%).

Moreover this finding showed that the patients who were directly accessed to the hospital with providing rt-PA treatment had a shorter onset-to-rtPA time 170 versus 208 minutes,  $p < 0.05$ ) than referral from other hospitals. This result is consistent with Kim et al. (2014) indicated that the patients who were directly admitted to stroke center had a shorter onset-to-door time (61 versus 120 minutes,  $p < 0.001$ ) and onset-to-rtPA time 103 versus 155 minutes,  $p < 0.001$ ) than those referred from other hospitals.

For referral time to the hospital provide stroke care, the mean of referral time was 107.47 minutes (SD 91.55) with a range of 25-555 minutes. Only

32.1% of participants had been referred within 60 minutes that recommended guideline by American Heart Association/American Stroke Association (Jauch et al., 2013). The guidelines for the early management of patients with acute ischemic stroke suggested that stroke care quality improvement should be an ongoing process for every hospital. One example of this process improvement is to shorten the door-to-needle time to <60 minutes. For every 15-minute reduction of door-to-needle time, there is a 5% lower odds of in-hospital mortality (adjusted OR, 0.95; 95% CI, 0.92–0.98;  $P=0.0007$ ) (Jauch et al., 2013).

The result from univariate logistic regression analysis revealed that the level of first hospital registers was not found to affect the early neurological recovery both 24 hours and 3 days. This finding disagree with previous study demonstrated that direct admission was associated with a good outcome with an odds ratio of 2.03 (95% CI 1.051–3.917,  $p = 0.035$ ), after adjusting for baseline variables (Kim, et al., 2014).

#### **5.3.1.5 Years experience of triage nurse**

Overall years experience of triage nurse, the averages number of years of emergency nursing experience was 7.1 (SD 5.50), ranging from 1 to 30 years. A half of triage nurses (49.1%) had experience of emergency care less than five years. For accuracy of triage, all patients who arrived within 4.5 hours should have been coded as a triage Level 2 (or Level 1 if truly in need of immediate resuscitation). If they were coded a Level 3, 4, or 5 the triage was considered inaccurate. The overall accuracy rate was 97.47%. Previous studies of triage accuracy have identified accuracy rates of 50% to 76 % (Holdgate et al., 2007; Wilper et al., 2008; Atzema et al., 2009). Because accuracy in triage is critical, acuity assignment affects the prioritization of limited medical resources among patients in acute need of medical care. (Vatnoy, Fossum, Smith, & Slettebo, 2013). Triage level designation decisions are a nursing function that could lead to patient outcomes. Due to reduce patient waiting times and improve patient flow has led to the introduction of a number of strategies such as fast track and patient streaming.

The result from univariate logistic regression analysis revealed that the year experience of triage nurse was not found to affect the early neurological recovery both 24 hours and 3 days. All triage nurses in this study could assign a

97.47% accuracy rate in stroke patients who arrived within 4.5 hours. Similar to years of experience was not a predictor of accuracy in triage of patients with symptoms suggestive of acute myocardial infarction (Sanders & DeVon, 2016). In this finding, half of stroke patients had onset time to rt-PA hospital more than time period of rt-PA treatment (> 4.5 hours). Thus, these patients were not treated with intravenous rt-PA because of delay access to the hospital. The spontaneous improvement would appear to have been either minimally impaired at the time of baseline examination or insignificantly improved in terms of true functional recovery (Biller et al., 1990). Cramer (2008) reported that some degree of spontaneous behavioral recovery is usually seen in the weeks after stroke onset.

#### **5.3.1.6 Triage rating score**

On triage levels of acute ischemic stroke patients presented at the emergency department were emergency, urgency, semi-urgency, non-urgency, and critical (70.5%, 24.5%, 2.5%, 1.8% and 0.9%, respectively). The most commonly reported stroke symptoms on presentation to triage were limb weakness (94.5%), speech problems (69.1.2%), and facial weakness (67.3%). A small proportion of patients presented with a loss of coordination (15.5%) while 1.4 % complained abnormal vision. As previously stated, the major of stroke symptoms on presentation to triage were limb weakness (56%), speech problems (42%), and facial weakness (33%) (Mosley, Morphet, Innes, & Braitberg, 2013).

This study found that the stroke patients, who potentially treated with thrombolysis (presented within 3.5 hours), 96.87 % were allocated critical triage and an emergent category (category 1 or 2). On the other hand, 3.12% (3 of 96 stroke patients) were allocated a category 4 or 5 (semi-urgent and non-urgent). In this group had presenting symptoms with facial weakness without limb weakness and vertigo. The results are consistent with Mosley, Morphet, Innes, & Braitberg (2013) demonstrated that the examination of patient triage categories identified around three quarters of acute stroke patients presenting within 2 hours from symptom onset (71%) were allocated a triage category 1 or 2. Moreover, they found that acute stroke patients were four times more likely to receive an emergency triage priority category (category 1 or 2) if they presented with facial weakness (OR 4.36), twice as likely to receive a category 1 or 2 if they presented with speech problems (OR 1.94). Additionally, loss

of coordination and resolving symptoms were negatively associated with triage category 1 or 2.

For door to physician time, the patients who were assigned a triage category 1 or 2 had seen by physician 17.58 minute (range 4-70 minutes). In addition, the National Institute of Neurological Disorders and Stroke (NINDS) and American Stroke Association recommend that stroke patients who present to an Emergency Department (ED) should be seen by a medical practitioner within 10 min from arrival (Marler et al., 2000; Jauch et al., 2013).

### **5.3.1.7 Compliance to clinical practice guideline for acute ischemic stroke**

The findings suggest that most of patients (68.7%) were compliance to clinical practice guideline for acute ischemic stroke and adherence to guidelines for the early management of patients with acute ischemic stroke is not associated with better early neurological recovery at 24 hours and 3 days. The recommended guidelines for treatment of acute ischemic stroke including door to physician  $\leq 10$  minutes, door to interpretation  $\leq 45$  minutes, and delivery of thrombolytic therapy within 60 minutes of the patients arrival in the ED (Jauch et al., 2013). This measure (DTN time  $<60$  minutes) has been associated with improved outcomes in several publications (Ahmed et al., 2010; Fonarow et al., 2010).

Many prospective and retrospective studies in the sample from 140 to 439 participants demonstrated that the clinical practice guideline can shorten time to treatment and investigations, and also increase the numbers of patients receiving timely treatments such as intravenous thrombolysis (Katzan et al., 2003; Mehdiratta & Caplan, 2006) and aspirin (Grotta et al., 2001). In another study, the use of clinical practice guideline in acute stroke patients from 257 to 439 participants was able to decrease post-stroke complication occurrence such as urinary tract infection (0.097 VS 0.05), pressure sore (0.0259 VS 0.0253), pneumonia, and fall (Kwan, Hand, & Sandercock, et al., 2004; Widjaja et al., 2002). Importantly, providing care following clinical practice guideline was able to improve early recovery in patients with acute ischemic stroke.

### 5.3.2 Individual Characteristics

#### 5.3.2.1 Admission stroke severity

The results from binary logistic regression analysis revealed that the neurological recovery at 24 hours after admission decreased in moderate by .095 (95%CI=.044-.205,  $p<.001$ ) and severe stroke by .126 (95%CI=.034-.465,  $p<.01$ ) compared with mild stroke severity. Similar finding was reported that the NIHSS score at admission was strongly associated with outcomes of acute hospitalization after multivariate adjustment. The odds ratio (OR) for moderate (versus mild) stroke patients to achieve excellent status was 0.04 (95% CI, 0.02-0.10), and for severe stroke the OR was less than 0.01 (95% CI, 0-0.05). The OR (95% CI) for moderate stroke patients to have good or improved outcome was 0.19 (0.10–0.36), for severe stroke 0.04 (0.01-0.13). The ORs for moderate and severe (versus mild) stroke patients to have better subsequent change in neurologic impairments were 5.18 (1.94-13.85) and 4.12 (1.38-12.30); to remain stationary 0.43 (0.19-0.96) and 0.15 (0.06-0.36), respectively. Consistently, other study has found that the initial severity ratings were strongly related to final hospital discharge disposition, LOS, and hospital charges (all  $p$  values  $<.001$ ). Ninety percent of patients with mild strokes were ultimately discharged to home, whereas only one third of patients with severe strokes improved enough to go home from the acute hospital setting (Reynolds et al., 2001).

However, the study finding indicated the neurological recovery in moderate stroke less than severe stroke (ORs .095, 95%CI=.044-.205,  $p<.001$  and .126, 95%CI=.044-.205,  $p<.001$ ). The result conforms to severe stroke patients had shorter hospital arrival time than moderate stroke (mean 156 min, SD 139.28 versus mean 494 min, SD 679.56,  $p<.001$ ). Similar the finding were reported that the levels of severity of stroke using the National Institute of Health Stroke Scale (NIHSS) and found that higher NIHSS scores or more severe stroke resulted in shorter hospital arrival time than lower NIHSS scores or less severe stroke (OR 0.92, 95% CI 0.88 - 0.97;  $p < 0.001$ ) (Faiz, Sundseth, Thommessen, & Ronning, 2013). Likewise, Inatomiet al. (2008) found that patients with higher NIHSS scores had shorter hospital arrival time than those with lower NIHSS scores (OR 0.98, 95% CI 0.95 - 1.01;  $p < 0.05$ ). Furthermore, Derexet al. (2002) have reported that levels of severity of stroke were associated with hospital arrival time of patients ( $\rho = - 0.261$ ;  $p = 0.001$ ).

As we can see, severe stroke patients had received intravenous rt-PA therapy more than moderate stroke patients (33% and 20%). This indicates severe stroke patients were good neurological recovery.

### 5.3.2.2 Age

The result showed that a mean age of ischemic patient were 64.35 years (range, 20 to 98 years) and 20-60 years (40.9%), 61-80 years (40.9%), 12.3% more than 80 years. On binary logistic regression analysis, age >80 years decreased neurological recovery at 24 hours after treatment by .361(95%CI=.120-1.085,  $P<.05$ ) compared with younger than 60 years age. The finding was similar to that in a study of Tseng, & Chang (2006) showed that for every increase of 1 year in age, the odds for an excellent outcome at discharge declined approximately 5% ( $p = 0.002$ ). And related to previous study indicated that relative improvement decreased with increasing age: patients younger than 55 years showed an improvement of 67 % of the maximum possible improvement compared which only 50 % for patients above 55 years (adjusted  $R^2 = 0.120$ ,  $\beta_{age} = -0.130$ ,  $p < 0.001$ ) (Kugler, Altenhoner, Lochner, Ferbert & Hessian Stroke Data Bank Study Group ASH, 2003).

There are some reasons for explaining this result. Firstly, the study found that acute stroke patients who were older than 80 years old had longer hospital arrival times than those who were equal to or older than 60 years old (mean 680 minutes and 425 minutes, respectively). The results are consistent with Kim et al. (2011) have reported that older patients had longer hospital arrival time than younger patients (OR 1. 95% CI 1.024 - 1.089;  $p < 0.01$ ). Chang, Tseng, and Tan (2004) also found that patients who were younger than 65 years of age had longer hospital arrival time than those who were 65 years old or older ( $p = 0.05$ ).

However, the earlier study investigated among patients 80 years, the rate of neurological improvement in those receiving thrombolytic treatment was higher than the rate in those patients not receiving thrombolytic treatment (58.8% vs. 14.1%,  $p < 0.01$ ). They concluded that thrombolysis increases the rate of neurological improvement in patients aged 80 years (Ong et al., 2014).

### 5.3.2.3 Admission blood pressure

This finding, systolic blood pressure was  $\leq 140$  mmHg in 15.5%, 141-180 mmHg in 56.8%, 181-220 mmHg in 24.5% and  $>220$  mmHg in 3.2%. Consistently, in one observational study, the systolic blood pressure was  $>139$  mmHg in 77% and  $>184$  mmHg in 15% of patients on arrival at the ED (Qureshi et al., 2007). The majority of patients will demonstrate increased blood pressure in response to acute ischemic stroke (Qureshi, 2008). Blood pressure typically decreases spontaneously during the acute phase of ischemic stroke, starting within 90 minutes after onset of stroke symptoms (Ahmed, Nasman, & Wahlgren, 2000).

The result from univariate logistic regression analysis revealed that the admission blood pressure was not found to affect the early neurological recovery both 24 hours and 3 days. By contrast, previous study found that high baseline, maximum, and mean level of systolic BP profiles were each inversely associated with favorable outcome (OR=0.84, 95% CI: 0.74 to 0.94; OR=0.82, 95% CI: 0.73 to 0.91; OR=0.81, 95% CI: 0.71 to 0.93, respectively) and associated with an increased risk of parenchymal hemorrhage within the first 7 days (OR=1.27, 95% CI: 1.07 to 1.51; OR=1.49, 95% CI: 1.27 to 1.75; OR=1.52, 95% CI: 1.23 to 1.87; respectively) in recombinant tissue plasminogen activator-treated patients (Yong & Kaste, 2008). Willmot, Leonardi-Bee, Bath (2004) revealed that high admission systolic blood pressure (SBP) is associated with poorer outcome in patients who are not treated with rt-PA.

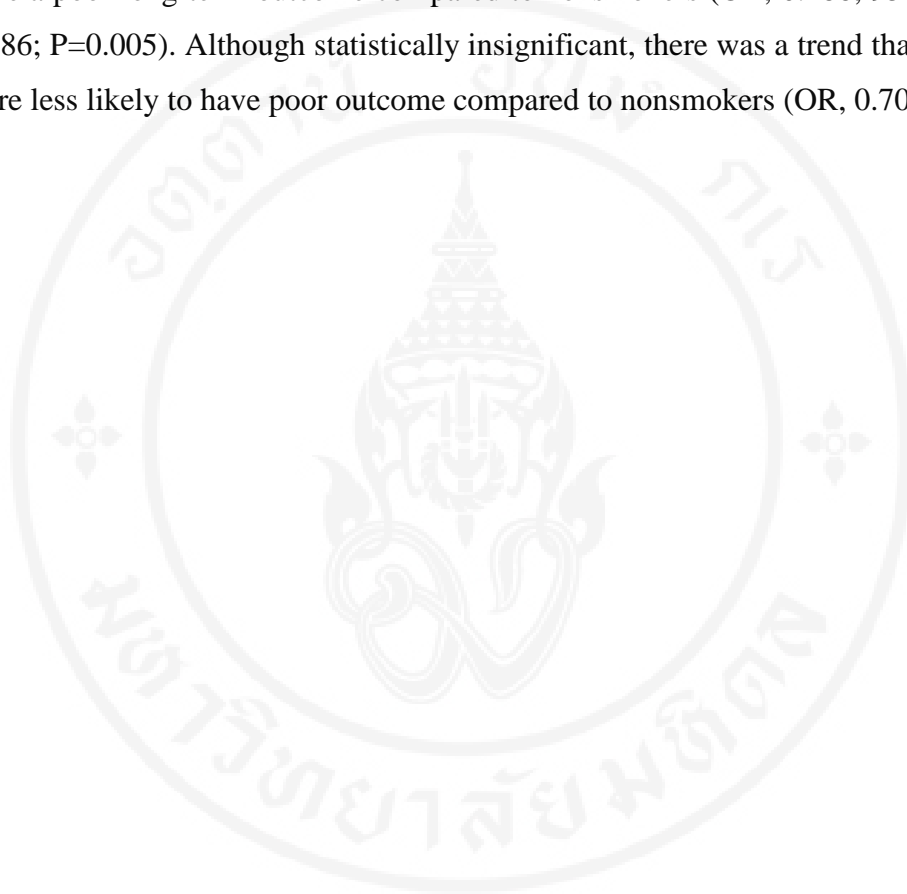
## 5.3.3 Health Behaviors

### 5.3.3.1 Smoking Status

Of 220 patients entered, 74(32.7%) were identified as current smokers, 29(13.2%) as ex-smokers, and 119 (54.1%) as nonsmokers. The finding of univariate logistic regression analysis revealed that the smoking status was not found to affect the early neurological recovery both 24 hours and 3 days. By contrast, the previous study reported that among the patients with ischemic stroke smokers who received thrombolysis had a significantly greater improvement at 24 hours after treatment and lower mortality over 1 year later than nonsmokers. However, the impact

of smoking on stroke prognosis for patients who did not receive thrombolysis was not settled (Ovbiagele & Saver, 2005).

In addition, Bang et al. (2007) demonstrated that smoking status remained a strong independent predictor; current smokers were less likely to have a poor long-term outcome compared to nonsmokers (OR, 0.286; 95% CI, 0.119–0.686;  $P=0.005$ ). Although statistically insignificant, there was a trend that ex-smokers were less likely to have poor outcome compared to nonsmokers (OR, 0.709;  $P=0.556$ ).



## **CHAPTER VI**

### **CONCLUSION AND RECOMMENDATIONS**

This chapter is organized into two sections. The first section is conclusion. The second focus on recommendations for nursing practice, nursing education, health policy, and further study.

#### **6.1 Conclusion**

The purpose of this study was to investigate the predictive predictors of early neurological recovery at 24 hours and day 3 after admission in patients with acute ischemic stroke. These factors included the distance from place of symptom attack to the hospital, the level of first hospital visits, specialty of physician, triage nurse, triage rating score, onset-to-rt-PA time, compliance to clinical practice guideline, age, admission blood pressure, admission stroke severity, and smoking status. Five instruments were used to assess all subjects including: 1) the Patient's Personal information questionnaire, 2) Clinical characteristics questionnaire, 3) Time form record, 4) The National Institutes of Health Stroke Scale (NIHSS), 5) Clinical practice guideline for patients with acute ischemic stroke

The study was conducted from January to May 2016 at 8 hospitals in southern region of Thailand that able to provide thrombolytic drug in patient with acute ischemic stroke. A total of 220 acute ischemic stroke patients were approached to participate into the study.

The participants of this study were male (55.9%) and female (44.1%). The mean age was 64.35 years, ranging from 20 to 98 years and most was married (75.0%). The majority (71.4%) had a primary school level education, and was farmer or gardener (38.6%). Half of the participants had income 5,000-15,000 Bath per month (49.5%) and most (76.8%) used Universal Coverage as their health care service payment.

Most of the patients (99.5%) were diagnosed ischemic stroke at emergency room. One-third of them were smokers (32.7%). The participants had underlying disease, i.e. Hypertension (73.2%), Dyslipidemia (36.4%), Diabetes Mellitus (26.8%) and Ischemic stroke/TIA (12.7%). Most of patient (56.8%) in this study had systolic blood pressure between 141 and 180 mmHg. The participants had symptoms occurring at home including weakness of limb (94.5%), abnormal speech (73.2%), weakness of facial muscle (29.2%), loss of balance/dizziness (26.4%) and abnormal vision (1.4%). Seventy-five percent of participants decided access to the hospital by weakness of limb. The witness was family member (82.2%) while five percent (5%) were alone when symptom occurred. Most patients (36.8%) had symptom onset during 6:01-12:00 am.

The mean of distance from place of symptom onset to the hospital that can provide rt-PA was 24.58 (SD 22.03) kilometers (range 0-130 kilometers) and nearly half of all patients (42.7%) had the distance 10 kilometers from hospital. Most of patients (96.8%) went to hospital by Self-transportation. Only 0.9% of participants used emergency medical service. In two-third of participants (65.4%) went to the hospital with could perform intravenous rt-PA treatment consist of General hospital (44.5%) and Excellent hospital (20.9%), while nearly thirty five percents (34.5%) went to health care service with could not perform intravenous rt-PA including community hospital (28.6%), primary care unit (3.2%) and private clinic (2.7%). The mean time of onset time to hospital was 477.55 minutes (SD 620.17) with a range of 1 - 3,470 minutes. For referring time, the mean time of referral system was 107.47 minutes (SD 91.55) with a range of 25-555 minutes. Only 32.1% of participants had been referred within 60 minutes recommended guideline of referral system.

For in-hospital services, the triage levels of acute ischemic stroke patients presented at the emergency department were emergency, urgency, semi-urgency, non-urgency, and critical (70.5%, 24.5%, 2.5%, 1.8% and 0.9%), respectively. Approximately forty five percents of participant (45.5%) were assigned to stroke fast track system where as more than a half (54.5%) were not assigned because they went to hospital with delay time > 4.5 hours. Intravenous rt-PA therapy was performed in 29 cases (13.18%). The mean onset to needle (rt-PA) time was 185.83 minutes (SD

46.51), ranging 62-240 minutes. Only 2 participants received intravenous rt-PA within 90 minutes.

For overall triage nurse experience, the averages number of years of emergency nursing experience was 7.1 (SD 5.50), ranging from 1 to 30 years. A half of triage nurses (49.1%) had experience of emergency care less than five years. For characteristics of physician who treated acute ischemic stroke patients were internal medicine 68.2%, neurologist 22.7%, general physician 8.2%, and emergency physician 0.9%. Most of patients (68.7%) were compliance to clinical practice guideline for acute ischemic stroke.

In non receiving rt-PA therapy group, a total of 191 who had recovery group had younger than the non recovery group ( $61.06 \pm 13.55$  versus  $67.94 \pm 13.67$ ,  $p = .001$ ) and had mean score of NIHSS less than non recovery group ( $4.83 \pm 4.88$  versus  $8.66 \pm 4.42$ ,  $p = .000$ ). The 2 groups did not differ between male and female (recovery group, 44:39; non recovery group, 61:47,  $P = .635$ ). Similarly, all risk factors including hypertension, diabetes, dyslipemia, and smoking are no difference ( $P = .368$ ,  $.457$ ,  $.567$  and  $.855$ , respectively). For Onset-to-door time, there are no significant differences between the recovery group and the non recovery group ( $583.05 \pm 645.79$  versus  $495.91 \pm 648.57$ ,  $P = .358$ )

For interpretation of the influencing factors, multivariate logistic regression was used to answer the predictive factors influencing early neurological recovery in patients with acute ischemic stroke at 24 hours and day 3 after treatment. The eleven theoretical related factors composed of the distance from place of symptom attack to the hospital, the level of first hospital registers, specialty of physician, triage nurse, triage rating score, onset-to-rt-PA time, compliance to clinical practice guideline, age, admission blood pressure, admission stroke severity, and smoking. Each variable was first investigated for its associations with neurological recovery as well as each outcome of interest. For purpose of the study, variables whose respective associations had  $p\text{-value} \leq 0.15$  were considered to be confounding factors. The results revealed that four variables had  $p\text{-value} < 0.15$  including admission stroke severity ( $p\text{-value} = .000$ ), onset-to-rt-PA time ( $p\text{-value} = .001$ ), age, ( $p\text{-value} = .002$ ), and specialty of physician ( $p\text{-value} = .069$ ).

The results of multivariate logistic regression analysis of related factors associated with the early neurological recovery at 24 hours after treatment in acute ischemic stroke patients. The goodness-of-fit model for the factors influencing a neurological recovery at 24 hours with -2 Log L and AIC statistic shown that M<sub>3</sub> model is minimum AIC value (AIC = 235.163). The result provides three predictor's contribution to the early neurological recovery at 24 hours. The odds ratio significantly demonstrated that three independent variables effect on early neurological recovery at 24 hours after treatment including stroke severity, onset time to rt-PA and age. The odds ratio (Exp(B)) value and Wald criterion significantly demonstrated that neurological recovery at 24 hours after admission decreased in moderate by .095(95%CI=.044-.205, p<.001) and severe stroke by .126 (95%CI=.034-.465, p<.01) compared with mild stroke severity. In addition, the stroke patients who had onset time to rt-PA within 3 hours and 3.0-4.5 hours increased the neurological recovery at 24 hours 22.22 times (95%CI=5.454-90.527, P<.001) and 17.282 times (95%CI=3.079-97.001, P<.01) compared with not received rt-PA treatment. Lastly, age >80 years decreased neurological recovery at 24 hours after treatment by .361(95%CI=.120-1.085, P<.05) There for, the final model could be represented as;

Log odds of early neurological recovery at 24 hours = .992 - 2.355stroke severity (moderate) - 2.068stroke severity(severe) +3.101 time to rt-PA(within 3 hours) + 2.850 time to rt-PA(3.0-4.5 hours) - .582age(60-80 years) -1.019 Age(>80 years)

The findings of multivariate logistic regression analysis of related factors associated with the early neurological recovery at 3 days after treatment in acute ischemic stroke patients. The result provides three predictor's contribution to the early neurological recovery at 3 days. The odds ratio significantly demonstrated that three independent variables effect on early neurological recovery at 3 days after treatment including stroke severity, onset time to rt-PA and age. The odds ratio (Exp(B)) value and Wald criterion significantly demonstrated that neurological recovery at 3 days after admission decreased in moderate by .10 (95%CI=.050-.209, p<.001) and severe stroke by .09 (95%CI=.028-.312, p<.001) compared with mild stroke severity. Whereas the stroke patients who had onset time to rt-PA within 3 hours and within 3.0-4.5 hours increased the neurological recovery at 3 days 16.95 times

(95%CI=5.454-90.527,  $P<.05$ ) and 14.43 times (95%CI=3.018-68.982,  $P<.01$ ) compared with not received rt-PA treatment. In the other hand, age is not significant in this model. There for, the final model could be represented as;

Log odds of early neurological recovery at 3 days = 1.557 - 2.283stroke severity (moderate) - 2.377stroke severity(severe) +2.830time to rt-PA(within 3 hours) + 2.669time to rt-PA(3.0-4.5 hours).

## **6.2 Recommendations**

The findings of this study contributed to nursing practice, nursing education, future nursing research, and health care system as presented below.

### **6.2.1 For nursing practice**

1) The finding emphasize an importance of delay in arrival to the hospital is the major reason seen in exclusion of patients with acute ischemic stroke for intravenous thrombolysis. Nurses who work with high risk patient and chronic illness clinic must clear information about early recognition of stroke signs and symptoms and call 1669, and arrive quickly enough to be eligible for these therapies. Especially in old age group, family members must have awareness and rapid response to acute-onset stroke symptoms.

2) Stroke team should speed the clinical assessment, the performance of diagnostic studies, and decisions for early management and try to adherence the guidelines for the early management of acute ischemic stroke.

3) Nurses who work in community hospital that cannot provide intravenous rt-PA treatment are alert to stroke symptoms, early identification and rapid refer to stroke center for appropriate treatment.

### **6.2.2 For health care system**

1) Ongoing the need for public awareness campaigns to increase knowledge of stroke symptoms and facilitate patients being able to access urgent treatment.

2) Local mass media should inform the public of appropriate EMS (1669) number for early access to the hospital.

3) Referral network system should be developed to early access to the hospital that able to treat by intravenous rt-PA.

### **6.2.3 Recommendations for further study**

1) A prospective study evaluate long term outcome in the ischemic stroke patients with non receiving rt-PA treatment.

2) A situation analysis of emergency and unit management for stroke patient in hospital that lack of neurologists and nurse case manager for stroke.

## **6.3 Limitation of the Study**

There are several limitation of this study

1. The cutoff score of the NIHSS effect on outcome, as demonstrated by the trials of thrombolytic therapy. This study categorized the NIHSS as mild (0-6), moderate (7-15), or severe ( $\geq 16$ ) (Tseng & Chang, 2006). However, the NIHSS can divide another categories, such as Minor stroke (0 - 4), Moderate stroke (5 - 15), Moderate to severe stroke (16 - 20), Severe stroke (21 - 42). Difference of the NIHSS categories may be influence recovery outcome.

2. A 3 days outcome might not be adequate for the assessment of the residual dependency of patients who survived, because more time is likely to be needed for full functional recovery. However, according to a previous analysis of the data from stroke clinical trials, global disability status at 3 days can be a reliable proxy of 3-month disability outcomes.

3. A further limitation is the fact that because adherence to clinical practice guideline has been defined as either receiving recommended care or the care provided was not specified as recommended care, this may have meant that recommended care was considered, but an alternative was provided, perhaps on the basis of a patient's preference, for example. The researcher agrees that personalizing care does not always comply with non adherence.

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**APPENDIX A**  
**LIST OF CONTENT VALIDITY EXPERTS**

**1. Assoc.Prof. Sombat Muengtaweepongsa**

Division of Neurology, Department of Internal Medicine, Faculty of  
Medicine, Thammasat University

**2. Assist. Prof. Dr.Sarunya Koositamongkol**

Assistant professor, Department of Medical Nursing, Faculty of Nursing,  
Mahidol University

**3. Mrs. Urai Kummak**

Head nurse of Stroke Unit, Thammasat University Hospital

## APPENDIX B

### RESEARCH INSTRUMENT

**แบบสอบถามวิจัย เรื่อง ปัจจัยที่มีผลต่อการฟื้นตัวทางระบบประสาทระยะแรกในผู้ป่วยโรคสมองขาดเลือดเฉียบพลัน (Factors influencing early neurological recovery in patients with acute ischemic stroke)**

**ส่วนที่ 1 แบบบันทึกข้อมูลทั่วไป**

ID code .....

**เก็บข้อมูลจากเวชระเบียน**

1. เพศ  ชาย  หญิง
2. อายุ.....ปี
3. สิทธิการรักษา  เบิกราชการ  ประกันสังคม  หลักประกันสุขภาพถ้วนหน้า
4. ประวัติโรคประจำตัว
  - HT  DM  Dyslipidemia  TIA  CAD/MI
  - Old ischemic stroke  Old ICH  AF
5. ยาที่รับประทานเป็นประจำ (ตอบได้มากกว่า 1 ข้อ)
  - ACEI  ARB  CCB  Thiazide  Loop diuretic
  - Statin  Fibrate  Antiplatelet  Oral hypoglycemic drug
  - Other.....
6. โรงพยาบาลแรกที่ผู้ป่วยไปรับการรักษาเมื่อเกิดอาการในครั้งนี้
  - สถานีอนามัย/ โรงพยาบาลสุขภาพตำบล
  - โรงพยาบาลชุมชน
    - สามารถให้ rt-PA ได้  ไม่สามารถให้ rt-PA ได้
  - โรงพยาบาลทั่วไป
    - สามารถให้ rt-PA ได้  ไม่สามารถให้ rt-PA ได้
  - โรงพยาบาลศูนย์
    - สามารถให้ rt-PA ได้  ไม่สามารถให้ rt-PA ได้

7. โรงพยาบาลที่รักษาปัจจุบันเป็นโรงพยาบาลแรกที่ผู้ป่วยเข้ารับการรักษาหรือไม่  
 ใช่  ไม่ใช่

**เก็บข้อมูลจากการสัมภาษณ์ผู้ป่วย**

8. สถานภาพสมรส  โสด  คู่  หย่า  หม้าย  แยกกันอยู่
9. ระดับการศึกษา  
 ไม่ได้เรียนในระบบ  ประถมศึกษาตอนต้น  ประถมศึกษาตอนปลาย  
 มัธยมศึกษาตอนต้น  มัธยมศึกษาตอนปลาย/ปวช.  อนุปริญญา/ปวส.  
 ปริญญาตรี  ปริญญาโท  ปริญญาเอก
10. อาชีพ  
 รับราชการ  รัฐวิสาหกิจ  ค้าขาย  เกษตรกรรม  ทำนา  ทำสวน  ทำ  
 ไร่  รับจ้าง  งานบ้าน  ธุรกิจส่วนตัว
11. รายได้ .....บาท/เดือน
12. ประวัติโรคในครอบครัว  
 โรคหลอดเลือดสมอง  พ่อ  แม่  พี่หรือน้อง  บุตร  
 โรคหลอดเลือดหัวใจ หรือโรคกล้ามเนื้อหัวใจขาดเลือด  พ่อ  แม่  
 พี่หรือน้อง  บุตร
13. ประวัติการสูบบุหรี่  
 ไม่เคยสูบบุหรี่  
 เคยสูบบุหรี่มา.....ปี สูบวันละ.....มวน และเลิกสูบบุหรี่.....ปี.....เดือน  
 สูบบุหรี่มาเป็นเวลา.....ปี.....เดือน สูบวันละ.....มวน และปัจจุบันยังสูบบุหรี่
14. ประวัติการดื่มสุรา  
 ไม่เคยดื่มสุรา  
 เคยดื่มสุรามานาน.....ปี และเลิกดื่มมา.....ปี.....เดือน  
 ดื่มสุรามานาน.....ปี.....เดือน ดื่มวันละ.....ขวด และปัจจุบันยังดื่มอยู่
15. เวลาที่เกิดอาการ.....น.
16. บุคคลที่อยู่ด้วยขณะเกิดอาการ  
 บุคคลในครอบครัว  เพื่อนบ้าน  เพื่อนร่วมงาน  อยู่คนเดียว  
 คนอื่นๆ ระบุ.....

17. ผู้ป่วยมาโรงพยาบาล โดย

- มาเอง     เพื่อนร่วมงานนำส่ง     เพื่อนบ้านนำส่ง     รถมูลนิธิ
- รถ อบต.     รถ EMS     รถ refer ระหว่าง รพ. กับ รพ.
- อื่นๆระบุ.....

18. ระยะทางจากสถานที่ที่เกิดอาการ ถึง รพ. ที่รักษาปัจจุบัน .....กิโลเมตร

**ส่วนที่ 2 แบบบันทึกข้อมูลเกี่ยวกับโรคและการรักษาโรคหลอดเลือดสมอง**

**เก็บข้อมูลจากสัมภาษณ์ผู้ป่วย**

1. อาการที่เกิดขึ้นกับท่านในครั้งนี้ คือ (ตอบได้มากกว่า 1 ข้อ)

- หน้าเบี้ยว มีอาการอ่อนแรงของใบหน้าซีกใดซีกหนึ่ง
- แขนอ่อนแรง/ ชา    ซีก     ซ้าย     ขวา
- ขา อ่อนแรง    ซีก     ซ้าย     ขวา
- พูดไม่ชัด / พูดตะกุกตะกะ / พูดไม่ออก/ พูดไม่เป็นคำพูด
- เวียนศีรษะ เดินเซ บ้านหมุน เดินทรงตัวไม่ได้

2. อาการที่ทำให้ท่านตัดสินใจมาโรงพยาบาล

- หน้าเบี้ยว มีอาการอ่อนแรงของใบหน้าซีกใดซีกหนึ่ง
- แขนอ่อนแรง/ ชา
- ขา อ่อนแรง
- พูดไม่ชัด / พูดตะกุกตะกัก / พูดไม่ออก/ พูดไม่เป็นคำพูด
- เวียนศีรษะ เดินเซ บ้านหมุน เดินทรงตัวไม่ได้
- อาการอื่นๆ.....

**เก็บข้อมูลจากเวชระเบียน**

3. Vital signs แรกรับที่ห้องฉุกเฉิน

T.....°C, P.....ครั้ง/นาที, R.....ครั้ง/นาที,

BP...../.....mmHg, O<sub>2</sub>sat.....%, DTX ..... mg/dl

4. ระดับการคัดแยกโดยพยาบาล

- critical     emergency     urgency     semi- urgency     non- urgency

5. ER diagnosis

- Ischemic stroke     TIA     Stroke mimics     อื่นๆ ระบุ.....

## 6. ตำแหน่งการเกิดโรคหลอดเลือดสมอง

- Large-artery atherosclerosis (embolus/thrombosis)
- Cardioembolism (high-risk/medium-risk)
- Small-vessel occlusion (lacune)
- Stroke of other determined etiology
- Stroke of undetermined etiology

## 7. ผู้ป่วยได้เข้าสู่ stroke fast track หรือไม่

- ใช่       ไม่ใช่ เพราะ.....

## 8. การรักษาโดย รับ rt-PA

- ได้รับ       ไม่ได้รับ เนื่องจาก.....

## 9. ภาวะแทรกซ้อนหลังการรักษา

- No complication
- Bleeding เกิดอาการวันที่.....เวลา.....
- Progressive stroke เกิดอาการวันที่.....เวลา.....
- IICP            เกิดอาการวันที่.....เวลา.....
- Pneumonia    เกิดอาการวันที่.....เวลา.....
- UTI             เกิดอาการวันที่.....เวลา.....
- DVT            เกิดอาการวันที่.....เวลา.....
- อื่นๆ ระบุ.....เกิดอาการวันที่.....เวลา.....

## 2.3 เก็บข้อมูลจากพยาบาลวิชาชีพ

## 10. Triage ผู้ป่วย โดย

- พยาบาลวิชาชีพ ประสบการณ์ทำงานที่แผนกอุบัติเหตุฉุกเฉิน .....ปี
- อื่นๆระบุ.....ประสบการณ์ทำงานที่แผนกอุบัติเหตุฉุกเฉิน .....ปี

## 11. พยาบาล Triage ผ่านอบรมหลักสูตรเฉพาะทาง (ตอบได้มากกว่า 1 ข้อ)

- หลักสูตรพยาบาลเวชปฏิบัติทั่วไป
- หลักสูตรพยาบาลเวชปฏิบัติฉุกเฉิน
- หลักสูตรพยาบาลอุบัติเหตุฉุกเฉิน
- หลักสูตรพยาบาลศัลยกรรมอุบัติเหตุ
- หลักสูตรการพยาบาลผู้ป่วยโรคหลอดเลือดสมอง

- การพยาบาลผู้ป่วยประสาทวิทยาและประสาทศัลยศาสตร์
- อื่นๆระบุ.....

**2.4 เก็บข้อมูลจากแพทย์**

12. แพทย์ที่ให้การรักษา

- Neurologist
- Internal Medicine
- Emergency physician
- General physician

**ส่วนที่ 3 แบบบันทึกเวลาในการรักษาโรคหลอดเลือดสมอง**

รายการ	เวลา	หมายเหตุ
เริ่มมีอาการ	น.	
มาถึง ER รพ. แรก	น.	
มาถึง ER รพ. ที่ 2 (กรณี refer)	น.	
เริ่ม triage	น.	
triage เสร็จ	น.	
เริ่มได้รับการตรวจโดยแพทย์	น.	
เริ่มส่ง LAB	น.	
แพทย์ดูผล LAB	น.	
เริ่มทำ CT brain	น.	
CT brain เสร็จ	น.	
แพทย์อ่านผล CT brain	น.	
เริ่มได้ยา rt-PA	น.	
เริ่มการรักษากรณีที่ไม่ได้ rt-PA	น.	
จำหน่ายจาก ER	น.	
ออกจาก ER	น.	
ถึง stroke unit	น.	

**ส่วนที่ 4 NIHSS (The National Institutes of Health Stroke scale)**

Item	Scale Definition	score	แรกจับ	ก่อนเริ่ม การรักษา	หลังรักษา 24 hr	หลังรักษา 3 วัน
เวลาที่ ประเมิน			วันที่..... เวลา.....	วันที่..... เวลา.....	วันที่..... เวลา.....	วันที่..... เวลา.....
Level of consciousness	Alert	0				
	Drowsy	1				
	Obtunded	2				
	Coma/unresponsive	3				
Orientation questions (2)	Answers both correctly	0				
	Answers 1 correctly	1				
	None correct	2				
Response to commands (2)	Performs both tasks correctly	0				
	Performs 1 task correctly	1				
	Performs neither	2				
Gaze	Normal	0				
	Partial gaze palsy	1				
	Complete gaze palsy	2				
Visual fields	No visual field defect	0				
	Partial hemianopia	1				
	Complete hemianopia	2				
	Bilateral hemianopia	3				
Facial movement	Normal	0				
	Minor facial weakness	1				
	Partial facial weakness	2				
	Complete unilateral palsy	3				

**ส่วนที่ 4 NIHSS (The National Institutes of Health Stroke scale) (ต่อ)**

Item	Scale Definition	score	แรกจับ	ก่อนเริ่ม การรักษา	หลังรักษา 24 hr	หลังรักษา 3 วัน
Motor function (arm) :Left arm	No drift	0				
	Drift before 5 seconds	1				
	Falls before 10 seconds	2				
	No effort against gravity	3				
	On movement	4				
Motor function (arm) : Right arm	No drift	0				
	Drift before 5 seconds	1				
	Falls before 10 seconds	2				
	No effort against gravity	3				
	On movement	4				
Motor function (leg) : Left leg	No drift	0				
	Drift before 5 seconds	1				
	Falls before 5 seconds	2				
	No effort against gravity	3				
	On movement	4				
Motor function (leg) : Right leg	No drift	0				
	Drift before 5 seconds	1				
	Falls before 5 seconds	2				
	No effort against gravity	3				
	On movement	4				
Limb Ataxia	No ataxia	0				
	Ataxia in 1 limb	1				
	Ataxia in 2 limbs	2				
Sensory	No sensory loss	0				
	Mild sensory loss	1				
	Severe sensory loss	2				

**ส่วนที่ 4 NIHSS (The National Institutes of Health Stroke scale) (ต่อ)**

Item	Scale Definition	score	แรกเริ่ม	ก่อนเริ่ม การรักษา	หลังรักษา 24 hr	หลังรักษา 3 วัน
Language	Normal	0				
	Mild aphasia	1				
	Severe aphasia	2				
	Mute or global aphasia	3				
Articulation	Normal	0				
	Mild dysarthria	1				
	Severe dysarthria	2				
Extinction or inattention	Absent	0				
	Mild(Loss 1 sensory modality lost)	1				
	Severe (Loss 2 modality lost)	2				
<b>Total score</b>		42				

**ส่วนที่ 5 Clinical Practice Guideline for Ischemic Stroke**

<b>CPG for Ischemic Stroke</b>	<b>Yes</b>	<b>No</b>	<b>Noted</b>
<b>Onset time &lt; 4.5 hr.</b>			
1. เข้า Stroke fast track			
2. Emergency lab CBC, BS, BUN, Cr, Coagulogram, Electrolyte, EKG			
3. Emergency non contrast CT brain or MRI $\leq$ 45 min			
4. Consider indications and contraindications for thrombolytic therapy			
5. Intravenous thrombolytic therapy (Door to needle time $\leq$ 60 min)			
<b>General management</b>			
6. ให้ oxygen ให้ $O_2\text{sat} > 94\%$			
7. ควบคุมระดับความดันโลหิตให้ $< 180/105$ mmHg. อย่างน้อย 24 hr. หลังให้ยา rt-PA			
8. การควบคุมระดับน้ำตาล <input type="checkbox"/> ภาวะน้ำตาลในเลือดต่ำ (BS $< 60$ mg./dl.) ให้แก้ไขให้อยู่ในเกณฑ์ปกติ <input type="checkbox"/> ถ้า BS สูง ควบคุมให้อยู่ในระดับ 140-180 mg./dl.			
9. ถ้า $T > 38.0$ °C ต้องหาสาเหตุและได้รับยาลดไข้			
10. ให้ antiplatelet ภายใน 48 hr. ถ้าไม่มีข้อห้าม			
11. stroke rehabilitation within 48 hr.			
12. Swallowing test within 24 hr. or before giving any food NPO กรณี - Severe vomiting - Massive infarct / ICH surgery? - Upper GI hemorrhage - Seizures at onset			

**ส่วนที่ 5 Clinical Practice Guideline for Ischemic Stroke (ต่อ)**

CPG for Ischemic Stroke	Yes	No	Noted
<b>Onset time 4.5-72 hr.</b>			
1. Emergency lab CBC, BUN, Cr, Coagulogram, Electrolyte, EKG			
2. Emergency non contrast CT brain or MRI within 24 hr.			
<b>General management</b>			
3. ให้ oxygen ให้ O <sub>2</sub> sat > 94%			
4. ให้ยาลดความดันโลหิต ให้ความดันลดลง 15% ภายใน 24 ชั่วโมงแรก โดยให้ BP<220/120 mmHg			
5. การควบคุมระดับน้ำตาล <input type="checkbox"/> ภาวะน้ำตาลในเลือดต่ำ (BS < 60 mg./dl.) ให้แก้ไขให้อยู่ในเกณฑ์ปกติ <input type="checkbox"/> ถ้า BS สูง ควบคุมให้อยู่ในระดับ 140-180 mg./dl.			
6. การทดแทนสารน้ำ เมื่อ BP<100/70 mmHg. โดยให้เป็นชนิด isotonic solution			
7. ให้ antiplatelet ภายใน 48 hr. ถ้าไม่มีข้อห้าม			
8. stroke rehabilitation within 48 hr.			
9. Swallowing test within 24 hr. or Before giving any food NPO กรณี - Severe vomiting - Massive infarct / ICH surgery - Upper GI hemorrhage - Seizures at onset			

## APPENDIX C

### **Preliminary Analysis: Testing the Assumptions for logistic regression analysis**

General assumptions of multivariate logistic regression analysis should be tested to ensure the validity of statistic calculation. The data were in accordance with the following linearity and multicollinearity.

#### **Multicollinearity**

Multicollinearity refers to a situation in which two or more explanatory variables in a multiple logistic regression model are highly linearly related, meaning that one can be linearly predicted from the others with a substantial degree of accuracy. Three indicators were used to detect multicollinearity: (1) correlation coefficient between independent variables above 0.85 (Munro, 2001); (2) tolerance values less than 0.19 and variance inflation factors (VIF) more than 5.3; and (3) all condition indices above a threshold value of 30, and identifying variables with variance proportion were above or equal to .90. If there were two or more coefficients, indicated the multicollinearity problem (Hair JR., Black et al. 2010).

The multicollinearity assessment was calculating the tolerance that should be more than 0.19 and variance inflation factors (VIF) that should be less than 5.3. The results displayed in the Table 4.10 revealed that all tolerance values were more than 0.19 that ranged from 0.32 to 0.68. There were no VIF values higher than 5.3 that ranged from 1.47 to 3.13. Thus, the assumption of no multicollinearity problem was accepted.

**Table A1** Testing for Multicollinearity of Tolerance Values and Variance Inflation Factors (VIF) (n=220)

Variable	Collinearity Statistic	
	Tolerance	VIF
Age	.437	2.114
Admission SBP	.605	1.653
Stroke severity	.404	2.476
Nurse experience	.350	2.855
Distance	.445	2.247
Onset-to- rt-PA time	.681	1.468
Triage rating score	.319	3.133
physician Specialty	.513	1.947
first hospital register	.474	2.112
Smoking	.631	1.584
Compliance to CPG	.345	2.902

In conclusion, The logistic regression analysis which concerns an important criterion for analysis is non-multicollinearity problem (Hair JR., Black et al. 2010). The testing the assumptions of this study, linearity and multicollinearity, had no evidence problems. This study can continue to use binary logistic regression analysis by using SPSS.

## **BIOGRAPHY**

<b>NAME</b>	Miss Orapen Sukhavulli
<b>DATE OF BIRTH</b>	30 August 1973
<b>PLACE OF BIRTH</b>	Nakhon Si Thammarat, Thailand
<b>INSTITUTIONS ATTENDED</b>	Kuakarun College of nursing, 1996 Bachelor of Nursing Science. Mahidol University, 2002 Master of Nursing Science (Adult Nursing) Mahidol University, 2016 Doctor of Philosophy (Nursing)
<b>SCHOLASHIP RECEIVED</b>	The commission on Higher education, Ministry of Education, Walailak University
<b>POSITION &amp; OFFICE</b>	Instructor, School of Nursing, Walailak University Thaiburi, Thasala, Nakhon Si Thammarat, 80160