Predicting Risk Factors of Working Aged Hemorrhagic Stroke Patients in a Tertiary Teaching Hospital in Chiang Mai

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Abstract

Stroke is the third leading cause of morbidity and mortality in Thailand accounting for a significant and increasing share of hospital costs. The purpose of this project is to study the epidemiology of the prevalence and its predicting factors of working aged hemorrhagic stroke (HS) patients admitted at a tertiary teaching hospital in Chiang Mai, Thailand.

We conducted a five-year retrospective descriptive study. The subjects in this study were patients diagnosed with HS, between 15-59 years of age, and admitted to a tertiary teaching hospital in Chiang Mai, Thailand from January 2009 to December 2013. A total of 404 working aged adults who had HS were admitted to the hospital during this review period; 60.9% males and 39.1% females. Nearly 70% of patients were between 46-59 years of age ($M = 47.5$, $SD = 9.8$). Of the patients admitted to the hospital, 76.7% were transferred there from other hospitals. Intracerebral hemorrhage was present in 59.7% of patients. Severe HS occurred in 35.9% of the patients with a Glasgow Coma Score from 3-8. Approximately 69% of the working aged HS patients required surgery. The top five identified risk factors for HS were hypertension (83.4%), hyperlipidemia (38.9%), alcohol consumption (21.5%), smoking (15.3 %), and drug non-adherence (14.9%).

We found significantly associated risk factors in working-aged HS by multivariate analysis among male gender ($p < .001$), drug non-adherence ($p = .047$), and hypertension ($p = .048$). Raising awareness to reduce risk behavior and health promotion in the community are the keynotes for health care providers in working-aged HS prevention.

Keywords: predicting risk factors, hemorrhagic stroke, working aged

Hemorrhagic stroke (HS) is caused by the rupture of weakened arteries in the brain or surrounding the brain. The blood accumulates and compresses the surrounding brain tissue causing the brain tissue in that area to weaken and die (American Heart Association & American Stroke Association, 2017). HS is life-threatening and often requires an operation, most frequently a craniotomy to remove the hematoma or inserted external ventriculostomy drainage to reduce the increased intracranial pressure in the brain. There are two types of HSs: an intracerebral hemorrhage (ICH) and a subarachnoid hemorrhage. Together they comprise between 22-30% of all strokes in East Asia (Burke & Venketasubramanian, 2006; Zhang et al., 2011). HS is often fatal or can cause permanent neurologic disability. The HS mortality rate in the United States is between 40 and 50% (Woo et al., 2004). In Korea, the fatality rate is 40% at 1 month and 54% at 1 year period. Between 12-39% of survivors can achieve long-term functional independence (An, Kim, & Yoon, 2017).

The prevalence of stroke in Thailand is estimated to be 1.88% of the population 45 years and older (Suwanwela, 2014). In Thailand among stroke sufferers of all kinds, 59.6% are male and 42.8% are people between 15-59 years of age (Areechokchai, Vijitsoonthornkul, Pongpan, & Maeakhian, 2017). The population of Thailand may be divided into three major age groups: youth (aged under 15), working age (aged 15-59), and elderly (aged 60 and older).

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Table 1. *Characteristic of Working Aged HS Patients (N = 404)*

Characteristic of Working Aged HS Patients	n (%)
Gender	
Male	246 (60.9)
Age	
≤ 45	125 (30.9)
> 45	279 (69.1)
M (SD)	47.5 (9.8)
Accessibility	
Transferred from other hospitals	310 (76.7)
Admitted directly	94 (23.3)
Diagnosis	
SAH	163 (40.3)
ICH	241 (59.7)
GCS at Admission	
GCS ≤ 8	145 (35.9)
GCS > 8	259 (64.1)
M (SD)	10.4 (3.9)
Operation	
Non-Operation	124 (30.7)
Operation (subgroups)	280 (69.3)
Craniotomy	206 (51.0)
EVD	84 (20.8)
Craniectomy	24 (5.9)
V-P shunt	11 (2.7)
Coiling	9 (2.2)
Re-operation	69 (17.1)

Note. EVD = external ventriculostomy drainage; GCS = Glasgow Coma Score; HS = hemorrhagic stroke; ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage.

The percentage of Thai youth and working aged population will continue to decline from the year 2010 to 2040, while that of the elderly will increase continuously from 13.2% in 2010 to 32.1% in 2040 (Foundation for Older Persons' Development, 2015). The incidence of stroke in the Thai working aged demographic is a major public health problem and has a negative impact on the economy. It can also be a burden on the families as victims can be left disabled and require ongoing care and support. This problem is compounded as the Thai society is becoming an increasingly elderly society (Foundation for Older Persons' Development, 2015).

Previous studies found that HS is related to hypertension, alcohol consumption, anticoagulant use, diabetes mellitus, serum cholesterol levels more than 200 mg/dl, body mass index greater than 25, genetics, and hyperuricemia. Another emerging risk factor is poor kidney function (Centers for Disease Control and Prevention, 2017; Daniel, & Bereczki, 2004; Feigin, 2005; Ikram, Wieberdink, & Koudstaal, 2012; Wang, Dong, Qi, Huang, & Hou, 2013). The severity of disability, likelihood of death, lengths of hospital stay, and cost of treatment of HS patients are higher than ischemic stroke (Gioldasis, 2008; Reed, Blough, Meyer, & Jarvik, 2001; Yoneda et al., 2005). ICH patients had a higher baseline stroke severity, resulting in longer hospitalization, higher disability

rates at discharge, higher mortality rates, and higher medical costs (Chiu et al., 2010; Christensen, 2009; Gioldasis, 2008; Reed et al., 2001; Yoneda et al., 2005). Previous studies have looked at risk factors associated with HS in many countries, including Thailand, but not specific to Northern Thailand and not specific to the working aged population. Research into the specific risk factors associated with HS in this demographic could promote primary prevention and therefore, reduce the burden of stroke. The purpose of this study was to identify the risk factors associated with working aged HS patients who underwent treatment in a tertiary teaching hospital in Chiang Mai, a tertiary care center in Northern Thailand.

Method

Study Design

The Ethics Committee of the Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, approved this study (NUR-2557-2100). Patients included in this study ranged from 15-59 years and were given ICD-9-CM Diagnosis Code I60 or I61. Code I60 indicates non-traumatic subarachnoid hemorrhage, and Code I61 indicates non-traumatic intrac-

Table 2. *Source of Admission by GCS*

GCS Admission	Transferred From Other Hospitals n (%)	Admitted Directly n (%)	p-value
3 – 8	120 (38.7)	25 (26.6)	.037*
9 – 15	190 (61.3)	69 (73.4)	

Note. GCS = Glasgow Coma Score; * *p* < .05.

erebral hemorrhage. We gathered data on the patients from the hospital's electronic medical records; we performed a secondary analysis on this data. The patients were diagnosed with HS and admitted to the Neurosurgical Intensive Care Unit, the Neurosurgical Critical Care Unit, and the Acute Stroke Unit during the period from January 2009 to December 2013.

The general demographic information pertained to age and sex while the medical data consisted of the Glasgow Coma Score (GCS) at admission, subgroups of HS (ICH and subarachnoid hemorrhage), surgical treatment, and the risk factors associated with HS (i.e., hypertension, hyperlipidemia, regular alcohol consumption, drug non-adherence with anti-hypertensive medications, smoking, diabetes mellitus, prior stroke, diagnosed underlying neurological problem, chronic kidney disease, and coagulopathy). The GCS is a neurological scale used to assess the level of consciousness of the patients on admission. The initial score correlates with the severity of brain injury and prognosis. The GCS provides a score in the range 3 (worst prognosis) to 15 (best prognosis). Patients with scores equal to or less than 8 are usually comatose and will have severe disability, scores of 9-13 indicate the likelihood of moderate disability, and 14-15 indicate a good chance for a full recovery (Biau Organization, n.d.; Traumaticbraininjury.com, n.d.).

Statistical Analysis

We used the STATA 10 program to analyze the demographic data using descriptive statistics. Risk factors and comorbidity were analyzed using frequencies and percentages. Logistic multiple regression was used to analyze associated risk factors in working-aged HS patients. Other covariates such as age, sex, hypertension, hyperlipidemia, alcohol drinking, drug non-adherence, smoking, diabetes mellitus, prior stroke, neurological problem, kidney problem, and anticoagulant drug use were controlled by using a multivariable logistic analysis. The unavailable logistic regression was used to identify the possible independent risk factors for stroke. We included the clinically significant variables and all variables that had a *p*-value less than .01 in the multivariable analysis model. Multivariable logistic regression analysis and step-backward method were used to identify the independent risk factors for stroke. We

considered a *p*-value less than .05 statistically significant.

Results

Our sample size was calculated based on a previous study which found that 45.9% of strokes among Thais were hemorrhagic strokes (Bandasak, Narksawat, Tangkanakul, Chinvarun, & Siri, 2011). To calculate sample size in this study, the formula *n* = $Z^2P(1-P)/d^2$ was used and provided a precision of 5% (Pourhoseingholi, Vahedi & Rahimzadeh, 2013). Using this formula, the recommended sample size was 382 cases. During the study period, we identified 647 hemorrhagic stroke patients. However, 404 met our inclusion criteria of being aged 15-59 years, which comprised our study sample. Table 1 shows the characteristics of the patients. The majority were male (60.9 %), and the mean age was 47.5 years (*SD* = 9.8). At the time of admission, 145 HS patients had suffered a severe stroke and had a GCS between 3 and 8. Two hundred and eighty of the HS patients required surgery while the remainder only needed supportive treatment. The three major surgeries performed were craniotomy, external ventriculostomy drainage, and craniectomy. Patients transferred from secondary hospitals (*n* = 120) had a GCS between 3 and 8 compared with 25 patients who admitted directly to the hospital in this study (Table 2).

Five principal risk factors were identified. Table 3 describes the risk factors associated with the HS patients. Univariate analysis indicated the significant risk factors were being male (*p* < .001) and drug non-adherence of antihypertension (*p* = .042). A multivariate analysis confirmed the same two risk factors, male gender (*p* < .001, *OR* = 2.43, 95% CI [1.60- 3.69] and drug non-adherence (*p* = .047, *OR* = 1.88, 95% CI [1.01-3.50]) were significant with the addition of hypertension (*p* = .048, *OR* = 1.81, 95% CI [1.01-3.26]; Table 4).

Discussion

The present study indicated that males accounted for more than half of our HS patients. This was similar to others studies that found a higher ICH incidence in males than in females in Greece, Southern Norway, Australia, Japan, and East China (Gokhale, Caplan, & James, 2015; Zhang et al., 2011).

The mean age of patients in our study was 47.5 years (*SD* = 9.8) years. We found that 69.1% of our stoke victims were aged 46-59 years, while 30.9% were aged 15-45 years. These results are similar to a study at a similar hospital (i.e., a tertiary hospital in a developing country, Bangladesh; Hussain, Mohammad, et al., 2015). In that study, 67.1% of the patients were over 45 years of age, and 33.9% were between 15-45 years of age. We speculate that, alt-

Table 3. *Risk Factors in Working Aged HS Patients by Univariate Analysis*

Risk factor	n (%)	Crude OR	95% CI	p-value
Male	246 (60.9)	2.508	1.661-3.787	< .001***
Age > 45	279 (69.1)	1.435	0.936-2.198	0.098
Hypertension	337 (83.4)	0.597	0.338-1.053	0.075
Hyperlipidemia (>200 mg/dl)	157 (38.9)	0.880	0.575-1.347	0.558
Alcohol drinker	87 (21.5)	1.138	0.697-1.852	0.604
Smoker	62 (15.3)	1.175	0.672-2.054	0.571
Drug non-adherence	60 (14.9)	1.865	1.023-3.401	0.042*
Diabetes mellitus	49 (12.1)	1.078	0.584-1.988	0.877
Old CVA	26 (6.4)	1.564	0.663-3.687	0.307
Neurological problem	18 (4.5)	0.839	0.324-2.172	0.717
Heart problem	16 (4.0)	0.900	0.199-4.076	0.891
Kidney problem	15 (3.7)	0.765	0.272-2.153	0.604
Coagulopathy	12 (3.0)	3.485	0.754-16.116	0.110

Note. CVA = cerebrovascular accident*;* HS = hemorrhagic stroke;*** $p < .001$; * $p < .05$.

hough both Bangladesh and Thailand are considered to be developing countries, Thailand is an upper income developing country with differences in lifestyle, access to health care, and other socio-economic factors that impact these results. Although only a small proportion of working aged people experience a stroke, the results are nonetheless significant as these working aged survivors may become dependent, unable to participate in the workforce, and require assistance for the rest of their lives. The effect of this is a significant loss of economic productivity and a prolonged financial burden, which has a negative impact on their families, communities, the health care system, and the nation as a whole.

The mean GCS at admission was 10.4 (*SD* = 3.9), which indicated a moderate HS. There were 145 (35.9%) patients with a GCS ranging from 3-8, showing severe disability (Biau Organization, n.d.; Traumaticbraininjury.com, n.d.). There was a large number of patients (*n* = 310) who were transferred from other hospitals. The physicians from outlying regions tend to transfer their patients to the hospital in this study who require the most intense treatment. At admission, 26.6% of patients admitted directly to the hospital in this study had a GCS ranging from 3-8, while 38.7% of patients transferred from outlying hospitals had a GCS in the same range (*p* = < .037).

HS is a clinical emergency requiring urgent surgical and medical intervention. Recent advances in the organization of acute stroke care, and improved understanding of the evolving pathophysiology together with advances in acute pharmacological therapy, including neuroprotective approaches, are changing the way that acute stroke is managed around the world (Davis, Lees, & Donnan, 2006). During the period under study, the hospital had the primary responsibility of treating patients with severe or complicated medical needs who required the most modern medical technology and interventions. The hospi-

tal also had the responsibility to act as a mentor and to promote best practices and integrate care for patients at all stages of treatment. After the period of study, the National Health Ministry promoted the establishment of stroke units in all secondary and tertiary hospitals in Thailand. Some additional hospitals in Northern Thailand have already established stroke units and now have the potential to perform surgery and treat stroke patients with thrombolysis. We anticipate that this development will reduce the number of stroke patients who will be transferred to the hospital under study. The majority (69.3 %) of HS patients in this study required surgery. Some patients required more than one surgical procedure. The top three surgeries were craniotomy, external ventriculostomy drainage, and craniectomy. More than half (51.0%) of the HS patients had craniotomies to remove a hematoma in the brain to decompress the brain tissue. Eighty-four (20.8%) patients had external ventriculostomy drainage to reduce hydrocephalus, which may occur after HS because blood components occlude the cerebrospinal fluid drainage pathway. Twenty-four (5.9%) craniectomies were performed in order to reduce secondary injuries from brain edema (Abdeen, Aboul-Henein, Orz, & El-Metainy, n.d.; Bhattathiri, Gregson, Prasad, & Mendelow, 2006; Bu et al., 2016; Chen, Luo, Reis, Manaenko, & Zhang, 2017).

The significant predicting risk factors for working-aged HS patients were male, drug non-adherence for antihypertensive drugs, and hypertension. A study done in China suggested that males were at greater risk for HS because they had lifestyle differences, such as cigarette smoking and alcohol drinking. Also, there is no vascular protection of endogenous estrogen in males and it may contribute to the risk of stroke in men (Zhang et al., 2011). Hypertension is a main risk factor for HS, specifically untreated hypertension (Woo et al., 2004). Our study is

Table 4. *Risk Factor in Working Aged HS Patients by Multivariate Analysis*

Risk factor	Adjusted *OR*	95% *CI*	*p*-value
Male	2.43	1.60-3.69	< .001***
Drug non-adherence	1.88	1.01-3.50	0.047*
Hypertension	1.81	1.01-3.26	0.048*

Note. Adjusted by sex, age > 45, drug non adherence and hypertension; HS = hemorrhagic stroke; *** *p* < .001; * *p* < .05.

similar to a systematic review of risk factors for intracerebral hemorrhage in the general population that found male sex and hypertension (Ariesen, Claus, Rinkel, & Algra, 2003). Our results are consistent with the previous study showing that medication non-adherence was associated with insufficient blood pressure control and increased risk of incident stroke (Cummings et al., 2013; Hussain, Azad, et al., 2015).

Non-medication adherence was associated with working-aged victims who were young, working, and presented with overweight or obesity as found in a study in Brazil (Demoner, de Paula Ramos, & Pereira, 2012). The reasons for drug non-adherence may be due to normalization of blood pressure, side effects of the medications, forgetting to use the medication, cost of medication, fear of mixing alcohol and medication, ignoring the need for continuing the treatment, use of an alternative treatment, fear of intoxication, fear of hypotension, and fear of mixing the medication with other drugs (Andrade, Vilas-Boas, Chagas, & Andrade, 2002).

A multinational study found an association between low age, low self-efficacy, respondents' perception of their illness, and cost-related barriers with medication non-adherence (Morrison et al., 2015). Individuals with hypertension who fail to take their prescribed antihypertensive medication experience a substantially increased risk of fatal stroke (Herttua, Martikainen, Batty, & Kivimäki, 2016). A retrospective cohort study in Korea about the effect of adherence to antihypertensive medications found a significant association between poor adherence and non-adherence to medication with a higher risk of stroke (Lee, Jang, & Park, 2017).

A systematic review of 97 articles published between 1979 and 2009, of the impact of the intervention on medication adherence and blood pressure control in patients with hypertension, found that improving knowledge of medications had potential clinical value in improving adherence with antihypertensive therapy (Gwadry-Sridhar, 2013). In a study in Spain, a team of pharmacists provided specific education on medication adherence and hypertension to some patients who were taking anti-hypertensives. There was a significant improvement in antihypertensive medication adherence compared to a control group who did not receive this education (*p* < .05; Fikri-Benbrahim, Faus, Martínez-Martínez, & Sabater-Hernández, 2013). Another study found that adherence to medications was positively correlated to increasing age (*p* < .001), the presence of hypertension (*p* < .05), and a more positive attitude toward health (*p* < .001; Alefishat, Abu Farha, & Al-Debei, 2017).

We suggest that there is a particular need for primary prevention and a need to address the significant associated risk factors. There is also a need to provide more information to working aged stroke victims to enhance their knowledge of hypertension and HS. We postulate that such measures can lead to a more positive attitude toward their health and a greater sense of self-efficacy, which in turn may affect adherence rates in patients (Morrison et al., 2015). Increased medication adherence should lead to more normal blood pressure and fewer negative outcomes. These educational programs could be incorporated into the current efforts to manage the patient's hypertension.

A prime responsibility of the nursing professional is to empower patients to look after their own health needs. For patients with hypertension, this involves helping patients to understand their disease and to realize the importance of medication adherence to antihypertensive drugs so that their blood pressure may be brought under control to reduce the risk of HS. Case management by nurses in the community is one way of addressing this issue. Case managers can offer outreach services to working aged adults who are known to have hypertension and proactively encourage these adults to learn about their disease and take measures to reduce the risk factors leading to HS. Knowledge sharing among medical professionals in the community and associated hospitals is an important aspect of identifying and contacting this group and encouraging their involvement in various preventive measures, especially medication adherence.

There is a need for further research to establish which approaches will be most effective in increasing drug compliance in the working aged group. Future study should have as its goal the development of an overall and integrated model of care and outreach to reduce the various factors that increase the risk of HS.

Limitations

This retrospective study was limited to using medical records already on file. Patient histories were sometimes sketchy as the patients were often in medical distress and could not provide information, which then had to be obtained from their relatives. Some of the transferring hospitals either did not have complete medical files on the transferred patients or

that information was not supplied to the receiving hospital.

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