Original Article

Predicting Factors of Poor Outcome of Hemorrhagic Stroke Patients

Triamvisit S, MSN, APN, RN[1], Chongruksut W, PhD, RN[2], Watcharasaksilp W, MD[3], Rattanasathien R, MSN, APN, RN[4], Saisuwan S, RN[4], Chaiwang S, MSN, RN[1], Jaiyen P, RN[1]

[1] Neurosurgical Critical Care Unit, Nursing Division, Chiang Mai University Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

[2] Research Unit, Department of Surgery, Chiang Mai University Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

[3] Neurosurgery Unit, Department of Surgery, Chiang Mai University Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

[4] Acute Stroke Unit, Nursing Division, Chiang Mai University Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Background: Stroke is the leading cause of morbidity and mortality, accounting for a significant and increasing share of hospital costs in Thailand.

Objective: The purpose of the present research was to study predicting factors of poor outcome at the time of discharge of hemorrhagic stroke (HS) patients, who underwent treatment in Chiang Mai University Hospital.

Materials and Methods: A five-year cross-sectional retrospective study was conducted. The subjects of the present study were patients diagnosed with HS, 15 years and older, admitted to Chiang Mai University Hospital between January 2009 and December 2013. The modified Rankin Scale (mRS) at the time of discharge was used to classify the patient outcomes. The good outcome group (mRS of less than 4) and poor outcome (mRS of 4 or more) were compared. Predictors of poor outcomes consisting of demographic data and known risk factors were identified through multiple regression analysis.

Results: Six hundred forty-seven patients with HS underwent treatment during the study period. At the time of discharge, 431 (66.6%) of patients had poor outcome and 328 (50.9%) had to be transferred back to a secondary hospital. The significant predictors of poor outcome by multivariate analysis were Glasgow Coma Score (GCS) at admission of 8 or less (adj OR 12.6, 95% CI 7.2 to 22.1), infection (adj OR 2.7, 95% CI 1.7 to 4.2), male gender (adj OR 1.9, 95% CI 1.3 to 2.9), operative treatment (adj OR 2.0, 95% CI 1.3 to 3.0), hypertension (adj OR 2.1, 95% CI 1.2 to 3.6), hyperlipidemia (adj OR 1.0, 95% CI 0.9 to 1.0), and ICH (adj OR 1.6, 95% CI 1.0 to 2.4).

Conclusion: The major finding from the present study was that two-thirds of the patients had poor outcomes. Hospital acquired infection must be screened and detected promptly. Health education may improve patient outcomes by promoting self-awareness in HS patients such as complying with antihypertensive medicine and controlling cholesterol within the normal limits.

Keywords: Outcomes, Predicting factors, Hemorrhagic stroke

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Stroke is one of the worldwide leading causes of morbidity and mortality[1]. Nearly six million died and another five million are left permanently disabled. Disability may include loss of vision and/or speech, paralysis, and confusion[1]. In Thailand, stroke is the third leading cause of death and disability. The Thai Stroke Society reported the stroke incidence rate of 257 cases per 100,000 population in 2008, and stroke mortality rate of 21 cases per 100,000 population in 2009[2,3]. Hemorrhagic stroke (HS) is caused by the rupture of an artery in the brain, and 20% of strokes are HS. The mortality rate in the United States is between 40% and 50%[4]. There are two subtypes of HS, intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). An ICH happens when a blood vessel in the brain leaks blood into the brain. A SAH happens when there is bleeding under the outer

Correspondence to:

Watcharasaksilp W.

Neurosurgery Unit, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

Phone: +66-53-935532

Email: wwatchar@gmail.com

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membranes of the brain and into the thin fluid-filled space surrounds the brain. HS can cause extensive damage to the brain and is the most lethal of all strokes. The severity of disability and risk of death, length of stay (LOS), and cost of treatment of HS patients are higher than ischemic stroke[5-8].

The modified Rankin Scale (mRS) at the time of discharge was used to classify the patient outcomes by measuring the degree of disability of the patients who have had a stroke[9,10]. The scale arranges from 0 to 6 as follow: 0=no symptoms at all, 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 and 6=dead[9,10]. A score between 0 and 3 is considered a good outcome, a score between 4 and 6 is a poor outcome.

There have been few studies on the outcomes for HS in Thailand, nor study of the factors associated with outcomes. There has been almost no research about the factors specific to Northern Thailand. This secondary data analysis study was conducted to describe the outcomes of HS, and its associated risk factors of HS patients admitted to Chiang Mai University (CMU) Hospital Northern Thailand between January 2009 and December 2013.

Materials and Methods

Study design

The present study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. The study population included patients aged 15 years and older, ICD-9-CM Diagnosis Code I60 or I61. Code I60 indicates non-traumatic SAH and Code I61 indicates non-traumatic ICH. All data were gathered from the hospital's electronic medical records. Secondary analysis was performed on this data. The subjects of the present study were admitted to CMU Hospital between January 2009 and December 2013. The patients who were less than 15 years or had incomplete electronic medical records were excluded.

The general demographic information pertained to age and sex while the medical data consisted of Glasgow Coma Score (GCS) at admission, subgroups of HS (ICH and SAH), 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 to 15. Patients with scores equal to or less than 8 are usually comatose and will have severe disability. Scores of 9 to 13 indicate likelihood of moderate disability and 14 to 15 a good chance for full recovery[11,12].

The mRS was used to classify the patient outcomes at the time of discharge. A mRS score between 4 and 6 is considered a poor outcome while a score between 0 and 3 is considered a good outcome[9,10]. The poor outcome (mRS of 4 or more) and good outcome group (mRS of less than 4) were compared.

Predictors of poor outcomes consisting of demographic data and known risk factors were identified through logistic regression analysis.

Statistical analysis

The Stata software version 12.0 was used to analyze the demographic data using descriptive statistics. Risk factors and comorbidity were reported by frequencies and percentages. Logistic multiple regression was used to analyze associated risk factors of poor outcome in HS patients. The present study was controlled for other covariates such as age, sex, operative treatment, infection, hypertension, hyperlipidemia, alcohol drinking, drug non-adherence, smoking, diabetes mellitus, prior stroke, and LOS greater than 14 days by using a multivariable logistic analysis. The univariable logistic regression was used to identify the possible independent risk factors associated with poor outcome. The clinically significant variables and all variables having a p-value less than 0.2 were included in the multivariable analysis model. Multivariable logistic regression analysis and step-backward method were used to identify the independent risk factors for poor outcomes of HS. A p-value less than 0.05 was considered statistically significant.

Results

The sample size was calculated based on a previous study that found that 20.3% of strokes among Thais were HS[13]. To calculate the sample size in the present study, the formula $n = Z^2_{1-\alpha/2} P(1-P) / d^2$ was used and provided a precision of 5%[14,15]. Using this

Table 1. Outcomes of hemorrhagic stroke patients at discharge (n = 647)

Variables	n (%)
mRS at discharge	
Range	2 to 6
Good outcome (0 to 3)	216 (33.4)
Poor outcome (4 to 6)	431 (66.6)
Type of discharge	
Discharge	187 (28.9)
Referred to the secondary hospital	328 (50.7)
Against advice	69 (10.7)
Death	63 (9.7)

mRS=modified Rankin Score

Table 2. Characteristics of hemorrhagic stroke patients (n = 647)

Characteristics	n (%)
Age (year), Mean±SD	56.2±14.5
Male, Mean±SD	54.7±14.5
Female, Mean±SD	58.3±14.4
Sex	
Male	368 (56.9)
Female	279 (43.1)
Risk factors/co-morbidity	
Hypertension	533 (82.4)
Hyperlipidemia (>200 mg/dl)	241 (37.2)
Binge drinking	139 (21.5)
Smoking	103 (15.9)
Drug non-adherence	102 (15.8)
Diabetes mellitus	74 (11.4)
Prior stroke	33 (5.1)
Accessibility	
Refer	499 (77.1)
Direct admission	148 (22.9)
GCS	
Admission, Mean±SD	10.2±3.9
• GCS >8	406 (62.8)
• GCS ≤8	241 (37.2)
Subtypes of hemorrhagic stroke	
SAH	246 (38.0)
ICH	401 (62.0)
Operation	
No	204 (31.5)
Yes	443 (68.5)
Reoperation	109 (16.8)
Infection	
No	385 (59.5)
Yes	262 (40.5)
Pre-hospitalized	16 (2.5)
Other hospital	10 (1.5)
At the present hospital	236 (36.5)
2 or more sites of infection	57 (8.8)
LOS (day)	
≤14	434 (67.1)
>14	213 (32.9)

GCS=Glasgow Coma Score; ICH=intracerebral hemorrhage; SAH=subarachnoid hemorrhage; LOS=length of stay; SD= standard deviation

formula, the selected a sample size was 430 cases. During the study period, 664 HS patients were included. However, 647 met inclusion criteria of being aged 15 years or older. Of the 647 HS patients at time of discharge, 431 (66.6%) had poor outcomes and 328 (50.7%) of the patients were transferred back to secondary hospitals (Table 1). The mean age was 56.2±14.5 years and 368 (56.9%) were male. The top five risk factors in order of frequency were hypertension, hyperlipidemia (greater than 200 mg/dl), alcohol drinking, smoking, and medical non-adherence. Of the 647 studied cases, 499 (77.1%) of the patients were transferred from secondary hospitals. The mean baseline GCS on admission was 10.2 (SD 3.9), 406 (62.8%) had GCS greater than 8 where 401 (62.0%) had ICH and 443 (68.5%) underwent a surgical procedure, and 262 (40.5%) had an infection where 236 (36.5%) infections occurred while patient was at CMU hospital. Infections in two or more sites occurred in 57 (8.8%) of the patients. Two hundred thirteen (32.9%) were hospitalized for more than two weeks (Table 2).

The associated factors, including demographic data, risk factors, and comorbidities (i.e., hypertension, dyslipidemia, binge drinking, smoking, medical non-adherence, diabetes, and prior stroke), type of HS, infection, and LOS were analyzed. Employing univariable analysis, the significant predictors of poor outcome were identified as male gender, ICH, GCS at admission of 8 or less, older than 45 years, surgical treatment, reoperation, infection, two or more sites of infection, hypertension, hyperlipidemia (more than 200 mg/dl), prior stroke, and LOS more than two weeks (Table 3).

Multivariable analysis indicated the significant risk factors for poor outcome were GCS at admission (adjusted OR 12.6, 95% CI 7.2 to 22.1; p<0.001), infection during hospitalization (adjusted OR 2.7, 95% CI 1.7 to 4.2; p<0.001), male gender (adjusted OR 1.9, 95% CI 1.3 to 2.9, p<0.01), operative treatment (adjusted OR 2.0, 95% CI 1.3 to 3.0; p<0.01), hypertension (adjusted OR 2.1, 95% CI 1.2 to 3.6;

Table 3. Associated factors of poor outcome hemorrhagic stroke patient by univariable analysis

Variables	n (%)	Crude OR	95% CI	p-value
Male	263 (61.0)	1.7	1.2 to 2.3	0.003**
ICH	292 (67.7)	2.1	1.5 to 2.9	<0.001***
GCS: admission ≤ 8	224 (52.0)	12.7	7.5 to 21.5	<0.001***
Age >45 years	359 (83.3)	1.6	1.1 to 2.4	0.018*
Operation	326 (75.6)	2.6	1.9 to 3.7	<0.001***
Reoperation	88 (20.4)	2.4	1.4 to 3.9	0.001**
Infection	217 (50.3)	3.9	2.6 to 5.6	<0.001***
Two or more sites infection	49 (11.4)	3.3	1.6 to 7.2	0.002**
Accessibility; referring from other hospital	340 (78.9)	1.3	0.9 to 1.9	0.133
Hypertension	375 (82.8)	2.5	1.6 to 3.7	<0.001***
Hyperlipidemia (>200 mg/dl)	167 (40.7)	1.0	0.9 to 1.0	<0.001***
Binge drinking	95 (22.0)	1.1	0.7 to 1.7	0.273
Smoking	68 (15.8)	1.0	0.6 to 1.5	0.889
Drug non-adherence	70 (16.2)	1.1	0.7 to 1.8	0.639
Diabetes mellitus	52 (12.1)	1.2	0.7 to 2.1	0.479
Prior stroke	29 (6.7)	3.8	1.3 to 10.9	0.014*
LOS >14 days	160 (37.1)	1.8	1.3 to 2.6	0.001**

GCS=Glasgow Coma Score; ICH=intracerebral hemorrhage; LOS=length of stay; OR=odds ratio; CI=confidence interval

* p<0.05, ** p<0.01, *** p<0.001

Table 4. Predicting factors of poor outcome hemorrhagic stroke patient by multivariable analysis

Variable	Adjusted OR	95% CI	p-value
GCS: admission	12.6	7.2 to 22.1	<0.001***
Infection	2.7	1.7 to 4.2	<0.001***
Male	1.9	1.3 to 2.9	0.002**
Operation	2.0	1.3 to 3.0	0.002**
Hypertension	2.1	1.2 to 3.6	0.008**
Hyperlipidemia	1.0	0.9 to 1.0	0.033*
ICH	1.6	1.0 to 2.4	0.047*

GCS=Glasgow Coma Score; ICH=intracerebral hemorrhage; OR=odds ratio; CI=confidence interval

* p<0.05, ** p<0.01, *** p<0.001

p<0.01), hyperlipidemia (adjusted OR 1.0, 95% CI 0.9 to 1.0; p<0.05), and ICH (adjusted OR 1.6, 95% CI 1.0 to 2.4; p<0.05) (Table 4).

Discussion

In the present study, the prevalence of poor outcomes of patients with HS was quite high. These patients required assistance and constant nursing care. About half of these patients (50.7%) could not go home and were transferred back to the secondary hospitals. CMU Hospital received all patients who had severe and/or complicated conditions from all the secondary hospitals in Northern Thailand. Most of the patients by definition, required extensive medical and surgical intervention, such patients may be predisposed to having poor outcomes.

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 of 3 to 15. The maximum score is 15, which indicates the best prognosis. The minimum score is 3 indicating the worst prognosis. Patients with scores equal to or less than 8 are usually comatose and will have severe disability. Scores of 9 to 13 indicate likelihood of moderate disability and 14 to 15 a good chance for full recovery[11,12]. In the present study, GCS at admission of 8 or less was significantly associated with poor outcomes in HS patients. This result is similar to other studies[16-18]. Since GCS is always used to assess level of consciousness, the lower the GCS the patient has, the greater severity of illness the patient will have. This was similar to the studies that showed the good outcomes were related to higher GCS[19].

In the present study ICH and operative treatment were significant predictors of poor outcomes in patients with HS. ICH has the highest morbidity and mortality of all types of stroke[20].

ICH is the most harmful type of HS and is a leading cause of disability and mortality[21,22]. The fatality rate of ICH is high (40% at one month and

54% at one year), and only 12% to 39% of survivors can achieve long-term functional independence[23]. Complications of ICH include hematoma expansion, perihematomal edema with increased intracranial pressure, intraventricular extension of hemorrhage with hydrocephalus, seizures, venous thrombotic events, hyperglycemia, increased blood pressure, fever, and infections[24]. To improve outcomes, surveillance is needed to prevent complications. Early detection and optimum management are effective in reducing adverse effects early in the course of stroke and improving prognosis[24]. Early surgery had a favorable outcome compared with initial conservative treatment[20]. Patients who underwent surgical treatment showed a longer survival rate. Operative treatment can relieve pressure in the brain and repair torn arteries. Certain medications can help manage symptoms, such as painkillers to ease severe headaches. Drugs may be necessary to control blood pressure and seizures to prevent secondary injuries[25]. Treatment approaches for ICH include early diagnosis and hemostasis, aggressive management of blood pressure, open surgical and minimally invasive surgical techniques to remove clot, techniques to remove intraventricular blood, and management of intracranial pressure. These approaches improve clinical management of patients with intracerebral hemorrhage and promise to reduce mortality and increase functional survival[26].

Hypertension is a significant predictor of ICH and a significant predictor of poor outcomes for HS[22,23,27]. Effective control of blood pressure is important in preventing spontaneous ICH[27,28].

In the present study, hyperlipidemia was a significant predictor of poor outcomes. This is not supported by a systematic review and meta-analysis that found total cholesterol level is inversely associated with risk of HS[5]. Higher level of low-density lipoprotein cholesterol seems to be associated with lower risk of HS. High-density lipoprotein cholesterol level seems to be positively associated with risk of ICH[5].

The gender difference influencing the risk of HS has been identified in several studies. Three hundred sixty-eight (56.9%) patients in the present study were male while 279 (43.1%) female. Male gender was a significant risk factor associated with poor outcomes. Many reasons have been given including genetic factors, higher prevalence of hypertension in males[26,27], risk behaviors such as uncontrolled hypertension, excessive alcohol consumption, smoking, and hyperlipidemia. As well, there is no vascular protection of endogenous estrogen in male. This may contribute to the risk of stroke in male[29].

The most serious risk factor leading to poor outcome is hospital acquired infection. HS patients with infection are at almost three times greater risk for poor outcomes (Table 4). Infections can be controlled and managed. The authors suggest that stringent precautions be taken to prevent infections in HS patients. Controlling infections will reduce the prevalence of poor outcomes.

In the present study, the mean age of HS was 56.2±14.5 years (Table 2). The incidence of stroke in the Thai working aged group is a major public health problem and has a negative impact on the country economy. It can also be a burden on the families as patients can be left disabled and require ongoing care and support. This problem is compounded as the Thai society is becoming an increasingly elderly society[30]. 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[31].

These significant preventable risk factors of poor outcome in the present study need to be addressed. There is also a need to provide more information to working aged group about stroke, enhance their knowledge of hypertension, and HS. Increased medication compliance should lead to more normal blood pressure and fewer negative outcomes. Health education may improve patient outcomes by promoting self-awareness in HS patients such as drug adherence to antihypertensive drugs. These educational programs could be incorporated into the current efforts to manage the patient's hypertension[31]. 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 and cholesterol stay within normal limits.

Limitation

This retrospective study was limited to using medical records already on file. Patient histories were sometimes sketchy as the patients were often in 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.

Conclusion

There is a need for further research to establish which approaches will be the most effective in increasing drug compliance to antihypertensive drugs. Future study should have its goal as to develop an over-all and integrated model of care to reduce the various factors that increase the risk of HS that occurred in late working age stroke victims compared with previous researches.

What is already known on this topic?

Patients with HS had higher mortality rates, higher disability rates at discharge, resulting in longer hospitalization, and higher medical costs. It has a disproportionately large economic impact by leaving victims disabled before their most productive years. The previous studies found that poor outcome of HS was related to volume of intracerebral hemorrhage in the brain and initial hospitalization GCS.

What this study adds?

This paper provided an overview of a five-year retrospective study of more than six hundred HS patients. The significant factors associated poor outcome by multivariate analysis were GCS at admission, infection during hospitalization, male gender, operative treatment, hypertension, and hyperlipidemia. The most serious risk factor leading to poor outcome is hospital acquired infection. This study suggested that stringent precautions be taken to prevent infections in HS patients. Controlling infections will reduce the prevalence of poor outcomes. There is also a need to provide more information to enhance the target group's knowledge of increasing medication adherence and avoid risk behaviors to the HS victims. These should lead to fewer negative outcomes.

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Conflicts of interest

The authors declare no conflict of interest.

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