Risk Factors for Stroke and Predictors of One-Month Mortality

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ABSTRACT

Background: Stroke is the third most common cause of death in Malaysia. The prevalence of risk factors and predictors of mortality of stroke in Malaysia are poorly understood.

Aim: To identify the prevalence of major risk factors for stroke and to determine predictors of one-month mortality.

Method: Prospective study of all stroke patients admitted to Penang Hospital between December 1998 and November 1999. All patients were subjected to brain CT. Predictors of one-month mortality: systolic and diastolic hypertension, hyperglycaemia, type of stroke, age $\geq$70, poor Glasgow coma score (GCS) on admission and deterioration of score were assessed.

Results: A total of 246 (139 male and 107 female) patients were included. Median age was 65 years. Hypertension was the commonest risk factor (71.5%) followed by diabetes mellitus (40.2%) and hyperlipidaemia (37%). 74.8% of the cases were ischaemic in origin and 25.2% haemorrhagic. Mortality at one month was 20.3%. Using multivariate analysis and logistic regression, deterioration of GCS (OR=46.04), poor GCS on admission (OR=12.35) and haemorrhagic stroke (OR=3.45) were independent predictors of one-month mortality.

Conclusion: Hypertension and diabetes mellitus are the commonest risk factors of stroke among patients admitted to a tertiary hospital in Malaysia. Significant predictors of one-month mortality include the admission GCS, deterioration of GCS and haemorrhagic stroke.

Keywords: Ischaemic stroke, haemorrhagic stroke, Glasgow coma scale

INTRODUCTION

Stroke is classified into ischaemic and haemorrhagic stroke. Ischaemic stroke accounts for 69 to 91 percent while haemorrhagic stroke 9 to 31 percent of a first ever stroke[1-4]. Stroke occurs predominantly in middle and late years of life. Most ischaemic strokes occur between the ages of 71 and 80 years while most haemorrhagic strokes between 60 and 70 years[3]. Stroke is the third most common cause of death after ischaemic heart disease and cancers, not only in developed countries, but worldwide[5]. Therefore, it is an important public health problem and a burden to health care providers and to the community at large because of the amount of effort that has to be invested in the planning and provision of health care. In Scotland the cost of each stroke to the National Health Service in 1988 was about 6000 pounds sterling, not including the cost of the family-doctor[6]. Therefore, it is important to identify the risk factors for primary prevention.

In one study in Denmark, the major risk factors identified for stroke were smoking, hypertension and hyperlipidaemia[7]. In Turkey, hypertension, hyperlipidaemia and diabetes mellitus were the major risk factors identified[8], whereas in Israel, hypertension was the most common risk factor followed by ischaemic heart disease and diabetes[9]. The minor differences in the prevalence of stroke risk factors in different countries are probably due to differences in culture, disease patterns, living habits and distribution of various ethnic groups. However the major risk factors of stroke in Malaysia have not been widely studied.

The Besancom Stroke Registry[10] reported an in-hospital mortality of 13.6%, with the highest morality in patients with primary intracranial haemorrhage. Independent predictors for poor outcome were: age >70, patient who deteriorated within 48 hours of admission, initial loss of consciousness, complete motor deficit, major cognitive syndrome, hyperglycaemia, female and regressive stroke onset. Age, intracerebral bleed, diabetes mellitus and cardiac disease were also poor predictors of outcome in the study by Lefkovits et al[11]. The overall in-hospital mortality was 19%. The present study evaluated these predictors of mortality in Malaysian stroke patients.

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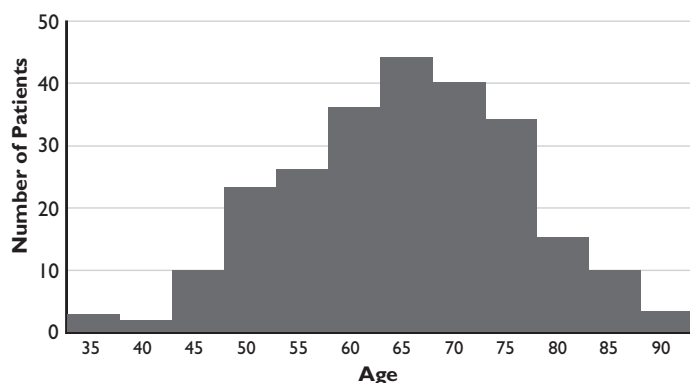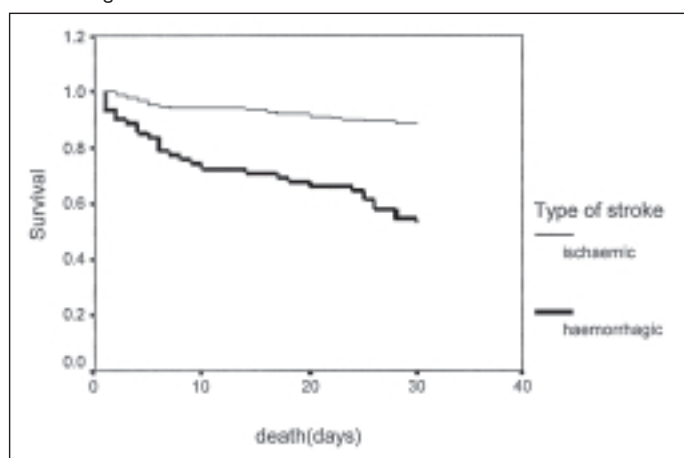
METHODS

This was a prospective case-control study. All patients admitted to Penang Hospital between 1/12/1998 and 30/11/1999 with a clinical diagnosis of stroke were included in the study. All patients routinely had a brain CT within 24 hours of admission to determine the type of stroke. On admission, patients and/or relatives were interviewed to obtain information pertaining to the onset of stroke and pre-existing risk factors, including hypertension, diabetes mellitus, hyperlipidaemia, smoking, ischaemic heart disease, atrial fibrillation and previous transient ischaemic attacks. Hypertension, diabetes mellitus, smoking, ischaemic heart disease (with/without ECG changes) and previous transient ischaemic attack were based on the history from patient or close relatives. Whereas hyperlipidaemia (total cholesterol >5.7mmol/l and triglyceride >2.3mmol/l) and atrial fibrillation were based on blood test and ECG done during admission. A thorough physical examination was performed. Baseline investigations included a full blood count, renal profile, random blood glucose, erythrocyte sedimentation rate, VDRL, electrocardiography and fasting lipid profile. Patients were then followed up in

the hospital and reassessed one month after onset of stroke in the clinic or through the phone to ascertain whether they were still alive. Predictors of one-month mortality: systolic and diastolic hypertension, hyperglycaemia, type of stroke, age ≥70, poor Glasgow coma score (GCS) on admission and deterioration of score were assessed during this period.

STATISTICAL ANALYSIS

All data were entered and analysed using SPSS version 10.0. All comparisons of risk factors between ischaemic and haemorrhagic stroke were analysed using the Chi-square test. Comparisons of age, duration of hospital stay, GCS, blood glucose, and systolic and diastolic blood pressure on admission between ischaemic and haemorrhagic stroke were analysed using the student t test. The predictors of one-month mortality were assessed using multivariate analysis and logistic regression. Survival rate was calculated using the Kaplan-Meier method.

RESULTS

Demographic Data

A total of 246 patients were included during the study period from 1 December 1998 to 30 November 1999. There were 139 men and 107 women. The mean age was 65 ± 11 years (range: 33 to 91 years). 33.7% of patients were aged ≥70 years (Fig. 1). Chinese accounted for 55.7% (n=137) of patients, Malays 28.9% (n=71), Indians 14.2% (n=35) and others 1.2% (n=3). The median duration of hospital stay was 4 days (range: 1 to 72 days). Only 52.8% of patients presented to hospital on the day of stroke onset. Ischaemic stroke accounted for 74.8% of strokes and haemorrhagic stroke 25.2%. Only 5.3% of all patients had a history of previous stroke.

Risk factors

Hypertension (71.5%) was the commonest risk factor for stroke in this study, followed by diabetes mellitus (40.2%), hyperlipidaemia (37%), smoking (35%), ischaemic heart disease (23.2%), previous transient ischaemic attack (5.3%) and atrial fibrillation (4.5%). However, if risk factors were analysed according to type of stroke, hypertension (70.1%) still remained the commonest risk factor followed by diabetes mellitus (45.1%) and hyperlipidaemia (41.8%) for ischaemic stroke, whereas for haemorrhagic stroke, the major risk factors were hypertension (75.8%), smoking (30.6%) and diabetes mellitus (25.8%) (Table I). In this study, there was no significant difference in the occurrence of hyperlipidaemia in both types of stroke (p=0.22). However, in patients ≥70 years of age, hyperlipidaemia was

more commonly present in those with ischaemic than haemorrhagic stroke (p=0.048,) but the numbers were small (50 patients only). Unfortunately 36.6% of patients had no lipid profiles or incomplete data. Hypertriglyceridaemia was present in only 7.3% of all stroke patients.

Predictors of one month mortality

In this study, one-month mortality was 20.3% and the majority were patients with haemorrhagic stroke (58%). About half of the mortalities occurred during the first week of the illness. On admission, haemorrhagic stroke patients had a lower Glasgow coma score, lower blood glucose level, higher incidence of hemiplegia, higher systolic and diastolic blood pressure compared to ischaemic stroke patients (Table II).

Using multivariate analysis and logistic regression, worsening of the GCS (p<0.0001), GCS $\leq$8 on admission (p=0.001) and haemorrhagic stroke (p=0.035) were the independent predictors of one-month stroke mortality with odds ratios of 46.04, 12.35 and 3.45 respectively (Table III). Only 17.4% of patients with worsening of the GCS survived at the end of one month whereas 94% of those without deterioration survived. For those who presented with a GCS $\leq$8, 81.3% died at the end of one month compared to 11.2% of those with a better GCS. About half of haemorrhagic stroke patients died after one month compared to only 11.2% of those with ischaemic stroke (Fig. 2). Other characteristics such as age $\geq$70, hemiplegia, systolic blood pressure $\geq$160, diastolic blood pressure $\geq$100 and random blood glucose $\geq$8 mmol/l on admission were not predictors of death (Table III).

DISCUSSION

Stroke is the third most common cause of death in Malaysia and the number one killer in those aged >65 years in the Ministry of Health hospitals in 1995. Since the average lifespan of the population in Malaysia is increasing, stroke incidence is also expected to increase. Consequently, stroke is, and will continue to exert a great impact on the health system because of the high costs in treatment and rehabilitation of stroke patients. Therefore risk factor identification and modification are important strategies in stroke prevention[12].

In the present study, ischaemic stroke constituted 74.8% and haemorrhagic stroke 25.2% of all patients studied. This composition is broadly similar to most studies conducted in this part of the world[1,2]. Colombo et al[3] showed that the majority of haemorrhagic strokes occurred between 61-70 years of age while ischaemic strokes between 71-80 years. However this

Table I. Risk factors in ischaemic and haemorrhagic strokes.

Risk factors	Ischaemic stroke n=	Haemorrhagic stroke n=	p value
Hypertension	129 (70.1%)	47 (75.8%)	0.39
Diabetes	83 (45.1%)	16 (25.8%)	0.007
Hyperlipidaemia	77 (41.8%)	14 (22.6%)	0.22
Smoking	67 (36.4%)	19 (30.6%)	0.41
IHD	52 (28.3%)	5 (8.1%)	0.001
TIA	11 (6%)	2 (3.2%)	0.4

Table II. Characteristic of ischaemic and haemorrhagic stroke patients.

	Ischaemic stroke n=	Haemorrhagic stroke n=	p value
Age	65 ± 10	64 ± 11	0.36
Male	106 (57.6)	33 (53.2)	0.55
Ethnic: Chinese	99 (53.8)	38 (61.3)	
Malay	52 (28.3)	19 (30.6)	
Indian	32 (17.4)	3 (4.8)	
Others	1 (0.5)	2 (3.3)	
Days of stay	5.7 ± 7.5	8.5 ± 9.5	0.038
GCS on admission	14 ± 2	11 ± 4	<0.0001
Systolic BP	165 ± 34	188 ± 34	<0.0001
Diastolic BP	95 ± 17	105 ± 19	<0.0001
Blood glucose	9.16 ± 5.2	7.9 ± 3.3	0.03
Worsening of GCS	21 (11.4)	25 (40.3)	<0.0001
Hemiplegia	51 (27.7)	34 (54.8)	<0.0001
Death	21 (11.4)	29 (46.8)	<0.0001

Note: ( ) in percentage.

Table III. Predictors of one-month mortality.

Predictors	p value	Odd Ratio	Confidence Interval
Worsening GCS	<0.0001	46.04	14.25 - 148.73
GCS <8	0.001	12.35	2.82 - 54.10
Haemorrhagic stroke	0.035	3.45	1.09 - 10.87
Age >70	0.057	2.98	0.97 - 9.16
Hemiplegia	0.81	1.15	0.36 - 3.68
Systolic BP >160	0.65	1.39	0.34 - 5.65
Diastolic BP >100	0.59	1.45	0.38 - 5.58
RBS >8 mmol/l	0.97	1.02	0.34 - 3.68

study showed no difference in terms of presenting age of both types of stroke.

The ethnic breakdown, where the majority of patients were Chinese, followed by Malays, Indians and other races, represents the unique racial distribution of the population in Penang. In comparison, with Jaya

et al[13] Malays were the majority because of the difference racial distribution in northeast Malaysia.

Hypertension was the commonest risk factor identified overall and for both types of stroke. Studies conducted in Turkey[8], Israel[9], France[10], Ireland (ischaemic stroke)[14] and India (ischaemic stroke)[15] showed similar results. Diabetes mellitus ranked second, but only for ischaemic stroke, as expected. However, smoking was found to be the major stroke risk factor, followed by hypertension and hyperlipidaemia in a study conducted by Bak et al in Denmark[7]. Diabetes mellitus and ischaemic heart disease were less important risk factors in their study. Therefore, different prevalence rates of risk factors are present in different countries. The finding in the present study that diabetes mellitus, ischaemic heart disease and hyperlipidaemia are risk factors favouring ischaemic rather than haemorrhagic stroke in patients over 70 years is supported by Jorgensen et al[4].

There is now evidence that hyperlipidaemia is also a risk factor for ischaemic stroke although all relevant studies included patients with concomitant ischaemic heart disease. Trials using statins to lower cholesterol have shown about a 29% reduction in stroke incidence[16-19]. Hyperlipidaemia, a feature in 37% of patients, was the third major risk factor in the present study. Unfortunately lipid profile results were missing or incomplete in 36.6% of patients. There was no significant difference in the occurrence of hyperlipidaemia in both types of stroke (p=0.22) in this study. However, if only patients older than 70 years were analysed, the difference in prevalence rates was statistically significant in favour of ischaemic stroke (p=0.048). This result is in contrast to the results obtained through a large meta-analysis[20] in which such a relationship between hypercholesterolaemia and stroke was only seen in patients less than 45 years of age.

The overall one-month stroke mortality in this study was 20.3%. The one-month mortality rate was higher in patients with haemorrhagic stroke (46.8%) than ischaemic stroke (11.4%). The Ege Stroke Registry[8] reported an overall 30-day mortality rate of 19.7%, also with a higher mortality rate in haemorrhagic (29%) compared to ischaemic stroke (17%). The 28-day case fatality rate for all strokes in the Perth Community Stroke Study was 24%[21] while the Oxfordshire Community Stroke Project[22] reported an overall 30-day case fatality rate of 19%, cerebral infarction case fatality rate of 10% and intracerebral haemorrhage case fatality rate of 50%. Jaya et al[13] who reported one-month mortality of 34%, was relatively high compared to this study and

other studies[8,21,22]. In the WHO MONICA Project[23] involving 16 European and two Asian centres from 1985 to 1987, the incidence of stroke was, in general, higher among populations in Eastern than in Western Europe. It was also relatively high in the Chinese population studied, particularly among women. The case-fatality rates at 28 days varied from 15% to 49% among men and from 18% to 57% among women.

In this study 15.4% of stroke patients died during the first three weeks of stroke onset. Colombo et al[3] reported a similar three-week mortality (12%). In the present study, half of the total stroke deaths at one month occurred during the first week. Stegmayr et al[24] found that patients in Eastern Europe (Novosiborsk) compared to those from Western Europe (Northern Sweden) had a higher 28-day fatality rate in both men (35.2% vs. 14.3%) and women (30.9% vs. 15.3%). In their study, 35.7% and 75.3% of the total mortality occurred during the first week of stroke onset in Novosiborsk and Northern Sweden, respectively.

Worsening of the GCS, a GCS of ≤8 and haemorrhagic stroke were identified as independent risk factors for stroke mortality in this study. The Besancon Stroke Registry in France[10] also showed that deterioration at 48 hours (OR 10.1) and initial loss of consciousness (OR 4.5) were independent predictors of mortality. Other independent risk factors identified in that study were age ≥70, complete motor deficit and hyperglycemia on admission, but these were not independent predictors in the present study. Coma at stroke onset also was shown to be an independent predictor of mortality by Terent and Anderssen[25], Benedetti et al[26] and Chambers et al[27]. Benedetti et al[26] also showed that other predictors of mortality were the presence of paralysis, impaired ocular motility and certain neuroradiological parameters (lesion size on brain CT), of which the latter two predictors were not assessed in this study.

Haemorrhagic stroke was the other important predictor of mortality identified. The poorer prognosis in haemorrhagic than ischaemic stroke is probably due to the lower GCS at presentation (average GCS 11 vs. 14), more rapid deterioration (40.3% vs. 11.4% of patients) and the greater frequency of complete paralysis at presentation. A greater number of patients with haemorrhagic (46.8%) than ischaemic stroke (11.4%) died. Jover-Saenz et al[28] and Mbala et al[29] reported similar findings.

Age ≥70 years was not an independent predictor of mortality in this study but there was a trend towards significance (p=0.057). This was probably because the

number of patients was not large enough. Colombo et al[3] showed that coma at the onset, haemorrhagic stroke and old age were the predictors of mortality in 503 stroke patients in their study. Chambers et al[27] also supported that old age was a predictor of short-term mortality.

Hypertension, diabetes mellitus and hyperlipidaemia were the major risk factors of stroke identified in the present study. This study also supported the role of hyperlipidaemia as a risk factor for ischaemic stroke in patients older than 70 years of age, but further prospective observational studies need to be done to confirm this result given the small number of patients in this study. Overall one-month mortality was 20.3%. Poor GCS with deterioration of score and haemorrhagic stroke were the independent predictors of one-month mortality. Stroke patients with a GCS ≤ 8 on admission, worsening of GCS after 48 hours and haemorrhagic stroke had one-month survival rates of 18.7%, 17.4% and 53.2% respectively.

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