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ORIGINAL ARTICLES

Predictors of in-hospital mortality in primary intracerebral haemorrhage in East coast of Peninsular Malaysia

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Abstract

Background and Objectives: Despite much medical progress, stroke remains a leading cause of death and disability. The aim of our study was to analyze the frequency of various risk factors and determine predictors of in-hospital mortality among primary intracerebral hemorrhage (PICH) patients, thus providing insight in developing therapeutic strategies to improve the outcome. *Methods:* A prospective study conducted at a tertiary care hospital. *Results:* A total of 160 patients (108 male and 52 female) were evaluated. Their ages ranged from 25 to 85 years (mean age was 58.3 ± 11.4 years). Hypertension was the commonest risk factor (74.4%), followed by diabetes mellitus (18.8%) and cigarette smoking (36.3%). The commonest location of ICH was lobar (43.8%) followed by basal ganglia / internal capsule (28.1 %) and multilobar (13.1%). The overall in-hospital mortality was 32.5 %. About one third (32.7%) of the deaths occurred within first 24 hours, this rose to 38.5% within first 2 days and 84.6% within one week. The significant independent predictors of acute in- hospital mortality were Glasgow Coma Scale (GCS) on admission, posterior fossa bleed (OR 11.01; 95% CI 3.21 to 37.81), hematoma volume >60ml (OR 4.72; 95% CI 1.34 to 16.64), mid line shift (OR 3.32; 95% CI 1.05 to 10.50) and intraventricular extension of haemorrhage (OR 5.69; 95% CI 2.24 to 14.47).
Conclusion: Low GCS score, posterior fossa bleed, and large hematoma volume were main indicators of mortality following PICH in East coast of Peninsular Malaysia.

INTRODUCTION

Intracerebral haemorrhage (ICH) accounts for 10 to 15 percent of all cases of stroke in the West but higher percentages of 20-30% have been reported among Asian population.[1-3] It remains the deadliest and most disabling form of stroke worldwide with high early mortality.[1,4,5] In Malaysia, it is the third commonest cause of death, and number one killer in those aged 65 and above.[6] Its burden is likely to increase in coming years due to increase in longevity leading to growing elderly population.[7] It has been reported that race and ethnicity influence the risk and associated outcome.[8] In a comparative study, PICH was found to be more common among Malaysians than Australians.[9]

ICH is widely considered to be fatal, and withdrawal of care may occur early during hospitalization. Several prognostic models have been proposed and validated to help clinicians in predicting mortality and functional outcome.[10-12] They are potentially useful in clinical decision-making and suggest which patient groups outcome can be influenced by a particular intervention.[12] There is scanty information in the multi-racial society of Malaysia. This study thus aims to analyze the frequency of various risk factors and determine the predictors of in-hospital mortality among patients with PICH. This will provide insight in developing therapeutic strategies to improve the outcome.

METHODS

This prospective study was conducted between December 2007 and November 2009, in Hospital Tengku Ampuan Afzan (HTAA) Kuantan, a tertiary care centre affiliated to faculty of Medicine, International Islamic university Malaysia (IIUM). The study protocol was approved by

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the ethical committees of both the HTAA and the faculty of Medicine, IIUM. All consecutive patients with symptoms of stroke, who were brought to HTAA within few hours to 24 hours of onset of symptoms, were initially evaluated at the emergency department and subsequently subjected to computerized tomography (CT) scan of the brain. Only patients with PICH who were admitted to medical wards/ICU were included in this study. Patients or their close relatives were approached by study personnel during the hospitalization, and informed consent was sought for enrolment into the study. They were interviewed to obtain information pertaining to the onset of stroke and any pre-existing illnesses such as hypertension, diabetes mellitus, heart disease, use of warfarin or any recreational drugs. The patient's medical records were also reviewed for any previous illness and medication. PICH was defined as spontaneous extravasations of blood into brain parenchyma, not attributable to an underlying cause and documented by CT brain scan. Patients with secondary causes of ICH such as subarachnoid haemorrhage, vascular malformation, central nervous system tumour, trauma, hemorrhagic transformation of cerebral infarct or coagulation abnormalities were excluded. Hypertension was defined as "history of hypertension" instead of actual blood pressure readings at the time of admission. Diabetes mellitus was diagnosed if the patient was currently undergoing treatment for this disease. All patients were assessed by at least one researcher and followed up consistently by the designated research assistant until their discharge or death. Clinical variables of each patient such as GCS on arrival and further follow-up, body temperature, blood pressure, CT scan findings, any surgical intervention / complications, length of hospital stay and outcome at discharge were recorded in a standardized proforma. All patients received standard medical care, including management of blood pressure, raised intracranial pressure and other complicating illnesses. The patients were offered neurosurgical intervention if it was found indicated by the neurosurgical team. All CT scans were reviewed by a single experienced radiologist and the locations and volumes of hematomas were determined. The hematoma volume was calculated by using the formula (A × B × C)/2, where A is the largest diameter of the haemorrhage on the CT slice with the larger area of ICH and B is the largest perpendicular diameter on the same slice as A and C is the number of 1 cm slices containing haemorrhage.[13] Variables in relation to the region of haemorrhage included basal ganglia / internal capsule, cerebellum, brainstem, lobar and multilobar - (when more than one of the aforementioned topographies was affected). Secondary intraventricular extension of haemorrhage /mid line shift was also assessed. On the basis of volume of hematoma, patients were categorized into three groups, those with respectively volume < 30 ml, 30-60 ml and >60ml. Outcome variables included cerebral herniation, cardiac events (cardiac arrhythmia, failure or infarction), respiratory events (infection, embolism) and metabolic complications.

Statistical analysis

All data from 160 respondents was entered and analyzed using the IBM SPSS Statistics for Windows 19 (SPSS Inc, Chicago, IL, USA). Univariate analysis for each variable (demographic data, vascular risk factors, and neuroimaging features) was assessed using student's t-test and the chi-square test. Variables that were significantly related to mortality in univariate analysis or those considered important were subjected to multivariate analysis using binary logistic regression. A value of $p<0.05$ was considered to be significant.

RESULTS

Data on demographic characteristics and clinical variables considered for analysis are listed in Table 1. Of the 160 patients, 108 were male and 52 female. Their ages ranged from 25 to 85 years (mean age 58.3 ± 11.4 years). Common presenting features were headache and vomiting followed by loss of consciousness (33.1%), sudden loss of consciousness with focal neurological deficits (39.4%), hemiplegia or hemiparesis (25.0%) and fits (2.5%). On admission, the mean systolic blood pressure was 187± 37.64 mmHg and diastolic blood pressure 107± 23.2mmHg. The mean GCS score was significantly higher among patients who survived as compared to those who died. (12.8 ± 0.4 vs. 8.5 ± 0.5, $p < 0.001$) One third (32.7%) deaths occurred within the first 24 hours, 38.5% within first 2 days and 84.6 within first week of admission. Twenty three of our patients were advised for decompressive surgery but only 18 underwent the procedure, out of which 13 (72.2%) survived and 5 (27.8%) died. The mean duration between the time of admission and death was 4.3 ± 4.1 days. Causes of death included tentorial herniation (50 patients), pneumonia (7 patients), sepsis (5 patients), myocardial infarction

Table1: Socio-demographic and clinical profile of ICH patients included in the study

Characteristics	Alive % (n)	Deceased % (n)	p-value
Demographic			
Age (year) mean ± SD	58.3±11.6	58.3±11.2	0.973
Sex			
Male	65 (69.9)	28 (30.1)	0.447
Female	43 (64.2)	24 (35.8)	
Ethnic			
Malay	90 (68.7)	41 (31.3)	0.390
Chinese	16 (59.3)	11 (40.7)	
Others	2 (100.0)	0 (.0)	
Previous disease			
Hypertension			
Yes	79 (66.4)	40 (36.7)	0.608
No	29 (70.7)	12 (29.3)	
Defaulted medication			
Yes	31 (64.6)	17 (35.4)	0.876
No	55 (68.8)	25 (31.2)	
No known illness	22 (68.8)	10 (31.2)	
Diabetes mellitus			
Yes	19 (63.3)	11 (36.7)	0.589
No	89 (68.5)	41 (31.5)	
Ischemic heart disease			
Yes	10 (62.5)	6 (36.5)	0.653
No	98 (68.1)	46 (31.9)	
Hyperlipidemia			
Yes	28 (63.6)	16 (36.4)	0.520
No	80 (69.0)	36 (31.0)	
Cigarette smoking			
Yes	42 (72.4)	16 (27.6)	0.317
No	66 (64.7)	36 (35.3)	
Clinical findings			
GCS score on admission			
≤ 8	11 (25.0)	33 (75.0)	<0.001
9-12	36 (78.3)	10 (21.7)	
13 and above	61 (87.1)	9 (21.9)	
GCS reassessment after 24 hours			
Improved	61 (96.8)	2 (3.2)	<0.001
Static	37 (97.4)	1 (2.6)	
Deteriorate	10 (16.9)	49 (83.1)	
Blood pressure on arrival			
Systolic BP (mmHg)	185±36	192±41	0.416
Diastolic BP (mmHg)	108±24	107±23	0.605
Surgical intervention			
Yes	5 (27.8)	13 (72.2)	0.650
No	47 (33.1)	95 (66.9)	

Table 2: CT scan findings of patients with intracerebral haemorrhage included in the study

Site	Frequency Total	percent	Alive n (%)	Deceased n (%)	p value
Basal ganglia/ Internal capsule	45	28.1	39 (86.7)	6 (13.3)	.004
Lobar	70	43.8	47 (67.1)	23 (32.9)	
Cerebellum	14	8.8	8 (57.1)	6 (42.9)	
Brain stem	10	6.3	4 (40.0)	6 (60.0)	
Multilobar	21	13.1	10 (47.6)	11 (52.4)	
Midline shift, n (%)					
Yes	25	23.1	31	59.6	<0.001
No	83	76.9	21	40.4	
Intraventricular haemorrhage, n (%)					
Yes	20	18.5	32	61.5	<0.001
No	88	81.5	20	38.5	

(2 patients) and renal failure (2 patients). The locations of hematoma in order of frequency are shown in Table 2. The patients with basal ganglia/ internal capsule bleed had the best outcome in terms of survival (86.7 %). Mortality by volume of ICH is shown in Table 3. The significant predictors of acute in- hospital mortality at univariate analysis were lower GCS score, worsening of GCS, locations of hematoma, hematoma volume greater than 30 cc, the presence of mid line shift and evidence of intraventricular extension of haemorrhage. For multivariate analysis (Table 4), we omitted GCS as independent factor as it has high correlation with all other clinical manifestations. Further we compared patients with posterior fossa bleed (brain stem and cerebellar haemorrhage patients) versus anterior hemisphere (lobar, basal ganglia and multilobar involvement) to see if location of bleed was statistically significant. Our analysis revealed locations of hematoma, hematoma volume, mid line shift, and intraventricular extension of haemorrhage as the significant independent predictors of acute in- hospital mortality. Among our patients 4.4% took discharge against medical advice as they were told to have poor prognosis.

DISCUSSION

PICH has a high reported mortality rate of 35 to 52 %, out of which one-half of deaths occur within the first two days.[6,13-15] In the present study, the overall mortality rate was 32.5 % which is similar to the figures reported by the previous two Malaysian studies.[16,17] Both those studies were hospital based and employed similar methodology. One third (32.7%) of our patients died within first 24 hours following hospital admission and 38.5% within first 2 days, and 84.6% within one week. Our study is consistent with data from other groups.[10,13,18]This is expected as hematoma growth occurs during the first few hours after onset and is associated with early neurological deterioration and significant mortality.[19] Death is thought to occur inevitably from fatal brainstem dysfunction. This dynamic nature of ICH enlargement during the first several hours poses both a challenge and

Table 3: CT scan findings (volume of hematoma)

Volume (ml)	No. of cases	Patient's outcome Alive	n (%) Death
< 30	85	74 (87.1)	11 (12.9)
30 – 60	29	17 (58.6)	12 (41.4)
> 60	46	17 (37.0)	29 (63.0)

$p < 0.001$

Table 4: Predictors of in-hospital mortality among PICH patients

	B	SE	Wald	df	P	OR	95% CI	
Age	-0.011	0.018	0.369	1	0.544	0.99	(0.96,	1.02)
Male	-0.109	0.453	0.058	1	0.810	0.90	(0.37,	2.18)
Midline shift	1.199	0.588	4.164	1	0.041	3.32	(1.05,	10.50)
Ventricular haemorrhage	1.739	0.476	13.331	1	< 0.001	5.69	(2.24,	14.47)
Bleeding volume			8.185	2	0.017			
30-59 mL	1.554	0.6	6.701	1	0.010	4.73	(1.46,	15.33)
60 mL or more	1.551	0.644	5.807	1	0.016	4.72	(1.34,	16.64)
Posterior fossa bleed	2.399	0.629	14.536	1	< 0.001	11.01	(3.21,	37.81)
Constant	-2.538	1.179	4.632	1	0.031	0.08		

Binary logistic regression. B=Regression coefficient, SE=Standard Error, df=degree of freedom, OR=Odds Ratio. Hosmer and Lemeshow Test, $\chi 2$ =4.044, df =8, P=0.853. ROC 0.855 (95% CI 0.790, 0.920)

an opportunity for intervention. Ideally all these patients should be admitted to neuro-intensive care or stroke unit, where experienced stroke nursing care and close attention to vital signs can be monitored by a dedicated stroke team, so that effective treatment can be administered during the acute phase. Recent reports suggest improved outcome in stroke patients cared for by stroke teams and in stroke units, even in the worst initial prognostic groups.[20-22] Our mortality rate could have been reduced further, if our patients were managed in an acute stoke unit.

The view on prognosis of ICH is widely pessimistic among the public and physicians, and therefore early withdrawal of care during hospitalization is not unexpected. This is despite the fact that in many cases prognosis may not be as grim as initially judged.[23, 24] If withdrawal of care is factored into analysis, it may feature as one of the most important predictor of death in ICH.[20,24] Although hematoma volume and initial GCS score are valuable in predicting early outcome, decisions regarding withdrawal of medical care need to be individualized. According to American Heart Association (AHA) and American Stroke Association (ASA) guideline (2010) for management of spontaneous ICH, withdrawal of medical support or issuance of "do not resuscitate" (DNR) orders within the first day of hospitalization are predictors of poor outcome independent of clinical factors. Among our patients 4.4% took discharge against medical advice as they were told to have poor prognosis. In East coast of Peninsular Malaysia, once the relatives are told about the grim prognosis, it is customary for them to ask for the patient to be discharged home for a dignified death amidst their families. The final hours are spent in prayers and performing some religious rituals in which all the family members and close friends participate. This perhaps may add more pressure to seek for early withdrawal of medical care in cases of PICH.

The mean age of our patients was 58.3 years and this figure is comparable to previous Malaysian studies.[16,17] Western studies have reported older mean age.[25] The ethnic composition consisted of 81.9% Malays, 16.9 % Chinese and 1.3 others. The ethnic Malays were the majority because our hospital is situated in an area with large Malay rural population. The mean length of hospital stay in this study was 6.1 days which is shorter than that reported in previous studies.[15, 25, 26] The local practice of family taking responsibility of long term care probably accounts for the short hospital stay in this study. We investigated many of the well-known risk factors for early death in our analysis. Neither was age > 65 years nor gender, an independent predictor of mortality in this study as previously reported.[15]

Hypertension has been reported as the most common significant and independent risk factor for ICH[27,28] and treatment of hypertension with reduction in stroke.[29] Untreated hypertension is highly prevalent among patients and is a significant risk factor for hemorrhagic stroke.[30] The incidence of PICH is substantially greater among those who have ceased their antihypertensive medication.[31] Recently a high mean arterial blood pressure at admission was reported to be an independent predictor of early death in patients with ICH.[18]

Among our patients 74.4% had history of hypertension, out of which 30.0% had defaulted treatment. Twenty percent of our patients had no known prior illness and ICH was the first manifestation of their disease. Our patient's had high blood pressure readings on admission, the mean systolic blood pressure of 188 mmHg and diastolic blood pressure 108 mmHg, which was similar to previous Malaysian studies.[16,17] However neither history of hypertension nor blood pressure readings at admission predicted poor outcome in our analysis. Some authors have reported diabetes mellitus as an independent risk factor of early mortality[18,32], while others reported smoking as a risk factor for ICH.[33] However, our data did not show any statistically significant difference in mortality rates among the hypertensive, diabetic or those who were smoking.

In our study the most frequent sites of bleeding were lobar (43.8%) and basal ganglia region/ internal capsule (28.1%), which was in conformity with previous studies.[16,17] Site of bleeding had influence on the mortality, which was lowest among our patients with basal ganglia/ internal capsule bleed. On the other hand patients with multilobar involvement and brain stem bleed had higher mortality as shown in Table 2. GCS of <8, worsening of the GCS, volume of hematoma >than 30ml, midline shift and intraventricular extension of haemorrhage were identified as independent risk factors for early mortality in this study, which was similar to earlier studies.[16,17,24]

This is the first study that was conducted mainly among rural population in Malaysia. The strength of this study is its prospective design, confirmatory CT of all patients; strict inclusion criteria and strong institutional support. Further, all the patients were followed up consistently by one designated investigator. However it has several limitations. Many patients with mild stroke who did not report to a hospital may have been excluded. Further the assessment was done merely during the in-patient period and hence the mortality after discharge was not included in the analysis.

In conclusion, this study in East coast of Peninsular Malaysia showed that the significant independent predictors of acute in- hospital mortality were GCS of <8, locations of hematoma, hematoma volume, mid line shift and intraventricular extension of haemorrhage. Among our patients, untreated hypertension was the commonest risk factor and this guides our strategy for effective and early therapeutic intervention.

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DISCLOSURE

Conflict of interest: None

REFERENCES

1. Sutherland GR, Auer RN. Primary intracerebral haemorrhage. *J Clin Neurosci* 2006; 13:511-7.
2. Garibi J, Bilbao G, Pomposo I, Hostalot C. Prognostic factors in a series of 185 consecutive spontaneous supratentorial intracerebral haematomas. *Br J Neurosurg* 2002; 16:355-61.
3. Asian Acute Stroke Advisory Panel (AASAP). Stroke epidemiological data of nine Asian countries. *J Med Assoc Thai* 2000; 83: 1-7.
4. Flaherty ML, Haverbusch M, Sekar P, *et al*. Long-term mortality after intracerebral haemorrhage. *Neurology* 2006; 66: 1182-6.
5. Dennis M.S. Outcome after brain hemorrhage. *Cerebrovasc Dis* 2003; 16 (suppl1): 9-13.
6. Venketasubramanian N. The epidemiology of stroke in ASEAN countries - A review. *Neurol J Southeast Asia* 1998; 3:9-14.
7. Bonita R, Beaglehole R, Asplund K. The worldwide problem of stroke. *Cur Opin Neurol Neurosurg* 1994; 7: 5-10.
8. Gorelick PB. Cerebrovascular Disease in African Americans. *Stroke* 1998; 29: 2656-64.
9. Ng WK, Goh KJ, George J, Tan CT, Biard A, Donnan GA. A Comparative study of stroke subtypes between Asian and Caucasian in two hospital based stroke registries. *Neurol J Southeast Asia* 1998; 3: 19-26.
10. Nilsson OG, Lindgren A, Brandt L, Saveland H. Prediction of death in patients with primary intracerebral hemorrhage: a prospective study of a defined population. *J Neurosurg* 2002; 97: 531-6.
11. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke* 2001; 32: 891-7.
12. Manno EM, Atkinson JL, Fulgham JR, Wijdicks EF. Emerging medical and surgical management strategies in the evaluation and treatment of intracerebral hemorrhage. *Mayo Clin Proc* 2005; 80:420-33.
13. Kothari RU, Brott T, Broderick JP, *et al*. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke* 1996; 27: 1304-5.
14. Juvela S. Risk factors for impaired outcome after

spontaneous intracerebral hemorrhage. *Arch Neurol* 1995; 52:1193-200.
15. Qureshi AL, Safdar K, Weil J. Predictors of early deterioration and mortality in Black Americans with intracerebral hemorrhage. *Stroke* 1995; 26:1764-7.
16. Ong TZ, Raymond AA. Risk factors for stroke and predictors of one-month mortality. *Singapore Med J* 2002; 43:517-21.
17. Sia SF, Tan KS, Waran V. Primary intracerebral haemorrhage in Malaysia: in-hospital mortality and outcome in patients from a hospital based registry. *Med J Malaysia* 2007; 62: 308-12.
18. Tetri S, Juvela S, Saloheimo P, Pyhtinen J, Hillbom M. Hypertension and diabetes as predictors of early death after spontaneous intracerebral hemorrhage. *J Neurosurg* 2009; 110:411-7.
19. Broderick JP, Diringer MN, Hill MD, *et al*. Determinants of intracerebral hemorrhage growth: an exploratory analysis. *Stroke* 2007; 8:1072-5.
20. Zahuranec DB, Brown DL, Lisabeth LD, *et al*. Early care limitations independently predict mortality after intracerebral hemorrhage. *Neurology* 2007; 68:1651-7.
21. Diringer MN, Edwards DF. Admission to a neurologic/ neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. *Crit Care Med* 2001; 29(3):635-40.
22. Ronning OM, Guldvog B, Stavem K. The benefit of an acute stroke unit in patients with intracranial haemorrhage: a controlled trial. *J Neurol Neurosurg Psychiatry* 2001; 70:631–4.
23. Hemphill JC III, Newman J, Zhao S, Johnston SC. Hospital usage of early do-not-resuscitate orders and outcome after intracerebral hemorrhage. *Stroke* 2004; 35:1130-4.
24. Becker KJ, Baxter AB, Cohen WA, et al. Withdrawal of support in intracerebral hemorrhage may lead to self-fulfilling prophecies. *Neurology* 2001; 56: 766-72.
25. Colombo A, Faglioni P, Marzullo M, Scarpa M, Sorgato P. Risk factors and short term prognosis in ischemic and hemorrhagic attacks: review of 503 patients admitted to Neurologic Clinic of Modena. *Riv Neurol* 1989; 59:1-7.
26. Van Straten A, Van Der Meulen JH, Van Den Bos GA, Limburg M. Length of hospital stay and discharge delays in stroke patients. *Stroke* 1997; 28:137-40.
27. Davenport RJ, Dennis MS, Wellwood I, Warlow CP. Complications after acute stroke. *Stroke* 1996; 27:415-20.
28. Woo D, Sauerbeck LR, Kissela BM, *et al*. Genetic and environmental risk factors for intracerebral hemorrhage: preliminary results of a population-based study. *Stroke* 2002; 33:1190-6.
29. Collins R, Peto R, MacMahon S, *et al*. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990; 335:827.
30. Woo D, Haverbusch M, Sekar P, Kissela B, Khoury J, Schneider A, Kleindorfer D**.** Effect of untreated hypertension on hemorrhagic stroke**.** *Stroke* 2004; 35:1703-8.
31. Thrift AJ, McNeil JJ, Forbes A, Donnan GA. Three important sbgroups of hypertensive persons at greater risk of intracerebral hemorrhage. *Hypertension* 1998; 31:1223-9.
32. Arboix A, Massons J, Garcia-Eroles L. Diabetes is an independent risk factor for in-hospital mortality from acute spontaneous intracerebral hemorrhage. *Diabetes Care* 2000; 23:1527-31.
33. Kurth T, Kase CS, Berger K, Gaziano JM, Cook NR, Buring JE. Smoking and risk of hemorrhagic stroke in women. *Stroke* 2003; 34:2792-5.