

# Prediction of functional outcome in patients with primary intracerebral hemorrhage by clinical-computed tomographic correlations

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**Background:** Primary intracerebral hemorrhage (PICH) remains the deadliest and most disabling form of stroke. The aim of our study was to determine the potential predictors for survival and neurological recovery in PICH patients by clinical-computed tomographic (CT) correlation. **Materials and Methods:** A prospective study conducted among PICH patients at a tertiary care hospital. The clinical and CT scan findings were correlated with the functional outcome using modified Rankin scores (mRS) of 0-5 at discharge and during six months follow-up. **Results:** The clinical and CT findings in 160 (93 male and 67 female) eligible adult patients with age range from 25 to 85 years (mean age  $58.30 \pm 11.44$  years) were analyzed. The mean Glasgow Coma Scale [GCS] score was significantly higher among survivors. ( $12.8 \pm 0.4$  vs.  $8.5 \pm 0.5$ ,  $P < 0.001$ ) Based upon the pattern of the CT findings, the best outcome in terms of survival was for the patients with ICH in basal ganglia/internal capsule region (86.7 %), followed by lobar hemorrhage (67.1%). Good functional outcome was associated with a hematoma volume of less than 30 ml. At discharge majority of the survivors were functionally dependent 76 (70.4%) and only 32 (29.6%) achieved functional independence. The significant independent predictors of in-hospital survival were GCS score  $> 9$  (OR 10.8; 95% CI 4.061 to 28.719), basal ganglia/internal capsule bleed (OR 9.750; 95% CI 2.122 to 45.004), hematoma volume  $< 30$  ml (OR 11.476; 95% CI 4.810 to 27.434), no mid line shift (OR 4.901; 95% CI 2.405 to 9.987) and no intraventricular extension of hemorrhage (OR 7.040; 95% CI 3.358 to 14.458). **Conclusion:** Outcome and functional status at discharge were well correlated with the initial CT scan findings and GCS score.

**Key words:** Computed tomography scan, glasgow Coma Scale, modified Rankin score, primary intracerebral hemorrhage, rehabilitation, survival

## INTRODUCTION

Intracerebral hemorrhage (ICH) accounts for 20-30% of all cases of stroke among Asian population approximately twice higher than that in the West.<sup>[1-3]</sup> It remains the deadliest and most disabling form of stroke worldwide with high early mortality.<sup>[4-6]</sup> Functional outcome in survivors is also poor with fewer than 20% being independent at six months.<sup>[7]</sup> At present there is no convincing evidence of benefit from any medical treatment, and the role of surgery remains controversial.<sup>[8,9]</sup> An early and accurate prediction of ICH outcome in the emergency department is crucial for decision-making, as well as in assessing patient prognosis.<sup>[10-13]</sup> There is evidence to suggest that

aggressive care can increase the chances of survival and physical independence, even in the worst initial prognostic group.<sup>[14,15]</sup> Under these circumstances, identification of factors which may influence the quality of care is crucial as most therapeutic decisions have to be individualized.

Once an ICH occurs, the most efficient way to localize the hemorrhage is non-contrast Computed Tomography (CT) of the brain. It is the main imaging modality recommended for the initial emergency evaluation of acute stroke due to its exquisite sensitivity for the detection of blood.<sup>[16-18]</sup> It is also readily available with short acquisition time, and applicable to almost any patient, with results that are relatively easy to interpret. CT scan usually defines the size, location of the hemorrhage, shift of midline structures and presence of hydrocephalus.<sup>[19]</sup> Sixty to 70% of PICH is hypertension related and, in the elderly, amyloid angiopathy accounts for up to one-third of the cases.<sup>[20]</sup> Hemorrhages due to hypertension are well circumscribed, homogeneous, and in typical locations (putamen/internal capsule, caudate nucleus, thalamus, pons, or cerebellum), while ICH related to

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amyloid angiopathy are mostly lobar, usually multiple but occasionally cerebellar.<sup>[21]</sup>

The GCS score is now a standard neurological assessment tool. Low GCS score, large hematoma volume, midline shift and the presence of ventricular blood on the initial CT scan have been consistently shown to predict high mortality rate. Only a few studies from the West have attempted to identify factors related to a favorable functional outcome in these patients.<sup>[22,23]</sup> Despite the higher rates of ICH in this part of the world, no study has attempted to identify factors related to a good functional outcome among PICH patients in Malaysia. Hence, the present study was contemplated to determine the potential predictors of good functional outcome by clinical-computed tomographic correlation. The modified Rankin score (mRS) was used for the assessment of functional status among survivors, as this scale is able to provide an overall estimate of the level of functional dependence in a given stroke survivor.<sup>[24]</sup>

## MATERIALS AND METHODS

### Study design

All the 172 patients admitted at the hospital Tengku Ampuan Afzan (HTAA) Kuantan Malaysia from December 2007 till November 2009, within few hours to 24 hrs of onset of symptoms, were initially observed at the emergency department to check for vital signs and subsequently subjected to CT scan of brain. They were then sent to the ward for further care.

### Inclusion and exclusion criteria

PICH was defined as spontaneous extravasation of blood into brain parenchyma not attributable to an underlying cause and documented by brain CT. Based on review of baseline clinical data and the results of CT imaging, patients with secondary causes of ICH such as subarachnoid hemorrhage, vascular malformation, central nervous system tumor, antecedent trauma (subdural hematoma/epidural hematoma/brain contusion) or hemorrhagic transformation of cerebral infarct or coagulation abnormalities were excluded.

### Ethics

The study protocol was approved by the ethical committees of both the hospital HTAA and the affiliated faculty of Medicine, International Islamic university Malaysia (IIUM). Patients or their close relatives were approached by study personnel during the hospitalization and informed consent was sought for enrolment into the study.

Only 160 patients who fulfilled the inclusion criteria were eventually enrolled. Patients or their close relatives were interviewed to obtain information pertaining to the onset of

stroke and any pre-existing risk factors like hypertension, diabetes mellitus, use of warfarin or any medication. The patient's previous records were also reviewed for hypertension, diabetes mellitus and current medication. 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 on admission and followed up consistently by the designated research assistant until their discharge. Clinical variables of each patient, such as GCS on arrival and further follow-up, body temperature, blood pressure, CT imaging findings, any surgical intervention/complications, length of hospital stay and outcome at discharge were recorded into a standardized proforma. The choice of subsequent clinical management, for example management of blood pressure, surgical evacuation, raised intracranial pressure and other complicating illnesses in the ward was left at the discretion of the treating physician.

All CT scans were downloaded directly to a workstation where they 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  $(A \times B \times C)/2$ , where A and B are the largest perpendicular diameters of the hematoma measured on the CT scan, and C is the number of slices multiplied by the slice thickness. Variables in relation to the region of hemorrhage included basal ganglia region/internal capsule, cerebellum, brainstem, lobar and multi lobar hemorrhage - (when more than one of the aforementioned topographies were affected).<sup>[25]</sup> Secondary intraventricular extension of hemorrhage/mid line shift was also assessed. Mass effect was defined as the presence of midline shift displacement by 0.5 mm on cranial CT. On the basis of volume of hematoma, patients were categorized into three groups; less than 30 ml, 30-60 ml and more than 60 ml.<sup>[11]</sup>

Patient functional outcome was evaluated at discharge and during follow-up for up to six months in the neurology clinic by mRS 0 to 5 (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. Patients with mRS of (0 - 2) were considered to have good functional outcome as they were functionally independent while those with mRS of (3 - 5) were considered as functionally dependent.<sup>[24]</sup>

Stroke rehabilitation was started as soon as the patient's conditions permitted in the ward and in this task family members and caregivers were also involved, so that it is continued at home. Functionally dependent survivors were subsequently followed up in the stroke rehabilitation clinic.

### 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 (with Yates correction if needed). Variables that were significantly related to survival 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

Demographic characteristics and clinical variables of PICH are summarized in Table 1. Of 160 patients, 93 were male and 67 female, with age range from 25 to 85 years (mean age  $58.30 \pm 11.44$  years). Among our patients hypertension was the commonest risk factor (74.4%) followed by diabetes mellitus (18.8%), and cigarette smoking (36.3%). More than half (54.4%) of the patients were on medication prior to onset of stroke, out of which 30.0% had defaulted treatment.

Common clinical presentations varied from deranged sensorium (39.4%), headache accompanied by nausea, vomiting and loss of consciousness (33.1%), sudden neurological deficit (25.0%) to seizures (2.5%). Patients who presented with headache and loss of consciousness had worse outcome  $<0.001$ .

The mean systolic blood pressure on admission was  $187 \pm 37.64$  mmHg and diastolic blood pressure  $107 \pm 23.2$  mmHg. The mean GCS score was significantly higher among patients who survived ( $12.8 \pm 0.4$  vs.  $8.5 \pm 0.5$ ,  $P < 0.001$ ). One third (32.7%) deaths occurred within the first 24 hrs, 38.5% within first two days and 84.6% within first week from the onset. The mean length of hospital stay for all cases was  $6.1 \pm 4.6$  days and  $7.0 \pm 4.6$  days among live discharges. Twenty three patients were advised for decompressive surgery but only 18 underwent the procedure, out of which 13 (72.2%) survived and 5 (27.8%) died. Correlation between CT scan findings affecting in hospital survival is depicted in Table 2. Basal ganglia/internal capsule and lobar hemorrhage were more frequent sites of ICH than other regions. The best outcome in terms of survival was for the patients with hemorrhage in basal ganglia/internal Capsule region, which was 86.7%. Patients with no midline shift had a better prognosis (79.8%

vs. 44.6%,  $P < 0.001$ ). The significant predictors of acute in-hospital survival at univariate analysis were GCS score of  $>8$ , locations of hematoma and hematoma volume less than 30 ml. For multivariate analysis, GCS was omitted as independent factor as it has high correlation with all other clinical manifestations. After multivariate analysis, significant predictors of survival and neurological recovery

**Table 1: Socio-demographic and Clinical Profile of ICH patients included in the study**

Characteristics	Alive % (n)	Deceased % (n)	P value
Demographic			
Age (year) mean $\pm$ SD	58.3 $\pm$ 11.6	58.3 $\pm$ 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 (0.0)	
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			
Diabetes mellitus	22 (68.8)	10 (31.2)	
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			
$\leq 8$	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 24hrs			
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 $\pm$ 36	192 $\pm$ 41	0.416
Diastolic BP (mmHg)	108 $\pm$ 24	107 $\pm$ 23	0.605
Surgical intervention			
Yes	5 (27.8)	13 (72.2)	0.650
No	47 (33.1)	95 (66.9)	

GCS=Glasgow Coma Scale, Deceased patients=Death in hospital, SD=Standard deviation

**Table 2: Univariate and multivariate analyses for factors affecting in-hospital survival**

	Crude or	95% CI Crude or		P	Adjusted or*	95% CI Adjusted or		P
		LL	UL			LL	UL	
Age (years)	1.000	0.972	1.030	0.993				
Male	1.296	0.665	2.526	0.447				
Race								
Malay	1.509	0.644	3.537	0.344				
Chinese	1							
Clinical presentation					1			
Deranged sensorium	1							
Neurological deficits	0.188	0.050	0.698	0.013	0.562	0.122	2.601	0.461
Headache and loss of consciousness	0.079	0.022	0.281	<0.001	0.192	0.045	0.813	0.025
Fits	0.243	0.019	3.118	0.277	0.132	0.009	1.959	0.141
GCS on admission								
8 and lower	1							
9-12	10.800	4.061	28.719	<0.001				
13 and above	20.333	7.651	54.040	<0.001				
GCS after 24 hours								
Static	1							
Deteriorated	0.006	0.001	0.045	<0.001				
Improved	0.824	0.072	9.410	0.876				
Bleeding site								
Internal capsule/ Basal ganglia	9.750	2.112	45.004	0.004	18.82	2.841	124.676	0.002
Lobar	3.065	0.787	11.942	0.106	20.546	3.168	133.235	0.002
Multilobar	1.364	0.296	6.283	0.691	18.604	2.286	151.399	0.006
Cerebellum	2.000	0.384	10.409	0.410	2.896	0.397	21.115	0.294
Brain stem	1				1			
No midline shift	4.901	2.405	9.987	<0.001	3.947	1.212	12.855	0.023
No inter-ventricular extension	7.040	3.358	14.758	<0.001	5.317	1.969	14.352	0.001
Hematoma volume								
<30 or =	11.476	4.801	27.434	<0.001	3.861	0.995	14.985	0.051
>30 but=or<60	2.417	0.934	6.255	0.069	1.13	0.319	3.994	0.85
>60	1				1			
No hypertension	1.224	0.565	2.650	0.609				
No diabetes mellitus	1.257	0.548	2.881	0.589				
Not smoking	0.698	0.345	1.413	0.318				
No hyperlipidemia	1.270	0.612	2.633	0.521				
No decompression surgery	1.286	0.433	3.822	0.650				

\*Hosmer-Lemeshow  $\chi^2=6.098$ ; df=8, P=0.523; or, odds ratio

were ICH volume, ICH location and absence of mid line shift or intraventricular extension of hemorrhage, while ICH volume of <30 ml was associated with good functional outcome [Table 3].

At the time of discharge majority of the survivors were functionally dependent 77 (70.6%) and only 32 (29.4%) had achieved functional independence. Patients coming from far flung areas that were unwilling to come for follow-up at HTAA, were referred to their local hospitals. After one month 87 patients came for follow up, 48 (55.2%) were functionally independent while 39 (44.8 %) were still dependent. Four patients had developed severe depression requiring psychiatric intervention. After about six months follow-up, five patients were lost due to default in treatment

**Table 3: Correlation between volume of hematoma and rankin's score**

	N	Independent		Dependent		P
		n	%	n	%	
Less than 30 ml	75	26	34.7	49	65.3	0.039
30 ml or more	33	5	15.2	28	84.8	

Independent=mRS of (0- 2); Dependant=mRS of (3-5)

and invalid telephone number, 69 (84.1%) were independent and 13 (15.9%) were still dependent.

## DISCUSSION

PICH has a high reported mortality rate of 40 to 50%.<sup>[11,26-28]</sup> In the present study, the overall mortality rate was

32.5% which was similar to the figures reported by the previous two Malaysian studies.<sup>[28,29]</sup> One third (32.7%) of our patients died within first 24 hrs following hospital admission and 38.5% within first two days, similar to previous studies.<sup>[9,11]</sup>

According to some studies level of consciousness on hospital admission and hematoma volume are the most robust outcome predictors.<sup>[7,30]</sup> In our study, patients who presented with headache followed by loss of consciousness had worst outcome. Clinical presentation alone is insufficient to predict outcome, because ICH is not a static phenomenon and expansion of cerebral hematoma of any topography occurs early in about 27% of cases, which can be detected by repeat CT scans.<sup>[31,32]</sup> This results in secondary brain damage and is the primary cause of neurological deterioration after the first day.<sup>[32,33]</sup> A good clinical status on admission should not therefore lead to complacency.

In the present study we evaluated the contribution of various well-known risk factors to the outcome. The mean age of patients was 58.30 years and this figure is comparable to previous Malaysian studies.<sup>[28,29]</sup> Western studies have reported older mean age.<sup>[34]</sup> 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.<sup>[27,34,35]</sup> The local practice of family taking responsibility of long term care probably accounts for the short hospital stay in this study.

Hypertension has been reported as the most common significant and independent risk factor for ICH,<sup>[36,37]</sup> and treatment of hypertension with reduction in stroke.<sup>[38]</sup> Sixty to 70% of PICH are related to rupture of small penetrating arteries and arterioles that have been damaged by chronic arterial hypertension or amyloid angiopathy.<sup>[20]</sup> Recently a high mean arterial blood pressure at admission was reported to be an independent predictor of early death in ICH patients.<sup>[39]</sup> Among our patients 74.4% had history of hypertension, out of which 30.0% had defaulted treatment. Twenty percent had no known prior illness and ICH was the first presentation. Further our patient's had high blood pressure readings on admission, similar to previous Malaysian studies.<sup>[28,29]</sup> Some studies have reported diabetes mellitus as an independent risk factor of early mortality<sup>[39,40]</sup> while others reported smoking as a risk factor for ICH.<sup>[41]</sup> The effect of cholesterol (hyperlipidemia) is uncertain, but recent evidence suggests that therapeutic reduction of cholesterol level reduces the incidence of stroke overall but is associated with a small increase in

the risk of ICH.<sup>[42]</sup> However, our data did not show any statistically significant difference in outcome rates among the hypertensive, diabetic or those who were smoking. Neither was age >65 years nor gender, an independent predictor of mortality in this study as previously reported.<sup>[27]</sup> The independent predictors are used in clinical decision making and attempt to prognosticate outcome. Hence while making decision these factors need to be considered.

The ICH volume has been found a strong predictor and often divided into three groups representing small, medium and large hematoma size.<sup>[11,43]</sup> While the specific volume cut points vary depending on the specific model, small hematomas have often been considered as 30 ml and large hematomas as 60 ml. Among our patients hematoma volume of <30 ml was a predictor of good functional outcome  $P < 0.039$ .

Our sites of bleeding on neuroimaging were in conformity with previous studies.<sup>[28,29,43]</sup> Site of bleeding had influence on survival, which was highest among our patients with basal ganglia region/internal capsule bleed. On the other hand patients with multilobar and brain stem bleed had higher mortality as shown in Table 2.

Eighteen of our patients underwent decompressive surgery out of which 13 (72.2%) survived. Although statistically insignificant, these preliminary findings probably determine a change in the management of patients of PICH to improve outcome. Conducting a larger prospective study might serve to confirm these trends in improvement.

To our knowledge, this is the first study in Malaysia to determine the potential predictors of good functional outcome by clinical-computed tomographic correlation. PICH patients are often neurologically devastated on presentation and functional recovery depends on family support, the patient's motivation, ability to learn as well as the quality and intensity of therapy. Over the 6 months follow up; an increasing number of our patients achieved functional independence, which may be attributed to stroke rehabilitation and physiotherapy services provided by our hospital. However spontaneous neurological recovery and natural improvement with family support is also an important factor to be considered.<sup>[44]</sup> The strict inclusion criteria and strong institutional support are the strengths of our study. Further, all the patients were followed up consistently by one designated investigator.

## CONCLUSION

The functional status at discharge was well correlated with the initial CT scan findings and GCS score. Therefore

CT scan which is readily available, with results that are relatively easy to interpret is a useful tool in clinical decision making and predicting likely functional independence.

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