# **ORIGINAL PAPER**



# Formulation of a radiological scoring system to prognosticate patients with primary intracerebral haemorrhage

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#### ABSTRACT

**Background.** Primary intracerebral haemorrhage is a neurological condition associated with high morbidity and mortality. Outcome prediction is necessary to allocate the available resources in such cases judicially. Our study aims to identify the radiological predictors of in-hospital mortality based on a plain CT study of the brain at admission and to develop a prognostic scoring system based on them.

**Material and methods.** We collected the clinical and radiological data from 182 consecutive patients who presented with primary spontaneous ICH. Bivariate analysis of radiological predictors of in-hospital mortality was undertaken using unadjusted logistic regression. Those variables found to have significance were put into a multivariate logistic regression model. The Results of multivariate logistic regression were treated as a foundation for developing the scoring system.

**Results**. The mortality rate in our series was 23.6% (N = 43). After multivariate analysis, Midline shift (MLS), presence or absence of intraventricular haemorrhage (IVH), Volume of ICH and Location of haematoma were significant predictors of mortality. Based on the identified radiological variables, a five-score prognostic scoring system (AUROC = 0.925, 95% CI 0.887–0.964)) was developed, with higher scores indicating higher mortality. **Conclusions**. The established scoring system, MIVL, may help physicians to do better patient counselling regarding outcomes.

# Introduction

Primary spontaneous intracerebral haemorrhage (PSICH) accounts for about 4–14% of all forms of stroke and carries a high mortality rate approach-

ing 40% [1–6]. Both medical and surgical treatments are available, but which modality would benefit an individual patient is yet to be clear [7, 8]. Clinical decisions regarding management

strategies are not often straightforward, given the ethical, moral and medical aspects involved in it. It is critical to strike the right balance between excessive but futile healthcare inputs on one side and dangerous self-fulfilling prophecies on the other. Such decisions assume paramount importance, especially when the resources are limited, to allocate them to the right patient with a high overall chance of survival. Literature is rife with several complex prognostic models, including clinical, biochemical, and radiological parameters but a scoring system based on radiological variables alone is lacking [9]. Therefore, in this study, we aim to define the radiological predictors of in-hospital mortality in PSICH based on information gathered from a plain CT scan of the brain obtained at admission and to develop a scoring system that can be adapted in such settings to enable easy exchange of objective prognostic information between healthcare professionals across various disciplines.

# Materials and methods

After obtaining approval from the institutional ethics committee, we retrospectively analysed the data collected as a part of a single-centre prospective cohort study of primary ICH undertaken at our tertiary care teaching hospital. Patients who presented with PSICH to our hospital between May 2017 and May 2018 were recruited for the study. The patients or their responsible bystanders consented to the study. Basic demographic information and a detailed clinical history to reveal the chronology of events were collected. The Glasgow Coma Scale (GCS) score on admission and history of hypertension, diabetes mellitus, alcoholism and smoking were also recorded. For the study, the primary intracerebral haematoma was defined as spontaneous blood leakage into the supratentorial brain parenchyma, documented by a plain CT study of the brain. In-hospital mortality was defined as mortality occurring within the first 30 days of admission. Patients with infratentorial bleeds, age above 80 years, with multiple haemorrhages, presenting after 24 hrs of ictus and with secondary ICH due to any cause were excluded from the study.

A plain CT scan of the brain performed on admission was analysed, and the parameters

such as volume of haematoma, midline shift (MLS), intraventricular haemorrhage (IVH), presence or absence of hydrocephalus, side of haematoma and location of haematoma (deep/ superficial) were noted. The volume of haematoma was measured by the method described by Kothari et al. [10] using the formula ABC/2, where A is the measure in the measurement of the most substantial haemorrhage dimension, B the diameter at 90 degrees to A, and C is the number of slices with haemorrhage multiplied by its thickness. For defining the location, the axial CT cut passing through the foramen of Monro was taken. First, a vertical line is drawn through the midline, and another line 2cm lateral to this line on either side is adjusted to scales. Next, two horizontal lines are drawn along this cut's most prominent anterior and posterior portion of the lateral ventricles. If the haematoma occupies the rectangle bounded by these four lines, it is classified as deep or zone 1. The primary outcome was in-hospital mortality, which was defined as death in the hospital during the current admission or within 30 days after. In-hospital mortality was considered a poor outcome, and the absence of this was defined as recovery the study.

All data were analysed using SPSS software version 16.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were stated as means with standard deviations, and categorical variables as percentages. The association between individual radiological parameters and outcome were first estimated using bivariate logistic regression analysis. Then, those radiological parameters showing statistical significance were analysed using a multivariate logistic regression model. Two continuous variables, hematoma volume and MLS were dichotomized using maximum sensitivity and specificity values obtained from the receiver operating curve (ROC). The regression coefficients of each factor in the multivariate logistic model were transformed into a risk score by dividing them by the smallest regression coefficient among the variables and then rounding the quotients to the nearest integer for developing the risk scoring system. Model performance consisting of the area under the receiver operating curve (AUROC) and Hosmer-Lemeshow goodness-of-fit test were further assessed. A p-value less than 0.05 was considered significant.

# Results

The initial cohort included a total of 201 cases. After applying all the inclusion and exclusion criteria, 182 subjects were recruited for the study. Males constituted 56.6% (N = 103) of our subjects. The whole cohort had a mortality rate of 23.6% (N = 43). The mean age was 62.90 years (median 64.5 years, range 31 to 79 years). Most, 53.84% (N = 98), presented with headache and altered sensorium. Headache alone was the presenting symptom in 20.3% (N = 37) patients, while 25.8% (N = 47) were unconscious at presentation. Prominent risk factors identified were hypertension 112 (61.5%), smoking 108 (59.3%), diabetes mellitus 61 (33.5%), and alcohol intake 58 (31.9%) in that order. Mortality was high within the first 48 hours of ictus (N = 20, 46.5%), and their presenting GCS were also significantly low (7 vs 13, P < 0.001). The mean hospital stay was 11 days. Most were managed along aggressive medical lines (88.4%, N = 161), while a surgical procedure was performed in 11.5% of patients (N = 21). Craniotomy and evacuation were done in 8.8% (N = 16) of patients, and external ventricular drainage alone in 2.7% (N = 5). A significant difference in outcome was not observed between the medical and surgical groups (P = 0.119).

The haematoma volume ranged from 4 ml to 230 ml (mean 45.5 ml). Patients with poor outcomes had a mean haematoma volume of 93.9 ml compared to 27.6 ml in those with recovery. The midline shift for the whole series ranged from 0 to 12 mm, with a mean of 2.8 mm. **Figures 1** and **2** show a ROC that was made to test the predictive accuracy of these variables (haematoma volume and MLS). IVH was present in 31.9% (N = 58) and hydrocephalus in 36% (N = 66) of subjects.



Diagonal segments are produced by ties.





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Figure 2. ROC (Receiver operating curve) shows the accuracy of volume of haematoma for a favourable outcome.

**Table 1.** Results of bivariate Logistic regression analysis.

SI No	Radiological variable	P-value	OR	95% confidence interval (lower–upper)
1	Midline shift	0.00	25.938	10.288-65.412
2	Volume	0.00	7.395	3.275-16.697
3	Intraventricular haemorrhage	0.00	6.988	2.541-19.214
4	Hydrocephalus	0.062	0.510	0.252-1.033
5	Zone	0.00	12.061	5.125-28.366
6	Site	0.826	0.926	0.466-1.839

Haematoma volume, MLS, IVH and location of haematoma attained statistical significance for in-hospital mortality on bivariate analysis (see **Table 1**). Haematoma volume and MLS were closely correlated with GCS. (Pearson correlation -0.663 and -0.612, respectively, P < .001). GCS was significantly low in patients with IVH and hydrocephalus (P < 001). On multivariate analysis MLS, the presence or absence of IVH, the volume of ICH and the location of haematoma were significant predictors of mortality (see **Table 2**).

The final risk prediction model contained four variables statistically significantly associated with in-hospital mortality in the multivariate

Table 2. OR for in-hospital mortality.

Predictor variable	OR (95% CI)	P-value
Intraventricular haemorrhage		
Present	6.7 (2.16–20.71)	0.001
Absent	-	
Volume		
>30ml	4.7 (1.4–15.1)	0.009
≤30ml	_	
Midline shift		
>6mm	14.5 (4.8-43.7)	0.001
≤6mm	-	
Zone		
1	4.7 (1.5-14.8)	0.007
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logistic regression analysis. The regression coefficients of all variables in the risk prediction model were transformed into risk scores, as demonstrated in Table 3.The risk scoring system, named MIVL, contained the following variables: 1) Midline shift ( $\leq 6$  mm vs >6 mm), 2) Intraventricular haemorrhage (present or absent), 3) Volume ( $\leq 30$  ml vs >30 ml), 4) Location of hematoma (deep vs superficial) as defined above. The sum of scores ranged from a minimum of 0 to a maximum of 5. No patient with a score of 0 died, while 18 (94.7%) patients with a score of 5 expired 30 days after admission (see Figure 3). The Hosmer-Lemeshow test yielded a *P* value of 0.438, indicating ade-

## Table 3. Determinants of the score.

Variable	Regression	Risk
	coefficient	score
Intraventricular haemorrhage		
Absent	0	0
Present	1.903	1
Volume of haemorrhage		
≤30 ml	0	0
>30ml	1.548	1
Midline shift		
≤6mm	0	0
>6mm	2.680	2
Zone of hematoma		
Zone 2	0	0
Zone 1	1.566	1



Figure 3. The Y-axis shows in-hospital mortality and the X-axis showing the MIVL score.



Figure 4. ROC curve for components of the score.

quate goodness-of-fit of the model. In the evaluation of the predictive accuracy of the model, the MIVL score was able to achieve an area under the curve (AUROC) of 0.925. **Figure 4** represents the ROC curve for components of score.

# Discussion

Any prognostic scoring model must be simple and accurate, though it would be counterintuitive to assume to be both. In this study, we attempted to develop a simple scoring system based on radiological parameters only to prognosticate patients with primary spontaneous supratentorial intracerebral bleed. Clinical grading scales serve the purpose of providing consistency and standardisation of prognostication in neurological conditions. The intracerebral haemorrhage (ICH) score, one of the first available scores, is the most widely used for prognostication purposes to estimate 30-day mortality following spontaneous ICH [11]. The score is based on the location and volume of ICH, presence of IVH, GCS on admission and age of the patient. The score ranged from 0 (best outcome) to 6 (worst outcome). Thirty-day mortality rates for ICH scores 1, 2, 3 and 4 were 13%, 26%, 72% and 97%, respectively. In their cohort, no patient with a score of 0 died, and all patients with a score of 5 died. No patient had a score of 6 in their cohort.

Mc Cracken et al., in a review of 554 patients, have found that the ICH score did not accurately predict mortality [12]. Patient survival exceeded the ICH score predicted mortality regardless of the intervention. The score ranged from 0 to 11, and 85% of the patients with a FUNC score of 11 reached functional independence at 90 days [14]. Clinical and radiological variables are often combined in many models, which would, however, lead to a problem of collinearity because the radiological variables reflect the clinical condition rather than the cause.

The mass effect produced by the haematoma and associated oedema caused MLS and was a significant prognostic variable in our study. There was a good correlation between haematoma volume and MLS (Pearson's correlation 0.706, P < 0.05). Though it is reasonable to assume higher mortality to a higher degree of MLS, the literature does not uniformly endorse this. In several studies, MLS has not been a statistically significant predictor of outcome [15]. One reason is that many of these studies have included infratentorial haemorrhages also, where MLS may be absent. Infratentorial haemorrhages per se constitute a distinct cohort from treatment and prognostic points of view and hence excluded them from our study. The shift of midline structures is also closely linked to brain atrophy. An atrophied brain may tolerate more blood without producing much mass effect. Fogelholm et al.

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demonstrated a significant relationship between MLS and outcome [16]. The shift of midline structures has been the most robust outcome predictor in our study and has been weighted more with a score of two points, which would mean that the prognostic implication of midline shift is more in spontaneous bleed.

IVH is consistently associated with poor outcomes across several studies. IVH was associated with a worse outcome in our study, with an OR of 6.7 (P < 0.001). Leira et al. [17] showed a 2.6 times chance of neurological deterioration following IVH. Blood is an irritant and can make the patient seizure-prone when collected in the ventricles. It can also obstruct the CSF pathways and produce hydrocephalus. Both these mechanisms augment the morbidity, along with the primary cause. Diringer et al. found that the shift of the pineal body and hydrocephalus were significant predictors of mortality [18]. Our cohort's hydrocephalus had no significant predictor on bivariate analysis (OR 0.51, 95% CI 0.252-1.033), which may result from IVH causing hydrocephalus and including both variables + in a single model will lead to the problem of collinearity Ex vacuo hydrocephalus may accompany old age, so IVH-associated hydrocephalus can be difficult to distinguish We have excluded hydrocephalus in our model due to these reasons.

The volume of haematoma is a significant prognosis predictor in several models. We have also identified volume as a important predictor of poor outcomes (P < 0.001). Haematoma volumes have been dichotomized into more than or less than 30 ml based on a trade-off between maximum sensitivity and specificity as predicted from ROC, enhancing its ease of usage. Though CT scanners could measure the volume of hematoma more accurately, we have used the ABC/2 method, considering the end users' ease of calculation. Moreover, this method has been found to be accurate with good inter-rater reliability.

Al-Mufti et al. researched various prognostic variables that could affect the outcome [19]. The most studied radiological predictors were the location, expansion, and volume of haematoma, swirl sign, spot sign, peri-haematoma oedema, IVH and hydrocephalus. Broderick et al. [20] have conducted a study of 30-day mortality based on ICH volume. For volumes more than 60cm<sup>3</sup>, they have reported 93% mortality for deep and 71% mortality for lobar locations. The location of haematoma also attained statistical significance in our model, with a score of one attributed to deep locations. In a similar study, Flemming et al. [21] described 40 ml as a critical volume which would predict a bad outcome. We used the ROC curve and identified 39 ml as the optimum cut-off volume for poor outcome (sensitivity 79.6%, specificity 83%), while a generally accepted cut-off is set at 30 ml. A worse outcome has also been attributed to haematoma expansion, a volume increase of more than one-third [22].

Brain damage following ICH occurs in three stages [23]. Primary artery rupture and bleeding occur in the first stage, haematoma expansion in the second stage, and brain oedema in the third stage. Hematoma expansion occurs in the first six hours in about 30% of cases, accounting for the high mortality observed on the first day of ictus. After 24 hours, haematomas seldom enlarge [24]. We also observed that 46.5% of deaths occurred in the first 48 hours. By that time, the brunt of the brain damage might have occurred. This pathophysiological profile has clinical repercussions. It may be one reason early surgical intervention does not offer an advantage over aggressive medical counterparts regarding outcomes or functional independence. Some authors believe that surgical treatments are making a comeback [25], but we could not document any significant outcome advantage in our surgical group (P = 0.119). Though assuming that the outcomes may be worse for dominant side haemorrhages may be reasonable, we could not identify significance for a particular side. A higher frequency of putaminal haemorrhages was observed on the side of dominant A1 [26].

Different studies have attempted to elucidate prognostic information from radiological data in ICH. The leakage of contrast into the haematoma is called the spot sign [27] and is a grave prognostic marker. It is an indication of active haemorrhage. Delgado Almandoz et al. [28] have developed a spot sign scoring system to predict mortality and poor outcome. But this required a contrast CT scan, which is only sometimes taken as a first-line investigation. The swirl sign, which is classically described in epidural haematoma, can also be seen in intracerebral haemorrhages. This sign shows a low attenuated area with irregular density in the haematoma. If this sign is present, it is an independent predictor of death at one month [29]. Li Q et al. [30] described the blend sign as the presence of two areas within the haematoma, one relatively hypoattenuating area with an adjacent hyperattenuating area with well-defined margins visible to the naked eye. There should be at least an 18-Hounsfield-unit difference between the two areas. This sign was observed only in 16.9% of patients, but if present, has got 95.5% specificity for predicting haematoma growth. Another sign described by Qi Li et al. is the black hole sign [31]. This is an area of hypoattenuation with clearly visible borders within an area of hyper attenuation with a difference of 28 Hounsfield units. The sign was specific for predicting haematoma growth and was present in 14.6% of patients. Of all the above radiological signs, the spot sign was the most reliable outcome predictor [32]. The heterogeneity of density of the haematoma itself is a marker of poor outcome [33]. However, the signs mentioned above are not present in all patients and hence cannot be uniformly applied to all patients.

# Conclusion

In summary, based on radiological data alone, the MIVL score is an easy scoring system for risk stratification and prognostication of patients with supratentorial ICH. The score is simple and will enable an exchange of prognostic information between healthcare professionals across various disciplines, even if clinical data needs to be included, but not to be used as the best indicator of prognosis. The model has been primarily intended to be used in places where resources are limited to take appropriate decisions regarding referral, intensive care or operative interventions and patient counselling regarding the potential outcome. However, the relatively small number of patients in our cohort and its single institutional nature are major limitations of our study.

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#### Statement of ethics

The Institutional Ethics Committee granted the ethical approval.

#### **Authors contribution**

KK, HG, and JJ prepared the concept and design. KK, HG, and JJ undertook the methodology and wrote the original draft. In addition, JJ did a critical review and final editing.

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#### **Conflict of interest statement**

The authors declare no potential conflicts of interest concerning this article's research, authorship, or publication.

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