Bangladesh Journal of Neuroscience 2019; Vol. 35 (2): 78-85

Prognostic significance of Intracerebral Hemorrhage Score in predicting 30-day mortality in Chittagong Medical College Hospital

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Abstract:

Background:*Prognosticating the outcome of Intracerebral Hemorrhage (ICH) at the time of admission is important to customize treatment in a cost-effective manner in such cases. ICH sore is a widely used prognosticating tool but yet not evaluated in our setting. This study was aimed to assess the prognostic factors influencing outcome and validating the ICH score for prediction of 30-day mortalityin hospitalized patients with ICH.* ***Materials and methods:****This prospective observational study was conducted in Chittagong Medical College Hospital, Bangladesh among 105 consecutively admitted patients aged 18 years and above with a computed tomography evidence of spontaneous ICH. ICH score was calculated soon after confirmation of diagnosis. Primary outcome measure was 30-day mortality after admission. Modified Rankin Scale (mRS) was used to assess outcome at discharge and at 30-day follow up.* ***Results:****A total of 104 patients were analyzed. Mean age of this cohort was 59.30±19.91 years. At 30 days all 27 patients with an ICH score of 0 survived, whereas those having scores of 1, 2, 3, and 4 had 5.9%, 33.3%, 46.2% and 88.9% mortality, respectively. ICH score was good for discriminating 30-day mortality with having an area under the ROC curve of 0.886 (95% CI:0.816-0.956; p<0.001]. For patients scoring above 2, the rate of poor functional outcome (mRS score e”4) approaches 100%. On the other hand, 18.5% of patients with score of 0 and 64.7% of patients with a score of 1 are not functionally independent after 30 days.* ***Conclusion:****In conclusion, the present study has demonstrated that the ICH score is a strong prognostic indicator of ICH outcomes (30-day mortality and 30-day functional outcome) among hospitalized patients in Bangladesh.*

Key words:*Intracerebral Hemorrhage; Intracerebral Hemorrhage Score; Prognosis; Bangladesh.*

Background:

Intracerebral hemorrhage (ICH) is the second most common cause of stroke and accounts for 10-20% of all strokes[1,2]. The incidence of ICH is increasing over the years[3] and ICH remains the most dreadful among stroke subtypes with a 30-day mortality of 40%–50%[4]. Though the exact scenario of Bangladesh is not known due to scarcity of

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published literature it can be assumed that, the incidence of ICH is higher in comparison to the western population[1,5], and the population at risk is younger compared to the western developed world[6]. Considering the poor long-term outcome for spontaneous ICH patients, an effective prognosticating scale is important to optimize the management plan for careful use of available resources, especially in low to middle income countries[7]. The ICH score is one of the simple and functional methods in this regards.It is determined as the sum of specific point values for each of the five characteristics (GCS score, age e”80 years, ICH volume, presence of IVH, and infratentorial origin), with weighting of potential points for each characteristic based on strength of outcome association[8].

However, for wider applicability of a risk-stratification scale, such as the ICH score, it must be useful outside the cohort of patients from which it was developed. So, external validation to determine whether the ICH score could accurately risk-stratify patients in a cohort independent of that from which it was developed was done in different population. Till date several studies in abroad have shown the external validity of ICH score but the study population and the hospital settings were completely different from ours[6,9-14]. Published study on ICH score in Bangladesh is very limited and the external validity of ICH score is not aimed in any study yet. So, it is necessary to prove its efficacy as a predictor of adverse outcome of ICH in Bangladeshi population.

Contemplating this background, this study was planned to evaluate the role of ICH score in predicting 30-day mortality in patients with ICH presenting and getting admitted in a tertiary care hospital of Bangladesh.

Materials and methods:

This prospective observational study was performed in Chittagong Medical College Hospital, Chattogram, Bangladesh. It is a 1313 bedded tertiary care hospital and one of the largest hospitals in Bangladesh. Patients with ICH are usually admitted in different Medicine, Neurology and Neurosurgery wards of this hospital.

All patients with a computed tomography (CT) evidence of spontaneous ICH above the age of 18 years were included in this study. Patients or attendantswho denied formal consent, patients with coagulation abnormalities, aneurysmal hematomas, and vascular malformations,past history of stroke, patients having ICH secondary to a brain tumor or trauma, patients with a past history of stroke and patients who were undergone surgical procedure were excluded.

Sample size was determined for the comparison of the area under a Receiver Operating Characteristics Curve (ROC) curve. A sample of 71 patients would suffice for a 90% power to detect a difference of 0.3 between the area under the curve (AUC), under the null hypothesis of AUC = 0.5 (no diagnostic accuracy) and the alternative hypothesis of AUC = 0.8 (moderate diagnostic accuracy), at a significance level of 0.05. However, considering the lost to follow up and to further increase the power of the study finally 105 patients were included in the study

Patients with a suspected diagnosis of acute stroke were subjected to an urgent noncontrast CT scan of the brain as soon as possible. Soon after, those diagnosed as ICH was enrolled and physically examined along with an evaluation for ICH scores. The scores used for 30-day mortality prediction was based on the ûrst evaluation after the enrollment. The data of the study subjects was collected by oral questionnaire regarding age, sex, education level, and risk factors for ICH (hypertension, diabetes, alcoholism, smoking, and anticoagulant and antiplatelet medications). Pulse, blood pressure (BP), respiratory rate, temperature, and GCS score was noted on admission. Hypertension and diabetes was diagnosed as having a previous diagnosis of these conditions by a registered physician or patients on anti-hypertensive or anti diabetic medications. Smoking was defined ever or never smokers. Obesity was defined as waist circumference >90cm in males and >80cm in females. Poor functional outcome was defined as mRS score e”4 at 30 days.As it was an observational study, the treatment protocol of the patient had not been interrupted and he/she had got the treatment as per available hospital protocol.

Patients of the study were monitored until discharge or death to observe the outcome. For those who had died within 30 days during the hospital stay, the cause of death was documented from the case record files. Those who was discharged before 30 days, a follow-up visit was arranged after 30 days of admission. Some patients who failed to attend the follow-up visit, telephonic follow-up was done.Primary outcome was defined as mortality assessment at 30-day after ICH. A patient who survived and discharged was followed up in the outpatient department and over telephone regarding their final outcome.

Continuous data were expressed as mean ± standard deviation (SD) and categorical variables were presented as percentages or proportions. The entire cohort was divided into survivor and non-survivor groups. Between these two groups, continuous and categorical variables were analyzed. Student's t-test was used to analyze continuous variableswhile categorical variables were compared by means of Chi-square test. Multivariate analysis, with the 30 day mortality as dependent variable, on variables found to be significant by univariate analysis, was performed finally. The discriminatory values of ICH score for predicting 30-day mortality was studied using ROC curve analyses with calculation of AUC. $p < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS version 23.0.

Informed consent was obtained from competent patients before enrollment. In patients who were unable to give fully informed consent, assent was obtained from a legal representative. The study protocol was approved by the Ethical Review Committee of Chittagong Medical College (Memo number: CMC/PG/2019/543) on June 20, 2019.

Results:

Out of 105 enrolled patients one was lost to follow up and rest 104 were included in the final analysis. Out of 104 patients 81 patients survived and rest 23 died in 30 days following enrollment. Overall, the mean age of the study subjects was 59.3 years and there was female predominance. In univariate analysis, mean age (p=0.04) but not the age group of e”80 years was significantly associated with 30 days mortality. (Table I). Majority of the patients were hypertensive (76%) and about half of them were obese (49%). However, DM, IHD alcohol drinking habit, smoking and tobacco leaf use was present in 16.3%, 19%, 1.9%, 36.5% and 27.9% respectively. There was no association of these factors with 30-day mortality.The frequency of IVH, hydrocephalus and hemorrhage with a volume of 30 cc or higher were significantly higher among the subjects who died (p<0.05).Those who survived had a higher GCS than those who died, the difference being statistically significant (p<0.001).In this cohort only 8.7% patients had infratentorial ICH and it was not associated with 30-days mortality (Table I.

In this cohort of 104 patients with ICH, 34 (32.7%) patients had ICH score 1. No patients had ICH score 5 and above (Table II). Present study demonstrated that, 30-day mortality increases as ICH Score increases. No patient with an ICH Score of 0 died. Majority of patients (88.9%, 8/9) with an ICH Score of 4 died. The 30-day case fatality for the entire cohort was 22.1% (23/104; 95% CI, 14.13%–30.07%).

Figure 1 contrasts the “observed mortality” vs “expected mortality” as predicted by the ICH Score. Mortality increased with ICH score, but not to the extent previously reported. In particular, the largest discrepancy between observed and expected mortality was demonstrated among patients with ICH Scores of 3 (46% vs 72%, P<0.01).

The areas under ROC curve for the ICH score was 0.886 (95% CI: 0.816-0.956; p<0.001) (Figure 2). The ROC suggested a sensitivity of 90% at cutoff value of 3 with specificity of 71%.

In the present cohort, ICH score was found to be predictive of poor functional outcome (mRS score $\geq$4) at 30 days after discharge. From Figure 6 it is apparent that for all patients scoring above 2, the rate of poor functional outcome approaches 100%. On the other hand, 18.5% of patients with score of 0 and 64.7% of patients with a score of 1 are not independent after 30 days.

Variables that had a p value of <0.05 in univariate analysis were selected for the multivariate regression analysis (Table 3). GCS score, the

Table-I

Socio-demographic variables of the 104 patients with ICH and association of 30-day mortality with these variables

Variables	Total (n=104)	Survival (n=81)	Death (n=23)	p value
Age (years)				
<80	93 (89.4%)	75 (80.6%)	18 (19.4%)	0.063*
≥80	11 (10.6%)	6 (54.5%)	5 (45.5%)	
Mean ±SD	59.30±19.91	57.91±12.79	64.17±12.69	0.040†
Sex				
Female	56 (53.8%)	45 (80.4%)	11 (19.6%)	0.512‡
Male	48 (46.2%)	36 (75.0%)	12 (25.0%)	
Risk factors				
Hypertension	79 (76.0%)	63 (79.7%)	16 (20.3%)	0.480‡
Diabetes mellitus	17 (16.3%)	12 (70.6%)	5 (29.4%)	0.430*
Obesity[a]	51 (49.0%)	41 (80.4%)	10 (19.6%)	0.546‡
IHD	2 (1.9%)	1 (50.0%)	1 (50.0%)	0.368*
Smoking	38 (36.5%)	28 (34.6%)	10 (43.5%)	0.289‡
Tobacco leaf use	29 (27.9%)	23 (28.4%)	6 (26.1%)	0.998‡
Alcohol drinking	2 (1.9%)	1 (50.0%)	1 (50.0%)	0.368*
GCS				
13-15	54 (51.9%)	51 (94.4%)	3 (5.6%)	<0.001*
5-12	46 (44.2%)	30 (65.2%)	16 (34.8%)	
3-4	4 (3.8%)	0 (0%)	4 (100%)	
Hematoma volume				
<30 cc	75 (72.1%)	66 (88.0%)	9 (12.0%)	<0.001‡
e”30 cc	29 (27.9%)	15 (51.7%)	14 (48.3%)	
Location				
Supratentorial	95 (91.3%)	75 (78.9%)	20 (21.1%)	0.402*
Infratentorial	9 (8.7%)	6 (66.7%)	3 (33.3%)	
IVH[a]	45 (43.3%)	27 (60.0%)	18 (40.0%)	<0.001*
Hydrocephalus	9 (8.7%)	3 (33.3%)	6 (66.7%)	0.003*

Data are expressed as frequency (percentage) if not mentioned otherwise. *p value derived from Fischer’s exact test; ‡ p value derived from Chi-square test; †p value derived from Student’s t-test; Significant values are in bold face.IVH; Intraventricular hemorrhage.

Table-II

30-days mortality rate for the Entire Cohort of 104 patients with ICH and Stratified by ICH Score

ICH score	n (%)	Case fatality rate at 30-day, n (%)	95% Confidence intervals
0	27 (25.9%)	0 (0%)	0-0
1	34 (32.7%)	2 (5.9%)	0.02-13.82
2	21 (20.2%)	7 (33.3%)	13.14-53.46
3	13 (12.5%)	6 (46.2%)	19.09-73.30
4	9 (8.7%)	8 (88.9%)	68.38-100
Entire cohort	104 (100%)	23 (22.1%)	14.13-30.07

Table-III

Multivariate logistic regression analysis of predictive 30-days mortality in 104 patients with ICH

Variables	β	Odds ratio (OR)	95% CI of OR		P value
			Lower	Upper	
Age	0.037	1.04	0.98	1.09	0.196
GCS	-0.398	0.67	0.52	0.86	0.002
Hematoma volume (≥30 cc)	1.565	4.78	1.23	18.57	0.024
IVH	0.084	1.09	0.24	4.98	0.914
Hydrocephalus	2.111	8.25	1.11	61.24	0.039

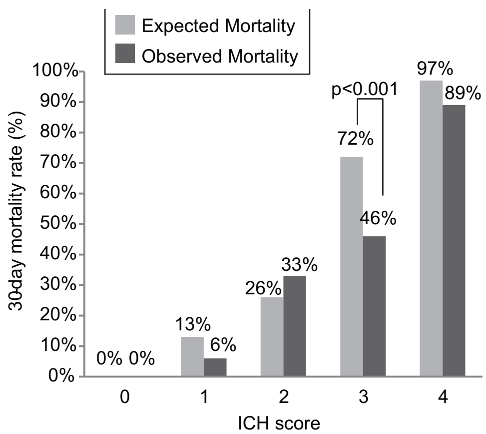

Fig.-1: *30-day mortality rate by presenting ICH score (Blue bars show expected mortality rate based on the original ICH score. Red bars show observed mortality rates in our patient cohort. Significant differences were seen between patients with ICH scores of 3).*

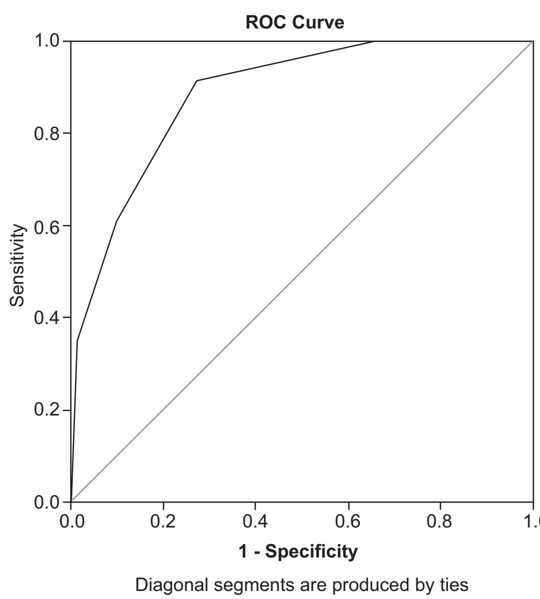

Fig.-2: *Receiver operating characteristic (ROC) curve for ICH score in predicting 30-day mortality outcome.*

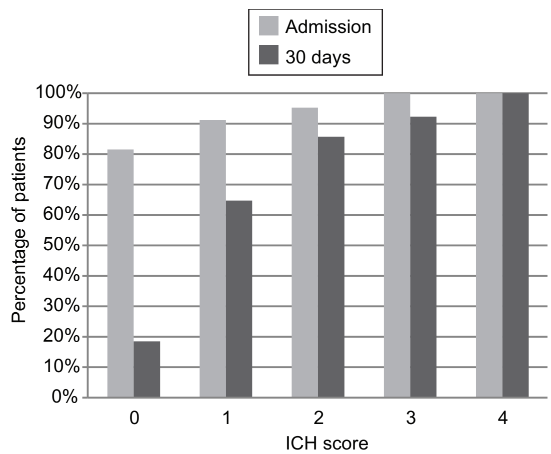

Fig.-3: *The ICH score and proportion of patients with modified Rankin score of e”4 at admission and one month after discharge.*

hematoma volume (≥30 cc), and the presence of hydrocephalous were independent predictors of 30-daymortality (p = 0.002, p=0.024 and p=0.039 respectively).

Discussion:

In this prospective study in Bangladesh, we have demonstrated that the ICH score is a valid prognostic indicator of 30-day case fatality. The overall 30-day mortality rate in the present cohort was 22.1%. When stratified by ICH scores, the mortality rate was significantly lower than the predicted mortality, which has been previously reported, in patients with ICH score 3. The observed mortality rate in the present study was similar to that predicted in Hemphill’s ICH score for the other ICH scores[8]. Historically quoted 30-day mortality rates of 72% for scores of 3 were based on a sample size of 32 patients for ICH score of 3 in the original cohort where the ICH score was developed[8]. In our patient population, the total number of patients with an ICH Score of 3 was only 13, of which 6 died (mortality rate of 46.2%). Difference in the sample sizes might be responsible for these differences in the observed and expected mortality rate between original and present study cohort.

The pattern and demography of spontaneous ICH in Bangladesh is different from the western world but quite similar to our neighboring country India. The mean age of the patients in the present study was 59.30 (±19.91) years, which is predominantly younger in comparison to the western population where the mean age was 70–79 years[8,9,15]. However, most of the available studies from Bangladesh and India report mean ages of 55-65 years[6,14,16]. Only 10.6% patients were above the age of 80 in the present study. The United Nations report states that the average life expectancy of a Bangladeshi at birth is 72.72 years[17]. Thus, most of our population fail to live beyond the age of 80 which is one of the cutoff criteria for the existing ICH scoring system. This was evident from our observation that none of the patients in this study group had an ICH score of 5. In the present study male to female representation was almost equal (46.2% versus 53.8%). Several other studies also observed such non-significant gender differences[14,18]. Hypertension was the most prevalent risk factor in the current cohort(76%) followed by obesity (49%). IHD, smoking, and alcohol abuse were less prominent risk factors in the present study. This pattern was more or less similar to the findings from the study in and around our country[19,20].

The 30 day mortality of patients with spontaneous ICH has been reported as ranging from 25 to 52%[10,21,22]. The low rate at 22.1% in our study might be explained by our exclusion criteria. Patients with an initial absence of brainstem reflexes in whom the non-treatment concept was clear were not included in the study group. Concerning the short term outcome (after 30-days), 21 (20.19%) patients had mRSscore d”2 (slight disability to no symptom at all) and 66 (63.46%) had mRS score ≥4 (moderately severe disability to dead). In a meta analysis, Van Asch et al. presented a functional outcome with independency rates of between 12 and 39% corresponding to the findings of present study[23].

Multivariate analysis of the components of ICH score in our study subjects revealed that GCS and hematoma volume (e”30cc) were strong predictors of 30-day mortality. However, the infratentorial origin of hemorrhage and IVH despite having high odds for death was not signiûcantly associated with the mortality prediction, which is in contradiction with the previous studies[8,24]. This discordance could possibly be due to very small number of patients having infratentorial hemorrhage (8.7% infratentorial versus 91.3% supratentorial), which could not reach statistical signiûcance. Most of the patients with IVH in the present study had associated hematoma volume of e”30 cc. So, the IVH was not revealed as an independent predictor of 30-day mortality though this variable had highly significant association ($p<0.001$) with 30-day mortality in univariate analysis. Age 80 years or older was an independent predictor of mortality in the original study of the ICH score[8]. The lack of association between age of 80 years or older and mortality in the present study may be due to the small number (11/104; 10.6%) of patients older than 80 years.

The present study also demonstrated that, the radiological feature hydrocephalus was an independent predictor of 30-day mortality. Diringer et al. demonstrated for the first time the impact of hydrocephalus on outcome from ICH[25]. Hydrocephalus was associated with a considerably higher mortality and fewer patients being discharged to home in their study. In agreement to our study, univariate and multivariate analyses indicate that hydrocephalus was an independent predictor of outcome in that study [25]. Later on, this factor is validated by other study[6].

The Hemphill ICH score has been validated numerous times in the literature, with a pooled AUC of 0.8 in an international meta-analysis[26]. In the present study the AUC for the ICH score was 0.886 (95% CI: 0.816-0.956; $p < .001$) which was consistence with other studies[26].

The results of the present study also support the validity of the ICH score in predicting early functional outcome in addition to mortality. This is consistent with the study of Jamoraet al[11]. But in disagreement with the study that have evaluated outcome too early at discharge without accounting for the eventual improvement in function over time[12].

Strength and limitations:The strengths of our study include the prospective nature of the data collection and the blinding of image analysis and prognostic score determination to survival status. ICH grading scores are not routinely used for clinical care at our hospital and were determined retrospectively for this study, thus preventing them from influencing care decisions and, hence, prognosis. We were able to ascertain the outcome status of almost all of the patients with otherwise complete data and only 1 out of 105(<1%) could not be traced. However, lack of long-term follow-up of patients after discharge from the hospital and sample from a single hospital were some of the limitations of the present study. Moreover, we could not establish the true strength of association of infratentorial origin of hemorrhage and age e"80years because of the small number of subjects in these respective categories.

Conclusion:In conclusion, our study has demonstrated that the ICH score is a prognostic indicator of ICH for both30-day mortality and 30-day functional outcome among hospitalized patients in Bangladesh.A numerical scoring system like ICH score can improve the consistency among the physicians regarding severity of ICH which in turn can help during counseling the caregivers.

Recommendations:As the ICH score was observed to have a good discriminative power for predicting 30-day mortality in patients with ICH, present study recommended routine assessment of ICH scores in patients with ICH in admission. However, results of the current study need to be confirmed by further prospective, multicenter studies with larger sample size.

Acknowledgement:
Dr. Pradip Kumar Kayasthagir, Dr. Md. Mahabubul Alam Khandker, Dr. S A M Masihuzzaman (Alpha), Dr. TouhidurRahman, Dr. Zaman Ahmed, Dr. AnwarulKibria, Dr. AkramulAzam, Dr. FaridUddin Ahmed, Dr. Sanjay Saha.

Contribution of authors:
MSE: Conception, designing, data collection, data analysis, manuscript drafting & final approval

MH: Conception, Manuscript drafting & final approval

SM: Manuscript drafting & final approval

Conflict of Interests: The authors declare no conflict of interest in this study.

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