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Predictors of Outcome in Intracerebral Hemorrhage and Performance of Hemphill ICH Score and GVS Score

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Abstract

Background: The outcome of intracerebral hemorrhage (ICH) is gloomy. There are several scoring systems for predicting its outcome. **Objective:** The purpose of the present study was to observe the predictors of outcome in ICH patients and to assess the performance of 'Hemphill ICH score' and 'GVS score'. **Methodology:** This cohort study involved patients of ICH admitted within 72 hours of acute event in July to December 2017 in the Department of Neurology at National Institute of Neurosciences (NINS) & Hospital, Dhaka, Bangladesh. Clinical and radiological data at admission and in-hospital events were obtained from medical records. Patients who were discharged from the hospital were interviewed at 30th day after event by face to face interview or over telephone. Follow up data was not found for 4 patients. **Results:** This study involved 115 patients of ICH [median age 60 years (interquartile range, IQR 50-70); 46% (53/115) female]. In-hospital and 30-day mortality of the ICH patients was 22% (25/115: 95% CI 15-30%) and 38% (42/111; 95% CI 29–48%) respectively. There was almost perfect agreement between Hemphill ICH score and GVS score ($p<0.001$ and $\kappa=0.862$). Kaplan-Meier survival curves of patients with different Hemphill ICH scores revealed significant difference among them; which was also true for patients with different GVS scores (by log-rank test, $p<0.001$ for both). The area under the curve (AUC) for the Hemphill ICH score to predict mortality was 0.70 (95% CI, 0.60–0.80) and for the GVS score 0.74 (95% CI, 0.64–0.83). In bivariate logistic regression, NIHSS score, GCS score, blood glucose at admission, nosocomial pneumonia, ICH volume, midline shift along with both Hemphill ICH and GVS score were observed to predict mortality at 30 days ($p<0.05$ for all). In two separate models adjusting for blood glucose and nosocomial pneumonia, every 1-point increase in the Hemphill ICH score and GVS score increases the mortality risk by 2.35 fold (adjusted OR: 2.35; 95% CI 1.33-4.16; $p=0.003$) and 2.99 fold (adjusted OR: 2.99; 95% CI 1.57-5.72; $p=0.001$) respectively. **Conclusions:** Both Hemphill ICH and GVS score have comparable predicting ability of outcome in ICH. In addition to components of scoring systems, occurrence of nosocomial pneumonia and blood glucose seems important. *[Journal of National Institute of Neurosciences Bangladesh, January 2021;7(1): 3-9]*

Keywords: Intracerebral hemorrhage; Hemphill ICH score; GVS score

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Introduction

Stroke is recognised as an important cause of mortality and morbidity worldwide as it is the second most common cause of death and the third most common

cause of disability[1-2]. Broadly there are two subcategories of stroke: ischemic and hemorrhagic. About 10.0% to 15.0% of stroke is hemorrhagic which is again subdivided into hemorrhage into brain parenchyma known as intracerebral haemorrhage (ICH) and hemorrhage into subarachnoid space known as subarachnoid haemorrhage (SAH)[3].

Among the different types of stroke, ICH is more common in low income countries and has a higher risk of morbidity and mortality than ischemic stroke and SAH[3,4]. It has a 30-days mortality of around 40% and worldwide it remains a big concern for neuroscientists[5]. To predict the prognosis of ICH it is important to know which factors are related to outcome. There have been a number of prediction models that have been developed for ICH[4,6–12]. Among them, most widely used prediction model is the Hemphill ICH score developed by Hemphill et al[4].

According to Hemphill ICH scoring system, independent predictors for 30-days mortality in ICH are greater ICH volume (score 0 if <30cm^3, score 1 if ≥30 cm^3) ,infratentorial location of ICH (score 0 if supratentorial, score 1 if infratentorial), low score on Glasgow Coma Scale (GCS) (score 0 if 13-15, score 1 if 5-12, score 2 if 3-4), older age (score 0 if <80 years, score 1 if ≥80 years), and intraventricular extension of the hemorrhage (score 0 if no, score 1 if yes)[4]. On the other hand, Mukherjee et al. proposed a simplified model for prediction of prognosis of ICH and named it as 'GVS score'[6]. The 'GVS' represents the three components of the scoring system where 'G' stands for GCS score (score 0 if 13-15, score 1 if 5-12, score 2 if 3-4), 'V' for volume of hemorrhage (score 0 if <30cm^3, score 1 if ≥30 cm3) and 'S' for site of hemorrhage (score 0 if supratentorial, score 1 if intraventricular or cerebellar and score 2 if brain stem). Despite its simplicity, the GVS score was observed to have substantial agreement with Hemphill ICH score[6]. Following the initial study of the authors proposing GVS score, it has not been validated by further studies. In this background, the present study was carried out to observe the predictors of outcome in ICH patients and to assess the performance of Hemphill ICH as well as GVS score.

Methodology

This was a retrospective cohort study carried out through review of medical records of stroke patients admitted during July 2017 to December 2017 in a single unit of the Department of Neurology of National Institute of Neurosciences (NINS) & Hospital, Dhaka, Bangladesh. The patients with acute ICH who presented within 72 hours of event and confirmed by computed tomography (CT) scan were enrolled. Clinical and radiological data recorded at admission were noted. ICH volume was measured on the initial CT scan of brain by using ABC/2 method. In this method A was the greatest diameter on the largest hemorrhage slice, B was the diameter perpendicular to A and C was the number of axial slices with hemorrhage multiplied by the slice thickness[13]. Patients were monitored for in-hospital events like surgical intervention, complications or death. Patients who were discharged from the hospital

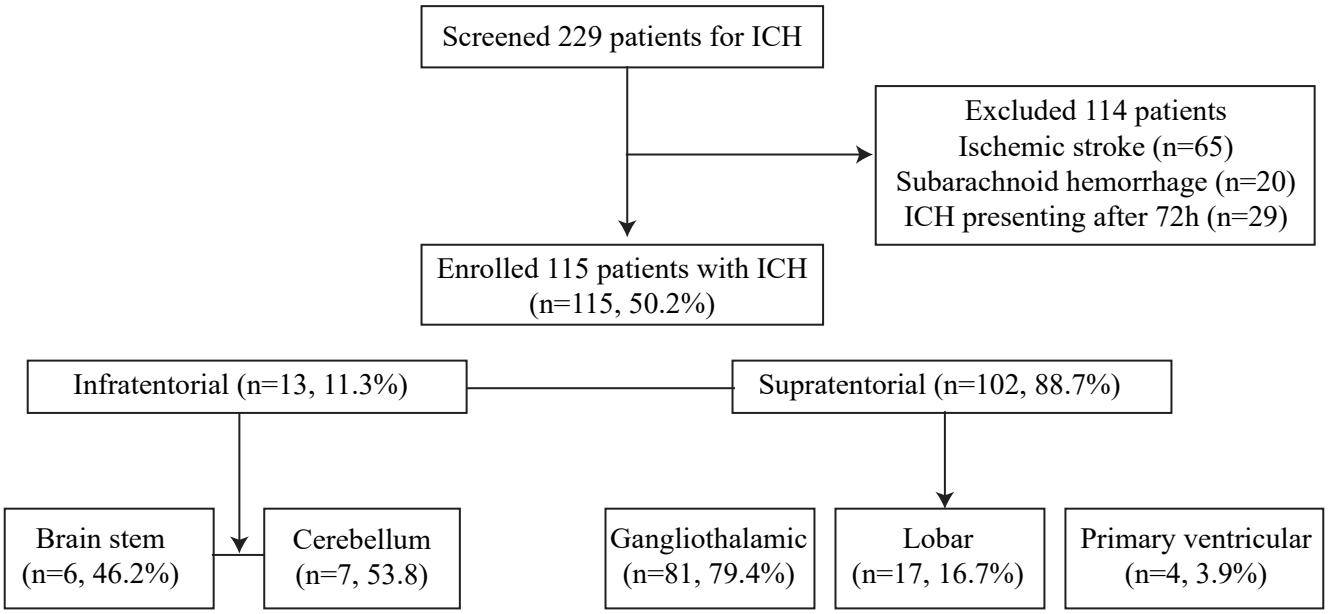

Figure I: The scheme of enrollment and radiological subtypes of ICH (ICH: Intracerebral hemorrhage)

were followed up at 30th day after the stroke event. Those who failed to attend NINS were followed up over telephone for modified Rankin Scale (mRS) score. The study was approved by the local ethical committee. Statistical analysis was performed by using Statistical Packages for Social Sciences (SPSS 22.0) (SPSS Inc, Chicago, IL, USA). Quantitative data were expressed as mean and standard deviation or median and interquartile range; and qualitative data were expressed as frequency and percentage. Normality of data was tested by Kolmogorov-Smirnov and Shapiro-Wilk test. 95% confidence limit was taken. Agreement of Hemphill ICH and GVS score was assessed by kappa test. Kaplan-Meier survival curve was constructed for participants of the study with different points in Hemphill ICH and GVS score separately and log-rank test was done to compare the difference in survival. Bivariate logistic regression was done to evaluate the predictors of 30-day mortality. Thereafter two separate multivariate logistic regressions adjusted for significant predictors in bivariate model was done to evaluate the Hemphill ICH score and GVS score as predictors. Receiver operating characteristic (ROC) curve was used to evaluate the performance of both the scores.

Results

A total number of 229 patients were screened during the study period and among them 115 of CT-confirmed ICH patients were included (Figure I).

The median age of the participants was 60 (IQR 50-70) years and 46 (53/115) were female. Their median Hemphill ICH score as well as GVS score was 2 (IQR 2-3 & 1-3 for Hemphill ICH and GVS score respectively). Median hospital stay was 6 (IQR-5-7) days and in-hospital mortality was 22% (25/115: 95% CI 15-30%) (Table 1).

Table 1: Demographic and clinical parameters of the study participants (n=115)

Characteristics		Frequency
Age (years; median and IQR)		60 (50-70)
Sex	Male	62 (53.9)
	Female	53 (46.1)
History of hypertension		89 (77.4)
History of diabetes mellitus		20 (17.4)
Previous stroke		12 (10.4)
Family history of stroke		25 (21.7)
History of cardiac disease		6 (5.2)
History of smoking		32 (27.8)
Duration of symptoms (hours; median and IQR)		24 (10-48)
NIHSS score on admission (median and IQR)		22 (14-27)
GCS score on admission (median and IQR)		8 (7-12)
Systolic BP (mm Hg; median and IQR)		160 (145-180)
Diastolic BP (mm Hg; median and IQR)		100 (80-100)
Blood glucose at admission (mmol/L; median and IQR)		8.3 (6.9-10.2)
Pre-event mRS score		0 (0-0)
Hemphill ICH score (median and IQR)		2 (2-3)
GVS score (median and IQR)		2 (1-3)
Nosocomial pneumonia		12 (10.4)
Surgical measures		4 (3.5)
Hospital stay (days; median and IQR)		6 (5-7)
In-hospital Mortality		25 (21.7)

Within parentheses are percentages over column total if not mentioned otherwise; IQR: Interquartile range; NIHSS: National Institute of Health Stroke Scale; GCS: Glasgow Coma Scale; mRS: modified Rankin scale

Among the study participants, 4 out of 115 (3.5%) had no follow up data at 30 days. In the remaining 111 participants, the 30-day case fatality was 38% (42/111); 95% CI 29–48%. The 30-day case fatality for patients with a Hemphill ICH score of 0, 1, 2, 3 and 4 was 0.0%,

Table 2: Agreement of Hemphill ICH score and GVS score

	GVS score					Total
	0	1	2	3	4	
Hemphill ICH score						
0	3 (100.0)	-	-	-	-	**3**
1	-	25 (96.2)	-	-	-	**25**
2	-	1 (3.8)	40 (90.9)	3 (7.7)	-	**44**
3	-	-	4 (9.1)	33 (84.6)	-	**37**
4	-	-	-	3 (7.7)	3 (100.0)	**6**
Total	**3**	**26**	**44**	**39**	**3**	

$p<0.001$, $\kappa=0.862$; within parentheses are percentages over column total

12.0%, 37.0%, 54.0% and 67.0% respectively. On the other hand, the 30-day case fatality for patients with an GVS score of 0, 1, 2, 3 and 4 was 0.0%, 12.0%, 33.0%, 58.0% and 100.0% respectively (Figure II). There was almost perfect agreement between Hemphill ICH score and GVS score ($p<0.001$ and $\kappa=0.862$) (Table 2).

Kaplan-Meier survival curves of patients with different Hemphill ICH scores revealed significant difference among them; which was also true for patients with different GVS scores (by log-rank test, $p<0.001$ for both) (Figure III).

In bivariate logistic regression, National Institute of Health Stroke Scale (NIHSS) score, GCS score and blood glucose at admission, nosocomial pneumonia, ICH volume, midline shift along with both Hemphill ICH and GVS score were observed to predict mortality at 30 days in the participants ($p<0.05$) (Table 3).

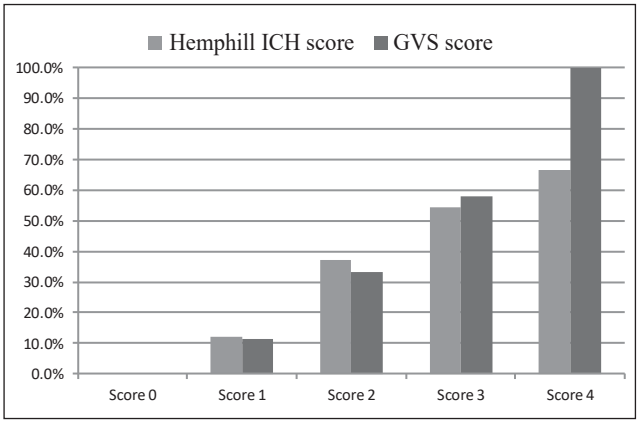

Figure II: Case fatality of the intracerebral hemorrhage patients (n=111) at 30 days stratified by Hemphill ICH score and GVS score (for Hemphill ICH score 0, 1, 2, 3, 4: n= 2, 25, 43, 35, 6 and for GVS score 0, 1, 2, 3, 4: n=2, 26, 42, 38, 3 respectively; no patients had Hemphill ICH score 5-6 or GVS score 5)

Table 3: Predictors of prognosis (30-day mortality) including ICH and GVS score by bivariate logistic regression

Variables	OR (95% CI)	P value
Age, per year increase	1.02 (0.98-1.05)	0.370
Female sex	0.77 (0.36-1.67)	0.511
Systolic blood pressure, per mm of Hg increase	1.00 (0.99-1.02)	0.747
Diastolic blood pressure, per mm of Hg increase	1.01 (0.99-1.03)	0.485
Admission NIHSS score, per unit increase	1.26 (1.15-1.38)	**<0.001**
Admission GCS score, per unit increase	0.65 (0.53-0.78)	**<0.001**
Random blood glucose, per mmol increase	1.27 (1.10-1.47)	**0.001**
White cell count, per unit increase	1.02 (0.91-1.14)	**0.767**
Prior history of hypertension	1.18 (0.45-3.08)	**0.735**
Prior history of diabetes	1.24 (0.45-3.39)	**0.674**
Time from symptom onset to hospital presentation, per hour increase	1.01 (0.99-1.02)	0.603
Hyponatremia	1.44 (0.54-3.83)	0.467
Renal impairment	2.03 (0.86-4.77)	0.104
Nosocomial pneumonia	10.47 (2.17-50.60)	0.029
ICH volume, per cm^3 increase	1.02 (1.01-1.02)	**<0.001**
Presence of IVH	1.29 (0.58-2.87)	0.540
Midline shift, per mm increase	1.25 (1.12-1.39)	**<0.001**
Infratentorial hemorrhage	0.45 (0.12-1.75)	0.252
Hemphill ICH score	2.52 (1.51-4.20)	**<0.001**
GVS score	3.42 (1.91-6.12)	**<0.001**

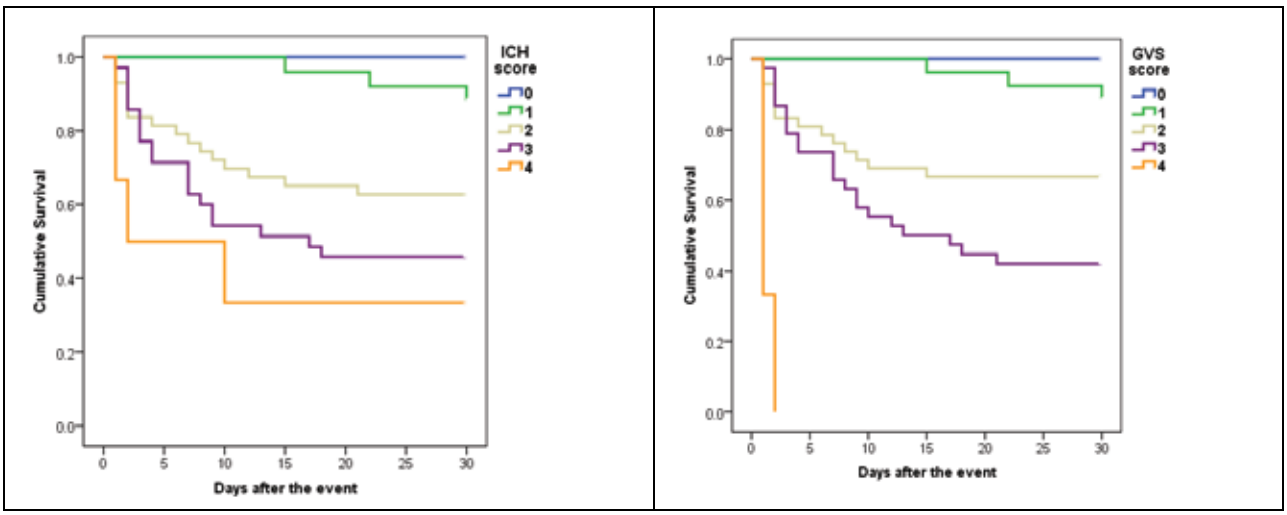

Figure III: Kaplan-Meier survival curve of patients with different Hemphill ICH score and GVS score (left and right panel respectively) revealed significant difference among them (by log-rank test, $p<0.001$ test for both)

In a model adjusting for blood glucose and aspiration pneumonia, it was observed that there is 2.35-fold increase in mortality risk for every 1-point increase in the Hemphill ICH score (adjusted OR: 2.35; 95% CI 1.33-4.16; p=0.003). In another model with same adjustment, we observed 2.99-fold increase in mortality for every 1-poit increase in the GVS score (adjusted OR: 2.99; 95% CI 1.57-5.72; p=0.001) (Table 4).

Table 4: Hemphill ICH score and GVS score in prediction of 30-day mortality when adjusted for blood glucose and pneumonia in two separate model of multivariate logistic regression

Scores	*R2	aOR (95% CI)	P value
Hemphill ICH score	o.290	2.35 (1.33-4.16)	0.003
GVS score	0.313	2.99 (1.57-5.72)	0.001

*Cox and Snell

The area under the curve (AUC) for the Hemphill ICH score to predict mortality was 0.70 (95% CI, 0.60–0.80), and for the GVS score was 0.74 (95% CI, 0.64–0.83) (Figure IV).

Discussion

The current study evaluated the in-hospital and 30-day mortality of ICH patients admitted within 72-hours of event in a referral neuroscience institute of Dhaka and observed 22.0% and 38.0% mortality respectively. Along with increasing Hemphill ICH and GVS score, lower GCS score, higher blood glucose at admission, pneumonia, higher ICH volume and midline shift in CT scan were observed to be associated with higher mortality at 30 days. There was almost perfect agreement between Hemphill ICH and GVS score. Despite its simplicity, the GVS score AUC was not below Hemphill ICH score.

In spite of advancements in medical service, case fatality rate of ICH patients is not decreasing worldwide[5]. Outcome of ICH patients in our study was comparable to those found by different studies in home and abroad[14–16]. However, our study was conducted in the in-patient department of a neuroscience institute situated in the capital of the country and so it may be generalizable to only those who present to this hospital for care. GCS score was observed to be a good predictor of mortality in ICH patients by both present and previous studies[9,14,17,18], though it was primarily developed for evaluating patients of head injury. As a result, GCS score is invariably incorporated in popular ICH outcome predicting scales. Despite its limitations especially in aphasic patient, GCS remains a simple and reliable tool to assess outcome of ICH patients. NIHSS score originally used for assessing the severity of ischemic stroke, was also observed to be a good predictor of outcome in current as well as in other studies[19,20]. However, it takes a few minutes to assess NIHSS score and it may not be as simple as applying GCS at bedside.

Initial CT scan of brain has an important role in predicting outcome of patients with ICH. Volume of hematoma was unequivocally seen to be associated with mortality[9,14,17,18,21]; which is also true for our study. Although it was observed that ABC/2 formula tends to overestimate intracerebral hematoma volume in comparison to computer-assisted volumetric analysis

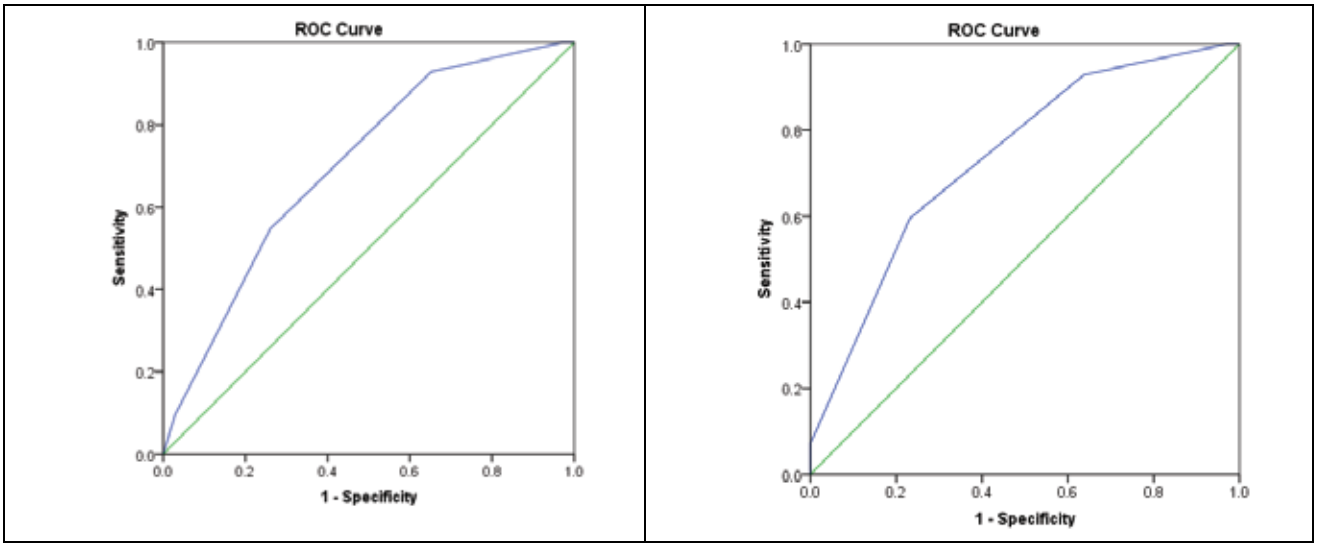

Figure IV: Receiver operating characteristic (ROC) curve for prediction of mortality in patients with intracerebral hemorrhage: left panel Hemphill ICH score, right panel GVS score

(CAVA)[22], it is still useful as an rapid and reliable method[23]. Intraventricular hemorrhage (IVH) adds a point in both Hemphill ICH and GVS score and has been considered to be a poor prognostic factor in various studies[9,15,16]. But the present study as well as some other studies could not appreciate its relationship to ICH outcome[18,24]. Faigle et al[25] observed a differential impact of IVH over ICH outcome in different races. Indeed, few authors opined that ICH with ventricular extension and no hydrocephalus may not increase mortality or severe disability[24]. So the direct relationship of IVH to outcome in ICH is not often observed. Mass effect of the hematoma induces neuronal injury; and midline shift in CT scan of brain is a simple way to quantify it. The present study also observed higher mortality in patients with higher midline shift. While it is acknowledged that midline shift is associated with poor outcome in patients with ICH[26], it has not been included in either ICH or GVS score. One explanation may be the relationship of hematoma volume measurement with midline shift as replacing hematoma volume with midline shift in ICH score resulted almost similar predictive capacity[27]. Site of hemorrhage in ICH is also included in both Hemphill ICH and GVS score and infratentorial location had been observed to be strongly related to mortality[9,18,28]. However, hemorrhage into the brain stem or cerebellum does not carry equal risk. Brain stem hemorrhage is particularly observed to be related to mortality[29] and hence it is given more weight in GVS score. The current study could not relate it to outcome probably due to small proportion of patients in infratentorial hemorrhage group (13/115; 11%).

Nosocomial pneumonia is a frequent complication among ICH patients. We observed around one in ten patients of ICH developed pneumonia, rate of which is comparable to previous studies[30,31]. Likewise, mortality in ICH patients with pneumonia was also higher in our as well as in other studies[32]. Occurrence of pneumonia may add more predicting power for negative outcome in ICH patients and may be considered while modifying the current scoring scales. Blood glucose is also not included in any of the predicting scores and studies did not confirm a strong and consistent association[33–37]. The present study observed an association of higher blood glucose at admission to mortality which is supported by a meta-analysis published in 2014[38]. In multivariate regression analysis we adjusted for pneumonia and blood glucose in two separate models for predicting ability of ICH and GVS score. Both the scores had good predicting ability with increase in one-point score result in more than two-fold increase chance of mortality. There was almost perfect agreement of ICH and GVS score with comparable AUC and mortality after 30 days of event. It seems that both the scores are good at predicting outcome of ICH patient. Due to its simplicity GVS score may be strongly considered in our setting.

Conclusion

In conclusion, both ICH and GVS score have comparable predicting ability of outcome in ICH. In addition to components of scoring systems, occurrence of nosocomial pneumonia and blood glucose seems important in our setting.

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