Outcome prediction in spontaneous intracerebral hemorrhage: A comparative study of ICH,WFNS,and GVS scoring systems

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ABSTRACT

A good predicting scoring system for intracerebral hemorrhage (ICH) has been a concern for decades as this will help in guiding the treatment and prognostication. The most widely accepted one is the Hemphill ICH score, but this conventional scoring system requires complex memorization and calculation making it difficult to apply in clinical practice. Hence, there is a need for a simpler and more accurate scoring system for ICH for prognosis that can be readily determined. This study was undertaken to compare simple scoring systems, such as WFNS, GVS and ICH scores, in predicting in-hospital mortality and outcomes at discharge and at three months in patients with spontaneous ICH. This study was carried out in the Department of Neurosurgery and Department of Neurology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Materials and Methods

Patients with primary spontaneous ICH aged ≥ 16 years admitted in the Department of Neurosurgery and Neurology participated in the study. The ICH, WFNS and GVS scores were measured at the earliest possible time during admission by a single observer. Modified Rankin scale (mRS) was measured at discharge and at three-months follow up. Mortality was used as the primary outcome measure.

Results

A total of 130 patients were included in the study. The mean age of the study population was 60.7 ± 16 years. There was an increase in mortality rate among ICH cases with higher scores of ICH, WFNS and GVS. The area under ROC curve for ICH, WFNS and GVS scores for prediction of mortality was 0.895 (95 % CI; 0.838 - 0.952; $p < 0.001$), 0.876 (95 % CI; 0.813 - 0.938; $p < 0.001$) and 0.887 (95 % CI; 0.823 - 0.950; $p < 0.001$), respectively, suggesting a good discrimination ability of all these three scores in predicting death. All three scores showed good discrimination ability of good outcomes but only fair prediction of bad outcome.

Conclusions

Both GVS and WFNS scores are simple, easy to use and comparable to ICH score for the prediction of mortality and good outcome in patients with spontaneous ICH. All three scores are inferior for the prediction of bad outcome. ICH score is marginally better than other two scores in all outcome subgroups but was not statistically significant. In all three outcomes, ICH score was marginally better but comparable with the other two scores.

Keywords: **GVS score, ICH, ICH score, WFNS score**

Introduction

Stroke is the second leading cause of death worldwide, and one of the leading causes of disability[1,2]. With increasing life expectancy, the burden of stroke is likely to increase worldwide specially in low and middle income countries (LMIC)[3,4]. Though intracerebral hemorrhage (ICH) accounts for only 10 - 20 % of all strokes, the mortality and long-term disability associated with it are disproportionally high[5,6].

Case-fatality at one month is over 40 % (20–70 %)[7-10] increasing to 54-58 % at one-year[11,12]; and two-thirds of survivors remain in moderate to severely disabled status[13]. Because ICH is associated with high mortality and long-term disability, it is desirable to have a scoring system that accurately predicts the likely outcome of patients, and helps stratify patients with very poor prognosis from patients who would otherwise benefit from aggressive treatment[14]. Ideally, any method of predicting outcome should be reliable, simple, accurate and reproducible[15]. Various prognostic scoring systems are in use - but not all are practical. These models usually include criteria related to neurological condition, laboratory parameters and neuroimaging findings. While these models may predict outcome, they vary in complexity[16].

In 2001, the ICH score was introduced by Hemphill et al. and later cited by a few other studies[17-21] as a tool for predicting 30-day mortality[22]. Hemphill ICH score is currently the most widely accepted scoring system. But this conventional scoring system requires complex memorization and calculation, making it difficult to apply in clinical practice in emergency settings. To simplify the prognostic scoring system for ICH without compromising the precision, Behrouz et al. (2015) proposed World Federation of Neurological Societies (WFNS) score as an alternative for predicting prognosis in ICH[23.] They concluded that WFNS classification was as accurate as the ICH score but has the advantage of being simple to use and versatile with only clinical evaluation and without incorporating radiological data[23]. Another scoring system, known as GVS (GCS, volume of hematoma and site) score, was proposed by Mukherjee et al. (2016) for prediction of outcome in ICH at three-month and one-year duration[24]. They concluded that the small number of variables used in the GVS score compared to ICH score is a clear advantage for the physicians, especially in the emergency settings.

WFNS and GVS scores were compared with ICH score for the prediction of outcome in two separate studies[23,24]. Both studies concluded that WFNS and GVS scores were as accurate as ICH score but with an added advantage of being easy to use. There are the only two studies comparing GVS vs ICH scores and WFNS vs ICH scores, respectively. GVS and WFNS scores are not validated on other cohort of patients and they were not compared together with standard ICH score in a single study. So, for the validation of their findings in Nepalese population, we have made an attempt to compare these three scoring systems, namely WFNS, GVS, and ICH scores, in predicting in-hospital mortality and outcomes at discharge and at three-month follow up.

Methods

This was the quantitative prospective observational study conducted in the department of Neurosurgery and Neurology, Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal. All patients with the diagnosis of primary spontaneous ICH aged ≥ 16 years admitted in Neurosurgery and Neurology Department were included in the study. The duration of the study was one-year (April, 2017 to March, 2018). Nonprobability (convenience) sampling method was utilized to select the required sample. Sample size was calculated, by using formula $n = z^2 p (1-p)/ e^2$ (where n is sample size, Z is the Z statistic for level of confidence, p is the proportion of an attribute, and e is the level of precision). The case-fatality at one month (p) was taken as 40 % as reported by Van Asch et al. in 2011[12]. With 95 % confidence interval (z = 1.96), expecting 10 % margin of error (e = 0.1) and expecting drop-out 10 % of 92, i.e. ~ 9, required sample size was calculated to be 101.

As per the study protocol, in eligible patients who met inclusion criteria, ICH, WFNS and GVS scores were recorded at the time of admission. Each component of all scores was tested independently. If a patient was under sedative and/or neuromuscular blocking agent, the scores was taken at the earliest possible time of spontaneous awakening trial.

GVS Score was proposed by Mukherjee et al. for prediction of prognosis in ICH[24]. GVS is an abbreviation of its components and the sum of individual points described as in table 1. GVS Scores for ICH ranged from 0 to 5; whereas Hemphill ICH score ranged from 0 to 6[22.] Three letters GVS (G =

Glasgow Coma Score, V = Volume of blood, S = Site of hematoma) coined from first capital letter of its component words is easy to memorize.

Table 1: GVS Scoring System

Components	Points
1. GCS (G)	
3 – 4	2
5 – 12	1
13 – 15	0
2. Volume (V)	
^{3} 30 mL	1
< 30 mL	0
3. Site of bleed (S)	
Brain stem	2
Intraventricular hemorrhage	1
Cerebellar	1
Supratentorial	0

Axial CT scan was used to calculate volume of hematoma using computer software. Computed Tomography (CT) is very sensitive for identifying acute hemorrhage and is still considered as the "gold standard". With CT, exact hematoma dimensions can be measured and evaluated in the context of the clinical examination.

Patients were managed according to the Guidelines for the Management of Spontaneous Intracerebral Hemorrhage of AHA/ASA (2015) and then discharged once they were neurologically stable. Outcomes were documented as scores on the modified Rankin scale (mRS)[25,26], which is a reliable stroke outcome scale with scores ranging from 0 (no symptoms at all) to 6 (dead). Outcome was labeled as good outcome when mRS of 2 or less, poor outcome when mRS is 3 – 5 and mortality (death) when mRS is 6. Outcome was recorded as in-hospital mortality, at the time of discharge and at three-month follow-up.

Data collection was done by filling the proforma. Qualitative data was expressed in proportion and percentage, and quantitative data as mean (M) and standard deviation (SD). Descriptive statistics was expressed in tables, graphs and charts, whenever applicable. For the inferential statistics, tests like student's t test and Pearson Chi^2 test were used. Sensitivity and specificity were calculated and plotted in the receiver-operating curve (ROC); and the area under the curve (AUC) was calculated to determine the discrimination ability of all the scores. The *p* value less than 0.05 was taken as statistically significant.

The consents from the patients or his/her legal guardians were obtained before they were enrolled in the research. Approval of the research was taken from Institutional Review Board, Institute of Medicine (IOM), Tribhuvan University Teaching Hospital, Kathmandu Nepal. No harm was caused because of the study. Every patient had the right to withdraw from the study, at any point of time, if he/she wished to do so.

Results

During the one-year study period, 151 patients were admitted with the diagnosis of spontaneous primary intracerebral hemorrhage. Out of these, 21 patients were excluded for various reasons. These 130 cases were classified based on GCS, ICH volume, location of intracranial bleed, age and neurological deficit into all three scoring systems - ICH, WFNS and GVS scores.

The age of the study population ranged from 20 to 101 years (mean, 60.7±16 years). Highest number of ICH patients (40, 30.7%) were in 60-70 years age group, and 82 patients (63.0%) belonged to age group of 40-70 years. Only 15 patients (11.5%) were 80 years or above. There were altogether 88 male and 42 female patients with male to female ratio of 2.1:1.

With regards to the location of bleed, the common sites were basal ganglia and lobar bleed, 36.9% and 35.4%, respectively. According to the clinical history, hypertension was documented in 87 of the patients (66.9%). Intraventricular bleed was seen in 51 patients (39.2%). On calculation, the mean volume of the intracranial bleed was 25±16.6 ml. Regarding ICH volume, 80 (61.5%) had volume less than 30 ml; and 50 (38.5%) had volume of 30 ml or more. The overall mean GCS was 10.9±4.0. 55 patients (42.3%) had GCS score of 14–15 and 14 patients (10.7%) had GCS of 3–4. (Fig. 3) Only 8 patients (6.0%) underwent surgical treatment; whereas majority of cases (122) were managed conservatively.

Distribution of mRS scores at discharge and in three months is as shown in Figure 1. 49 (37.7%) had good outcome, 41 (31.5%) had bad outcomes and 40 (30.8%) had mortality.

The mortality increased with the increasing ICH score of the patients. No patients with ICH score of 0 died; whereas all the patients with ICH score of 5 died. Good outcome was seen in 96.6% of the patients with ICH score of 0 and 65.6% of the patients with ICH score of 1. Patients with ICH score between 2-5 had no 'good outcomes'.

Similarly, mortality increased with higher WFNS scores. The majority (87.5%) of the patients with WFNS score of 5 died. Good outcome was seen in lower WFNS scores -84.6 % of patients with WFNS score of 1 had good outcome.

When comparing GVS score with outcome, mortality increased with higher GVS score- with 100% mortality in GVS scores of 4 and 5. Good outcome was seen in 93.5% in GVS score of 0 and in 62.1% with GVS score of 1, whereas none of the patients with GVS score between 3-5 had good outcomes.

Discrimination is how well a model can predict the correct outcome, which in this study was tested by plotting the area under receiver-operating characteristic (ROC) curve. The area under ROC curve for ICH, WFNS and GVS scores for prediction of mortality at three months was 0.895 (95% CI; 0.838-0.952; p<0.001), 0.876 (95% CI; 0.813- 0.938; p<0.001) and 0.887 (95% CI; 0.823-0.950; p<0.001) suggesting a good discrimination ability of all three scores in predicting mortality as shown in figure 5. Statistical inference - all these three scoring systems

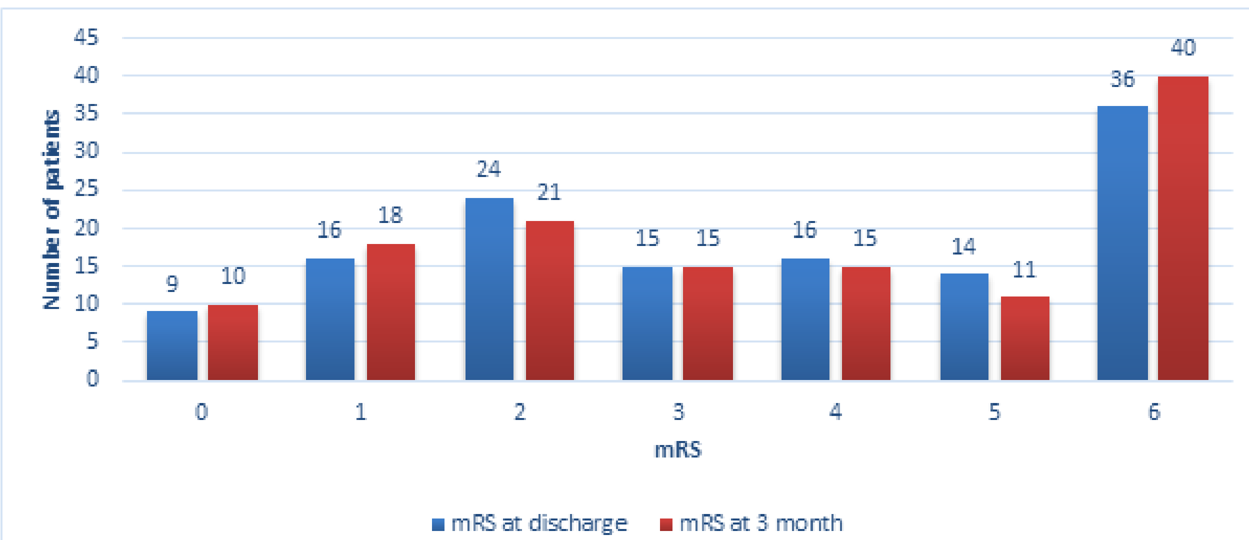

Figure 1: Distribution of mRS Scores

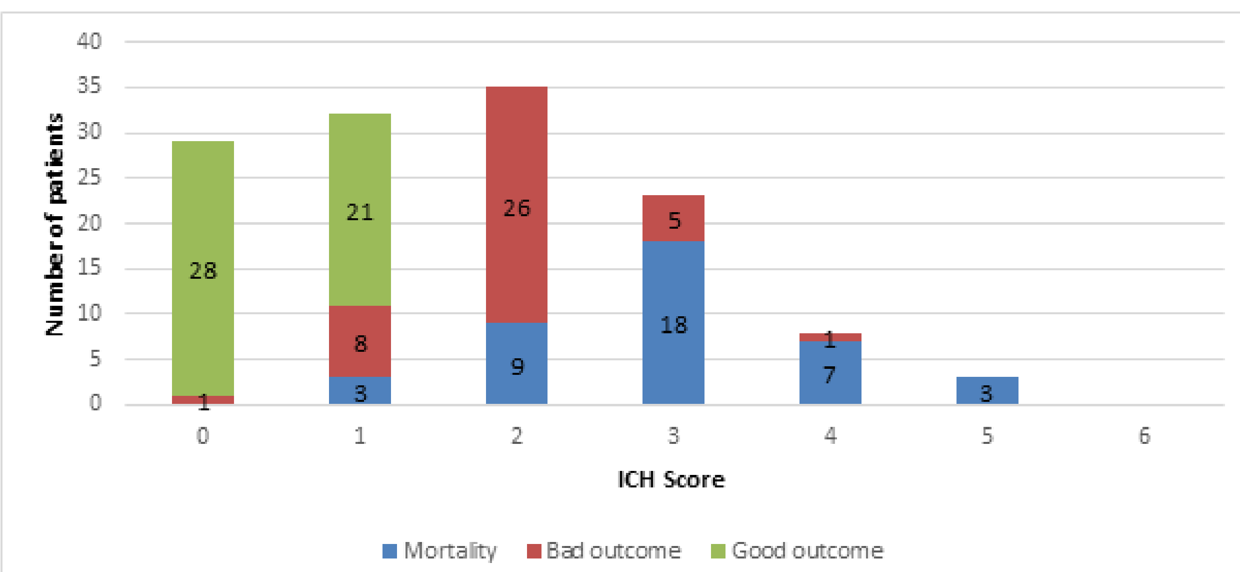

Figure 2: ICH Score and Outcome Distribution

Figure 3: WFNS Score and Outcome Distribution

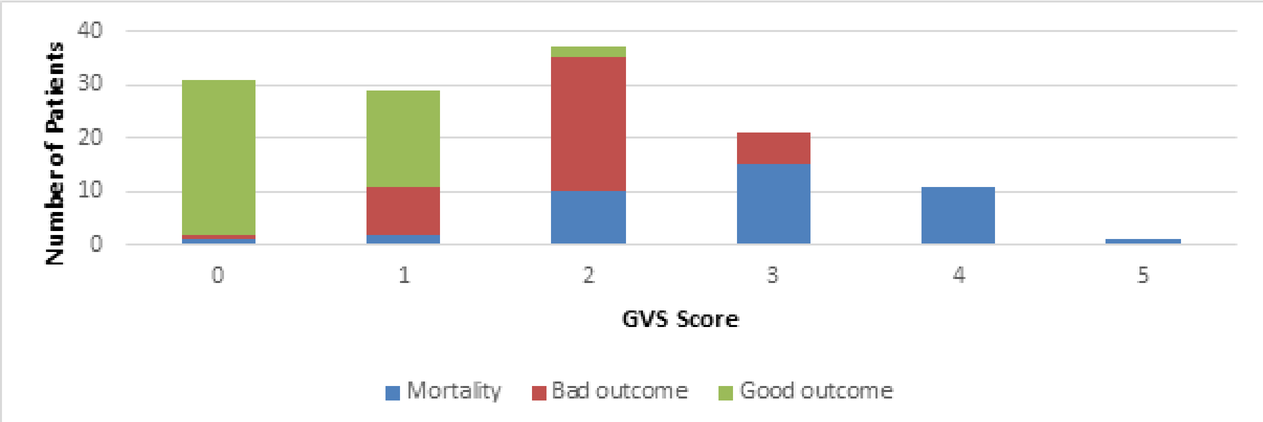

Figure 4: GVS Score and Outcome Distribution

may predict mortality at the time of presentation.

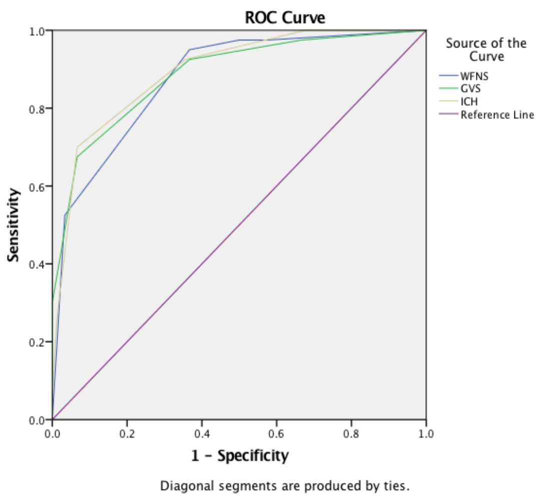

Figure 5: ROC Curve for Mortality

The area under ROC curve for GCS for prediction of bad outcome was 0.613 (95% CI; 0.517-0.708; *p*=0.039), 0.576 (95% CI; 0.479-0.674; *p*<0.162) and 0.601 (95% CI; 0.506-0.696; *p*=0.066) for ICH, WFNS and GVS scores, suggesting a fair discrimination ability of all three models in predicting bad outcome. In other words, all these three scoring systems may not be able to predict bad outcomes as good as for mortality.

Area under ROC curve for ICH, WFNS and GVS scores for good outcome was 0.962 (95 % CI; 0.922 - 0.991; p < 0.0001), 0.911 (95 % CI; 0.859 - 0.963; p < 0.0001) and 0.943 (95 % CI; 0.905 - 0.981; p < 0.0001). All the three scoring system can predict good outcome better than bad outcomes.

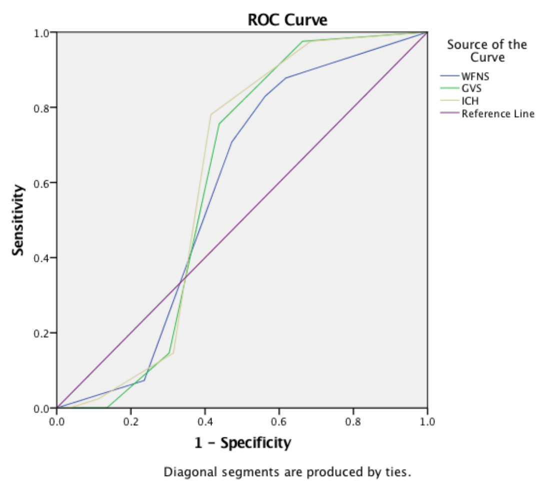

Figure 6: ROC Curve for Bad Outcome

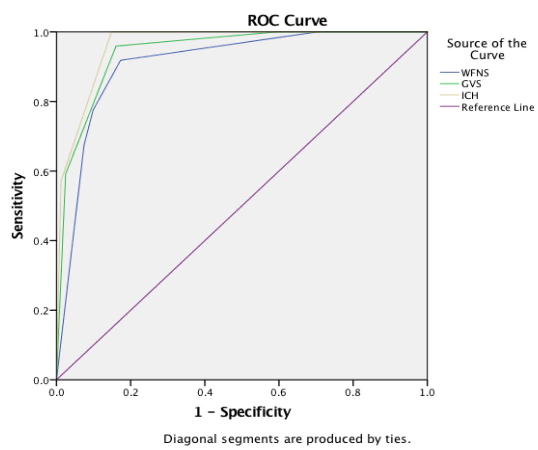

Figure 7: ROC Curve for Good Outcome

Discussion

Despite several recent large clinical trials of medical or surgical interventions[27,28], ICH is a disease with no proven treatment. However, there is a great interest in understanding and using outcome predictors for ICH. Numerous observational studies have been performed to develop prediction models and scores for ICH outcome[21,29-34] and only ICH score has been externally validated and extensively used. However, ICH score is complex and cumbersome to use in emergency situations and by physicians without special training. In order to simplify without decreasing the accuracy, WFNS and GVS scores have been recently proposed to predict morbidity and mortality[23,24]. We attempted to compare all three scores for the prognostication of ICH for mortality and functional outcome at three months, using mRS scale in our institution.

No patient with an ICH Score of 0 died in our study, whereas all patients with an ICH Score of 5 died. Thirty-day mortality rates for patients with ICH Scores of 1, 2, 3 and 4 were 9.4%, 26.0%, 78. % and 87.5% respectively. No patient had an ICH Score of 6 because no patient with an infratentorial ICH had a hematoma volume of 30 ml or more. Our finding was similar to the one reported by Hemphill et al[22]. In their study no patient with an ICH score of 0 died, whereas all patients with an ICH score of 5 died. Furthermore, 30 - day mortality rates for patients with ICH scores of 1, 2, 3 and 4 were 13%, 26%, 72% and 97 %, respectively[22]. Godoy et al.[18] reported that for patients with ICH scores of 1, 2, 3 and 4, the mortality rates were 2.9%, 30.8%, 61.1% and 88.2% respectively, showing an exponential increase in 30-day mortality with higher ICH score (*p*<0.0001; Cuzick's test for trend). In the study by Clarke et al.[19] in 2004, each increase in the ICH score was associated with a progressive increase in 30-day mortality (*p*<0.01 for trend). All the findings from various aforementioned series were similar to our study.

AUC for mortality for ICH score was 0.895 in our study which corroborates well with the other published series. The range of AUC for mortality varied from 0.76–0.92 in various series which were comparable to our study[19-21,23,34-36]. In our study, AUC for good outcome for ICH score was 0.962. It was higher than that found in most of other studies showing more discriminatory power. It was 0.821 in the study of Ruiz-Sandoval et al.[21], 0.776 in Ji et al.[35] and 0.831 in Weimar et al.[34].

Comparing the AUC for ICH and WFNS score in our study, it was found to be 0.895 and 0.876 for mortality, 0.613 and 0.576 for bad outcome and 0.962 and 0.911 for good outcome. So, discrimination ability was high for mortality and good outcome and only fair for bad outcome in our series. AUC was slightly better for ICH score than WFNS but was comparable for all three types of outcomes. In the study by Behrouz et al.[23] values were slightly higher for WFNS score in contrast to our study. In their study, AUC estimate was 0.92 for ICH and 0.93 for the WFNS score for mortality, 0.90 and 0.91 for bad outcome and 0.85 and 0.86 for good outcome showing excellent discrimination ability for all three outcomes by both scores. So, our results were comparable for predicting good outcome and mortality but had significantly less ability for prediction of bad outcome than that by Behrouz et al. [23]. WFNS score from 1 to 5 was 30.0%, 5.3%, 10.0%, 36.1% and 24.1% in our study. The mortality rate increased exponentially as the score increased - rate from score 1 to 5 were 2.6%, 0%, 7.7%, 36.2% and 87.5%, respectively. The zero mortality with WFNS score 2 may be due to the small number of patients (seven) in that group.

AUC for ICH and GVS score were comparable for all three types of outcomes, and it was slightly better for ICH score. For mortality, it was 0.895 and 0.887; for bad outcome, it was 0.613 and 0.601; and for good outcome, it was 0.963 and 0.943 respectively. So, GVS score was also a good predictor of mortality and good outcome like ICH score, but both showed only fair prediction of bad outcome. In our study, GVS score distribution from 0 to 5 was 23.8%, 22.3%, 28.5%, 16.1%, 8.4% and 0.7%, respectively. GVS score distribution from 0 to 4 was 22.2%, 26.7%, 27.4%, 18.9% and 4.5% respectively in the study by Mukherjee et al.[23]. Increase in GVS score was associated with adverse outcome in our study similar to the study by Mukherjee et al.[23]. GVS score of 0 to 5 associated with increasing risk of mortality at three months: 3.2%, 6.9%, 27%, 71.4%, 100% and 100% in our study. Our findings of rising GVS score with increased mortality also correlates similarly in study by Mukherjee et al.[23] - 32%, 52%, 71%, 80% and 86% for GVS score 0 to 4. Also, higher GVS score was associated with less chance of good outcome- GVS score of 0 to 2 had 93.5%, 62.1% and 5.4% chances of good outcome. In study by Mukherjee et al.[24] it was associated with 42%, 24% and 20% chances of good outcome from GVS 0 to 2 scores.

Limitations

1. This is a single center hospital-based study.
2. Long-term outcome of patients was not assessed in our study due to time constraints.
    - The functional outcome was assessed up to three months only.
    - Trend of improvement of functional outcome was not fully evaluated.
3. Cognitive status of our patients was not evaluated. Both functional and cognitive status may continue to improve well beyond three months; therefore, additional assessments may prove beneficial in future studies

Conclusions

Both GVS and WFNS scores are simple, easy to use and comparable to ICH score for the prediction of mortality and good outcome in patients with spontaneous ICH. All three scores are inferior for the prediction of bad outcome. ICH score is slightly better than other two scores in all outcome subgroups but was not significant. Further larger studies involving multiple centers with a long-term outcome evaluation may be required to better clarify the predictive ability of three scoring systems.

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