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Associated with the 30-Day Outcome of Spontaneous Cerebellar Hemorrhage

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Abstract **Original Research Article**

***Background*:** Spontaneous cerebellar hemorrhage (SCH) is a potentially life-threatening condition that results in early neurological deterioration, significant disability, and adverse consequences. Therefore, knowledge of the factors that potentially affect the outcome is crucial for a sound clinical decision-making framework and implementing efficient therapeutic measures. ***Objectives*:** This study aimed to identify possible clinical, radiological, and therapeutic factors associated with 30-day outcomes in patients with acute SCH. ***Methods*:** Sixty-six computerized tomography (CT) diagnosed cases of SCH above 18 years of age who were admitted and managed in the Department of Neurosurgery of Chittagong Medical College Hospital from October 2021 to September 2022 were enrolled prospectively in this study based on inclusion and exclusion criteria. Data regarding demographic, clinical, radiographic, and treatment modalities was recorded. The 30-day outcome was assessed by the Glasgow Outcome Scale (GOS) score and analyzed. A poor outcome was defined by GOS ≤3. ***Results*:** The mean age was 65.6±10.8 years and 56.1% were male. The median Glasgow Coma Scale (GCS) score on admission was 13 [interquartile range (IQR) = 8-14]. Twenty-five patients (37.9%) underwent surgical management [evacuation of the cerebellar hemorrhage and placement of an external ventricular drain (EVD) in 7 (28%); EVD alone in 12 (48%), and only evacuation in 6 (24%) cases of surgically managed] and 41 (62.1%) were treated conservatively. The 30-day mortality rate was 36.4%. Regarding 30-day outcomes, 47% (31) of patients had a poor outcome after 30 days. On univariate analysis, GCS score on admission, hematoma size, hematoma volume, ventricular extension, 4th ventricle obstruction, hydrocephalus, tight posterior fossa, ratio between transverse diameter of cerebellar hematoma and posterior fossa, intervention type, and need for mechanical ventilation were significantly associated with 30-day poor outcome. In multivariate analysis, only the GCS score on admission was a significant predictor of a 30-day poor outcome [odds ratio (OR) = 0.28; 95% confidence interval (CI) = 0.12–0.66; P = 0.003]. For prediction of a 30-day poor outcome, receiver operating characteristic (ROC) curve analysis confirmed that the best cut-off point was a GCS score of 11 on admission [area under the curve (AUC): 0.94, 95% CI = 0.88–0.98, P < 0.001] with the sensitivity of 94.3% and specificity of 87.1%. ***Conclusion*:** The 30-day outcome of SCH patients mostly depends on admission GCS score. A higher GCS score on their admission is strongly associated with a 30-day favorable outcome.
Keywords: 30-Day Mortality, Cerebellar Hemorrhage, Outcome, Associated Factors.

INTRODUCTION

SCH patients are being diagnosed at various levels of health care and attracting medical attention at higher centers on a regular basis. SCH is widely regarded as a rapidly progressive condition that necessitates prompt allocation and management decisions. Because of the high mortality and morbidity rates, predictors of early mortality are extremely clinically useful. SCH varies by race and age with an annual incidence of 12 to 31 per 100000 people [1]. The incidence of intracranial hemorrhage (ICH) in Asia, especially in the Indian subcontinent is higher in comparison to the western population, and the population at risk is the younger group [2]. The one-year mortality associated with SCH can be as high as 64% [3]. Unfortunately, the association between predictor and early outcome has not been systematically investigated, and published studies in Bangladesh were scary. SCH is a subtype of ICH that accounts for <15% of all spontaneous brain bleeds. Spontaneous cerebellar hemorrhage (SCH) causes mass lesion within the small posterior fossa threatens to compress the anatomic proximity brainstem and the fourth ventricle and can lead to life-threatening complications such as acute obstructive hydrocephalus, brainstem compression, or herniation. There aren't many recent articles available that discuss the outcomes of SCH patients prospectively, both those who have had surgery and those who haven't [4], set out to investigate whether surgery can be justifiable if performed in poor clinical grade in patients with SCH. The mortality rate is generally higher than those patients with other type of ICH. The verification of the short- term vital prognosis at the onset of the disease is especially significant since it forms the basis for taking appropriate therapeutic and tactical decisions [5, 6]. Hence, predictors for early mortality, poor short-term and long-term outcomes for SCH patients, is important to develop the management plan for careful use of available resources, especially in developing countries with limited resources [7]. Fast diagnosis and specific emergency treatment strategies especially surgical treatment are more often necessary in cases of cerebellar hemorrhage compared to supratentorial ICHs. Management of grave cases and treatment of patients in good neurological condition may be straightforward; however, the group of patients between these two extremes poses a trouble in decision making during treatment. Patients, who survived frequently suffer from lifelong disabilities and remain dependent on others for care which increases the health burden with associated socio-economic problems. The AHA guidelines, however, advocate for emergency surgery in patients with spontaneous cerebellar ICH of >3cm, or those showing signs of brainstem compression and/or hydrocephalus [8]. As a result, there is no commonly accepted management strategy for SCH [3-9]. Most reported studies have compared retrospectively the clinical course of conservatively and surgically treated patients to identify predictive indicators for the clinical outcomes from which treatment conclusions can be derived. However, compared to supratentorial lesion, the risk factors related to clinical and radiological findings are not well established in case of SCH. A better understanding of prognosis and associated factors in SCH could reduce variability in clinical trials and in clinical management by allowing more effective targeting of therapies [9, 10], set to o determines the association of surgical hematoma evacuation with clinical outcomes in cerebellar ICH. They found that unoperated patients were younger, and had a lower GCS on admission. They observed that both death and the unfavorable outcome was more common among the operated cases than the unoperated patients. [11], retrospectively reviewed all medical records of patients diagnosed with ischemic and hemorrhagic cerebellar strokes; during 2002-2018, in the Hospital of Thailand. To address this knowledge gap, this study was conducted to describe the demographic, clinical, biochemical, and radiological factors associated with the 30- day outcomes of patients with SCH admitted to a government tertiary care hospital in Bangladesh.

MATERIALS AND METHODS

Type of Study: Prospective observational descriptive study.

Place of Study: Department of Neurosurgery, Chittagong Medical College Hospital, Chattogram, Bangladesh.

Study Period: October 2021 to September 2022.

Study Population: All the patients admitted to the Department of Neurosurgery of CMCH with a diagnosis of SCH during the study period.

Sample Technique: Consecutive sampling considering the inclusion and exclusion criteria.

Sample Size: To estimate the sample size following formula was used: Finally, it was possible to include 66 patients in the study.

Inclusion Criteria:

Admitted patients were included if

1. Diagnosed as SCH.
2. Age more than 18 years.

Exclusion Criteria:

1. Secondary cerebellar hemorrhage is caused by neoplasm, aneurysm, arteriovenous malformation, cavernoma, trauma or hemorrhagic transformation of a cerebellar infarct, and hemorrhage after thrombolysis.
2. Hemorrhage extending to, or originating from the brainstem.
3. Patients with the initial absence of brainstem reflexes on admission.
4. The presence of accompanying supratentorial hemorrhage.
5. Refusal to participate in the study.

Data Collection Procedure

This study included 82 computerized tomography diagnosed cases of SCH over the age of 18 who were admitted and transferred to the Department of Neurosurgery at Chittagong Medical College Hospital. Based on inclusion and exclusion criteria, 16 patients were excluded: 7 had GCS 3 with nonreacting pupil, 2 had secondary cerebellar hemorrhage, and 3 patients' legal guardians declined to participate in the study procedure. Four patients were dropped out due to failure to attend follow-up appointments, one was an immigrant Rohingya, and other phone numbers were disconnected. Finally, 66 patients were enrolled. On admission, data regarding basic demographic profile (age and sex), scrutiny of cerebrovascular risk profile, a detailed physical examination, routine laboratory testing, and brain imaging were collected by direct supervision or from the history sheets for all patients. The initial neurologic state was evaluated by the GCS and clinical evaluation was performed by ICH score.

Outcome Assessment and Follow-Up

Final follow-ups were done 30 days post-attack and GOS scores were noted. The patient's party was counseled to bring the patient at follow-up after 30 days at the hospital outdoors when patients were examined physically including a neurological examination. For those patients who could not come at due time, information was collected over the telephone through structured interviews (Appendix-AİI and İIİ) with the patient or the responsible attendant. In circumstances where a responsible attendant would not be available, data were collected by direct visits or by providing allowances to attend outdoors for weak economic conditions. If the death occurred within 30 days, the time of death was collected and noted.

Data Analysis

Data were recorded in the form of an Excel worksheet. After completion of data collection, they were fed into SPSS version 23 for processing analysis. Continuous data were expressed as mean ± standard deviation (SD) for normally distributed data or median and 25%–75% interquartile range for non-normally distributed data. Categorical variables were presented as percentages (%) or proportions. The study population was divided into 30-day poor and good outcomes by GOS. Between these groups, continuous and categorical variables were analyzed. Student's *t*-tests were used to analyze normally distributed continuous variables, while Mann– Whitney's U-test was used for no normally distributed continuous variables. Categorical variables were compared using the Chi-square test. Variables with $P < 0.05$ on univariate analysis for good outcome 30-day after SCH were included in multivariate logistic regression analysis to determine the independent predictors of 30-day functional outcome. Results were reported as OR together with a 95% CI. The discriminatory values of the ICH score and GCS for predicting 30-day poor outcomes were studied using ROC curve analyses with the calculation of the AUC. An optimal cutoff value of the ICH score and GCS score for predicting a poor 30-day outcomes was defined by calculating Youden's index. Survival was estimated and compared between surgically managed and conservatively managed groups using the Kaplan-Meier method, and differences in survival between groups were assessed using the log-rank test. P < 0.05 was considered statistically significant.

RESULTS

A total of 82 patients were screened and 66 of them were found to full fill the eligibility criteria for the study. The final analysis included these 66 patients. Results and observations of the present study were described in the following tables and charts.

Table 1: Association between demographic characteristics and outcome of the patients (n=66)

Characteristics		30-day outcome		P value
		Good (n=35)	Poor (n=31)	
Age				
	Mean ±SD	63.2±10.5	68.3±10.7	0.054‡I
	Range			
Sex				
	Female	17 (48.6)	12 (38.7)	0.420*
	Male	18 (51.4)	19 (61.3)	

Data were expressed as frequency (%) if not mentioned otherwise. *Chi-square test; ‡Independent sample t-test. SD: Standard deviation.

Table 1 shows that mean age of the patients with poor outcomes (68.3±10.7 years) was higher than the patients with good outcomes (63.2±10.5 years), but the difference failed to reach statistical significance (p=0.054). Similarly, sex had no significant association with 30-day outcome (p=0.42).

Table 2: Association between baseline clinical characteristics and outcome of the patients (n=66)

Characteristics		30-day outcome		P value
		Good (n=35)	Poor (n=31)	
Comorbidity				
Hypertension		31 (88.6)	22 (71.0)	0.073*
Diabetes mellitus		7 (20.0)	7 (22.6)	0.798*
H/O Antiplatelet		3 (8.6)	7 (22.6)	0.113*
Interval[a], hours		24.0 (12.0-48.0)	20.0 (12.0-48.0)	0.806†
Presenting symptoms				
	Altered consciousness	10 (28.6)	28 (90.3)	<0.001*

Characteristics		30-day outcome		P value
		Good (n=35)	Poor (n=31)	
	Vomiting	15 (42.9)	15 (48.4)	0.652*
	Vertigo	18 (51.4)	5 (16.1)	0.003*
	Ataxia	11 (31.4)	4 (12.9)	0.073*
	Seizure	1 (2.9)	0 (0)	1.0**
Examination findings				
	DBP, mmHg.	90 (80-100)	90 (80-100)	0.469†
	SBP, mmHg.	160 (130-170)	160 (140-160)	0.339†
	GCS	13 (12-14)	7 (5-8)	<0.001†
	RBS, mg/dl	151.7 (127.8-198.0)	158.4 (131.4-225.0)	0.322†

Data were expressed as frequency (%) or median (IQR). *Chi-square test; ‡Independent sample t-test. †Mann-Whitney U test; aFrom symptom onset to admission; **Fisher's exact test.

Table 2 shows that the presence of any comorbidity, hypertension, diabetes mellitus, and pretreatment with antiplatelet had no association with the 30-day outcome. Similarly, median interval from symptoms onset to admission was similar between the two groups (p=0.806). Among the presenting symptoms, only the altered level of consciousness was significantly associated with the outcome (p<0.001), patients with poor outcomes reported more frequently (90.3%) than the patients with good outcomes (28.6%). Similarly, the median GCS at presentation was significantly lower among the patients with poor outcomes than the patients with good outcomes (7 versus 13, p<0.001). The mean blood pressure and RBS levels were similar in the two groups (p>0.05).

Table 3: Association between baseline radiological findings and outcome of the patients (n=66)

Characteristics		30-day outcome		P value
		Good (n=35)	Poor (n=31)	
Hematoma size, cm		3.0 (2.5-3.5)	4.0 (3.0-4.5)	0.001†
Hematoma volume, ml		10.0 (8.0-15.0)	22.0 (14.0-32.0)	<0.001†
Intraventricular extension		16 (45.7)	25 (80.6)	0.005
Hydrocephalus		19 (54.3)	30 (96.8)	<0.001
4th ventricle obstruction				
	Grade I	12 (34.3)	1 (3.2)	<0.001*
	Grade II	20 (57.1)	9 (29.0)	
	Grade III	3 (8.6)	21 (67.7)	
Ratioa (%)		30.0 (24.0-35.0)	38.0 (30.0-43.0)	<0.001†
Location of hematoma				
	Right	15 (42.9)	10 (32.3)	0.066*
	Left	16 (45.7)	10 (32.3)	
	Vermis	4 (11.4)	11 (35.5)	
Basal effacement				
	Grade I	21 (60.0)	4 (12.9)	<0.001*
	Grade II	14 (40.0)	14 (40.0)	
	Grade III	0 (0)	13 (41.9)	
Tight posterior fossa		13 (37.1)	26 (83.9)	<0.001*

Data were expressed as frequency (%) or median (IQR). *Chi-square test; †Mann-Whitney U test; aCerebellar hematoma/posterior fossa (maximum transverse diameter).

Table 3 shows that the mean hematoma size, hematoma volume, and ratio of the cerebellar hematoma and posterior fossa (maximum transverse diameter) were significantly higher in patients with poor outcomes than the patients with good outcomes (p <0.05). Similarly, the presence of Intraventricular extension, higher graded of 4th ventricular obstruction, hydrocephalus, and presence of tight posterior fossa was associated with poor outcome (p<0.05). A higher proportion of patients with poor outcomes had Intraventricular extension, higher graded of 4th ventricular obstruction, hydrocephalus, and tight posterior fossa than their counterparts.

Table 4: Association between treatment modalities used and outcome of the patients (n=66)

Characteristics	30-day outcome		P value
	Good (n=35)	Poor (n=31)	
Management			
Surgery	7 (20.0)	18 (58.1)	0.001*
Conservative	28 (80.0)	13(41.9)	
Interval[a], hour	76 (72-96)	42 (29-108)	0.458†
Interval[b], hour	48 (26-52)	16 (10-27)	0.014†
Type of surgery (n=25)			
EVD insertion	3 (42.9)	9 (50.0)	0.342*
Suboccipital craniectomy and evacuation of hematoma	3 (42.9)	3 (16.7)	
Combined EVD and evacuation	1 (14.3)	6 (33.3)	
Need Mechanical ventilation	3 (8.6)	17 (54.8)	<0.001**

Data were expressed as frequency (%) or median (IQR). *Chi-square test; †Mann-Whitney U test; [a]From symptom onset to surgery; [b]From admission to surgery; **Fisher's exact test. EVD: External ventricular drainage,

Table 4 shows that type of intervention, (conservative or surgical) had a significant association with outcome (p=0.001), the outcome was poor in higher proportion of patients managed surgically, than those managed conservatively. However, the type of surgical intervention with evacuation and EVD placement or with EVD placement alone or evacuation alone had no significant effect on the outcome. A significantly higher proportion of the patient who need mechanical ventilation had poor outcomes (P<0.001).

Table 5: Logistic regression analysis with a 30-day poor outcome as the dependent variable

Variables	B	P value	OR (95% CI for OR)
GCS on admission (per point)	-1.261	0.003	0.28 (0.12-0.66)
Hematoma volume (per 1 ml increase)	0.082	0.457	1.09 (0.87-1.35)
Presence of ventricular extension on admission CT scan	0.843	0.433	2.32 (0.28-19.14)
Presence of hydrocephalus	1.551	0.288	4.72 (0.27-82.37)
Ratio[a] (%)	-0.207	0.186	0.81 (0.60-1.11)
4th ventricle obstruction			
Grade I	Reference		
Grade II	0.635	0.689	1.89 (0.08-42.36)
Grade III	2.668	0.247	14.41 (0.16-131.02)
Presence of tight posterior fossa	-2.549	0.092	0.08 (0.01-1.51)
Managed surgically	2.817	0.150	16.73 (0.36-77.00)

OR: Odds ratio; CI: Confidence interval. [a]Cerebellar hematoma/posterior fossa (maximum transverse diameter)

A multivariate binary logistic regression analysis was performed using the variables which had a significant association with outcome in univariate analysis, with the 30-day poor outcome as the dependent variable (Table 5). Only the initial GCS score of patients with SCH (OR = 0.28 per one point change in GCS score, 95% CI = 0.12-0.66, P = 0.003) was a significant predictor of 30-day poor outcomes. This means that each additional increase of one point in GCS at admission is associated with a decrease in the odds of an SCH patient having a 30-day poor outcome. In other words, one point decrease in the admission GCS would increase the risk of a 30- day poor outcomes by 72%.

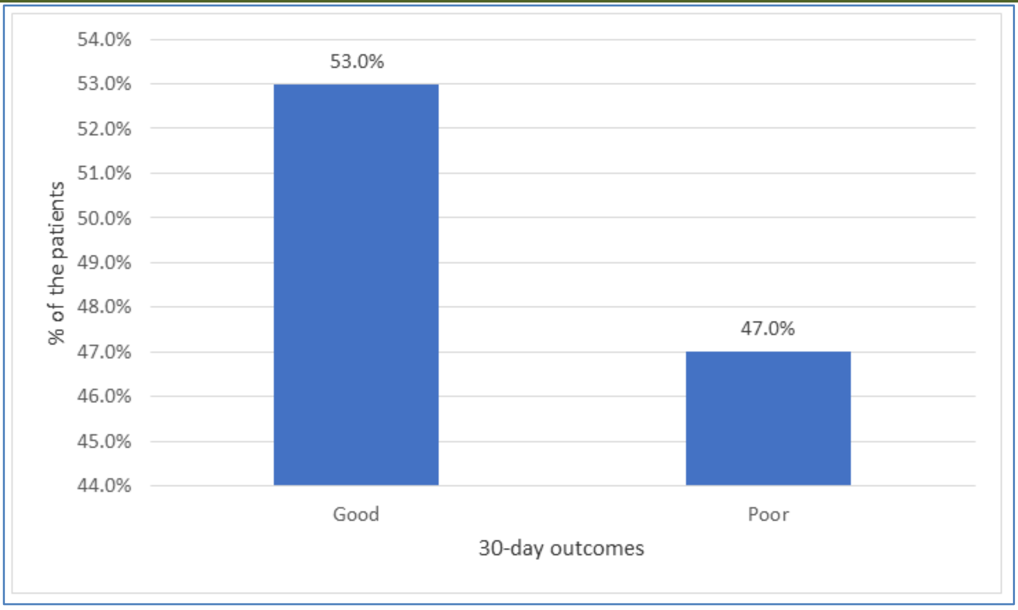

Figure 1: Distribution of the patients based on their 30-day outcomes.

At the final follow-up (30-day), out of 66 patients, 35 (53%) patients had a good outcome and other 31 (47%) patients had poor outcomes (Figure 1).

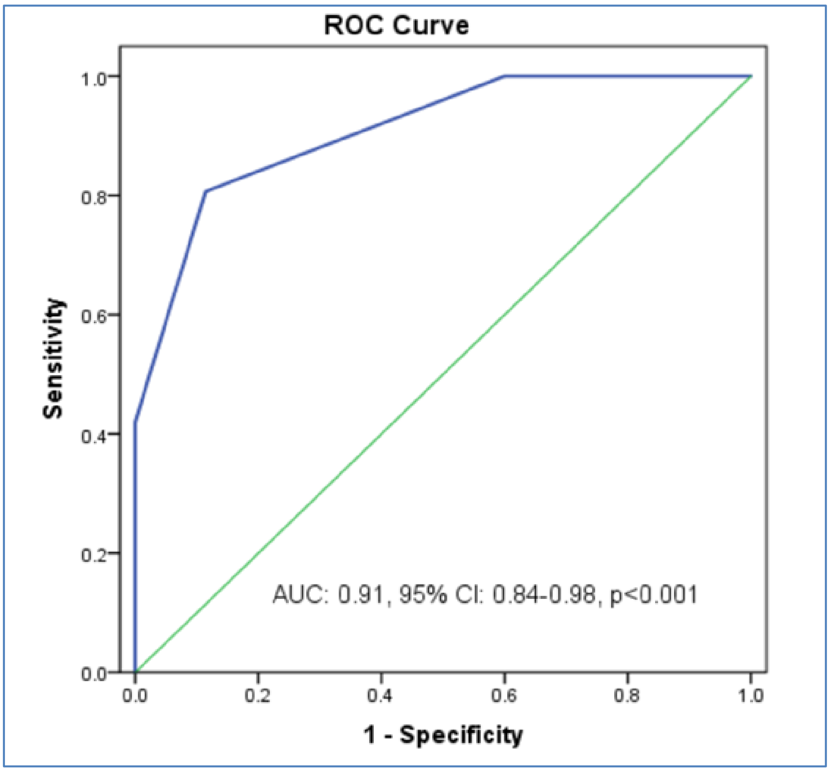

Figure 2: The ROC curve of the correlation between ICH score on admission and 30-day poor outcome.

To determine the relationship between the ICH score on the initial presentation and the risks of poor outcome after 30 days, the ROC curve was generated (Figure 2). The AUC for ICH score on presentation was 0.91 ($p<0.001$, 95% CI: 0.84-0.98). The best cutoff value of the ICH score on the presentation for the prediction of a 30-day poor outcome was 2.5 (sensitivity 88.6% and specificity 80.6%).

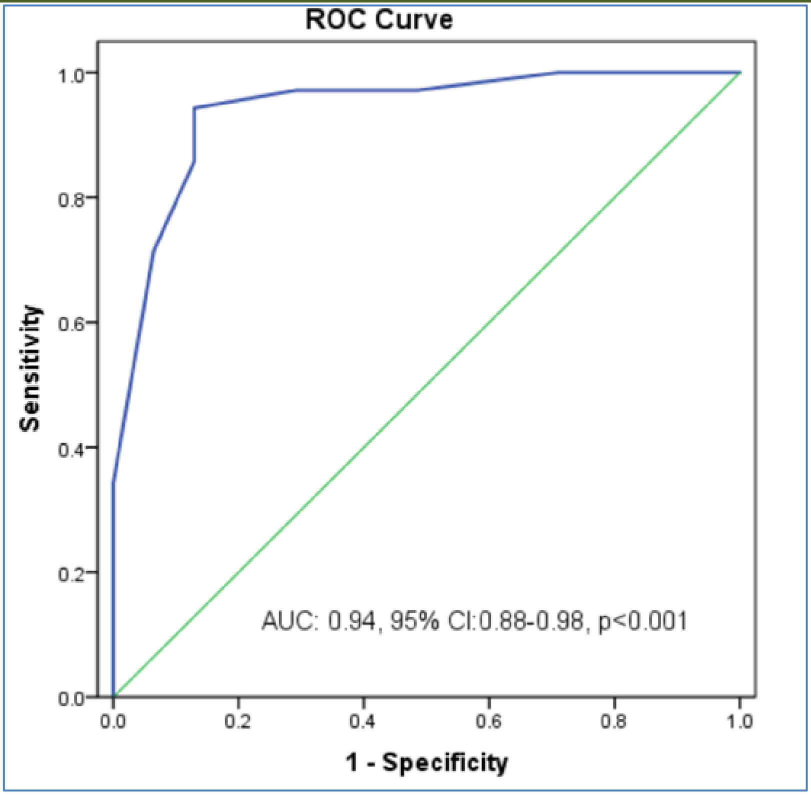

Figure 3: The ROC curve of the correlation between GCS on admission and 30-day poor outcome.

The AUC of 0.94 points to the high diagnostic utility of GCS as a predictor of 30-day poor outcomes (Figure 3). ROC curve analysis demonstrated a GCS score cut-off of 11 to be the best predictor of poor outcome at 30-days with a sensitivity of 94.3% and specificity of 87.1%.

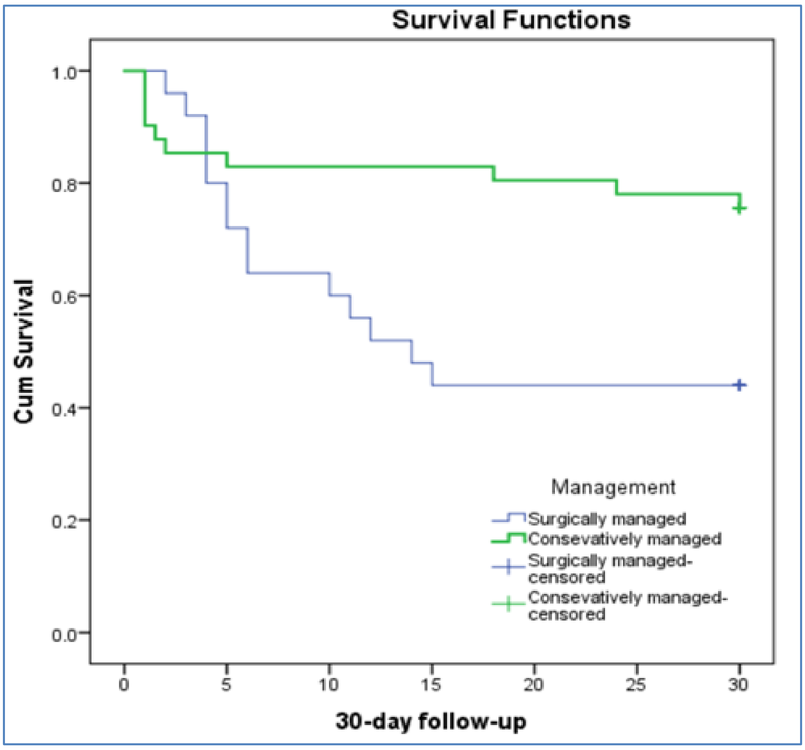

Figure 4: Kaplan-Meier curves showing the 30-day survival of patients with SCH after enrollment stratified according to the management procedure.

The studied patients were divided into two groups according to their management type (surgically versus conservatively). The 30-day mortality rates were 56% (14/25) and 24% (10/41) in the surgically and conservatively managed groups, respectively. The overall survival was assessed by the Kaplan–Meier curve (Figure 4), it showed significantly higher mortality in the conservative group in the initial period (log-rank test, p=0.013), but at the later stage significantly higher proportion of surgically managed cases expired than their counterpart (Breslow test, p=0.029; Tarone-Ware test, p=0.019).

Discussion

This prospective observational study investigated the association of different clinical, radiological, and therapeutic factors on the 30-day outcome of SCH patients whether managed surgically or conservatively to determine any of these factors could predict the prognosis. The results of the current study proved that the admission GCS score was a strong influencing factor of outcome in SCH patients. Regarding the 30-day outcomes, 53% of patients had a good outcome consistent with previous findings of various studies [12- 14]. In our study, 36.4% mortality has been noted, which is similar to or corresponds with mortality reported in the literature between 18 and 75% early mortality after SCH [14,15]. This study reported that the mean age of 63.2±10.5 years had a better outcome than the mean age of 68.3±10.7 years which is not statistically significant [16], observed that there is strong correlation between advance age and unfavorable outcome, which is not supported by our prospective observational study and [12]. That means advanced age and an unfavorable outcome do not correlate significantly. We found that altered level of consciousness is the most frequent symptom (57.6%), where patients with poor outcomes were reported more frequently (90.3%) than patients with good outcomes. The impaired conscious state seen in cerebellar hemorrhage can largely be attributed to the development of hydrocephalus, resulting in intracranial hypertension and/or direct brain stem compression [12- 17], have consistently reported that initial impaired consciousness (GCS) is a vital influencing factor for poor outcomes after SCH whilst *[16], do* not significant association before surgery on 6-month or long-term outcomes. The present study confirmed this association between initial GCS and outcome where median GCS at presentation was significantly lower among the patients with poor outcomes and vice versa. The AUC of 0.94 points to the high diagnostic utility of GCS and ROC curve analysis demonstrated a GCS score cutoff of 11 as the best predictor of poor outcome at 30 days, with a sensitivity of 94.3% and specificity of 87.1% was accordance with [14], who stated GCS score cutoff 10 as the significant predictor of the 30-day mortality. This means, one point decrease in the admission GCS would increase the risk of a 30-day poor outcome by 72%. Due to the diversity of the presentation, patients present early to late according to their severity or deterioration. We found no statistical correlation between the outcome and symptoms onset to admission, found accordance with [10- 18]. Our study showed that hematoma volume (particularly values over 15 ml), diameter of hematoma (> 3.5 cm) and the ratio of the maximum transverse diameter of the cerebellar hematoma/posterior fossa (> 33%) were significantly associated with poor outcome in univariate logistic analysis but not in multivariate model and were in good agreement with several studies [13- 20]. CBH/PF ratio >35%, a new parameter introduced by [13- 17], stated that hemorrhage in the cerebellar vermis was associated with an unfavorable outcome but in our study location of the hematoma no association with prognosis. Several studies have mentioned the presence of or developing hydrocephalus at admission, compression of the fourth ventricle, obliteration of the basal cistern and tight posterior fossa in neuroimages as indications for neurosurgical interventions and as prognostic factors in patients with SCH [12- 18]. In our study, IV extension, hydrocephalus, a higher grade of 4th ventricular obstruction, and a tight posterior fossa were associated with a negative prognosis of SCH. But the radiological parameters did not reach statistical significance in the multivariate logistic analysis. The ICH score, first introduced by [21], was a simple and reliable scale for predicting 30-day mortality in patients with spontaneous intracerebral hemorrhage. Accordance to [18], in our study we too found that the AUC for ICH score on presentation was 0.91 (p<0.001, 95% CI: 0.84-0.98) and the best cutoff value of the ICH score on the presentation for the prediction of a 30-day poor outcome was 2.5 (sensitivity 88.6% and specificity 80.6%). A standard treatment guideline for SCH management has not yet been established. In the present study, the outcome was poor in a higher proportion of patients managed surgically and they had less favorable clinical and radiological findings and a delay in presentation due to referral [10], showed that surgical hematoma evacuation, compared with conservative treatment, was not associated with improved functional outcome where [14], found that the 30-day outcome was higher in patients treated surgically than in patients treated conservatively, but this was statistically insignificant. The role of surgical treatment for SCH is controversial. However, subgroup analysis showed a potential benefit [22]. A significantly higher proportion of patients who needed mechanical ventilation had poor outcomes. The strength of the present prospective study was to find out the related associated factors affecting the 30-day outcome of SCH patients managed both surgically and conservatively. Based on this study, decision-making dilemma between surgery and conservative will overcome. Further large- scale studies incorporating patients from the different centers will be able to clarify the predictors of short-term outcomes following SCH more clearly.

CONCLUSION

The current investigation demonstrated that the 30-day outcome of SCH patients mostly depends on their admission GCS score. A higher GCS score on admission is strongly associated with a favorable 30-day outcome. A standard treatment guideline for SCH management has not yet been established. In the present study, the outcome was poor in a higher proportion of patients managed surgically and they had less favorable clinical and radiological findings and a delay in presentation due to referral. Showed that surgical hematoma evacuation, compared with conservative treatment, was not associated with improved functional outcome.

CONFLICT OF INTEREST: None.

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