

## Original Article

# Prediction of 30-day mortality in spontaneous cerebellar hemorrhage

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## Abstract

**Background:** Cerebellar hemorrhage is a potentially life-threatening condition and an understanding of the factors influencing outcome is essential for sound clinical decision-making.

**Methods:** We retrospectively evaluated data from 50 consecutive patients who suffered a first spontaneous cerebellar hemorrhage (SCH) from 2005 to 2014, analysing their short-term outcomes and identifying possible clinical, radiological and therapeutic risk factors for poor prognosis and death within 30 days.

**Results:** Among 50 patients with first SCH, the mean age was  $72 \pm 10$  years. Median Glasgow Coma Scale (GCS) score on admission was 11 [interquartile range (IQR) = 7–11]. Among 50 patients, 19 patients (38%) underwent surgical hemorrhage evacuation with placement of an external ventricular drain (EVD), 12 patients (24%) received an EVD only and 19 patients (38%) were treated conservatively. The 30-day mortality rate was 36%. In multivariate analysis only the GCS score on admission was a significant predictor of 30-day mortality [odds ratio (OR) = 0.598; 95% confidence interval (CI) = 0.406–0.879;  $P = 0.009$ ]. For prediction of 30-day mortality, receiver operating characteristic curve analysis confirmed that the best cut-off point was a GCS score of 10 on admission [area under the curve: 0.882, 95% CI = 0.717–1,  $P < 0.001$ ].

**Conclusion:** Lower GCS score on admission was associated with increased 30-day mortality and poorer short-term outcome in patients with SCH. For patients with a GCS score  $< 10$  on admission, it is important to balance the possibility of survival afforded by further therapy against the formidable risk of significant functional disability and poor quality of life.

**Key Words:** 30-day mortality, cerebellar hemorrhage, prognosis, risk factors

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## INTRODUCTION

Cerebellar hemorrhages constitute about 10% of all intracerebral hemorrhages and about 15% of cerebellar strokes.<sup>[15,24]</sup> Spontaneous cerebellar hemorrhage (SCH) can occur in the cerebellar hemispheres, the vermis or in both of these regions simultaneously, and it may extend into the ventricular system. Hypertension is the most common identifiable risk factor for SCH,

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with a reported incidence of between 36 and 89% of cases.<sup>[19]</sup> There are also other less frequent causes such as coagulopathy (including the use of antiplatelet and anticoagulant drugs) and amyloid angiopathy.<sup>[2,9]</sup> Remote cerebellar hemorrhage as a result of the release of large volumes of cerebrospinal fluid following supratentorial or spinal surgery is also well described in the literature.<sup>[16,21,26]</sup> Intracerebellar hemorrhages are associated with high mortality and morbidity.<sup>[27,29,34]</sup> However, there are no prospective randomized trials evaluating outcomes in these patients, and due to the variations in the patient cohorts, clinical settings and treatment strategies in the available studies, there is still uncertainty about which risk factors significantly influence outcome in patients with SCH.<sup>[8,10,35,36]</sup>

We performed a study to analyze the short-term course of patients suffering from SCH and evaluate different possible outcome predictors, including patient- and treatment-related factors (medical versus surgical therapy) in our analysis.

## MATERIALS AND METHODS

We retrospectively analyzed data from 50 consecutive patients treated in our tertiary academic centre between January 2005 and December 2014, all diagnosed with a first episode of isolated SCH. The exclusion criteria were secondary cerebellar hemorrhage caused by trauma, tumours, cavernomas, arteriovenous malformations or aneurysms, hemorrhagic transformation of a cerebellar infarct, the presence of accompanying supratentorial or brainstem hemorrhage, incomplete medical records and patients with initial absence of brainstem reflexes on admission.

### Study design

This is a single-centre retrospective study. To evaluate the short-term outcome and define possible risk factors for an unfavourable prognosis among patients with first SCH, we created a data file including the following parameters: age, sex, initial neurologic status, the presence of cardiovascular comorbidities, previous consumption of antiplatelet and/or anticoagulant drugs, radiographic features and type of treatment (medical or surgical). The major end-points in our study were death within 30 days, functional status at follow-up (a maximum of 30 days after ictus) and recurrent cerebellar hemorrhage or ischemic stroke.

Neurological outcome was measured using the modified Rankin scale (mRS).<sup>[37]</sup> The overall outcome was defined as favourable if the mRS score was  $\leq 2$  and unfavourable when the mRS score was  $\geq 3$ . The initial neurologic status was determined according to the Glasgow Coma Scale (GCS) score<sup>[33]</sup> at the time of arrival of the patient in our emergency department and before the start of any treatment.

The initial imaging data, mainly head computed tomography (CT) scans (LightSpeed VCT, GE Medical Systems, Milwaukee, WI, USA), were reviewed to determine the location and dimension of each SCH, the presence of intraventricular hemorrhage (IVH), and radiological signs of hydrocephalus. The hematoma volume was estimated on the initial head CT scan using the ABC/2 method, in which A is the greatest diameter on the largest hemorrhage slice, B is the diameter perpendicular to A and C is the number of axial slices with bleeding multiplied by the slice thickness.<sup>[5]</sup> A diagnosis of hydrocephalus was based on signs including effacement of basal cisterns, enlargement of ventricles and the presence of transependymal oedema. These imaging studies (mostly head CT scans) were performed in our institution and there was always a written radiological report approved by a consultant radiologist. The findings contained in the written radiological report for each patient were compared with our own assessments to control for any inter-observer variability.

### Treatment protocol

All patients were treated according to the standard of care in our institution. Alert patients with hemorrhage of maximal diameter  $< 3$  cm and without radiological evidence of hydrocephalus were treated conservatively in a neurointensive care unit. Unconscious patients and patients with a decreased consciousness level and hemorrhage diameter  $> 3$  cm were treated surgically, by means of evacuation of the bleeding through a suboccipital craniectomy and placement of an external ventricular drain (EVD). In cases of hemorrhage  $< 3$  cm but with IVH resulting in clinical and/or radiological signs of hydrocephalus, an EVD alone was placed. However, the decision for surgery was individualized in each case, taking into account patient comorbidities. Comatose patients with absent brainstem reflexes on admission received conservative therapy and/or palliative care and were excluded from the study because of the high likelihood of very poor outcome.

### Statistical analysis

First, univariate logistic regression was used to assess the strength of association between the collected variables and short-term outcome, using 30-day mortality as a dependent variable. Independent variables included age, gender, GCS score, arterial hypertension, use of anticoagulant or antiplatelet medications (use of antiplatelet drugs and anticoagulants were evaluated separately), maximal hemorrhage diameter and hemorrhage location, presence of IVH, hydrocephalus and the choice of therapy (conservative/medical versus surgical). Multivariate analysis was performed as a second step, using 30-day mortality as a dependent variable, and incorporating independent variables showing significance

or a trend towards significance in the univariate analysis. A Hosmer-Lemeshow test was used to assess the goodness of fit of the multivariate model. Results are reported as odds ratios (OR) together with 95% confidence intervals (CI). For the GCS on admission that appeared significant in the multivariate correlations, the receiver operating characteristic (ROC) curve analysis was applied for identification of the clinically relevant cut-off value. The diagnostic accuracy was judged based on the value of the area under the curve (AUC). The significance level was set to 0.05. Analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL, USA).

## RESULTS

A total of 50 patients (mean age  $72 \pm 10$  years; 30 males and 20 females) diagnosed with a first episode of SCH fulfilled the inclusion criteria. The median GCS score on admission was 11 [interquartile range (IQR) 7–13, range 3–15]. In this cohort, 84% of patients ( $n = 42$ ) had a pre-existing diagnosis of arterial hypertension.

Use of a hemostasis-altering medication prior to ictus was identified in 34 patients (68%), who had been prescribed either antiplatelet ( $n = 20$ ) or anticoagulant therapy ( $n = 14$ ). 30 patients (61.6%) suffered a unilateral cerebellar hemorrhage and 12 patients (19.8%) experienced midline (vermian) hemorrhage. In 8 patients (18.6%) the hemorrhage was diffuse. The average hematoma diameter was  $3.97 \pm 1.66$  cm, corresponding to a volume of  $35.56 \pm 32.75$  ml (range 0.5–130.36 ml). IVH was found on the initial head CT scan of 36 patients (72%). Incipient hydrocephalus with compression of the fourth ventricle was apparent on the admission CT scan of 28 patients (54%). Among the 50 included patients, no patient developed a second hemorrhage or ischemic stroke within our short-term follow-up.

Nineteen patients (38%) underwent surgical evacuation of the cerebellar hemorrhage and placement of an EVD within 72 hours after ictus; 12 patients (24%) received an EVD alone and 19 (38%) were treated conservatively. The main characteristics of our cohort are summarized in Table 1.

### 30-day outcome

Eighteen patients died within 30 days of the occurrence of hemorrhage, representing a 30-day mortality of 36%. An unfavourable outcome (mRS  $\geq 3$ ) was documented in 30 patients (60%) at the end of short-term follow-up [Figure 1].

### Logistic regression

The univariate analysis showed admission neurological status according to GCS score and maximal diameter

**Table 1: Characteristics of 50 patients with spontaneous cerebellar hemorrhage**

Patients ( <i>n</i> )	50
Male/female, <i>n</i> (%)	30 (60)/20 (40)
Age (years), mean $\pm$ SD	72 $\pm$ 10
GCS on admission, median $\pm$ (IQR 25-75%)	11 (7-13)
GCS = 3-8, <i>n</i> (%)	15 (30)
GCS = 9-12, <i>n</i> (%)	10 (20)
GCS = 13-15, (%)	15 (30)
Comorbidities	
Hypertension, <i>n</i> (%)	42 (84)
Use of AC or AP, <i>n</i> (%)	34 (68)
Hemorrhage characteristics	
Location	
Unilateral, <i>n</i> (%)	53 (61.6)
Midline, <i>n</i> (%)	17 (19.8)
Diffuse, <i>n</i> (%)	16 (18.6)
IVH, <i>n</i> (%)	36 (72)
Hemorrhage maximal diameter (cm), mean $\pm$ SD	3.97 $\pm$ 1.66
Hemorrhage volume (ml), mean $\pm$ SD	35.56 $\pm$ 32.75
Presence of hydrocephalus on admission CT scan, <i>n</i> (%)	28 (54)
Treatment	
Surgery and EVD, <i>n</i> (%)	19 (38)
EVD alone, <i>n</i> (%)	12 (24)
Conservative, <i>n</i> (%)	19 (38)

AC: Anticoagulation therapy, AP: Antiplatelet therapy, EVD: External ventricular drainage, GCS: Glasgow Coma Scale, IVH: Intraventricular hemorrhage, SD: Standard deviation, IQR: interquartile range

of the hemorrhage on initial head CT scan to be significant predictors of death within 30 days after ictus. The presence of hydrocephalus and IVH on initial head CT scan was not significantly associated with increased 30-day mortality [Table 2]. In a second step we performed a multivariate logistic regression analysis using these variables, with the 30-day fatality as dependent variable. Only the initial GCS score of patients with SCH (OR = 0.598 per one point change in GCS score, 95% CI = 0.406–0.879,  $P = 0.009$ ) was a significant predictor of 30-day mortality [Table 2].

The type of intervention, whether conservative or surgical, or with evacuation and EVD placement or with EVD placement alone, had no significant effect on outcome. However, it must be noted that the characteristics of the patients across each of the three treatment groups in this retrospective and non-randomized study were significantly different, particularly regarding the initial GCS score and the dimensions of the hemorrhage on initial head CT scan.

Performing a ROC analysis an optimal GCS score cut-off value of 10 was identified (AUC: 0.882, 95% CI = 0.717–1,  $P < 0.001$ ) [Figure 2]. The patients in our cohort who had an initial GCS score  $< 10$  had

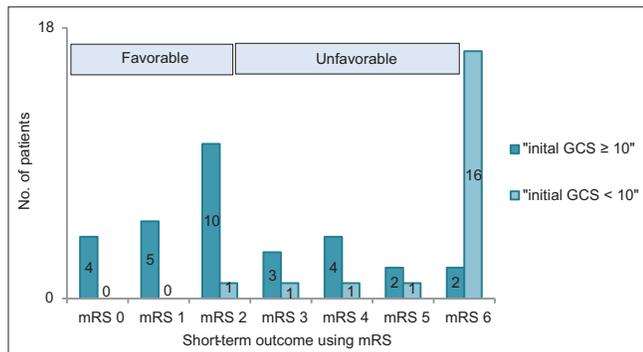
an in-hospital mortality of approximately 89% and experienced an unfavourable outcome (mRS  $\geq 3$ ) in approximately 97% of cases [Figure 1].

A further analysis was performed to evaluate for the presence of a potential effect of the timing of surgical intervention on 30-day patient outcome. All 19 patients who underwent operative evacuation of the hemorrhage had this surgery within 72 hours of hemorrhage. This surgery was performed within 6 h and after 6 h of hemorrhage ictus in 14/19 patients (median 3.3 h) and 5/19 patients (median 34 h), respectively. There was no significant difference between these groups in terms of 30-day outcome (mortality 40% in patients operated within 6 h versus 43% in patients operated after 6 h,

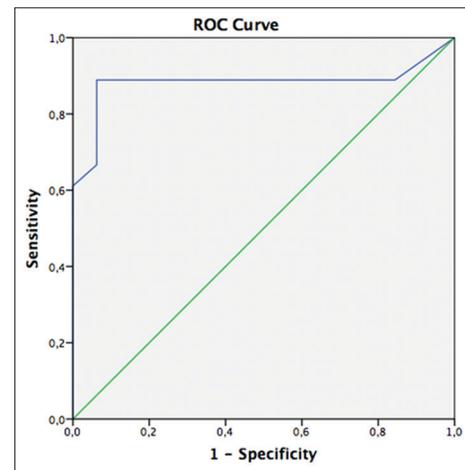
$P = 0.912$ ; morbidity 77% in patients operated within 6 h versus 80% in patients operated after 6 h,  $P = 0.947$ ).

## DISCUSSION

The 30-day mortality was 36% in our study, which is within the wide range of between 18 and 75% early mortality after cerebellar hemorrhage reported in the literature.<sup>[1,18,19,28,35]</sup> Regarding short-term outcome, 60% of patients had an



**Figure 1:** Distribution of favourable and unfavourable outcome according to the mRS in our cohort 30 days after hemorrhage and its relationship to initial neurological status (GCS score <10 versus GCS score  $\geq 10$ )



**Figure 2:** The ROC curve of the correlation between GCS on admission and 30-day mortality. The AUC of 0.882 points to the high diagnostic utility of GCS as a predictor of 30-day mortality. ROC curve analysis demonstrated a GCS score cut-off of 10 to be the best predictor of mortality at 30 days (AUC: 0.882, 95% CI = 0.717–1,  $P < 0.001$ )

**Table 2: Logistic regression analysis with 30-day mortality as the dependent variable**

	Univariate		Multivariate*	
	OR (95% CI)	P	OR (95% CI)	P
Age (per year)	1.022 (0.936-1.085)	0.475	-	-
Sex (female)	0.930 (0.285-3.301)	0.904	-	-
GCS on admission (per point)	0.538 (0.391-0.741)	<0.001	0.598 (0.406–0.879)	0.009
<b>Comorbidities</b>				
Hypertension	0.548 (0.32-1.014)	0.678	-	-
Use of AP	1.476 (0.367-5.585)	0.588	-	-
Use of AC	1.222 (0.267-5.592)	0.796	-	-
<b>Imaging features</b>				
Location of hemorrhage				
Unilateral	Reference	0.712		
Midline	1.437 (0.343-4.399)	0.528		
Diffuse	1.347 (0.454-4.578)	0.472		
Presence of IVH	4.008 (0.936-24.620)	0.060	3.448 (0.301-39.514)	0.320
Diameter (per 1 ml increase)	1.009 (1.004-1.014)	0.001	1.285 (0.680-2.429)	0.439
Presence of hydrocephalus on admission CT scan	0.339 (0.098-1.177)	0.088	0.219 (0.028-1.731)	0.150
<b>Therapy</b>				
Conservative	Reference	0.810		
EVD insertion alone	1.528 (0.424-5.499)	0.517		
Hematoma evacuation and EVD insertion	1.527 (0.486-4.979)	0.482		

\*Data of 50 patients were included in this analysis, AC: Anticoagulation therapy, AP: Antiplatelet therapy, CI: Confidence interval, EVD: External ventricular drain, GCS: Glasgow Coma Scale, IVH: Intraventricular hemorrhage, OR: Odds ratio

unfavourable outcome after 30 days. Consistent with previously published studies, neither gender nor age were significant outcome predictors.<sup>[10,12,28,34]</sup>

Arterial hypertension is strongly associated with the occurrence of cerebellar hemorrhage and it is known to pre-exist between 36 and 89% of cases.<sup>[3,6,19,31]</sup> In our study, we too found a very high prevalence of pre-existing hypertension (about 84%). Moreover, 68% of the patients received anticoagulant or antiplatelet therapy prior to their hemorrhage. However, our analyses showed no significant association between 30-day outcome and the presence of arterial hypertension or the consumption of hemostasis-altering drugs (AP or AC).

In relation to possible prognostic risk factors for early outcome, our work demonstrated that initial neurological status according to GCS score is the only significant predictors of 30-day mortality after SCH. The patients in our cohort with an initial GCS score <10 had an in-hospital mortality of about 89% and suffered an unfavourable outcome (mRS  $\geq 3$ ) in approximately 97% of cases.

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.<sup>[28,34]</sup> In many studies, and consistent with our own results, initial impaired consciousness has been shown to be a strong risk factor for poor outcome after cerebellar hemorrhage.<sup>[8,11,12,14,17,19,20,28]</sup> It should be noted that there is conflicting evidence in this regard, with Tsitsopoulos *et al.*<sup>[34]</sup> demonstrating no significant effect of impaired consciousness before surgery on 6-month or long-term outcome. In contrast, St. Louis *et al.*<sup>[31]</sup> found that a GCS score of <8 and radiological evidence of acute hydrocephalus or IVH are the most significant predictors of early mortality.

Hydrocephalus is a clinical emergency in patients with SCH and its early diagnosis and rapid treatment have a positive impact on outcome; the developing of hydrocephalus has also been described in many studies as a significant risk factor of unfavourable outcome.<sup>[10,25,30]</sup> Hydrocephalus occurs owing to the mass effect of the hematoma with subsequent narrowing of the fourth ventricle or the aqueduct, or secondary to IVH.<sup>[13]</sup> However, the size of the hematoma and the degree of narrowing of the fourth ventricle are not necessarily correlated.<sup>[32]</sup> Hematoma location seems to have a stronger role and midline (vermian) hematomas are more likely to cause hydrocephalus than lobar ones.<sup>[22,35]</sup> The presence of hydrocephalus on the initial CT scan was not a significant risk factor for mortality or poor outcome in our work; however, this may be due to the low threshold for early EVD placement in our institution following a clinical or radiological diagnosis of hydrocephalus.

There is agreement that surgical evacuation of a cerebellar hemorrhage is indicated in unconscious

patients or following deterioration of consciousness.<sup>[4,38]</sup> In our study, the 30-day mortality was higher in patients treated surgically with hematoma evacuation and EVD placement compared with patients treated conservatively (41.45% versus 35.1%) but this was statistically not significant. However, patients who are treated surgically have ostensibly less favourable clinical and radiological findings, which may explain their high mortality and morbidity.<sup>[10]</sup>

We found no statistically significant correlation between advanced age and unfavourable outcome within the short-term follow-up period in this study. Some studies have found advanced age to be a strong predictor of an unfavourable outcome,<sup>[34]</sup> whilst others have not.<sup>[8]</sup> In this regard, we must draw attention to the short-term nature of our follow-up and the advanced age of our cohort (mean age 72 years).

Although not reflected in the results of our multivariate analysis, several studies have found particular radiological risk factors to be predictive of poor outcome, including large hemorrhage size,<sup>[7,10,17,20,22,23,25,39]</sup> midline location of hemorrhage<sup>[30]</sup> and the presence of IVH.<sup>[19,23,31,36]</sup>

With regard to the timing of surgical intervention, there was no discernible, statistically significant effect on morbidity or mortality afforded by surgery within 6 h in comparison to surgery performed within 72 h.

The principal limitation of our study is its non-randomized and retrospective nature. We also cannot rule out unmeasured confounding from comorbidities and the fact that decision-making may not always have corresponded to standardized institutional protocols.

Several studies have investigated patient outcomes after spontaneous cerebellar and our findings align with a number of reports about predictors of short-term outcome following hemorrhage. Further, our study suggests that the strategy of evacuating hemorrhages >3 cm in diameter, with a low threshold for EVD placement in the context by clinically or radiologically diagnosed hydrocephalus, is a valid approach, which may help to reduce the size of hemorrhage and the degree of hydrocephalus and fourth ventricle compression. Addressing these factors leaves initial GCS score alone as a significant risk factor for poor outcome. In addition, we clearly show that those patients with an initial GCS score of <10 represent a particularly high-risk group.

## CONCLUSION

The initial GCS score on admission is a significant predictor of short-term outcome and 30-day mortality in patients with SCH. For patients with a GCS score <10 on admission, it is important to weight the benefit of survival against the high risk of significant functional disability and poor quality of life that may be achieved

by intensified or extended therapy. The findings in our study may help physicians to recognize patient-specific predictive factors for poor outcome and identify those patients who are likely to suffer early mortality after SCH regardless of medical intervention. Such early prognostication has significant consequences for medical decision-making, the counselling of family members and, by avoiding futile treatment, resource utilisation.

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### Conflicts of interest

There are no conflicts of interest.

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