Association of surgical treatment with functional outcome in patients with spontaneous cerebellar hemorrhage

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Summary

Objective: To investigate the relation of surgical treatment with patient's 180-day outcome. *Subject and method*: Thirty-six patients who suffered a first spontaneous cerebellar hemorrhage (SCH) were treated with operation from January 2017 to March 2022. This study aimed to identify potential clinical and computed tomography (CT) features influencing outcomes after 6 months from ictus, and the association of surgical treatment with SCH patients. *Result*: The mean age was 62.9 years (IQR 43–83 years). Hypertension was the most common underlying disease (31 patients, 86.1%), followed by smoking (15 patients, 41.7%). 63.9% (23/36) of patients showed loss of consciousness at the initial presentation. Among 36 patients, 25 patients (70%) underwent surgical hemorrhage evacuation with the placement of an external ventricle drainage (EVD), 4 patients (10.4%) received an EVD only. The six-moth mortality rate was 33.33%, 12 patients (33.34%) had good outcome (modified Rankin Scale - mRS < 3). In multivariate analysis only the Glasgow coma scale (GCS) score and intracerebral hemorrhage (ICH) score on admission was significant predictor of six-month outcome ([odds ratio (OR) = 1.50, 95% confidence interval (CI): 1.08-2.08, p=0.01; OR = 0.32, CI: 0.10–1.05, p=0.03), respectively. *Conclusion:* Surgical treatment can be effective for selected patients without lower GSC scores on admission. However, a higher ICH score on admission was associated with a 180-day outcome in patients with SCH.

Keywords: Cerebellar hemorrhage, hypertension, external ventricular drainage.

1. Background

Spontaneous cerebellar hemorrhage (SCH) represents about 5 to 10% of all spontaneous intracerebral hemorrhage (ICH) [1], most commonly due to hypertension [2]. The reported mortality rate within 6 months can reach 50%, and approximately 60% of surviving patients had moderate or severe disability [3]. The treatment strategies for patients with SCH are based on the hematoma size and the absence or presence of hydrocephalus [4]. The severe SCH (diameter > 3cm) with obstructive hydrocephalus is the evidence for surgery as soon as possible [4]. Most neurosurgeons have strongly recommended clot evacuation (CE) for SCH treatment [2], [5], [6], as EVD alone was found to be ineffective in some cases [5], [7]. However, in some cases, such as elderly patients, most of whom have previous comorbidities are not suitable for CE. Several studies have shown that the presence of a single general risk factor such as hyperglycemia, low platelet count, a lower Glasgow Coma Scale (GCS) at admission, or a large hematoma volume on computed tomography (CT) might affect the survival outcome [8]. In this study, we retrospectively analyzed a consecutive series of patients with severe SCH treated with CE with or

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without EVD. In addition, we investigated the treatment's safety and outcome, including complications, results, and death rate and evaluated the factors influencing a patient's 180-day outcome.

2. Subject and method

Subject

From January 2017 to March 2022, a sample of patients with the first-time spontaneous cerebellar hemorrhage was consecutively admitted to our Stroke Department.

The primary inclusion criteria of these patients were as follows: (1) age ≥ 18 years; (2) cerebellar hemorrhage was confirmed by CT scans; (3) the hematoma was > 3cm in diameter. Patients with hematoma from trauma, tumors, cavernomas, vascular malformations, aneurysms, and hemorrhage transformation of cerebellar infarctions were excluded from this study. The institutional ethics committee approved our research protocol.

Intervention

Patients were diagnosed according to the guidelines for the primary prevention of stroke [3]. All patients were treated according to the standard recommendations in the guidelines of the American Heart Association/ American Stroke Association (AHA/ASA) [9]. Unconscious patients and patients with a decreased consciousness level and hemorrhage diameter > 3cm were treated by evacuation of the bleeding through suboccipital craniectomy. In cases of hemorrhage diameter < 3 cm but intraventricular hemorrhage (IVH) resulting in obstructive hydrocephalus, external ventricular drainage (EVD) was performed. Comatose patients with absent brainstem reflexes on admission received conservative therapy and/ or palliative care because of the likelihood of very poor outcomes.

ICH volumes were calculated using the ABC/2 formula, where A and B are the perpendicular maximal diameters of the lesion and C is the total length in the vertical plane, using CTs obtained just before operation [10]

The ICH score includes the following items: Glasgow Coma Scale score, age, infratentorial origin of ICH, cerebellar hemorrhage (CH) volume, and presence of IVH. The ICH Score was the sum of individual points assigned as follows: GCS score 3 to 4 (=2 points), 5 to 12 (=1), 13 to 15 (=0); age > =80 years yes (=1), no (=0); infratentorial origin yes (=1), no (=0); CH volume > =30 cm^3 (=1), < 30 cm^3 (=0); and intraventricular hemorrhage yes (=1), no (=0). The maximal score is 5 and the lowest score is 0.

The fourth ventricle appearance was divided into 3 grades, according to Kirollos et al. study, as following: Grade 1, the 4^{th} ventricle is in normal size and configuration, and located in the midline (if intraventricular hemorrhage is present, the cerebrospinal fluid is visible in the 4^{th} ventricle); Grade 2, the 4^{th} ventricle was partially compressed, distorted or shifting to the contralateral side (in cases of unilateral hematomas); Grade 3, the 4^{th} ventricle is completely obliteration with shift distorting the brainstem anteriorly and obliteration of the prepontine space (even if partial compression of the 4^{th} ventricle) [5].

Outcome evaluation

The primary outcome was the 6-month mortality rate. The secondary outcome was the long-term neurological functional status, evaluated by the modified Rankin Scale (mRS) score at 6 months. A poor outcome was defined as death or the dependency on daily living provided by others (mRS 4-6). Adverse events were also recorded, including reoperation, rebleeding, hydrocephalus, intracranial infection, and pulmonary infection.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation. Categorical variables such as gender, hematoma size, acute hydrocephalus, comorbidities, frequency of complication, death, mRS and causes of death were analyzed using Pearson's Chi-square test. All recorded data were statistically analyzed using the SPSS 20.0 software (SPSS Inc). First, univariate logistic regression was used to assess the strength of the association between the collected variables and the 180-day outcome, using the favourable 180-day outcome as a dependent variable. Independent variables included age, gender, GSC score, the location of hemorrhage a, presence of IVH, presence of hydrocephalus on CT scanner, compression of the 4th ventricle and ICH score. Next step, multivariate analysis was performed, using the 180-day outcome as a dependent variable, and incorporating independent variables showing significance or a trend towards significance in the univariate analysis. Finally, to assess the goodness of fit of the multivariate model, we used a Hosmer-Lemeshow test. Results are reported as odds ratios (OR) together with 95% confidence intervals (CI). p value<0.05 was considered to be statistically significant.

3. Result

3.1. Baseline characteristics

36 SCH patients were treated with CE with/ without EVD between January 2017 to March 2022. The baseline characteristics and clinical features are shown in Table 1.

Table 1. Baseline characteristics

Gender	Female	13
	Male	23
Age	62.9 years (IQR43-83)	
Clinical history		
Post stroke, n (%)	5 (13.9%)	
Hypertension, n (%)	31 (86.1%)	
Diabetes mellitus, n (%)	9 (25%)	
Smoking, n (%)	15 (41.7%)	
Heart valve disease, n (%)	1 (2.8%)	
Atrial fibrillation, n (%)	2 (5.6%)	
Chronic kidney disease, n (%)	3 (8.3%)	
Antiplatelet therapy, n (%)	2 (5.6%)	
Signs and symptoms at onset		
Headache	27 (75%)	
Nausea, vomiting	35 (86.1%)	
Loss of consciousness	23 (63.9%)	
Limb weakness	8 (22.2%)	
Initial systolic blood pressure (mmHg), median (IQR)	164 (IQR 110-220)	
Initial diastolic blood pressure (mmHg), median (IQR)	95 (IQR 70-124)	
Initial heart rate, median (IQR)	90 (IQR 70-125)	
Body temperature, median (IQR)	37 (36-37.5)	
GCS score at admission	9.72 ± 3.0	
≤ 8	13	36.1%
9-12	12	33.3%
> 12	11	30.6%
GCS before operation	8.7 ± 2.0	
≤ 8	14	38.9%
9-12	22	61.1%
> 12	0	0%

GCS Glasgow coma score, IQR interquartile range.

A total of 36 patients were identified (23 males, 63.9%). The mean age was 62.9 years (IQR 43–83 years). Hypertension was the most common underlying disease (31 patients, 86.1%), followed by smoking (15 patients, 41.7%). The mean initial heart rate on arrival at the hospital was 90bpm (IQR 70-125bpm), and the median systolic arterial blood pressure on arrival was 164mmHg (IQR 142-195mmHg). 63.9% (23/36) of patients showed loss of consciousness at the initial presentation. Otherwise, signs of increased intracranial pressure (e.g., nausea or vomiting) were presented in most patients.

3.2. Neuro-imaging

Neuroradiological characteristics and neuro-surgical treatment at presentation were listed in Table 2.

Table 2. Radiological characteristics at presentation and neuro-surgical treatments

Parameter	Spontaneous cerebellar hemorrhage (n = 36)	Percentage %
Brain images findings at presentation		
Hematoma maximum dimensions (mm), median (IQR)	44.7 (20-65)	
Hematoma volume (ml), median (IQR)	29.5 (15.2-97.5)	
Hematoma location		
Right hemisphere	16	44.4
Left hemisphere	6	16.7
Vermis	9	25
Involves more than two locations	5	13.9
Intraventricular hemorrhage	26	72.7
Intraventricular hemorrhage grades		
Grade I	13	36.1
Grade II	11	30.6
Grade III	12	33.3
Hydrocephalus	20	55.6
Obliteration of basal cistern	19	52.8
Compression of the 4th ventricle	8	22.2
ICH score (Median)	3 (2-4)	
Time from onset to neuro-surgery (hours), mean (SD)	34.5 ± 37.0	
Neuro-surgical treatments		
EVD only	4	10.4
Suboccipital decompressive craniectomy	7	19.6
Suboccipital decompressive craniectomy + EVD	25	70

EVD: external ventricular drainage

The median maximum hematoma dimension was 44.7mm (IQR: 20-65mm), and the median volume of 30.9ml (IQR: 20-65ml). Hydrocephalus in the initial image was presented in 20 patients (55.6%). The appearance of 4th ventricle compression was grade I in 13 (36.1%), grade II in 11 (30.6%), and grade III in 13 (33.3%) patients. Nineteen patients (54.2%) were found to be obliteration in the basal cistern.

Concerning the neurosurgical treatment, 25 patients (70%) received both suboccipital decompressive craniectomy and EVD, four patients (10.4%) with EVD only, and 7 patients (19.6%) with suboccipital craniectomy. None of the patients underwent re-operative craniectomy. The mean time between symptom onset to surgery was 34.5 ± 37.0 (hours).

180-day outcomes

Table 3. Clinical outcome at discharge and six-month follow-up

Time / Outcomes	Discharge	Percentage %	180 days follow-up	Percentage %
mRS (0-2)	5	13.89	12	33.33
mRS (3-6)	31	86.11	12	33.34
Mortality	6	16.7	12	33.33

Three patients who experienced rebleeding and severe edema died shortly after an emergency procedure at discharge. The mortality rate was 16.7% (six patients) at discharge. Among survivors, 5 patients (13.89%) achieved good neurological function (mRS < 3). An unfavourable outcome (mRS ≥ 3) was documented in 12 patients (33.33%) at the end of 180-day follow-up. Six patients (16.7%) required ventriculoperitoneal shunt (VPS) placement due to hydrocephalus.

3.3. Logistic regression

Table 4. Logistic regression analysis with favourable 180-day outcome as the dependent variable

	Univariate		Multivariate *	
	OR (95% CI)	p	OR (95% CI)	p
Age (year)	0.95 (0.88-1.04)	0.18		
Gender (male)	1.20 (0.28-5.15)	0.806		
GCS on admission (point)	1.53 (1.13-2.08)	0.007	1.50 (1.08-2.08)	0.01
Hypertension	0.71 (0.10-4.98)	0.734		
Imaging features				
Location of hemorrhage	1.10 (0.52-2.35)	0.80		
Diameter (per 1ml increase)	0.44 (0.20-0.96)	0.04	0.46 (0.18-1.08)	0.07
Presence of IVH	0.67 (0.15-3.03)	0.60		
Presence of hydrocephalus on CT scanner	0.46 (0.56-3.70)	0.46		
Compression of the 4th ventricle	1.15 (0.30-4.47)	0.84		
ICH score	0.31 (0.11-0.91)	0.03	0.32 (0.10-1.05)	0.03

IVH: Intraventricular hemorrhage, CT: Computed tomography, OR: Odds ratio.

*Data of 36 patients were included in this analysis.

The univariate analysis showed GCS score at admission and maximal diameter of the bleeding on initial head CT scan to be significant predictors of outcome at six-month follow-up (Table 4). On the other hand, IVH and hydrocephalus on the initial CT scanner were not significantly associated with the result. In the next step, we estimated a multivariate logistic regression analysis using these variables, with the six-month follow-up outcome as the dependent variable. The initial GCS score and ICH score of patients with SCH (OR = 1.50, 95% CI: 1.08-2.08, p=0.01; OR = 0.32, 95% CI: 0.10-1.05, p=0.03, respectively) were the significant predictors of six-month outcome (Table 4).

For the opponent of the reviewer about the results of the Table 4:

Look at OR can be interpreted that if initial GCS increase 1 point, favourable 180-day outcome will increase 1.50 time. The result shall be similar to ICH score. Maybe we have to calculate the ROC to find out the best cut-off of GCS o admission.

4. Discussion

4.1. Etiology of bleeding and initial clinical findings

The clinical presentation of cerebellar hemorrhage can range from symptoms mimicking ischemic stroke to catastrophic neurologic decline. The presence of symptoms largely depends on the size of the hematoma and the degree of perilesional edema. This study showed that the most common symptoms of SCH were nausea, and vomiting (86.1%), followed by headache (75%). In our study, 23 patients (63.9%) lost consciousness at the onset and 13 of them presented with GCS ≤ 8 and were immediately operated. The hematoma size in patients ranged from 20 to 65mm (median 47mm). 12 patients scored 8-12 on GCS. At admission, the median diastolic and diastolic blood pressure were 164 (IQR 110-220) and 95 (IQR 70-124), respectively, which was similar to the reported study [3].

The surgical evacuation was recently recommended in patients with the cerebellar hemorrhage who have unconsciousness or following the deterioration of consciousness [4], [9]. Treatment of patients with initially poor neurological condition is controversial due to the limited prospect for recovery and mainly poor outcome. So, we did not enroll the SCH patients with deep coma, lost brain stem reflexes or tetraplegia, deep coma and hematoma size > 5.0cm. Suboccipital craniectomy has been the main surgical intervention used for SCH until now and EVD is the treatment of an option for obstructive hydrocephalus in the setting of an IVH [5]. In our study, 25 patients (70%) received suboccipital decompressive craniectomy + EVD, and seven (19.6%) received suboccipital decompressive craniectomy. In addition, EVD was indicated for four patients (10.4%). Regarding the complications after the operation, meningitis was observed in 2 patients (5.6%). Pneumonia was noted in 10 patients (27.8%) and bacteremia in 2 patient (5.6%). Two patients had gastric bleeding after the operation 2 days. At the discharge, 3 patients died. Our follow-up revealed that the mortality rate was 33.33% (12/36), which was within the reported range of mortality rates between 20 and 50% in the literature [10]. In our study, the mean time of symptoms onset to operation was 34.5 ± 37.0 hours.

4.2. Factors with impact on clinical outcome

As reported in the previous study, high age was considered to be the most vital prognostic factor for an unfavorable outcome [2]. Surprisingly, in our series, some variables were not predictive of clinical outcome: Age and gender of the patients, hypertension, hematoma size on initial CT scan, acute hydrocephalus, and the presence of IVH (Table 4).

Hypertension is strongly associated with the occurrence of cerebellar hemorrhage, with the prevalence of between 36% and 89% [12], [13]. Our result showed that hypertension was the most common underlying disease (31 patients, 86.1%), followed by smoking (15 patients, 41.7%). However, our analyses showed no significant association between six-month outcome and the presence of hypertension.

The deterioration of consciousness state seen in cerebellar hemorrhage can be attributed to the development of hydrocephalus, resulting in intracranial hypertension and direct brain stem compression [14], [11]. Hydrocephalus is a clinical emergency in patients with SCH, and its early diagnosis and rapid treatment positively impact the outcome. In our study, 20 patients (55.6%) have hydrocephalus in the head CT imaging. Hydrocephalus can result from the mass effect of the hematoma with subsequent narrowing of the fourth ventricle or the aqueduct or secondary to IVH. St. Louis et al. followed 72 SCH patients and showed that hydrocephalus is the radiologic feature for predicting neurologic deterioration in patients with

SCH [15]. The presence of hydrocephalus on the initial CT scan was not a significant risk factor for mortality or poor outcome in our work (p=0.46); however this may be due to the early EVD placement in our institution following a clinical or radiological diagnosis of hydrocephalus. Al Safatli et al also demonstrated the same result [3].

Many studies showed the impaired consciousness in SCH patients can be largely attributed to the development of hydrocephalus and/or direct brain stem compression [3], [16]. Accumulating evidence has demonstrated that a low preoperative GCS score is strong risk factor for poor prognosis SCH after SCH. We found statistically significant correlation between preoperative GCS and the outcome within 180-day follow-up in this study (Table 4). Al Safatli et al. reported that initial neurological status according to GCS score is the only significant predictors of 30-day mortality after SCH [3]. Wu et al demonstrated that a preoperative GCS score ≤ 8 was strong predictor of mortality, reporting that SCH patients with GCS scores ≤ 8 were approximately 32 times more likely to die within the initial seven days [17].

ICH score was first introduced by Hemphill et al. in 2001 and was a simple and reliable scale for predicting 30-day mortality in patients with spontaneous intracerebral hemorrhage. The ICH score includes the following items: Glasgow Scale score, age, the infratentorial origin of ICH, cerebellar hemorrhage volume, and IVH. The maximal score is five, and the lowest point is 0. Therefore, the ICH score is more reliable than each of the above single factors. Several studies described the role of ICH score in predicting the outcome in patients with spontaneous ICH [18]. In our study, we found that ICH score to be the predictive for clinical outcome.

The limitation of our study is its non-randomized and retrospective nature. In addition, the decision-making may sometimes have corresponded to standardized institutional protocols. Multicenter randomized controlled trials are needed to confirm the effectiveness of different surgical techniques.

5. Conclusion

Decompressive craniectomy is still the most effective treatment for patients with severe spontaneous cerebellar hemorrhage. EVD may be another treatment option. The initial GCS score on admission and ICH score are significant predictors of 180-day outcome and mortality in patients with spontaneous cerebellar hemorrhage. Our study's findings may help physicians recognize patient-specific predictive factors for poor outcomes and identify patients likely to suffer mortality after spontaneous cerebellar hemorrhage, regardless of medical intervention.

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