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14-Day Mortality Predictive Factors in Surgically Treated Supratentorial Spontaneous Intracerebral Hemorrhage: A Retrospective Analysis Of 44 Patients

I Wayan Niryana*, Steven Awyono, Sri Maliawan, Nyoman Golden, Tjokorda Gde Bagus Mahadewa, Made Gemma Daniswara Maliawan, Kevin Kristian Putra, and Maria Monica

Neurosurgery Division, Surgery Department, Faculty of Medicine
Udayana University, Prof. Dr. IGNG General Hospital, Bali, Indonesia

*Corresponding author details: niryanawayan@gmail.com; I Wayan Niryana

ABSTRACT

Background: Spontaneous intracerebral hemorrhage accounts for 10-15% of cerebrovascular events. Various modalities of patient management, both conservatively and surgical. Despite its deadly nature and extensive studies, there is no standard model for predictive factors in intracerebral hemorrhage-related mortality. ***Methods***: A retrospective cohort analysis on patients with supratentorial spontaneous intracerebral hemorrhage who received surgical treatment for clot evacuation. Factors including age, sex, initial Glasgow Coma Scale score, the volume of the clot, existing intraventricular hemorrhage, existing subarachnoid hemorrhage, signs of cerebral herniation from head CT-Scan, duration of the surgery, and surgical technique were analyzed. ***Results:*** Data for 44 patients were included in this study. The mean age was 54.68 ±12.79 years old, with 64.6% of the sample being males. The mean GCS score of the sample is 9.3 ± 3.15. Subarachnoid hemorrhage was noticed in 34.1% of cases. Intraventricular hemorrhage extension was found in 27.3% of cases. Cerebral herniation on CT-scan was noticed in 50% of cases. Based on surgical characteristics, the mean surgical time is 194.84 ± 54.84 mins. Almost two-thirds of the cases performed craniectomy procedure 28 (63.6%). We found that subarachnoid hemorrhage (OR 5.77 [1.12 – 29.7]; p = 0.036) and cerebral herniation (OR 8.26 [1.91- 35.7]; p = 0.005) were considered as significant factors in predicting 14-day mortality after multivariate analysis. ***Conclusions***: Subarachnoid hemorrhage and cerebral herniation are good predictors of 14-day mortality in patients with sICH who are surgically treated. Earlier and shorter duration of the surgery showed no correlation to the outcome.

Keywords: intracerebral hemorrhage; stroke; 14-day mortality factors; craniotomy; craniectomy

INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) accounts for 10-15% of cerebrovascular events, with an incidence rate of 25 per 100,000 individuals annually.[1], [2] Despite rare occurrences compared to ischemic stroke, sICH remains the most deadly, disabling, and least treatable form of stroke.[3] It is more frequently linked with worse outcomes and long-term morbidity.[1]–[4] In fact, 25-50% of patients with sICH died within the first month.[2], [5] Thus, sICH has been declared the world's third most common cause of death.[6]

Various modalities of patient management, both conservatively and surgical, have been studied and continue to be developed to increase patient safety with intracerebral hemorrhage.[7] Surgery in sICH is aimed at removing clots while relieving tissue injury, decreasing local ischemia, and lowering intracranial pressure.[8] Although a profound understanding of the pathophysiology has been widely studied, sICH management, including indications for surgery, is still highly debated. The decision regarding the surgery varies for each individual.[7], [8] Surgery is especially lifesaving for patients with large sICH volume and rapid neurological deficit progression.[9]

Knowledge of predicting factors for sICH mortality is crucial to determine appropriate strategies and improving patient outcomes. Several studies have established models to forecast outcomes after sICH surgical evacuation. The ICH score is the most widely used predictor of 30-day mortality after intracerebral hemorrhage onset, which consists of intraventricular hemorrhage (IVH) presentation.[5] Other studies found female sex, a decrease of consciousness, multiple locations, infratentorial hemorrhage, hyperglycemia, and vascular malformation that lead to sICH as factors predicting early mortality of sICH in young adults.[1] Despite extensive studies regarding these factors, no available standard model can be used due to the weakness of the evidence obtained.[3] This study aimed to identify variables related to mortality in sICH patients undergoing surgery. We retrospectively examined a cohort of variables thought to affect mortality in spontaneous ICH patients undergoing surgery.

METHODS

Study population and design

We conducted a retrospective cohort analysis on patients with supratentorial sICH who received surgical treatment for clot evacuation at Prof. Dr. I.G.N.G. Ngoerah General Hospital from January 1, 2020, to December 31, 2021.

This hospital is a referral center in Bali, Indonesia. sICH was diagnosed with an acute neurological deficit with additional head Computed Tomography (CT) scan imaging indicating ICH without any history of trauma or surgery. The research protocol and informed consent in this study were approved by the Research Ethics Committee, Faculty of Medicine, Udayana University (529/UN14.2.2.VII.14/LT/2022). All data and information of patients were used for research only and followed the principle of privacy. The consent to participants was waived due to the retrospective design.

The following data were collected in a computerized database: age, sex, initial Glasgow Coma Scale (GCS) score, the volume of the clot, existing intraventricular hemorrhage, existing subarachnoid hemorrhage, signs of cerebral herniation from head CT-Scan, duration of the surgery, surgical technique, and mortality were investigated using medical records.

Patients meeting these criteria were included: 1) diagnosed with spontaneous supratentorial intracerebral hemorrhage according to history taking and head CT-Scan; 2) age of 17 years or older and underwent surgery to evacuate the blood clot. Subjects meeting any of the following were excluded: 1) having two or more surgeries related to an intracerebral hemorrhage, 2) being treated surgically with endoscopy, or treated surgically in another hospital then were referred to Prof. Dr. I.G.N.G. Ngoerah General Hospital for further treatment.

Some data were considered to discover factors that may lead to mortality in a spontaneous intracerebral hemorrhage. We considered age as one of the factors, being less than or more than 65 years old. GCS scores on admission were also evaluated, with a total of 3-6 or 7-15. Clot's volume of more than 50 cc, existing intraventricular hemorrhage, subarachnoid hemorrhage, and signs of cerebral herniation from preoperative head CT-Scan was also investigated.

We considered early surgery to be performed 24 hours from the onset and late undergoing surgery after 24 hours from the onset. We also classified the duration of surgery, being less than or more than 3 hours, as a predictive factor. Surgical techniques were classified by craniotomy or craniectomy, and it is not randomized performed.

Statistical Analysis

All statistical analyses were done using SPSS 24.0. Continuous variables are mentioned as mean with standard deviation (SD) or median with 25th and 75th percentiles, according to distribution manner. Using backward binary logistics, bivariate analysis for categorical variables was analyzed by Chi-Square to determine variables for multivariate analysis of 14-day mortality. *P* value ≤0.05 indicated statistical significance.

RESULTS

Between January 1st, 2020, and December 31st, 2021, 48 patients were surgically treated for supratentorial spontaneous ICH. After we performed the comprehensive patient selection, four patients did not meet the patient selection criteria, making the total sample 44 patients **(Figure 1)**.

A summary of patient characteristics is shown in **Table 1**. In this study group, the mean age was 54.68 ±12.79 years old, and 28 (64.6%) of the sample were males. More than two-thirds of the sample (79.6%) were under 50. The mean GCS score of the sample is 9.3 ± 3.15, with more than half of the sample having a GCS of 9-15. The mean volume of the clot was 63.73 ± 26.1 ml. Subarachnoid hemorrhage was noticed in 15 (34.1%) cases.

Intraventricular hemorrhage extension was found in 12 (27.3%) cases and most markedly on the lateral ventricle. Cerebral herniation on CT-scan was noticed in 22 (50%) cases. Based on surgical characteristics, the mean surgical time is 194.84 ± 54.84 min. Almost two-thirds of the cases performed craniectomy procedure 28 (63.6%).

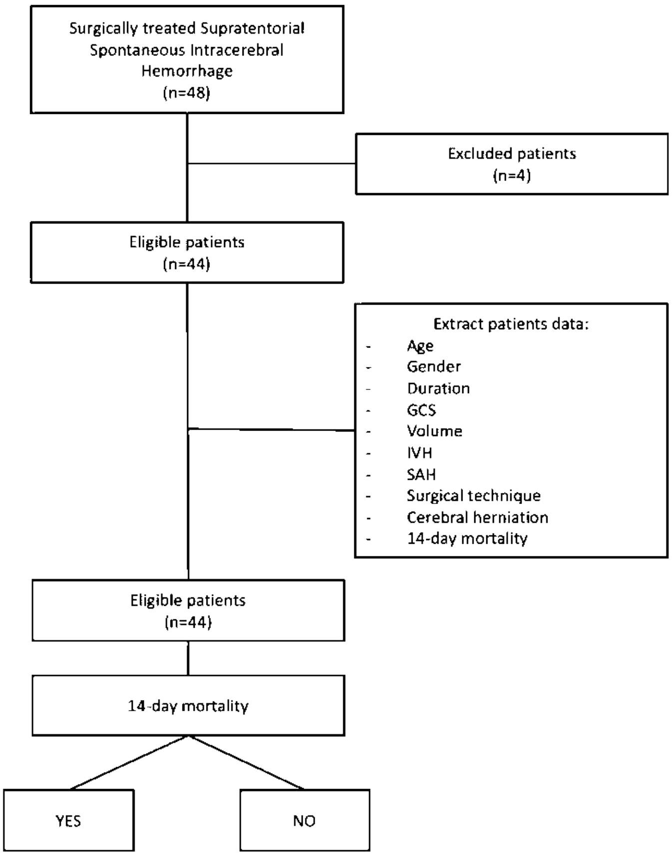

FIGURE 1: Patient flow diagram.

Multivariate Analysis Model to Predict 14-Day Mortality

The summary results of several analyses between outcome and 14-day mortality are displayed in Table 2. Bivariate analysis was conducted to identify potential influential factors that may impact the outcome. Based on the bivariate analysis, we excluded two variables for further analysis: age group and intraventricular hemorrhage; the rest were included as possible significant factors.

Backward binary logistics was then performed for those possible significant factors to conclude the most significant factors. Subarachnoid hemorrhage (OR 5.77 [1.12 – 29.7]; *p* = 0.036) and cerebral herniation (OR 8.26 [1.91- 35.7]; *p* = 0.005) were significant factors in predicting 14-day mortality.

TABLE 1: Patient's Characteristics.

		Frequency	Percentage (%)
Age	<65	35	79.5
	>65	9	20.5
Gender	Male	28	63.6
	Female	16	36.4
Duration	<180 mins	20	45.5
	≥180 mins	24	54.5
GCS	3-8	16	36.4
	9-15	28	63.6
Volume (ml)	<50	15	34.1
	≥50	29	65.9
IVH	Yes	12	27.3
	No	22	72.7
SAH	Yes	15	34.1
	No	29	65.9
Surgical Technique	Craniotomy	16	36.4
	Craniectomy	28	63.6
Cerebral Herniation	Yes	22	50
	No	22	50
14-day Mortality	Yes	23	52.3
	No	21	47.7

Abbreviations: GCS Glasgow Coma Scale; IVH Intraventricular hemorrhage; SAH Subarachnoid hemorrhage.

P value ≤0.05 indicated statistical significance. Subarachnoid hemorrhage and cerebral herniation were considered statistically significant predictors of 14-day mortality in surgically treated patients with sICH.

TABLE 2: Multivariate analysis of predictive factors for 14-day mortality.

		14-Day Mortality		*p-value*	OR
		Yes (n)	No (n)		
Age	<65	18 (51.4%)	17 (48.6%)	0.825	
	>65	5 (55.6%)	4 (44.4%)		
Duration	<180 mins	8 (40%)	12 (60%)	0.137	
	≥180 mins	15 (62.5%)	9 (37.5		
GCS	3-8	10 (62.5%)	6 (37.5%)	0.305	
	9-15	13 (46.4%)	15 (53.6%)		
Volume	<50	6 (40%)	9 (60%)	0.241	
	≥50	17 (58.6%)	12 (41.4%)		
IVH	Yes	7 (58.3%)	5 (41.7)	0.622	
	No	16 (50%)	16 (50%)		
SAH	Yes	12 (80%)	3 (20%)	**0.036**	**5.77**
	No	11 (37.9%)	18 (62.1)		
Surgical Technique	Craniotomy	10 (62.5%)	6 (37.5%)	0.305	
	Craniectomy	13 (46.4%)	15 (53.6%)		
Cerebral Herniation	Yes	17 (77.3%)	5 (22.7%)	**0.0005**	**8.26**
	No	6 (27.3%)	16 (72.7%)		

Abbreviations: GCS Glasgow Coma Scale; IVH Intraventricular hemorrhage; OR Odds ratio; SAH Subarachnoid hemorrhage.

DISCUSSION

Spontaneous ICH provides a very large burden for health workers and also the government. Although several managements, either medical or surgical, have been well developed, the incidence of sICH remains very high in populations.

In our study, the prevalence of spontaneous ICH is male predominance (63.6%), with a mean age of 54.68 ± 12.79. This finding is similar to several previous studies. Yacouba and colleagues, with their three-year prospective study, found that the mean age is 58.66 ± 13.6 and male predominance (68.1%).[10] Another study found mean age is 55.6 ± 11.8, with a slight tendency in the group aged> 55 years (50.6). They also found a male gender tendency (64%) with a mean age of 54.6 ± 11.4.[11]

The decision to perform surgery is based on lesion's volume, brain swelling, midline shifting, ability to control bleeding, and neurological status. Some publications advised minimally invasive surgery for a lesion less than 80 ml. Regarding volume, some authors recommended minimally invasive surgery (MIS) in volumes less than 80 ml. However, patients with poor neurological status and raised ICP are more suitable for a conventional craniectomy regardless of the volume.[12]

A superior outcome was discovered in superficial hemorrhage and surgical group patients in the STITCH (Surgical Trial in Intracerebral Hematoma) study that contained 83 centers and 1033 patients (OR, 0.69; 95% CI, 0.47-1.01). Meanwhile, in STITCH II, surgery was not superior to conservative treatment for lobar sICH with a GCS Score of 9-15 and a volume between 10-100 cc. Furthermore, a subgroup analysis showed better outcomes with a GCS score of 8012, age over 65 years, and hemorrhage volume over 35 cc. This corresponds with multiple studies such as randomized clinical trial (RCT) in China by Morioka et al. and an RCT by Bhaskar et al.[12], [13]

Luzzi et al. found that ICH surgery had the best outcome in patients with lobar hemorrhage with volume over 30 cc and a GCS score of 9-15. In patients with hemorrhage volumes under 15 cc and no indications of neurological deterioration, conservative treatment should be taken into account.[13] However, any substantial cerebellar hemorrhage must be removed as quickly as possible, considering how close the hemorrhage is to the critical anatomical structure, brainstem, and fourth ventricle.[14]

MIS for sICH can be carried out already and has shown good results. Miller et al. found that endoscopic evacuation had a better outcome for patients with a GCS score of more than 5 with a clot volume of more than 15 cc. Prasad et al. also showed better results for MIS using endoscopic or stereotactic than conventional craniotomy. Li et al. performed a comparison study of MIS and craniotomy lobar supratentorial sICH with more than 60 cc volume and poor GCS score (4-8).[13]

Jang et al. performed a study on 70 patients. They found that patients treated with MIS tended to have lower volume compared to the craniotomy group, with lower evacuated lesions in the MIS group. Nevertheless, the Minimally Invasive Surgery and rTPA in ICH evacuation (MISTIE) II trial found that MIS was superior to the craniotomy group based on intraoperative blood loss, intensive care unit hospitalization, overall hospital stay, surgical duration, mortality, and infections.[12]

Intrahemorrhage urokinase administration following clot evacuation using the stereotactic technique was discovered to be more effective for deep-seated hemorrhage with a volume of 30-60 cc and a GCS score of 9-14. Akhigbe et al. found that stereotactic evacuation reduced the mortality rate in supratentorial hemorrhage with a volume of 45 cc (OR, 0.74; 95% CI, 0.61- 0.0; p=0.003).[13]

Yao et al. found that decompressive craniectomy must be performed in comatose patients, with shifting over 5 mm, a volume of 30-60 cc, an intraventricular expansion, and any signs of raised ICP.[13] Hayes et al. found trends of younger age, female sex, larger hemorrhage volume, and worse neurological status in the decompressive craniectomy group compare to the craniotomy group.[15]

Regarding surgical timing, Wang et al. found that early surgery (7-24 hours) had the best outcome, ultra-early surgery (≤7 hours) had the highest rebleeding rate, and delayed surgery had more severe complications. However, different timing should be applied to patients with cerebellar hemorrhage >3 cm, rapidly deteriorating neurological status, brainstem compression, and hydrocephalus.[12], [13]

The gold examination standard for intracerebral hemorrhage is computed tomography due to its short duration and high sensitivity. CT-Scan could evaluate the hemorrhage's location, size, and shape and the presence of hydrocephalus and midline shift. A hyperdense lesion is the classic finding in sICH, indicating an acute state of the hemorrhage. The hemorrhage will start lysis on day 4, indicating the subacute phase, and will appear isodense in a brain CT-Scan, then it becomes hypodense and resembles CSF in the chronic phase.[14]

Elkhatib et al. conducted a study on 136 samples with acute primary ICH. In this study, they found that 58 patients (43%) had an irregular-shaped of hemorrhage, 55 patients had heterogenous density sICH density, and 24 patients had CTA spot signs on their imaging.[16]

Hegde et al. performed a study on 119 patients. Upon the sample populations, mostly the hemorrhages were situated on the basal ganglia region compared to the lobar (84.03% vs. 15.9%) and right side compared to the left side (57.1% vs. 42.8%). Other notable radiological findings include an intraventricular extension in 44 patients and 27 in the surgical and conservative groups, respectively. This study also found hydrocephalus in 29 patients, 14 in the surgical group and the rest in the conservative group.[17]

Øie et al. found that the most often affected location of sICH was the deep structure (45%), followed by lobar (41%), cerebellar (8%), and brainstem (5%). Hemorrhages had an average volume of 33.1 cc. Of this population, 186 patients (41.2%) had an intraventricular hemorrhage, and a pure intraventricular hemorrhage was found in 0.7% of the samples.[2]

A mixed hypodensity and hyperdensity lesions within the hemorrhage on non-contrast CT suggest ongoing bleeding.[16] CT angiography may also help identify vascular malformation and visualize the enhancing foci inside the hemorrhage called "spot sign," indicating contrast extravasation. Spot sign helps determine the risk for hemorrhage expansion.[14], [16] Hemorrhage expansion was primarily seen in patients with a shorter duration between symptom onset and initial CT.[16] Wada et al. did a study of spontaneous ICH on 39 patients, which revealed lesion expansion in 10 out of 13 patients with spot signs.[18]

Another visible sign observed on non-contrast CT is the *swirl sign*, which visualizes a hypodensity lesion within the lesion. This sign denotes persistent blood extravasation within the lesion. Boulouis et al. did a large retrospective cohort analysis of 1,029 patients that revealed about 53% of patients with expanding lesions had this sign, as opposed to 21.9% of patients without lesion expansion ($p<0.001$).[18]

Perilesional edema is seen as early as 1 hour after ICH, peaks at seven days, lasting weeks after injury. The larger the ICH volume, the larger the perilesional edema and the worse the patient outcome.[18]

Accompanying ICH, IVH may also be present, mainly in large ICH ($p<0.001$). IVH could fill the ventricular system, blocking the CSF flow and causing obstructive hydrocephalus. Thus, IVH was found to increase the 2.6-fold risk of early neurological deterioration ($p<0.001$), while hydrocephalus will significantly increase the 90-day mortality rates (OR 1.26, 95% CI 1.13–1.42, $p < 0.0001$).[18]

Magnetic Resonance Imaging (MRI) could also be used to detect a hemorrhage. However, CT-Scan is more suitable in the acute setting due to time, cost, and patient tolerance. The appearance of sICH on MRI changes over time due to the change in the molecular components of the clot. Oxyhemoglobin inside the hemorrhage is catabolized to deoxyhemoglobin, extracellular methemoglobin, and hemosiderin. First, acute ICH will appear hypointense on T1-weighted images and hyperintense on T2-weighted images because of oxyhemoglobin. As oxyhemoglobin undergoes catabolism to deoxyhemoglobin (after 1-3 days), hemorrhage appears hypointense on both the T1 and T2 weighted images. On days 3rd to 7th, the hemorrhage is at the early subacute pre-lysis phase. In this phase, the lesion will appear hyperintense on T1 and hypointense on T2 due to intracellular methemoglobin. Next, ICH will appear bright after weeks on both T1 and T2 due to extracellular methemoglobin (late subacute post-lysis phase). Finally, hemosiderin formation in the chronic phase will occur the same as deoxyhemoglobin on T1 and T2 without concomitant vasogenic edema.[14]

ICH is often accompanied by subarachnoid hemorrhage (SAH), especially in ruptured cerebral aneurysms. These circumstances are linked to a poorer admission grade and unfavorable outcomes without considering the volume of the ICH.[19] Some studies have included SAH to predict mortality and morbidity after an ICH using a new ICH score at their institution. They found that subarachnoid and intraventricular extension of an ICH is related to a worse outcome.[20] Another study also considered SAH as one of the prognostic factors in determining the mortality rate in patients with ICH. However, the result was not significant, especially as an independent predictor for mortality.[21] In our study, we concluded that the presence of SAH in ICH patients was related to determining their 14-day mortality rate.

The dynamic mass effect of the hemorrhage that results in raised intracranial pressure (ICP) is the main factor contributing to brain herniation in ICH patients.[22] Malignant outcome was found in which brain edema leads to a significant mass effect that leads to midline shift. The evidence of existing herniation also determines our treatment for ICH patients.[23] As a separate risk factor, cerebral herniation syndrome is related to a higher risk of in-hospital death. Chen et al. pointed out that sICH patients with brain herniation frequently experienced acute respiratory distress syndrome, necessitating tracheal intubation.[24]

Other studies also mentioned that treating increased ICP is necessary to prevent the potential risk of brain herniation, thus lowering the mortality rate.[25] This is in accordance with our study, which mentioned brain herniation as one of the predictors of the 14-day mortality rate.

Several limitations should be considered in evaluating our study. We do not have any comorbidity data of the patients as it may also contribute to their prognosis. Currently, there is no epidemiological data regarding surgically treated patients with sICH.

CONCLUSIONS

In conclusion, this study found that subarachnoid hemorrhage and cerebral herniation are good predictors of 14-day mortality in patients with sICH who are surgically treated. Earlier and shorter duration of the surgery showed no correlation to the outcome. Further study regarding this issue is required with additional variables such as comorbidity, hemorrhage location, IVH, and SAH grading, as these variables may contribute to mortality in patients with sICH.

LIST OF ABBREVIATIONS

sICH; Spontaneous Intracerebral Hemorrhage
IVH; Intraventricular Hemorrhage
CT-Scan; Computed Tomography Scan
GCS; Glasgow Coma Scale
SD; Standard Deviation
OR; Odds Ratio
MIS; Minimally Invasive Surgery
STITCH; Surgical Trial in Intracerebral Hematoma
MISTIE; Minimally Invasive Surgery and rTPA in ICH evacuation
MRI; Magnetic Resonance Imaging
SAH; Subarachnoid Hemorrhage
ICP; Intracranial Pressure

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