

## Diastolic Blood Pressure as a Predictor of Mortality in Intracerebral Hemorrhage Stroke Patients with Hypertension

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### Abstract

**Background:** Intracerebral hemorrhage (ICH) stroke contributes to a considerable number of deaths, ranging between 30% and 40% of the overall stroke mortality. The incidence of stroke increases with higher blood pressure. High blood pressure at the onset of ICH stroke is a strong predictor for mortality and morbidity. This study aimed to explore the role of diastolic blood pressure as a predictor of death in ICH stroke patients.

**Methods:** Data on 113 ICH stroke patients with chronic hypertension were collected from the medical records of patients treated in the Neurology ward of Dr. Hasan Sadikin General Hospital Bandung, Indonesia, in 2019. Data collected were patient characteristics, hypertension status, systolic and diastolic blood pressures, and patient outcome. Analysis was then performed using the Mann-Whitney test.

**Results:** This study revealed a positive correlation ( $p=0.031$ ) between diastolic blood pressure and death in ICH stroke patients with chronic hypertension.

**Conclusions:** High diastolic blood pressure is associated with mortality in ICH stroke patients with chronic hypertension.

**Keywords:** Diastolic, intracerebral hemorrhage, predictor, stroke, systolic

### Introduction

Stroke is a common cerebrovascular disease in which intracerebral hemorrhage (ICH) constitutes 10% to 15% of all strokes. The global incidence of ICH range is from 10 to 20 cases per 100,000 population.<sup>1-4</sup> Riset Kesehatan Dasar (Riskesdas) 2018 in Indonesia has shown the stroke prevalence is 10.9/mil.<sup>5</sup> Stroke is the leading cause of death in the neurology, and most of the stroke-related death is due to ICH. The mortality rate of ICH stroke is found to be higher in low- and middle-income countries, and the majority of stroke-related deaths that occurred in this area are younger than 60 years old. In hospital-based studies, the 30-day mortality ranges between 30% and 40%.<sup>6</sup>

Chronic hypertension is reported to be a major risk factor for ICH stroke. This chronic

hypertension is found in 78–88% of patients with ICH stroke.<sup>1-4</sup> According to the Joint National Committee (JNC) VII, the risk of a stroke starts when blood pressure is reaching 115/75 mmHg and will double for every 20mmHg systolic and 10 mmHg diastolic pressure increase. Systolic and diastolic blood pressures play a role in the occurrence of stroke. However, several studies suggested that starting from the age of 50 years old, diastolic blood pressure tends to decrease; thus, systolic blood pressure has a profound influence on the occurrence of stroke.<sup>7</sup>

An important mechanism involving hypertension as the risk for ICH stroke is the rupture of penetrating arteries triggered by chronic hypertension and an acute increase in normal arterial and capillary blood pressure. Chronic hypertension can result in changes in arterioles, which include fibrinoid necrosis,

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lipohyalinosis, medial degeneration, and microaneurysm formation.<sup>8</sup>

Decreased level of consciousness is the most important prognostic sign among patients suffering from ICH strokes. Patients with a decrease in consciousness show a poor prognosis. All ICH stroke patients with a very severe decrease of consciousness died in the acute phase. Other factors that lead to poor prognosis in the acute phase of the ICH stroke are age, a poor score of 'National Institute of Stroke Scale' (NIHSS), location of the ruptured blood vessel, high hematoma volume (>30 cc), high leukocyte count and random blood sugar (RBS) score, midline shift, hematoma expansion, secondary subarachnoid hemorrhage (SAH), hydrocephalus, and high blood pressure at the onset.<sup>3,6-9</sup> High blood pressure at the onset of the ICH stroke is one of the predictors of high mortality and morbidity. Uncontrolled blood pressure in patients with ICH stroke leads to a poor prognosis in the form of a recurrent stroke or death. A sustained increase in blood pressure can cause the patient to have an enlarged hematoma.<sup>3</sup>

Previous studies have explored the role of systolic blood pressure and mean arterial pressure (MAP) score and their relationship with mortality in stroke patients with hypertension as the risk factor. Our study specifically sought to understand the role of diastolic blood pressure as a predictor of mortality in ICH stroke patients with hypertension as the risk factor.

## Methods

This was a cross-sectional analytic observational study using retrospective secondary data from medical records of patients treated at the Neurology Ward Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. Those patients were diagnosed as having ICH stroke with hypertension as the risk factor, and data were collected throughout the year 2019. The inclusion criteria of those patients were ICH stroke patients with head CT scan images but without contrast, presenting a hemorrhage that matched the type of hemorrhage caused by hypertension. Patients with signs of infection at presentation, diabetes mellitus (DM), and primary subarachnoid hemorrhage were excluded. Each patient record was coded anonymously to ensure confidentiality during statistical analysis. The protocol study was approved by the Research Ethics Committee of Universitas Padjadjaran.

Data were analyzed statistically by first

testing the numerical data normality using the Shapiro-Wilk test. To compare the means of the numerical data that were normally distributed, the unpaired t-test was used. Meanwhile, the Mann-Whitney test was used for data that were not normally distributed. The categorical data were tested using the Chi-Square test with the Kolmogorov-Smirnov and Exact-Fisher tests used as the alternative tests when the requirements of the Chi-Square test could not be met. The p-value  $\leq 0.05$  was considered significant.

## Results

Total data from 113 ICH stroke patients were collected. The majority of the patients were male (51.3%) and <60 years of age (64.6%). The mean systolic blood pressure was  $179.6 \pm 21.5$  mmHg and diastolic pressure was  $101.1 \pm 10.9$  mmHg. The mean arterial pressure (MAP) of the subjects was  $127.0 \pm 12.7$  mmHg. The predominant symptom of intracranial high pressure observed was a decrease in consciousness or somnolence in 70 (61.9%) patients. The average leukocyte count was  $11,676.5 \pm 3,623.8$  and the average random blood sugar level was  $127.8 \pm 35.8$ . Most of the ICH strokes were located in basal ganglia and internal capsule (40.7%) with secondary SAH presentation (39.8%), the midline shift (9.7%) and hydrocephalus (11.5%) (Table 1).

The outcome of patients with intracerebral hemorrhage stroke based on age and gender were compared, resulting in no statistical difference between patients' outcome and age or gender as shown in Table 2.

The outcome of patients with intracerebral hemorrhage stroke was compared based on various blood examinations, showing that the mean of leucocyte was higher in patients who died compared to those who were alive. Interestingly, the blood glucose was tended to higher in patients who had died, although the difference was not statistically significant.

The patient outcome was further compared based on increased intracranial pressure symptoms, including the level of consciousness which were decreased consciousness (somnolence), decreased consciousness (soporose), headache, vomiting, and seizure. The results showed that decreased consciousness (soporose) was a statistically significant difference between patient outcomes. Patients who had died were more soporose.

Blood pressure parameters observed, including systolic, diastolic, and mean arterial

**Table 1 Characteristic of Patients with Intracerebral Hemorrhage Stroke at Dr. Hasan Sadikin General Hospital year 2019**

Characteristic	n (%)
Gender	
Male	58 (51.3)
Female	55 (48.7)
Age category	
<60 years old	73 (64.6)
> 60 years	40 (35.4)
Systolic blood pressure	
Mean±Std	179.6±21.5
Median	180.0
Range (min-max)	120.0–240.0
Diastolic blood pressure	
Mean±Std	101.1±10.9
Median	100
Range (min-max)	80–150
Mean arterial pressure	
Mean±Std	127.0±12.7
Median	126.7
Range (min-max)	93.3–170
Leukocyte count	
Mean±Std	11,676.5±3,623.8
Median	11,440
Range (min-max)	4,650–26,530
Random blood sugar level	
Mean±Std	127.8±35.8
Median	120.0
Range (min-max)	81.0–338.0
Symptoms of high intracranial pressure	
Somnolence	70 (61.9)
Soporosis	18 (15.9)
Headache	48 (42.5)
Vomiting	43 (38.1)
Seizure	4 (3.5)
NIHSS score	
Mean±Std	11.5±4.9
Median	11
Range (min-max)	3–25
Radiology results	
Location of hemorrhage	
Basal ganglia/internal capsule	46 (40.7)
Thalamus	30 (26.5)
Pons	9 (8.0)
Cerebellum	6 (5.3)
Lobar	14 (21.2)
Important radiological features	
Secondary SAH	45 (39.8)
Midline shift	11 (9.7)
Hydrocephalus	13 (11.5)

Note: NIHSS=National Institute of Stroke Scale; SAH= subarachnoid hemorrhage; Std= standard deviation. Categorical data were presented in number/frequency and percentage; numerical data was presented in mean, median, standard deviation, and range.

**Table 2 Outcome of Patients with Intracerebral Hemorrhage Stroke based on Age and Gender**

Variable	Patient Outcome		p-value
	Alive (n=90) n (%)	Dead (n=23) n (%)	
Age category			0.059
<60 year	62 (68.9)	11 (47.8)	
>60 year	28 (31.1)	12 (52.2)	
Gender			0.135
Male	43 (47.8)	15 (65.2)	
Female	47 (52.2)	8 (34.8)	

pressure were all statistically higher in patients who had died as shown in Table 5.

The CT head scan features based on the location, including basal ganglia/internal capsule, thalamus, pons, cerebellum, lobar, presence of secondary SAH, midline shift,

and hydrocephalus were compared between patients who survived and patients who died. Results showed that the location in secondary SAH, midline shift, and hydrocephalus more occurred in the patients who died.

**Table 3 Outcome of Patients with Intracerebral Hemorrhage Stroke based on Blood Examination and NIHSS Score**

Variable	Patient Outcome		p-value
	Alive (n=90) n (%)	Dead (n=23) n (%)	
Leukocyte count(/mm <sup>3</sup> )			0.0001 *
Mean±Std	11,060.1±3,167.5	14,088.7±4,315.9	
Median	10,795	14,320	
Range (min-max)	4,650–26,530	7,330–26,000	
Leukocyte category			0.065
<10000/mm <sup>3</sup>	34 (37.8)	4 (17.4)	
> 0000/mm <sup>3</sup>	56 (62.2)	19 (82.6)	
Random blood sugar level (mg/dl)			0.091
Mean±Std	123.0±27.2	146.6±55.4	
Median	120	132	
Range (min-max)	81–240	92–338	
Random blood sugar category			0.001 *
<140 mg/dl	76 (84.4)	12 (52.2)	
>140 mg/dl	14 (15.6)	11 (47.8)	
NIHSS score			0.0001 *
Mean ± Std	10.4±4.5	15.5±4.1	
Median	10	15	
Range (min-max)	3–20	10–25	
NIHSS category			0.012 *
Mild	11 (12.2)	0 (0.0)	
Moderate	58 (64.4)	11 (47.8)	
Severe	21 (23.3)	12 (52.2)	

Note: NIHSS= National Institute of Stroke Scale; Std standard deviation; \*p <0.05.

**Table 4 Comparison of Various Increased Intracranial Pressure Symptoms and Outcome of Patients with Intracerebral Hemorrhage Stroke**

Variable	Patient Outcome		p-value
	Alive (n=90) n (%)	Dead (n=23) n (%)	
Somnolence**			
Yes	59 (65.6)	11 (47.8)	0.118
No	31 (34.4)	12 (52.2)	
Soporosis**			
Yes	7 (7.8)	11 (47.8)	0.0001*
No	83 (92.2)	12 (52.2)	
Headache			
Yes	41 (45.6)	7 (30.4)	0.190
No	49 (54.4)	16 (69.6)	
Vomiting			
Yes	32 (35.6)	11 (47.8)	0.279
No	58 (64.4)	12 (52.2)	
Seizure			
Yes	3 (3.3)	1 (4.3)	1.000
No	87 (96.7)	22 (95.7)	

Note: \*= p <0.05; \*\*Decreased consciousness

### Discussions

This study has found several predictors of death in patients with ICH stroke; i.e. decreased consciousness, poor NIHSS score, leukocytosis, high random blood sugar level, secondary SAH, midline shift, hydrocephalus,

systolic blood pressure, MAP, and diastolic blood pressure.

Decreased level of consciousness is the most important sign of poor prognosis in patients with ICH stroke. Decreased consciousness in patients with ICH stroke is caused by the effect of mass and increased intracranial pressure or

**Table 5 Comparison of Blood Pressure and Outcome of Patients with Intracerebral Hemorrhage Stroke**

Variable	Patient Outcome		p-value
	Alive (n=90)	Dead (n=23)	
Systolic blood pressure			
Mean±Std	176.7±19.3	190.9±26.3	0.018 *
Median	180	190	
Range (min-max)	120-220	140-240	
Diastolic blood pressure			
Mean±Std	100.2±10.7	104.4±11.2	0.031 *
Median	100	100	
Range (min-max)	80-150	80-120	
MAP			
Mean±Std	125.4±11.9	133.2±14.3	0.004 *
Median	126.7	133.3	
Range (min-max)	93-170	100-160	

Note: MAP mean arterial pressure; \* p<0.05; Std standard deviation

**Table 6 Comparison of CT-head Scan Feature based on Location and the Outcome of Patients with Intracerebral Hemorrhage Stroke**

Variable	Patient Outcome		p-value
	Alive (n=90) n (%)	Dead (n=23) n (%)	
Basal ganglia/internal capsule			
Yes	38 (42.2)	8 (34.8)	0.517
No	52 (57.8)	15 (65.2)	
Thalamus			
Yes	22 (24.4)	8 (34.8)	0.316
No	68 (75.6)	15 (65.2)	
Pons			
Yes	6 (6.7)	3 (13.0)	0.313
No	84 (93.3)	20 (87.0)	
Cerebellum			
Yes	5 (5.6)	1 (4.3)	1.000
No	85 (94.4)	22 (95.7)	
Lobar			
Yes	10 (22.2)	4 (17.4)	0.613
No	70 (77.8)	19 (82.6)	
Secondary SAH			
Yes	28 (31.1)	17 (73.9)	0.0001 *
No	62 (68.9)	6 (26.1)	
Midline shift			
<0.5 cm	9 (10.0)	2 (8.7)	0.0001 *
> 0.5 cm	5 (5.6)	12 (52.2)	
No	76 (84.4)	9 (39.1)	
Hydrocephalus			
Yes	2 (2.2)	11 (47.8)	0.0001 *
No	88 (97.8)	12 (52.2)	

Note: SAH= subarachnoid hemorrhage, \*= p<0.05

direct involvement of the reticular activation system of the brainstem.<sup>8</sup>

NIHSS is a stroke-specific quantitative scale that examines levels of consciousness, language function, neglect, visual field, eye movement, facial symmetry, motor strength, sensory, and coordination. NIHSS has been originally designed as a research tool to measure basic data in clinical trials on acute stroke patients. This scale is widely used as a clinical assessment tool to evaluate stroke patients, determine appropriate treatment, and can be considered to have a better predictive factor for neurological outputs in ICH stroke compared to the Glasgow Coma Scale (GCS) only. NIHSS correlates with the objective measure of stroke severity. Increasing NIHSS score reflects an unfavorable ICH stroke output. Poor NIHSS score is associated with

hematoma volume at the onset of the ICH stroke.<sup>10</sup>

A high leukocyte count at onset is one of the predictors of death in patients with ICH stroke. Several reports have shown that in patients with ICH stroke, a correlation is found between increased leukocyte count at onset and initial neurological deterioration that will then lead to poor outcomes. Early leukocytosis is significantly associated with early neurological deterioration and mortality. Leukocytosis in ICH stroke patients is caused by increased catecholamine release and corticosteroid production that positively correlates with the hemorrhage volume.<sup>11</sup>

The random blood sugar level is associated with a high risk of mortality among ICH stroke patients. Studies have shown that patients with elevated random blood sugar levels have

a higher incidence of brain complications and more extensive hemorrhage, recurrent hemorrhage, blood barrier destruction leading to brain edema exacerbation, neuronal apoptosis, and poor functional outcomes. A study showed that elevated random blood sugar level in patients with ICH stroke was an independent predictor of mortality in non-diabetic patients. Hyperglycemia in acute neurological injuries is associated with catecholamine surge and immune stress response. The elevated random blood sugar level reflects the severity of the stroke as a stress reaction to a serious brain injury.<sup>12</sup>

Secondary SAH, midline shift, and hydrocephalus are the next predictors of death in this study. Patients with ICH stroke are often deteriorating during the first 24–48 hours after onset. This deterioration can be explained by the ongoing hemorrhage but it is most frequently associated with the development of edema around the lesion, the effect of lesion on the blood flow, metabolism in the brain, brain tissue shift, and herniation. Mass-induced effects in patients with hematomas are more common than in patients with ischemia due to the volume of additional substances that add to the edema. Mostly, the effect of the hematoma pressure on the hemisphere results in the midline shift without herniation of the brain. When the effect of mass is severe, the brain tissue swells or protrudes into a different compartment, which is referred to as the process of herniation. A shift in the brain tissue can also cause compression or expansion of blood vessels and infarction of the area that receives blood supply from the artery and secondary hemorrhage. Blood can also enter the ventricular space, which will substantially increase the mortality risk. The ventricular system can also be compressed in various places. Hematomas in the putamen or cerebral lobes can damage the Monro foramen, causing dilatation of the contralateral lateral ventricles. The thalamus hematoma often blocks and compresses the third ventricle, causing hydrocephalus of both lateral ventricles. Cerebral hemorrhage can compress the IV ventricles or cerebral aqueduct, causing obstructive hydrocephalus from the third and lateral ventricles. Brain tissue shift, herniation, secondary infarction, blood entering the ventricles, and hydrocephalus lead to the worsening of the ICH stroke clinical signs and symptoms.<sup>8</sup>

Hypertension is the most important risk factor for ICH stroke. A meta-analysis on 68 blood pressure reduction trials showed that

a reduction of 10 mmHg of the systolic blood pressure and 5 mmHg of diastolic blood pressure is associated with a reduction in the incidence of stroke by 36% and a reduction in the mortality caused by cardiovascular disease by 16%.<sup>13</sup> In many cases, patients with ICH stroke are assigned in the hypertensive crisis criteria. In a hypertensive crisis, the systolic blood pressure reaches 180 mmHg and the diastolic pressure becomes very high, up to 120 mmHg.<sup>14,15</sup> The role of systolic and diastolic blood pressures in ICH stroke cannot be ignored because each of them independently affects the blood vessels.<sup>16</sup> A previous study has reported that high diastolic blood pressure damages the endothelium of the intracerebral arteries, causing rupture of the blood vessels.<sup>17</sup> ICH stroke occurs spontaneously when a weak blood vessel in the brain ruptures and increases the intracranial pressure, causing damage to brain cells around the hematoma. High blood pressure is associated with hematoma growth expansion that results in poorer functional outcomes and increased mortality risk. One-third of patients with ICH stroke rapidly develop hematoma during the first few hours of the stroke. The leaking blood also displaces and compresses the surrounding tissue.<sup>18</sup>

The limitation of this study is that this study has been conducted in a single center hospital, therefore, a larger multicenter study is recommended to further validate the result. Another limitation is that no data available on the blood volume of the hemorrhage image from the head CT Scanasthis might be important predictors of death in ICH stroke.

In conclusion, diastolic blood pressure can be used as a predictor of death in ICH stroke patients with hypertension as the risk factor.

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