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## ARTICLE INFO

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#### Article history

Received 19-05-2023  
Revisited 26-06-2023  
Accepted 23-09-2023  
Available online 30-09-2023

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#### Please cite this article in APA 7<sup>th</sup> edition style as:

Aulia, N.N., Syifak S. &  
Yuniati, D. (2023). Analysis  
of Factors Influencing  
Mortality in Patients with  
Intracerebral Hemorrhagic  
Stroke. *Jurnal Ilmiah  
Kedokteran Wijaya*  
Kusuma, 12(2), 124-131,  
<http://dx.doi.org/10.30742/jikw.v12i2.2880>

## Analysis of Factors Influencing Mortality in Patients with Intracerebral Hemorrhagic Stroke

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### Abstract

Stroke is a cerebrovascular disease that causes sudden neurological deficits due to the interruption of blood supply to the brain, resulting in the disruption of brain function. It is ranked as the second most common cause of death worldwide and leads to the highest number of disabilities globally. The incidence of this disease is 10-20 cases per 100,000 population, reaching 15% of all strokes worldwide yearly. The highest mortality rate was 20.3% after 48 hours and 18.3% less than 48 hours. This number is greater than the death rate in stroke infarction. This study aims to analyze the factors influencing mortality in patients with intracerebral hemorrhage (ICH). This type of research is observational analytic research. The design used is cross-sectional. This study was approved by the Health Ethics Committee of the Jemursari Islamic Hospital in Surabaya. The sampling technique uses total sampling. The total sample of this study was 65 patients. The sample in this study were all ICH stroke patients who were treated at RSI JS Surabaya from January 2019 to December 2021. Statistical analysis in this study used the chi-square correlation test. The results showed that the duration of hospitalization and bleeding volume had a significant correlation with the mortality in stroke patients ( $p$ -value<0.05) with OR (95% CI) are 0.243 (0.082-0.723) and 0.154 (0.048-0.500) respectively. Bleeding volume has a correlation with mortality in this study. However, this study has only fewer samples and it can't be generalized.

**Keywords:** bleeding volume, intracerebral hemorrhage, mortality in stroke, stroke, stroke outcome

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## Original Research Article

### INTRODUCTION

Stroke is a cerebrovascular disease that causes neurological deficits that occur suddenly due to the cessation of blood supply to the brain, resulting in disruption of brain function. Disruption of cerebral blood flow can be caused by the rupture of an artery or blockage in the blood vessels of the brain (Broderick et al., 1993; de Oliveira Manoel et al., 2016). Stroke is placed as the second most common death cause in the world and results in the highest number of disabilities in the world. Mortality risk in this disease is highest in the first weeks after hemorrhagic stroke and the overall case fatality in a month has been studied and reported to be approximately 40% (An et al., 2017; Gaist et al., 2013). The incidence of this disease is 10-20 cases per 100,000 population and reaches 15% of all hemorrhagic strokes worldwide each year (Benjamin et al., 2018; Janis et al., 2013). According to data in 2014 by Indonesia reported that the prevalence of strokes was 32.9% in Indonesia. The highest mortality rate in Indonesia was due to hemorrhagic stroke, the mortality rate was 20.3% after 48 hours and 18.3% less than 48 hours. This number is greater than the mortality rate in stroke infarction. A total of 52% of patients died within the first month and only 20% lived independently during 6 months. Apart from

causing high morbidity and mortality, ICH stroke also has important implications in the economic field (Alerhand & Lay, 2017). According to the previous study, the sociodemographic characteristics of patients can be risk factors for ICH and the mortality of ICH. The increasing age can also increase the incidence of ICH, while the overall incidence was greater in women than in men (Hong et al., 2013; Jolink et al., 2015). And the other hand, the outcome of patients with ICH is various, it depends on the volume of bleeding, location of bleeding, and other factors including age, gender, ethnicity, other underlying diseases, and the history of hospitalization. In women, the number of childbirths may be associated with the risk of ICH. The age of patients seems to take an important role, patients with older age are more likely to have more than one non-communicable disease, which leads to the mortality and poor prognosis of ICH. These factors may increase the severity of ICH stroke (An et al., 2017; Yudiarto et al., 2014). According to the CT scan of the brain, the location of the hematoma is in the frontal lobe (13%), parietal lobe (9%), temporal lobe (6%), occipital lobe (1%), thalamus (18%), basal ganglia (16%), cerebellum (8%), and brainstem (1%), and 28% of patients had hematomas in more than one of these locations (Faghih-Jouybari et al., 2021). The location of the hematoma may determine the condition of the patient (Morotti & Goldstein, 2016). A previous study also reported that mortality was higher as the volume of hematoma increased, and the lethal volume of parenchymal hemorrhage in ICH patients varied according to the location (Ahammed et al., 2017; Broderick et al., 2021; Panchal et al., 2015).

In an ICH stroke, a hematoma will form which can last up to 6 hours. Large-volume hematomas can destruct the anatomical structures of the brain, and lead to neurological deficits and space-occupying effects that can cause increased intracranial pressure (Broderick et al., 2021; Magid-Bernstein et al., 2022). Hematoma volume of more than 30 cc is associated with an increased mortality rate due to ICH stroke, with a high mortality rate of up to > 90% in hematoma volumes of more than 60 cc. The occurrence of perihematomal edema and hematoma expansion results in secondary brain injury and worsens clinical outcomes (Duan et al., 2016).

Many factors affect the clinical outcome of ICH stroke patients (Lioutas et al., 2020). A study in Bangladesh showed that the volume of intracerebral hemorrhage was a strong and easy-to-use predictor of 30-day mortality in patients with ICH stroke (Ahammed et al., 2017; Houben et al., 2018). There are preventive strategies (Parry-Jones et al., 2020) including strict control of blood pressure (target is 180/105 mmHg) and avoidance of any antithrombotic medication in the first 24 hours following the infusion of rtPA 52. However, once ICH occurs, it is unclear how best to treat this in ICH so, the number of the mortality in ICH is still high. According to the previous study, the management of ICH stroke patients is to control the BP to prevent the bleeding volume however, these efforts still result in a high level of mortality in ICH stroke patients (Alerhand & Lay, 2017; Morotti & Goldstein, 2016; Panchal et al., 2015). Based on the background, the aim of this study was to analyze the factors influencing mortality in patients with intracerebral hemorrhage. Even though the volume of bleeding is one of the most easily identifiable signs using a CT-Scan imaging examination, this study was necessary because we need to know the precise other influencing elements that may contribute to the mortality of ICH stroke patients. CT scan imaging of the brain can detect the presence of ICH which looks white with a hypodensity area around it (McGurgan et al., 2021; Stephen & Cappi, 2017). The Jemursari Islamic Surabaya Hospital is the only type B hospital in Wonocolo District, Surabaya City, and this research has never been done there. The findings of this study should help clinicians predict and enhance the clinical outcomes of stroke patients to lower mortality and morbidity.

## MATERIALS AND METHODS

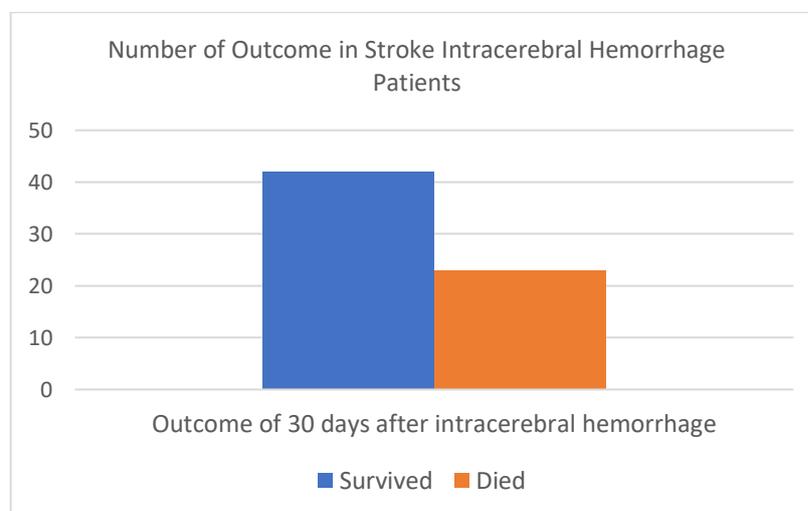
This type of research is observational analytic research. The design used is cross-sectional. This study was approved by the Health Ethics Committee of the Jemursari Islamic Hospital in Surabaya with an ethical number No. 002/KEPK-RSISJS/I/2023. The sampling technique uses total sampling from the patients in Jemursari Islamic Hospital. The total sample of this study was 65 patients. The sample in this study were all ICH stroke patients who were treated at RSI JS Surabaya from January 2019 to December 2021. All the variables including age, sex, duration of hospitalization, bleeding volume, and

location of hemorrhage were obtained from the medical record. The inclusion criteria in this study were ICH stroke patients who had clinical examinations or experienced stroke symptoms and had head CT scans without contrast. The exclusion criteria in this study were patients with subarachnoid hemorrhage, patients with intraventricular hemorrhage, and patients who did not have a completed medical record which can be a bias in the result. There is no limitation of age or sex in this study.

The research instrument uses all the completed medical records that match the required sample criteria. The result of bleeding volume, and location of hemorrhage was observed and calibrated at the same time. The CT scan result of each patient in this study was observed by three neurologists according to the head CT scans that were conducted in Jemursari Islamic Hospital. All the neurologists gave the same reading of the patient's CT scan. Statistical analysis in this study used the chi-square correlation test ( $p\text{-value} < 0.05$ ). In addition, odds ratio figures are also displayed to determine risk factors that are in accordance with the research objectives.

## RESULTS

The incidence of death in stroke patients 30 days after the stroke event, based on figure 1. appears that the number of patients who live is more than those who die. All patients in this study were stroke patients who were receiving treatment such as control of blood pressure and the use of antithrombotic agents and were also hospitalized for a day or more. Based on this study, the average duration of hospitalization for patients who died from stroke was 5 days and the average volume of bleeding was 64.9 cc.



**Figure 1.** Number of deaths 30 days after stroke intracerebral hemorrhage

Based on the analysis of the frequency distribution of patients in this study, it was found that more male patients died after having a stroke (78.3%). In this study, it was also found that patients aged  $< 56$  years died more (52.2%) while those who lived were aged  $\geq 56$  years (54.8%). In patients who were hospitalized for less than 6 days, more died (69.6%). Meanwhile, there are more survivors who have experienced hospitalization  $\geq 6$  days after the stroke incident.

Table 1. shows that more patients who experienced bleeding  $\geq 20$  cc died (78.3%). While the location of the bleeding in the patients in this study was mostly supratentorial, most of the patients who died experienced supratentorial (73.9%) and infratentorial (26.1%) bleeding, however, there were also more patients who lived in this study. who experienced supratentorial bleeding (90.5%).

**Table 1.** Distribution of patient characteristics

Variable	Frequency (%)	
	Survived	Died
<b>Sex</b>		
Male	24 (57.1%)	18 (78.3%)
Female	18 (42.9%)	5 (21.7%)
<b>Age</b>		
≥ 56 years old	23 (54.8%)	11 (47.8%)
< 56 years old	19 (45.2%)	12 (52.2%)
<b>Duration of Hospitalization</b>		
< 6 days	15 (35.7%)	16 (69.6%)
≥ 6 days	27 (64.3%)	7 (30.4%)
<b>Bleeding Volume</b>		
≥ 20 cc	15 (35.7%)	18 (78.3%)
< 20 cc	27 (64.3%)	5 (21.7%)
<b>Location of Hemorrhage</b>		
Infratentorial	4 (9.5%)	6 (26.1%)
Supratentorial	38 (90.5%)	17 (73.9%)

**Table 2.** Result of correlation test between sex, age, duration of hospitalization, Bleeding volume, and location of hemorrhage with the outcome post intracerebral hemorrhage in stroke patients

Variable	OR	95% Confidence Interval	P-value
Sex	0.370	0.116-1.186	0.094
Age	1.321	0.477-3.659	0.593
Duration of Hospitalization	0.243	0.082-0.723	0.011*
Volume of Hemorrhage	0.154	0.048-0.500	0.001*
Location of Hemorrhage	0.298	0.074-1.196	0.077

\*There is a significant correlation (p-value<0.05)

Based on Table 2, the Pearson chi-square correlation test showed that the duration of hospitalization and volume of hemorrhage had a significant relationship with the incidence of death in stroke patients. The short duration of hospitalization in this study was due to the dying patients, and it was not because patients were discharged. According to this study, patients who were admitted for less than 6 days had a higher incidence of dying from a stroke by 0.243 times than patients who were hospitalized for ≥ 6 days. Whereas patients who experience bleeding ≥ 20 cc have a risk of dying from a stroke by 0.154 times compared to patients who experience bleeding < 20 cc. Age, gender, and location of bleeding showed no significant association with the incidence of death in stroke patients in this study.

## DISCUSSION

Based on this study, most of the patients lived during follow-up. There were more surviving patients than dead patients. Intracerebral hemorrhage is indeed a disease with a fairly high mortality rate. Several factors can predict mortality from ICH. These factors were the size of the hematoma, its location, and the Glasgow Coma Scale (GCS) score of the patient at the first hospitalization (Radu et al., 2020; Safatli et al., 2016). Follow-ups carried out for 30 days showed a mortality that could reach 50%, most deaths occurred in the first 24 hours after the bleeding. One of the factors that can cause death is the occurrence of hydrocephalus or the presence of intraventricular hemorrhage (Ahammed et al., 2017; Benjamin et al., 2018).

A study by Pinho et al. found that mortality in ICH after 1 month was 36.3%, after 3 months was 35.3%, and after 12 months was 50.7%. In this study, it was found that factors that can predict mortality are old age, the severity of the degree of neurological deficit as measured by the Glasgow Coma Scale or the National Institutes of Health Stroke Scale (NIHSS) (Pinho et al., 2019)

In this study, in general, the male sex was dominated in both the living and dead groups. In the death group, men predominated with 18 patients (78.3%). Analysis of the relationship between gender was not statistically significant. According to a study by Forman et al., which examined the incidence of ICH in the elderly, found a predominance of the female sex with 68.2% (Forman et al., 2020). Even so, in general, ICH is indeed more common in male patients, with a predilection for Asian and African populations (Rajashekar & Liang, 2023). A similar study was conducted by Radu et al., in Romania. This study found that the incidence of ICH was found to be more common in men (53%) than in women. In addition, this study found that women who suffer from ICH are significantly older than men (Radu et al., 2020)

In this study, the majority of patients in the age group <56 years died (52.2%). In the group  $\geq$  56 years most of the patients were still alive at follow-up (54.8%). Analysis of the relationship to the age variable is not statistically significant. The incidence of ICH is indeed increasing with age, especially in patients who are over 55 years old (Rajashekar & Liang, 2023). It was found that the incidence of ICH was 5.9 per 100,000 of the population at the age of 35-54 years, 37.2 per 100,000 of the population in the 55-74 years age group, and 176.3 per 100,000 population in the 75-94 years age group (An et al., 2017). Based on a study by Radu et al. it was found that the average age is 69.1 years. As many as 7.55% of patients were under 50 years old, 16.9% were aged 51-60 years, 26.42% were aged 61-70 years, and 49.06% were aged over 71 years. This study also found no relationship between age and hospital mortality (An et al., 2017). Most of the deaths found in the hospital were related to ICH itself (66.7%) while the rest were attributed to complications or other underlying diseases. In this study, all patients under the age of 50 did not experience death, while 67% of patients aged 51-60 years died in hospital (Radu et al., 2020).

In this study, it was found that more patients who were hospitalized <6 days died (69.6%). In the analysis of the relationship, it was found that the duration of hospitalization of less than 6 days was more at risk of dying from stroke by 0.245 times compared to patients who were hospitalized for  $\geq$  6 days. The study by Kim et al., found that the length of stay in ICH was longer compared to other strokes. In this study, the length of stay in ICH patients was 28.9 days, which is shorter than stroke infarction which was only 15 days (Kim et al., 2013). There are several factors (Kang et al., 2017) that lead to a longer length of stay, namely the presence of comorbidities, complications, and surgery (Patel et al., 2020). Kim et al., found that the longer the hospitalization time, the higher the death rate. In addition, Kim et al. also found that hemorrhagic strokes have a higher mortality rate than infarct strokes. Death is indeed one of the factors that reduce hospitalization time. Kim et al. found that 52.5% of patients died within the first 7 days of hospitalization (An et al., 2017).

According to the bleeding volume, more patients who experienced bleeding  $\geq$  20 cc died (78.3%). Analysis of the relationship showed that patients who experienced bleeding  $\geq$  20 cc had an increased risk of dying from stroke by 0.154 times compared to patients who experienced bleeding < 20 cc. Patients who have a bleeding volume of more than 60 ml also have a mortality rate of up to 90% (Rajashekar & Liang, 2023). Large volumes of bleeding have been associated with a poor prognosis of ICH. Bleeding size  $\geq$  30 cc is associated with a poor prognosis (An et al., 2017).

Based on the location of the bleeding, the patients who died had more supratentorial bleeding (73.9%) compared to infratentorial bleeding. However, many surviving patients also had supratentorial hemorrhage (90.5%). Analysis of the relationship to the bleeding location variable was not statistically significant. In a study by Patel et al., it was found that patients with infratentorial ICH had worse clinical manifestations and severity compared to ICH in other locations (Duan et al., 2016b). Patients with the worst degree of disease severity and prognosis come from patients with ICH that occur in the

brainstem (Forman et al., 2020). In a previous study, the location of the infratentorial hematoma was associated with 30-day mortality (Faghih-Jouybari et al., 2021; Lioutas et al., 2020).

## CONCLUSION

Based on this study, it can be concluded that the volume of intracerebral hemorrhage has a significant correlation with the 30-day mortality in stroke patients with intracerebral hemorrhage at Jemursari Islamic Hospital. The volume of intracerebral hemorrhage can be used as a mortality predictor in patients with intracerebral hemorrhage stroke. The duration of hospitalization also has a correlation with the mortality in patients with intracerebral hemorrhage stroke at Jemursari Hospital in Surabaya. However, most of the bleeding experienced by patients in this study was supratentorial rather than infratentorial. Yet, there was a limitation of this study, the number of samples in this study is quite a bit and it can't be generalized. So, we suggest conducting a larger number of samples for further study.

## CONFLICT OF INTEREST

All authors declare that there is no conflict of interest in this study.

## ACKNOWLEDGEMENTS

All the authors would like to express their gratitude towards all the parties who supported this research including the Rector, the Dean of the Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, and Jemursari Islamic Hospital, Surabaya, Indonesia.

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