



Volume 4 Number 1, January 2024

Comparison of Recurrent Stroke in Patients with First Stroke Ischemic and Hemorrhagic in Soetomo General Academic Hospital

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Article info

Article History:

Received Oct 6, 2023

Revised Jan 20, 2023

Accepted Jan 26, 2023

Published Jan 31, 2024

Keywords:

Improving mortality
Secondary prevention
Stroke
Stroke management
Recurrent stroke

ABSTRACT

Introduction: Stroke is the leading cause of mortality and disability in Indonesia, as well as being the major cause of death and disability-adjusted life years (DALY) lost worldwide. Recurrent stroke is one of the most common complications of stroke after discharge, despite being highly preventable. **Objective:** This study aimed to compare the differences in recurrent stroke profiles between patients with first stroke ischemic and hemorrhagic strokes. **Methods:** The study was done by collecting secondary data from medical records and the stroke registry at Dr. Soetomo General Academic Hospital over a period of six months (January–July 2020). **Result:** This study examined 36 samples that met the inclusion criteria. The results revealed that patients who experienced their first stroke of the ischemic type had a 2.5-fold higher incidence of recurrent stroke than those who suffered a hemorrhagic type. Except for one case, the majority of patients had the same type of stroke as the first. The most frequent modifiable risk factors seen in these two types of strokes are hypertension and physical inactivity. It was found that there were still 5% of the risk factors for which secondary prevention had not been carried out optimally with antidyslipidemic, antidiabetic, or antihypertensive drugs. The most common acute treatment for ischemic stroke is antiplatelet therapy, either single or dual therapy. Up to 90% of hemorrhagic strokes were treated conservatively, and in one patient, extraventricular drainage was performed. **Conclusion:** There were more stroke patients with a first stroke of hemorrhagic type that presented with NIHSS scores in the severe to very severe range, and the average length of hospitalization in this group was longer.

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INTRODUCTION

According to 2010 Global Burden Disease Research, stroke is the world's second-largest cause of death.^{1,2} Its prevalence in Indonesia, according to the Ministry of Health's 2018 Basic Health Research, was 10.9 per 1,000 people, making it the primary cause of death in 2019.³ Stroke is not only a threat to life, but it is also the leading cause of disability, particularly in the elderly, and it contributes significantly to the loss of productive years both nationally and globally.⁴

Based on the underlying pathology, strokes are divided into two types: ischemic and hemorrhagic. Approximately 80% of strokes are ischemic, resulting from cerebral vascular occlusion, while hemorrhagic strokes happen when cerebral vessels rupture and cause bleeding.⁵ Recurrent stroke, a common complication post-discharge, exhibits a significantly higher mortality rate compared to first-time stroke occurrences. Effective stroke prevention hinges on identifying and managing modifiable risk factors, with nearly half of stroke-related deaths being preventable through such measures.^{6,7,8}

Optimal acute first stroke management and secondary prevention play crucial roles in minimizing patient losses and preserving quality of life. Control of major risk factors, including hypertension, diabetes mellitus, hyperlipidemia, and lifestyle modifications, forms the foundation for effective prevention strategies.^{9,10,11} Secondary prevention for ischemic stroke involves diet modification, aerobic exercise, aspirin, statins, and antihypertensive drugs. Patient education is integral to enhancing awareness and fostering medication compliance.¹²

Existing stroke prevention strategies frequently concentrate on the coagulation cascade, utilizing antiplatelet and anticoagulant medication. However, adjusting treatment to stroke subtypes is essential for reducing the risk of recurrence. More study on the relationship between stroke types and recurrent stroke is needed, which might lead to more specific management strategies.^{13,14} The primary objective of this investigation is to delineate the risk factors associated with recurrent stroke and compare recurrence incidence across different stroke types.

OBJECTIVE

This study aimed to identify risk factors for recurrence in each type of stroke, compare the incidence of recurrence between stroke types, and compare patient outcomes, acute treatment, length of hospital stays, and secondary prevention efforts between groups of patients with first stroke ischemic and hemorrhagic strokes who had recurrent stroke. It is hoped that having this information available would

help justify therapeutic choices and recommend secondary prevention in order to reduce the number of recurrent strokes.

METHODS

This was a retrospective descriptive study that used medical records and the stroke registry to identify patients with recurrent stroke at the inpatient installation of Soetomo General Academic Hospital, Surabaya. This study used total sampling, which included all patients who met the inclusion criteria. Patients included in this study were inpatients diagnosed with recurrent strokes by a neurology specialist at Soetomo General Academic Hospital between January and July 2020. Exclusion criteria for this study were inpatients with recurrent stroke where the type of the first stroke (ischemic or hemorrhagic) was unknown, as well as patients whose first stroke was classified as a mixed cerebrovascular disease. Data regarding type of current and previous stroke, risk factors related, therapy and management given, and length of stay were recorded in Microsoft Excel. The data was described, grouped by variable, and presented in frequency distribution tables.

RESULTS

A total of 36 patients were eligible for this study.

Type of first stroke

Recurrent strokes were more common in patients with a first stroke of ischemic type than hemorrhagic type (2.6:1), all of which were followed by ischemic recurrent strokes. Meanwhile, among ten patients with a hemorrhagic first stroke, one patient (10.0%) had a recurrent ischemic stroke, while the rest had a recurrent hemorrhagic stroke (90.0%).

Table 1. Frequency of distribution based on type of first stroke and recurrent stroke

Type of First Stroke	Frequency		Type of Recurrent Stroke			
	n	%	Ischemic		Hemorrhagic	
			n	%	n	%
Ischemic	26	72.2	26	100.0	-	-
Hemorrhagic	10	27.8	1	10.0	9	90.0

Territorial stroke is the most common feature found in patients with ischemic stroke, while the remaining eleven patients had lacunar stroke. In patients with hemorrhagic stroke, it was found that the incidence of intracerebral hemorrhage (ICH) compared to subarachnoid hemorrhage is (4.5:1). Intraventricular hemorrhage that leads to an increase in intracranial pressure can be found in two patients.

Table 2. Frequency of distribution based on CT imaging of the recurrent stroke

Type of Recurrent Stroke	CT Imaging					
	Lacunar	Territorial	ICH	ICH	ICH	SAH
				+	+	+
			IVH	SAH	IVH	
Ischemic	11	16	-	-	-	-
Hemorrhagic	-	-	6	1	1	1

Risk factors of stroke

The age group with the highest number of recurrent strokes in the ischemic group was 50–59 (42.3%). Physical inactivity was the most common

modifiable risk factors in this group, accounting for 25 patients (100.0%), whereas hypertension affected 21 patients (80.8%). The most prevalent age group among hemorrhagic patients was 60–69 (50.0%). The most common modifiable risk factors found in this group were hypertension, found in 10 patients (100.0%), and physical inactivity, found in 9 patients (90.0%). In this group, the percentage of patients with diabetes mellitus was higher than that of patients who had dyslipidemia, in contrast to the previous group. The complete list of risk factors is displayed in Table 3.

Table 3. Frequency of distribution of stroke risk factors based on stroke type

Type of Stroke	Ischemic		Hemorrhagic		
	n	%	n	%	
Unmodifiable					
Age	≤ 49	5	19,23	2	20,00
	50-59	11	42,31	3	30,00
	60-69	7	26,92	5	50,00
	≥ 70	3	11,54	0	0,00
Gender	Male	18	69,23	6	60,00
	Female	8	30,77	4	40,00
Modifiable					
Hypertension	21	80,77	10	100,00	
Dyslipidemia	15	57,69	2	20,00	
Diabetes Mellitus	11	42,31	6	60,00	
Smoking	14	53,85	3	30,00	
Diet and physical activity	High sodium diet	19	79,17	5	55,55
	Physical inactivity	25	100,00	9	90,00

Stroke management

Table 4 contains a comparison of secondary prevention measures to prevent recurrent strokes. These include the use of antihypertensive, antidyslipidemic, and antidiabetic drugs, as well as education regarding a low-sodium diet. Data were also gathered on the curative management of the recurrent stroke. Most patients with ischemic stroke are treated with antiplatelet agents, while the majority of patients with

hemorrhagic stroke are managed conservatively. In both groups, citicoline was also given to help the recovery of nerve cells. The majority of the patient outcomes were discharged with improved status. More than half of the patients in the ischemic and hemorrhagic groups arrived at the hospital after more than 24 hours from the initial onset of symptoms. The most common reason for patient delays is waiting for the family.

Table 4. Frequency of distribution of stroke management aspect based on stroke type

	First stroke ischemic		First stroke hemorrhagic	
	n	%	n	%
Secondary prevention				
Antihypertensive drugs	19	73,08	10	100,00
Antidyslipidemic drugs	13	50,00	2	20,00
Antidiabetic drugs	7	26,92	5	50,00
Low sodium diet	26	100,00	10	100,00
Curative management				
rt-PA	-	0,00		
Aspirin	17	65,38		
Clopidogrel	11	42,31		
Cilostazol	1	3,85		
Warfarin	1	3,85		
Citicoline	14	53,85	2	20,00
Conservative			9	90,00
Surgical (EVD)			1	10,00

Table 4. Frequency of distribution of stroke management aspect based on stroke type

	First stroke ischemic		First stroke hemorrhagic	
	n	%	n	%
Patient outcome				
Improved and discharged	23	88,46	8	80,00
Passed away	3	11,54	2	20,00
Onset-presentation time				
<4.5 hours	4	17,39	2	20,00
4.5 – 24 hours	6	26,09	2	20,00
>24 hours	13	56,52	6	60,00
Reason for delay				
Remote hospital distance	4	20,00	2	40,00
Waiting for family	8	40,00	3	60,00
Ignorance of stroke signs	3	15,00	-	-
Transportation constraints	5	25,00	-	-

Length of hospitalization

The shortest length of stay for the first stroke ischemic group was 3 days, and the longest was 20 days. The average length of stay in this group was 7.3 days; when only patients that are improved and discharged are taken into consideration, this average was increased to 7.8 days. In patients with strokes of hemorrhagic type, the shortest length of hospitalization was 2 days, and the longest was 16 days. The average length of stay in this group was 7.8 days; when only patients that are improved and discharged are included, the average was increased to 10.8 days. The data is described in detail in Table 5.

Table 5. Length of hospitalization comparison based on stroke type

First stroke type	Length of hospitalization			
	Min	max	mean	Corrected mean*
Ischemic	3	20	7,3	7,8
Hemorrhagic	2	16	7,8	10,8

*average length of hospitalization of patients who are improved and discharged

DISCUSSION

Among the 36 patients, the first stroke in 26 patients was ischemic, while in 10 patients it was hemorrhagic. The most common type of recurrent ischemic stroke was territorial stroke in 16 patients and lacunar stroke in 11 patients. This higher incidence of recurrent ischemic stroke is in accordance with the Recurrent Stroke Quality and Epidemiology (RESQUE) study, which also stated that the incidence of recurrent ischemic stroke due to blockage of large blood vessels was higher than that of small vessel obstruction with a ratio of 1.3:1.¹⁵ A total of seven patients who presented with recurrent hemorrhagic stroke had stroke features of ICH; one patient had combined features of SAH and ICH stroke; and one patient had features of SAH alone. Almost all patients experienced the same type of recurrent stroke as the

first stroke, with the exception of one patient with a hemorrhagic first stroke who had a recurrent ischemic stroke with CT features of lacunar infarction. ICH strokes are twice as often followed by recurrent ICH strokes as ischemic strokes, according to previous systematic review.¹⁶ This indicates that there are different vascular processes underlying the two types of stroke.

Patients aged 50–59 (42.31%) had the highest rate of recurrent ischemic strokes, with almost 90% ranging between 50 and 69. This study found that men had more recurrent ischemic strokes than women, which was consistent with previous research.¹¹ In this group, hypertension was the most common modifiable risk factor, accounting for 80.77% of patients, followed by diabetes mellitus (42.31%), and dyslipidemia (34.61%). Half of the patients smoked, 19 had a high-sodium diet, and all were physically inactive. Most of patients with the first stroke of hemorrhagic type were in the age group of 60–69 years. There were no cases over the age of 70, and the incidence was higher in males than females (1.5:1).

Hypertension was found to be a risk factor in all patients in this group, whereas dyslipidemia was present in 20.0% and diabetes mellitus in 60.0% of the patients. ICH caused by hypertension has a high recurrence rate, reaching 13.7% after 5 years; hence, blood pressure management is critical in preventing recurrent stroke. Smoking habits were found in 30% of patients, and 50% had a high-sodium diet. Nine out of 10 patients claimed physical inactivity. Based on a previous expert review, smoking raises carboxyhemoglobin, increases platelet aggregation and fibrinogen levels, and reduces HDL levels. The direct toxic effects of cigarette chemicals can contribute to atherosclerosis, increasing the risk of stroke.¹⁷ In this study, risk factors for a high-sodium diet were given to patients who chose a score > 3 on a subjective question about their salty eating habits from a list of 1–5 choices. Physical inactivity is defined as not engaging in any moderate-to-heavy-intensity activities for more than 10 minutes in a single day.

The majority of patients with ischemic stroke received aspirin (65.38%), 42.31% received clopidogrel, and one patient (3.85%) received warfarin. Clopidogrel was combined with cilostazol in one patient and with aspirin in three others. Aspirin, clopidogrel, and cilostazol are pharmacological antiplatelet agents that inhibit ADP-mediated platelet aggregation as well as intervene in the arachidonic acid metabolic pathway. These three agents target different stages. Antithrombotic agents are utilized not just for the management of acute ischemic stroke but also for secondary prevention. The AHA/ASA recommends short-term dual antiplatelet therapy (DAPT) between 21 and 90 days after stroke onset for patients with early non-cardioembolic ischemic stroke who present less than 24 hours from onset. After that time, antiplatelet therapy can be maintained with a single antiplatelet (SAPT). The recommended method of administering DAPT is to combine aspirin and clopidogrel. Patients who do not match these criteria can immediately use SAPT as a secondary prevention modality for recurrent stroke.¹⁸

Conservative management was performed in almost all patients with hemorrhagic stroke, with the exception of one patient who had External Ventricular Drainage (EVD) due to increased intracranial pressure caused by SAH and IVH in the patient. Blood pressure reduction for patients with acute ICH is aimed primarily at preventing hematoma expansion. According to the AHA/ASA guidelines for the management of acute ICH, blood pressure reduction can be aggressively reduced until the target systolic blood pressure below 140 is reached within a few hours after the onset of ICH. Constant monitoring of vital signs, neurological assessment, cardiovascular status, and glucose levels in conservatively managed patients can help to minimize mortality by avoiding hyperglycemia or hypoglycemia.¹⁹ Installation of an EVD should be considered if there is obstructive hydrocephalus in an ICH patient with intra-ventricular hemorrhage (IVH). This installation is meant to keep intracranial pressure under control while avoiding complications that might worsen the patient's condition.²⁰

A previous study found that early surgical choices lead to a better patient outcome in patients with lobar hemorrhage, however for the supratentorial intracerebral type of hemorrhage, initial conservative management is adequate.²¹ In general, the shorter the time between the onset of stroke symptoms, the patient's admission to the hospital, and the patient's treatment, the less neurologic deficit there is and the better the prevention of future worsening. The majority of patient delays are due to distance and transportation difficulties. To enhance prehospital stroke patient treatment, health facilities in distant locations may develop an EMS (emergency medical

system) team and village ambulances on standby with an integrated 3D system (detection, delivery, and dispatch).^{13,22} Other causes of a patient's delay in coming to the hospital include waiting for relatives and not knowing the symptoms of a stroke. As a result, raising awareness among the patient's family and others about the early signs and symptoms of stroke is critical to avoiding more serious effects. One way to enhance prehospital stroke management is to socialize and educate people about the early symptoms of stroke by introducing acronyms such as F.A.S.T. by the WHO or SeGeRa ke RS by the Indonesian Ministry of Health.^{23,24,25}

The average length of hospital stays between patients with first stroke ischemic and hemorrhagic was 7 days. If the average calculation only includes patients who were discharged with improved outcomes, there is a difference in the length of hospitalization: patients with a first stroke hemorrhagic stroke spend an average of 10–11 days in the hospital, whereas patients with a first stroke ischemic stroke spend 7–8 days. Hemorrhagic strokes are often more severe than ischemic strokes, with a higher mortality rate and a longer recovery period.²¹ The severity of the stroke when the patient arrives at the hospital is one factor that affects the length of treatment. One way to determine stroke severity is the National Institutes of Health Stroke Scale (NIHSS) score.

The length of hospital stay was impacted by the patient's initial NIHSS score, gender, and smoking status.²⁶ The majority of patients with their first ischemic stroke were classified as having a moderate-to-severe stroke for both the initial and final NIHSS scores. Meanwhile, patients with a first stroke hemorrhagic had an initial NIHSS score distribution that ranged from moderate to severe, with 85% of patients scoring mild to moderate-severe on the final NIHSS. For the NIHSS scores of patients recorded at the time of their admission to the health facility, the hemorrhagic group had a lower average score of 5.7 than the ischemic group, which was 7.4. This suggests that patients who have had previous hemorrhagic strokes are more likely to have a severe stroke than patients who have had a previous ischemic stroke. A comparison of the initial and final NIHSS scores showed that the ischemic group had a larger increase in the average NIHSS score of 3.3 points than the hemorrhagic group, which had only an increase of 0.8. A previous study concluded that blood pressure is a predictor of improvement in the NIHSS score, with patients with high blood pressure during acute stroke experiencing clinical deterioration compared to those without hypertension.²⁷ Blood pressure and bleeding volume in patients with hemorrhagic strokes have an impact on clinical improvement and outcomes.²⁸ As a result, blood pressure control and effective acute

management play an important role in determining the prognosis and preventing further recurrent strokes.

CONCLUSION

The recurrence of stroke in the first ischemic stroke is 2.5-fold higher than the first hemorrhagic stroke, and a change in stroke type is only found in 1 patient. The most common risk factor in both groups is hypertension, and there are still 5% of risk factors that have not undergone secondary prevention. Therefore, education, especially regarding regular monitoring and consistent medication, is crucial in preventing recurrent strokes. Treatment with dual antiplatelet therapy has the potential, as shown in some studies, to reduce the risk of recurrent strokes and may be more considered in the management of acute ischemic stroke.

The majority of patients experience delays in seeking healthcare, so creating an alert environment and awareness of early signs play a crucial role in the management of both acute and recurrent pre-hospital strokes. Patients with recurrent strokes who have previously experienced hemorrhagic strokes generally present with worse stroke severity, with higher NIHSS scores than the ischemic group, and require longer hospitalization. Hence, secondary management is essential to minimize the occurrence of further strokes and reduce the disability, decrease in productivity, and economic losses that are consequences of stroke.

Acknowledgment

We thank the Department of Neurology, Faculty of Medicine, Universitas Airlangga, Indonesia and Dr. Soetomo Hospital which has facilitated this study.

Conflict of Interest

All authors have no conflict of interest in writing this article.

Ethic Consideration

This study has been approved by the ethics committee of Dr. Soetomo General Academic Hospital with ethical letter of exemption Ref. No.: 0216/LOE/301.4.2/XI/2020.

Funding

No funding was received for this study.

Author Contribution

The first author designed the concept, collected and analyzed the data, and wrote the manuscript. The second and third authors provided independent consultations for the review and revision of the manuscript.

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